CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

A Brief History, Current Status Report And Options for Next steps

Prepared for CIRM outside reviewers prior to October 13-15, 2010 on-site review

Index —

Introduction

The California Institute for Regenerative Medicine has matured into a deliberative, targeted funding agency in the nearly six years since 59 percent of California voters approved the initiative, Proposition 71, that created the agency in November 2004 http://www.cirm.ca.gov/AboutCIRM_Prop71
The agency has awarded 364 grants and loans for research and facilities to 54 institutions totaling $1.07 billion. About half of those commitments have been disbursed. This progress comes despite years of litigation and delays. A series of court cases were resolved in CIRM's favor in May of 2007 and the state issued the first bonds under the initiative in October, nearly three years after the vote. The agency was able to fund its first round of grants a year earlier, in April 2006, through a loan from the state's general fund arranged by Governor Arnold Schwarzenegger and through the generous support of individuals. To date, the agency has issued 22 rounds of funding.

CIRM has established systems and processes for soliciting, evaluating, and monitoring high quality, targeted research projects and to do this in an ethically sound manner (Link to 2006 Scientific Strategic Plan at http://www.cirm.ca.gov/meetings/pdf/2006/12/120706_item_7.pdf) It has seeded the stem cell research field in California with a greatly expanded workforce and dedicated facilities. It is now entering a second phase in which it can build on this robust foundation and deliver on its goal of accelerating this research toward the clinic (Link to 2009 Scientific Strategic Plan Update at http://www.cirm.ca.gov/files/PDFs/Publications/2009_Strategic_Plan-2.pdf)

The systems developed by CIRM have produced results. As of August 10, CIRM funding contributed toward the work published in 584 journal articles (Appendix 5 - List of Publications). Twenty-three percent of those have been in high profile journals, and the CIRM grantee was first or last author on 75 percent of all 584 papers. Seventeen shared lab facilities are up and running providing specialized equipment, facilities and training necessary to carry out stem cell protocols. Six of these labs were funded for specific Techniques Training Courses as well. Of the 12 major facilities grants that were awarded $271 million in May of 2008, two projects have been completed and opened this spring, three more are scheduled to open in October of this year and all but one of those remaining are scheduled for completion by December, 2011. These dedicated stem cell facilities and CIRM's predictable and sustained funding stream have clearly impacted the ability of California institutions to recruit in this field. We have documented more than 100 faculty-level recruits since 2006 (Appendix 6 - Faculty Level Recruits). CIRM-funded research has contributed to moving two candidate therapeutics into phase I FDA-approved clinical trials. (Appendix 38, A new Political-Financial Paradigm for Medical Research: The California Model)

These apparent successes notwithstanding, CIRM is now exploring whether or not its focus, systems and processes are optimal. Is a focus on pluripotent-derived therapies the optimal strategy to benefit patients? Are we attracting and selecting the research proposals that are most likely to accelerate the field toward therapies? Are we providing effective oversight to maximize the pace and success of individual projects and the synergy between projects? As we think about system gaps and process improvements, which should garner the greatest attention and assets?

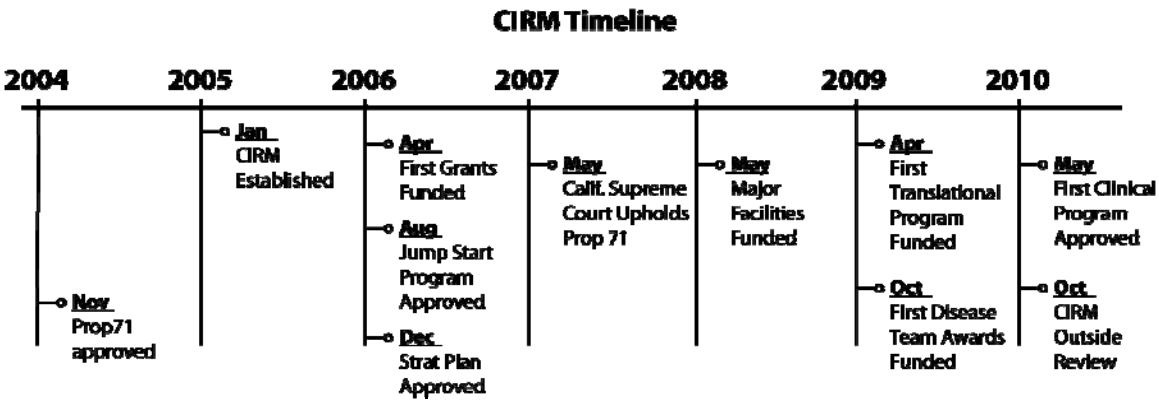


Figure 1. CIRM was tangled in court cases for more than two years but used the time to set up its processes and to issue two rounds of grants through borrowed and donated funds.

Getting Started

CIRM's governing board conducted an organizing meeting in December 2004 and it held its first business meeting in January, at which time the agency hired its first staff. The board met monthly the first year setting up procedures for creating its working groups for peer review, facilities and ethical standards; selecting the members of those groups; determining which city would host the agency; and numerous other start-up activities. (For a more extensive discussion regarding Proposition 71 and its requirements refer to Report of the Office of the Chair to External Reviewers.)

During that first year, the agency was quick to create the processes necessary to fund promising science. CIRM issued its first Request for Applications (RFA) – for training grants – in May, organized the 15-member Grant Review Group to judge the applications in August and the Board approved the first awards at its September meeting. But by that time litigation had been filed preventing the agency from raising money through bonds, and the grants were put on hold. By December, staff had written an Interim Grants Administration Policy (GAP) able to handle the limited scope of training grants, pending available funds. Also, the board had adopted the National Academy of Science's standard for human embryonic stem cell research as interim standards.

In 2006, a slowly growing staff started to formalize and clarify the policies and procedures created in the first year. In April the agency used funds from Bond Anticipation Notes (BANs) to issue the first round of awards, the training grants approved the prior September. The BANs, from wealthy supporters of CIRM, would not have been taken out as bonds if the plaintiffs had succeeded in their challenge to Proposition 71 and would have been converted to gifts to the state. During the second half of the year the agency issued three RFAs that were known as the Jump Start Program: SEED grants to bring new investigators and innovative ideas into human embryonic cell research, Comprehensive grants to support mature projects of researchers with a track record in stem cell research, and Shared Labs to provide critical infrastructure and training in human embryonic stem cell use. Also, mid-year 2006 the board approved the agency's policy on medical and ethical standards after a year of

work by the committee charged with developing the standards. Most important, the board and staff completed the Scientific Strategic Plan, which was approved by the board at its December 2006 meeting.

THE SCIENTIFIC STRATEGIC PLAN — The agency developed the plan over a period of 14 months having sought the advice of more than 170 scientists, ethicists, patient advocates and public and private representatives. Work on the plan began with a scientific meeting that brought leading stem cell scientists together to discuss the challenges and opportunities of this emerging field on October 1-2, 2005, "Stem Cell Research: Charting New Directions for California." A team from PricewaterhouseCooper facilitated later stages of the effort. Three smaller scientific conferences on specific topics followed along with two focus group meetings. The Board devoted two full meetings to developing the mission statement, values and strategic principals.

The centerpiece of the plan is two sets of goals for CIRM, 10 five-year goals (Appendix 2 – CIRM 5 Year Goals annotated with success-to-date) and 10 ten-year goals (Appendix 3 – CIRM 10 Year Goals annotated with success-to-date). Collectively, those goals set aim on providing evidence that cell replacement therapy using derivatives of human embryonic stem cells is effective for at least one disease, producing a rich pipeline of therapeutic candidates for other diseases, and laying a broad foundation of knowledge about stem cells and disease mechanisms on which future research can build new therapies.

The 2006 Strategic Plan was intended to be a living document. In recognition of the field's rapid development, the agency updated the plan in 2009 (Appendix 4 – 2009 Strategic Plan Key Revisions). That update maintains the aims of the 2006 plan but increases focus on a "pipeline to cures" (Fig. 2) with significant increases in funding for translational and clinical programs and through five specific strategies:

• **Acceleration of Therapeutic Discoveries**, by fostering teams, retaining flexibility to respond to advances in the field, actively managing the development portfolio, capturing data on our progress and sharing that data, fostering the sharing of expertise, promoting partnership with industry, initiating the linkage of stem cell and immunology researchers to enable studies of immune tolerance, encouraging creative basic research proposals that can lead to new development targets and impact the pace of delivery for therapies already moving toward the clinic;
• **Working to Create More Regulatory Certainty**, nationally by monitoring and fostering discussion with regulatory bodies and locally by improving, where appropriate, research policy and the regulations governing the ethical conduct of CIRM-funded research, an example is the creation of the Regenerative Medicine Consortium that fosters substantive discussion with the FDA;
• **Provide Public Education**, by taking a leadership role in educating and informing the general public, including special interest groups and California students of all ages to increase support for stem cell research and for CIRM, examples include an active outreach program to patient advocate groups and building four curriculum modules for high school teachers;
• **Confirm Economic Benefit to California,** by collecting and analyzing information on the impact of CIRM as an economic engine that would justify an additional mechanism for sustaining CIRM financially, including commissioning a two-pronged economic impact assessment with one looking at immediate job creation and tax revenue and the other building a model for assessing the long-term cost saving of regenerative therapies;

• **Create Operational Excellence,** by re-examining CIRM's internal operations so as to improve administrative efficiency, financial accountability, communication, education and teamwork, including developing more robust and detailed budget and expenditure documentation.

Figure 2. CIRM's mission requires funding for the full continuum of the research pipeline from basic to clinical, but with added emphasis in the translational "valley of death" where funding for preclinical development tends to be scarce.

The underlying strategy remains the same in both documents, which is to realize our mission by funding infrastructure and the pipeline of research through Phase II clinical trials. Funding infrastructure, both facilities and intellectual resources, affords California the ability to create and sustain a leadership position in stem cell research. Pipeline research encompasses foundational research, both fundamental stem cell biology and the development of tools and technologies necessary to progress in the field. Most important for our mission, the pipeline funding strategy also includes all levels of translational "applied" research that is critical to bringing benefits of the field to patients.

The agency implements its funding strategy through a series of competitive and targeted initiatives, each with defined objectives and timelines. Solicitations for proposals that address these initiatives are carried out through a formal Request For Applications (RFA) and continue with peer review, pre-funding administrative review and active monitoring during the duration of the grant period. Since the issuance of a single RFA in 2005, CIRM will have issued a total of 22 research and facilities RFAs as of September 2010, a remarkable accomplishment for a start-up agency.

RFAs for which Applications Have Been Peer Reviewed

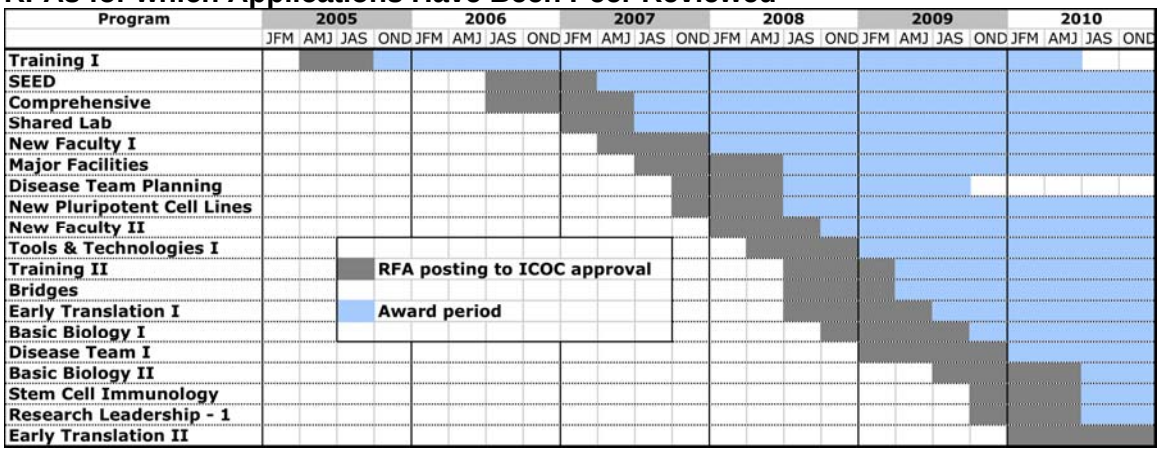


Figure 3. As of September 3, CIRM has processed 1,036 applications through the Grants Working Group (plus 700 Pre-applications). CIRM's grant cycle is approximately 7-9 months from application due date to funding approval, compared to NIH's cycle, which is typically 11 months.

THE GRANT REVIEW PROCESS — Establishing a proper scientific review process was critical from the outset of the agency. The refinement of this process has been ongoing to address our developing spectrum of funding initiatives and specific challenges encountered along the way.

Proposition 71 defines some of the legal parameters around which a review process would be built. Regulations state that grant applications must be evaluated by the Scientific and Medical Research Funding Working Group (GWG) composed of 15 scientist members, "nationally recognized in the field of stem cell research", and 7 patient advocate members from the governing board, the Independent Citizens Oversight Committee (ICOC) (Appendix 7 – Grants Working Group Members). The GWG is required to make funding recommendations to the ICOC, which then makes the final funding decisions. Award recommendations must be based on a competitive evaluation by the GWG and only the scientist members are allowed to score applications for scientific merit.

Within this legal construct, CIRM looked to existing science funding agencies, especially the NIH for guidance. In general, most of CIRM's standard practices related to grant review have been adopted from NIH policies, including rules for non-disclosure, confidentiality, and conflict of interest. There are several important differences, however, that are unique to CIRM.

A primary difference might best be considered a strategic or philosophical one. The goal for CIRM is not simply to fund good science, but specifically to fund good science that will achieve our core mission. As such, our competitive calls for applications are targeted towards specific objectives articulated in our strategic plan and are not general calls meant to support all aspects of stem cell science. CIRM issues Requests For Applications (RFAs) that are similar to NIH and NSF, but unlike these agencies, CIRM does not have a regular open application cycle. Whereas the NIH can process about 50,000 R01 grant applications per year through its approximately 250 study sections, CIRM effectively has only one study section, the GWG, which focuses effort on one RFA at a time.

Another difference is the conduct of the review. Although the scientific peer review component is quite standard, an additional programmatic component that is chaired by patient advocate members is unique. Once applications have been evaluated for scientific merit (usually by 3 expert reviewers), discussed by the review panel (GWG), and assigned a scientific score, the applications undergo a programmatic review. The GWG considers the entire group of applications taking into account the overall rankings by score, the specific objectives of the RFA and of the mission of CIRM. Although the scientific score is fixed, the GWG may change the ranking of an application for strategic purposes, such as adjusting for balance in the overall portfolio. For example, applications that address a topic that is underrepresented might be increased in rank (despite a lower but still meritorious score) and recommended over others that are already highly represented. The GWG, as a whole, votes on which applications will be recommended for funding to the ICOC using both scientific merit and programmatic considerations. (For more detail on programmatic review refer to Chair's Report.)

An initial challenge for CIRM was working within a framework that assigned scientific review responsibilities to only 15 members. CIRM quickly recognized that the breadth

and depth of reviewer expertise needed broadening not only to address the scope of proposals within an RFA but also the expected range of RFA topics spanning from basic stem cell biology to clinical trials to training and facilities. We now recruit the 15 members appropriate for any specific review panel from a pool of 136 board-approved members and alternates. We also actively supplement this selected core of 15 with additional non-voting reviewers who contribute expert evaluations as "Specialist Reviewers".

The conventional peer review of applications is resource intensive and limits the number of applications that can be reasonably and adequately reviewed. This has presented another challenge to CIRM as it is not feasible for the GWG to adequately review much more than 60 applications in response to a standard RFA, and even fewer for complex projects like the Disease Teams. For perspective, an average NIH study section (~24 members) will be assigned review of 60-90 applications but will score and discuss 50% or less. A single CIRM RFA, like Basic Biology Awards, can solicit up to 300 applications. Managing this number of applications would require review across multiple GWG sessions, significantly increase the time to award, and reduce the capacity to handle additional RFAs. To solve this issue, CIRM has previously set limits on the number of applications that it will accept from any given organization. It has relied on the applicant institutions to select those proposals that it believes are the most competitive to submit to CIRM. Although these institutional limits have worked to limit the sheer number of applications received by CIRM, such limits have in some cases also prevented often less senior or less influential scientists from bringing their ideas forward.

Due to concerns over limiting applications per institution, CIRM has developed a pre-application process (Appendix 8– PreApplication Process [PreApp] Description). This process applies only to RFAs that are re-issued on a regular basis. Within this process, teams of external scientific experts and internal science officers identify brief proposals that are likely to be most competitive and responsive to an RFA and invite those investigators to submit full applications. The PreApp process adds about 2 months to the timeline between the release of an RFA and the final approval of awards by the Board. Still, the overall timeframe from PreApp due date to issuance of the Notice of Grant Award (NGA) is about 2 to 3 months shorter than the average NIH cycle of 11 months from application due date to NGA. Applicants who are not selected to submit full applications have the opportunity to submit a new application a year or more later when the RFA is re-issued.

This year's Disease Team II award uses another method for managing application number and quality. Successfully competing for a planning grant is a pre-condition to submitting a final full application. This technique should improve the quality of final applications while ensuring that the number of full applications is manageable.

Overall, CIRM has built (and continues to improve on) a review process that is tuned to our strategic goals, is efficient, and is valued by both reviewers and applicants. (Appendix 9 – Details of CIRM's application and review process) (Appendix 10– CIRM Grantee Survey Data).

Running in parallel with the science team's work with grants review and subsequent project oversight is the work of the Grants Management Office. This group does extensive checking pre-award and post-award to ensure all applicants are adhering to

CIRM's Grants Administration Policy (GAP), Medical and Ethical Standards and other policies. (Link to Regulations Governing CIRM Grants)

BUSINESS SYSTEMS — As a state agency, CIRM was required to develop a clear set of written rules for grant administration. The agency is keenly aware of its obligations as steward of public funds and the need to account for their use. We have tried to develop grant administration rules that enable us to meet these needs while minimizing the burden on grantees. CIRM's accounts are audited annually and the agency went through an extensive audit of its business practices by the Bureau of State Audits (Appendix 11– BSA Audit and Appendix 12 - CIRM Response). The State Controller's Office did a separate audit of Grants Management in 2008. CIRM was also reviewed by the state's good business practices unit, The Little Hoover Commission, in 2009 (Appendix 13 – Little Hoover Commission Report Executive Summary). Part of that commission's recommendations resulted in legislation passed by the legislature in Sacramento and being considered for signature by the governor (Appendix 14 -- SB1064) (For more detail on accountability standards see Chair's Report.)

Most CIRM grantees are accustomed to administering research awards that operate under NIH rules. When we could, we have adopted compatible approaches, so that grantees would not have to learn a new set of rules and procedures.

In some instances, Proposition 71 imposed requirements that would not allow us to adopt NIH rules. For example, Proposition 71 allows for reimbursement of indirect costs, but includes requirements that are inconsistent with the indirect cost rates used by NIH. Though we have done what we could to harmonize our requirements, grantee institutions express frustration with deviations from familiar requirements.

In other instances, NIH rules were simply a poor fit with CIRM's goals. One reason for diverging from NIH requirements is due to the narrower focus of CIRM's research program compared to that of the NIH. CIRM grantees are expected to work toward specific aims outlined in their applications. Under CIRM's requirements Principal Investigators (PIs) are expected to consult with CIRM scientific staff before making significant changes to their aims or research plan. For the same reason, CIRM also expects progress reports to include sufficient information to evaluate progress toward aims. In both areas, we have found that some investigators accustomed to NIH grants have had difficulty understanding CIRM's expectations. However, more often than not, the dialogue that develops between the grantee and the CIRM scientific program office is viewed as beneficial by the researcher. Under certain circumstances, CIRM has terminated grants for lack of progress, generally because the research being conducted was not in compliance with the objectives of the RFA. Going forward, CIRM is using objective milestones to measure progress and ensure accountability in its applied research such as the Disease Teams.

INTELLECTUAL PROPERTY — Proposition 71 required CIRM's board to establish intellectual property policies that appropriately balanced the desire to generate a fair return to California taxpayers with the need to ensure that research would not be unreasonably hindered by such policies. To accomplish this challenging task, the Board created the "IP Task Force," which presided over public comment on 17 rounds of draft regulations, held 15 public meetings, conducted surveys of more than 20 funding entities to determine best practices and interviewed more than 100 people. (For more on IP policies see Chair's Report.)

The first set of IP regulations were for non-profit organizations and went into effect February 10, 2006. These interim regulations were then submitted for review to the state's Office of Administrative Law, and went into effect formally on July 14, 2007. A later set of regulations covered for-profit organizations. These were recently consolidated into one controlling set of regulations that applied to both for-profit and non-profit entities. (A link to those regulations is at http://www.cirm.ca.gov/cirm-operations/Regulations.)

In each case, three core principles served as cornerstones of the regulation. The first is that CIRM does not own any intellectual property arising from its funding. The second is the requirement that grantees make a reasonable effort to bring their inventions to practical use. The third is the notion that non-exclusive licenses were preferred over exclusive licenses as this would more likely lead to increased competition and hence lower prices of any CIRM funded therapeutic. (Appendix 15 - CIRM IP Regulations and Frequently Asked Questions.)

MEDICAL AND ETHICAL STANDARDS —CIRM developed the first comprehensive set of regulations governing the conduct of human embryonic/pluripotent stem cell research. Rules governing the ethical conduct of CIRM-funded research were required by Proposition 71, so the agency reviewed the landscape of regulations, such as the Common Rule, and focused its efforts where there were gaps relevant to the stem cell field. Interim regulations were approved by the ICOC in late 2005. As illustrated in Figure 4, the Scientific & Medical Accountability Standards Working Group (SWG) developed and the ICOC approved final standards in a one-year period.

These standards were developed following California's open meetings rules and administrative law requirements. CIRM and the SWG held 9 public meeting to develop specific policy recommendations. During these meetings, extensive public comment was considered. Further, CIRM staff responded in writing to over 100 written comments from research institutions, patient advocates, interest groups and the public. The process culminated with the approval of final standards making California the first state to have comprehensive ethical standards for human embryonic stem cell research. They incorporate the Common Rule for the protection of human subjects as well as some additional requirements discussed further on page 25.

Figure 4. CIRM developed the first comprehensive set of medical and ethical standards in 12 months incorporating a process that involved extensive public deliberation and comment.

THE SCIENCE PROGRAM

CIRM maintains a two-pronged funding strategy, supporting infrastructure and the full research pipeline. The agency views infrastructure broadly and supports facility construction, acquisition of key service equipment and intellectual resources with training programs starting at community college and running through graduate programs, post doctoral fellowships and specialized training for active investigators. The latter is largely through its Shared Lab program, many of which offered courses for specialized stem cell lab techniques and protocols. CIRM's investment in both infrastructure and pipeline research is shown in Figure 5 and further broken down in Figure 6 below.

INTELLECTUAL RESOURCES — CIRM's programs to build intellectual resources in the state span the complete spectrum of research participation and experience levels, from undergraduate biology students to leading, established investigators. All of these programs, from the Bridges to Stem Cell Research (Bridges) and Research Training grants to the New Faculty Awards and Research Leadership program, have at their core the direct participation in laboratory research in support of CIRM's mission. The Bridges program funds undergraduates and masters level students from California State Universities and community colleges. Training grants fund graduate students, post doctoral and clinical fellows. The SEED grants were designed to bring new investigators into the field of human embryonic stem cell research, and the New Faculty Awards are five-year early career grants. The Research Leadership program provides funding for the recruitment of world-class, generally mid-career scientists to California institutions.

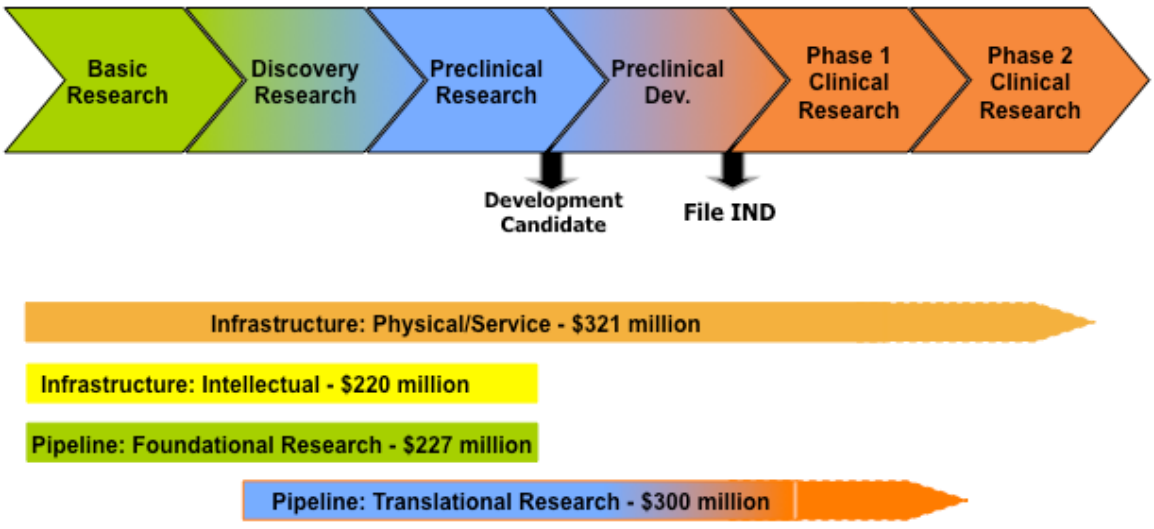


Figure 5. CIRM Investment in Infrastructure and Pipeline Research, as of July 2010. Within infrastructure, "physical" includes CIRM Major Facilities and Shared Lab grants and "Intellectual Resources" includes, Training grants, the Bridges program, New Faculty Awards, and CIRM Research Leadership Awards

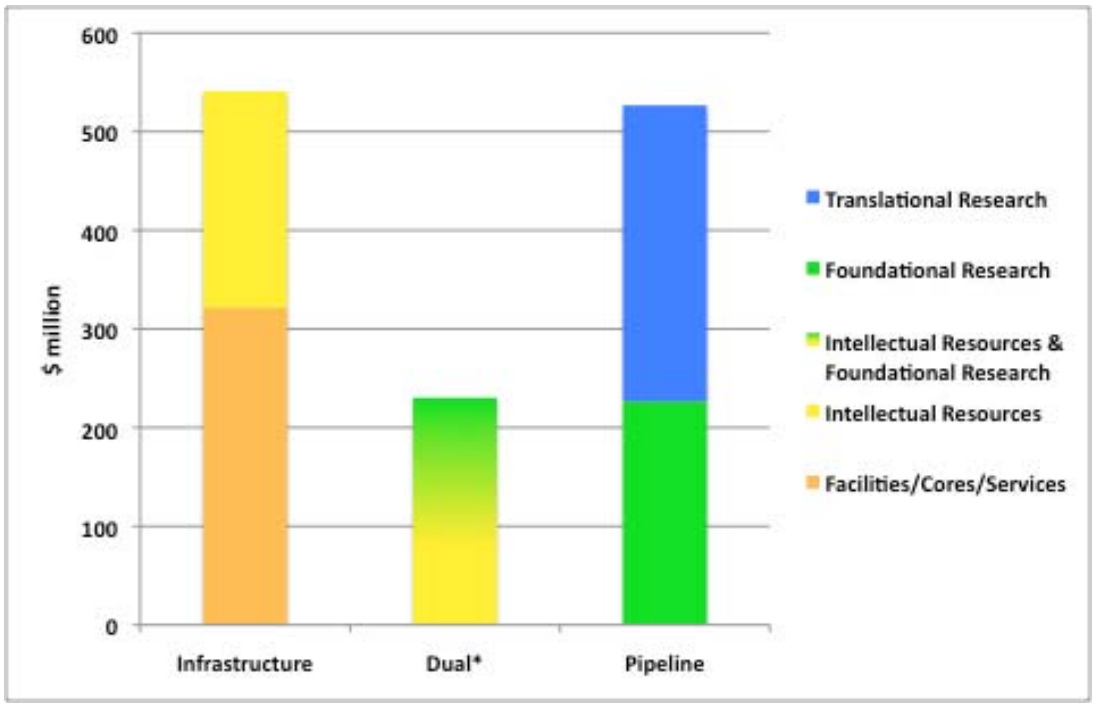


Figure 6. CIRM Investment in Infrastructure and Pipeline Research as of July 2010. The Dual category highlights the overlap not captured in the categorization. Specifically, New Faculty Awards, included in Intellectual Resources, are also an investment in foundational research. Similarly, the Jump Start SEED and Comprehensive programs included in Foundational Research is a dual investments in intellectual resources.

The first of the programs intended to build intellectual resources were the Research Training grants, which support pre-doctoral, post-doctoral, and clinical fellows. Training Program I, CIRM's first ever awards, supported 16 institutional training programs and engaged approximately 170 trainees per year, and involved 219 labs over three years. The recently initiated Training Program II increases support to 17 programs and approximately 196 trainees per year. Fellows supported by these two grant programs have contributed to 358 research publications as of August 10, 2010.

The Bridges initiative supports research opportunities for undergraduate and masters level students, particularly from California State Universities and community colleges. This program seeks to expand the pool of laboratory personnel trained in techniques essential for stem cell biology and to provide exposure to this field to students who otherwise might not consider more advance educational opportunities. The 160 trainees per year in the 16 Bridges programs participate in research internships in laboratories in research-intensive universities and biotech companies.

The New Faculty Awards encourage and support the next generation of clinical and scientific leaders in stem cell research. These awards provide five years of funding for research projects conducted by newly independent principal investigators. Two rounds of New Faulty Awards yielded 45 recipients (Appendix 16 – New Faculty Award Recipients).

CIRM's Research Leadership Award program is a new initiative to foster recruitment of established or emerging leaders in stem cell science. These grants provide six years of salary and research support intended to enable these researchers to pursue highly innovative projects. CIRM plans to fund eight of these awards over the next two years. One has been awarded to date (Appendix 17 – Recipient CV).

The agency's first research grants, part of the "jump start" program, were the SEED and Comprehensive awards intended to rapidly energize stem cell science in California. The SEED grants focused on bringing new ideas and new investigators into the field by providing two year funding for novel projects focused on human embryonic stem cells. The Comprehensive grants provide four years of support for mature, ongoing studies on human embryonic stem cells by scientists with established records of accomplishment in the field. CIRM funded 73 SEED and 28 Comprehensive awards.

RFA	Program Period	Grants Awarded	Funds Committed
Training I	2006-2010	16	$38.9 million
Training II	2009-2011	17	$45.2 million
Bridges	2009-2011	16	$23.9 million
New Faculty I	2008-2013	22	$55.4 million
New Faculty II	2009-2014	23	$61.3 million
Research Leadership	2011-2018	8*	$44 million*
SEED	2007-2010	73	$45.3 million
Comprehensive	2007-2011	28	$72.0 million

* projected; approved in Concept Proposal

Table 1. CIRM activity in developing intellectual resource

FACILITIES INFRASTRUCTURE — CIRM made early strategic investments to establish dedicated space and equipment free of federal funding for the conduct of research on human embryonic stem cell lines without regard to federal limits. The Shared Labs and Stem Cell Techniques Course program, a $50 million investment, had the goal of supporting the creation of core laboratories for use by multiple investigators at both the grantee institution and neighboring institutions. In addition to creating a safe harbor for this work, the program provides an expertise resource, both through linked CIRM funded hESC Techniques courses and through the shared expertise of persons operating and utilizing the facility. Shared Lab directors have told CIRM that continued funding for operations of a core lab/resource such as these would contribute immensely to advancing the field by not requiring all investigators/labs to have hands-on pluripotent cell technical expertise.

The Major Facilities program, a $271 million investment to build stem cell research centers in California, had the additional purpose of expanding research capacity and capabilities and bringing stem cell-related researchers together in a collaborative setting. This was a forward looking capacity building program to position California for continued leadership in stem cell related biomedical research. It had the added benefit of bringing in an additional $560 million in leverage funding for construction from the institutions and private donors. Additional institutional commitments for faculty recruitments packages and other costs brought the total leverage funds to $880 million and total project funding

to $1.1 billion (Appendix 18– Major Facilities Leverage Chart). The seven largest of these awards were for "CIRM Institutes" that have pledged to put basic, translational, and clinical researchers side-by-side in the new buildings in an effort to expedite the transition from bench to bedside for CIRM-funded discoveries.

The major facilities construction is providing 13,000 job-years of employment in California during the recent economic downturn. (Appendix 19 – Economic Analysis Impact Report on Major Facilities.)

PIPELINE STRATEGY — CIRM's pipeline strategy is anchored by a core set of repeating RFAs (every 12-24 months) which span the stages of research – from basic foundational biology through clinical research (Figure 7). This strategy is reflected in the update to the Scientific Strategic Plan, which provides for the timely re-issuance of core RFAs. This provides predictability to California's researchers and permits deferred applicants to improve and resubmit their applications. Other RFAs are introduced as needed to address focused pipeline considerations. For example, the Targeted Clinical Development RFA was introduced specifically to provide a funding opportunity to those innovators who are leading the field by pursuing clinical development of novel cell therapies derived from pluripotent stem cells.

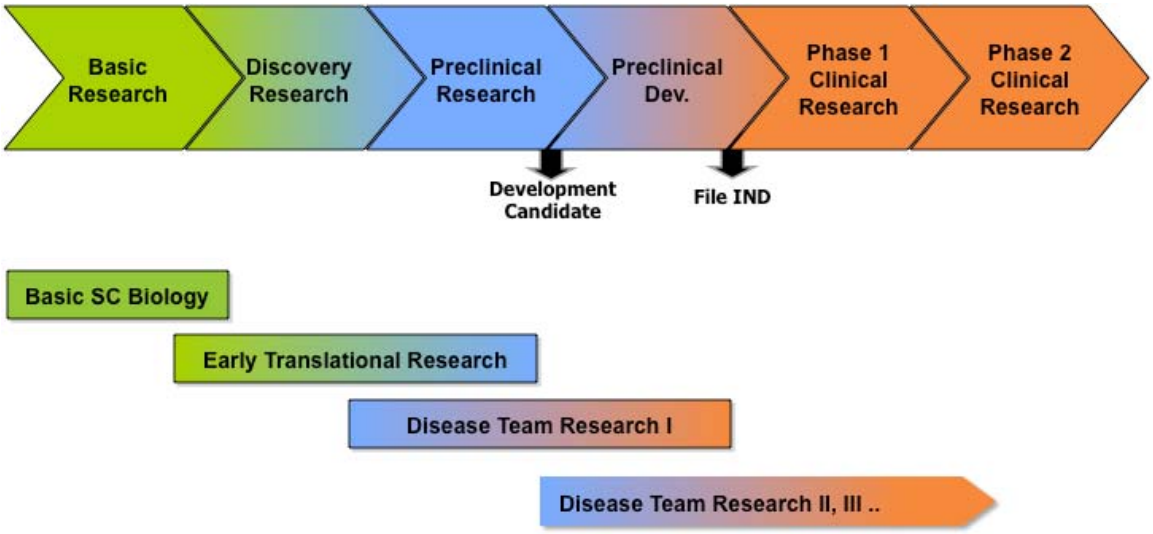


Figure 7. CIRM's core grants fit into the successive phases of the research pipeline.

FOUNDATIONAL BIOLOGY — CIRM's initiatives in Basic Biology focus on transformative research that provides novel insights into cellular and molecular mechanism underlying stem cell biology. These studies provide an essential foundation for deriving cells and developing cell therapy approaches appropriate for clinical translation. Key areas of research concentration have included investigations of stem cell pluripotency and self-renewal, cellular differentiation pathways, and mechanisms of reprogramming.

Within these broad areas, various projects have focused on signaling pathways regulating critical stem cell functions, epigenetic mechanisms mediating stem cell fate, role of the microenvironment in maintaining pluripotency and modulating differentiation, molecular determinants of cellular reprogramming towards induced pluripotency, and direct reprogramming. CIRM has sought to support projects that explore novel mechanisms, pathways or cellular events and investigations that will have a major impact on stem cell research and regenerative medicine.

Highest priority for funding under these initiatives has been studies of and with human pluripotent and progenitor cells; this priority reflects a commitment to support research not likely to be funded by other sources and projects that might not otherwise be pursued due to the slower and more formidable technical challenges of working with human cells. Some 70 percent of CIRM's research projects involve work with human embryonic stem cells although many of those involve comparisons between types of cells.

The Basic Biology RFAs constitute CIRM's core programs in foundational scientific studies. These programs have run in two successive annual cycles yielding 28 grants funded for a total of $38.7 million. Basic Biology awards provide up to $300,000 per year in direct research funds for up to three years. A third Basic Biology competition is currently underway.

Other CIRM initiatives have also supported research into basic processes and mechanisms in stem cell biology. A majority of the SEED and Comprehensive grants are focused on basic biology. Additionally, most of the projects supported by the New Faculty awards are concerned with fundamental stem cell research.

RFA	Program Period	Grants Awarded	Funds Committed
Basic Biology I	2009 - 2012	12	$16.3 million
Basic Biology II	2010 - 2013	16	$22.4 million
Basic Biology III	2011 - 2014	25*	$45 million*
SEED	2007 - 2010	43§	$25.9 million§
Comprehensive	2007 - 2011	17§	$24.1 million§
New Faculty I	2008 - 2013	18§	$43.6 million§
New Faculty II	2009 - 2014	19§	$48.6 million§

* projected; approved in Concept § portion of program grants/funds for basic research

Table 2. Summary of CIRM programs supporting fundamental studies.

As of August 10, CIRM funding resulted in authorship on 584 articles. Appendix 20 has narrowed that group down to 41 papers in the most high profile journals and for which the CIRM grantee was the PI. Here are a few examples:

From the SEED grants, R. Blelloch of UCSF published in *Nature* the discovery that two distinct classes of microRNA orchestrate embryonic stem cell self-renewal through opposing regulation of self-renewal genes.

From the Comprehensive grants, D. Srivastava of Gladstone published in *Cell* the first report that committed cardiac fibroblasts can be directly reprogrammed into cardiomyocytes without passing through a pluripotent or progenitor stage.

From New Faculty grants, K Baldwin of Scripps published in *Nature* one of two papers demonstrating for the first time that mouse iPSCs are fully pluripotent and can generate viable, fertile, adult progeny via tetraploid complementation.

From the Tools and Technologies grants, H. Blau of Stanford published in *Cell Stem Cell* a study revealing that two key regulatory components, Rb and ARF, play a central role in maintaining the differentiation state of muscle cells and that inactivation of these components can restore proliferative and regenerative properties to terminally differentiated muscle cells.

CREATING A DEVELOPMENT PORTFOLIO — To support the development of stem cell-based therapies for patient benefit, CIRM created repeating programs aimed at building a development portfolio. These include the CIRM Early Translational, Disease Team and Targeted Clinical Development initiatives. CIRM's total activity in translational research is summarized in the following table.

RFA	Program Period	Grants Awarded	Funds Committed
Early Translational I	2009 - 2012	16 §	$71.6 million
Early Translational II	2011 - 2014	20* §	$80.0* million
Disease Team I	2010 - 2014	14	$225.0 million
Disease Team II	2012 - 2016	12*	$243.3* million
Targeted Clinical Development	2011 - 2014	2*	$50.0* million

* projected; approved in Concept §Early Translational I includes 8 Development Candidate (DC) Awards; ET II includes projected 10 DC Awards

Table 3. Summary of CIRM's total activity in translational research.

Because translational research is inherently a multidisciplinary endeavor, CIRM structured the RFAs for these initiatives to ensure that the most qualified scientists are involved in these projects. International collaborative funding partnerships and co-principal investigators enable multiple thought leaders to work toward a common goal. Grants and loans fund both companies and non-profit institutions, so that teams can blend expertise from industry and academia. CIRM issued the first round of Early Translation and Disease Teams in 2009, and the resulting CIRM Development Portfolio is illustrated in Figure 8 below. The Targeted Clinical Development RFA, which will fund early clinical trials for pluripotent-derived cells, was released in August 2010 and the second round of Early Translational and Disease Team awards are in preparation for awarding in late 2010 and early 2012, respectively.

The first round of Early Translational grants had two distinct goal options for the applicants. They could propose identifying a development candidate, either small molecules or biologics or cell therapy derived from stem cell research, or they could propose developing tools to overcome bottlenecks for cell therapies on the path to the clinic. Eight awards were made in each category in April 2009. The therapeutic focused projects are conducting pre-clinical proof of concept research as well as preliminary safety studies with the goal of preparing a development candidate suitable for moving into IND-enabling development in anticipation of use in humans. The bottleneck projects

aim to overcome technical hurdles in advancing potential therapies to the clinic such as developing sensitive standardized teratoma assays and tools for imaging cells after transplantation.

The first round of Disease Team grants had the objective of filing within four years an approvable Investigational New Drug (IND) application to begin a clinical trial. This first round was open to candidate drug molecules, biologics or cell therapies derived from stem cell research, and to potential therapeutics in all diseases and injuries. The Board approved 14 teams in October 2009. To help teams stay focused on the primary goal of the IND filing, CIRM developed an active management concept for projects in this late translational research stage. CIRM staff worked with teams in the immediate post-award period to ensure that project plans and milestones adequately addressed the regulatory requirements for IND filing within the four-year timeframe, and to develop activity-based budgets.

For the four teams that included international Collaborative Funding Partners, CIRM worked with the funding agencies in each country to ensure mutually agreed upon processes were followed (see page 23 and Appendix 21– Sample Memorandum of Understanding). Two of the fourteen Disease Teams have industry leadership (PI or Co-PI), however, an additional eight teams have industry participation as subcontractors, suppliers, or consultants. A priority for CIRM will be to actively engage industry in these applied research programs where therapeutic development expertise is critical.

An important strategic question is whether we are attracting and selecting the research proposals that are most likely to enable CIRM to fulfill its mission to deliver stem cell-derived therapies to the clinic. These first rounds of translational programs were “very open” in the types of projects that would meet the requirements of the RFA. All stem cell types and multiple therapeutic approaches (biologic, small molecule, and cell therapy) were eligible, as were all disease and injury targets. The resulting Development Portfolio (Figure 8) shows a mix of stem cell types that are the source (adult SC, hESC, iPSc) or the proposed therapeutic target (cancer stem cell or endogenous stem cell). Of the 22 projects, 18 are cell therapies or combination products (8 of which are gene-modified cell therapies); 2 are small molecule approaches; 1 monoclonal antibody, and 1 protein (data not shown).

The regulatory requirements for stem cell therapies are still being established. While there are general guidances, the regulatory pathway for these therapies, especially pluripotent-derived cellular therapies remains uncertain. Thus, the majority of CIRM’s development portfolio is considered novel from a regulatory review perspective. CIRM anticipates that reducing the regulatory uncertainty will be a key factor in successfully meeting the goals of the Disease Team program and therefore is engaged in a number of initiatives with the FDA described on pages 30-31.

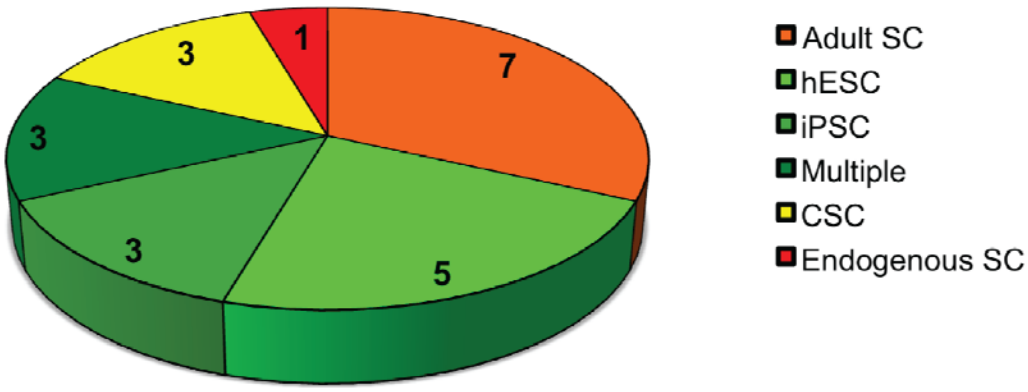


Figure 8. Development Portfolio – 2010 by Stem Cell Type. 18 projects include a stem cell (Adult SC, hESC, iPSC, or multiple including hESC or iPSC) as the therapeutic candidate; the 3 Cancer Stem Cell projects (yellow) include 2 small molecule and 1 monoclonal antibody approaches; the endogenous stem cell (red) is the target of a protein therapeutic.

CIRM is also in the process of establishing a clinical Oversight Advisory Committee (OAC) comprised of external experts in cellular therapy development, regulation, and specific disease areas to assist the CIRM President and staff in reviewing these projects. The OAC will provide advice at key junctures, defined in the grant approval process as critical milestones, as the agency decides to continue projects as planned, continue projects with modifications, or to discontinue projects, based on the presentation of scientific findings. The disease distribution of projects under active management in these translational and preclinical projects is illustrated in Figure 9 and their stage along the pipeline is indicated in Figure 10.

Two of these disease teams have already achieved major milestones. USC's P. Cannon, who is working with the team headed by J. Zaia of City of Hope has published a proof of principle paper in Nature Biotech August 2010 on the team's effort to create blood-forming stem cells that can produce HIV-resistant T cells. Her team showed that in mice human HSC/progenitors modified by zinc-finger nucleases that target and break the CCR5 gene in a manner similar to the natural CCR5 mutation were capable of engraftment and control of HIV replication. Also, K. Aboody of City of Hope has received FDA approval in June 2010 to begin a clinical trial with neural stem cells that home to brain tumors and act as carriers for an enzyme that converts a pro-drug to an active cancer chemotherapeutic agent. While this is a different agent and a different protocol than the one she has proposed for the CIRM disease team, the cell source is the same. The ability to cite a previously accepted drug master file on the cell source should facilitate approval of the CIRM funded IND **a**pplication.

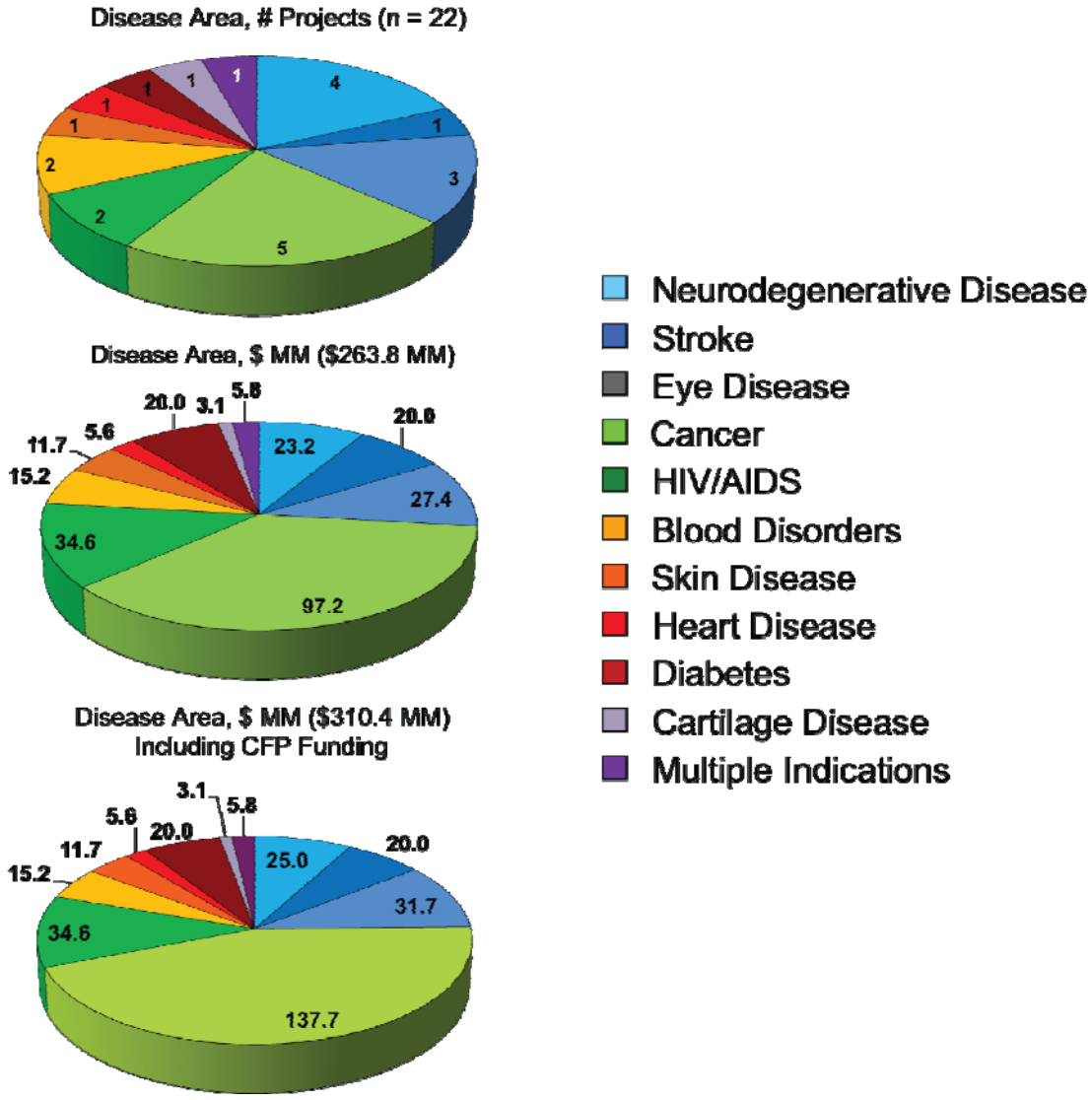


Figure 9. CIRM 2010 Development Portfolio: Disease Distribution. CFPs are international Collaborative Funding Partners, in this case from Canada and the UK.

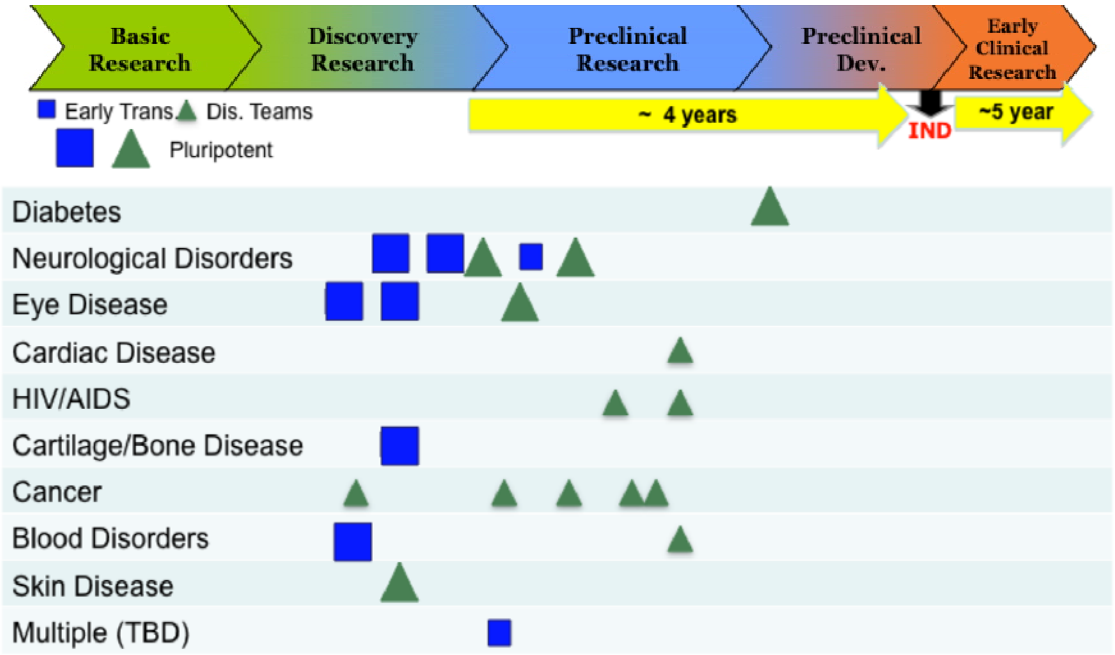


Figure 10. CIRM Development Portfolio – 2010. The markers indicate where the project is in the development pipeline.

ASSESSING THE RESEARCH PORTFOLIO

By the end of 2010 CIRM will have issued 22 research and facilities RFAs, most of which are still active (see Figure 11).

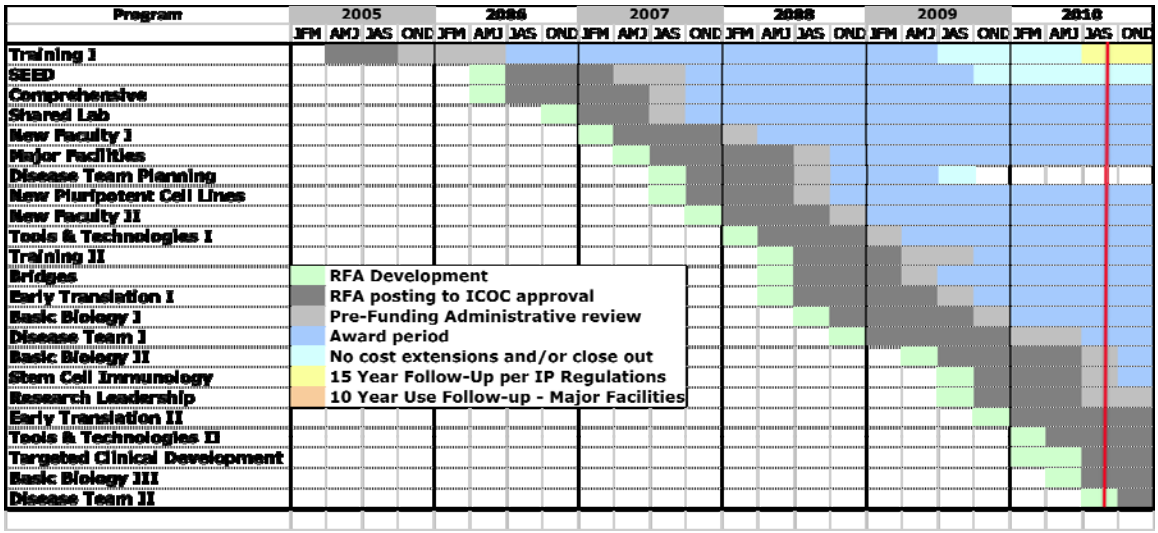


Figure 11. CIRM Funding Programs: The red line indicates the stage in the program lifecycle for all of CIRM's funding programs.

The process from posting to Board approval of award averages seven to nine months. However, each RFA takes up considerably more time from the Science Office staff both pre-application and post award (Appendix 22 - Science Office Activities Per Grant). Staff first develops the concept behind a particular RFA, takes that to the board for approval,

and then spends one to two months refining the area of focus and other aspects of the RFA before posting. The full process is depicted in Figure 12 below.

Many different inputs determine the focus of each RFA. The overriding parameter is always the mission and strategic goals of the agency, but many real-time assessments of the current state of the field come into play. CIRM's internal scientific expertise filters information from meetings, the literature, CIRM-organized or funded workshops, input from our grantees and data provided on existing grant progress reports. The science team is vigilant about monitoring for portfolio gaps.

Staff-organized workshops have proven invaluable in bringing the leading thinkers on a given topic together to look for gaps in the field or best opportunities going forward. Examples include: the autism workshop pointed out the real potential of iPS cell lines to define the phenotype of the various types of disease in this broad spectrum disorder, and the workshop on stem cells in drug development showed the potential as well as significant hurdles in scaling up stem cell screening for target molecules and for toxicity testing. (Appendix 23– CIRM Workshops).

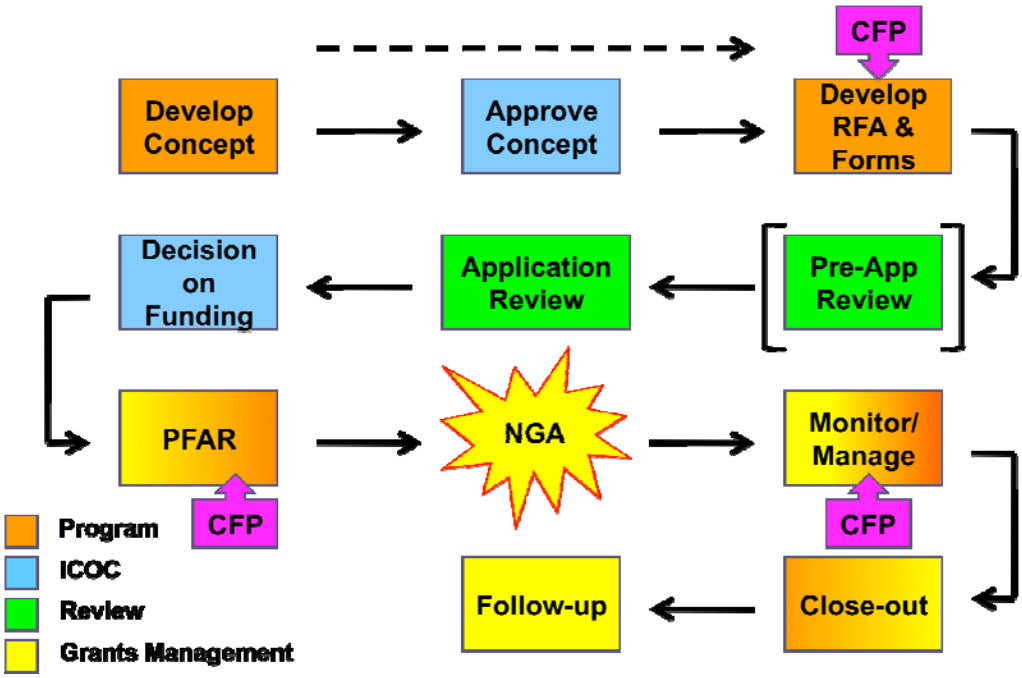


Figure 12. CIRM Award Process. Boxes reflect key functions throughout the award process. Color of the boxes refers to primary responsibility for activities associated with each function, e.g. Program Office, Review Office, ICOC (Independent Citizens Oversight Committee, CIRM's governing board), Grants Management Office. CFP refers to CIRM's collaborative funding partners, who, when they participate in a given RFA program, participate during the steps noted. NGA is Notice of Grant Award which is the official contract issued after staff pre-funding administrative review (PFAR).

CIRM has also funded 14 matching grants up to $50,000 each to help California institutions develop high-level symposia and conferences on specific topics. They have brought in leading experts from around the world to address issues ranging from stem

cells in pediatric disease to regulatory issues and numerous disease-centric conferences. (Appendix 24 – Conference Grants).

During the life of the grant the science office actively follows each project, in particular through annual progress reports. (Progress reports for translational and disease team awards are received biannually and quarterly, respectively.) Discussions following these reports have been able to redirect several projects that were not making sufficient progress to goal. Where PIs were unwilling to work within the objective of the RFA and the goals stated in the application, three projects were terminated.

OUTCOMES — CIRM is still in the early days of assessing outcome. Of the issued RFAs only two are completed and the awards closed out, Training I and Disease Team Planning. One RFA is near close out, the SEED program. Progress to the five-year and ten-year strategic goals outlined in the 2006 strategic plan is detailed in Appendix 2 and Appendix 3.

In summary, CIRM has made significant progress toward most of these goals. Half of the five-year goals have been met and the others are on a plausible track for completion in the next year or two, within the five-year window of when the first grants were awarded in 2006. The one difficult goal here is # VI demonstrating immune tolerance, but 19 awards have been launched under the recent RFA for Cell Transplantation Immunology.

CIRM grantees have published papers advancing progress toward nearly all of the ten-year goals. They have made sufficient progress to believe these goals are achievable. Goal #1, which is proof-of-principal that transplanted cells derived from pluripotent cells can be used to restore function for at least one disease is challenging to achieve within the 10-year timeframe, but progress may be accelerated with the new RFA for support of clinical studies. However, with the historic high failure rate for all potential therapies at this juncture, it is premature to predict CIRM success on this goal and lends weight to Management's desire to ensure funding for this end of the pipeline extends long enough to enable this goal.

CIRM-sponsored research has facilitated rapid translation to the clinic of traditional small molecule therapies developed using stem cell research. CIRM research support has contributed to the rapid translation of two such programs into the clinic. Preclinical research supported by a SEED grant to the lead investigator and CIRM Training Grant I funding to two CIRM scholars demonstrated that a JAK2 inhibitor (TG101348) could block aberrant erythroid differentiation of polycythemia vera progenitors. The studies also provided direct in vivo evidence that a particular mutation in JAK2 (JAK2V617F) is necessary and sufficient to drive aberrant myeloid differentiation characteristic of polycythemia vera. This work was published (Geron, I. et al., Cancer Cell 4:321, 2008) but more importantly provided the basis for Phase I clinical trials by TargeGen of the JAK2 inhibitor TG101348 in polycythemia vera patients. The trial was completed and plans for further studies are under development. (Appendix 25 – First Clinical Trial Funded by CIRM)

Similarly, a CIRM SEED-funded grantee conducted research and was a co-author on a publication showing that hedgehog signaling was required for maintenance of cancer stem cells in chronic myelogenous leukemia (Zhao C., et al., Nature 458:776, 2009). The researcher has continued the research funded under a CIRM New Faculty II Research award and reported to CIRM on preclinical studies on leukemic cancer stem

cells with a small molecule inhibitor of the hedgehog pathway. Based in part on these studies, Pfizer has initiated Phase I clinical testing of the hedgehog inhibitor in chronic myelogenous leukemia this year.

IMPACT OF CLOSED OUT GRANTS — The Research Training Program I showed significant indicators of success. Over the past three years, the training grants have supported 279 pre-doctoral students and postdoctoral and clinical fellows across 219 distinct laboratories. Those trainees, "CIRM Scholars," have contributed to 358 publications as of August 10. Although it is still early to access full outcomes, we know that many with MD degrees are practicing medicine with an intimate knowledge of stem cells and their potential. And many have moved on to continue training at top stem cell research laboratories. Outstanding examples of CIRM Scholar achievements include: research leading to the founding of a biotechnology company and contributions to research that has led to a Phase 1 clinical trial.

Former CIRM Scholars continue to contribute to stem cell research in California. For example, Dr. Kathryn Ivey, a CIRM Scholar from 2006 to 2009, is currently the Director of the Stem Cell Core at the Gladstone Institutes, which provides resources for the study of iPSC and hESC. Dr. Lousie Laurent, a CIRM Scholar form 2006 to 2008, currently holds a faculty appointment at UCSD and recently published work that highlights the lack of ethnic/racial diversity among existing hESC lines. Dr. Emin Maltepe, a CIRM Scholar from 2006 to 2007, is currently an Assistant Professor of Pediatrics and Biomedical Sciences at UCSF. Dr. Ann Zovein, a CIRM Scholar from 2006 to 2009, is currently an Assistant Professor at the Cardiovascular Research Institute at UCSF. Dr. Mathew Blurton-Jones, a CIRM Scholar from 2006 to 2007, is currently a faculty member in the Department of Neurobiology and Behavior at UC Irvine. Dr. Nil Emre, a CIRM Scholar from 2006 to 2007, is a stem cell scientist at BD Biosciences. Dr. Edward Hsiao, a CIRM Scholar from 2006 to 2009, is an endocrinologist in the Department of Craniofacial and Mesenchymal Biology at UCSF. Dr. Laura Perin, a CIRM Scholar from 2006 to 2009, is an Assistant Professor at Children's Hospital Los Angeles.

Many other trainees have also taken on positions outside of California. For example, Dr. Derrick Rossi, a CIRM Scholar in 2006, is now Principal Faculty at the Harvard Stem Cell Institute. Dr. Michael Dorsi, a CIRM Scholar from 2008-2009, is a practicing neurosurgeon in Baltimore. Dr. Ichiro Nakano, a CIRM Scholar from 2006 to 2008, is an Associate Professor at Ohio State University Medical Center.

What may perhaps be most impressive is that the training programs have catalyzed the development and maintenance of a robust stem cell community at the host institutions. The program, through its courses, seminars, and mentoring brings together many faculty in a variety of ways that spur increased collaboration and community.

This has in turn enhanced the recruitment of top students in what is a very competitive program. The number of applications in the UC Berkeley program at the graduate student level, for example, went up eight fold between its Training I first year and its Training II first year, with overall applications during that period up three fold. The program also has helped attract faculty from outside the state to join this emerging community. It is itself an effective recruitment and retention tool.

Finally, the research that the agency supports via this program clearly synergizes with other CIRM funded programs to accelerate research and generate new ideas. Just as an

example, we know that work performed by two CIRM Scholars and a SEED award have contributed to the testing of a drug, currently in Phase I clinical trials noted above.

It is clear that CIRM has built a momentum and critical foundation with these training programs. The leaders of stem cell programs at these training institutions have unequivocally and unanimously stated to CIRM the importance of funding these programs to help sustain the advancement of their research.

The Research Training Program II is now supporting 17 programs that offer training to 198 trainees per year. In addition to students and fellows tethered to these specific training grants, many other trainees are gaining experience through CIRM's routine research awards, with 1,248 total trainees cited as working on any CIRM grant as of June 2010 (Appendix 26 – All CIRM Trainees).

Disease Team Planning awards were clearly effective in producing higher quality applications for the Disease Team Awards. Given the relative small size of the planning awards, $50,000, and the major commitment of the Disease Team awards, averaging $14 million and many up to $20 million, this was a good investment:

- Out of 22 DT Planning Award recipients, 19 submitted 18 pre-applications for the Disease Teams (86%) – two groups consolidated into one
- Out of those 18 pre-applications, 13 were invited to submit full applications (72%) (For the RFA as a whole, 32 of 73 pre-applicants were invited to go forward.)
- Out of those 13 full applications, 10 were ultimately awarded DT grants (77%)
- Out of the 14 DT grants awarded, 10 were given to DT Planning Award recipients (71%) - *However Stanford independently provided Planning funding to two additional Stanford PI led teams including one that succeeded in securing a Disease Team grant, so 11 of 14 had funded planning phases and only three of the 53 pre-aps without a funded planning phase succeeded.*

(Planning grants for Disease Team II will be $100,000 and will be a required as a prerequisite for a full Disease Team submission.)

The Bridges program, even though it is only a little more than a year old, has already resulted in interns securing jobs at internship labs or extending their training period through additional support provided by the host labs. A few examples: at Humboldt State three of seven interns have been hired as research technicians and one has been accepted into a PhD program; at CSU Long Beach of four trainees two have been offered jobs in their internship labs, a third is continuing with a master's program and a fourth plans to apply for a PhD program; and at San Jose State four students from the first cohort have been hired as research technicians— two at Stanford University, one at Escape Therapeutics, Inc., and one at the Parkinson's Institute—two interns are entering PhD programs, one in Microbiology at the University of Hawaii and one in Bioinformatics at University of Iowa, and two interns are completing Master's programs.

COLLABORATIVE FUNDING LEVERAGES RFA POTENTIAL — Scientific inquiry occurs without regard to state and national boundaries. CIRM's Collaborative Funding program (CFP) fosters the natural inclination of California's scientists to pursue their objectives through collaborations with colleagues having special capacities and resources around the globe.

The CFP program has proven to be an effective tool to leverage CIRM's financial and intellectual capital to further its mission. Collaborative funding optimizes the use of

resources, avoids duplication and creates a critical mass of excellence across a wide range of specialties. CIRM currently has Memorandum of Understanding agreements with funding agencies in seven countries:
• Cancer Stem Cell Consortium (CSCC) of Canada;
• State of Victoria in Australia;
• Japan Science and Technology agency (JST) in Japan;
• Ministry of Science and Innovation (MICINN) in Spain;
• Medical Research Council (MRC) in the United Kingdom;
• Federal Ministry of Education and Research (BMBF) in Germany; and
• Ministry of Science Technology (MOST) in China.

Discussions with several other nations including Sweden, The Netherlands, France, India, Israel, South Korea and Scotland are underway, as are negotiations specifically with the state of Andalucia in Spain, the national Australian government, the East England Stem Cell Network within the UK and with Canada to consider broadening that agreement beyond cancer stem cells. CIRM also has formed relationships with the State of Maryland and the New York Stem Cell Foundation and is in discussion with several other states. (Appendix 21- Sample Memoranda of Understanding.)

CIRM has established general criteria for selecting and evaluating potential Collaborative Funding Partner countries. Countries with an established or emerging stem cell research community and a stable funding environment are evaluated. The prevailing laws and ethical standards governing research in potential partner countries are considered. Perhaps most importantly, CIRM favors partner countries with scientific communities that already are established and productive (Appendix 28 -- PubMed Publications by Country), or are developing, strong scientific ties to the California stem cell research community. This reflects CIRM's operating principle that collaborative funding arrangements should be "driven from the bottom up." To that end, the CIRM leadership meets frequently with the heads of Californian Institutes to discuss desirable collaboration partners. CIRM also frequently co-sponsors workshops for California scientists and their international colleagues to discuss overlapping and synergistic areas of research interest.

In just the first 18 months of this program, our collaborators agreed to fund over $50 million in research and development work to join their scientists with California scientists funded by CIRM. Our partners were prepared to dedicate twice that amount to collaborative teams involving California scientists. In many cases, the funds contributed by our collaborators represent new funding, which but-for the CFP program, might not have been dedicated to stem cell research. Our collaborative partners are involved in RFAs which span CIRM's entire funding pipeline including Basic Biology, Early Translational, Immunology and Disease Teams.

RFA	CSCC	JST	MRC	Victoria	Total
Early Translation				$3,868,934	$3,868,934
Disease Teams	$36,414,513		$8,394,738		$44,809,251
Basic Biology		$900,000			$900,000
Immunology				$1,094,454	$1,094,454
	$36,414,513	$900,000	$8,394,738	$4,963,388	$50,672,639

Table 4. Collaborative Funding Partner RFA participation.

The fundamental structure of all CFP relationships is the same. Funded projects are evaluated and monitored as a single, integrated effort. Collaborative proposed projects are neither favored nor given any special consideration in the grant review process. They must compete at the Grants Working Group level on the scientific merits just like every other application. For selected projects, CIRM agrees to fund the work done in California while our partners agree to fund the work done in their jurisdictions. Once projects are funded, CIRM and its collaborator together monitor technical progress across the full scope of the subject research. Periodic performance reports are submitted to both funders on a fully integrated basis. This entire structure is documented in a binding Funding Agreement, which CIRM enters with each funding partner (Appendix 27 – Sample CFP Funding Agreement).

Managing the Portfolio

As of August 1, CIRM has 308 awards under management. Although the agency manages each type of award with specific criteria, outcome is the common focus for all awards. Our Grants Administration Policy and IP policy uniformly dictate at least annual progress reporting, publication and invention disclosure, and reporting of any licensing activity. The annual grantee meeting also provides valuable input on progress, as do other smaller meetings, workshops and conferences.

An important aspect of CIRM's management is the initial and subsequent ongoing relationship between the agency's program officers and the grantees. This provides an opportunity to establish a positive, collaborative relationship, clarify some of our rules and highlight our expectations.

Given the urgency of our mission and our focus on outcomes, CIRM places considerable emphasis on progress reporting both in the information requested and its internal review. The degree of oversight ties to the RFA type. Fundamental research programs have an annual reporting schedule. Science officers focus on progress against aims, with recognition that, particularly in basic research, aims may evolve as the science evolves. CIRM has a prior approval process in place when work deviates significantly from that approved by the Board. For the larger translational research programs (Early Translational and Disease Team Awards) CIRM monitors progress more frequently and is more actively involved in the management of these projects, particularly in assuring complete and appropriate milestones and timelines. For these awards, progress reporting may be biannually (Early Translational) or quarterly (Disease Teams), and projects are subject to evaluation by an Oversight Advisory Committee made up of outside experts.

THE BUSINESS SIDE OF GRANT MANAGEMENT — With expertise in the financial and compliance aspects of grants administration, the Grants Management Office staff ensure that grants and loans are awarded, administered and terminated in accordance with the agency's established policies and procedures. Once an application is approved for funding by the Board, the Grants Management Office initiates an administrative review to ensure that all funding criteria are met and notes special terms or conditions to include in the Notice of Grant Award (NGA), or Notice of Loan Award. The NGA is the agreement between CIRM and the Grantee (both Institution and Principal Investigator)

containing all terms and conditions of the award (Appendix 29-- Activities of the Grants Management Office Per Grant).

During the active grant period, Grants Management ensures that all required reports are submitted by the Grantee and reviewed internally, and closely tracks the status of each grant on a real time basis. They engage in an on-going dialogue with the grants administrators at the institutions to ensure expectations are set and met.

Clear business processes and a robust software system are essential for these processes. CIRM developed business processes with the advice of a former NIH Senior Grant Administrator, the expertise of the experienced staff in the Grants Management Office, university facilities management experts, and accounting and financial consultants. The agency spent two years reviewing the available options for an off-the-shelf grants administration software with enough flexibility to support CIRM's still-evolving, unique business requirements. The Grants Management Office developed business processes and interim tracking and reporting systems in parallel with this software search. This approach has allowed CIRM to confidently opt to develop custom software to manage the hundreds of complex grants that are actively being tracked at any one time and will ease the transition from the interim reporting tools to the custom software, which is partially built at this time.

MEDICAL AND ETHICAL STANDARDS AND COMPLIANCE — CIRM's medical and ethical standards regulations incorporate the Common Rule and California state regulations to ensure uniformity with established research protections. CIRM imposes some additional review, oversight and donor protections not required by other agencies. The agency requires voluntary and informed consent for all biological specimens without the exemption for medical waste that is in the federal guidelines. It mandates review for all research involving human oocytes or embryos; a stem cell oversight committee must determine use of embryos or oocytes has scientific justification. Also, CIRM put in place some special protections for oocyte donors.

CIRM Standards Working Group has met two to three times a year since adoption of the standards to review the field and verify that the standards still mesh with current scientific practice. The group has proposed minor modification to the standards four times and those amendments have been adopted by the Board. The standards evaluation process is described in a white paper, entitled Advancing Effective Research Oversight: CIRM's Evaluation Initiatives, which can be found at http://www.cirm.ca.gov/sites/default/files/PDFs/Standards/CIRM_Evaul_Initiative_white_paper.pdf). In addition, three reports generated by the process may be found on the Standards home page: http://www.cirm.ca.gov/WorkingGroup_Standards.

The following are two examples of the changes that have been made:

• Consistent with the National Academy of Sciences, the Standards Working Group had recommended that all gamete donors provide consent for the donation of embryos for stem cell derivation, but the group came to realize that prior to the NAS and CIRM guidelines some embryos were created without these consents and that retrospective application of this consent standard was inappropriate, so the SWG created an exemption for cell lines created from such embryos.

• The original regulation restricted the use of cells and tissue for which any donor was paid. This restriction resulted in embryos created for reproduction with gametes from paid donors being disqualified. This created inconsistency with the NAS guidelines and the 2009 NIH guidelines, so the SWG revised the restriction to allow embryos created for reproduction, but no longer required for family planning, to be donated for CIRM-funded research.

The agency, through its board, weighed in on another more recent cell line issue. In 2010, uncertainty emerged regarding the status of stem cell lines previously approved by NIH (the "Bush" lines). Many lines were not in the NIH Human Embryonic Stem Cell Registry and there was concern among researchers that experiments involving previously approved lines could not continue. To alleviate uncertainty and allow further development of foundational research CIRM issued a policy statement that all previously approved lines may be used in CIRM-sponsored research.

The CIRM "Compliance Program" is designed to evaluate and support grantee compliance with the institute's regulations and contracts. The program includes site visits to grantee institutions. During site visits CIRM staff perform a regulatory review to evaluate compliance with CIRM Medical and Ethical Standards Regulations and Grants Administration Policy.

More specifically, CIRM staff reviews the activity of the institution's Stem Cell Research Oversight (SCRO) committee for particular applications to see if they are consistent with regulatory requirements. During this process CIRM provided recommendations to two institutions regarding the need for more explicit procedures and policies to govern their SCRO operations. The agency has also worked with two institutions to ensure compliance with AALAC (animal care accreditation) requirements. Compliance review also identified one patent that had not been reported to CIRM and that has been addressed.

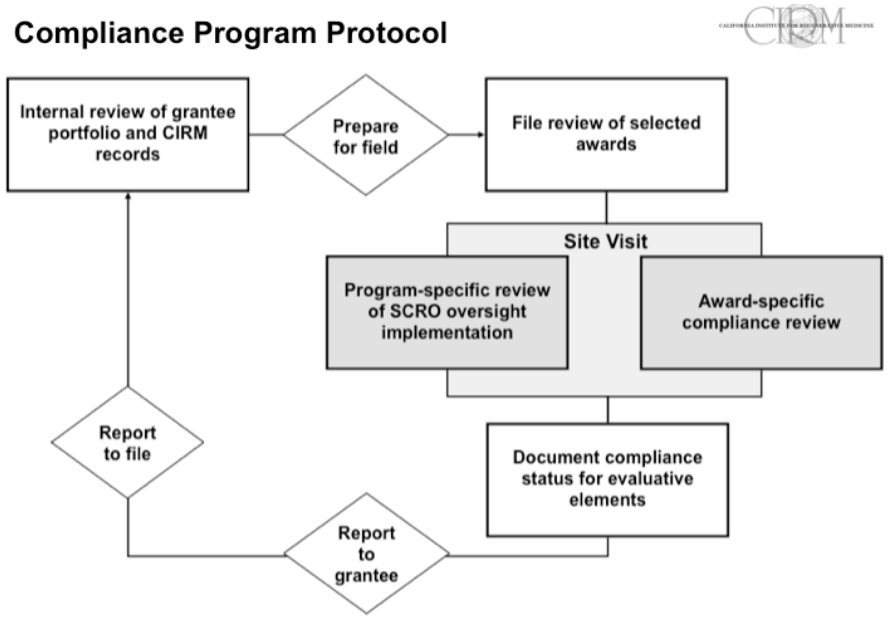


Figure 13. CIRM's protocol for performing regulatory compliance review of specific grant awards.

Operations and Administration

CIRM's funding stream is unique. It does not come from state tax revenues but instead is generated by the sale of general obligation state bonds. CIRM is continuously appropriated for its full $3 billion authorization. This has insulated CIRM from most of the financial woes that have plagued California for the past few years. During this period, the State has continued to sell bonds and has raised $1.03 billion for CIRM. CIRM uses these funds to finance all of the agency's programs including its internal operations. Management of bond sales is coordinated through the Office of the Chair. Since the State Treasurer often wants verifications on how the money is used, it frequently requires input from members of CIRM's operations and science staff.

CIRM faces challenges as it strives to meet its mission because it will always be restricted to a small staff and a limited operating budget. Proposition 71 caps CIRM's overhead expenditures over the lifetime of its current funding authority to 6 percent of $3 billion, excluding legal costs, or a total of $180 million. Compared to industry norms, this is a very low rate for administration and management and it means that CIRM must be strategic and judicious in planning its operations. As comparisons the American Cancer Society spends 6.9 percent on administration plus an added 20.2 percent for fundraising and the Muscular Dystrophy Association spends 7.5 percent on administration plus an added 14.1 percent on fundraising.

When CIRM awarded its first grants in FY 2005-6 it had 22 employees who had created the framework for CIRM's research strategy. Since then the funding programs have grown enormously as indicated in the table below. During this same period the size of the staff and CIRM's operating budget have increased slowly. The agency currently has 44 fulltime employees, compared to its legal maximum of 50 employees. However, even if that cap is removed through legislation currently pending in the state capital we do not envision CIRM's staff surpassing 60 due to the 6 percent limitation on operational expenditures. If it did the funds for operations could easily be expended before the granting programs are complete. This is discussed in more detail later in this briefing.

Because of the limitations on staff numbers and the magnitude of its mission, CIRM has focused its hiring on highly trained individuals. About half of the fulltime employees have MD or PhD degrees and several have MS or MA degrees. Another 10-15% have postgraduate professional degrees (law, business).

Employees are grouped into four administrative units, the largest being the Science Office which manages the granting programs from inception (developing the RFAs) through close-out, including the review process and all monitoring (annual progress reports, milestone evaluations, and all financial and regulatory compliance). The Office of Administration includes communications, finance, human resources and management of the office space, while the Office of the President oversees all activities and includes the legal team. (Appendix 1 -- Organizational Chart)

The fourth administrative unit is the Office of the Chair, which is lead by the ICOC Chair and includes the Vice-Chairs and the staff that manages Board activities and the Chair's other responsibilities (Appendix 30-- Duties of the Board, the Chair and the President as set out in Prop 71). Materials related to Board governance and the details of the bond financing will come under separate cover from this office. Many of CIRM's processes

and procedures are impacted by language in Proposition 71 and these will be discussed in that document.

FISCAL YEAR	GRANT PAYMENTS (Cumulative)	VALUE OF PROGRAMS UNDER MANAGEMENT	NUMBER OF ACTIVE AWARDS	NUMBER OF STAFF POSITIONS	OPERATING BUDGET*
2005/06	12,112,251	38,912,252	16	22	766,062 **
2006/07	12,112,251	209,942,953	134	26	5,889,137
2007/08	270,608,516	562,337,381	207	31	6,887,283
2008/09	385,156,804	783,018,780	276	37	8,814,230
2009/10	521,157,118	1,013,642,440	303	44	10,269,761

* Excluding direct legal costs
** Excluding $3.9 million from charitable donations used to support operations in FY 05/06

Table 5. Between 2006 and today, CIRM programs have grown dramatically. The total value of the programs under management* has increased 26 fold and the number of active grants has increased 19 times (Figure 14). [*Programs under management is the total value of all programs active as of June 30, 2010. It is equal to the cumulative value of all program commitments minus the value of those programs that have terminated – Training 1, Disease Team Planning and some SEED]

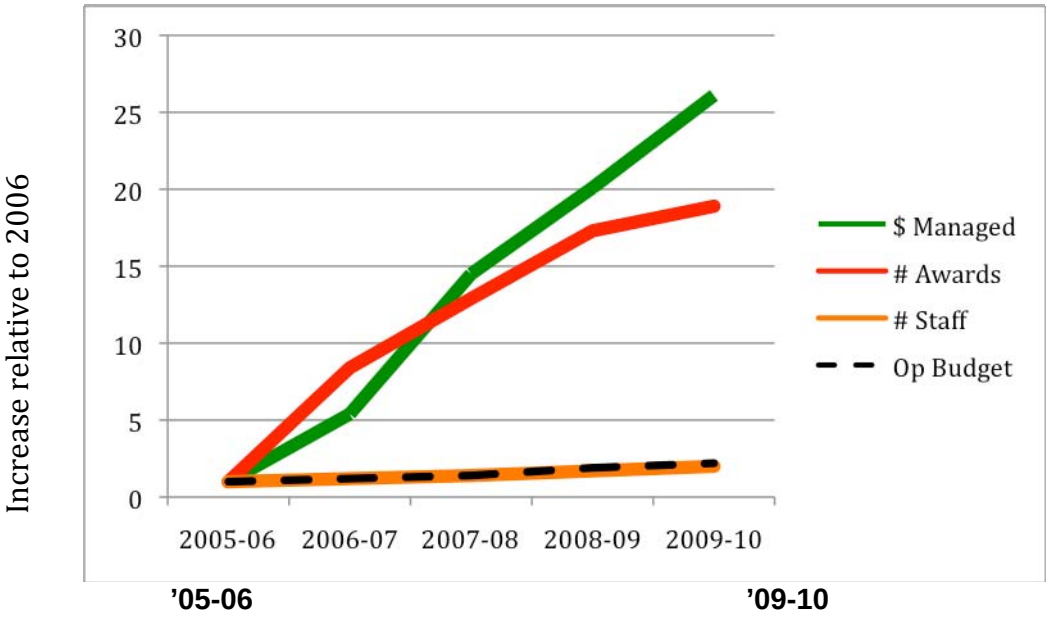


Figure 14. During this same period CIRM's operating budget (black/dashed) and staff size (orange) have increased about 2X. Dark green line is dollar value of programs under management and the red line is active grants. . For this graph the total operating budget figure used for FY 05/06 was $4.7 million, including funds from charitable donations.

The Office of Administration, led by the Vice President, Operations, is responsible for the internal operations of the Institute, including development and oversight of the annual budget, an annual financial audit, approving contracts (in conjunction with the legal team) tracking all expenditures, creation of a staffing plan that proactively addresses staffing needs and the retention of top employees, updating and maintaining the Institute's web site, developing and delivering a communications plan, overseeing the use of office space and providing the IT support required for the Institute to operate efficiently and steward its grant portfolio.

This team has also taken responsibility for tracking and forecasting the expenditure of CIRM's authorized $3 billion for the purposes of predicting the Institute's longevity and for developing research funding strategies that will enable the Institute to meet its goals (page 21). It is assessing the economic impact of CIRM's research investments through commissioned studies and is working with members of the legal and grants management teams to ensure that CIRM's Major Facilities meet their promise to serve as major engines for stem cell research in California.

Since 2005 CIRM has undergone several audits. Financial audits are performed annually (since 2005) and a committee chaired by the State Controller reviews the results. No significant deficiencies have been reported. In 2007 the Bureau of State Audits conducted an audit of CIRM's performance. That audit generated 12 recommendations, all of which have been satisfied (Appendix 11 – BSA Audit and Appendix 12 - CIRM Response to Audit). Finally, in 2008 the Controller's Office audited CIRM's compliance with Proposition 71 relative to conflict-of-interest, grant administration, administrative expenses and expenditures. No serious deficiencies were identified (Appendix 31 – Office of State Controller Audit).

OUTREACH — CIRM has established extensive programs to explain its mission and science product to various constituents, from the general public and legislators to other groups in the stem cell research community and regulatory bodies.

While the agency has used traditional media relations to generate more than 1,500 articles in the past two and half years, including many front-page articles in major papers, it relies most heavily on digital media to reach the public with explanations of its work. CIRM's communications team has created a robust web site with broad content at a lay level including very detailed pages on 18 diseases, which patient advocates have found useful. They have also created 29 videos explaining CIRM funding of stem cell research that that have been viewed more then 66,000 times in the past year.
http://www.youtube.com/cirmtv
CIRM's page on Flickr has 59 images of stem cells that have been viewed more than 91,000 times in the past year.
http://www.flickr.com/photos/cirm
The agency's web site gets more than 11,000 unique visitors a month. (Highlights of news coverage and the digital media are in Appendix 39.)
http://www.cirm.ca.gov/

In addition, CIRM arranges for its grantees to speak directly to public audiences through a series of town meetings in major markets in the state each spring. It also organizes Stem Cell Awareness Day, an effort that reaches across state and national boundaries to create more opportunities for stem cell researchers to reach out to the public. The

principal activity in California last year was to place CIRM grantees into high school classrooms for the day to give guest lectures. Grantees who had been given a slide deck that had been tested at the high school level reached more than 5,000 students last September.
http://www.stemcellday.com/SCAD_Links.html
Stem Cell Awareness Day this year is October 6 and a number of CIRM's collaborative funding partners are planning various levels of participation.

CIRM's communications office has also teamed up with a group of researchers and educators at UC Berkeley to develop four high school curriculum modules that are available for any teacher to use on the agency web site.
http://www.cirm.ca.gov/Stem_Cell_Education_Portal
The modules are linked to specific sections of the California science curriculum guidelines so that teachers can easily fit stem cells into the mandatory curriculum. Each module can be taught in a day or a week depending on how many of the related activities teachers choose to use. Staff just completed an evaluation of the modules with a team of outside experts and is making modifications prior to a marketing roll out to teachers that will begin at the California Science Teachers Association annual meeting October 22-23.

PARTNERING IN THE STEM CELL COMMUNITY — CIRM has strong relationships with many other groups in the stem cell research community. The President was a founding board member of the International Society for Stem Cell Research (ISSCR) and the agency co-hosted the ISSCR annual meeting in San Francisco in June of this year. CIRM's Chief Communications Officer serves on ISSCR's education committee. The agency was a founding member of the Interstate Alliance on Stem Cell Research, which was founded in 2007 and provides a forum for information exchange and collaborative planning. CIRM's Senior Officer for Medial and Ethical Standards co-chairs the Alliance. CIRM also joined the Alliance for Regenerative Medicine (ARM) at its inaugural meeting in September 2009 and became a founding member. This group has a strong focus on lobbying from the perspective of promulgating regulations and garnering funding needed to move regenerative therapies through the translational space to the clinic, and to gain reimbursement for proven therapies. The President is co-chair of the Science and Technology Committee and serves on the Board with the General Counsel as alternate.

On the federal level, CIRM's collaborations began in 2005 when it partnered with the National Academies of Science to hold a workshop on ethical issues around stem cell research. CIRM leadership has had several meetings with the leaders of the National Institutes of Health and helped to orchestrate constructive responses to NIH's proposed regulations to allow broader use of existing human embryonic cell lines following President Obama's decision March 9, 2009 to allow federal funding of this work. The agency has had extensive interactions with the Food and Drug Administration (FDA) and has interfaced with the European Medicines Agency (EMA).

The primary objectives of our FDA and EMA initiatives are to take a leadership role in creating more certainty to the regulatory approval process for stem cell therapies and to educate our grantees as to what the regulatory requirements are. It is critical for the success of this field that innovative stem cell therapies reach the clinic. Pluripotent therapies, in particular, have faced significant hurdles in this regard, and have found

themselves placed on clinical hold by the FDA. Without a clear regulatory pathway, inefficiencies result and the ability to attract private investment becomes more difficult.

However, this is a new area with new safety issues and insufficient analytical tools to inform regulatory decision-making. CIRM believes that the regulatory pathway will become more easily traversed if CIRM invests in developments that could better inform regulatory decision making and by creating forums for leading experts in the field to share their approaches with FDA and others for addressing challenges in proving safety and efficacy.

To this end CIRM, through the work of its General Counsel, has founded the Regenerative Medicine Consortium (RMC), which has wide membership from industry and some key academics. The agency has obtained FDA's participation in RMC-sponsored webinars (open to all interested parties) and roundtable discussions of topics of mutual interest, which are attended by members of the RMC and FDA. The first webinar held was well received by the science community and there are plans to continue offering webinars on various topics of interest to the stem cell field. The next webinar is planned for September 28th and it will focus on preclinical models. In addition, CIRM and the RMC have held one roundtable with the FDA and a second meeting will be held October 8th. Likewise the agency has developed a good working relationship with the European Medicines Agency (EMA). CIRM was invited to participate on a panel held by EMA's Committee on Advanced Therapies to discuss its first efforts at formulating a policy on stem cell regulation.

With similar goals in mind, CIRM is considering offering seed funding to jumpstart the creation of a public access journal in translational science as it relates to regenerative medicine. The agency believes the field will be accelerated if it has a high profile journal where such research can be aggregated and where negative data is welcomed and published on a fast track.

INDUSTRY ENGAGEMENT — CIRM has recognized the importance of fostering industry participation in the development of therapeutics. As stated by one CIRM PI, "traditionally, research, drug development and clinical medicine were three separate endeavors. CIRM created a funding mechanism that breaks the barriers to this critical interaction." Eliminating these barriers provides access to industry's extensive experience in regulatory matters, knowledge of drug development in general and potential to offer additional development capital in the future. In addition, by funding California companies involved in stem cell research, CIRM helps support California's economy.

Industry participation in CIRM programs includes:

- **Companies awarded CIRM grants** (serving as PI or Co-PI):
    - ViaCyte
    - Calimmune
    - BioTime
    - VistaGen Therapeutics
    - Gamma Medica-Ideas
    - Vala Sciences
    - Fluidigm
    - iPierian

- **Companies receiving CIRM funding through subcontracts:**
    - Approximate number: 27+ subcontracts with companies in Disease Team I
    - Examples of Companies: Life Technologies (scale-up, differentiation and purification of ESC's to astrocyte precursors), Progenitor Cell Therapy (development and manufacture of neural stem cells)

In addition to the foregoing, we are beginning to see investments by industry and funding institutions in companies that have benefitted from CIRM funding. By way of example,

- ViaCyte reports that "very soon after our announcement about the Tools and Translational grants awarded to us, we were notified that we were selected to be the first and only biotechnology company to be funded by the EU through its 7th Framework Programme. This collaboration will provide slightly over 1 million Euros over the next 5 years."
- iPierian has attributed its ability to attract a recent Series B $28M funding round, in part, to the prospect of obtaining CIRM funding.
- TargeGen - CIRM has funded, in part, research relating to the use of a small molecule inhibitor of the JAK2 pathway which is owned by TargeGen. That research by Dr. Catriona Jamesison, a CIRM grantee, resulted in a high impact publication. TargeGen is currently being acquired by Sanofi-Aventis which is interested in the Jak2 inhibitor.

Going Forward

CIRM is an unusual research funding organization because it is continuously appropriated to invest a finite amount of money ($3 billion) over a limited period of time (minimum of 10 years). It also has a very ambitious mission that promises new stem cell-based therapies that will be available to all Californians within this funding period or soon thereafter.

This is an especially daunting agenda because stem cell science is still a very young field that is changing rapidly. Approaches that show clinical promise today may not be the ones leading the way a few years from now. Therefore, in designing its research programs CIRM must balance the desire to invest heavily today with the need to have adequate funds available in the future to push therapies into the clinic.

As described above, CIRM is committed to a regular, rotating set of core RFAs that will support research from basic science to early phase clinical trials, with the greatest investments made near the clinical end of the pipeline. Basic Biology RFAs are slated to repeat annually with a targeted value of about $45 million. In comparison, Early Translational and Disease Team RFAs will repeat ever 15 and 24 months respectively, but they carry much larger values: $80 million and $240 million (see Table 3, page 15). In addition, other RFAs are planned that deal with more specialized needs, including specific research bottlenecks, training, recruitment of world-class researchers and support of facilities. Based on these expectations and other assumptions explained in

Appendix 32 management expects that the Board would approve its last RFA in mid-2016 and would expend the full $3 billion by the end of FY 2020-21, as shown in Figure 15.

This raises issues related to the strategy of CIRM's spending. Stem cell research is a relatively young discipline that it is progressing at an extraordinarily fast pace. Should CIRM speed up its rate of investment in order to maximize the pace of the science or should it reserve more funds for later in its lifespan so that it is in a position to take advantage of advances that have not yet been realized? This issue, which is discussed more thoroughly in Appendix 32, is one that has no uniformity of opinion among the Board. Because this is such an important, fundamental issue, we request that the review committee make it a significant focus of its discussions and recommendations.

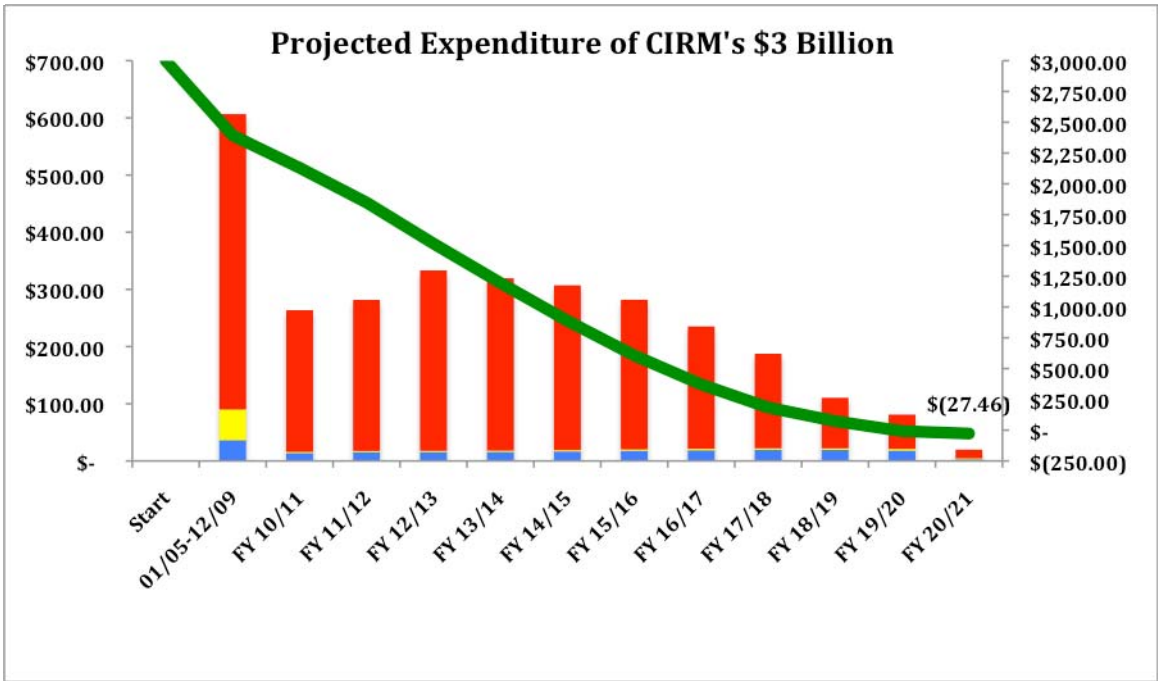


Figure 15. Expenditure of CIRM's $3 billion based on current rate of scheduled awards. The columns in this graph show the annual expenditures for research and facilities (red), operations (blue) and other expenses (yellow – capitalized interest, bond issuance) based on an RFA schedule listed in Appendix 32. The first column on the left (Jan 05-Dec 09) is based on actual expenditures and the others are projections. For each column the values are indicated by the numbers along the vertical axis on the left (in $millions). The green line indicates the total amount of CIRM's $3 billion authorization remaining to be expended with the amounts indicated along the vertical axis on the right (in $millions). Thus the line begins at $3 billion (upper left) and declines to zero in FY 20/21 (lower right).

OUR LOAN PROGRAM — Going forward, CIRM's program to fund industry research via loans should become an increasingly important part of the agency's portfolio, but whether this materializes remains to be seen. Unlike revenue generated under CIRM's intellectual property provisions, the revenue generated from the loan program, by the terms of Proposition 71, is re-circulated back to CIRM directly and is not remitted to

California's General Fund. Thus the loan program could play an important role in continued funding of CIRM's overall mission.

CIRM's loan program is in its first year of implementation. Earlier this year, the Disease Team RFA served as a useful pilot. It was in this RFA that loans were first offered. In advance of the Board meeting scheduled for review and approval of these awards, the Board held a Loan Task Force public meeting seeking input. Representatives from venture capital funds and industry were invited to speak and attend. During the public meeting, both supportive comments and constructive criticisms were received. For instance, a representative from Burrill & Company stated that "From our point of view, on balance, the program is fantastic and the terms associated with it for companies pursuing both nonrecourse and recourse loans are on balance pretty fair." Areas identified as problematic included: acceleration provisions, warrant coverage requirements, the potential for repayment prior to commercialization of the product, the inability to bifurcate the form of award such that in joint academic and industry teams the academic would receive a grant and the commercial entity a loan, the interest rate charged, and objections to having to comply with certain CIRM IP requirements which are perceived as increasing the cost of capital.

In response to this input, the Board approved a set of amendments that are in the process of being codified. These amendments addressed a number of the concerns voiced at the hearing and submitted in correspondence. The proposed amendments include: a significantly altered acceleration provision which eliminates the potential for acceleration to occur upon certain events that do not provide for a cash infusion, a change of the interest rate to LIBOR +2%, a provision allowing the loan recipient to unilaterally extend the term of a loan up to 10 years, and a revised schedule for warrant coverage. To permit continued flexibility to maximize the effectiveness of the loan terms, the new set of amendments provides that the forgoing terms are guidelines in nature and become operative only in the event that the Board at the request of the President does not change the terms as part of an RFA. An outline of the new proposed terms is attached as Appendix 33.

Two rounds of funding suggest CIRM loans may not yet be optimized to attract industry, but the numbers are small and we do not know the rationale behind industry's choices. Most recently CIRM posted its Early Translation II award that permitted applicants seeking funding in an amount greater than $3 million to choose between a loan or grant. Of the 45 applicants that were invited to submit a full application 5 were for profit entities and one requested a loan. Under the Disease Team I RFA, when a PI was from a for-profit entity and the Co-PI was from an academic institution, then the only funding mechanism available was a loan which covered all of the work under the RFA. We saw that designations between PI and co-PI switched between the pre-application and full application stage in one instance. The switch involved changing the commercial entity to co-PI in a joint academic-industry team. Whether this was done strictly to avail themselves of a grant over a loan is uncertain. It does suggest, however, that efforts need to be undertaken to identify and correct any barriers that may impede the success of the loan program.

OTHER APPROACHES TO ATTRACT ADDITIONAL FUNDING —While CIRM's funding of $3 billion is a sizeable investment, when one considers the cost of developing a drug it is clear that significantly more funding will be required to bring many of these new therapies to patients. For this reason, venture capital companies, the

pharmaceutical industry and large biotechnology companies are critical for financial support of the stem cell industry. In addition, continued engagement of national and international funding agencies and foundations in collaborative funding of RFAs will serve to leverage CIRM's investments.

Engaging industry in efforts to leverage CIRM funds has many advantages. It creates a potential source of follow on financing through either an equity investment by the biotechnology or pharmaceutical company or through a licensing arrangement where industry funds the phase III clinical trial. In addition to the financial benefits, industry's direct participation in academic–industry research collaborations brings critical expertise to these projects. Biotech and pharmaceutical company participation on such teams, as we have seen recently with our Disease Teams, will ensure that the research progresses in such a way as to maximize its ability to reach the clinic cost effectively.

CIRM staff is considering various approaches to engage industry and venture capital. One such approach is to host a conference in which PI's showcase their work to various representatives from industry and venture capital companies. To date, CIRM has been apprised of approximately 75 CIRM funded inventions, although the data have yet to be fully collected and tabulated. A conference presenting these works could help foster licensing and investment in these new areas. Other activities by CIRM can include acting as a clearing house that provides information on CIRM funded inventions, and on development candidates that are being investigated with CIRM funding.

In addition to these more traditional funding approaches, another approach to engage industry is through its participation in co-funding of RFA's. Just recently MaRS Innovation announced that it had entered into a co-funding agreement with Johnson and Johnson's Corporate Office of Science and Technology. MaRS Innovation is a non-profit organization funded, in part, through the government of Canada's Networks of Centers of Excellence with the mission of commercializing the discoveries and intellectual property of 14 research universities and health centers in Toronto. In a press release the Vice President for MaRS Innovation stated: "This co-managed fund represents a unique public-private partnership that is strategic for MI as it provides a complementary mechanism to address the commercialization gap…" While Proposition 71 would have certain constraints on the structure of an industry supported RFA, and perhaps some perception issues could arise, it may be possible to structure an arrangement in such a manner that would be acceptable to both CIRM and an industry partner.

As discussed above, CIRM's Collaborative Funding Partner program has been very productive with total approved funding of $50M to date from funding organizations outside of the United States. Continuing these relationships will be very advantageous. It is possible that as a result of the difficult economic climate we expect that in the short term we may not see aggressive investment by the international community at the rate that we did at the start of our program. Nonetheless, other countries and entities outside of the U.S. and nationally have expressed new interest and funding from these sources may serve to replace any from our earlier participants.

NEXT STEPS IN INTELLECTUAL PROPERTY — At present, CIRM does not fund patent costs as part of its grants. The decision to patent remains with the institution and in these difficult economic times, pressure to reduce costs may result in some institutions not filing important patents. We have confirmed that technology transfer offices at California institutions often do not file internationally for patents. Also,

anecdotally, some scientists have voiced concern that their universities have completely foregone patents on their inventions. While not all inventions warrant the expense of patenting, some valuable patenting opportunities may be lost in the current climate. This could endanger the ability of projects to attract follow-on financing, which depends on the strength of the underlying patent rights.

CIRM has contacted a number of funding institutions to determine their practices around patent costs. A number of foundations do in fact provide patent funding, including the Welcome Trust, the Canadian Stem Cell Network and the Myelin Repair Foundation. In addition, these organizations dedicate resources to support out-licensing and other commercialization support services, including assistance in contract negotiations.

Now that CIRM has shifted its focus from funding the physical and intellectual infrastructure needed to support stem cell research to the translation of this research to the clinic the agency must develop policies and staffing to support translation. Critical to this endeavor is evaluating whether and to what extent to support the funding of patent costs.

One approach would be to model a program similar to the Myelin Repair Foundation, which has full control of the patenting process or the Wellcome Trust's Strategic Translation Awards program where the Wellcome Trust pays for patent costs and takes the lead on licensing and commercialization programs. Under this approach, CIRM would need to hire qualified staff and use a panel of outside experts to provide counsel on the commercial viability of CIRM funded inventions.

Another approach that provides for moderate control and is less hands-on would entail CIRM providing patent funding in addition to the grant award for inventions warranting such investment, based on input from an external advisory committee, and let the individual institutions manage the patenting process. Rather than have control over out-licensing activities, CIRM would simply facilitate such partnerships through a clearing house or repository identifying funded inventions, hosting annual workshops where venture capitalists and industry are invited to hear summaries of grantee projects.

Finally, CIRM can simply permit grantees to dedicate a certain percent of awarded funds for patent costs, placing the full decision on patenting on the funded institution.

It would be helpful if the review committee provided its perspective on the optimal approach for engaging in commercialization support – including patent funding, out-licensing support services, and joint funding of RFAs (as discussed in the previous section). During informal discussions with California's academic institutions, there was naturally keen interest in CIRM funding of patent costs, even if that meant that there would be some repayment obligations arising from successful out-licensing or commercialization. However, the process or impact of CIRM's evaluation process for determining which inventions to fund was not considered. The merits of the moderate control approach discussed above are certainly recognized. However, in addition to the funding support, such a program would require resources to oversee and manage the program. At a minimum there appears to be strong external support for CIRM to act as a clearinghouse for available IP and to host periodic meetings with potential funders.

OUR SCIENCE PROGRAM — Stem cell science and CIRM are maturing in parallel. Much of the agency's current scientific direction is reflected in the adjustments to the

2006 Scientific Strategic Plan contained in the 2009 Update. A summary of those revisions are in Appendix 4. Most notably, we have placed a greater emphasis on moving toward the clinic, with a higher percent of our portfolio in the translational segments of the pipeline. We have also consolidated some of the RFAs envisioned in 2006 into a few core grants and tried to build enough flexibility into those core grants to be responsive to unexpected discoveries in the field.

With direction from its Board in December 2009, CIRM has renewed its emphasis on pluripotent-derived products, and issued the Targeted Clinical Development RFA in that category in August. Through this RFA, CIRM will foster those innovators who are willing to lead the field in conducting clinical development of these highly innovative novel cell therapies derived from pluripotent stem cells that may offer unique benefit with well-considered risk to persons with disease or injury. The agency is continuing to build its development portfolio with recurring programs in Early Translation and Disease Teams. As additional rounds of these applied RFAs come forward for review, it may be prudent to take into account the existing development portfolio so that CIRM is not simply investing in projects with very similar approaches for the same or closely related disease. To date, management has not been enabled by the Board to adjust the CIRM portfolio in this way.

To support CIRM's projects in their path toward human trials, the agency is stepping up its activities with the Regenerative Medicine Consortium, the Alliance for Regenerative Medicine and the International Society for Cell Therapy to reduce regulatory uncertainty for cell-based therapies. It is also looking into the possibility of providing access to GMP-derived cell lines to jump start clinical projects.

There have been suggestions from industry for CIRM to issue an industry-only RFA as an alternative to the current routine of RFAs that encourage academic-industry partnerships but are open to applicants from either sector. What is necessary to get fast and efficient hand-off of potential products to industry? There is a strong possibility that many cell therapies will be made available to patients through a model similar to the Bone Marrow Transplant Unit or IVF Clinic that have remained hospital-based with industry involvement only in providing specific reagents and tools needed for cell production and manipulation procedures? (See "Alpha Clinic Model" in Appendix 35)

As part of CIRM's commercialization support initiative the agency has and will continue to engage in a number of activities that will facilitate and foster the formation of academic – industry partnerships, enhance the attractiveness of CIRM Funded Therapies, by for example seeking to negotiate caps on royalties owed on underlying technology of the CIRM Funded Invention (see *CellStemCell* article in Appendix 34). In addition there is strong interest in serving as a clearinghouse for available IP and to host periodic meetings with potential funders.

CORE PROGRAMS AND NEW INITIATIVES — In addition to the translational repeating RFAs, CIRM has continued its recurring funding rounds for basic science and for new technologies. With stem cell science evolving so rapidly, this foundational research is key to staying at the cutting edge of what will lead to tomorrow's pre-clinical tools. For example, the discovery of iPS cells in 2007 led to funding of an iPS-based Disease Team grant just two years later. Discoveries in direct reprogramming this year in animal models will likely lead to new avenues to potential human work in the near future.

While it maintains the core programs, CIRM staff is considering a number of other initiatives. Programs in early stages of consideration include:

• a fibroblast/iPSC bank that samples the population heterogeneity of the major human diseases of interest to CIRM as a resource for basic research. Thousands of iPSCs made by exactly the same method could be used to explore the basis of complex diseases, development of "disease in a dish" technology and for high throughput screening for the identification of new therapeutic candidate molecules and biologics. CIRM needs to decide the best way to foster such a resource and whether it should be in partnership with another agency. CIRM has held one workshop on ethical issues involved in patient sampling and banking, and the whitepaper from that workshop can be found at http://www.cirm.ca.gov/files/PDFs/Standards/SWG_5_2010_Workshop_Report_7_31_10.pdf. A second workshop involving multiple agencies on the issues of clinical sample procurement, method of derivation of iPS cell lines and banking/access issues is scheduled for November 2010.

• the application of sequencing technologies to pluripotent stem cells and their differentiated progenitors. These studies would take advantage of major genome/epigenome sequencing capacity in California and apply this to populations of iPSCs derived for different diseases to provide readout of RNA expression, miRNA expression, chromatin states and transposon variants. This can be expanded into the variety of lineages differentiated in iPSCs and ESCs by origin that would include various diseases. This would enable analyses on how genetic variation influences biological networks in cell-based models of disease. This would provide ways into determining how genetic variation is involved in the expression of complex human diseases. This linkage may be achieved by co-location of CIRM funded stem cell labs with major genomic institutes.

• a specific RFA around Somatic Cell Nuclear Transfer (SCNT) to create an international collaborative effort with other states/jurisdictions to develop human SCNT lines. The agency organized a workshop on the topic in June 2010 with the U.K.'s Medical Research Council. A report on that workshop is in the process of being edited and we hope to be able to share it with the review committee by October.

• a project to foster targeted studies in iPSCs and neural transposon activity in differentiation and development, particularly in relation to autism, epilepsy and mental retardation.

• a creativity program for undergraduate and graduate students to encourage multi-disciplinary study and exposure to bring new dimensions into stem cell science and regenerative medicine.

• the development in California of Alpha Stem Cell Clinics (Appendix 35) that would establish tertiary medical centers with dedicated clinical staff, cell biologists, molecular biologists, patient counselors and the necessary GMP and GLP facilities for cell and tissue isolation, cell culture and expression, cell modification and transplantation. The Alpha Clinics would be the hub of initial rollout of cell-based therapies to patients and eventually would include connections to under-resourced areas of the community.

Also, CIRM Shared Labs have proven highly valued both at the institutions that house them as well as by neighboring institutions that utilize them. CIRM is considering renewing the funding for operating these facilities; should it proceed along that route or should it expect host institutions to set up charge-back systems to keep them running.

REFINANCING CIRM — At the current rate of funding CIRM expects to award the last of it original $3 billion in bond funding in 2016. Those last grants are likely to be four-year Disease Team Awards, so the agency would continue to steward those original funds at least through FY 2019-20 and probably into the next fiscal year.

However, many at CIRM and many observing our work believe that the stem cell field may have matured to the point that it may be most attractive for investment around the time CIRM awards the last of its currently authorized bonds. Discussions have begun regarding ways to extend the funding of the agency. As discussed above there may be some interest in partnership arrangements between investors and CIRM. This may necessitate some revisions of CIRM IP policies to enable pooled or some carried interest in IP that is of interest to investors. The current loan program may add a small increment of recycled funds as loans are repaid, but a robust funding stream would most likely require renewed authorization of state general obligation bonds. This could be done via a second ballot initiative triggered by either a signature gathering campaign or by legislation. Both have major political challenges especially in the current economic climate. Over the next three years, as the health of the California economy improves, firm decisions will need to be made on whether CIRM should seek additional funding, and if so, how much, and via what avenue?

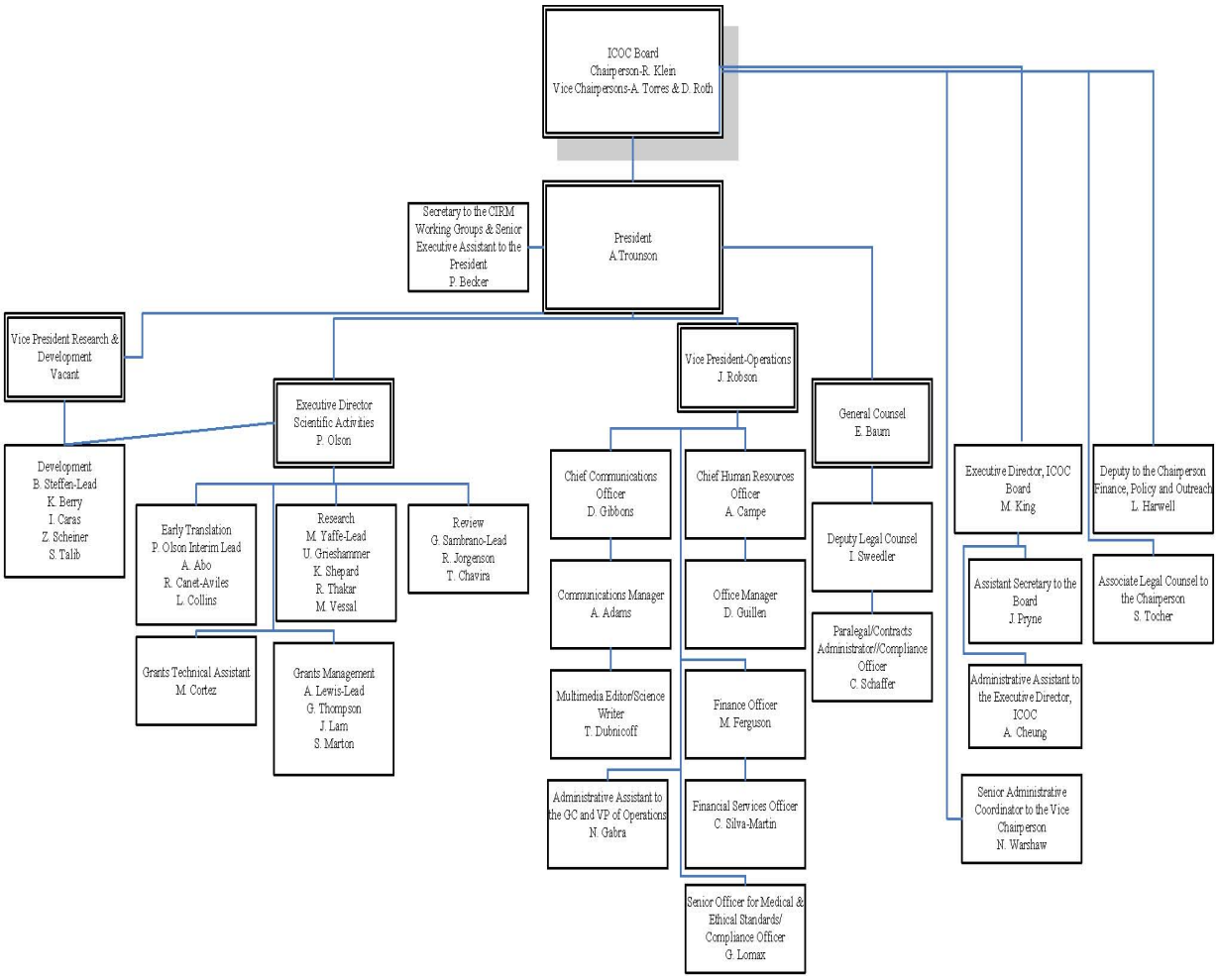
Also, in light of any conclusions the committee draws, the agency would like to know the group's recommendations regarding the best possible timing for any further outside review of its future direction and momentum.

APPENDICES

1. Organizational Chart ►
2. Five-year goals from Strategic Plan and results to date ►
3. Ten-year goals from Strategic Plan and results to date ►
4. 2009 Strat Plan key revisions ►
5. All publications with CIRM funding ►
6. Faculty level recruits to California since 2006 ►
7. Grants Working Group members ►
8. Pre-application (PreAp) process ►
9. Grants Working Group details of review process ►
10. Data from PI grantee survey ►
11. Bureau of State Audits (BSA) report ►
12. CIRM responses to BSA ►
13. Little Hoover Commission executive summary ►
14. Senate Bill 1064 ►
15. Summary of CIRM Intellectual Property (IP) regulations ►
16. New Faculty Award recipients ►
17. Leadership Award CV from Reya ►
18. Major Facilities leverage chart ►
19. Economic analysis of impact of CIRM major facilities grants ►
20. Papers in highest profile journals ►
21. Collaborative Funding Partner sample MOU ►
22. Science Office activity per grant ►
23. Workshops organized by CIRM ►
24. Conferences developed by grantees with CIRM conference grants ►
25. First clinical trial fostered by CIRM funding ►
26. All trainees attached to any CIRM grant ►
27. Collaborative Funding Partner sample funding agreement ►
28. Pub Med data by country over time ►
29. Grants Management Office activity/grant list ►
30. Duties of the Board, the Board Chair and the President ►
31. Office of State Controller audit ►
32. Analysis of duration of CIRM expenditures►
33. Proposed new loan terms ►
34. Cell Stem Cell article ►
35. Alpha Clinic model for therapy roll-out ►
36. Brief staff bios ►
    A. Senior Staff duties and responsibilities ►
37. Staff patents and publications ►
38. Book Chapter on a new paradigm for funding research ►
39. Folder of media highlights and CIRM web information ►

APPENDIX 1

1. Organizational Chart



*Personnel in the Office of the Chair will report to the Chairperson and Vice Chairperson and through them to the President.

9/1/10

[Back to Appendices]

2. Five-year goals from Strategic Plan and results to date

Five-Year Goals (to 2011)

These five-year goals will be milestones to gauge our progress:

Goal I: CIRM grantees will have six therapies based on stem cell research in pre-clinical development.

CIRM defines "preclinical development" or "IND-enabling preclinical development" as the stage of translational research that includes those activities required to enable regulatory approval for the initiation and conduct of a clinical trial with a given therapeutic candidate. Examples of such activities include process scale-up and production under current Good Manufacturing Practices (cGMP), toxicology and other required safety studies and pivotal preclinical pharmacology studies.

Progress: In late October 2009, CIRM invested $225 million dollars and CIRM's Collaborative Funding Partners invested an additional S44.8 million in Disease Team Research Awards I comprising 14 awards to projects in various stages of translation ranging from late discovery research to early preclinical development. The goal for Disease Team I projects is an IND submission within four years. It is from the projects of this program that CIRM anticipates achieving this milestone.

Outcomes:

- **14 Disease Team I Projects**
  - 1 therapeutic candidate in preclinical development
  - Through 2011, an estimated ten Disease Team I projects are expected to reach a Go/No Go decision point for IND enabling preclinical development; **a Go decision for 30% of these would result in achievement of this milestone**.
- A CIRM New Faculty grantee is performing preclinical research and development in the context of an ongoing clinical trial for treating melanoma with genetically modified CD34 cells. Specifically, an improved vector is being developed and will be produced under current Good Manufacturing Practices (cGMP). Following testing in preclinical models, the new vector could be could be incorporated into a parallel clinical study within the next year or two.
- One CIRM-funded publication describes the preclinical studies of small molecular inhibitor currently in Phase I/II clinical trials:
  - Geron, I., et al. "Selective inhibition of JAK2-driven erythroid differentiation of polycythemia vera progenitors." *Cancer Cell*, 13:321, 2008. **PI: C. Jamieson (SEED, UCSD).** Demonstrated that a JAK2 (signaling kinase) inhibitor could block aberrant erythroid differentiation of polycythemia vera progenitors. Study also provided direct in vivo evidence that a particular mutation in JAK2 (JAK2V617F) is necessary and sufficient to drive aberrant myeloid differentiation characteristic of polycythemia vera. This work provided the basis for Phase I clinical trials of the JAK2 inhibitor *TG101348 in polycythemia vera patients*.
- A publication that was co-authored by a CIRM SEED-funded grantee showed that hedgehog signaling was required for maintenance of cancer stem cells in chronic myelogenous leukemia (CML) (Zhao C., et.al., Nature 458:776, 2009). The researcher, now funded under a CIRM New Faculty II Research award, has subsequently reported in her progress report on preclinical studies on leukemic cancer stem cells with a small molecule inhibitor of the hedgehog pathway. Based in part on these studies, Pfizer has initiated Phase I clinical testing of that inhibitor in CML this year.

Goal II: CIRM grantees will have developed new methods for making stem cell lines.

Progress: CIRM has funded numerous projects seeking to develop or optimize methods for generating new stem cell lines. In addition to deriving new human embryonic stem cell lines from blastocysts, CIRM grantees are exploring the use of transcription factors, chemicals, proteins, cell fusion, nuclear transfer, and small RNAs for generating induced pluripotent stem cells (iPSC) or other cell types. Investigators are creating and using new methods for producing stem cell lines with desired properties such as disease- or patient-specific phenotypes, ethnic and genetic diversity, expression of reporter constructs, correction of genetic defects, or production of therapeutic agents. In total, CIRM has funded about 75 projects with the goal of deriving, engineering or refining a human stem cell line for research and/or development purposes. While this goal was specifically targeted with the New Cell Lines Awards, these projects have been captured and supported by nearly all of CIRM's research programs including the SEED, Comprehensive, New Faculty, Tools and Technology, Early Translational, Basic Biology and Disease Team Initiatives.

Outcomes: While most of CIRM's grants addressing this goal have only initiated within the last 1-2 years, a number of projects have led to significant discoveries and insights.

- Data from progress reports indicate that about 20 research grants thus far have generated novel insights and methods, many of which have yet to be published.
- To date, CIRM grantees have produced 21 publications documenting work using small molecules and microRNAs to induce pluripotency and make significant refinements to stem cell line derivations. Examples include the following:
    - Li, W., et al. "Generation of human induced pluripotent stem cells in the absence of exogenous Sox2." *Stem Cells*, October 2009. **PI: S. Ding (New Faculty, Scripps).** This publication reports that a specific inhibitor of GSK-3 can induce the reprogramming of mouse embryonic fibroblasts transduced by only two factors, Oct4 and Klf4. The further addition of an inhibitor of LSD-1 can cause the reprogramming of human primary keratinocytes. This work is a step on the road toward purely chemical methods of reprogramming.
    - Byrne, J. A., et al. "Enhanced generation of induced pluripotent stem cells from a subpopulation of human fibroblasts." *PLoS ONE*, September 2009. **PI: R. Reijo-Pera (New Cell Lines, Stanford).** This paper reports that a cell surface marker, SSEA3, can be used to identify and isolate a subpopulation of fibroblasts with an enhanced propensity to reprogram to iPSCs. This finding provides a relatively simple method for improving the efficiency of reprogramming.
    - Judson, R.L., et al. "Embryonic stem cell-specific microRNAs promote induced pluripotency." *Nature Biotechnology*, April 2009. **PI: R. Blelloch (SEED, UCSF)**. This report demonstrates that introduction of microRNAs specific to embryonic stem cells enhances the production of mouse induced pluripotent stem (iPS) cells. The paper suggests that these microRNAs are downstream effectors of cMyc during reprogramming, however, unlike cMyc, they induce a homogeneous population of iPS cell colonies.

Goal III: CIRM grantees will have successfully created disease-specific stem cell lines for four diseases.

Progress: CIRM has funded over 25 grants with a goal of developing disease- or patient- specific stem cells lines targeting around 20 disorders. While yet to be published, data from progress reports indicates that at least a dozen such lines have been successfully created and are being used to generate novel findings (see below).

Outcomes:

- Disease- or patient-specific stem cell lines (embryonic, induced pluripotent or cancer stem cell) have been created for the following disorders: Rett Syndrome, frontotemporal dementia, Marfan Syndrome, Monosomy X, various trisomies, muscular dystrophy, Alzheimer's Disease, Long QT Syndrome, cancer.
- One publication has resulted from this work thus far:
    - Song H., et al., "Modeling disease in human ESCs using an efficient BAC-based homologous recombination system." *Cell Stem Cell*, January 2010. **PI: Y. Xu (Comprehensive, UCSD).** This paper described a novel method to disrupt specific genes in hESCs and thereby generate models of disease-specific hESC lines. The authors demonstrated proof-of-principle with two genes, ATM and p53, which are mutated in ataxia telangiectasia (AT) and several types of cancer, respectively. Dr. Xu's group has begun to characterize hESC lines lacking ATM and p53, which will be valuable resources in the study of AT and p53-related cancers as well as the development of novel therapies for these diseases.

This strategic goal has been met; lines for more than 4 disorders have been derived.

<u>Goal IV</u>: CIRM grantees will have developed methods for growing stem cells in defined media.

Progress: CIRM has funded 13 grants that are focused on developing methods or identifying molecules or tools that enable stem cells to grow effectively in defined, xeno-free media. In addition, efforts to develop GMP-grade cell lines or therapy candidates amongst CIRM's Development Portfolio projects could lead to insights that could further impact this goal.

Outcomes:

- Data from progress reports indicate that about 15 grants have generated new, unpublished insights in this area. Some of the highlights include:
    - Use of defined, xeno-free conditions for more efficient derivation of patient-specific stem cell lines
    - Use of screening platforms and microfluidic technologies to rapidly identify ligands, chemicals and matrix formulations that promote stem cell expansion and pluripotency or replace non- defined components of culture media
    - Identification of specific molecules or compounds that promote differentiation to specific lineages including neural, cardiac and hematopoietic cell fates
- Thus far, 5 publications addressing this strategic goal have resulted from CIRM funding, including:
    - Swistowski, A., et al. "Xeno-free defined conditions for culture of human embryonic stem cells, neural stem cells and dopaminergic neurons derived from them." *<u>PLoS ONE</u>*, July 2009. **PI: X. Zeng (Shared Labs, Buck Institute).** This paper describes the use of chemically defined, xeno-free media to propagate hESCs, differentiate them into human neural stem cells,

induce dopaminergic neuron precursors and mature these precursors into neurons expressing midbrain and A9 dopaminergic markers (the cells lost in Parkinson's disease). The grantee writes that this "four-step scalable process is readily transferable to a Good Manufacture Practice (GMP) facility for the production of functional dopaminergic neurons from hESCs for potential clinical uses."

- Brafman, D., et al. "Defining long-term maintenance conditions of human embryonic stem cells with arrayed cellular microenvironment technology." *Stem Cells Dev*, March 2009. **PIs: K. Willert (Shared Labs, UCSD), S. Chien (SEED, UCSD).** This publication describes the use of array technology to identify fully defined and optimized conditions for the culture and proliferation of hESCs. The authors screened extracellular matrix proteins and other signaling molecules in order to develop and characterize a defined culture system for the long-term self-renewal of three independent hESC lines.

This strategic goal has been met.

Goal V: CIRM will have enabled establishment of a stem cell bank.

CIRM is considering establishing a bank of iPSC cell lines from patients for research use and is conducting a workshop to further explore this. In addition, CIRM has developed a process for registering human embryonic and other pluripotent stem cell lines derived with CIRM-funding. By March 2010 CIRM had received complete documentation for 12 lines.

These lines and supporting documentation may be found at: http://www.cirm.ca.gov/CIRMCellLines. After March 2010, CIRM grantees reported that they thought it would be most efficient to register hESC lines with NIH (CIRM recognized NIH Registry Lines as acceptable for research) and forgo a second CIRM registration process. Given the general interest in NIH registration, CIRM no longer actively promoted registration of hESC lines. However, as a result of the August 2010 decision by Judge Royce Lambert which resulted in a halt to NIH cell line evaluation and registration, we have begun reminding grantees of the CIRM registration option.

Goal VI: CIRM-funded investigators will have demonstrated methods for inducing immune tolerance in animal models.

Progress: In June of 2010**,** CIRM's Stem Cell Transplantation Immunology Awards were issued to 19 investigators whose efforts are specifically devoted to understanding and overcoming immune rejection of stem cell-derived tissues. In addition to probing the immunogenic properties of stem cells, these investigators are exploring a variety of approaches for inducing tolerance or enabling transplanted tissues to evade host immunity. Several of CIRM's Disease Team Grantees will also address this goal by devising appropriate immunosuppression strategies as part of their preclinical development plan. It is possible that pioneering work by these groups could inform the design of similar approaches in the broader stem cell research community.

Outcomes:

- 19 Grants awarded in the area of Stem Cell Transplantation Immunology: Approaches to be explored include use of tolerogenic dendritic cells; induction of central tolerance; mixed chimerism; regeneration of thymic epithelium; manipulation of regulatory T cells or NK cells; engineering the adaptive immune system; reducing the immunogenicity of stem cells; use of *in utero* methods; various specialized biologic strategies

- In addition to the above, CIRM has previously funded 5 awards that address this strategic goal. Data from early progress reports indicate that CIRM researchers have successfully developed a tool for modulating HLA expression on hESC-derived hematopoietic stem cells. Others have optimized and refined protocols for differentiating pluripotent stem cells into defined populations of T cells and dendritic cells.

Goal VII: CIRM will have increased the workforce of stem cell researchers in California.

As of July 2010, CIRM has funded 560 undergraduate and graduate students, postdoctoral fellows and clinical fellows through its training grants and has jumpstarted the careers of 45 promising investigators through its New Faculty grants. We have also documented that more than 100 faculty-level researchers have moved to California's non-profit institutions from around the world since CIRM began operations. More recently, CIRM has implemented the Research Leadership Awards to enable top California institutions to recruit the most productive and rapidly rising stem cell scientists from out of state. The first round of this program led to the successful recruitment of Dr. Robert Wechsler-Reya, who will be relocating his laboratory from Duke University to the Sanford-Burnham Medical Research Institute in La Jolla, CA. (See appendix # 17).

This strategic goal has been met.

Goal VIII: CIRM grantees will have established tools for toxicity testing based on stem cell research.

Progress: CIRM has funded two projects that explicitly target the development of an assay system for predicting or evaluating toxicity. In addition, a third project seeks to identify agents that are toxic to hESCs, the insights from which could inform our understanding of developmental/reproductive toxins and their mechanisms of action. CIRM funds another 15 projects that are seeking to develop more authentic, mature cardiomyocytes or hepatocytes, the basic tools that are needed for toxicity studies. CIRM will continue to address this goal by targeting additional applications through future Basic Biology, Early Translational and Tools and Technology initiatives.

Outcomes:

- Preliminary, unpublished data from progress reports suggests that thus far, two projects have yielded specific tools (reporter lines, patient-specific stem cell derivatives) that could be useful for predicting or evaluating developmental or cardiotoxicity.
- CIRM grantees have made excellent progress in elucidating the molecular basis of lineage specification towards the cardiac or hepatic fate, including the notable recent publication:
    - Duan, Y., et al., "Differentiation and characterization of metabolically functioning hepatocytes from human embryonic stem cells." *Stem Cells*, February 2010. **PI: M. Zern (Comprehensive, UC Davis).** This paper describes the multi-step differentiation of hESCs into cells with many of the markers and metabolic activities characteristic of primary human liver cells. While these hESC-derived hepatocytes may not be fully equivalent to mature hepatocytes, they represent an important step towards that goal and a potentially valuable tool for toxicity testing.

Goal IX: CIRM will have enabled effective partnerships in stem cell research between scientific teams in non-profit and commercial sectors.

CIRM has funded multiple industry/nonprofit collaborations encompassing a variety of relationships and will continue to do so, particularly as more of its programs enter the translational and clinical landscapes. These partnerships are best illustrated by the Disease Team Awards, in which teams are effectively leveraging the disparate resources and skills that will be necessary to bring such complex and ambitious projects to fruition. Examples include:

- 2 projects with co-principal investigators at industry and non-profit organizations
- 8 projects with academic principal investigators that include CIRM-funded, industry-based subcontracts for critical activities including GMP manufacturing, vector development, preclinical safety studies, sample and data analysis, project management, and access to specific reagents, supplies or technologies

This strategic goal has been met.

Goal X: CIRM will have established national and international collaborations in stem cell research that will allow us to leverage the comparative advantage of California and our collaborators to advance toward therapies.

CIRM has established 10 such partnerships and is actively pursuing additional agreements. From these programs, a total of 11 collaborative projects have emerged.

- **Funding Agreements**

  State of Victoria, Australia
  Canadian Cancer Stem Cell Consortium (CSCC)
  Medical Research Council, UK (MRC)
  Juvenile Diabetes Research Foundation (JDRF)
  Japanese Science and Technology Agency (JST)
  Spanish Ministry of Science and Innovation (SMSI)
  Federal Ministry of Education and Research, Germany (BMBF)
  Maryland Technology Development Corporation, Maryland, US
  Chinese Ministry of Science and Technology
  New York Stem Cell Foundation

- **Awarded Projects (as of August, 2010)**
  4 Disease Team Awards (with MRC, CSCC)
  1 Basic Biology Award (with JST)
  2 Transplantation Immunology Awards (with State of Victoria)
  4 Early Translational Awards (with State of Victoria)

This goal has been met.

[Back to Appendices]

APPENDIX 3

3. Ten-year goals from Strategic Plan and results to date

Ten-Year Goals (to 2017)

CIRM commited to the following ten-year goals:

Goal I: CIRM grantees will have clinical proof-of-principle that transplanted cells derived from pluripotent cells can be used to restore function for at least one disease.

CIRM issued a Targeted Clinical Development RFA in August 2010. This award will support up to two programs where a key objective is to provide preliminary evidence of clinical efficacy for a cell therapy derived from human pluripotent stem cells that could lead to more definitive efficacy studies. In addition, the Early Translational and Disease Team Research Awards will continue to build CIRM's pipeline of potential pluripotent-derived cell therapies.

Goal II: CIRM-sponsored research will have generated therapies based on stem cell research in Phase I or Phase II clinical trials for 2-4 additional diseases.

Progress: As described previously, CIRM has funded a "Development Portfolio" of 22 potential therapeutic candidates, a number that may double in 2010-2011 with funding of the Early Translational II and Disease Team II Awards. See Five Year Goal, 1.

Outcomes: CIRM has, in part, sponsored research leading to a Phase I/II clinical trial for a small molecule inhibitor of the JAK2 pathway for treating polycythemia vera and a Phase I clinical trial for a small molecule inhibitor of the hedgehog pathway for treating CML. If only a few additional IND applications emerge from the 20+ potential therapeutics in CIRM's current pipeline, this goal will be achieved.

Goal III: CIRM funded projects will have achieved sufficient success to attract private capital for funding further clinical development of stem cell therapies.

CIRM funded research is only just starting to move toward the clinic, yet accomplishment of this goal appears to be on target considering the long timeline. Companies, such as iPierian Inc., have attributed their ability to attract funding, in part, because of the prospect of obtaining CIRM funding. Also, CIRM has funded, in part, research relating to the use of a small molecule inhibitor of the JAK2 pathway (owned by TargeGen) which resulted in a high impact publication prompting further research in this area. Now TargeGen is in the midst of being purchased by Sanofi-Aventis which is interested in the Jak2 inhibitor.

Goal IV: CIRM will have funded new approaches for achieving immune tolerance for transplantation that are in pre-clinical development.

Progress: See Five Year Goal VI.

Outcomes: One of CIRM's Disease Team Projects is currently in Preclinical Development and is pursuing a novel encapsulation strategy to prevent immune rejection, thereby addressing this goal directly. Knowledge and insights gained from this effort may elicit broader insights that could be applicable to other stem cell transplantation paradigms. Similarly, several other cell therapy candidates in CIRM's development portfolio may progress within the next few years into IND-enabling

development, thereby engaging in the creation or optimization of additional immune-modulation strategies.

Goal V: Using stem cell research, CIRM-funded investigators will have established proof of principle in preclinical animal models for the treatment of 6-8 diseases.

Progress: As described previously, CIRM's Development Portfolio, which will continue to grow over the next few years, presently comprises 22 projects that are seeking to demonstrate, or already have demonstrated, proof of principle in preclinical models of disease or injury. Furthermore, several additional grants from CIRM's other programs have also led to insights and methods that could impact this goal.

Outcomes:

- Diseases represented in CIRM's current Development Portfolio include type 1 diabetes, glioblastoma, cancer (both hematologic and solid tumor), macular degeneration, epidermolysis bullosa, stroke, ALS, HIV, anemia, arthritis, Parkinson's disease, cardiovascular damage and Huntington's disease.
- Analysis of recent progress reports from CIRM's ongoing grants indicate that several projects have made headway towards this goal. Examples include:
    - Demonstration of efficacy of hESCs in a model of radiation damage, immunotherapy for melanoma, and retinal degeneration
    - Progress towards establishing proof of principle for cardiovascular disease, intestinal disorder, myeloproliferative disorder, muscular dystrophy, multiple sclerosis, and HIV
- Although publications have yet to emerge from CIRM's developmental portfolio projects, some earlier research programs have provided supporting rationale for the use of hESC and their derivatives for regenerative medicine. Examples include:
    - Rossi, S. L., et al. "Histological and functional benefit following transplantation of motor neuron progenitors to the injured rat spinal cord." *PLoS ONE*, July 2010. **PI: H. Keirstead (Comprehensive, UC Irvine).** This publication describes the transplantation of hESC-derived motor neuron progenitors (MNPs) to treat a rat model of spinal cord injury. While these MNPs didn't integrate at the site of injury, they improved endogenous neuronal survival, neurite branching and performance on a balance beam task, presumably through trophic effects.
    - Acharya, M., et al. "Rescue of radiation-induced cognitive impairment through cranial transplantation of human embryonic stem cells." *Proc. Natl. Acad. Sci. USA,* November 2009. **PI: C. Limoli (SEED, UCI).** This paper demonstrated the potential for hESCs to ameliorate radiation-induced tissue injury (such as that which occurs during treatment of certain cancers), and that such strategies may provide useful interventions for reducing the adverse effects of irradiation on cognition.
    - Blurton-Jones, M., et al. "Neural stem cells improve cognition via BDNF in a transgenic model of Alzheimer disease." *Proc. Natl. Acad. Sci. USA*, July 2009. **PI: F. LaFerla (SEED, UC Irvine), Postdoctoral trainee: M. Blurton-Jones.** This paper reported memory improvement following mouse NSC transplant in a mouse model of Alzheimer's disease. Dr. LaFerla is the recipient of an Early Translational award to expand upon these findings using hESC-derived NSCs.

- Sun, L. et al. "Mesenchymal stem cell transplantation reverses multiorgan dysfunction in systemic lupus erythematosus mice and humans." *Stem Cells*, June 2009. **PI: S. Shi (New Faculty, USC).** This paper reported that allogeneic mouse mesenchymal stem cell (MSC) transplant improved multiple organ function and measures of immune function in a mouse model of systemic lupus erythematosus (SLE). This paper further demonstrated the safety and efficacy of allogeneic hMSC transplant in 4 human SLE patients, but that part of the study was performed in China and not funded by CIRM.

Goal VI: CIRM-funded investigators will have created disease-specific cell lines for 20-30 diseases and used them to gain new information about pathogenesis, to identify new drug targets and to discover new therapeutics.

Progress and Outcomes: See progress for Five Year Goal III. Given that CIRM researchers have already developed a dozen such lines, it is very likely that this goal will have been met well in advance of initial expectations.

Goal VII: CIRM will have enabled development of new procedures for the production of a variety of stem and/or progenitor cells that meet GMP requirements.

Progress: CIRM is currently funding about 30 grants that either directly or indirectly impact this goal. Included among these are:

- 5 grants developing methods or cell lines for GMP production
- 18 translational cell therapy projects (in CIRM's current Development Portfolio) which will, if successful, develop GMP and GMP-compatible methods, cell lines and banks over the course of their progression towards an IND application
- 5 projects addressing quality control of cell preparations, assays for detecting teratomas, assurance of cell integrity and functionality
- Also see Five Year Goal IV: 11 additional grants seeking to develop defined media conditions could lead to insights that may indirectly impact this goal

Outcomes: While still in the early stages, several projects have generated preliminary data by comparing and evaluating growth and behavior parameters for multiple pluripotent cell lines using different conditions and media formulations for expansion.

Goal VIII: Through research sponsored by CIRM and others, a thorough description of the steps of differentiation leading to the production of the various cells of the body will have been achieved.

Progress: CIRM has funded about 125 projects that could inform our understanding of the mechanisms by which cell identity is established. CIRM will continue to target additional studies in this area, particularly through the ongoing Basic Biology Initiative. Currently funded grants include:

- About 50 grants studying specification of neural fate
- About 20 grants investigating the cardiac lineage
- About 15 grants focused on hematopoietic and/or immune differentiation

- Multiple grants focused differentiation towards skeletal muscle, liver, pancreas, retinal epithelium, trophoblast and other early lineages
- One or two grants each exploring specification of lung, kidney, vascular, skin, sensory cells, bone/cartilage, germ cells, intestine, and/or dental fates

Outcomes: Major strides have been made in understanding differentiation into many cell lineages. Most of CIRM's strategic impacts, thus far, have been towards this goal and derive largely from the earliest rounds of research funding, the SEED, Comprehensive and New Faculty Awards.

- Analysis of recent progress reports from CIRM's SEED, Comprehensive New Faculty programs suggest that 58 grants thus have had measurable impacts on this strategic goal, many of which have yet to be published
- To date, CIRM grantees have produced 51 publications detailing aspects of the differentiation process of stem/progenitor cells into various phenotypes. Some notable examples include the following:
    - Oshima, K., et al. "Mechanosensitive hair cell-like cells from embryonic and induced pluripotent stem cells." *Cell*, May 2010. PI: S. Heller (Comprehensive, Stanford). In this study, the authors describe a stepwise protocol for directing mouse embryonic stem and induced pluripotent stem cells towards a hair cell-like fate. Hair cells are specialized mechanosensory cells that play a central role in hearing and balance. Cells produced from this methodology possessed sterociliary bundles and responded to mechanical stimulation. This study lays the foundation for future therapeutic advances for treating hearing loss due to hair cell damage.
    - Cordes, K.R., et al. "miR-145 and miR-143 regulate smooth muscle cell fate and plasticity." *Nature,* 2009. **PI: D. Srivastava (Comprehensive, Gladstone Institute)** MicroRNAs are regulators of myriad cellular events, but evidence for a single microRNA that can efficiently differentiate multipotent stem cells into a specific lineage or regulate direct reprogramming of cells into an alternative cell fate has been elusive. These findings demonstrate that a specific microRNA can direct the smooth muscle fate and that a combination of microRNAs functions to regulate the quiescent versus proliferative phenotype of smooth muscle cells.
    - Karumbayaram, S., et al. "Directed differentiation of human-induced pluripotent stem cells generates active motor neurons." *Stem Cells*, April 2009. **PI: W.E. Lowry (SEED, UCLA).** The authors found that human induced pluripotent stem (iPS) cells could be differentiated to form motor neurons with a similar efficiency as hESCs. This represents the first demonstration that human iPS-derived cells are able to generate electrically active motor neurons and demonstrates the feasibility of using iPS-derived motor neuron progenitors and motor neurons in regenerative medicine applications and *in vitro* modeling of motor neuron diseases.
    - Oh, S., et al. "Stem cell fate dictated solely by altered nanotube dimension." *Proc. Natl. Acad. Sci. USA*, January 2009. **PI: S. Chien (Comprehensive, UCSD); Trainee: S. Oh.** This paper demonstrated that engineered microenvironments can be used to direct the fate of stem cells. In this case, the dimensions of nanotubular-shaped surface structure (geometric cues) could be manipulated to either augment human mesenchymal stem cell (hMSC) adhesion, or specify

differentiation into osteoblasts.

<u>Goal IX</u>: Through research sponsored by CIRM and others, the mechanisms regulating the self-renewal and oncogenic potential of embryonic stem cells and their derivatives will have been identified and characterized.

Progress: CIRM has funded about 100 grants with the potential to impact this goal. Included amongst these projects are:

- Those that elucidate oncogenic mechanisms (genetic instability, tumor suppressor function) in stem cells
- Mechanisms of self-renewal in pluripotent, adult and cancer stem cells
- Mechanisms by which pluripotency can be established or maintained
- Non-viral methods for induction of pluripotency
- Evaluation and mitigation of teratoma risk in stem cells and their derivatives

Outcomes: Analyses of progress reports indicate that about 40 projects have had substantial and/or measurable impacts on this goal, many of which have yet to be published. In addition, CIRM funding has contributed to more than 30 publications describing the mechanisms regulating the self-renewal and oncogenic potential of embryonic stem cells and their derivatives. These publications include:

- Hawkins, R. D., et al. "Distinct epigenomic landscapes of pluripotent and lineage-committed human cells." *Cell Stem Cell*, May 2010. **PI: B. Ren (New Faculty II, Ludwig Institute).** This paper reported that hESCs differ vastly from their lineage-committed progeny in their DNA modification profile, or epigenome. The group analyzed different types of DNA modifications in different cell types using high-throughput, genome-wide approaches. The differences they discovered between hESCs and their differentiated progeny may comprise novel epigenetic mechanisms underlying pluripotency and lineage commitment in human cells.
- Lee, A. S., et al., "Effects of cell number on teratoma formation by human embryonic stem cells." *Cell Cycle*, August 2009. **PI: J. Wu (SEED, Comprehensive, Stanford).** In this paper Dr. Wu's group utilized fluorescent reporter genes and long-term, non-invasive imaging techniques to determine the minimum number of hESCs required for teratoma formation in immunodeficient mice. They found that a minimum of 100,000 hESCs transplanted into the heart and 10,000 hESCs into skeletal muscle were required, demonstrating that both cell number and transplant site play important roles in teratoma formation.
- Gaspar-Maia, A., et al. "Chd1 regulates open chromatin and pluripotency of embryonic stem cells." *Nature*, July 2009. **PI: Miguel Ramalho-Santos (SEED & New Cell Lines, UCSF).** This paper reports the identification of a protein, Chd1, required for hESC self-renewal and pluripotency as well as the epigenetic mechanism responsible for this regulation. This discovery will impact work on stem cell differentiation, reprogramming and oncogenicity.
- Xu, N., et al. "MicroRNA-145 regulates OCT4, SOX2, and KLF4 and represses pluripotency in human embryonic stem cells." *Cell*, May 2009. **Trainee: Na Xu (UC Santa Barbara).** This paper reports the identification of a novel microRNA regulator of hESC self-renewal and pluripotency. The authors demonstrated that this microRNA directly regulates known

transcription factors responsible for pluripotency, and its expression inhibits hESC self-renewal. This is an important discovery with implications for controlling the differentiation and potential oncogenicity of hESCs.

Goal X: CIRM will have enabled development of new methods for tissue replacement based on stem cell research.

Progress: CIRM is funding a significant number of grants that address this goal:

- 16 grants exploring the use of matrices, biomaterials, co-culture techniques or scaffolding to control cell fate/ improve cell authenticity or function
- An additional 13 grants exploring the effects of cellular microenvironment or niche on cell behavior

Outcomes: While most grants in this area were funded only recently, CIRM investigators have already generated novel insights with the potential to impact our understanding of tissue architecture, particularly in the areas of cardiac biology but also in such organs as the eye, the brain, intestine and liver.

- CIRM has contributed funding towards 28 publications that focus on tissue engineering, tissue regeneration/replacement, and/or microenvironment interactions of stem cells. Notable examples include:
    - Gilbert, P. M., et al. "Substrate Elasticity Regulates Skeletal Muscle Stem Cell Self-Renewal in Culture." *Science*, July 2010. **PI: H. Blau (Tools & Technologies I, Stanford).** In this groundbreaking study, the authors report that freshly isolated muscle stem cells (MuSCs) could be maintained on a bioengineered substrate that recapitulates key biophysical and biochemical niche features. Furthermore, these MuSCs contributed extensively to muscle regeneration when transplanted into mice. This study provided novel evidence that by recapitulating physiological tissue rigidity, propagation of adult muscle stem cells was possible, renewing the promise of cell-based therapies for treating muscle wasting diseases.
    - Yu, J., et al. "The use of human mesenchymal stem cells encapsulated in RGD modified alginate microspheres in the repair of myocardial infarction in the rat." *Biomaterial*, June 2010. **PI: R. Lee (Comprehensive, UCSF).** The combination of scaffold material and cell transplantation therapy has been extensively investigated in cardiac tissue engineering. However, many polymers are difficult to administer or lack the structural integrity to restore left ventricle function. This study developed a technique using human mesenchymal stem cells (hMSCs) encapsulated in RGD modified alginate microspheres that were capable of facilitating myocardial repair. The surface modification and microencapsulation techniques were successfully combined with cell transplantation, which led to the maintenance of left ventricle geometry, preservation of left ventricle function, increase of angiogenesis and improvement of cell survival.
    - Nakayama, K. H., et al. "Decellularized rhesus monkey kidney as a three-dimensional scaffold for renal tissue engineering." *Tissue Eng Part A*, February 2010. **PI: A. Tarantal (Comprehensive, UC Davis). Trainee: K. H. Nakayama.** This paper describes the optimization of kidney decellularization techniques and the characterization of the resulting

structures. The authors demonstrate that decellularized kidney sections retain critical properties necessary for use as a three-dimensional scaffold. This study represents an important first step toward new strategies for renal tissue engineering and repair.

[Back to Appendices]

APPENDIX 4

4. 2009 Strategic Plan key revisions

Revisions to the 2006 Strategic Plan (excerpt from Plan Update)

Building upon the values and foundation expressed in the first Plan, the specific strategic objectives of the 2009/2010 Strategic Plan Update are as follows:

1. **Acceleration of Therapeutic Discoveries**
   A. Develop Teams: Design an effective research program by linking the critical stakeholders together as committed teams to deliver clinical applications in regenerative medicine.
   B. Respond to Scientific Discoveries: Create the flexibility in ongoing grants to accommodate the rapidly evolving developments in stem cell science and regenerative medicine.
   C. Actively Manage Portfolio: Map a plan for accelerating progress to meet CIRM's demanding 10-to-14-year therapy goals through the "pipeline to cures" by more efficiently organizing CIRM's portfolio to bridge CIRM-funded basic stem cell research and translational, pre-clinical, and clinical research.
   D. Capture and Share Data. Develop robust systems for capturing and evaluating the results of CIRM-funded programs and for sharing these data in ways that accelerate the field
   E. Share Expertise and Collaborate: Propose new ways for CIRM to lead stem cell science and regenerative medicine by developing more formal mechanisms for sharing expertise and collaborations with partners in the scientific community, both nationally and around the world.
   F. Partner with Industry: Enhance CIRM's relationships with the venture capital, biotechnology and pharmaceutical industries -- relationships essential to delivering lifesaving therapies based on stem cell research to patients.

2. **Regulatory Certainty**. Consider methods for monitoring and improving, where appropriate, research policy and the regulations governing the ethical conduct of CIRM-funded research

3. **Public Education**. Encourage the development of a "stem cell science culture" in California by taking a leadership role in educating and informing the general public, including special interest groups and California students of all ages. Identify new procedures and methodologies that will expand public understanding and support of CIRM's research and development operations.

4. **Economic Benefit to California.** Collect and analyze information on the impact of CIRM as an economic engine and as an additional mechanism for sustaining CIRM financially.

5. **Operational Excellence.** Re-examine CIRM's internal operations so as to improve administrative efficiency, financial accountability, communication, education and teamwork.

APPENDIX 4

(Continue Excerpt from Plan Update)

SUMMARY OF STRATEGIC ADJUSTMENTS RECOMMENDED — IN ORDER TO ACHIEVE THE STRATEGIC OBJECTIVES NOTED ABOVE, ADJUSTMENTS TO THE 2006 STRATEGIC PLAN ARE NECESSARY. TO DO THIS, CIRM SOUGHT INPUT FROM THE RESEARCH INSTITUTIONS, THE GENERAL PUBLIC, INDUSTRY, PATIENT ADVOCATES, AND OTHER STAKEHOLDERS. THE FOLLOWING RECOMMENDATIONS ARE THE RESULT OF THAT CONSULTATION.

Funding Focus and Strategy

1. The CIRM Governing Board has already approved the allocation of up to $210 million for Disease Team awards, which represents a near doubling of the funds allocated to this award category in 2006. CIRM received considerable support from many different constituents for these multi-disciplinary teams, as a valuable tool for CIRM's efforts on the clinical side of the research pipeline. The Disease Teams should subsume the Clinical and Tissue Engineering RFAs that were forecast in 2006.

2. CIRM clearly needs to continue to fund the full spectrum from basic to clinical research, but with NIH now able to fund basic embryonic research, CIRM can direct more of its basic science funding to two areas not well represented in NIH's portfolio. It can fund very directed projects that try to unlock a fundamental truth that was found to be unknown and blocking in a translational or clinical project—the critical path from bedside to the bench. It can also fund highly innovative basic projects that can sometimes yield a step-change in our understanding of a particular area.

3. In light of recent science advances in using stem cells as research tools CIRM has begun to fund molecular therapeutics based on stem cells and high throughput screening of stem cell and progenitor cell assays. As stem cell science advances in drug development, disease modeling, and small molecule drug discovery, CIRM should apply its resources in these fields in ways that are in accordance with Proposition 71—funding those projects which involve stem cell research that have the most promise of advancing the field toward therapies, but that have limited capacity to attract alternative funding.

4. CIRM has consolidated many of the RFAs envisioned in 2006, in part because it was not feasible to manage 12 grant cycles per year, but more so, in order to move toward a smaller number of core grants, which are predictable for grantees and can have rolling priorities that reflect that state of the stem cell science at the moment of each RFA (see page 27). CIRM received considerable support from researchers for these core grants and plans to proceed in that direction.

5. The need to engage immunology in stem cell and regenerative medicine is critical and little progress has been achieved to date in attracting immunologists to address the areas of inducing immune tolerance for allogenic cell and tissue graft survival, the need for new types of immune modulation and the apparent role of the immune system in tissue regeneration. CIRM needs to engage immunologists in working with stem cell researchers to provide the data and strategies that are essential for stem cell transplants in a wide range of diseases and injuries. An immunology and stem cell RFA is proposed and a proactive strategy is proposed to attract central and peripheral immunologists and transplant scientists into collaborative partnerships with

stem cell scientists. (This round of grants has been executed with $25 million allotted to 19 projects each with stem cell scientists and immunologist working together.)

Collaborations

6. CIRM has embarked on a series of agreements with funding entities from other countries in order to foster collaborations between Californian researchers and top stem cell scientists around the world. The agreements signed to date are outlined on page 27. In order to gain further global leverage of California's investment, CIRM plans to add several additional high ranked countries to this list that are strategically important for collaboration to Californian researchers. Similar agreements are under discussion with states and foundations within the US, and CIRM is looking for opportunities for partnership arrangements with federal agencies. Already a regular quarterly meeting forum has been agreed with the FDA through the Office of the President and General Counsel.

7. CIRM has begun to proactively engage with industry recognizing the need and benefit of partnering with California's vibrant biotechnology, pharmaceutical and venture capital communities to translate basic discovery research into clinical application. A number of operational changes, outlined beginning on page 22, are being made to facilitate these collaborations. CIRM has also recently appointed Elona Baum as General Counsel. She is a strategic thinker with 12 years experience at Genentech Inc. who is experienced in aligning agreements in the corporate sector and addressing complicated legal issues that involve private and public partnerships. Furthermore, CIRM proposes to recruit an experienced individual to staff (Vice President R&D) to assist in the translation-clinical research phase and who can enhance the prospects of clinical applications by working closely with teams of academic-medical-biotech-pharma interests.
(End of excerpt from Plan Update)

[Back to Appendices]

APPENDIX 5

5. All Publications with CIRM Funding

Title	Authors	Journal	Date	PMID
Molecular analyses of human induced pluripotent stem cells and embryonic stem cells	Chin MH, Pellegrini M, Plath K, Lowry WE	Cell Stem Cell	8/6/2010	20682452
Direct reprogramming of fibroblasts into functional cardiomyocytes by defined factors	Ieda M, Fu JD, Delgado-Olguin P, Vedantham V, Hayashi Y, Bruneau BG, Srivastava D	Cell	8/6/2010	20691899
Transient inactivation of Rb and ARF yields regenerative cells from postmitotic mammalian muscle	Pajcini KV, Corbel SY, Sage J, Pomerantz JH, Blau HM	Cell Stem Cell	8/6/2010	20682446
PNPASE regulates RNA import into mitochondria	Wang G, Chen HW, Oktay Y, Zhang J, Allen EL, Smith GM, Fan KC, Hong JS, French SW, McCaffery JM, Lightowlers RN, Morse HC 3rd, Koehler CM, Teitell MA	Cell	8/6/2010	20691904
Lung organogenesis	Warburton D, El-Hashash A, Carraro G, Tiozzo C, Sala F, Rogers O, Langhe SD, Kemp PJ, Riccardi D, Torday J, Bellusci S, Shi W, Lubkin SR, Jesudason E	Curr Top Dev Biol	8/5/2010	20691848
Vitamin C promotes widespread yet specific DNA demethylation of the epigenome in human embryonic stem cells	Chung TL, Brena RM, Kolle G, Grimmond SM, Berman BP, Laird PW, Pera MF, Wolvetang EJ	Stem Cells	8/4/2010	20687155
Histological and functional benefit following transplantation of motor neuron progenitors to the injured rat spinal cord	Rossi SL, Nistor G, Wyatt T, Yin HZ, Poole AJ, Weiss JH, Gardener MJ, Dijkstra S, Fischer DF, Keirstead HS	PLoS ONE	7/29/2010	20686613

APPENDIX 5

Title	Authors	Journal	Date	PMID
Live cell monitoring of hiPSC generation and differentiation using differential expression of endogenous microRNAs	Kamata M, Liang M, Liu S, Nagaoka Y, Chen IS	PLoS ONE	7/28/2010	20676373
Centromere Protein A dynamics in human pluripotent stem cell self renewal, differentiation and DNA damage	Ambartsumyan G, Gill RK, Perez SD, Conway D, Vincent J, Dalal Y, Clark AT	Hum Mol Genet	7/22/2010	20650959
Mapping the first stages of mesoderm commitment during differentiation of human embryonic stem cells	Evseenko D, Zhu Y, Schenke-Layland K, Kuo J, Latour B, Ge S, Scholes J, Dravid G, Li X, Maclellan WR, Crooks GM	Proc Natl Acad Sci U S A	7/19/2010	20643952
Epigenetic memory in induced pluripotent stem cells	Kim K, Doi A, Wen B, Ng K, Zhao R, Cahan P, Kim J, Aryee MJ, Ji H, Ehrlich LI, Yabuuchi A, Takeuchi A, Cunniff KC, Hongguang H, McKinney-Freeman S, Naveiras O, Yoon TJ, Irizarry RA, Jung N, Seita J, Hanna J, Murakami P, Jaenisch R, Weissleder R, Orkin SH, Weissman IL, Feinberg AP, Daley GQ	Nature	7/19/2010	20644535
Substrate elasticity regulates skeletal muscle stem cell self-renewal in culture	Gilbert PM, Havenstrite KL, Magnusson KE, Sacco A, Leonardi NA, Kraft P, Nguyen NK, Thrun S, Lutolf MP, Blau HM	Science	7/15/2010	20647425
miRNAs regulate SIRT1 expression during mouse embryonic stem cell differentiation and in adult mouse tissues	Saunders LR, Sharma AD, Tawney J, Nakagawa M, Okita K, Yamanaka S, Willenbring H, Verdin E	Aging (Albany NY)	7/15/2010	20634564

APPENDIX 5

Title	Authors	Journal	Date	PMID
Characterization of axon guidance cue sensitivity of human embryonic stem cell-derived dopaminergic neurons	Cord BJ, Li J, Works M, McConnell SK, Palmer T, Hynes MA	Mol Cell Neurosci	7/13/2010	20637284
High throughput tracking of pluripotent human embryonic stem cells with dual FRET molecular beacons	King FW, Liszewski W, Ritner C, Bernstein HS	Stem Cells Dev	7/12/2010	20624034
Kinetic phases of distribution and tumor targeting by T cell receptor engineered lymphocytes inducing robust antitumor responses	Koya RC, Mok S, Comin-Anduix B, Chodon T, Radu CG, Nishimura MI, Witte ON, Ribas A	Proc Natl Acad Sci U S A	7/12/2010	20624956
Phosphorylation stabilizes Nanog by promoting its interaction with Pin1	Moretto-Zita M, Jin H, Shen Z, Zhao T, Briggs SP, Xu Y	Proc Natl Acad Sci U S A	7/9/2010	20622153
Hematopoietic stem cell quiescence promotes error-prone DNA repair and mutagenesis	Mohrin M, Bourke E, Alexander D, Warr MR, Barry-Holson K, Le Beau MM, Morrison CG, Passegué E	Cell Stem Cell	7/7/2010	20619762
MicroRNAs as regulators of differentiation and cell fate decisions	Ivey KN, Srivastava D	Cell Stem Cell	7/2/2010	20621048
An early T cell lineage commitment checkpoint dependent on the transcription factor Bcl11b	Li L, Leid M, Rothenberg EV	Science	7/2/2010	20595614
Chromatin regulation by Brg1 underlies heart muscle development and disease	Hang CT, Yang J, Han P, Cheng HL, Shang C, Ashley E, Zhou B, Chang CP	Nature	7/1/2010	20596014
Parallel gateways to pluripotency: open chromatin in stem cells and development	Koh FM, Sachs M, Guzman-Ayala M, Ramalho-Santos M	Curr Opin Genet Dev	7/1/2010	20598875
Placenta as a newly identified source of hematopoietic stem cells	Lee LK, Ueno M, Van Handel B, Mikkola HK	Curr Opin Hematol	7/1/2010	20571394

APPENDIX 5

Title	Authors	Journal	Date	PMID
Chronic myeloid leukemia: mechanisms of blastic transformation	Perrotti D, Jamieson C, Goldman J, Skorski T	J Clin Invest	7/1/2010	20592475
Variations of X chromosome inactivation occur in early passages of female human embryonic stem cells	Dvash T, Lavon N, Fan G	PLoS ONE	6/25/2010	20593031
Genetic modification of airway progenitors following lentiviral gene delivery to the amniotic fluid of murine fetuses	Mishra S, Wang X, Smiley N, Xia P, Hong CM, Senadheera D, Bui KC, Lutzko C	Am J Respir Cell Mol Biol	6/25/2010	20581098
Platelet-derived growth factor receptor beta is critical for zebrafish intersegmental vessel formation	Wiens KM, Lee HL, Shimada H, Metcalf AE, Chao MY, Lien CL	PLoS ONE	6/25/2010	20593033
Tandem E2F binding sites in the promoter of the p107 cell cycle regulator control p107 expression and its cellular functions	Burkhart DL, Wirt SE, Zmoos AF, Kareta MS, Sage J	PLoS Genet	6/24/2010	20585628
Alternative control: what's WASp doing in the nucleus?	Teitell MA	Sci Transl Med	6/23/2010	20574067
Comparison of reprogramming efficiency between transduction of reprogramming factors, cell-cell fusion, and cytoplast fusion	Hasegawa K, Zhang P, Wei Z, Pomeroy JE, Lu W, Pera MF	Stem Cells	6/22/2010	20572011
The use of human mesenchymal stem cells encapsulated in RGD modified alginate microspheres in the repair of myocardial infarction in the rat	Yu J, Du KT, Fang Q, Gu Y, Mihardja SS, Sievers RE, Wu JC, Lee RJ	Biomaterials	6/19/2010	20566215
PET imaging of the immune system: immune monitoring at the whole body level	Singh AS, Radu CG, Ribas A	Q J Nucl Med Mol Imaging	6/18/2010	20559199

APPENDIX 5

Title	Authors	Journal	Date	PMID
Immature B cell progenitors survive oncogenic stress and efficiently initiate Ph+ B-acute lymphoblastic leukemia	Signer RA, Montecino-Rodriguez E, Witte ON, Dorshkind K	Blood	6/18/2010	20562326
BMP-2/6 heterodimer is more effective than BMP-2 or BMP-6 homodimers as inductor of differentiation of human embryonic stem cells	Valera E, Isaacs MJ, Kawakami Y, Izpisúa Belmonte JC, Choe S	PLoS ONE	6/17/2010	20567515
Reporter-based isolation of induced pluripotent stem cell- and embryonic stem cell-derived cardiac progenitors reveals limited gene expression variance	van Laake LW, Qian L, Cheng P, Huang Y, Hsiao EC, Conklin B, Srivastava D	Circ Res	6/17/2010	20558827
RB's original CIN	Sage J, Straight AF	Genes Dev	6/15/2010	20551167
Indian hedgehog regulates intestinal stem cell fate through epithelial-mesenchymal interactions during development	Kosinski C, Stange DE, Xu C, Chan AS, Ho C, Yuen ST, Mifflin RC, Powell DW, Clevers H, Leung SY, Chen X	Gastroenterology	6/10/2010	20542037
Nuclear reprogramming to a pluripotent state by three approaches	Yamanaka S, Blau HM	Nature	6/10/2010	20535199
Well-defined, size-tunable, multifunctional micelles for efficient paclitaxel delivery for cancer treatment	Luo J, Xiao K, Li Y, Lee JS, Shi L, Tan YH, Xing L, Holland Cheng R, Liu GY, Lam KS	Bioconj Chem	6/10/2010	20536174
HIV-1 Vif versus the APOBEC3 cytidine deaminases: An intracellular duel between pathogen and host restriction factors	Wissing S, Galloway NL, Greene WC	Mol Aspects of Med	6/9/2010	20538015
Next-generation genomics: an integrative approach	Hawkins RD, Hon GC, Ren B	Nat Rev Genet	6/8/2010	20531367

APPENDIX 5

Title	Authors	Journal	Date	PMID
Association between mitochondrial DNA variations and Alzheimer's disease in the ADNI cohort	Lakatos A, Derbeneva O, Younes D, Keator D, Bakken T, Lvova M, Brandon M, Guffanti G, Reglodi D, Saykin A, Weiner M, Macciardi F, Schork N, Wallace DC, Potkin SG	Neurobiol Aging	6/8/2010	20538375
Parthenogenic blastocysts derived from cumulus-free in vitro matured human oocytes	McElroy SL, Byrne JA, Chavez SL, Behr B, Hsueh AJ, Westphal LM, Pera RA	PLoS ONE	6/7/2010	20539753
Wnt proteins are self-renewal factors for mammary stem cells and promote their long-term expansion in culture	Zeng YA, Nusse R	Cell Stem Cell	6/4/2010	20569694
Cell replacement therapies to promote remyelination in a viral model of demyelination	Tirotta E, Carbajal KS, Schaumburg CS, Whitman L, Lane TE	J Neuroimmunol	6/1/2010	20627412
Migration of engrafted neural stem cells is mediated by CXCL12 signaling through CXCR4 in a viral model of multiple sclerosis	Carbajal KS, Schaumburg C, Strieter R, Kane J, Lane TE	Proc Natl Acad Sci U S A	6/1/2010	20534452
Mitochondrial DNA mutations in disease and aging	Wallace DC	Environ Mol Mutagen	6/1/2010	20544884
Disease research and drug development models based on genetically altered human embryonic stem cells	Song H, Xu Y	Discov Med	5/30/2010	20587338
Surface immobilization of hexa-histidine-tagged adeno-associated viral vectors for localized gene delivery	Jang JH, Koerber JT, Gujraty K, Bethi SR, Kane RS, Schaffer DV	Gene Ther	5/27/2010	20508598
myc maintains embryonic stem cell pluripotency and self-renewal	Varlakhanova NV, Cotterman RF, Devries WN, Morgan J, Donahue LR, Murray S, Knowles BB, Knoepfler PS	Differentiation	5/26/2010	20537458

APPENDIX 5

Title	Authors	Journal	Date	PMID
Alternative splicing regulates mouse embryonic stem cell pluripotency and differentiation	Salomonis N, Schlieve CR, Pereira L, Wahlquist C, Colas A, Zambon AC, Vranizan K, Spindler MJ, Pico AR, Cline MS, Clark TA, Williams A, Blume JE, Samal E, Mercola M, Merrill BJ, Conklin BR	Proc Natl Acad Sci U S A	5/24/2010	20498046
Expression of migration-related genes is progressively upregulated in murine Lineage^{-}Sca-1^{+}c-Kit^{+} population from the fetal to adult stages of development	Ciriza J, García-Ojeda ME	Stem Cell Res Ther	5/20/2010	20637061
Connexin 43 mediates the tangential to radial migratory switch in ventrally derived cortical interneurons	Elias LA, Turmaine M, Parnavelas JG, Kriegstein AR	J Neurosci	5/19/2010	20484649
Bone morphogenetic protein-2 and -6 heterodimer illustrates the nature of ligand-receptor assembly	Isaacs MJ, Kawakami Y, Allendorph GP, Yoon BH, Izpisua Belmonte JC, Choe S	Mol Endocrinol	5/19/2010	20484413
Global and local fMRI signals driven by neurons defined optogenetically by type and wiring	Lee JH, Durand R, Gradinaru V, Zhang F, Goshen I, Kim DS, Fenno LE, Ramakrishnan C, Deisseroth K	Nature	5/16/2010	20473285
Mechanosensitive hair cell-like cells from embryonic and induced pluripotent stem cells	Oshima K, Shin K, Diensthuber M, Peng AW, Ricci AJ, Heller S	Cell	5/14/2010	20478259
Antithrombogenic modification of small-diameter microfibrous vascular grafts	Hashi CK, Derugin N, Janairo RR, Lee R, Schultz D, Lotz J, Li S	Arterioscler Thromb Vasc Biol	5/13/2010	20466974

APPENDIX 5

Title	Authors	Journal	Date	PMID
Distinct epigenomic landscapes of pluripotent and lineage-committed human cells	Hawkins RD, Hon GC, Lee LK, Ngo Q, Lister R, Pelizzola M, Edsall LE, Kuan S, Luu Y, Klugman S, Antosiewicz-Bourget J, Ye Z, Espinoza C, Agarwahl S, Shen L, Ruotti V, Wang W, Stewart R, Thomson JA, Ecker JR, Ren B	Cell Stem Cell	5/7/2010	20452322
In Light of Evolution IV: The Human Conditions Sackler Colloquium: Bioenergetics, the origins of complexity, and the ascent of man	Wallace DC	Proc Natl Acad Sci U S A	5/5/2010	20445102
Metabolic oxidation regulates embryonic stem cell differentiation	Yanes O, Clark J, Wong DM, Patti GJ, Sánchez-Ruiz A, Benton HP, Trauger SA, Desponts C, Ding S, Siuzdak G	Nat Cell Biol	5/2/2010	20436487
The utility of routine surveillance blood cultures in asymptomatic hematopoietic stem cell transplant patients	Kanathezhath B, Shah A, Secola R, Hudes M, Feusner JH	J Pediatr Hematol Oncol	5/1/2010	20445421
Wnt proteins promote bone regeneration	Minear S, Leucht P, Jiang J, Liu B, Zeng A, Fuerer C, Nusse R, Helms JA	Sci Transl Med	4/28/2010	20427820
Hydrogel matrix to support stem cell survival after brain transplantation in stroke	Zhong J, Chan A, Morad L, Kornblum HI, Fan G, Carmichael ST	Neurorehabil Neural Repair	4/27/2010	20424193
Pluripotent stem cells in neurodegenerative and neurodevelopmental diseases	Marchetto MC, Winner B, Gage FH	Hum Mol Genet	4/23/2010	20418487
Allele-specific methylation is prevalent and is contributed by CpG-SNPs in the human genome	Shoemaker R, Deng J, Wang W, Zhang K	Genome Res	4/23/2010	20418490

APPENDIX 5

Title	Authors	Journal	Date	PMID
Preparation of adult muscle fiber-associated stem/precursor cells	Conboy MJ, Conboy IM	Methods Mol Biol	4/20/2010	20405365
In vitro culture and analysis of adult hippocampal neural progenitors	Peltier J, Agrawal S, Robertson MJ, Schaffer DV	Methods Mol Biol	4/20/2010	20405360
Isolation of adult hippocampal neural progenitors	Peltier J, Ormerod BK, Schaffer DV	Methods Mol Biol	4/20/2010	20405359
Viral packaging and transduction of adult hippocampal neural progenitors	Peltier J, Schaffer DV	Methods Mol Biol	4/20/2010	20405362
In vivo analysis of engrafted adult hippocampal neural progenitors	Robertson MJ, Peltier J, Schaffer DV	Methods Mol Biol	4/20/2010	20405361
A PIN diode controlled dual-tuned MRI RF coil and phased array for multi nuclear imaging	Ha S, Hamamura MJ, Nalcioglu O, Muftuler LT	Phys Med Biol	4/14/2010	20393229
Dlx5 and Dlx6 regulate the development of parvalbumin-expressing cortical interneurons	Wang Y, Dye CA, Sohal V, Long JE, Estrada RC, Roztocil T, Lufkin T, Deisseroth K, Baraban SC, Rubenstein JL	J Neurosci	4/14/2010	20392955
Regulated expansion of human pancreatic beta-cells	Pais E, Park J, Alexy T, Nikolian V, Ge S, Shaw K, Senadheera S, Hardee CL, Skelton D, Hollis R, Crooks GM, Kohn DB	Mol Ther	4/13/2010	20389286
HOXA9 regulates BRCA1 expression to modulate human breast tumor phenotype	Gilbert PM, Mouw JK, Unger MA, Lakins JN, Gbegnon MK, Clemmer VB, Benezra M, Licht JD, Boudreau NJ, Tsai KK, Welm AL, Feldman MD, Weber BL, Weaver VM	J Clin Invest	4/12/2010	20389018

APPENDIX 5

Title	Authors	Journal	Date	PMID
Assessment of mitochondrial membrane potential using an on-chip microelectrode in a microfluidic device	Lim TS, Dávila A, Wallace DC, Burke P	Lab Chip	4/12/2010	20383402
Oligonucleotide-based tools for studying zebrafish development	Shestopalov IA, Chen JK	Zebrafish	4/12/2010	20392138
Development of a new RF coil and gamma-ray radiation shielding assembly for improved MR image quality in SPECT/MRI	Ha S, Hamamura MJ, Roeck WW, Muftuler LT, Nalcioglu O	Phys Med Biol	4/6/2010	20371909
MicroRNA-9 coordinates proliferation and migration of human embryonic stem cell-derived neural progenitors	Delaloy C, Liu L, Lee JA, Su H, Shen F, Yang GY, Young WL, Ivey KN, Gao FB	Cell Stem Cell	4/2/2010	20362537
CD133 expression in chemo-resistant Ewing sarcoma cells	Jiang X, Gwye Y, Russell D, Cao C, Douglas D, Hung L, Kovar H, Triche TJ, Lawlor ER	BMC Cancer	3/26/2010	20346143
Isolation, cultivation and characterization of adult murine prostate stem cells	Lukacs RU, Goldstein AS, Lawson DA, Cheng D, Witte ON	Nat Protoc	3/25/2010	20360765
Molecular and cellular approaches for diversifying and extending optogenetics	Gradinaru V, Zhang F, Ramakrishnan C, Mattis J, Prakash R, Diester I, Goshen I, Thompson KR, Deisseroth K	Cell	3/18/2010	20303157
Inhibition of proteolysis of Delta-like-1 does not promote or reduce T-cell developmental potential	Gravano DM, Manilay JO	Immunol Cell Biol	3/16/2010	20231851
Microfluidic image cytometry for quantitative single-cell profiling of human pluripotent stem cells in chemically defined conditions	Kamei K, Ohashi M, Gschweng E, Ho Q, Suh J, Tang J, For Yu ZT, Clark AT, Pyle AD, Teitell MA, Lee KB, Witte ON, Tseng HR	Lab Chip	3/16/2010	20390128
Ofd1, a human disease gene, regulates the length and distal structure of	Singla V, Romaguera-Ros M, Garcia-Verdugo JM, Reiter JF	Dev Cell	3/16/2010	20230748

Title	Authors	Journal	Date	PMID
centrioles				
MiDReG: A method of mining developmentally regulated genes using Boolean implications	Sahoo D, Seita J, Bhattacharya D, Inlay MA, Weissman IL, Plevritis SK, Dill DL	Proc Natl Acad Sci U S A	3/15/2010	20231483
Cortical plasticity induced by inhibitory neuron transplantation	Southwell DG, Froemke RC, Alvarez-Buylla A, Stryker MP, Gandhi SP	Science	2/26/2010	20185728
Multipotent mesenchymal progenitor cells are present in endarterectomized tissues from patients with chronic thromboembolic pulmonary hypertension	Firth AL, Yao W, Ogawa A, Madani MM, Lin GY, Yuan JX	Am J Physiol Cell Physiol	2/24/2010	20181931
Inhibition of HIV-1 infection by a unique short hairpin RNA to chemokine receptor 5 delivered into macrophages through hematopoietic progenitor cell transduction	Liang M, Kamata M, Chen KN, Pariente N, An DS, Chen IS	J Gene Med	2/24/2010	20186995
Protective effect of human amniotic fluid stem cells in an immunodeficient mouse model of acute tubular necrosis	Perin L, Sedrakyan S, Giuliani S, Da Sacco S, Carraro G, Shiri L, Lemley KV, Rosol M, Wu S, Atala A, Warburton D, De Filippo RE	PLoS ONE	2/24/2010	20195358
Cardiac myocyte force development during differentiation and maturation	Jacot JG, Kita-Matsuo H, Wei KA, Chen HS, Omens JH, Mercola M, McCulloch AD	Ann N Y Acad Sci	2/23/2010	20201894
Embryonic stem cell-derived endothelial cells engraft into the ischemic hindlimb and restore perfusion	Huang NF, Niiyama H, Peter C, De A, Natkunam Y, Fleissner F, Li Z, Rollins MD, Wu JC, Gambhir SS, Cooke JP	Arterioscler Thromb Vasc Biol	2/18/2010	20167654

APPENDIX 5

Title	Authors	Journal	Date	PMID
Development of an MR-compatible SPECT system (MRSPECT) for simultaneous data acquisition	Hamamura MJ, Ha S, Roeck WW, Muftuler LT, Wagenaar DJ, Meier D, Patt BE, Nalcioglu O	Phys Med Biol	2/17/2010	20164533
Decellularized rhesus monkey kidney as a three-dimensional scaffold for renal tissue engineering	Nakayama KH, Batchelder CA, Lee CC, Tarantal A	Tissue Eng Part A	2/16/2010	20156112
Haematopoietic stem cells derive directly from aortic endothelium during development	Bertrand JY, Chi NC, Santoso B, Teng S, Stainier DY, Traver D	Nature	2/14/2010	20154733
Neurogenic radial glia in the outer subventricular zone of human neocortex	Hansen DV, Lui JH, Parker PR, Kriegstein AR	Nature	2/14/2010	20154730
Imaging of CTLA4 blockade-induced cell replication with 18F-FLT PET in patients with advanced melanoma treated with tremelimumab	Ribas A, Benz MR, Allen-Auerbach MS, Radu C, Chmielowski B, Seja E, Williams JL, Gomez-Navarro J, McCarthy T, Czernin J	J Nucl Med	2/11/2010	20150263
Cellular histone modification patterns predict prognosis and treatment response in resectable pancreatic adenocarcinoma: results from RTOG 9704	Manuyakorn A, Paulus R, Farrell J, Dawson NA, Tze S, Cheung-Lau G, Hines OJ, Reber H, Seligson DB, Horvath S, Kurdistani SK, Guha C, Dawson DW	J Clin Oncol	2/8/2010	20142597
Genomic code for Sox10 activation reveals a key regulatory enhancer for cranial neural crest	Betancur P, Bronner-Fraser M, Sauka-Spengler T	Proc Natl Acad Sci U S A	2/5/2010	20139305
Upregulation of Oct-4 isoforms in pulmonary artery smooth muscle cells from patients with pulmonary arterial hypertension	Firth AL, Yao W, Remillard CV, Ogawa A, Yuan JX	Am J Physiol Lung Cell Mol Physiol	2/5/2010	20139178
Stem cells and the niche: a dynamic duo	Voog J, Jones DL	Cell Stem Cell	2/5/2010	20144784

APPENDIX 5

Title	Authors	Journal	Date	PMID
Polycomb-like 2 associates with PRC2 and regulates transcriptional networks during mouse embryonic stem cell self-renewal and differentiation	Walker E, Chang WY, Hunkapiller J, Cagney G, Garcha K, Torchia J, Krogan NJ, Reiter JF, Stanford WL	Cell Stem Cell	2/5/2010	20144788
Differentiation and characterization of metabolically functioning hepatocytes from human embryonic stem cells	Duan Y, Ma X, Zou W, Wang C, Behbahan IS, Ahuja TP, Tolstikov V, Zern MA	Stem Cells	2/4/2010	20135682
Dynamic changes in the human methylome during differentiation	Laurent L, Wong E, Li G, Huynh T, Tsirigos A, Ong CT, Low HM, Kin Sung KW, Rigoutsos I, Loring J, Wei CL	Genome Res	2/4/2010	20133333
CHD7 cooperates with PBAF to control multipotent neural crest formation	Bajpai R, Chen DA, Rada-Iglesias A, Zhang J, Xiong Y, Helms J, Chang CP, Zhao Y, Swigut T, Wysocka J	Nature	2/3/2010	20130577
Molecular imaging of stem cell transplantation in myocardial disease	Chung J, Yang PC	Curr Cardiovasc Imaging Rep	2/3/2010	20396619
Screening the mammalian extracellular proteome for regulators of embryonic human stem cell pluripotency	Gonzalez R, Jennings LL, Knuth M, Orth AP, Klock HE, Ou W, Feuerhelm J, Hull MV, Koesema E, Wang Y, Zhang J, Wu C, Cho CY, Su AI, Batalov S, Chen H, Johnson K, Laffitte B, Nguyen DG, Snyder EY, Schultz PG, Harris JL, Lesley SA	Proc Natl Acad Sci U S A	2/2/2010	20133595
Propagation of human embryonic and induced pluripotent stem cells in an indirect co-culture system	Abraham S, Sheridan SD, Laurent LC, Albert K, Stubban C, Ulitsky I, Miller B, Loring JF, Rao RR	Biochem Biophys Res Commun	2/1/2010	20117095
Initial investigation of preclinical integrated SPECT and MR imaging	Hamamura MJ, Ha S, Roeck WW, Wagenaar DJ, Meier D, Patt BE, Nalcioglu O	Technol Cancer Res Treat	2/1/2010	20082527

APPENDIX 5

Title	Authors	Journal	Date	PMID
Hemoglobin Hakkari: an autosomal dominant form of beta thalassemia with inclusion bodies arising from de novo mutation in exon 2 of beta globin gene	Kanathezhath B, Hazard FK, Guo H, Kidd J, Azimi M, Kuypers FA, Vichinsky EP, Lal A	Pediatr Blood Cancer	2/1/2010	19852066
Synthetic surfaces for human embryonic stem cell culture	Kolhar P, Kotamraju VR, Hikita ST, Clegg DO, Ruoslahti E	J Biotechnol	2/1/2010	20132848
Histone demethylase LSD1 regulates neural stem cell proliferation	Sun G, Alzayady K, Stewart R, Ye P, Yang S, Li W, Shi Y	Mol Cell Biol	2/1/2010	20123967
The histone demethylase UTX enables RB-dependent cell fate control	Wang JK, Tsai MC, Poulin G, Adler AS, Chen S, Liu H, Shi Y, Chang HY	Genes Dev	2/1/2010	20123895
Cell-based immunotherapy with mesenchymal stem cells cures bisphosphonate-related osteonecrosis of the jaw-like disease in mice	Kikuiri T, Kim I, Yamaza T, Akiyama K, Zhang Q, Li Y, Chen C, Chen W, Wang S, Le AD, Shi S	J Bone Miner Res	1/29/2010	20200952
MicroRNAs control hepatocyte proliferation during liver regeneration	Song G, Sharma AD, Roll GR, Ng R, Lee AY, Blelloch RH, Frandsen NM, Willenbring H	Hepatology	1/28/2010	20432256
MicroRNA function is globally suppressed in mouse oocytes and early embryos	Suh N, Baehner L, Moltzahn F, Melton C, Shenoy A, Chen J, Blelloch R	Curr Biol	1/28/2010	20116247
Notch signaling distinguishes 2 waves of definitive hematopoiesis in the zebrafish embryo	Bertrand JY, Cisson JL, Stachura DL, Traver D	Blood	1/27/2010	20107232
Genetic studies on the functional relevance of the protein prenyltransferases in skin keratinocytes	Lee R, Chang SY, Trinh H, Tu Y, White AC, Davies BS, Bergo MO, Fong LG, Lowry WE, Young SG	Hum Mol Genet	1/27/2010	20106865
Aberrant alternative splicing and extracellular matrix gene expression in mouse models of myotonic dystrophy	Du H, Cline MS, Osborne RJ, Tuttle DL, Clark TA, Donohue JP, Hall MP, Shiue L, Swanson MS, Thornton	Nat Struct Mol Biol	1/24/2010	20098426

Title	Authors	Journal	Date	PMID
	CA, Ares M Jr			
Human amniotic fluid as a potential new source of organ specific precursor cells for future regenerative medicine applications	Da Sacco S, Sedrakyan S, Boldrin F, Giuliani S, Parnigotto P, Habibian R, Warburton D, De Filippo RE, Perin L	J Urol	1/22/2010	20096867
BubR1- and Polo-coated DNA tethers facilitate poleward segregation of acentric chromatids	Royou A, Gagou ME, Karess R, Sullivan W	Cell	1/22/2010	20141837
Genome-wide prediction of transcription factor binding sites using an integrated model	Won KJ, Ren B, Wang W	Genome Biol	1/22/2010	20096096
Molecular signatures of quiescent, mobilized and leukemia-initiating hematopoietic stem cells	Forsberg EC, Passegué E, Prohaska SS, Wagers AJ, Koeva M, Stuart JM, Weissman IL	PLoS ONE	1/20/2010	20098702
Murine embryonic stem cell-derived pyramidal neurons integrate into the cerebral cortex and appropriately project axons to subcortical targets	Ideguchi M, Palmer TD, Recht LD, Weimann JM	J Neurosci	1/20/2010	20089898
MicroRNA let-7b regulates neural stem cell proliferation and differentiation by targeting nuclear receptor TLX signaling	Zhao C, Sun G, Li S, Lang MF, Yang S, Li W, Shi Y	Proc Natl Acad Sci U S A	1/19/2010	20133835
Quantitative analysis of cellular inflammation after traumatic spinal cord injury: evidence for a multiphasic inflammatory response in the acute to chronic environment	Beck KD, Nguyen HX, Galvan MD, Salazar DL, Woodruff TM, Anderson AJ	Brain	1/19/2010	20085927

APPENDIX 5

Title	Authors	Journal	Date	PMID
Beta1 integrin establishes endothelial cell polarity and arteriolar lumen formation via a Par3-dependent mechanism	Zovein AC, Luque A, Turlo KA, Hofmann JJ, Yee KM, Becker MS, Fassler R, Mellman I, Lane TF, Iruela-Arispe ML	Dev Cell	1/19/2010	20152176
Ultrafast optogenetic control	Gunaydin LA, Yizhar O, Berndt A, Sohal VS, Deisseroth K, Hegemann P	Nat Neurosci	1/17/2010	20081849
Human neural stem cell grafts modify microglial response and enhance axonal sprouting in neonatal hypoxic-ischemic brain injury	Daadi MM, Davis AS, Arac A, Li Z, Maag AL, Bhatnagar R, Jiang K, Sun G, Wu JC, Steinberg GK	Stroke	1/14/2010	20075340
Requirement for deoxycytidine kinase in T and B lymphocyte development	Toy G, Austin WR, Liao HI, Cheng D, Singh A, Campbell DO, Ishikawa TO, Lehmann LW, Satyamurthy N, Phelps ME, Herschman HR, Czernin J, Witte ON, Radu CG	Proc Natl Acad Sci U S A	1/13/2010	20080663
Kruppel-like factor 4 (KLF4) prevents embryonic stem (ES) cell differentiation by regulating nanog gene expression	Zhang P, Andrianakos R, Yang Y, Liu C, Lu W	J Biol Chem	1/13/2010	20071344
Role of nitric oxide signaling in endothelial differentiation of embryonic stem cells	Huang N, Fleissner F, Sun J, Cooke J	Stem Cells Dev	1/11/2010	20064011
G(s) G-protein-coupled receptor signaling in osteoblasts elicits age-dependent effects on bone formation	Hsiao EC, Boudignon BM, Halloran BP, Nissenson RA, Conklin BR	J Bone Miner Res	1/8/2010	20200944
Modeling disease in human ESCs using an efficient BAC-based homologous recombination system	Song H, Chung SK, Xu Y	Cell Stem Cell	1/8/2010	20074536

APPENDIX 5

Title	Authors	Journal	Date	PMID
p53 and stem cells: new developments and new concerns	Zhao T, Xu Y	Trends Cell Biol	1/8/2010	20061153
Opposing microRNA families regulate self-renewal in mouse embryonic stem cells	Melton C, Judson RL, Blelloch R	Nature	1/6/2010	20054295
Restricted ethnic diversity in human embryonic stem cell lines	Laurent LC, Nievergelt CM, Lynch C, Fakunle E, Harness JV, Schmidt U, Galat V, Laslett AL, Otonkoski T, Keirstead HS, Schork A, Park HS, Loring JF	Nat Methods	1/1/2010	20038950
Functional and transcriptional characterization of human embryonic stem cell-derived endothelial cells for treatment of myocardial infarction	Li Z, Wilson KD, Smith B, Kraft DL, Jia F, Huang M, Xie X, Robbins RC, Gambhir SS, Weissman IL, Wu JC	PLoS ONE	12/31/2009	20046878
Intranasal administration of PEGylated transforming growth factor-alpha improves behavioral deficits in a chronic stroke model	Guerra-Crespo M, Sistos A, Gleason D, Fallon JH	J Stroke Cerebrovasc Dis	12/30/2009	20123220
Suppression of Alk8-mediated Bmp signaling cell-autonomously induces pancreatic {beta}-cells in zebrafish	Chung WS, Andersson O, Row R, Kimelman D, Stainier DY	Proc Natl Acad Sci U S A	12/29/2009	20080554
Jarid2/Jumonji coordinates control of PRC2 enzymatic activity and target gene occupancy in pluripotent cells	Peng JC, Valouev A, Swigut T, Zhang J, Zhao Y, Sidow A, Wysocka J	Cell	12/24/2009	20064375
A highly efficient short hairpin RNA potently down-regulates CCR5 expression in systemic lymphoid organs in the hu-BLT mouse model	Shimizu S, Hong P, Arumugam B, Pokomo L, Boyer J, Koizumi N, Kittipongdaja P, Chen A, Bristol G, Galic Z, Zack JA, Yang O, Chen IS, Lee B, An DS	Blood	12/17/2009	20018916

APPENDIX 5

Title	Authors	Journal	Date	PMID
Electrophysiological challenges of cell-based myocardial repair	Chen HS, Kim C, Mercola M	Circulation	12/15/2009	20008740
miR-19 is a key oncogenic component of mir-17-92	Olive V, Bennett MJ, Walker JC, Ma C, Jiang I, Cordon-Cardo C, Li QJ, Lowe SW, Hannon GJ, He L	Genes Dev	12/15/2009	20008935
Accumulation of a differentiation regulator specifies transit amplifying division number in an adult stem cell lineage	Insco ML, Leon A, Tam CH, McKearin DM, Fuller MT	Proc Natl Acad Sci U S A	12/14/2009	20018708
Non-cardiomyocytes influence the electrophysiological maturation of human embryonic stem cell-derived cardiomyocytes during differentiation	Kim C, Majdi M, Xia P, Wei K, Talantova M, Spiering S, Nelson B, Mercola M, Chen HS	Stem Cells Dev	12/10/2009	20001453
De novo design of saccharide-peptide hydrogels as synthetic scaffolds for tailored cell responses	Liao SW, Yu TB, Guan Z	J Am Chem Soc	12/9/2009	19908839
Engineering antigen-specific T cells from genetically modified human hematopoietic stem cells in immunodeficient mice	Kitchen SG, Bennett M, Galić Z, Kim J, Xu Q, Young A, Lieberman A, Joseph A, Goldstein H, Ng H, Yang O, Zack JA	PLoS ONE	12/7/2009	19997617
Tunable shrink-induced honeycomb microwell arrays for uniform embryoid bodies	Nguyen D, Sa S, Pegan JD, Rich B, Xiang G, McCloskey KE, Manilay JO, Khine M	Lab Chip	12/7/2009	19904398
ChIP-Seq of transcription factors predicts absolute and differential gene expression in embryonic stem cells	Ouyang Z, Zhou Q, Wong WH	Proc Natl Acad Sci U S A	12/7/2009	19995984
Floxin, a resource for genetically engineering mouse ESCs	Singla V, Hunkapiller J, Santos N, Seol AD, Norman AR, Wakenight P, Skarnes WC, Reiter JF	Nat Methods	12/6/2009	19966808

APPENDIX 5

Title	Authors	Journal	Date	PMID
GABAergic interneuron dysfunction impairs hippocampal neurogenesis in adult apolipoprotein e4 knockin mice	Li G, Bien-Ly N, Andrews-Zwilling Y, Xu Q, Bernardo A, Ring K, Halabisky B, Deng C, Mahley RW, Huang Y	Cell Stem Cell	12/4/2009	19951691
Protective effects of human iPS-derived retinal pigment epithelium cell transplantation in the retinal dystrophic rat	Carr AJ, Vugler AA, Hikita ST, Lawrence JM, Gias C, Chen LL, Buchholz DE, Ahmado A, Semo M, Smart MJ, Hasan S, da Cruz L, Johnson LV, Clegg DO, Coffey PJ	PLoS ONE	12/3/2009	19997644
Electrophysiological properties of human induced pluripotent stem cells	Jiang P, Rushing S, Kong CW, Fu J, Lieu DK, Chan C, Deng W, Li R	Am J Physiol Cell Physiol	12/2/2009	19955484
Current-controlled electrical point-source stimulation of embryonic stem cells	Chen MQ, Xie X, Wilson KD, Sun N, Wu JC, Giovangrandi L, Kovacs GT	Cell Mol Bioeng	12/1/2009	n/a
Induction of chondrogenesis from human embryonic stem cells without embryoid body formation by bone morphogenetic protein 7 and transforming growth factor beta1	Nakagawa T, Lee SY, Reddi AH	Arthritis Rheum	11/30/2009	19950276
Anatomic demarcation of cells: genes to patterns	Chang HY	Science	11/27/2009	19965461
The geoepidemiology of immune thrombocytopenic purpura	Deane S, Teuber SS, Gershwin ME	Autoimmun Rev	11/27/2009	19945546
Designing materials to direct stem-cell fate	Lutolf MP, Gilbert PM, Blau HM	Nature	11/26/2009	19940913
Mesenchymal stem cells derived from human gingiva are capable of immunomodulatory functions and ameliorate inflammation-related tissue destruction in experimental colitis	Zhang Q, Shi S, Liu Y, Uyanne J, Shi Y, Shi S, Le AD	J Immunol	11/18/2009	19923445

APPENDIX 5

Title	Authors	Journal	Date	PMID
In vivo kinetics of embryonic stem cell viability following transplantation into the injured murine myocardium	Chung J, Kee K, Barral JK, Dash R, Weissman I, Quertermous T, Robbins RC, Nishimura DG, Reijo-Pera RA, Yang PC	Circulation	11/14/2009	n/a
Tumor-like stem cells derived from human keloid are governed by the inflammatory niche driven by IL-17/IL-6 axis	Zhang Q, Yamaza T, Kelly AP, Shi S, Wang S, Brown J, Wang L, French SW, Shi S, Le AD	PLoS ONE	11/11/2009	19907660
G(i)-coupled GPCR signaling controls the formation and organization of human pluripotent colonies	Nakamura K, Salmonis N, Tomoda K, Yamanaka S, Conklin BR	PLoS ONE	11/10/2009	19936228
Rescue of radiation-induced cognitive impairment through cranial transplantation of human embryonic stem cells	Acharya MM, Christie LA, Lan ML, Donovan PJ, Cotman CW, Fike JR, Limoli CL	Proc Natl Acad Sci U S A	11/10/2009	19901336
FoxO3 regulates neural stem cell homeostasis	Renault VM, Rafalski VA, Morgan AA, Salih DA, Brett JO, Webb AE, Villeda SA, Thekkat PU, Guillerey C, Denko NC, Palmer TD, Butte AJ, Brunet A	Cell Stem Cell	11/6/2009	19896443
Alternative splicing in the differentiation of human embryonic stem cells into cardiac precursors	Salomonis N, Nelson B, Vranizan K, Pico AR, Hanspers K, Kuchinsky A, Ta L, Mercola M, Conklin BR	PLoS Comput Biol	11/6/2009	19893621
A histone demethylase is necessary for regeneration in zebrafish	Stewart S, Tsun ZY, Izpisua Belmonte JC	Proc Natl Acad Sci U S A	11/6/2009	19897725
Mitochondrial energetics and therapeutics	Wallace DC, Fan W, Procaccio V	Annu Rev Pathol	11/3/2009	20078222
High-content screening of primary neurons: ready for prime time	Daub A, Sharma P, Finkbeiner S	Curr Opin Neurobiol	11/2/2009	19889533

APPENDIX 5

Title	Authors	Journal	Date	PMID
Parsing the niche code: the molecular mechanisms governing hematopoietic stem cell adhesion and differentiation	Forsberg EC, Smith-Berdan S	Haematologica	11/1/2009	19880773
The occurrence and management of fluid retention associated with TKI therapy in CML, with a focus on dasatinib	Masiello D, Gorospe G 3rd, Yang AS	J Hematol Oncol	11/1/2009	19909541
Labeling human embryonic stem cell derived cardiomyocytes with indocyanine green for noninvasive tracking with optical imaging: an FDA compatible alternative to firefly luciferase	Boddington SE, Henning TD, Jha P, Schlieve CR, Mandrussow L, Denardo D, Bernstein HS, Ritner C, Golovko D, Lu Y, Zhao S, Daldrup-Link HE	Cell Transplant	10/29/2009	19878626
Human DAZL, DAZ and BOULE genes modulate primordial germ-cell and haploid gamete formation	Kee K, Angeles VT, Flores M, Nguyen HN, Reijo Pera RA	Nature	10/28/2009	19865085
Finding distal regulatory elements in the human genome	Heintzman ND, Ren B	Curr Opin Genet Dev	10/23/2009	19854636
Generation of human-induced pluripotent stem cells in the absence of exogenous Sox2	Li W, Zhou H, Abujarour R, Zhu S, Young Joo J, Lin T, Hao E, Schöler HR, Hayek A, Ding S	Stem Cells	10/16/2009	19839055
Immune influence on adult neural stem cell regulation and function	Carpentier PA, Palmer TD	Neuron	10/15/2009	19840551
Cytokines and CNS development	Deverman BE, Patterson PH	Neuron	10/15/2009	19840550
Hypoxia selectively inhibits KCNA5 channels in pulmonary artery smooth muscle cells	Firth AL, Platoshyn O, Brevnova EE, Burg ED, Powell F, Haddad GH, Yuan JX	Ann N Y Acad Sci	10/15/2009	19845612

APPENDIX 5

Title	Authors	Journal	Date	PMID
Ly6d marks the earliest stage of B-cell specification and identifies the branchpoint between B-cell and T-cell development	Inlay MA, Bhattacharya D, Sahoo D, Serwold T, Seita J, Karsunky H, Plevritis SK, Dill DL, Weissman IL	Genes Dev	10/15/2009	19833765
Human DNA methylomes at base resolution show widespread epigenomic differences	Lister R, Pelizzola M, Dowen RH, Hawkins RD, Hon G, Tonti-Filippini J, Nery JR, Lee L, Ye Z, Ngo QM, Edsall L, Antosiewicz-Bourget J, Stewart R, Ruotti V, Millar AH, Thomson JA, Ren B, Ecker JR	Nature	10/14/2009	19829295
Regulative recovery in the sea urchin embryo and the stabilizing role of fail-safe gene network wiring	Smith J, Davidson EH	Proc Natl Acad Sci U S A	10/12/2009	19822764
Roles of integrins in human induced pluripotent stem cell growth on matrigel and vitronectin	Rowland TJ, Miller LM, Blaschke AJ, Doss EL, Bonham AJ, Hikita ST, Johnson LV, Clegg DO	Stem Cells Dev	10/7/2009	19811096
Genome integrity: linking pluripotency and tumorgenicity	Deng W, Xu Y	Trends Genet	10/2/2009	19801173
Magnetic resonance imaging of human embryonic stem cells	Chung J, Yamada M, Yang PC	Curr Protoc Stem Cell Biol	10/1/2009	19653198
Dendritic cell vaccination combined with CTLA4 blockade in patients with metastatic melanoma	Ribas A, Comin-Anduix B, Chmielowski B, Jalil J, de la Rocha P, McCannel TA, Ochoa MT, Seja E, Villanueva A, Oseguera DK, Straatsma BR, Cochran AJ, Glaspy JA, Hui L, Marincola FM, Wang E, Economou JS, Gomez-Navarro J	Clin Cancer Res	10/1/2009	19789309
Molecular aging and rejuvenation of human muscle stem cells	Carlson ME, Suetta C, Conboy MJ, Aagaard P, Mackey A, Kjaer M, Conboy I	EMBO Mol Med	9/30/2009	20049743

APPENDIX 5

Title	Authors	Journal	Date	PMID
Energetics, epigenetics, mitochondrial genetics	Wallace DC, Fan W	Mitochondrion	9/28/2009	19796712
Ago2 immunoprecipitation identifies predicted microRNAs in human embryonic stem cells and neural precursors	Goff LA, Davila J, Swerdel MR, Moore JC, Cohen RI, Wu H, Sun YE, Hart RP	PLoS ONE	9/28/2009	19784364
Enhanced generation of induced pluripotent stem cells from a subpopulation of human fibroblasts	Byrne JA, Nguyen HN, Reijo Pera RA	PLoS ONE	9/23/2009	19774082
Identification by automated screening of a small molecule that selectively eliminates neural stem cells derived from hESCs but not dopamine neurons	Han Y, Miller A, Mangada J, Liu Y, Swistowski A, Zhan M, Rao MS, Zeng X	PLoS ONE	9/23/2009	19774075
Acting locally and globally: Myc's ever-expanding roles on chromatin	Varlakhanova NV, Knoepfler PS	Cancer Res	9/22/2009	19773445
Transcriptional signature and memory retention of human-induced pluripotent stem cells	Marchetto MC, Yeo GW, Kainohana O, Marsala M, Gage FH, Muotri AR	PLoS ONE	9/18/2009	19763270
Keeping an eye on retinoblastoma control of human embryonic stem cells	Conklin JF, Sage J	J Cell Biochem	9/16/2009	19760644
nAChRs mediate human embryonic stem cell-derived endothelial cells: proliferation, apoptosis, and angiogenesis	Yu J, Huang NF, Wilson KD, Velotta JB, Huang M, Li Z, Lee A, Robbins RC, Cooke JP, Wu JC	PLoS ONE	9/15/2009	19753305
A home away from home: challenges and opportunities in engineering in vitro muscle satellite cell niches	Cosgrove BD, Sacco A, Gilbert PM, Blau HM	Differentiation	9/12/2009	19751902
Genomic analysis suggests that mRNA destabilization by the microprocessor is specialized for the auto-regulation of Dgcr8	Shenoy A, Blelloch R	PLoS ONE	9/11/2009	19759829

APPENDIX 5

Title	Authors	Journal	Date	PMID
Modeling conduction in host-graft interactions between stem cell grafts and cardiomyocytes	Chen MQ, Yu J, Whittington R, Wu JC, Kovacs GT, Giovangrandi L	Conf Proc IEEE Eng Med Biol Soc	9/3/2009	19964687
Conduction analysis in mixed cardiomyocytes-fibroblasts cultures using microelectrode arrays	Roy S, Chen MQ, Kovacs GT, Giovangrandi L	Conf Proc IEEE Eng Med Biol Soc	9/3/2009	19964347
Injectable myocardial matrix as a scaffold for myocardial tissue engineering	Singelyn JM, Dequach JA, Christman KL	Conf Proc IEEE Eng Med Biol Soc	9/3/2009	19964956
Relative roles of TGF-beta1 and Wnt in the systemic regulation and aging of satellite cell responses	Carlson ME, Conboy MJ, Hsu M, Barchas L, Jeong J, Agrawal A, Mikels AJ, Agrawal S, Schaffer DV, Conboy IM	Aging Cell	9/2/2009	19732043
Sleep homeostasis modulates hypocretin-mediated sleep-to-wake transitions	Carter ME, Adamantidis A, Ohtsu H, Deisseroth K, de Lecea L	J Neurosci	9/2/2009	19726652
Investigating the role of the extracellular environment in modulating hepatic stellate cell biology with arrayed combinatorial microenvironments	Brafman DA, de Minicis S, Seki E, Shah KD, Teng D, Brenner D, Willert K, Chien S	Integr Biol (Camb)	9/1/2009	20023766
A new feeder-free technique to expand human embryonic stem cells and induced pluripotent stem Cells	Denham M, Leung J, Tay C, Wong RC, Donovan P, Dottori M, Pebay A	Open Stem Cell J	9/1/2009	n/a
Na+/Ca2+ exchanger is a determinant of excitation-contraction coupling in human embryonic stem cell-derived ventricular cardiomyocytes	Fu JD, Jiang P, Rushing S, Liu J, Chiamvimonvat N, Li RA	Stem Cells Dev	8/31/2009	19719399
Versatile synthesis and rational design of caged morpholinos	Ouyang X, Shestopalov IA, Sinha S, Zheng G, Pitt CL, Li WH, Olson AJ, Chen JK	J Am Chem Soc	8/26/2009	19708646

APPENDIX 5

Title	Authors	Journal	Date	PMID
Effects of cell number on teratoma formation by human embryonic stem cells	Lee AS, Tang C, Cao F, Xie X, van der Bogt K, Hwang A, Connolly AJ, Robbins RC, Wu JC	Cell Cycle	8/24/2009	19597339
A study on the interactions between heparan sulfate proteoglycans and Wnt proteins	Fuerer C, Habib SJ, Nusse R	Dev Dyn	8/24/2009	19705435
Reduction of seizures by transplantation of cortical GABAergic interneuron precursors into Kv1.1 mutant mice	Baraban SC, Southwell DG, Estrada RC, Jones DL, Sebe JY, Alfaro-Cervello C, García-Verdugo JM, Rubenstein JL, Alvarez-Buylla A	Proc Natl Acad Sci U S A	8/24/2009	19706400
Posterior malformations in Dact1 mutant mice arise through misregulated Vangl2 at the primitive streak	Suriben R, Kivimäe S, Fisher DA, Moon RT, Cheyette BN	Nat Genet	8/23/2009	19701191
iPS cells: insights into basic biology	Ramalho-Santos M	Cell	8/21/2009	19703387
Detection of protein ubiquitination	Choo YS, Zhang Z	J Vis Exp	8/19/2009	19692941
Notch1 represses osteogenic pathways in aortic valve cells	Nigam V, Srivastava D	J Mol Cell Cardiol	8/18/2009	19695258
Identification and characterization of posttranslational modification-specific binding proteins in vivo by mammalian tethered catalysis	Spektor TM, Rice JC	Proc Natl Acad Sci U S A	8/18/2009	19706462
Phosphoproteomic analysis of human embryonic stem cells	Brill LM, Xiong W, Lee KB, Ficarro SB, Crain A, Xu Y, Terskikh A, Snyder EY, Ding S	Cell Stem Cell	8/7/2009	19664994
L1 retrotransposition in human neural progenitor cells	Coufal NG, Garcia-Perez JL, Peng GE, Yeo GW, Mu Y, Lovci MT, Morell M, O'Shea KS, Moran JV, Gage FH	Nature	8/5/2009	19657334

APPENDIX 5

Title	Authors	Journal	Date	PMID
Derivation of functional retinal pigmented epithelium from induced pluripotent stem cells	Buchholz DE, Hikita ST, Rowland TJ, Friedrich AM, Hinman CR, Johnson LV, Clegg DO	Stem Cells	8/5/2009	19658190
New regulatory mechanisms of TGF-beta receptor function	Kang JS, Liu C, Derynck R	Trends Cell Biol	8/3/2009	19648010
Adult mice generated from induced pluripotent stem cells	Boland MJ, Hazen JL, Nazor KL, Rodriguez AR, Gifford W, Martin G, Kupriyanov S, Baldwin KK	Nature	8/2/2009	19672243
The pathophysiology of mitochondrial disease as modeled in the mouse	Wallace DC, Fan W	Genes Dev	8/1/2009	19651984
Chronic myeloproliferative diseases with and without the Ph chromosome: some unresolved issues	Goldman JM, Green AR, Holyoake T, Jamieson C, Mesa R, Mughal T, Pellicano F, Perrotti D, Skoda R, Vannucchi AM	Leukemia	7/30/2009	19641523
Inhibition of mTOR attenuates store-operated Ca2+ entry in cells from endarterectomized tissues of patients with chronic thromboembolic pulmonary hypertension	Ogawa A, Firth AL, Yao W, Madani MM, Kerr KM, Auger WR, Jamieson SW, Thistlethwaite PA, Yuan JX	Am J Physiol Lung Cell Mol Physiol	7/24/2009	19633069
Neural stem cells improve cognition via BDNF in a transgenic model of Alzheimer disease	Blurton-Jones M, Kitazawa M, Martinez-Coria H, Castello NA, Müller FJ, Loring JF, Yamasaki TR, Poon WW, Green KN, Laferla FM	Proc Natl Acad Sci U S A	7/24/2009	19633196
CD47 is upregulated on circulating hematopoietic stem cells and leukemia cells to avoid phagocytosis	Jaiswal S, Jamieson CH, Pang WW, Park CY, Chao MP, Majeti R, Traver D, van Rooijen N, Weissman IL	Cell	7/23/2009	19632178
PARP-1 deficiency increases the severity of disease in a mouse model of multiple sclerosis	Selvaraj V, Soundarapandian MM, Chechneva O, Williams AJ, Sidorov MK, Soulika AM, Pleasure DE, Deng W	J Biol Chem	7/23/2009	19628872

APPENDIX 5

Title	Authors	Journal	Date	PMID
Signed weighted gene co-expression network analysis of transcriptional regulation in murine embryonic stem cells	Mason MJ, Fan G, Plath K, Zhou Q, Horvath S	BMC Genomics	7/20/2009	19619308
A regulatory pathway involving Notch1/beta-catenin/Isl1 determines cardiac progenitor cell fate	Kwon C, Qian L, Cheng P, Nigam V, Arnold J, Srivastava D	Nat Cell Biol	7/20/2009	19620969
Digital RNA allelotyping reveals tissue-specific and allele-specific gene expression in human	Zhang K, Li JB, Gao Y, Egli D, Xie B, Deng J, Li Z, Lee JH, Aach J, Leproust EM, Eggan K, Church GM	Nat Methods	7/20/2009	19620972
Regeneration of the mammalian inner ear sensory epithelium	Wei D, Yamoah EN	Curr Opin Otolaryngol Head Neck Surg	7/15/2009	19617827
Naturally derived myocardial matrix as an injectable scaffold for cardiac tissue engineering	Singelyn JM, Dequach JA, Seif-Naraghi SB, Littlefield RB, Schup-Magoffin PJ, Christman KL	Biomaterials	7/14/2009	19608268
Xeno-free defined conditions for culture of human embryonic stem cells, neural stem cells and dopaminergic neurons derived from them	Swistowski A, Peng J, Han Y, Swistowska AM, Rao MS, Zeng X	PLoS ONE	7/14/2009	19597550
Nkx6-1 controls the identity and fate of red nucleus and oculomotor neurons in the mouse midbrain	Prakash N, Puelles E, Freude K, Trümbach D, Omodei D, Di Salvio M, Sussel L, Ericson J, Sander M, Simeone A, Wurst W	Development	7/10/2009	19592574
TACE-mediated ectodomain shedding of the type I TGF-beta receptor downregulates TGF-beta signaling	Liu C, Xu P, Lamouille S, Xu J, Derynck R	Mol Cell	7/10/2009	19595713

APPENDIX 5

Title	Authors	Journal	Date	PMID
Specific loss of histone H3 lysine 9 trimethylation and HP1gamma/cohesin binding at D4Z4 repeats is associated with facioscapulohumeral dystrophy (FSHD)	Zeng W, de Greef JC, Chen YY, Chien R, Kong X, Gregson HC, Winokur ST, Pyle A, Robertson KD, Schmiesing JA, Kimonis VE, Balog J, Frants RR, Ball AR Jr, Lock LF, Donovan PJ, van der Maarel SM, Yokomori K	PLoS Genet	7/10/2009	19593370
Chd1 regulates open chromatin and pluripotency of embryonic stem cells	Gaspar-Maia A, Alajem A, Polesso F, Sridharan R, Mason MJ, Heidersbach A, Ramalho-Santos J, McManus MT, Plath K, Meshorer E, Ramalho-Santos M	Nature	7/8/2009	19587682
Polysialic acid governs T-cell development by regulating progenitor access to the thymus	Drake PM, Stock CM, Nathan JK, Gip P, Golden KP, Weinhold B, Gerardy-Schahn R, Bertozzi CR	Proc Natl Acad Sci U S A	7/8/2009	19587240
Methods for analysis of brain tumor stem cell and neural stem cell self-renewal	Nakano I, Kornblum HI	Methods Mol Biol	7/7/2009	19582420
Common variable immunodeficiency: etiological and treatment issues	Deane S, Selmi C, Naguwa SM, Teuber SS, Gershwin ME	Int Arch Allergy Immunol	7/5/2009	19571563
miR-145 and miR-143 regulate smooth muscle cell fate and plasticity	Cordes KR, Sheehy NT, White MP, Berry EC, Morton SU, Muth AN, Lee TH, Miano JM, Ivey KN, Srivastava D	Nature	7/5/2009	19578358
Utility of PDL progenitors for in vivo tissue regeneration: a report of 3 cases	Feng F, Akiyama K, Liu Y, Yamaza T, Wang TM, Chen JH, Wang B, Huang G, Wang S, Shi S	Oral Dis	7/2/2009	20355278
Deletion of Pten expands lung epithelial progenitor pools and confers resistance to airway injury	Tiozzo C, De Langhe S, Yu M, Londhe VA, Carraro G, Li M, Li C, Xing Y, Anderson S, Borok Z, Bellusci S, Minoo P	Am J Respir Crit Care Med	7/2/2009	19574443

APPENDIX 5

Title	Authors	Journal	Date	PMID
Induced pluripotent stem cells and embryonic stem cells are distinguished by gene expression signatures	Chin MH, Mason MJ, Xie W, Volinia S, Singer M, Peterson C, Ambartsumyan G, Aimiuwu O, Richter L, Zhang J, Khvorostov I, Ott V, Grunstein M, Lavon N, Benvenisty N, Croce CM, Clark AT, Baxter T, Pyle AD, Teitell MA, Pelegrini M, Plath K, Lowry WE	Cell Stem Cell	7/2/2009	19570518
Pluripotent stem cell-derived gametes: truth and (potential) consequences	Mathews DJ, Donovan PJ, Harris J, Lovell-Badge R, Savulescu J, Faden R	Cell Stem Cell	7/2/2009	19570509
Improving orthogonal tRNA-synthetase recognition for efficient unnatural amino acid incorporation and application in mammalian cells	Takimoto JK, Adams KL, Xiang Z, Wang L	Mol Biosyst	7/2/2009	19668857
Bone marrow-derived mesenchymal stem cells in fibrin augment angiogenesis in the chronically infarcted myocardium	Huang NF, Lam A, Fang Q, Sievers RE, Li S, Lee RJ	Regen Med	7/1/2009	19580402
Mutations in CBL occur frequently in juvenile myelomonocytic leukemia	Loh ML, Sakai DS, Flotho C, Kang M, Fliegauf M, Archambeault S, Mullighan CG, Chen L, Bergstraesser E, Bueso-Ramos CE, Emanuel PD, Hasle H, Issa JP, van den Heuvel-Eibrink MM, Locatelli F, Stary J, Trebo M, Wlodarski M, Zecca M, Shannon KM, Niemeyer CM	Blood	7/1/2009	19571318
Bendamustine therapy in chronic lymphocytic leukemia	Masiello D, Tulpule A	Expert Opin Pharmacother	7/1/2009	19527193

APPENDIX 5

Title	Authors	Journal	Date	PMID
Fibroblast growth factor 10 plays a causative role in the tracheal cartilage defects in a mouse model of Apert syndrome	Tiozzo C, De Langhe S, Carraro G, Al Alam D, Nagy A, Wigfall C, Hajihosseini MK, Warburton D, Minoo P, Bellusci S	Pediatr Res	7/1/2009	19581825
Mitochondrial dysfunction in CA1 hippocampal neurons of the Ube3a deficient mouse model for Angelman syndrome	Su H, Fan W, Coskun PE, Vesa J, Gold JA, Jiang YH, Potluri P, Procaccio V, Acab A, Weiss JH, Wallace DC, Kimonis VE	Neurosci Lett	6/26/2009	19563863
Comparison of gene-transfer efficiency in human embryonic stem cells	Cao F, Xie X, Gollan T, Zhao L, Narsinh K, Lee RJ, Wu JC	Mol Imaging Biol	6/24/2009	19551446
Maintaining retinal astrocytes normalizes revascularization and prevents vascular pathology associated with oxygen-induced retinopathy	Dorrell MI, Aguilar E, Jacobson R, Trauger SA, Friedlander J, Siuzdak G, Friedlander M	Glia	6/23/2009	19544395
Regenerative growth in Drosophila imaginal discs is regulated by Wingless and Myc	Smith-Bolton RK, Worley MI, Kanda H, Hariharan IK	Dev Cell	6/15/2009	19531351
Directing hepatic differentiation of embryonic stem cells with protein microarray-based co-cultures	Lee JY, Tuleuova N, Jones CN, Ramanculov E, Zern MA, Revzin A	Integr Biol (Camb)	6/12/2009	20023756
Hematopoietic cell development in the zebrafish embryo	Bertrand JY, Traver D	Curr Opin Hematol	6/10/2009	19491671
Characterization of a potent non-cytotoxic shRNA directed to the HIV-1 co-receptor CCR5	Shimizu S, Kamata M, Kittipongdaja P, Chen KN, Kim S, Pang S, Boyer J, Qin FX, An DS, Chen IS	Genet Vaccines Ther	6/10/2009	19515239
N-Myc regulates expression of pluripotency genes in neuroblastoma including lif, klf2, klf4, and lin28b	Cotterman R, Knoepfler PS	PLoS ONE	6/4/2009	19495417

APPENDIX 5

Title	Authors	Journal	Date	PMID
Renal ontogeny in the rhesus monkey (Macaca mulatta) and directed differentiation of human embryonic stem cells towards kidney precursors	Batchelder CA, Lee CC, Matsell DG, Yoder MC, Tarantal AF	Differentiation	6/3/2009	19500897
Early postnatal proteolipid promoter-expressing progenitors produce multilineage cells in vivo	Guo F, Ma J, McCauley E, Bannerman P, Pleasure D	J Neurosci	6/3/2009	19494148
Quo vadis, hair cell regeneration?	Brigande JV, Heller S	Nat Neurosci	5/26/2009	19471265
Endogenous remyelination is induced by transplant rejection in a viral model of multiple sclerosis	Hatch MN, Schaumburg CS, Lane TE, Keirstead HS	J Neuroimmunol	5/22/2009	19477025
CTLA4 blockade increases Th17 cells in patients with metastatic melanoma	von Euw E, Chodon T, Attar N, Jalil J, Koya RC, Comin-Anduix B, Ribas A	J Transl Med	5/20/2009	19457253
Efficient siRNA delivery into primary cells by a peptide transduction domain-dsRNA binding domain fusion protein	Eguchi A, Meade BR, Chang YC, Fredrickson CT, Willert K, Puri N, Dowdy SF	Nat Biotechnol	5/17/2009	19448630
A targeted neuroglial reporter line generated by homologous recombination in human embryonic stem cells	Xue H, Wu S, Papadeas ST, Spusta S, Swistowska AM, Macarthur CC, Mattson MP, Maragakis NJ, Capecchi MR, Rao MS, Zeng X, Liu Y	Stem Cells	5/14/2009	19544414
Cell cycle regulation by MicroRNAs in embryonic stem cells	Wang Y, Blelloch R	Cancer Res	5/12/2009	19435891
Molecular and magnetic resonance imaging of human embryonic stem cell-derived neural stem cell grafts in ischemic rat brain	Daadi MM, Li Z, Arac A, Grueter BA, Sofilos M, Malenka RC, Wu JC, Steinberg GK	Mol Ther	5/12/2009	19436269
A small molecule primes embryonic stem cells for differentiation	Zhu S, Wurdak H, Wang J, Lyssiotis CA, Peters EC, Cho CY, Wu X,	Cell Stem Cell	5/8/2009	19427291

Title	Authors	Journal	Date	PMID
	Schultz PG			
Wnt5a knock-out mouse as a new model of anorectal malformation	Tai CC, Sala FG, Ford HR, Wang KS, Li C, Minoo P, Grikscheit TC, Bellusci S	J Surg Res	5/8/2009	19577771
Tissue-engineered small intestine and stomach form from autologous tissue in a preclinical large animal model	Sala FG, Kunisaki SM, Ochoa ER, Vacanti J, Grikscheit TC	J Surg Res	5/3/2009	19665143
Receptor for advanced glycation end-products (RAGE) is an indicator of direct lung injury in models of experimental lung injury	Su X, Looney MR, Gupta N, Matthay MA	Am J Physiol Lung Cell Mol Physiol	5/1/2009	19411309
Stem cell and regenerative science applications in the development of bioengineering of renal tissue	Perin L, Giuliani S, Sedrakyan S, DA Sacco S, De Filippo RE	Pediatr Res	5/1/2009	18427289
MicroRNA-145 regulates Oct4, Sox2, and Klf4 and represses pluripotency in human embryonic stem cells	Xu N, Papagiannakopoulos T, Pan G, Thomson JA, Kosik KS	Cell	4/30/2009	19409607
Sustained in vitro intestinal epithelial culture within a Wnt-dependent stem cell niche	Ootani A, Li X, Sangiorgi E, Ho QT, Ueno H, Toda S, Sugihara H, Fujimoto K, Weissman IL, Capecchi MR, Kuo CJ	Nat Med	4/27/2009	19398967
A central role for the small GTPase Rac1 in hippocampal plasticity and spatial learning and memory	Haditsch U, Leone DP, Farinelli M, Chrostek-Grashoff A, Brakebusch C, Mansuy IM, McConnell SK, Palmer TD	Mol Cell Neurosci	4/24/2009	19394428
Dlx1&2 and Mash1 transcription factors control MGE and CGE patterning and differentiation through parallel and overlapping pathways	Long JE, Cobos I, Potter GB, Rubenstein JL	Cereb Cortex	4/22/2009	19386638

APPENDIX 5

Title	Authors	Journal	Date	PMID
A variable torque motor compatible with magnetic resonance imaging	Roeck WW, Ha SH, Farmaka S, Nalcioglu O	Rev Sci Instrum	4/22/2009	19405704
Molecular imaging of human embryonic stem cells	Narsinh KH, Cao F, Wu JC	Methods Mol Biol	4/20/2009	19405224
Cultivating liver cells on printed arrays of hepatocyte growth factor	Jones CN, Tuleuova N, Lee JY, Ramanculov E, Reddi AH, Zern MA, Revzin A	Biomaterials	4/17/2009	19375794
PhiC31 integrase for modification of stem cells	Jung WE, Calos MP	Emerging Technology Platforms for Stem Cells	4/17/2009	n/a
Parvalbumin neurons and gamma rhythms enhance cortical circuit performance	Sohal VS, Zhang F, Yizhar O, Deisseroth K	Nature	4/16/2009	19396159
Embryonic stem cell–specific microRNAs promote induced pluripotency	Judson RL, Babiarz JE, Venere M, Blelloch R	Nat Biotechnol	4/12/2009	19363475
Chronic exposure to fibrin and fibrinogen differentially regulates intracellular Ca2+ in human pulmonary arterial smooth muscle and endothelial cells	Firth AL, Yau J, White A, Chiles PG, Marsh JJ, Morris TA, Yuan JX	Am J Physiol Lung Cell Mol Physiol	4/10/2009	19363122
Hedgehog signalling is essential for maintenance of cancer stem cells in myeloid leukaemia	Zhao C, Chen A, Jamieson CH, Fereshteh M, Abrahamsson A, Blum J, Kwon HY, Kim J, Chute JP, Rizzieri D, Munchhof M, VanArsdale T, Beachy PA, Reya T	Nature	4/9/2009	19169242
Inositol phosphatase SHIP1 is a primary target of miR-155	O'Connell RM, Chaudhuri AA, Rao DS, Baltimore D	Proc Natl Acad Sci U S A	4/9/2009	19359473
Facilitated maturation of Ca2+ handling properties of human embryonic stem cell-derived cardiomyocytes by calsequestrin expression	Liu J, Lieu DK, Siu CW, Fu JD, Tse HF, Li RA	Am J Physiol Cell Physiol	4/8/2009	19357236

APPENDIX 5

Title	Authors	Journal	Date	PMID
Chapter 1 gene regulatory networks in neural crest development and evolution	Nikitina N, Sauka-Spengler T, Bronner-Fraser M	Curr Top Dev Biol	4/8/2009	19361687
Lentiviral vectors and protocols for creation of stable hESC lines for fluorescent tracking and drug resistance selection of cardiomyocytes	Kita-Matsuo H, Barcova M, Prigozhina N, Salomonis N, Wei K, Jacot JG, Nelson B, Spiering S, Haverslag R, Kim C, Talantova M, Bajpai R, Calzolari D, Terskikh A, McCulloch AD, Price JH, Conklin BR, Chen HS, Mercola M	PLoS ONE	4/8/2009	19352491
JunB protects against myeloid malignancies by limiting hematopoietic stem cell proliferation and differentiation without affecting self-renewal	Santaguida M, Schepers K, King B, Sabnis AJ, Forsberg EC, Attema JL, Braun BS, Passegué E	Cancer Cell	4/7/2009	19345332
Global levels of histone modifications predict prognosis in different cancers	Seligson DB, Horvath S, McBrian MA, Mah V, Yu H, Tze S, Wang Q, Chia D, Goodglick L, Kurdistani SK	Am J Pathol	4/6/2009	19349354
A Nurr1/CoREST pathway in microglia and astrocytes protects dopaminergic neurons from inflammation-induced death	Saijo K, Winner B, Carson CT, Collins JG, Boyer L, Rosenfeld MG, Gage FH, Glass CK	Cell	4/3/2009	19345186
Manipulation of an innate escape response in Drosophila: photoexcitation of acj6 neurons induces the escape response	Zimmermann G, Wang LP, Vaughan AG, Manoli DS, Zhang F, Deisseroth K, Baker BS, Scott MP	PLoS ONE	4/2/2009	19340304
Imaging of STAT3 signaling pathway during mouse embryonic stem cell differentiation	Xie X, Chan KS, Cao F, Huang M, Li Z, Lee A, Weissman IL, Wu JC	Stem Cells Dev	4/1/2009	18576943

APPENDIX 5

Title	Authors	Journal	Date	PMID
Targeted bisulfite sequencing reveals changes in DNA methylation associated with nuclear reprogramming	Deng J, Shoemaker R, Xie B, Gore A, LeProust EM, Antosiewicz-Bourget J, Egli D, Maherali N, Park IH, Yu J, Daley GQ, Eggan K, Hochedlinger K, Thomson J, Wang W, Gao Y, Zhang K	Nat Biotechnol	3/29/2009	19330000
Expanding the genetic code for biological studies	Wang Q, Parrish AR, Wang L	Chem Biol	3/27/2009	19318213
MicroRNA regulation of cardiovascular development	Cordes KR, Srivastava D	Circ Res	3/27/2009	19325160
Gene targeting in a HUES line of human embryonic stem cells via electroporation	Ruby KM, Zheng B	Stem Cells	3/26/2009	19544466
Natural and Synthetic Regulators of Embryonic Stem Cell Cardiogenesis	Willems E, Bushway PJ, Mercola M	Pediatr Cardiol	3/25/2009	19319460
Noninvasive de novo imaging of human embryonic stem cell-derived teratoma formation	Cao F, Li Z, Lee A, Liu Z, Chen K, Wang H, Cai W, Chen X, Wu JC	Cancer Res	3/24/2009	19318556
Optical deconstruction of parkinsonian neural circuitry	Gradinaru V, Mogri M, Thompson KR, Henderson JM, Deisseroth K	Science	3/19/2009	19299587
Mesenchymal stem cell transplantation reverses multiorgan dysfunction in systemic lupus erythematosus mice and humans	Sun L, Akiyama K, Zhang H, Yamaza T, Hou Y, Zhao S, Xu T, Le A, Shi S	Stem Cells	3/19/2009	19489103
Engineering microscale cellular niches for three-dimensional multicellular co-cultures	Huang CP, Lu J, Seon H, Lee AP, Flanagan LA, Kim HY, Putnam AJ, Jeon NL	Lab Chip	3/18/2009	19495458

APPENDIX 5

Title	Authors	Journal	Date	PMID
Histone modifications at human enhancers reflect global cell-type-specific gene expression	Heintzman ND, Hon GC, Hawkins RD, Kheradpour P, Stark A, Harp LF, Ye Z, Lee LK, Stuart RK, Ching CW, Ching KA, Antosiewicz-Bourget JE, Liu H, Zhang X, Green RD, Lobanenkov VV, Stewart R, Thomson JA, Crawford GE, Kellis M, Ren B	Nature	3/18/2009	19295514
Temporally precise in vivo control of intracellular signalling	Airan RD, Thompson KR, Fenno LE, Bernstein H, Deisseroth K	Nature	3/18/2009	19295515
A conserved mechanism for control of human and mouse embryonic stem cell pluripotency and differentiation by shp2 tyrosine phosphatase	Wu D, Pang Y, Ke Y, Yu J, He Z, Tautz L, Mustelin T, Ding S, Huang Z, Feng GS	PLoS ONE	3/17/2009	19290061
Molecular stages of rapid and uniform neuralization of human embryonic stem cells	Bajpai R, Coppola G, Kaul M, Talantova M, Cimadamore F, Nilbratt M, Geschwind DH, Lipton SA, Terskikh AV	Cell Death Differ	3/13/2009	19282867
Identification of putative endothelial progenitor cells (CD34+CD133+Flk-1+) in endarterectomized tissue of patients with chronic thromboembolic pulmonary hypertension	Yao W, Firth AL, Sacks RS, Ogawa A, Auger WR, Fedullo PF, Madani MM, Lin GY, Sakakibara N, Thistlethwaite PA, Jamieson SW, Rubin LJ, Yuan JX	Am J Physiol Lung Cell Mol Physiol	3/13/2009	19286928
Mesenchymal stem cell-mediated ectopic hematopoiesis alleviates aging-related phenotype in immunocompromised mice	Yamaza T, Miura Y, Akiyama K, Bi Y, Sonoyama W, Gronthos S, Chen W, Le A, Shi S	Blood	3/12/2009	19074727

APPENDIX 5

Title	Authors	Journal	Date	PMID
Distinct DNA methylation patterns characterize differentiated human embryonic stem cells and developing human fetal liver	Brunner AL, Johnson DS, Kim SW, Valouev A, Reddy TE, Neff NF, Anton E, Medina C, Nguyen L, Chiao E, Oyolu CB, Schroth GP, Absher DM, Baker JC, Myers RM	Genome Res	3/9/2009	19273619
Cdc37 regulates Ryk signaling by stabilizing the cleaved Ryk intracellular domain	Lyu J, Wesselschmidt RL, Lu W	J Biol Chem	3/5/2009	19269974
Personal genomics services: whose genomes?	Gurwitz D, Bregman-Eschet Y	Eur J Hum Genet	3/4/2009	19259127
Analyses of regenerative wave patterns in adult hair follicle populations reveal macro-environmental regulation of stem cell activity	Plikus MV, Widelitz RB, Maxson R, Chuong CM	Int J Dev Biol	3/4/2009	19378257
Controlling the selection stringency of phage display using a microfluidic device	Liu Y, Adams JD, Turner K, Cochran FV, Gambhir SS, Soh HT	Lab Chip	3/3/2009	19350081
Subpopulations of human embryonic stem cells with distinct tissue-specific fates can be selected from pluripotent cultures	King FW, Ritner C, Liszewski W, Kwan HC, Pedersen A, Leavitt AD, Bernstein HS	Stem Cells Dev	3/2/2009	19254177
Quantitative fluorescence tomography with functional and structural a priori information	Lin Y, Yan H, Nalcioglu O, Gulsen G	Appl Opt	3/1/2009	19252634
EphA4 as an effector of Twist1 in the guidance of osteogenic precursor cells during calvarial bone growth and in craniosynostosis	Ting MC, Wu NL, Roybal PG, Sun J, Liu L, Yen Y, Maxson RE Jr	Development	3/1/2009	19201948

APPENDIX 5

Title	Authors	Journal	Date	PMID
A systematic search for DNA methyltransferase polymorphisms reveals a rare DNMT3L variant associated with subtelomeric hypomethylation	El-Maarri O, Kareta MS, Mikeska T, Becker T, Diaz-Lacava A, Junen J, Nüsgen N, Behne F, Wienker T, Waha A, Oldenburg J, Chédin F	Hum Mol Genet	2/26/2009	19246518
Transforming growth factor-alpha induces neurogenesis and behavioral improvement in a chronic stroke model	Guerra-Crespo M, Gleason D, Sistos A, Toosky T, Solaroglu I, Zhang JH, Bryant PJ, Fallon JH	Neuroscience	2/25/2009	19248822
Parkin, PINK1, and DJ-1 form a ubiquitin E3 ligase complex promoting unfolded protein degradation	Xiong H, Wang D, Chen L, Choo YS, Ma H, Tang C, Xia K, Jiang W, Ronai Z, Zhuang X, Zhang Z	J Clin Invest	2/23/2009	19229105
Glycogen synthase kinase 3beta missplicing contributes to leukemia stem cell generation	Abrahamsson AE, Geron I, Gotlib J, Dao KH, Barroga CF, Newton IG, Giles FJ, Durocher J, Creusot RS, Karimi M, Jones C, Zehnder JL, Keating A, Negrin RS, Weissman IL, Jamieson CH	Proc Natl Acad Sci U S A	2/23/2009	19237556
Directed differentiation of human-induced pluripotent stem cells generates active motor neurons	Karumbayaram S, Novitch BG, Patterson M, Umbach JA, Richter L, Lindgren A, Conway AE, Clark AT, Goldman SA, Plath K, Wiedau-Pazos M, Kornblum HI, Lowry WE	Stem Cells	2/23/2009	19350680
Cardiac fibroblasts regulate myocardial proliferation through beta1 integrin signaling	Ieda M, Tsuchihashi T, Ivey KN, Ross RS, Hong TT, Shaw RM, Srivastava D	Dev Cell	2/17/2009	19217425
Derivation of human embryonic stem cell lines from biopsied blastomeres on human feeders with a minimal exposure to xenomaterials	Ilic D, Giritharan G, Zdravkovic T, Caceres E, Genbacev O, Fisher S, Krtolica A	Stem Cells Dev	2/17/2009	19222349

APPENDIX 5

Title	Authors	Journal	Date	PMID
Cell kinase activity assay based on surface enhanced Raman spectroscopy	Yue Z, Zhuang F, Kumar R, Wang I, Cronin SB, Liu YH	Spectrochim Acta A Mol Biomol Spectrosc	2/14/2009	19299194
Endogenous Wnt signaling maintains neural progenitor cell potency	Wexler EM, Paucer A, Kornblum HI, Palmer TD, Geschwind DH	Stem Cells	2/12/2009	19418460
Deconstructing stem cell tumorigenicity: a roadmap to safe regenerative medicine	Knoepfler PS	Stem Cells	2/12/2009	19415771
Mef2C is a lineage-restricted target of Scl/Tal1 and regulates megakaryopoiesis and B-cell homeostasis	Gekas C, Rhodes KE, Gereige LM, Helgadottir H, Ferrari R, Kurdistani SK, Montecino-Rodriguez E, Bassel-Duby R, Olson E, Krivtsov AV, Armstrong S, Orkin SH, Pellegrini M, Mikkola HK	Blood	2/11/2009	19211936
Chromatin remodelling factor Mll1 is essential for neurogenesis from postnatal neural stem cells	Lim DA, Huang YC, Swigut T, Mirick AL, Garcia-Verdugo JM, Wysocka J, Ernst P, Alvarez-Buylla A	Nature	2/11/2009	19212323
Narrowband magnetic particle imaging	Goodwill P, Scott G, Stang P, Conolly S	IEEE Trans Med Imaging	2/10/2009	19211340
Optimal timing of inner cell mass isolation increases the efficiency of human embryonic stem cell derivation and allows generation of sibling cell lines	Chen AE, Egli D, Niakan K, Deng J, Akutsu H, Yamaki M, Cowan C, Fitz-Gerald C, Zhang K, Melton DA, Eggan K	Cell Stem Cell	2/6/2009	19200798
The MLLgnant consequences of reverting to an embryonic transcriptional program	Jamieson C	Cell Stem Cell	2/6/2009	19200795
TOX3 regulates calcium-dependent transcription in neurons	Yuan SH, Qiu Z, Ghosh A	Proc Natl Acad Sci U S A	2/5/2009	19196971
Germ cell migration in zebrafish is cyclopamine-sensitive but Smoothened-independent	Mich JK, Blaser H, Thomas NA, Firestone AJ, Yelon D, Raz E, Chen JK	Dev Biol	2/4/2009	19389352

APPENDIX 5

Title	Authors	Journal	Date	PMID
Antioxidant or neurotrophic factor treatment preserves function in a mouse model of neovascularization-associated oxidative stress.	Dorrell MI, Aguilar E, Jacobson R, Yanes O, Gariano R, Heckenlively J, Banin E, Ramirez GA, Gasmi M, Bird A, Siuzdak G, Friedlander M	J Clin Invest	2/2/2009	19188685
E2A proteins maintain the hematopoietic stem cell pool and promote the maturation of myelolymphoid and myeloerythroid progenitors	Semerad CL, Mercer EM, Inlay MA, Weissman IL, Murre C	Proc Natl Acad Sci U S A	1/30/2009	19181846
Stem cell fate dictated solely by altered nanotube dimension	Oh S, Brammer KS, Li YS, Teng D, Engler AJ, Chien S, Jin S	Proc Natl Acad Sci U S A	1/28/2009	19179282
Role of the murine reprogramming factors in the induction of pluripotency	Sridharan R, Tchieu J, Mason MJ, Yachechko R, Kuoy E, Horvath S, Zhou Q, Plath K	Cell	1/23/2009	19167336
Embryonic stem cell-derived endothelial cells for treatment of hindlimb ischemia	Huang NF, Niiyama H, De A, Gambhir SS, Cooke JP	J Vis Exp	1/23/2009	19229180
Journal club. A cell biologist looks at the risk and promise of a new insight into stem cells and cancer	Knoepfler P	Nature	1/22/2009	19158746
Derivation of primordial germ cells from human embryonic and induced pluripotent stem cells is significantly improved by coculture with human fetal gonadal cells	Park TS, Galic Z, Conway AE, Lindgren A, van Handel BJ, Magnusson M, Richter L, Teitell MA, Mikkola HK, Lowry WE, Plath K, Clark AT	Stem Cells	1/22/2009	19350678
Neurosphere formation is an independent predictor of clinical outcome in malignant glioma	Laks DR, Masterman-Smith M, Visnyei K, Angenieux B, Orozco NM, Foran I, Yong WH, Vinters HV, Liau LM, Lazareff JA, Mischel PS, Cloughesy TF, Horvath S, Kornblum HI	Stem Cells	1/22/2009	19353526

APPENDIX 5

Title	Authors	Journal	Date	PMID
Defining long-term maintenance conditions of human embryonic stem cells with arrayed cellular microenvironment technology	Brafman D, Shah K, Fellner T, Chien S, Willert K	Stem Cells Dev	1/21/2009	19327010
Islet specific Wnt activation in human type II diabetes	Lee SH, Demeterco C, Geron I, Abrahamsson A, Levine F, Itkin-Ansari P	Exp Diabetes Res	1/20/2009	19165345
Microarray and cDNA sequence analysis of transcription during nerve-dependent limb regeneration	Monaghan JR, Epp LG, Putta S, Page RB, Walker JA, Beachy CK, Zhu W, Pao GM, Verma IM, Hunter T, Bryant SV, Gardiner DM, Harkins TT, Voss SR	BMC Biol	1/13/2009	19144100
Genic regions of a large salamander genome contain long introns and novel genes	Smith JJ, Putta S, Zhu W, Pao GM, Verma IM, Hunter T, Bryant SV, Gardiner DM, Harkins TT, Voss SR	BMC Genomics	1/13/2009	19144141
MicroRNA profiling of human-induced pluripotent stem cells	Wilson KD, Venkatasubrahmanyam S, Jia F, Sun N, Butte AJ, Wu JC	Stem Cells Dev	1/12/2009	19284351
An RNA code for the FOX2 splicing regulator revealed by mapping RNA-protein interactions in stem cells	Yeo GW, Coufal NG, Liang TY, Peng GE, Fu XD, Gage FH	Nat Struct Mol Biol	1/11/2009	19136955
Abeta-specific Th2 cells provide cognitive and pathological benefits to Alzheimer's mice without infiltrating the CNS	Cao C, Arendash GW, Dickson A, Mamcarz MB, Lin X, Ethell DW	Neurobiol Dis	1/8/2009	19167499
Molecular characterization of the human NANOG protein	Chang DF, Tsai SC, Wang XC, Xia P, Senadheera D, Lutzko C	Stem Cells	1/8/2009	19350681
MicroRNAs: opening a new vein in angiogenesis research	Fish JE, Srivastava D	Sci Signal	1/6/2009	19126861
Epigenetic regulation of X-inactivation in human embryonic stem cells	Dvash T, Fan G	Epigenetics	1/1/2009	19106643

APPENDIX 5

Title	Authors	Journal	Date	PMID
Epigenetic reprogramming and induced pluripotency	Hochedlinger K, Plath K	Development	1/1/2009	19168672
Carcinoma-produced factors activate myeloid cells through TLR2 to stimulate metastasis	Kim S, Takahashi H, Lin WW, Descargues P, Grivennikov S, Kim Y, Luo JL, Karin M	Nature	1/1/2009	19122641
Immunostaining of whole-mount and sectioned lamprey embryos	Nikitina N, Bronner-Fraser M, Sauka-Spengler T	Cold Spring Harb Protoc	1/1/2009	20147021
Whole-mount in situ hybridization on lamprey embryos	Nikitina N, Bronner-Fraser M, Sauka-Spengler T	Cold Spring Harb Protoc	1/1/2009	20147020
DiI cell labeling in lamprey embryos	Nikitina N, Bronner-Fraser M, Sauka-Spengler T	Cold Spring Harb Protoc	1/1/2009	20147019
Microinjection of RNA and morpholino oligos into lamprey embryos	Nikitina N, Bronner-Fraser M, Sauka-Spengler T	Cold Spring Harb Protoc	1/1/2009	20147018
Culturing lamprey embryos	Nikitina N, Bronner-Fraser M, Sauka-Spengler T	Cold Spring Harb Protoc	1/1/2009	20147017
The sea lamprey Petromyzon marinus: a model for evolutionary and developmental biology	Nikitina N, Bronner-Fraser M, Sauka-Spengler T	Cold Spring Harb Protoc	1/1/2009	20147008
Macrophage differentiation from embryoid bodies derived from human embryonic stem cells	Subramanian A, Guo B, Marsden MD, Galic Z, Kitchen S, Kacena A, Brown HJ, Cheng G, Zack JA	J Stem Cells	1/1/2009	n/a
ESCRT, autophagy, and frontotemporal dementia	Lee JA, Gao FB	BMB Rep	12/31/2008	19123971
Cells of adult brain germinal zone have properties akin to hair cells and can be used to replace inner ear sensory cells after damage	Wei D, Levic S, Nie L, Gao WQ, Petit C, Jones EG, Yamoah EN	Proc Natl Acad Sci U S A	12/30/2008	19064919
Germline competent embryonic stem cells derived from rat blastocysts	Li P, Tong C, Mehrian-Shai R, Jia L, Wu N, Yan Y, Maxson RE, Schulze EN, Song H, Hsieh CL, Pera MF,	Cell	12/26/2008	19109898

Title	Authors	Journal	Date	PMID
	Ying QL			
Differential trafficking of AMPA and NMDA receptors by SAP102 and PSD-95 underlies synapse development	Elias GM, Elias LA, Apostolides PF, Kriegstein AR, Nicoll RA	Proc Natl Acad Sci U S A	12/24/2008	19104036
Dissecting early regulatory relationships in the lamprey neural crest gene network	Nikitina N, Sauka-Spengler T, Bronner-Fraser M	Proc Natl Acad Sci U S A	12/22/2008	19104059
Isolation and characterization of neural crest stem cells derived from in vitro differentiated human embryonic stem cells	Jiang X, Gwye Y, McKeown SJ, Bronner-Fraser M, Lutzko C, Lawlor ER	Stem Cells Dev	12/19/2008	19099373
Integrated chemical genomics reveals modifiers of survival in human embryonic stem cells	Damoiseaux R, Sherman SP, Alva JA, Peterson C, Pyle AD	Stem Cells	12/18/2008	19074420
VEGF-mediated cross-talk within the neonatal murine thymus	Cuddihy AR, Ge S, Zhu J, Jang J, Chidgey A, Thurston G, Boyd R, Crooks GM	Blood	12/16/2008	19088378
Wnt/beta-catenin signaling acts at multiple developmental stages to promote mammalian cardiogenesis	Kwon C, Cordes KR, Srivastava D	Cell Cycle	12/13/2008	19066459
The adhesion molecule esam1 is a novel hematopoietic stem cell marker	Ooi AG, Karsunky H, Majeti R, Butz S, Vestweber D, Ishida T, Quertermous T, Weissman IL, Forsberg EC	Stem Cells	12/11/2008	19074415
Use of bioluminescent imaging to assay the transplantation of immortalized human fetal hepatocytes into mice	Choi MS, Catana AM, Wu J, Kim YS, Yoon SJ, Borowsky AD, Gambhir SS, Gupta S, Zern MA	Cell Transplant	12/8/2008	19069633

APPENDIX 5

Title	Authors	Journal	Date	PMID
Fate tracing reveals the endothelial origin of hematopoietic stem cells	Zovein AC, Hofmann JJ, Lynch M, French WJ, Turlo KA, Yang Y, Becker MS, Zanetta L, Dejana E, Gasson JC, Tallquist MD, Iruela-Arispe ML	Cell Stem Cell	12/4/2008	19041779
Non-cell-autonomous effect of human SOD1 G37R astrocytes on motor neurons derived from human embryonic stem cells	Marchetto MC, Muotri AR, Mu Y, Smith AM, Cezar GG, Gage FH	Cell Stem Cell	12/3/2008	19041781
Suppression of HLA expression by lentivirus-mediated gene transfer of siRNA cassettes and in vivo chemoselection to enhance hematopoietic stem cell transplantation	Hacke K, Falahati R, Flebbe-Rehwaldt L, Kasahara N, Gaensler KM	Immunol Res	12/2/2008	19048410
Applications of lentiviral vectors for shRNA delivery and transgenesis	Singer O, Verma IM	Curr Gene Ther	12/1/2008	19075631
Embryonic stem cell-specific microRNAs regulate the G1-S transition and promote rapid proliferation	Wang Y, Baskerville S, Shenoy A, Babiarz JE, Baehner L, Blelloch R	Nat Genet	12/1/2008	18978791
In vivo imaging of embryonic stem cells reveals patterns of survival and immune rejection following transplantation	Swijnenburg RJ, Schrepfer S, Cao F, Pearl JI, Xie X, Connolly AJ, Robbins RC, Wu JC	Stem Cells Dev	12/1/2008	18491958
Role of gap junctions in embryonic and somatic stem cells	Wong RC, Pera MF, Pébay A	Stem Cells Rev	12/1/2008	18704771
Generation of Cre-transgenic mice using Dlx1/Dlx2 enhancers and their characterization in GABAergic interneurons	Potter GB, Petryniak MA, Shevchenko E, McKinsey GL, Ekker M, Rubenstein JL	Mol Cell Neurosci	11/26/2008	19026749
A role for von Hippel-Lindau protein in pancreatic beta-cell function	Puri S, Cano DA, Hebrok M	Diabetes	11/25/2008	19033400

APPENDIX 5

Title	Authors	Journal	Date	PMID
Dlx1&2 and Mash1 transcription factors control striatal patterning and differentiation through parallel and overlapping pathways	Long JE, Swan C, Liang WS, Cobos I, Potter GB, Rubenstein JL	J Comp Neurol	11/24/2008	19030180
Selective blockade of 2-arachidonoylglycerol hydrolysis produces cannabinoid behavioral effects	Long JZ, Li W, Booker L, Burston JJ, Kinsey SG, Schlosburg JE, Pavón FJ, Serrano AM, Selley DE, Parsons LH, Lichtman AH, Cravatt BF	Nat Chem Biol	11/23/2008	19029917
Gene regulatory network subcircuit controlling a dynamic spatial pattern of signaling in the sea urchin embryo	Smith J, Davidson EH	Proc Natl Acad Sci U S A	11/22/2008	19104065
Identification of the critical extracellular matrix proteins that promote human embryonic stem cell assembly	Evseenko D, Schenke-Layland K, Dravid G, Zhu Y, Hao QL, Scholes J, Chao X, Maclellan WR, Crooks GM	Stem Cells Dev	11/20/2008	19021502
An integrated microfluidic culture device for quantitative analysis of human embryonic stem cells	Kamei K, Guo S, Yu ZT, Takahashi H, Gschweng E, Suh C, Wang X, Tang J, McLaughlin J, Witte ON, Lee KB, Tseng HR	Lab Chip	11/20/2008	19190791
Aging and cancer resistance in lymphoid progenitors are linked processes conferred by p16Ink4a and Arf	Signer RA, Montecino-Rodriguez E, Witte ON, Dorshkind K	Genes Dev	11/15/2008	19056891
Polysialic acid, a glycan with highly restricted expression, is found on human and murine leukocytes and modulates immune responses	Drake PM, Nathan JK, Stock CM, Chang PV, Muench MO, Nakata D, Reader JR, Gip P, Golden KP, Weinhold B, Gerardy-Schahn R, Troy FA 2nd, Bertozzi CR	J Immunol	11/15/2008	18981104
microRNA-138 modulates cardiac patterning during embryonic development	Morton SU, Scherz PJ, Cordes KR, Ivey KN, Stainier DY, Srivastava D	Proc Natl Acad Sci U S A	11/12/2008	19004786

APPENDIX 5

Title	Authors	Journal	Date	PMID
BCR-ABL-transformed GMP as myeloid leukemic stem cells	Minami Y, Stuart SA, Ikawa T, Jiang Y, Banno A, Hunton IC, Young DJ, Naoe T, Murre C, Jamieson CH, Wang JY	Proc Natl Acad Sci U S A	11/11/2008	19004799
Evolution of the neural crest viewed from a gene regulatory perspective	Sauka-Spengler T, Bronner-Fraser M	Genesis	11/10/2008	19003930
Epithelial stem cells of the prostate and their role in cancer progression	Lukacs RU, Lawson DA, Xin L, Zong Y, Garraway I, Goldstein AS, Memarzadeh S, Witte ON	Cold Spring Harb Symp Quant Biol	11/6/2008	19022743
Establishment of a normal hematopoietic and leukemia stem cell hierarchy	Chao MP, Seita J, Weissman IL	Cold Spring Harb Symp Quant Biol	11/6/2008	19022770
Wnt signaling mediates self-organization and axis formation in embryoid bodies	ten Berge D, Koole W, Fuerer C, Fish M, Eroglu E, Nusse R	Cell Stem Cell	11/5/2008	18983966
Bmp2 signaling regulates the hepatic versus pancreatic fate decision	Chung WS, Shin CH, Stainier DY	Dev Cell	11/1/2008	19000838
Cleavage of the Wnt receptor Ryk regulates neuronal differentiation during cortical neurogenesis	Lyu J, Yamamoto V, Lu W	Dev Cell	11/1/2008	19000841
Human amniotic fluid stem cells can integrate and differentiate into epithelial lung lineages	Carraro G, Perin L, Sedrakyan S, Giuliani S, Tiozzo C, Lee J, Turcatel G, De Langhe SP, Driscoll B, Bellusci S, Minoo P, Atala A, De Filippo RE, Warburton D	Stem Cells	11/1/2008	18719226
Generation of T lineage cells from human embryonic stem cells in a feeder free system	Galic Z, Kitchen SG, Subramanian A, Bristol G, Marsden MD, Balamurugan A, Kacena A, Yang O, Zack JA	Stem Cells	10/30/2008	18974209
Wnt-mediated self-renewal of neural stem/progenitor cells	Kalani MY, Cheshier SH, Cord BJ, Bababeygy SR, Vogel H, Weissman IL, Palmer TD, Nusse R	Proc Natl Acad Sci U S A	10/28/2008	18957545

APPENDIX 5

Title	Authors	Journal	Date	PMID
CompMoby: comparative MobyDick for detection of cis-regulatory motifs	Chaivorapol C, Melton C, Wei G, Yeh RF, Ramalho-Santos M, Blelloch R, Li H	BMC Bioinformatics	10/27/2008	18950538
Transcriptional and functional profiling of human embryonic stem cell-derived cardiomyocytes	Cao F, Wagner RA, Wilson KD, Xie X, Fu JD, Drukker M, Lee A, Li RA, Gambhir SS, Weissman IL, Robbins RC, Wu JC	PLoS ONE	10/22/2008	18941512
Contrasting expression of keratins 8, 18 and 19 in mouse and human embryonic stem cells	Maurer J, Nelson B, Ceceña G, Bajpai R, Mercola M, Terskikh A, Oshima RG	PLoS ONE	10/20/2008	18941637
Bringing down the ROS: a new therapeutic approach for PPHN	Firth AL, Yuan JX	Am J Physiol Lung Cell Mol Physiol	10/17/2008	18931050
ChromaSig: a probabilistic approach to finding common chromatin signatures in the human genome	Hon G, Ren B, Wang W	PLoS Comput Biol	10/17/2008	18927605
Miscreant myeloproliferative disorder stem cells	Jamieson CH, Barroga CF, Vainchenker WP	Leukemia	10/16/2008	18923436
Isolation and characterization of pluripotent human spermatogonial stem cell-derived cells	Kossack N, Meneses J, Shefi S, Nguyen HN, Chavez S, Nicholas C, Gromoll J, Turek PJ, Reijo-Pera RA	Stem Cells	10/16/2008	18927477
Mouse ES cells express endogenous shRNAs, siRNAs, and other Microprocessor-independent, Dicer-dependent small RNAs	Babiarz JE, Ruby JG, Wang Y, Bartel DP, Blelloch R	Genes Dev	10/15/2008	18923076
MyoD targets TAF3/TRF3 to activate myogenin transcription	Deato MD, Marr MT, Sottero T, Inouye C, Hu P, Tjian R	Mol Cell	10/10/2008	18851836
The pluripotent transcriptome	Grskovic M, Ramalho-Santos M	Stembook	10/10/2008	20614622
Mrc1 and DNA polymerase epsilon function together in linking DNA replication and the S phase checkpoint	Lou H, Komata M, Katou Y, Guan Z, Reis CC, Budd M, Shirahige K, Campbell JL	Mol Cell	10/10/2008	18851837

APPENDIX 5

Title	Authors	Journal	Date	PMID
Drosophila Kismet regulates histone H3 lysine 27 methylation and early elongation by RNA polymerase II	Srinivasan S, Dorighi KM, Tamkun JW	PLoS Genet	10/10/2008	18846226
Single-cell profiling identifies aberrant STAT5 activation in myeloid malignancies with specific clinical and biologic correlates	Kotecha N, Flores NJ, Irish JM, Simonds EF, Sakai DS, Archambeault S, Diaz-Flores E, Coram M, Shannon KM, Nolan GP, Loh ML	Cancer Cell	10/6/2008	18835035
A pluripotency and self-renewal program controls the expansion of genetically unstable cancer stem cells in pluripotent stem cell-derived tumors	Conway AE, Lindgren A, Galic Z, Pyle AD, Wu H, Zack JA, Pelligrini M, Teitell MA, Clark A	Stem Cells	10/2/2008	18832591
Cell cycle-dependent variation of a CD133 epitope in human embryonic stem cell, colon cancer, and melanoma cell lines	Jaksch M, Múnera J, Bajpai R, Terskikh A, Oshima RG	Cancer Res	10/1/2008	18829544
DNA shuffling of adeno-associated virus yields functionally diverse viral progeny	Koerber JT, Jang JH, Schaffer DV	Mol Ther	10/1/2008	18728640
Grapes(Chk1) prevents nuclear CDK1 activation by delaying cyclin B nuclear accumulation	Royou A, McCusker D, Kellogg DR, Sullivan W	J Cell Biol	9/29/2008	18824564
EWS-FLI1 causes neuroepithelial defects and abrogates emigration of neural crest stem cells	Coles EG, Lawlor ER, Bronner-Fraser M	Stem Cells	9/28/2008	18556509
Prox1 physically and functionally interacts with COUP-TFII to specify lymphatic endothelial cell fate	Lee S, Kang J, Yoo J, Ganesan SK, Cook SC, Aguilar B, Ramu S, Lee J, Hong YK	Blood	9/24/2008	18815287

APPENDIX 5

Title	Authors	Journal	Date	PMID
A novel activity of the Dickkopf-1 amino terminal domain promotes axial and heart development independently of canonical Wnt inhibition	Korol O, Gupta RW, Mercola M	Dev Biol	9/24/2008	18840423
Ependymal stem cells divide asymmetrically and transfer progeny into the subventricular zone when activated by injury	Gleason D, Fallon JH, Guerra M, Liu JC, Bryant PJ	Neuroscience	9/22/2008	18682279
A glucagon-like endocrine pathway in Drosophila modulates both lipid and carbohydrate homeostasis	Bharucha KN, Tarr P, Zipursky SL	J Exp Biol	9/19/2008	18805809
Retinoic acid synthesis and signaling during early organogenesis	Duester G	Cell	9/18/2008	18805086
Induction of fibroblast growth factor 10 (FGF10) in the ileal crypt epithelium after massive small bowel resection suggests a role for FGF10 in gut adaptation	Tai CC, Curtis JL, Sala FG, Del Moral PM, Chokshi N, Kanard RJ, Al Alam D, Wang J, Burns RC, Ford HR, Grishin A, Wang KS, Bellusci S	Dev Dyn	9/4/2008	18773490
Immunosuppressive therapy mitigates immunological rejection of human embryonic stem cell xenografts	Swijnenburg RJ, Schrepfer S, Govaert JA, Cao F, Ransohoff K, Sheikh AY, Haddad M, Connolly AJ, Davis MM, Robbins RC, Wu JC	Proc Natl Acad Sci U S A	9/2/2008	18728188
Culturing human embryonic stem cells with mouse embryonic fibroblast feeder cells	McElroy SL, Reijo Pera RA	Cold Spring Harb Protoc	9/1/2008	n/a
Culturing human embryonic stem cells in feeder-free conditions	McElroy SL, Reijo Pera RA	Cold Spring Harb Protoc	9/1/2008	n/a
Noninvasive human nuclear transfer with embryonic stem cells	McElroy SL, Reijo Pera RA	Cold Spring Harb Protoc	9/1/2008	n/a

APPENDIX 5

Title	Authors	Journal	Date	PMID
Regulatory networks define phenotypic classes of human stem cell lines	Müller FJ, Laurent LC, Kostka D, Ulitsky I, Williams R, Lu C, Park IH, Rao MS, Shamir R, Schwartz PH, Schmidt NO, Loring JF	Nature	8/24/2008	18724358
A biochemically defined system for coding joint formation in V(D)J recombination	Lu H, Shimazaki N, Raval P, Gu J, Watanabe G, Schwarz K, Swanson PC, Lieber MR	Mol Cell	8/22/2008	18722175
Cardiac differentiation of embryonic stem cells with point-source electrical stimulation	Chen MQ, Xie X, Hollis Whittington R, Kovacs GT, Wu JC, Giovangrandi L	Conf Proc IEEE Eng Med Biol Soc	8/21/2008	19163013
Parkinson-linked genes and toxins that affect neuronal cell death through the bcl-2 family	Ethell DW, Fei Q	Antioxid Redox Signal	8/20/2008	18715146
BMI-1 promotes Ewing sarcoma tumorigenicity independent of CDKN2A repression	Douglas D, Hsu JH, Hung L, Cooper A, Abdueva D, van Doorninck J, Peng G, Shimada H, Triche TJ, Lawlor ER	Cancer Res	8/15/2008	18701473
Stem/progenitor cells in lung development, injury repair, and regeneration	Warburton D, Perin L, Defilippo R, Bellusci S, Shi W, Driscoll B	Proc Am Thorac Soc	8/15/2008	18684721
miR-126 regulates angiogenic signaling and vascular integrity	Fish JE, Santoro MM, Morton SU, Yu S, Yeh RF, Wythe JD, Ivey KN, Bruneau BG, Stainier DY, Srivastava D	Dev Cell	8/11/2008	18694566
Distinct cardiogenic preferences of two human embryonic stem cell (hESC) lines are imprinted in their proteomes in the pluripotent state	Moore JC, Fu J, Chan YC, Lin D, Tran H, Tse HF, Li RA	Biochem Biophys Res Commun	8/8/2008	18503758
A comparative analysis of standard microtiter plate reading versus imaging in cellular assays	Bushway PJ, Mercola M, Price JH	Assay Drug Dev Technol	8/6/2008	18795873

APPENDIX 5

Title	Authors	Journal	Date	PMID
A dosage-dependent requirement for Sox9 in pancreatic endocrine cell formation	Seymour PA, Freude KK, Dubois CL, Shih HP, Patel NA, Sander M	Dev Biol	8/6/2008	18723011
The Fezf2-Ctip2 genetic pathway regulates the fate choice of subcortical projection neurons in the developing cerebral cortex	Chen B, Wang SS, Hattox AM, Rayburn H, Nelson SB, McConnell SK	Proc Natl Acad Sci U S A	8/4/2008	18678899
Engineering GPCR signaling pathways with RASSLs	Conklin BR, Hsiao EC, Claeysen S, Dumuis A, Srinivasan S, Forsayeth JR, Guettier JM, Chang WC, Pei Y, McCarthy KD, Nissenson RA, Wess J, Bockaert J, Roth BL	Nat Methods	7/30/2008	18668035
Chromatin immunoprecipitation from human embryonic stem cells	Bertani S, Kan A, Sauer F	J Vis Exp	7/22/2008	19066517
Multipotent somatic stem cells contribute to the stem cell niche in the Drosophila testis	Voog J, D'Alterio C, Jones DL	Nature	7/20/2008	18641633
Current status of tissue engineering in pediatric urology	Yamzon J, Perin L, Koh CJ	Curr Opin Urol	7/18/2008	18520763
How to assess a stem cell genome	Teitell MA	Nat Rep Stem Cells	7/10/2008	n/a
Stabilization of beta-catenin induces pancreas tumor formation	Heiser PW, Cano DA, Landsman L, Kim GE, Kench JG, Klimstra DS, Taketo MM, Biankin AV, Hebrok M	Gastroenterology	7/9/2008	18725219
Transcription factor MEF2C influences neural stem/progenitor cell differentiation and maturation in vivo	Li H, Radford JC, Ragusa MJ, Shea KL, McKercher SR, Zaremba JD, Soussou W, Nie Z, Kang YJ, Nakanishi N, Okamoto S, Roberts AJ, Schwarz JJ, Lipton SA	Proc Natl Acad Sci U S A	7/8/2008	18599437

APPENDIX 5

Title	Authors	Journal	Date	PMID
Marking embryonic stem cells with a 2A self-cleaving peptide: a NKX2-5 emerald GFP BAC reporter	Hsiao EC, Yoshinaga Y, Nguyen TD, Musone SL, Kim JE, Swinton P, Espineda I, Manalac C, deJong PJ, Conklin BR	PLoS ONE	7/2/2008	18596956
Allergic reactions to peanuts, tree nuts, and seeds aboard commercial airliners	Comstock SS, DeMera R, Vega LC, Boren EJ, Deane S, Haapanen LA, Teuber SS	Ann Allergy Asthma Immunol	7/1/2008	18681085
Multimodality evaluation of the viability of stem cells delivered into different zones of myocardial infarction	Hung TC, Suzuki Y, Urashima T, Caffarelli A, Hoyt G, Sheikh AY, Yeung AC, Weissman I, Robbins RC, Bulte JW, Yang PC	Circ Cardiovasc Imaging	7/1/2008	19808509
A gene regulatory network orchestrates neural crest formation	Sauka-Spengler T, Bronner-Fraser M	Nat Rev Mol Cell Biol	7/1/2008	18523435
Myocyte enhancer factor 2C as a neurogenic and antiapoptotic transcription factor in murine embryonic stem cells	Li Z, McKercher SR, Cui J, Nie Z, Soussou W, Roberts AJ, Sallmen T, Lipton JH, Talantova M, Okamoto S, Lipton SA	J Neurosci	6/25/2008	18579729
Human embryonic stem cell-derived oligodendrocyte progenitor cells express the serotonin receptor and are susceptible to JC virus infection	Schaumburg C, O'Hara BA, Lane TE, Atwood WJ	J Virol	6/25/2008	18579595
Probing for mitochondrial complex activity in human embryonic stem cells	Khvorostov I, Zhang J, Teitell M	J Vis Exp	6/17/2008	19066553
Imbalance between pSmad3 and Notch induces CDK inhibitors in old muscle stem cells	Carlson ME, Hsu M, Conboy IM	Nature	6/15/2008	18552838
Chronic myeloid leukemia stem cells	Kavalerchik E, Goff D, Jamieson CH	J Clin Oncol	6/10/2008	18539972
From MEFs to Matrigel 3: passaging hESCs from Matrigel onto Matrigel	Zhang J, Khvorostov I, Teitell M	J Vis Exp	6/10/2008	19066542

APPENDIX 5

Title	Authors	Journal	Date	PMID
From MEFs to Matrigel 2: splitting hESCs from MEFs onto Matrigel	Khvorostov I, Zhang J, Teitell M	J Vis Exp	6/9/2008	19066543
From MEFs to matrigel I: passaging hESCs in the presence of MEFs	Zhang J, Khvorostov I, Teitell M	J Vis Exp	6/4/2008	19066554
A voltage-sensing phosphatase, Ci-VSP, which shares sequence identity with PTEN, dephosphorylates phosphatidylinositol 4,5-bisphosphate	Iwasaki H, Murata Y, Kim Y, Hossain MI, Worby CA, Dixon JE, McCormack T, Sasaki T, Okamura Y	Proc Natl Acad Sci U S A	6/4/2008	18524949
A SPOT on the chromatin landscape? Histone peptide arrays as a tool for epigenetic research	Nady N, Min J, Kareta MS, Chédin F, Arrowsmith CH	Trends Biochem Sci	6/4/2008	18538573
Insights from a sea lamprey into the evolution of neural crest gene regulatory network	Sauka-Spengler T, Bronner-Fraser M	Biol Bull	6/1/2008	18574106
Transforming growth factor-β activation promotes genetic context-dependent invasion of immortalized melanocytes	Lo RS, Witte ON	Cancer Res	6/1/2008	18519684
Characterization of six new human embryonic stem cell lines (HSF7, -8, -9, -10, -12, and -13) derived under minimal-animal component conditions	Chavez SL, Meneses JJ, Nguyen HN, Kim SK, Pera RA	Stem Cells Dev	6/1/2008	18513167
Regulation of Abeta pathology by beclin 1: a protective role for autophagy?	Lee JA, Gao FB	J Clin Invest	5/22/2008	18497881
Multi-genetic events collaboratively contribute to Pten-null leukaemia stem-cell formation	Guo W, Lasky JL, Chang CJ, Mosessian S, Lewis X, Xiao Y, Yeh JE, Chen JY, Iruela-Arispe ML, Varella-Garcia M, Wu H	Nature	5/22/2008	18463637

APPENDIX 5

Title	Authors	Journal	Date	PMID
Multiple roles for Med12 in vertebrate endoderm development	Shin CH, Chung WS, Hong SK, Ober EA, Verkade H, Field HA, Huisken J, Stainier DY	Dev Biol	5/15/2008	18394596
A chemical approach to stem-cell biology and regenerative medicine	Xu Y, Shi Y, Ding S	Nature	5/15/2008	18480815
Gain- and loss-of-function approaches in the chick embryo	Sauka-Spengler T, Barembaum M	Methods Cell Biol	5/14/2008	18485300
Chemical technologies for probing embryonic development	Shestopalov IA, Chen JK	Chem Soc Rev	5/7/2008	18568156
Mouse hepatitis virus infection of the CNS: a model for defense, disease, and repair	Schaumburg CS, Held KS, Lane TE	Front Biosci	5/1/2008	18508518
Complex hair cycle domain patterns and regenerative hair waves in living rodents	Plikus MV, Chuong CM	J Invest Dermatol	5/1/2008	18094733
Characterization of human amniotic fluid stem cells and their pluripotential capability	Perin L, Sedrakyan S, Da Sacco S, De Filippo R	Methods Cell Biol	4/26/2008	18442645
Flk2+ common lymphoid progenitors possess equivalent differentiation potential for the B and T lineages	Karsunky H, Inlay MA, Serwold T, Bhattacharya D, Weissman IL	Blood	4/18/2008	18424665
An inducible transgene expression system for regulated phenotypic modification of human embryonic stem cells	Fu JD, Jung Y, Chan CW, Li RA	Stem Cells Dev	4/17/2008	18447646
High-efficiency stem cell fusion-mediated assay reveals Sall4 as an enhancer of reprogramming	Wong CC, Gaspar-Maia A, Ramalho-Santos M, Reijo Pera RA	PLoS ONE	4/16/2008	18414659
Multiple layers of molecular controls modulate self-renewal and neuronal lineage specification of embryonic stem cells	Yeo GW, Coufal N, Aigner S, Winner B, Scolnick JA, Marchetto MC, Muotri AR, Carson C, Gage FH	Hum Mol Genet	4/15/2008	18632700

APPENDIX 5

Title	Authors	Journal	Date	PMID
Cellular repair of CNS disorders: an immunological perspective	Chen Z, Palmer TD	Hum Mol Genet	4/15/2008	18632702
Illuminating the black box of reprogramming	Sridharan R, Plath K	Cell Stem Cell	4/10/2008	18397745
Comprehensive microRNA profiling reveals a unique human embryonic stem cell signature dominated by a single seed sequence	Laurent LC, Chen J, Ulitsky I, Mueller FJ, Lu C, Shamir R, Fan JB, Loring JF	Stem Cells	4/10/2008	18403753
In vitro and in vivo gene therapy vector evolution via multispecies interbreeding and retargeting of adeno-associated viruses	Grimm D, Lee JS, Wang L, Desai T, Akache B, Storm TA, Kay MA	J Virol	4/9/2008	18400866
It takes a PHD to SUMO	Peng J, Wysocka J	Trends Biochem Sci	4/9/2008	18406149
Gap junctions: multifaceted regulators of embryonic cortical development	Elias LA, Kriegstein AR	Trends Neurosci	4/8/2008	18403031
Regulation of self-renewal and pluripotency by Sox2 in human embryonic stem cells	Fong H, Hohenstein KA, Donovan PJ	Stem Cells	4/3/2008	18388306
Labeling stem cells with fluorescent dyes for non-invasive detection with optical imaging	Boddington S, Henning TD, Sutton EJ, Daldrup-Link HE	J Vis Exp	4/2/2008	19066580
Selective inhibition of JAK2-driven erythroid differentiation of polycythemia vera progenitors	Geron I, Abrahamsson AE, Barroga CF, Kavalerchik E, Gotlib J, Hood JD, Durocher J, Mak CC, Noronha G, Soll RM, Tefferi A, Kaushansky K, Jamieson CH	Cancer Cell	4/1/2008	18394555
Intra-endodermal interactions are required for pancreatic beta cell induction	Chung WS, Stainier DY	Dev Cell	4/1/2008	18410733

APPENDIX 5

Title	Authors	Journal	Date	PMID
Labeling hESCs and hMSCs with iron oxide nanoparticles for non-invasive in vivo tracking with MR imaging	Henning TD, Boddington S, Daldrup-Link HE	J Vis Exp	3/31/2008	19066574
Copy number variant analysis of human embryonic stem cells	Wu H, Kim KJ, Mehta K, Paxia S, Sundstrom A, Anantharaman T, Kuraishy AI, Doan T, Ghosh J, Pyle AD, Clark A, Lowry W, Fan G, Baxter T, Mishra B, Sun Y, Teitell MA	Stem Cells	3/25/2008	18369100
A new method, using cis-regulatory control, for blocking embryonic gene expression	Smith J, Davidson EH	Dev Biol	3/14/2008	18423438
SATB1 reprogrammes gene expression to promote breast tumour growth and metastasis	Han HJ, Russo J, Kohwi Y, Kohwi-Shigematsu T	Nature	3/13/2008	18337816
X-inactivation in female human embryonic stem cells is in a nonrandom pattern and prone to epigenetic alterations	Shen Y, Matsuno Y, Fouse SD, Rao N, Root S, Xu R, Pellegrini M, Riggs AD, Fan G	Proc Natl Acad Sci U S A	3/12/2008	18339804
Developmental competence of immature and failed/abnormally fertilized human oocytes in nuclear transfer	McElroy SL, Kee K, Tran N, Menses J, Giudice LC, Reijo Pera RA	Reprod Biomed Online	3/11/2008	18492373
Nucleofection mediates high-efficiency stable gene knockdown and transgene expression in human embryonic stem cells	Hohenstein KA, Pyle AD, Chern JY, Lock LF, Donovan PJ	Stem Cells	3/6/2008	18323409
MicroRNA regulation of cell lineages in mouse and human embryonic stem cells	Ivey KN, Muth A, Arnold J, King FW, Yeh RF, Fish JE, Hsiao EC, Schwartz RJ, Conklin BR, Bernstein HS, Srivastava D	Cell Stem Cell	3/5/2008	18371447

APPENDIX 5

Title	Authors	Journal	Date	PMID
Shrinky-dink hanging drops: a simple way to form and culture embryoid bodies	Chen CS, Pegan J, Luna J, Xia B, McCloskey K, Chin WC, Khine M	J Vis Exp	3/5/2008	19066572
A mouse model of mitochondrial disease reveals germline selection against severe mtDNA mutations	Fan W, Waymire KG, Narula N, Li P, Rocher C, Coskun PE, Vannan MA, Narula J, Macgregor GR, Wallace DC	Science	2/15/2008	18276892
Dispensable role of Drosophila ortholog of LRRK2 kinase activity in survival of dopaminergic neurons	Wang D, Tang B, Zhao G, Pan Q, Xia K, Bodmer R, Zhang Z	Mol Neurodegener	2/8/2008	18257932
Generation of human induced pluripotent stem cells from dermal fibroblasts	Lowry WE, Richter L, Yachechko R, Pyle AD, Tchieu J, Sridharan R, Clark AT, Plath K	Proc Natl Acad Sci U S A	2/8/2008	18287077
Human embryonic stem cell lines generated without embryo destruction	Chung Y, Klimanskaya I, Becker S, Li T, Maserati M, Lu SJ, Zdravkovic T, Ilic D, Genbacev O, Fisher S, Krtolica A, Lanza R	Cell Stem Cell	2/7/2008	18371431
Promoter CpG methylation contributes to ES cell gene regulation in parallel with Oct4/Nanog, PcG complex, and histone H3 K4/K27 trimethylation	Fouse SD, Shen Y, Pellegrini M, Cole S, Meissner A, Van Neste L, Jaenisch R, Fan G	Cell Stem Cell	2/7/2008	18371437
Enhanced cellular mobility guided by TiO2 nanotube surfaces	Brammer KS, Oh S, Gallagher JO, Jin S	Nano Lett	2/6/2008	18251515
Tissue-specific expression of Cre recombinase from the Tgfb3 locus	Yang LT, Li WY, Kaartinen V	Genesis	2/1/2008	18257072
On reversing the persistence of memory: hematopoietic stem cell transplant for autoimmune disease in the first ten years	Deane S, Meyers FJ, Gershwin ME	J Autoimmun	1/31/2008	18242059

APPENDIX 5

Title	Authors	Journal	Date	PMID
Osteoblast expression of an engineered Gs-coupled receptor dramatically increases bone mass	Hsiao EC, Boudignon BM, Chang WC, Bencsik M, Peng J, Nguyen TD, Manalac C, Halloran BP, Conklin BR, Nissenson RA	Proc Natl Acad Sci U S A	1/29/2008	18212126
Stem cell and regenerative science applications in the development of bioengineering of renal tissue	Perin L, Giuliani S, Sedrakyan S, DA Sacco S, De Filippo RE	Pediatr Res	1/24/2008	18319645
Cyclic dermal BMP signalling regulates stem cell activation during hair regeneration	Plikus MV, Mayer JA, de la Cruz D, Baker RE, Maini PK, Maxson R, Chuong CM	Nature	1/17/2008	18202659
CD133+ neural stem cells in the ependyma of mammalian postnatal forebrain	Coskun V, Wu H, Blanchi B, Tsao S, Kim K, Zhao J, Biancotti JC, Hutnick L, Krueger RC Jr, Fan G, de Vellis J, Sun YE	Proc Natl Acad Sci U S A	1/14/2008	18195354
Regulatory Priorities Governing Stem Cell Research in California: Relaxing Revenue Sharing & Safeguarding Access Plans	Tolley DC	Berkeley Technology Law Journal	1/1/2008	n/a
A novel bone morphogenetic protein signaling in heterotypic cell interactions in prostate cancer	Yang S, Pham LK, Liao CP, Frenkel B, Reddi AH, Roy-Burman P	Cancer Res	1/1/2008	18172312
Chronic myeloid leukemia stem cells	Jamieson CH	Hematology Am Soc Hematol Educ Program	1/1/2008	19074122
Maternal embryonic leucine zipper kinase is a key regulator of the proliferation of malignant brain tumors, including brain tumor stem cells	Nakano I, Masterman-Smith M, Saigusa K, Paucar AA, Horvath S, Shoemaker L, Watanabe M, Negro A, Bajpai R, Howes A, Lelievre V, Waschek JA, Lazareff JA, Freije WA, Liau LM, Gilbertson RJ, Cloughesy TF,	J Neurosci Res	1/1/2008	17722061

Title	Authors	Journal	Date	PMID
	Geschwind DH, Nelson SF, Mischel PS, Terskikh AV, Kornblum HI			
Kif3a constrains beta-catenin-dependent Wnt signalling through dual ciliary and non-ciliary mechanisms	Corbit KC, Shyer AE, Dowdle WE, Gaulden J, Singla V, Chen MH, Chuang PT, Reiter JF	Nat Cell Biol	1/1/2008	18084282
The N-end rule pathway is a sensor of heme	Hu RG, Wang H, Xia Z, Varshavsky A	Proc Natl Acad Sci U S A	12/27/2007	18162538
Functional sarcoplasmic reticulum for calcium handling of human embryonic stem cell-derived cardiomyocytes: insights for driven maturation	Liu J, Fu JD, Siu CW, Li RA	Stem Cells	12/25/2007	17872499
Efficient propagation of single cells Accutase-dissociated human embryonic stem cells	Bajpai R, Lesperance J, Kim M, Terskikh AV	Mol Reprod Dev	12/21/2007	18157870
Modifying ligand-induced and constitutive signaling of the human 5-HT4 receptor	Chang WC, Ng JK, Nguyen T, Pellissier L, Claeysen S, Hsiao EC, Conklin BR	PLoS ONE	12/19/2007	18338032
Regulated beta-cell regeneration in the adult mouse pancreas	Cano DA, Rulifson IC, Heiser PW, Swigart LB, Pelengaris S, German M, Evan GI, Bluestone JA, Hebrok M	Diabetes	12/14/2007	18083786
Sustained suppression of Bcr-Abl-driven lymphoid leukemia by microRNA mimics	McLaughlin J, Cheng D, Singer O, Lukacs RU, Radu CG, Verma IM, Witte ON	Proc Natl Acad Sci U S A	12/13/2007	18079287

APPENDIX 5

Title	Authors	Journal	Date	PMID
Enhanced paracrine FGF10 expression promotes formation of multifocal prostate adenocarcinoma and an increase in epithelial androgen receptor	Memarzadeh S, Xin L, Mulholland DJ, Mansukhani A, Wu H, Teitell MA, Witte ON	Cancer Cell	12/12/2007	18068633
Roles of ESCRT in autophagy-associated neurodegeneration	Lee JA, Gao FB	Autophagy	12/6/2007	18094607
Self renewal and multilineage differentiation in vitro from murine prostate stem cells	Xin L, Lukacs RU, Lawson DA, Cheng D, Witte ON	Stem Cells	11/25/2007	17641240
Ex vivo whole embryonic kidney culture: a novel method for research in development, regeneration and transplantation	Giuliani S, Perin L, Sedrakyan S, Kokorowski P, Jin D, De Filippo R	J Urol	11/19/2007	18006007
Renal differentiation of amniotic fluid stem cells	Perin L, Giuliani S, Jin D, Sedrakyan S, Carraro G, Habibian R, Warburton D, Atala A, De Filippo RE	Cell Prolif	11/15/2007	18021180
A spatially dynamic cohort of regulatory genes in the endomesodermal gene network of the sea urchin embryo	Smith J, Kraemer E, Liu H, Theodoris C, Davidson E	Dev Biol	11/9/2007	18061160
Probing cell type-specific functions of Gi in vivo identifies GPCR regulators of insulin secretion	Regard JB, Kataoka H, Cano DA, Camerer E, Yin L, Zheng YW, Scanlan TS, Hebrok M, Coughlin SR	J Clin Invest	11/8/2007	17992256
Epicardium-derived progenitor cells require beta-catenin for coronary artery formation	Zamora M, Männer J, Ruiz-Lozano P	Proc Natl Acad Sci U S A	11/7/2007	17989236
A gene regulatory network subcircuit drives a dynamic pattern of gene expression	Smith J, Theodoris C, Davidson EH	Science	11/2/2007	17975065
Neural stem cells improve memory in an inducible mouse model of neuronal loss	Yamasaki TR, Blurton-Jones M, Morrissette DA, Kitazawa M, Oddo S, LaFerla FM	J Neurosci	10/31/2007	17978032

APPENDIX 5

Title	Authors	Journal	Date	PMID
Tgfb1 expressed in the Tgfb3 locus partially rescues the cleft palate phenotype of Tgfb3 null mutants	Yang LT, Kaartinen V	Dev Biol	10/29/2007	17967447
The 5th International Society for Stem Cell Research (ISSCR) Annual Meeting, June 2007	Rajasekhar VK, Dalerba P, Passegué E, Lagasse E, Najbauer J	Stem Cells	10/25/2007	17962698
Bioelectricity and epimorphic regeneration	Stewart S, Rojas-Muñoz A, Belmonte JC	Bioessays	10/12/2007	17935197
Extent to which hairpin opening by the Artemis:DNA-PKcs complex can contribute to junctional diversity in V(D)J recombination	Lu H, Schwarz K, Lieber MR	Nucleic Acids Res	10/11/2007	17932067
H3K27 demethylases, at long last	Swigut T, Wysocka J	Cell	10/5/2007	17923085
Alternative splicing events identified in human embryonic stem cells and neural progenitors	Yeo GW, Xu X, Liang TY, Muotri AR, Carson CT, Coufal NG and Gage FH	PLoS Comput Biol	10/3/2007	17967047
A global analysis of genetic interactions in Caenorhabditis elegans	Byrne AB, Weirauch MT, Wong V, Koeva M, Dixon SJ, Stuart JM, Roy PJ	J Biol	9/26/2007	17897480
Gene expression patterns of human colon tops and basal crypts and BMP antagonists as intestinal stem cell niche factors	Kosinski C, Li VS, Chan AS, Zhang J, Ho C, Tsui WY, Chan TL, Mifflin RC, Powell DW, Yuen ST, Leung SY, Chen X	Proc Natl Acad Sci U S A	9/25/2007	17881565
Cancer stem cells and tumor metastasis: first steps into uncharted territory	Dalerba P, Clarke S	Cell Stem Cell	9/13/2007	18371356
Ancient evolutionary origin of the neural crest gene regulatory network	Sauka-Spengler T, Meulemans D, Jones M, Bronner-Fraser M	Dev Cell	9/4/2007	17765683

APPENDIX 5

Title	Authors	Journal	Date	PMID
An optical neural interface: in vivo control of rodent motor cortex with integrated fiberoptic and optogenetic technology	Aravanis AM, Wang LP, Zhang F, Meltzer LA, Mogri MZ, Schneider MB, Deisseroth K	J Neural Eng	9/4/2007	17873414
Fluorescence diffuse optical tomography with functional and anatomical a priori information: feasibility study	Lin Y, Gao H, Nalcioglu O, Gulsen G	Phys Med Biol	9/3/2007	17804882
A phenotypic small-molecule screen identifies an orphan ligand-receptor pair that regulates neural stem cell differentiation	Saxe JP, Wu H, Kelly TK, Phelps ME, Sun YE, Kornblum HI, Huang J	Chem Biol	9/1/2007	17884634
ISWI regulates higher-order chromatin structure and histone H1 assembly in vivo	Corona DF, Siriaco G, Armstrong JA, Snarskaya N, McClymont SA, Scott MP, Tamkun JW	PLoS Biol	8/28/2007	17760505
Gap junction adhesion is necessary for radial migration in the neocortex	Elias LA, Wang DD, Kriegstein AR	Nature	8/23/2007	17713529
Sirtuins: critical regulators at the crossroads between cancer and aging	Saunders LR, Verdin E	Oncogene	8/13/2007	17694089
Integrative genomic and functional analyses reveal neuronal subtype differentiation bias in human embryonic stem cell lines	Wu H, Xu J, Pang ZP, Ge W, Kim KJ, Blanchi B, Chen C, Südhof TC, Sun YE	Proc Natl Acad Sci U S A	8/10/2007	17693548
Conservation of hearing by simultaneous mutation of Na,K-ATPase and NKCC1	Diaz RC, Vazquez AE, Dou H, Wei D, Cardell EL, Lingrel J, Shull GE, Doyle KJ, Yamoah EN	J Assoc Res Otolaryngol	8/4/2007	17674100
ESCRT-III dysfunction causes autophagosome accumulation and neurodegeneration	Lee JA, Beigneux A, Ahmad ST, Young SG, Gao FB	Curr Biol	8/2/2007	17683935

APPENDIX 5

Title	Authors	Journal	Date	PMID
Dlx1 and Dlx2 control neuronal versus oligodendroglial cell fate acquisition in the developing forebrain	Petryniak MA, Potter GB, Rowitch DH, Rubenstein JL	Neuron	8/2/2007	17678855
Mouse models of prostate adenocarcinoma with the capacity to monitor spontaneous carcinogenesis by bioluminescence or fluorescence	Liao CP, Zhong C, Saribekyan G, Bading J, Park R, Conti PS, Moats R, Berns A, Shi W, Zhou Z, Nikitin AY, Roy-Burman P	Cancer Res	8/1/2007	17671224
Intrapulmonary delivery of bone marrow-derived mesenchymal stem cells improves survival and attenuates endotoxin-induced acute lung injury in mice	Gupta N, Su X, Popov B, Lee JW, Serikov V, Matthay MA	J Immunol	8/1/2007	17641052
Systematic identification of cis-regulatory sequences active in mouse and human embryonic stem cells	Grskovic M, Chaivorapol C, Gaspar-Maia A, Li H, Ramalho-Santos M	PLoS Genet	8/1/2007	17784790
Phosphoserine phosphatase is expressed in the neural stem cell niche and regulates neural stem and progenitor cell proliferation	Nakano I, Dougherty JD, Kim K, Klement I, Geschwind DH, Kornblum HI	Stem Cells	8/1/2007	17495110
Evidence of temporary airway epithelial repopulation and rare clonal formation by BM-derived cells following naphthalene injury in mice	Serikov VB, Popov B, Mikhailov VM, Gupta N, Matthay MA	Anat Rec (Hoboken)	7/27/2007	17661377
Deletion of Shp2 in the brain leads to defective proliferation and differentiation in neural stem cells and early postnatal lethality	Ke Y, Zhang EE, Hagihara K, Wu D, Pang Y, Klein R, Curran T, Ranscht B, Feng GS	Mol Cell Biol	7/23/2007	17646384
In utero intraventricular injection and electroporation of E15 mouse embryos	Walantus W, Castaneda D, Elias L, Kriegstein A	J Vis Exp	7/19/2007	18997887

APPENDIX 5

Title	Authors	Journal	Date	PMID
In utero intraventricular injection and electroporation of E16 rat embryos	Walantus W, Elias L, Kriegstein A	J Vis Exp	7/19/2007	18997884
Antithrombogenic property of bone marrow mesenchymal stem cells in nanofibrous vascular grafts	Hashi CK, Zhu Y, Yang GY, Young WL, Hsiao BS, Wang K, Chu B, Li S	Proc Natl Acad Sci U S A	7/17/2007	17615237
Switching of the core transcription machinery during myogenesis	Deato MD, Tjian R	Genes Dev	7/13/2007	17704303
Organotypic slice culture of E18 rat brains	Elias L, Kriegstein A	J Vis Exp	7/11/2007	18997883
The concentration of Nuf, a Rab11 effector, at the microtubule-organizing center is cell cycle regulated, dynein-dependent, and coincides with furrow formation	Riggs B, Fasulo B, Royou A, Mische S, Cao J, Hays TS, Sullivan W	Mol Biol Cell	6/20/2007	17581858
Phenotypic characterization of human colorectal cancer stem cells	Dalerba P, Dylla SJ, Park IK, Liu R, Wang X, Cho RW, Hoey T, Gurney A, Huang EH, Simeone DM, Shelton AA, Parmiani G, Castelli C, Clarke MF	Proc Natl Acad Sci U S A	6/12/2007	17548814
On the origin of the term "stem cell"	Ramalho-Santos M, Willenbring H	Cell Stem Cell	6/7/2007	18371332
Deficiencies in DNA damage repair limit the function of haematopoietic stem cells with age	Rossi DJ, Bryder D, Seita J, Nussenzweig A, Hoeijmakers J, Weissman IL	Nature	6/7/2007	17554309
Roles of alternative splicing in the functional properties of inner ear-specific KCNQ4 channels	Xu T, Nie L, Zhang Y, Mo J, Feng W, Wei D, Petrov E, Calisto LE, Kachar B, Beisel KW, Vazquez AE, Yamoah EN	J Biol Chem	6/7/2007	17561493
Age-related defects in B lymphopoiesis underlie the myeloid dominance of adult leukemia	Signer RA, Montecino-Rodriguez E, Witte ON, McLaughlin J, Dorshkind K	Blood	6/6/2007	17554060

APPENDIX 5

Title	Authors	Journal	Date	PMID
A chemical approach to stem cell biology	Emre N, Coleman R, Ding S	Curr Opin Chem Biol	5/10/2007	17493865
Gene-trapped mouse embryonic stem cell-derived cardiac myocytes and human genetics implicate AKAP10 in heart rhythm regulation	Tingley WG, Pawlikowska L, Zaroff JG, Kim T, Nguyen T, Young SG, Vranizan K, Kwok PY, Whooley MA, Conklin BR	Proc Natl Acad Sci U S A	5/7/2007	17485678
Controlling hair follicle signaling pathways through polyubiquitination	Huntzicker EG, AE Oro	J Invest Dermatol	4/22/2007	18408747
A conserved phosphatase cascade that regulates nuclear membrane biogenesis	Kim Y, Gentry MS, Harris TE, Wiley SE, Lawrence JC Jr, Dixon JE	Proc Natl Acad Sci U S A	4/9/2007	17420445
Multimodal fast optical interrogation of neural circuitry	Zhang F, Wang LP, Brauner M, Liewald JF, Kay K, Watzke N, Wood PG, Bamberg E, Nagel G, Gottschalk A, Deisseroth K	Nature	4/5/2007	17410168
Dysregulation of cardiogenesis, cardiac conduction, and cell cycle in mice lacking miRNA-1-2	Zhao Y, Ransom JF, Li A, Vedantham V, von Drehle M, Muth AN, Tsuchihashi T, McManus MT, Schwartz RJ, Srivastava D	Cell	3/29/2007	17397913
Loss of stem cell regenerative capacity within aged niches	Carlson ME, Conboy IM	Aging Cell	3/23/2007	17381551
A developmental view of microRNA function	Zhao Y, Srivastava D	Trends Biochem Sci	3/9/2007	17350266
DGCR8 is essential for microRNA biogenesis and silencing of embryonic stem cell self-renewal	Wang Y, Medvid R, Melton C, Jaenisch R, Blelloch R	Nat Genet	3/1/2007	17259983
Pancreatic development and disease	Cano DA, Hebrok M, Zenker M	Gastroenterology	2/21/2007	17258745
Length-dependent binding of human XLF to DNA and stimulation of XRCC4.DNA ligase IV activity	Lu H, Pannicke U, Schwarz K, Lieber MR	J Biol Chem	2/21/2007	17317666

APPENDIX 5

Title	Authors	Journal	Date	PMID
Identification of pancreatic cancer stem cells	Li C, Heidt DG, Dalerba P, Burant CF, Zhang L, Adsay V, Wicha M, Clarke MF, Simeone DM	Cancer Res	2/1/2007	17283135
SOX9 is required for maintenance of the pancreatic progenitor cell pool	Seymour PA, Freude KK, Tran MN, Mayes EE, Jensen J, Kist R, Scherer G, Sander M	Proc Natl Acad Sci U S A	1/31/2007	17267606
The prognostic role of a gene signature from tumorigenic breast-cancer cells	Liu R, Wang X, Chen GY, Dalerba P, Gurney A, Hoey T, Sherlock G, Lewicki J, Shedden K, Clarke MF	N Engl J Med	1/18/2007	17229949
Identification of a subpopulation of cells with cancer stem cell properties in head and neck squamous cell carcinoma	Prince ME, Sivanandan R, Kaczorowski A, Wolf GT, Kaplan MJ, Dalerba P, Weissman IL, Clarke MF, Ailles LE	Proc Natl Acad Sci U S A	1/16/2007	17210912
Aging, B lymphopoiesis, and patterns of leukemogenesis	Signer RA, Montecino-Rodriguez E, Dorshkind K	Exp Gerontol	12/20/2006	17184948
Postnatal deletion of Numb/Numblike reveals repair and remodeling capacity in the subventricular neurogenic niche	Kuo CT, Mirzadeh Z, Soriano-Navarro M, Rasin M, Wang D, Shen J, Sestan N, Garcia-Verdugo J, Alvarez-Buylla A, Jan LY, Jan YN	Cell	12/15/2006	17174898
Genetic Databases and Biobanks: Who Controls our Genetic Privacy?	Bregman-Eschet Y	Santa Clara Computer and High Tech Law Journal	11/1/2006	n/a
TRP channels and the regulation of vascular permeability: new insights from the lung microvasculature	Curry FR, Glass CA	Circ Res	10/27/2006	17068297
Multiple functions of Cerberus cooperate to induce heart downstream of Nodal	Foley AC, Korol O, Timmer AM, Mercola M	Dev Biol	10/26/2006	17123501
Channelrhodopsin-2 and optical control of excitable cells	Zhang F, Wang LP, Boyden ES, Deisseroth K	Nat Methods	10/3/2006	16990810

APPENDIX 5

Title	Authors	Journal	Date	PMID
Cancer stem cells: models and concepts	Dalerba P, Cho RW, Clarke MF	Annu Rev Med	9/26/2006	17002552
Identification of E2/E3 ubiquitinating enzymes and caspase activity regulating Drosophila sensory neuron dendrite pruning	Kuo CT, Zhu S, Younger S, Jan LY, Jan YN	Neuron	8/3/2006	16880123
Drosophila neuroblast asymmetric cell division: recent advances and implications for stem cell biology	Yu F, Kuo CT, Jan YN	Neuron	7/6/2006	16815328
Potential of stem-cell-based therapies for heart disease	Srivastava D, Ivey KN	Nature	6/28/2006	16810246

[Back to Appendices]

APPENDIX 6

6. Faculty level recruits to California Since 2006

*Those with an * have CIRM funding now; others have grant applications pending.*

National and International leadership level stem cell investigators who moved to California:

Henk Roelink, PhD, from Univ. of Washington to UC Berkeley

Dr. Krzysztof Kobielak, Ph.D., from Howard Hughes Medical Institute, Rockefeller University, New York to USC

Gregor Adams, Ph.D., from Massachusetts General Hospital / Harvard Medical School to USC

* Martin Pera, Ph.D., from Monash University (Australia) to USC

* Min Zhao, Ph.D., from University of Aberdeen, Scotland to UC Davis

Michael Clarke, M.D., from the University of Michigan to Stanford

*Stephan Heller, Ph.D., from Harvard to Stanford

*Peter Donovan, Ph.D., from Johns Hopkins to UC Irvine

*Jan Aileen Nolta, Ph.D., from Washington University to UC Davis

Gerhard Bauer, M.D., from Washington University to UC Davis

David Rowitch, M.D., from Harvard to UCSF

* Benoit Bruneau, Ph.D., from the Hospital for Sick Children in Toronto to a joint appointment at the Gladstone Institutes and UCSF

Michael Kahn, Ph.D., from University of Washington to USC;

M. Ian Phillips, Ph.D., from University of South Florida to USC

*Deepak Srivastava, M.D. from University of Texas to the Gladstone Institutes and UCSF

Markus Muschen, M.D., Ph.D., from Heinrich-Heine-Universitat Dusseldorf to Childrens Hospital Los Angeles and USC

Ronald Li, Ph.D., from Johns Hopkins to UC Davis

* Paul Knoepfler, Ph.D., from Fred Hutchinson Cancer Research Center to UC Davis

James Thomson, Ph.D., part time at UC Santa Barbara (while at University of Wisconsin)

Shinya Yamanaka, M.D., Ph.D., part time at Gladstone Institutes and UCSF (Kyoto University)

*Nissim Benvenisty, M.D., from Hebrew University to Cedars-Sinai

Michal Schwartz, Ph.D., part time at Cedars-Sinai (Weizmann Institute of Science)

Dan Gazit, Ph.D., D.M.D., from Hebrew University to Cedars-Sinai

Michael Beattie, PhD., from Ohio State to UCSF

Jacqueline Bresnahan, Ph.D., from Ohio State to UCSF

Eric Rulifson, Ph.D., from University of Pennsylvania to UCSF

Chris Murphy, Ph.D., from University of Wisconsin to UC Davis

William Murphy, Ph.D., from University of Nevada, Reno, to UC Davis

Brian Rutt M.D., from Canada to Stanford

Miles Wilkinson, Ph.D., from M.D. Anderson to UC San Diego

Kang Zhang, M.D., Ph.D., from University of Utah to UC San Diego

* Eduardo Marban, M.D., Ph.D., from John Hopkins Medical School to Cedars-Sinai

Linda Marban, Ph.D., from Johns Hopkins Medical School to Cedars-Sinai

Clive Svendsen, Ph.D., from University of Wisconsin to Stanford and then Cedars-Sinai

Bruno Peault, Ph.D., from University of Pittsburgh to UCLA

Jeffrey Fair, M.D., from Johns Hopkins Medical School to Cedarsl-Sinai

Emiliana Borrelli, from University of Naples, Italy, to UC Irvine

Paolo Sassone-Corsi, from University of Strassbourg, France, to UC Irvine

Jonathan Lakey, from University of Alberta, to UC Irvine

Leading junior faculty who moved to California:

* Lin He, PhD, from Cold Spring Harbor to UC Berkeley

Michael Rape, PhD, from Harvard to UC Berkeley

* Noburo Sato, Ph.D. from lab of Brivanlou at Rockefeller to UC, Riverside

* Qi-Long Ying, Ph.D. from lab of Austin Smith, Institute for Stem Cell Research at University of Edinburgh to USC

* Kara McCloskey, Ph.D. from Nerem's lab at Georgia Tech to UC Merced

* Xianmin Zeng, Ph.D. from Rao's lab at NIH to Buck; Institute

* Kathrin Plath, Ph.D., from Jaenisch's lab at MIT to UCLA

*Robert Blelloch, M.D., Ph.D., from Jaenisch's lab at MIT to UCSF

*Holger Willenbring, M.D., from Grompe's lab in Oregon to UCSF

April Pyle, Ph.D., from the Donovan lab at Johns Hopkins to UCLA

* Gage Crump, Ph.D., from Kimmel's lab at University of Oregon to USC

Tod Kippin, Ph.D., from Van Der Kooy's lab at University of Toronto to UC Santa Barbara

Leslie Lock, Ph.D., from the Donovan lab at Johns Hopkins to UC Irvine

Gautam Dravid, Ph.D., from Johns Hopkins to Childrens Hospital Los Angeles

Dennis Evseenko, M.D., Ph.D., from New Zealand to Childrens Hospital Los Angeles

Andrew Cuddihy, Ph.D., from Canada to Childrens Hospital Los Angeles

* Hanna Mikkola, M.D., Ph.D., from Harvard to UCLA

* William Lowry, Ph.D., from Rockefeller University to UCLA

* Bennett Novitch, Ph.D., from University of Michigan to UCLA

Ping Zhou, Ph.D., from Nolta lab at Washington University to UC Davis

Suzanne Pontow, Ph.D., from Nolta lab at Washington University to UC Davis

Camie Chan, Ph.D., from Johns Hopkins to UC Davis

Wenbin Deng, Ph.D., from Harvard/Children's Hospital Boston to UC Davis

* Chong-Xian-Pan, Ph.D., from the Indiana University to UC Davis

James Byrne, Ph.D., from Oregon Health Sciences University to Stanford

* David Traver, Ph.D. from Harvard to UC San Diego

* Mana Parast, M.D., Ph.D. from Harvard and Brigham and Women's in Boston to UC San Diego

Kun Zhang, Ph.D. from Harvard to UC San Diego

Adam Engler, PhD. from Princeton to UC San Diego

* Shyni Varghese, Ph.D. from Johns Hopkins to UC San Diego

Scott Olson, Ph.D., from Tulane to UC Davis

Martin Vidal, BVSc, Ph.D. from Louisiana State to UC Davis

Joseph Anderson, Ph.D., from Colorado State to UC Davis

* Kristin Baldwin, Ph.D., from Columbia University to Scripps

Anton Maximov, Ph.D. from UT Southwestern to Scripps

Diana Laird, Ph.D., from Memorial Sloan Kettering to UCSF

Katja Bruckner, Ph.D., from Harvard Medical School to UCSF

* Tippi Mackenzie, M.D., from Harvard and Brigham and Wormen's Hospital to UCSF

Ruben Fragoso, M.D., from Philadelphia to UC Davis

Bjorn Oskarsson, M.D., from Denver to UC Davis

Marius Wernig, Ph.D., from the Whitehead Institute to Stanford

John Sunwoo, M.D., from Washington University, St. Louis, to Stanford

Joshua Elias, Ph.D., from Harvard to Stanford

Hsun Theresa Ku, Ph.D., from Mt. Sinai to City of Hope

Takahiro Maeda, M.D., Ph.D., from Memorial Sloan Kettering to City of Hope

Alexander Kauffman, Ph.D., from University of Washington to UC San Diego

Ke Cheng, Ph.D., from University of Georgia to Cedars-Sinai

Hee Cheol Cho, Ph.D., from Excigen Corp. to Cedars-Sinai

Gail Thomas, Ph.D., from UT Southwestern to Cedars-Sinai

Lidia Szczepaniak, Ph.D., from UT Southwestern to Cedars-Sinai

Soshana Svendsen, from University of Wisconsin to Cedars-Sinai

* Atsushi Nakano, M.D., Ph.D., from Harvard and Massachusetts General Hospital to UCLA

APPENDIX 6

Pablo Ross, Ph.D., from Michigan State University to UC Davis

Paul Russell, Ph.D., from University of Wisconsin to UC Davis

Nanette Joyce, D.O., from Colorado State University to UC Davis

Daniella Bota, to UC Irvine from Duke University

Olivier Cinquin, from University of Wisconsin to UC Irvine

Norbert Fortin, from Boston University to UC Irvine

Marcelo Wood, to UC Irvine from University of Pennsylvania

Guiyun Yan to UC Irvine from SUNY Buffalo

Yi-Hong Zhou, from University of Arkansas to UC Irvine

[Back to Appendices]

APPENDIX 7

7. Grants Working Group Members

LN	FN	Expertise	Institute
Anderson	Judy	Muscular Dystrophy; Muscle Regeneration	University of Manitoba
Auerbach	Jonathan	Stem Cell Culture & Maintenance	GlobalStem Inc
Balber	Andrew	Immunology; Transplantation; Cell Therapy	Aldegen
Baron	Margaret	Hematopoiesis; Embryogenesis; Gene Expression	Mount Sinai School of Medicine
Bartholomew	Amelia	Stem Cell Biology; Transplantation Tolerance	University of Illinois-Chicago
Bhatia	Sangeeta	Bioengineering; Nanotechnology	Massachusetts Institute of Technology
Blazar	Bruce	Immunobiology of Transplantation; Pediatric BMT	University of Minnesota
Bokesch	Paula	Drug Development	Cubist Pharmaceuticals
Bonner-Weir	Susan	Diabetes	Joslin Diabetes Center
Boulton	Michael	Retinal Disease; SC Biology	University of Florida
Boyan	Barbara	Tissue Engineering; Bone/Cartilage Cell Biology	Georgia Institute of Technology
Brivanlou	Ali	Developmental Biology	The Rockefeller University
Brundin	Patrik	Neural Transplantation (PD)	Lund University
Bulte	Jeff	Cellular Imaging	John Hopkins University
Burger	Scott	Process Development; GMP Manufacturing	Advanced Cell & Gene Therapy
Cibelli	Jose	Stem Cell Biology; Pluripotency	Michigan State University
Clevers	Hans	Wnt Signaling & Cancer; Adult SCs	Hubrecht Institute
Cooke	Anne	Autoimmunity & Beta Cell Restoration	University of Cambridge, England
Cowan	Chad	Stem Cell Biology; *In vitro* Models of Disease	Massachusetts General Hospital
Cox	Charles	Pediatric Neurological/Brain Injury; Cellular Therapy	University of Texas Medical School at Houston
Daley	George	SC Biology & Reprogramming; Oncogenesis; Germline	Children's Hospital Boston

APPENDIX 7

LN	FN	Expertise	Institute
Diamond	Marc	Therapeutic Targets & Small Molecules (HD & Tauopathies)	Washington University School of Medicine
DiPersio	John	Leukemias; Bone Marrow Transplantation	Washington University School of Medicine
Donahoe	Patricia	Cancer	Massachusetts General Hospital
du Moulin	Gary	Quality Compliance for Cell Therapy/Tissue Engineering	Genzyme
Duncan	Ian D.	Neurodegenerative Disease (MS)	University of Wisconsin Medical
Eaton	Douglas	Cell Signaling	Emory University
Edelberg	Jay	Cardiovascular Disease Therapies & Biomarkers	Bristol-Myers Squibb Co.
Eggan	Kevin	Biology of Reprogramming; Neuromuscular System Disorders	Harvard University
El-Deiry	Wafik	Hematology-Oncology; Radiobiology	University of Pennsylvania
Emerson	Stephen	Hematopoietic Cells & Transplantation	Haverford University
Evans	Todd	Developmental & Molecular Biology	Albert Einstein College of Medicine
ffrench-Constant	Charles	Neurogenesis; Neurodegenerative Diseases (MS)	University of Cambridge
Fishell	Gordon	Developmental Genetics	NYU School of Medicine
Flake	Alan	*in utero* SC & Gene Therapy	Children's Hospital of Philadelphia
Furth	Mark	Adult Stem Cells; Differentiation	Wake Forest University
Gearhart	John	Mammalian Developmental Genetics; Stem Cell Biology	University of Pennsylvania
Gibbons	Gary	Vascular Biology, Cardiovascular Medicine	Morehouse School of Medicine
Glass	Jonathan	ALS, Axonal Degeneration	Emory University
Glicksman	Marcie	Assay Development; Preclinical Development	Brigham and Women's Hospital
Goodell	Margaret	Hematopoietic Stem Cells; Gene Therapy	Baylor College of Medicine
Gunter	Kurt	Regulatory Affairs & Therapy Development	Hospira Inc
Harfe	Brian	Developmental Biology; microRNA	University of Florida

APPENDIX 7

LN	FN	Expertise	Institute
Harvey	Richard	Cardiac Developmental Biology; Stem Cell Biology	Victor Chang Cardiac Research Institute
Hassell	John	Breast Cancer; Stem Cell Biology	McMaster University
Hefti	Franz	Drug Development; Neuroscience	Avid Radiopharmaceuticals, Inc.
Heimfeld	Shelly	Cellular Therapy; Hematopoietic Stem Cells	Fred Hutchinson Cancer Research Center
Hollander	Anthony	Chondrogenesis; Osteoarthritis; Tissue Engineering	University of Bristol
Jackson-Grusby	Laurie	Epigenetic Basis of Disease	Children's Hospital Boston
Jenkins	Marc	T Cell Biology; Vaccines & Autoimmunity; *in vivo* Imaging	University of Minnesota
Joyner	Alexandra	Developmental Biology	Memorial Sloan Kettering Cancer Center
Kerr	Douglas	Transverse Myelitis	Biogen Idec
Kiessling	Ann	Reproductive Biology; HIV	Harvard Institutes of Medicine
Kimble	Judith	SC Generalist; Organogenesis	University of Wisconsin
Korsgren	Olle	Islet allo- & xenotransplantation	Uppsala University Hospital
Krause	Diane	Hematopoietic Stem & Progenitor Cells	Yale University
Kulesa	Paul	Cell Migration; Imaging	Stowers Institute for Medical Research
Kung	Andrew	Tumor/Stem Cell Biology; Clinical Transplantation	Dana Farber Cancer Institute
Kurtzberg	Joanne	Stem Cell Transplantation	Duke University Children's Hospital
Lake	John	Liver; Solid Organ Transplantation	University of Minnesota
Lemischka	Ihor	Hematopoiesis	Mount Sinai School of Medicine
Lindvall	Olle	Neurogenesis & Neural Transplantation (PD, Stroke, Epilepsy)	University Hospital
Matsui	William (Bill)	SC & CSC biology; Clinical Oncology	John Hopkins University, Sidney Kimmel
McDevitt	Todd	Bioengineering; Myocardial Repair	Georgia Institute of Technology

APPENDIX 7

LN	FN	Expertise	Institute
McKenna	David	Development of Cellular-based Therapies; GMP Manufacturing	University of Minnesota Masonic Cancer Center
Mendez	Ivar	Neural Transplantation; Neurosurgery	Dalhousie University
Miller	Freda Diane	Adult Stem Cells; Neurobiology	The Hospital for Sick Children
Mills	Randall	Cell Therapy; Drug Development	Osiris, Inc.
Minger	Stephen L.	Stem Cell Biology; Neurobiology	King's College London
Morrison	Sean	Hematopoietic & Neural Stem Cells	University of Michigan
Mummery	Christine	Pluripotency & Differentiation to Cardiovascular Cells	Leiden University Medical Center
Navran	Stephen	Stem Cell Culture Methods & Applications	Synthecon, Inc
Niklason	Laura	Cardiovascular Tissue Engineering	Yale University
Nilson	John	Gametogenesis; Endocrinology	Washington State University
Odorico	Jon	Diabetes; Transplantation	University of Wisconsin
Orkin	Stuart	Hematopoiesis	Dana Farber Cancer Institute
Palecek	Sean	Pluripotency; Tissue Engineering; Biosensors	University of Wisconsin
Pavlath	Grace	Skeletal Muscle Growth & Repair	Emory University
Rasko	John	Hematology; Gene & Stem Cell Therapy	University of Sydney
Rasmussen	Ted	Chromatin Dynamics in Pluripotent Cells	University of Connecticut
Rauscher	Frank	Cancer	The Wistar Institute
Raymond	Pamela	Retinal Development & Regeneration	University of Michigan
Reisner	Yair	Immunology	Weizmann Institute of Science
Ricordi	Camillo	Islet Transplantation	University of Miami Miller School of Medicine
Robertson	Gail	Cardiac & Neuronal Electrophysiology	University of Wisconsin-Madison
Rojas	Mauricio	Stem Cells in Lung Repair & Injury	Emory University
Roncarolo	Maria Grazia	Immunological Tolerance; Pediatric Immunohaematology	San Rafaele Scientific Institute

APPENDIX 7

LN	FN	Expertise	Institute
Roos	Raymond	Neurodegenerative Diseases (ALS, MS)	The University of Chicago
Rosen	Michael	Cardiovascular Disease	Columbia University
Rosmarin	Alan	Hematology; Transcriptional Regulation	University of Massachusetts
Ross	Theodora	Hematopoiesis; Leukemia	University of Michigan
Rossant	Janet	Developmental & Stem Cell Biology	Hospital for Sick Children
Rosser	Anne	CNS Regeneration (HD, PD)	Cardiff School of Biosciences
Rothstein	Jeffrey	Neurological Disease (ALS)	Johns Hopkins University
Rubin	Josh	Biology & Treatment of Pediatric Brain Tumors	Washington University in St. Louis
Rubinstein	Pablo	Hematopoiesis	New York Blood Center
Rudnicki	Michael	Myogenesis; Transcriptional Regulation	Ottawa Health Research Institute
Russell	Alan	Chemical & Tissue Engineering	University of Pittsburgh
Sachs	David	Immunobiology of Transplantation; Xenotransplantation	Massachusetts General Hospital, HMS
Scadden	David	Stem Cell Microenvironments	Massachusetts General Hospital
Schneider	Michael D.	Cardiology; Molecular Genetics	Imperial College London
Schöler	Hans	SC Pluripotency & Germline Development	Max Planck Institute for Molecular Biomedicine
Schwob	Jim	Neural Assembly & Recovery; Olfactory Projection	Tufts University
Sharpless	Norman	Clinical Oncology; Tumor Suppressors in Aging & Cancer	The University of North Carolina School of Medicine
Sheridan	Steven	Cell-Based Assay Development	Millipore, Corp.
Simmons	Paul J.	Hematopoiesis; Mesenchymal Stem Cells	UT Houston IMM
Singh	Harinder	Hematopoietic Cell Differentiation; Immune System	University of Chicago
Sittampalam	G. Sitta	SC Pharmacology & Quantitative Biology in Drug Discovery	The University of Kansas Medical Center
Sladek	John	Neurodegenerative Diseases (PD);	University of Colorado

LN	FN	Expertise	Institute
		Transplantation	
Slukvin	Igor	Pluripotency; Gene Therapy; Hematopoiesis	University of Wisconsin
Stacey	Glyn	Stem Cell Standardization & Banking	NIBSC
Steer	Clifford	Liver & Neural Regeneration; microRNAs; Non-Viral Gene Therapy	University of Minnesota Medical School
Steindler	Dennis	Neurodegenerative Disease	The University of Florida
Stiles	Charles D.	Neuro-oncology; Genomics	Dana-Farver Cancer Institute, Harvard Medical School
Storb	Rainer	Hematopoiesis; SC Transplantation Biology; DMD	Fred Hutchinson Cancer Research Center
Strom	Stephen C.	Cancer of Liver & Prostate	University of Pittsburgh
Studer	Lorenz	Neurogenesis; Differentiation	Memorial Sloan-Kettering Cancer Center
Sykes	Megan	Transplantation; Immune Mechanisms	Massachusetts General Hospital
Tabar	Vivianne	Pluripotent & Neural Stem Cell Biology; Neurosurgery; Tumors	Memorial Sloan-Kettering Cancer Center
Takayama	Shuichi	Bioengineering; Nano/Micro Technologies	University of Michigan
Verfaillie	Catherine	Hematopoiesis; Mesenchymal Stem Cells	University of Minnesota
Voldman	Joel	Bioengineering; Fluid Mechanics; Microscopy	Massachusetts Institute of Technology
Wagers	Amy	Hematopoietic & Skeletal Muscle Stem Cells; Aging	Joslin Diabetes Center
Wagner	John	Lympho-hematopoietic Disorders; HSCT; UCB	University of Minnesota
Waldmann	Herman	Transplantation Tolerance Strategies	University of Oxford
Weiss	Samuel	CNS Biology; Neurogenesis; SC Therapy & Functional Recovery	University of Calgary
Wekerle	Hartmut	Neuroimmunology	Max Planck Institute of Neurobiology
Werner-Washburne	Margaret	Cell Biology; Growth Control; Genomics	University of New Mexico in Albuquerque

APPENDIX 7

LN	FN	Expertise	Institute
Whiteside	Theresa	Tumor Immunology & Immunotherapy	University of Pittsburgh Cancer Institute
Williams	David	Hematopoiesis; Gene Therapy	Children's Hospital Boston
Wirostko	Barbara	Ophthalmology; Clinical Development	Pfizer
Wright	Robin	Cell biology; organelles; microscopy	University of Minnesota, St. Paul
Yaffe	Michael	Protein Phosphorylation & Cell Cycle	Massachusetts Institute of Technology
Young	Wise	Neurodegenerative Disease (SCI)	W. M. Keck Center for Collaborative Neuroscience
Zandstra	Peter	Stem Cell Bioengineering; Signaling	University of Toronto
Zwaka	Thomas	Pluripotent Stem Cell Biology; Molecular Genetics	Baylor College of Medicine

[Back to Appendices]

APPENDIX 8

8. Pre-Application (PreAp) process

GWG Review Process for CIRM Pre-Applications

The goal of the pre-application (PreApp) review is to provide a greater opportunity to California scientists and organizations to compete in CIRM Requests for Applications (RFA). A larger pool of applicants provides a more diverse and more robust wealth of ideas from which to draw and achieve our mission. Identifying the best scientific ideas, however, requires the conduct of a rigorous scientific peer review. The conventional peer review of applications is resource intensive and limits the number of applications that can be reasonably and appropriately reviewed. To solve this issue, CIRM has previously set limits on the number of applications that it will accept from any given organization. It has relied on the applicant institutions to select those proposals that it believes are the most competitive to submit to CIRM. Although these institutional limits have worked to limit the sheer number of applications received by CIRM, such limits have in some cases also prevented often less senior or less influential scientists from bringing their ideas forward. We feel this works against our interest of fostering new ideas and the building of a integrated scientific community for stem cell research. We have therefore proposed the PreApp process described below as a possible solution. Similar PreApp procedures have been implemented by other funding agencies such as the National Science Foundation.

To be successful, the PreApp process must be capable of processing several hundred applications if necessary but must also be efficient and expeditious in identifying proposals that are most closely aligned with the RFA objectives and likely to be most competitive in a full application review. The PreApp process must balance acquiring the most pertinent information about a scientific proposal for proper review and minimizing the effort by applicants in conveying and submitting their idea. Another critical factor is that appropriate scientific expertise is sought to review the PreApps. Although the PreApp process can achieve all of the above, there are some consequences to utilizing this method. For example, toward maintaining efficiency and expediency we cannot practically request or collect written critiques for each PreApp reviewed and therefore cannot provide specific details to the applicants about why they did or did not succeed at this stage. In addition, the PreApp process will add about 2 months to the timeline between the release of an RFA and the final approval of awards by the ICOC.

The PreApp process utilizes a system of ranking that is similar to that used by other funding agencies to handle large volumes of pre-applications. The process described below is being applied in the same way to all PreApps including those with a collaborative funding partner. Those projects deemed to be most responsive and meritorious will be invited to submit full applications, which then undergo a full review by the Grants Working Group.

The PreApp process is coordinated and managed by CIRM Review Officers who do not participate in the scientific evaluation or selection of the PreApps.

APPENDIX 8

PreApp Processing

1. PreApps are received in electronic format.

2. PreApps are prepared for review:

- Eligibility confirmed (e.g., PI has degree required, institutional authority)
- PreApp data/content is transferred to CIRM's online review system.
- List of applicant individuals (personnel/consultants), organizations and any related business entities from applications is compiled electronically.

3. Conflict of Interest and Financial Disclosure

CIRM staff and scientific reviewers are provided with a personal login and password to the CIRM Review System web site to complete review tasks.

CIRM staff and scientific reviewers declare conflicts against comprehensive list of applicant individuals and organizations compiled from PreApps.

Scientific reviewers and CIRM staff reviewers in conflict with a PreApp cannot be assigned as reviewer of the PreApp, and must be recused from discussion, scoring and voting on the merits of the PreApp.

Scientific reviewers complete and submit a financial disclosure form that is examined for any possible conflicts of interest.

Review Assignments: External Scientific Reviewers

Each PreApp is assigned, based on relevant expertise, to two or three (depending on total number of PreApps received) scientific reviewers.

Reviewers are not assigned to any PreApp with which the reviewer has a conflict.

Approximately 15 to 40 scientific experts are sought for a given RFA depending on expertise needs and number of PreApps received.

Each scientific reviewer evaluates 15 to 40 proposals depending on type of RFA and content of the PreApp.

For their evaluation, reviewers are asked to carefully consider the RFA objectives and evaluate scientific merit against the criteria specified in the RFA. Reviewers are to place each assigned PreApp in one of 4 categories:

Do not invite, maybe invite, yes invite, or top application (optional, for the best 2 or 3 PreApp in their assignment list).

All reviewers access the PreApps and submit evaluations via a secure CIRM Review System web site. No written critiques are collected or requested.

Reviews are done independently and scientific reviewers do not see or have access to PreApps that are not specifically assigned to them.

Review Assignments: CIRM Science Officers

Each PreApp is assigned, based on relevant expertise, to two or three (depending on total number of PreApps received) CIRM Science Officers.

Reviewers are not assigned to any PreApp with which the reviewer has a conflict.

Approximately 7-10 CIRM Science Officers participate in the PreApp review.

Each CIRM Science Officer evaluates 15 to 40 proposals depending on type of RFA and content of the PreApp.

For their evaluation, CIRM Science Officers use the same criteria as the external scientific reviewers. However, CIRM Science Officers focus their evaluation on the responsiveness of the PreApp to the RFA objectives and consider the recommendations made by the external scientific reviewers. Reviewers place each assigned PreApp in one of 4 categories:

Do not invite, maybe invite, yes invite, or top application (optional, for the best 2 or 3 PreApp in their assignment list).

All reviewers access the PreApps and submit evaluations via a secure CIRM Review System web site. No written critiques are collected or requested.

Reviews are done independently from other Science Officers. However, Science Officers do have access to the evaluations from external scientific reviewers.

PreApp Evaluation Meeting:

Once all results are received, CIRM conducts a formal internal review meeting that is led by CIRM review officers who do not participate in the evaluation of PreApps.

Attendance at the internal review meeting is limited to those necessary to conduct the review including CIRM Science Officers, CIRM Review Officers, CIRM Legal Staff, the Chief Scientific Officer and the CIRM President. All attendees must declare conflicts against the full list of applicant individuals and institutions and certify their review of this list. Rules of confidentiality and non-disclosure apply.

During the closed session, the CIRM Review Officer presents the rules of confidentiality, non-disclosure, conflicts of interest and the process of review. The Review Officer also presents an overview of the RFA objectives and review criteria.

The recommendations from both external scientific reviewers and Science Officers on all PreApps are presented and discussed to identify the top 40- to 60 PreApps. The PreApps are ordered according to the level of enthusiasm across all reviewers with those having a unanimous recommendation to invite on top and a unanimous recommendation not to invite at the bottom.

The PreApps are considered and discussed taking into account any discrepancies among reviewers. Neither the CIRM reviewers nor the external reviewers will know what our funding partners have said about their preferences before making their recommendation.

For each application, the science officers take a majority vote to invite or not invite the applicant to submit a full application. The CIRM President and CIRM CSO do not participate in the vote unless the Science Officers are at a tie.

Invited applicants are then notified that CIRM will accept a full application to be reviewed by the Grants Working Group. The other applicants are notified that their PreApp has been deferred.

In the interest of improving this process we are also conducting a survey of applicants where they can anonymously tell us what they thought of the process and suggest improvements.

[Back to Appendices]

9. Grants Working group details of review process

Detailed Look at the CIRM Grants Review Process

The Grants Working Group (GWG) composed of 15 scientific members and 7 patient advocate members is responsible for reviewing the scientific and programmatic content of grant applications and making recommendations to the ICOC. The 15 scientific members that participate in a specific RFA review are drawn from approximately 130 currently appointed Regular or Alternate Grants Working Group Members. The expertise of the overall scientific membership centers on stem cells and regenerative medicine but spans a broad spectrum of knowledge across many diverse disciplines, fields, and backgrounds.

This document presents an overview of the process used by CIRM for conducting the review of full applications by the GWG.

Application Processing

1. Applications are received in hard copy and electronic formats.

2. Applications are prepared for review:

- Eligibility confirmed (e.g., PI has required minimum degree)
- Unallowable materials are removed.
- Application parts are formatted into PDF for reviewer viewing in online review system.
- List of applicant individuals (personnel/consultants), organizations and any related business entities from applications is compiled electronically.

3. Conflict of Interest and Financial Disclosure

CIRM staff, GWG scientific reviewers, and GWG patient advocates are provided with a personal login and password to the CIRM Review System web site to complete review tasks.

CIRM staff, GWG scientific reviewers, and GWG patient advocates declare conflicts against the comprehensive list of applicant individuals and organizations for the RFA.

GWG scientific reviewers and GWG patient advocates in conflict with an application cannot view the application, be assigned as reviewer of the application, and must be recused from discussion, scoring and voting on the application.

GWG scientific reviewers complete and submit a financial disclosure form that is examined for any possible conflicts of interest.

Review Assignments

Each GWG scientific reviewer is provided with a subgroup of application abstracts based on expertise to identify specific applications they can review or prefer not to review.

Each application is assigned to two or three GWG scientific reviewers based on expertise and indicated preferences. Review assignments are balanced among participating reviewers to achieve similar and reasonable workloads.

Specialist reviewers are recruited as needed to provide either additional expertise or fill specific areas of expertise that are not available among the GWG scientific reviewers. Specialists declare conflicts only against the specific applications for which their expertise is sought, complete a financial disclosure form, and do not see any other applications under review. Assignments for review are made only if no conflict is declared or identified.

All reviewers receive hard copies of assigned applications unless they prefer to view the applications online. The assigned applications are also available in the CIRM Review System web site.

GWG reviewers and GWG patient advocates may view all applications for which the specific individual has no conflict. Specialist reviewers only view assigned applications.

For each assigned application, GWG scientific reviewers and specialists submit a preliminary score and written critique (prior to the review meeting) via the CIRM Review System web site that specifically addresses the review criteria described in the RFA.

GWG Review Meeting

The review meeting must be publically posted on the CIRM web site. A public session is scheduled at the beginning of the meeting to conduct any GWG business that does not involve application review.

Attendance at the closed review session is limited to those necessary to conduct the review including CIRM staff and GWG members. Funding partner observers are also permitted to attend. All attendees must declare conflicts against the full list of applicant individuals and institutions and certify their review of this list. All meeting attendees and specialists participating by phone must sign a confidentiality and non-disclosure agreement.

During the closed session, the Senior Review Officer presents the rules of confidentiality, non-disclosure, conflicts of interest and the process of review. The Scientific Officer leading the RFA presents an overview of the RFA and review criteria.

The GWG review is conducted in two stages: scientific review followed by programmatic review.

During **scientific review**, the Chair of the GWG leads scientific members of the working group to evaluate and score individual applications for scientific merit.

Before beginning each review, the individuals who have a conflict of interest must leave the room. Once recused members are out of the room, the primary and secondary reviewers are identified. Each reviewer first states his/her preliminary score – a score of 100 is best, and 1 is worst. The primary reviewer then provides a very brief synopsis of the application, highlighting the overall goals of the application and major strengths or weaknesses relevant to the review criteria. The secondary reviewers then contribute

their comments. The application is then open for discussion by all. When there is no more discussion, the chair calls for each assigned reviewer to state a final score. Each scientific member of the GWG records his/her own final score for the application in individualized voting booklets. Reviewers are instructed that their individual score does not need to reflect a consensus score.

When applicable, specialist reviewers participate as secondary reviewers of assigned applications and contribute to the discussion, provide a preliminary score, but do not record an individual final score. Only GWG scientists contribute a final score.

The final score for an application represents the average of all individual scores recorded by the GWG scientists who have no conflict with the application.

If the review of an application results in thirty-five percent (35%) of the members of the GWG joining in a minority position, a minority report may be submitted to the board with the final recommendations.

During **programmatic review**, the working group evaluates the entire portfolio of applications taking into consideration the overall rankings by score, and the specific objectives of the RFA and of the mission of CIRM. The working group will make their final recommendations to the ICOC for funding or not funding of applications.

Programmatic review is led by the Vice-Chair of the GWG (a patient advocate) and is conducted in 2 steps.

In the first step, the GWG is presented with a frequency distribution histogram of the scientific scores (final average score) of all the applications. The distribution histogram contains no information that would allow GWG members to identify any particular application. With this visual tool, the GWG can consider any natural groupings in the overall scores that would identify the most meritorious applications. The GWG votes to draw an initial red line along the distribution histogram below which the scientific merit score does not justify a recommendation for funding. The GWG also votes to draw an initial green line which best identifies the most meritorious applications that should be recommended for funding. These initial funding lines establish the following tiers:

Tier 1: Recommended for Funding – For highly meritorious grant and loan applications that are recommended for funding to the ICOC.

Tier 2*: *Provisionally Recommended for Funding – For meritorious grant and loan applications that require further consideration by the ICOC. The GWG may change the designation as needed to reflect the appropriate communication to the ICOC regarding the merit of the applications in Tier 2.

Tier 3: Not Recommended for Funding – For grant or loan applications that are not recommended for funding at this time.

Once the GWG has established these initial funding lines – the GWG moves to the second step of programmatic review. In the second step, the identity (PI , title of project, funds requested) and score of each application is shown to the GWG in rank order in respective tiers. GWG members are asked to consider the rankings and where appropriate propose any changes to the funding recommendation of any application

based on programmatic grounds. Programmatic considerations may include, for example, that an appropriate range of diseases is addressed or a balance between innovation and feasibility is achieved. At this step, before any discussion of an individual application takes place, members and staff who are in conflict with the application leave the room and the recusals documented. The change in rank or tier of an application must first be proposed via a motion by a GWG member, agreed to by a second member, and finalized by a majority vote of the GWG members. When the GWG is satisfied with the programmatic order, a final vote is taken on the overall recommendations to the ICOC.

ICOC Approval

The recommendations of the GWG are presented to the ICOC in a public meeting of the board. A scientific score, funding recommendation, and summary of review are provided to the ICOC and public for each application. The summary of review includes the public abstract and statement of benefit provided by the applicant. Documents are redacted to remove any information that would identify the investigators or applicant organization.

The ICOC considers the GWG recommendations and any information that they feel is pertinent in making a final decision on funding or not funding of an application. The ICOC may consider any confidential and proprietary information contained in an application during a closed (non-public) session.

Applicants approved for funding by the ICOC are named in a press release immediately following the board meeting. Applicants are informed by CIRM of the ICOC decision. Approved applications then undergo an administrative review prior to the initiation of funding.

[Back to Appendices]

APPENDIX 10

10. Data from PI grantee survey

1. What type(s) of CIRM grant(s) do you hold?

New Faculty	SEED	Basic Biology	Disease Team Research	Early Translational	Training	Comprehensive
19% (24)	**18%** (23)	**16%** (20)	**10%** (13)	**10%** (13)	**9%** (12)	**9%** (11)

Bridges	New Cell Lines	Shared Labs	Tools & Technologies	Disease Team Planning	No Response
7% (9)	**7%** (9)	**6%** (8)	**6%** (8)	**4%** (5)	**5%** (6)

2. What is your position?

Professor	Associate Professor	Assistant Professor	CSO	Senior Scientist	Prinicipal Scientist	Other
53% (67)	**16%** (20)	**24%** (30)	**1%** (1)	**1%** (1)	**2%** (2)	**5%** (6)

3. CIRM's portfolio of RFAs is balanced and appropriate to achieve its mission of accelerating the pace toward therapies.

Agree	Somewhat Agree	Somewhat Disagree	Disagree	No Response
65% (82)	**16%** (20)	**14%** (18)	**5%** (6)	**1%** (1)

4. CIRM's application and review process seems appropriate.

Agree	Somewhat Agree	Somewhat Disagree	Disagree	No Response
67% (85)	**20%** (26)	**9%** (11)	**3%** (4)	**1%** (1)

5. For those RFAs when CIRM must limit the number of grants taken to full review, do you prefer: a) the pre-application process (where short applications are submitted and only the most responsive and competitive are invited to submit a full application), b) institutionally set limits (where your institution selects the one, two or three applications that may be submitted to CIRM), or c) other (please specify).

Pre-Applications	Institutional Limits	Other	No Response
85% (108)	**11%** (14)	**3%** (4)	**1%** (1)

6. Do you feel adequately informed of CIRM funding opportunities?

Yes	No	No Response
88% (112)	**10%** (13)	**2%** (2)

How do you currently learn about CIRM funding opportunities?

From my institution	CIRM website	Email from CIRM	Word of mouth	Other	No Response
62% (79)	**60%** (76)	**43%** (54)	**32%** (41)	**0%** (0)	**2%** (2)

7. Being a mission driven organization with a limited time frame to deliver, CIRM requires progress reports that are more detailed than most other funders. CIRM also monitors progress through site visits and the annual grantee meeting. Given the agency's goals and time frame this progress tracking is reasonable.

Agree	Somewhat Agree	Somewhat Disagree	Disagree	No Response
57% (72)	**26%** (33)	**12%** (15)	**4%** (5)	**2%** (2)

8. CIRM recognizes that the nature of science results in drift in the direction of research projects. The extent to which this will be permitted depends on the specific requirements of the RFA under which the award was granted, with some RFAs such as Basic Science allowing for more drift than translation RFAs that require tighter adherence to pre-set goals. Did you know CIRM requires prior approval for change in scope of a research project?

Yes	No	No Response
94% (119)	**6%** (7)	**1%** (1)

CIRM strives to make approval for change in direction as efficient as possible. The agency succeeds in this effort.

Agree	Somewhat Agree	Somewhat Disagree	Disagree	No Response
48% (61)	**20%** (25)	**6%** (8)	**2%** (3)	**24%** (30)

9. Do you communicate with your CIRM program officer or grant management officer regularly?

Yes	No	No Response
58% (74)	**39%** (50)	**2%** (3)

They are consistently helpful.

Agree	Somewhat Agree	Somewhat Disagree	Disagree	No Response
65% (82)	**10%** (13)	**4%** (5)	**1%** (1)	**20%** (26)

APPENDIX 10

10. CIRM has succeeded in fostering a community of researchers that creates synergy through shared knowledge and collaboration.

Agree	Somewhat Agree	Somewhat Disagree	Disagree	No Response
59% (75)	**29%** (37)	**6%** (8)	**4%** (5)	**2%** (2)

11. Do you use CIRM-funded shared lab facilities?

Yes	No	No Response
59% (75)	**39%** (50)	**2%** (2)

Do you think your institution will be able to maintain these facilities when CIRM funding for that lab ends?

Yes	No	Maybe	Not Applicable	No Response
26% (33)	**12%** (15)	**31%** (39)	**11%** (14)	**20%** (26)

12. Do you think CIRM's collaborative programs with the UK, Japan, Victoria Australia, Spain, Germany, China, New York and Maryland benefit your research and ability to collaborate?

Yes	No	No Response
47% (60)	**47%** (60)	**6%** (7)

Do you have out-of-state collaborators now?

Yes	No	No Response
46% (59)	**50%** (64)	**3%** (4)

13. CIRM is sufficiently aggressive in pursuing industry participation in its work and fostering academic/industry partnerships.

Yes	No	No Response
93% (118)	**0%** (0)	**7%** (9)

14. How has CIRM benefited your research?

Directly supported research via grant	Supported a trainee	Supported facilities used	Allowed hiring of additional research personnel	Facilitated collaboration	Supported work that led to publication	No Response
83% (105)	**64%** (81)	**56%** (71)	**53%** (67)	**48%** (61)	**44%** (56)	**3%** (4)

15. Has CIRM funding created data that allowed you to obtain grants from other organizations?

NIH	Foundations	Other	No Response
27% (34)	**13%** (17)	**12%** (15)	**54%** (69)

16. How has CIRM benefited your field of research?

Stimulated additional research	Contributed to the training of new researchers	Expanded available research facilities	Brought new scientists to the field	Other	No Response
81% (103)	**72%** (92)	**55%** (70)	**51%** (65)	**3%** (4)	**6%** (7)

[Back to Appendices]

11. Bureau of State Audit (BSA) Report

California Institute for Regenerative Medicine:
It Has a Strategic Plan, but It Needs to Finish Developing Grant-Related Policies and Continue Strengthening Management Controls to Ensure Policy Compliance and Cost Containment
HIGHLIGHTS

Our review of the California Institute for Regenerative Medicine (institute) revealed the following:

- The institute identified long-term research priorities and considered the industry's best practices to create its strategic plan, but it has yet to implement a process to assess annual progress toward attaining its strategic goals.
- A task force formulated draft policies for revenue sharing through a public deliberative process but, because of a lack of documentation, we could not independently evaluate any analyses of the information on which the task force members based their revenue-sharing policies.
- Although it has a grants administration policy for academic and nonprofit institutions, the institute is still developing a for-profit policy and is still implementing a monitoring process to ensure that grantees comply with the terms of their grants.
- The institute's recent policy revisions addressed our contracting concerns, but not all of our travel reimbursement concerns.
- The salary survey conducted by the institute and the compilation of the salary data collected contained enough errors, omissions, and inconsistencies that the institute cannot ensure that the salaries for certain positions comply with the requirements of the law.

RESULTS IN BRIEF

In 2004, voters approved the California Stem Cell Research and Cures Act (act), which authorized the issuance of $3 billion in bonds over 10 years to fund a stem cell research program and dedicated research facilities in California. The act established the California Institute for Regenerative Medicine (institute) as a state agency with the purpose of funding stem cell research activities. The goal of the research is to realize therapies, protocols, and medical procedures that, as soon as possible, will lead to curing or substantially mitigating diseases and injuries. The act directs the institute to give priority to research that has the greatest potential for therapies and cures and that cannot or is unlikely to receive timely or sufficient federal funding. The institute is responsible for supporting all stages of the process of developing cures and establishing appropriate regulatory standards and oversight bodies for research and facilities development.
To oversee the institute's operations, the act established the Independent Citizens Oversight Committee (committee). The act mandates that the committee develop annual and long term strategic research and financial plans for the institute. The committee adopted the institute's strategic plan during its December 2006 meeting. The plan outlines goals and objectives for spending $3 billion in general obligation bonds authorized by the act and provides a strategy that strives to meet the purpose and intent of the act.

APPENDIX 11

To create the strategic plan, the institute followed a planning process that outlined organizational responsibilities and timelines. The planning process enabled the institute first to analyze pertinent information and then to identify long-term research priorities. To consider the best practices of the industry, the institute consulted various expert stakeholders through interviews, conferences, and focus groups. In addition, the institute reviewed the strategic plans and the strategic planning processes of other entities. The strategic plan contains essential elements, including a mission statement and a set of goals for fulfilling the mission. The plan's goals depend on scientific discovery, so ensuring that they are achievable is challenging. However, the outlined goals are specific in nature and were adopted unanimously by the committee, along with the remainder of the institute's strategic plan, in December 2006. Our review concluded that the institute's approach to achieving its goals through specific initiatives is defined clearly. The plan contains an action plan for the first 1,000 days, as well as performance mechanisms and milestones to ensure accountability, assess performance, and gauge scientific progress at years three and seven of the 10-year strategic plan. However, the institute has not yet established a process to track management information from grantees to assess annual progress toward attaining its strategic goals.

The institute has developed several policies and procedures to advance implementation of the stem cell research program approved by voters, including policies that address intellectual property issues resulting from research funded by its grants to nonprofit and for-profit organizations. A particularly important concern for the institute is sharing revenues acquired from the commercialization of institute-funded discoveries. Under the act, the committee must establish standards that balance the State's opportunity to benefit from the patents, royalties, and licenses resulting from the activities funded by the institute with the need to ensure that essential research is not unreasonably hindered by intellectual property agreements. A task force established by the committee formulated draft policies for revenue sharing through a public deliberative process. The committee subsequently adopted the policies. The task force relied on the knowledge and judgment of its members and a broad assortment of information collected and summarized by the committee's vice chair (who served as the chair of the task force) and his deputy. Although we observed that the task force conducted extensive discussions of the information presented, neither the vice chair nor his deputy provided sufficient documentation to demonstrate how they evaluated the information they gathered and how they determined whether the information was appropriate for discussions that would lead to the formulation of the revenue-sharing policy. As a result, we could not independently evaluate any analyses they may have performed of the information on which the task force based its deliberations.

The committee's policies require that grantees provide a plan that ensures that uninsured Californians have access to all therapies developed as a result of the institute's grants. However, the committee has not yet adopted the appropriate language to define its expectations regarding access. Moreover, although the committee has identified standards for discount prices for drugs, it has not yet identified the appropriate benchmarks to use as a standard for establishing discount prices for nondrug therapies. In addition, the institute needs to develop a policy for administering certain grants. Although it has developed a grants administration policy for academic and nonprofit institutions, the institute is still developing a policy for administering future grants to for-profit organizations.

Moreover, it is still implementing a grants monitoring process that will contain the procedures used to ensure that grantees comply with the terms of their grants, including procedures for performing audits of grantees.

The committee has adopted conflict-of-interest policies to identify and prevent conflicts between the personal interests and the work duties of institute employees as well as members of the committee and the institute's working groups. However, the institute needs more effective policies and procedures. For example, its conflict-of-interest policy for the working group that evaluates applications for program grants does not include experts, known as specialists, who are invited to assist the working group.

The institute did not establish a contracting policy effectively ensuring that it received appropriate goods and services at reasonable prices. Based on language in the act, legal counsel for the institute concluded that it is governed by all the provisions of the Public Contract Code that affect the University of California (UC). Additionally, it is the institute's intent to model its policies substantially after those of UC. However, much of the institute's policy did not conform to UC policy. As a result, the institute awarded multiple contracts without a competitive-bidding process and did not maintain documents that demonstrated it received reasonable prices on the goods and services it purchased. In addition, the institute's travel reimbursement policy did not provide sufficient control over travel expenses. The institute originally adopted the travel reimbursement policy of the Department of Personnel Administration, but then revised the policy several times to conform more closely to the UC policy. In general, the revisions allowed travelers greater flexibility and more liberal reimbursements. For example, the institute removed maximum reimbursable amounts for some expenses, such as meals for committee meetings.

Moreover, the institute reimbursed costs for air travel and meals without sufficient documentation of travel expenses to ensure that its policies were followed. The revisions also made the policy confusing because they did not use consistent language, and some new provisions did not specify whether they replaced or supplemented existing policies. For instance, the policy contained multiple reimbursement rates for items such as meals but failed to provide clear guidance on when to use each rate.

In response to our concerns about contracting and travel reimbursements, the institute revised certain policies in December 2006. These policy revisions addressed our contracting concerns, but not all of our travel reimbursement concerns. For example, the institute has not revised the form that working group members use to claim travel reimbursement to include information specific enough to allow for a proper review of the claims, and its revised policy specifies that it applies only to institute staff and working group members, not to members of the committee. The institute has indicated to us that it is developing an internal procedures manual that will address additional contracting issues. In addition, the committee chair stated that the committee will consider amendments to the travel policy in the upcoming months.

Finally, the salary survey conducted by the institute and the compilation of the salary data collected contained enough errors, omissions, and inconsistencies that the committee and the institute cannot ensure that the salaries for certain positions comply with the requirements of the act. The institute plans corrective action.

RECOMMENDATIONS

The institute should develop a process to track management information reported annually by grantees, thereby providing accountability and enabling it to assess its annual progress in meeting its strategic goals.

The committee should ensure that it proceeds with its plan to identify the appropriate standard for providing uninsured Californians access to therapies developed with institute funds. Moreover, the committee should ensure that its intellectual property policies clearly convey to grantees its expectations for providing that access. In addition, the committee should identify practical benchmarks to use as a standard for discount prices for therapies and apply the standard to its policies for grants to nonprofit and for-profit organizations. The institute should complete its grants administration policy targeted toward for-profit organizations.

To monitor the performance of grantees effectively, the institute should complete the implementation of a grant monitoring process and the development of related procedures.

The institute should amend its conflict-of-interest policies to include any specialists it may invite to participate in stem cell research program activities, such as grant application review.

The institute should strictly follow its newly revised contracting policy, which addresses the concerns raised in our audit. The institute also should amend its travel reimbursement practices for meal reimbursement to ensure its policies are followed. Further, the committee should consider amendments to its travel reimbursement policy that will result in the reimbursement of reasonable and necessary travel expenses, as stated in the act, and that address the concerns we raised in the report.
To ensure that the methodology to set salary ranges complies with the act, the institute should proceed with its plan to resurvey any positions with salary ranges affected by the errors, omissions, and inconsistencies in its initial salary survey and salary-setting activities.

AGENCY COMMENTS

The institute agrees with our recommendations and states that the report makes a useful and important contribution to the institute's effort to operate as effectively and efficiently as possible and in full compliance with the law.

[Back to Appendices]

APPENDIX 12

12. CIRM responses to BSA

Report 2006-108—California Institute for Regenerative Medicine

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

(Report Number 2006-108, February 2007)

It Has a Strategic Plan, but It Needs to Finish Developing Grant-Related Policies and Continue Strengthening Management Controls to Ensure Policy Compliance and Cost Containment

In 2004 voters approved the California Stem Cell Research and Cures Act (act), which authorized the issuance of $3 billion in bonds over 10 years to fund a stem cell research program and dedicated research facilities in California. The act established the California Institute for Regenerative Medicine (institute) as a state agency with the purpose of funding stem cell research activities. The goal of the research is to realize therapies, protocols, and medical procedures that, as soon as possible, will lead to curing or substantially mitigating diseases and injuries. To oversee the institute's operations, the act established the Independent Citizens Oversight Committee (committee).

The Joint Legislative Audit Committee (audit committee) requested that the Bureau of State Audits (bureau) review the implementation of the act and the performance of the institute and the committee to the extent that the program is operating. The audit committee asked us to review and evaluate the strategic plan and related policies developed by the institute and the committee. In addition, the audit committee asked us to review and evaluate certain institute policies and procedures and related management controls to determine whether they are necessary and designed to carry out the intent of the act as well as other applicable laws and regulations, and to review the internal oversight structure of the institute and the committee.

The following table summarizes the auditee's progress in implementing the 12 recommendations the bureau made in the above referenced report. As shown in the table, as of its one-year response, the auditee had not fully implemented four of those recommendations. Based on the auditee's most recent response, it has fully implemented all recommendations within the report.

TOTAL REOMMENDATIONS	NOT IMPLEMENTED AFTER ONE YEAR	NOT IMPLEMENTED AS OF 2008-041 RESPONSE	NOT IMPLEMENTED AS OF MOST RECENT RESPONSE
12	4	3	0

Below are the recommendations that we determined were fully implemented, followed by the auditee's most recent response.

Recommendation #1:
The institute should fulfill its plans to develop a process to track management information reported annually by grantees, thereby providing accountability and enabling it to assess annual progress in meeting its strategic goals and initiatives.

Bureau's assessment of status: Fully implemented

Auditee's Response:
Introductory note: Recommendations 1 and 3 both refer to how CIRM manages grants that have been awarded, and information reported by grantees. For clarity, and with reference to the findings with which each recommendation was made, CIRM's response to Recommendation No. 1 will address the collection, tracking and use of substantive information from and about grantees; the response for Recommendation No. 3 refers to monitoring grantee compliance, including verification and audits of the information reported by grantees, and a grants management database system.

Progress reporting: Implementation completed Spring 2007

Grantees submit annual reports detailing scientific progress on the funded research project. Grantees also have reporting requirements triggered by certain events. For example, when a CIRM grantee publishes a scientific article reporting results of CIRM-funded research, the grantee must report that to CIRM within 60 days. CIRM uses these reports to compile and report information about CIRM-funded scientific progress. (Annual reporting requirements are set out in the grants administration policies. Event-based reporting requirements are set out there and in the intellectual property regulations.)

Each scientific progress report is reviewed by the assigned CIRM science officer. Grantees are required to provide data and figures to support the report, and may be asked for supplemental information if the report is incomplete or inadequate. 1 Science officers review the reports for several reasons:

1) Science officers review progress reports to determine whether the grantee is pursuing the agreed-upon research plan, and making adequate progress. This review includes reference back to the original application and prior progress reports, and requires grantees to provide updated data and figures. Due to the nature of scientific research, it is not uncommon that preliminary results require changes to the original research plan. Grantees may deviate from the original research plan, but only after obtaining prior approval from CIRM, which will be granted when the change would further CIRM's mission and the purposes for which the grant was awarded. Changes in research personnel are handled the same way. If the progress report indicates that such changes have occurred without CIRM's prior approval, or that adequate process has not been made, CIRM will take further action, as described below.

2) By understanding the progress and preliminary results of CIRM-funded research, CIRM's science officers are able to maintain current, cutting-edge knowledge of developments in the field. This knowledge helps to inform all aspects of CIRM's scientific programs.

3) A report may also indicate that a grantee is confronting an obstacle that has been addressed by another researcher (another CIRM grantee, or otherwise). The science

officer may be able to help move the research forward by facilitating communication between the researchers.

If it appears that a grantee is not making adequate progress, and that it would not be productive for it to continue, CIRM will notify that grantee that termination is being considered. The researcher and the grantee institution are given an opportunity to respond. In some instances, further dialog has allowed a project to continue subject to specified conditions. In other instances, CIRM has terminated grants.

For further details about the review of progress reports, please see two attached documents: A transcript of a presentation to CIRM's governing board, the ICOC, regarding CIRM's experience to date with progress reports, and a copy of the accompanying slides.

Additional methods for tracking and using grantee information

CIRM has developed and implemented a method for capturing and coding scientific information about the scope, progress and outcomes of funded research projects. As CIRM initiates the funding for a new project, most of the information from the grantee's original application is imported into CIRM's grants management database, which tracks all of the administrative information (names, key personnel, percent effort, institution, funding amounts, budget, etc.).
At the same time, the science officer assigned to the project will fill out a "Coding Form" which captures all of the relevant scientific and programmatic aspects. Examples of the latter include diseases addressed, types of cells used (embryonic, adult stem cell, iPS, etc.), basic approaches used, biological mechanisms investigated, lineages of stem cell derivatives being studied, whether or not a grant is basic or applied research and its approximate maturity (stage on the development pipeline); the intended outcome of the project (e. g. , cell therapy, biologic or small molecule, or bottlenecks addressed).

The database can be searched by any of the coded items, be they administrative or scientific. For example, CIRM can search the database for all grants that are investigating cancer, and see a list of projects, titles, amounts awarded, principal investigators, etc.

Recent examples of questions addressed by use of this information:

• What percentage of CIRM grants are pursuing embryonic stem cells vs. adult stem cells? What is the breakdown by amount of funding?

• How much cancer research is CIRM funding?

• Which grants are using cancer stem cells?

• Pie chart of the disease breakdown of CIRM grants.

• Which grants are pursuing therapies for diseases that affect under-represented minorities (HIV, SCD, diabetes)?

CIRM has used this data to answer questions about how CIRM is meeting the goals of its scientific strategic plan. It was also critical to the recent update of that plan, which relied on portfolio coding ("What are we funding?") and on CIRM's publication/patent databases ("What have we achieved?").

This information was also critical earlier this year, when the National Institutes of Health proposed new regulations about which cell lines would be eligible for study in federally funded research. The scientific community generally agreed that the proposed regulations would have unnecessarily impeded critical research. CIRM was able to quickly identify the relevant research projects and contact grantees for additional information, then prepare a chart identifying specific cell lines that could be affected, and the types of research for which each cell line was in use. Supplemented with data from other agencies, this chart was part of CIRM's comments on the proposed regulations, and provided the NIH with specific, well-supported examples. The NIH adopted final regulations that were generally consistent with CIRM's position.

Grantee meeting: Implementation Completed September 2008

As noted last year, CIRM held its first scientific conference for all CIRM grantees in September 2008, with over four hundred CIRM-funded scientists attending. The meeting featured lectures, posters, and interactive science activities. Leading U. S. and international scientists attended by invitation to stimulate discussions on chosen subjects of high priority. The next grantee conference is scheduled for March 2010.

Recommendation #2:

The committee should ensure that it follows through with its plan to identify the appropriate standard for providing uninsured Californians access to therapies developed using institute funds and to convey clearly to grantees its expectations for providing access in its intellectual property policies. In addition, the committee should identify practical benchmarks to use as a standard for discount prices for therapies and apply the standard to its policies for grants to nonprofit and for-profit organizations.

Bureau's assessment of status: Fully implemented

Auditee's Response:

Intellectual Property and Related Regulations

By the time of last year's update, CIRM had adopted its "Intellectual Property Requirements for Non-Profit Organizations" (17 Cal. Code Reg. §§ 100300 et seq.) and "Intellectual Property and Revenue Sharing Requirements for For-Profit Organizations" (17 Cal. Code Reg. §§ 100400 et seq.), and embarked on the process of combining them into a single, updated set of comprehensive regulations. CIRM's governing board, the Independent Citizens Oversight Committee (ICOC) has adopted the new regulations, "Intellectual Property and Revenue Sharing Requirements for Non-Profit and For-Profit Grantees" (17 Cal. Code Reg. §§ 100600 et seq.). The regulations include requirements for discount pricing and access (§ 100607).

Recommendation #3:

To monitor the performance of grantees effectively, the institute should complete the implementation of a grants monitoring process, including audits, and the development of related procedures.

Bureau's assessment of status: Fully implemented

Auditee's Response:

Introductory note:. Recommendations 1 and 3 both refer to how CIRM manages grants that have been awarded, and information reported by grantees. For clarity, and with reference to the findings with which each recommendation was made, CIRM's response to Recommendation No. 1 will address the collection, tracking and use of substantive information from and about grantees; the response for Recommendation No. 3 refers to monitoring grantee compliance, including verification and audits of the information reported by grantees, and a grants management database system.

Grants management system: Implementation completed September 2009

From the outset, CIRM has tracked the financial and scientific information reported by grantees. Initially, staff relied on spreadsheets and other standard office software to track the information.
These methods allowed staff to collect and analyze the information, but it was cumbersome, and intended as a temporary system.

Initially, CIRM sought development of a customized system that would handle all stages of the grantmaking process – application, expert review, issuance, funding, oversight and close-out. CIRM awarded a contract to Grantium, Inc. , and began working with Grantium on implementation.

With further experience, and based on systems analysis that occurred in the Grantium implementation process, CIRM staff concluded that a simpler approach would be more effective and less expensive, and could be implemented more quickly. CIRM already has custom-designed software, developed in-house, to handle the application and review process. That custom software continues to meet CIRM's needs for all stages of the grant process up to and including the ICOC's final funding decisions.

For post-award management, CIRM opted for an existing grants management product, MicroEdge GIFTS, that is widely used among grantmaking agencies. This software was much less expensive than it would have cost to continue development of a complete customized system. Because GIFTS is in widespread use, most of the grants management staff had prior experience with it, which expedited training. It has been installed and configured for CIRM's processes, and existing data has been transferred. CIRM's grants management staff now use GIFTS to manage post-award activities and reporting. As discussed in CIRM's response regarding Recommendation No. 1, this system allows tracking of substantive scientific information across all CIRM grants. Other examples of functionality:

• Centralized tracking of all documents, information and events associated with each grant

• Generates accurate up-to-date cash flow projections

• Coordinates the workflow of science officers and grants management staff, by tracking all pending tasks by grant or staff member.

• Enhanced data validation functions

• For applications approved by the ICOC, import of relevant application data

• Generates grant agreement, official payment requests, notices to grantees, and other grant-specific documents

Verification of Compliance

CIRM relies on multiple levels of oversight to verify that grantees comply with legal requirements and the terms of each grant:

1. Pre-Funding Administrative Review: Before initial funding of an award, CIRM staff verify that all requirements have been met.

2. Annual reporting: Financial and scientific reports allow CIRM to verify continued compliance and to monitor progress. Reports are actively reviewed, and further funding may be withheld until complete reports have been reviewed and approved.

3. Event-based reporting: Publications, invention disclosures and other significant events that occur during the course of the CIRM-funded research.

4 Institutional oversight: As is standard with this type of research funding, the grantee institutions have the primary responsibility for ensuring that researchers comply with all requirements. Institutions are required to maintain and follow oversight policies, and to investigate and report on misconduct.

5. On-site audits of grantee institutions:. CIRM staff visit grantee institutions to review policies and practices, and to test compliance by examining supporting documents for selected grants.

6. Independent audits:. Under recent amendments to CIRM's grant administration regulations, CIRM can require a grantee to commission an independent audit.

7. Referral: If serious misconduct occurs, CIRM may refer the matter to the Attorney General or other officials for investigation.

Prefunding Administrative Review

As reported in CIRM's prior responses, CIRM verifies eligibility before an award is issued, through its Prefunding Administrative Review (PFAR) process. Attached is a document setting out the PFAR process for non-profit grantees; a similar process is used for for-profit grantees.

Annual financial reporting

All grantees are required to report annually on their use of CIRM funds. Every financial report is scrutinized by the grants management staff to determine whether the reported use of funds complies with the CIRM-approved budget. Future funding can be withheld until CIRM has received and approved the annual financial and scientific reports. If reporting is incomplete or ambiguous, CIRM staff will request additional information or detailed supporting documentation. If the grantee has used funds for costs outside the approved budget, CIRM recovers those funds from the grantee, or reduces the next year's payment accordingly.

It is not uncommon for grantees to report that they have not spent all funds budgeted for the prior year; scientific research and the associated costs do not always follow a precise schedule. From a budgetary standpoint, CIRM will allow a grantee to carry over up to 25% of the annual budget, adding that amount to the budgeted amount for the following year. Any amount over 25% must be returned (or deducted from the following year's payment) unless CIRM approves the carryover for good cause.

Similarly, at the end of the grant period, grantees may petition for authorization to extend the grant for up to one year to complete the work with remaining funds. The "no-cost extensions" are generally granted when scientifically justified.

Annual scientific reporting

As discussed in CIRM's response regarding Recommendation No. 1, CIRM science officers review annual reports of scientific progress. In addition, CIRM staff confirm continued compliance with medical and ethical standards regulations, verifying current approvals from oversight committees for human subject research, animal research, and research using human embryonic stem cells.

Because the annual report includes a comprehensive summary of the year's activity, these reports sometimes reveal items that should have been reported earlier in the year, such as scientific publications or invention disclosures. Recognizing that grantees may not be familiar with all of CIRM's event-based reporting requirements, CIRM has explored ways to improve prompt compliance. For example, recognizing that scientists may not remember to notify CIRM when CIRM-funded research leads to an invention, CIRM is working with institutional technology transfer officers to incorporate CIRM reporting into their procedures.

Annual scientific progress reports include a summary that is intended for the general public. CIRM will soon begin posting the public progress summaries on its website, alongside the other information already posted for every CIRM-funded project.

Event-Based Reporting

Grantees are required to notify CIRM of certain events that may occur during (or after) the lifetime of a grant. For example, grantees are required to notify CIRM when they publish the results of CIRM-funded research, and provide an abstract written for the general public. CIRM summarizes selected publications on its research blog, and plans to post a searchable list on its website.

Without reports from grantees, CIRM would be unaware of many of these events, and thus unaware that a report is due. CIRM is working with grantee institutions to improve compliance, and developing alternative methods for obtaining this information. For example, CIRM science staff use keyword searches of the scientific literature to locate publications that should have been reported to CIRM.

Institutional oversight of researchers

Most CIRM grantees are accustomed to managing research funded by the National Institutes of Health and other federal agencies. In order to avoid confusion and simplify compliance, CIRM incorporates federal standards whenever possible. These standards rely on research institutions to ensure that their researchers comply with requirements, and to investigate and report on failure of compliance. This approach represents a balance between the need for accountability with institutional independence and academic freedom. CIRM has taken a similar approach. For example, CIRM does not specify a uniform policy for handling research misconduct. Instead, grantee institutions are required to maintain and follow acceptable policies regarding research misconduct, conflicts of interest, and protection of human and animal subjects.

Onsite Compliance Audits

CIRM's compliance audit program has been operating since June 2008. When a grantee institution is selected for audit, CIRM staff conduct an internal review of CIRM's files for that institution's grants, followed by a full onsite evaluation for selected grants. CIRM staff have conducted onsite audits at eight grantee institutions that account for approximately 60% of all CIRM grants. These reviews have generally found grantee institutions to be in compliance, though individual oversights were noted and corrected. In some instances, CIRM has requested improvements to institutional procedures.

Independent Audits

Under recent amendments to CIRM's grant administration regulations, CIRM can require a grantee to commission an independent audit. Proposition 71 places tight limits on the size of CIRM's staff and the funds available for operating expenses, so it would not be feasible for CIRM to routinely perform detailed financial audits of its grantees. With this supplemental authority, CIRM can now require an independent, professional audit if the grantee cannot adequately account for its use of CIRM funds.

[Back to Appendices]

APPENDIX 13

13. Little Hoover Commisiion executive summary

EXECUTIVE SUMMARY

Approved by voters in November 2004, Proposition 71 gave California the constitutional right to conduct a politically controversial type of stem cell research using human embryos.

The measure was a reaction to President George W. Bush's restrictions on federal funding for certain human embryonic stem cell research and a bid to jumpstart a new industry in California. Although private funding was not restricted, California voters responded by authorizing $3 billion in research funds to support stem cell science and create a new state agency, the California Institute for Regenerative Medicine (CIRM), to oversee the distribution of the money to universities, research institutes and biotechnology companies. The ballot measure also created a 29-member governing board, the Independent Citizens Oversight Committee (ICOC), to craft policies for CIRM and give final funding approval for research requests.

Although Proposition 71 passed with almost 60 percent of the vote, skepticism continues to surface from detractors, the media, members of the Legislature – even early backers – about the agency's ability to direct funding to science that will best lead to new medical treatments and cures. Much of the criticism has been directed at the ICOC, which is composed of officials from top universities, research institutes and the biotechnology industry, as well as advocates from disease groups that will benefit from the funding. The legality of this governance structure has been upheld by the courts, though what is legally allowable may not necessarily be optimal. As long as CIRM's governance structure exists in this form, skepticism will remain, generating scrutiny that will take away from CIRM's main focus – driving transformational scientific research and finding cures.

In April 2008, Senators Sheila Kuehl and George Runner asked the Little Hoover Commission to make recommendations on ways that CIRM's governance structure might be improved to better ensure public accountability and reduce conflicts of interest. The Commission has identified several recommendations to more adequately guide the state's unique investment in stem cell science – more than $6 billion once bonds are repaid – and improve the agency's efficiency in meeting the voters' goals.

In terms of outcomes, the governance structure and issues of transparency and accountability will be more critical to CIRM going forward. Despite the weaknesses of its existing governance structure, CIRM has been successful in getting money out the door quickly and establishing California as a global leader in stem cell science. Its investment of more than $700 million since 2004 has provided demonstrable results, including new and expanded facilities under construction, an influx of out-of-state and foreign scientists, published articles on research progress and growth in California's life-sciences industry. Moreover, it has leveraged the state's investment by attracting $900 million in matching funds. The Commission found that the method CIRM has developed to distribute grants, based on practices of leading federal grant-making entities, has been defensible, though room exists for process improvement. The Commission can see no downside to more transparency: Connecticut, for example, has not suffered from a lack of

interest from grant seekers by using its more open process for a state-run $100 million stem cell research program. CIRM, however, is moving in the other direction by introducing an additional, closed-door element of the review process that involves an internal staff screening of funding requests.

Criticism that CIRM's governing board remains an insiders' club undermines the legitimacy of the agency. Some 80 percent of the funds to date have been awarded to institutions with representatives on the ICOC. The fact that CIRM funding has gone largely to prestigious California universities and research institutes is hardly surprising and should be expected, given the goals of Proposition 71 and the considerable expertise resident in these research centers. Such institutions would be natural recipients of such research money under Proposition 71. Even though the names of the institutions applying for research funds are redacted during the review and approval process, criticism about the makeup of the agency's governing board was an issue the Commission heard repeatedly – and one that can be addressed by incorporating more transparency into CIRM's operations. For example, the frequent occurrence of members recusing themselves because of conflicts of interest shows a structural defect in the governing board.

Though CIRM's original grant distribution process follows a best-practices model, CIRM's organizational structure deviates from good-governance characteristics of corporate, nonprofit and public-sector boards. The rationale may have been reasonable in 2004, when human embryonic stem cell science was the subject of political controversy. The detailed provisions of the ballot initiative, which placed the governing board outside of the normal scope of accountability compared to other state agencies and boards, provided stability, diversity and the political protection to get the agency up and running. But today, only five years later, Proposition 71 already looks like a relic of another era. President Barack Obama is removing restrictions on federal funding for human embryonic stem cell research, and CIRM struggles at times against the rigidity of its governing statutes to adjust to the changing political and scientific landscape and plan for the future.

Much of Proposition 71 now seems overly prescriptive in defining the governance and oversight structure of CIRM. Among the weaknesses the Commission found:

- The 29-member board is too big and has had trouble assembling quorums.
- The board lacks truly independent voices to balance out those of interested board members.
- The founding board members' terms are too long and are not conducive to adding fresh perspectives about the agency's future given the rapid advancement of stem cell science.
- The multiple appointing authorities for board members cloud accountability.
- The board chair position, as structured, conflates day-to-day management with the independent oversight that the board is supposed to provide, straddling the roles of accountability and operations.
- The 50-person cap on CIRM staffing is arbitrary and has led to a potential overreliance on more expensive, outside contractors.
- A second arbitrary cap limits to 15 the number of out-of-state scientists that CIRM can use to conduct a first-level review of grant applications. To operate

within the cap, CIRM has created an internal pre-application triage process to ease the workload on the peer-review panel, but the process creates a layer of opacity when the agency should be striving for more public transparency.

Some of the Commission's recommendations for governance improvement can and should be adopted by the ICOC. The board has made internal changes on its own in the past. Other proposed reforms will require legislative action. There are limits, however, to how far the Legislature can amend CIRM's organizational structure without requiring another vote of the people – a tack the Commission has tried to avoid. A key provision in Proposition 71 stated that any legislative alteration must "enhance the ability of the institute to further the purposes of the grant and loan programs created by the measure."

The ability of the Legislature to amend statutes that have been enacted through voter initiatives, even when amendments are authorized, has been subject of occasional litigation, but the standards and criteria under which the Legislature can make these changes are vague.

Counsel for CIRM and the Americans for Cures Foundation provided the Commission with legal opinions that question whether some of the Commission's potential recommendations could be enacted into law without voter approval. In their view, the Commission's recommendations do not fall within the category of "permissible clarifications, but instead constitute impermissible policy alterations."

According to the Attorney General's Office and the Legislative Counsel, in the general sense, the courts have not provided clear guidance as to what constitutes a "permissible clarification" that "furthers the purpose of the grant and loan programs." Efforts to amend laws created by ballot measures often are subject to dispute, which can end up in litigation and must be resolved on a case-by-case basis on whether the intended change furthers the purpose of the initiative.

While the Commission understands there is a potential controversy here, which could lead to litigation, this is a sufficiently open question that persuades the Commission to recommend the following governance changes in the interest of furthering the purpose of Proposition 71 and improving the prospects for long-term success of the agency's mission.

That is, in improving efficiency and transparency at CIRM, the Commission believes that the recommendations will further the voters' mandate.

To that end, CIRM's governing board should be reduced to 15 members, to be selected from similarly diverse backgrounds as the current board, but injected with four truly independent voices from the business and science community who have no affiliations with CIRM-funded entities.

Board terms should be reduced to four years, to encourage new voices and debate. Such changes should be introduced as board members' terms expire.

To enhance accountability and transparency, the governor also should appoint a majority of its members, with confirmation by the state Senate, as is standard with many state boards. The newly recast board should be known simply as the Board of Directors, to more accurately reflect its composition.

To strengthen lines of communication and provide clear direction for the agency, the co-CEO management approach at CIRM should end, with the agency president placed in charge of all operations and the chair fulfilling only oversight duties, external affairs and board administration. The administrative limits set in Proposition 71 require a careful allocation of staffing and resources: the current overlapping roles of the president and the board chair complicate this effort, creating multiple reporting channels and functional redundancy.

The board should be given more flexibility to choose its own leadership. The statutory references to the nominating process, job duties and qualifications for board chair and vice chair should be modified, allowing the board to select a chair and vice chair from among its members. The board should determine an appropriate term for the chair and vice chair that allows for regular re-election or replacement based on performance.

While a leaner, more efficient board can bolster its oversight of CIRM, an existing outside entity should continue to monitor the agency's overall performance. The Citizens Financial Accountability Oversight Committee (CFAOC), led by the state controller and established by Proposition 71, already reviews financial audits of CIRM. The committee can enhance its mission by holding regular meetings to review CIRM's programmatic and strategic performance under authority already statutorily designated to it.

Expanding the role of the CFAOC would create an important, regular check on CIRM as it enters a critical stage of maturing from its start-up phase into an operational mode. Proposition 71 backers promoted CIRM as a fixed-duration experiment, with funding sunsetting after 10 years, but CIRM is launching a loan program to biotechnology companies, backed with stock warrants, that could provide a continuous revenue stream to the agency. A new strategic plan under consideration also lacks clarity on how funds will be spent in the future. What is clear is that CIRM leaders are positioning CIRM to exist beyond the 10 years promised to voters. The ICOC chair, for example, testified to the Commission about his desire to ask voters to extend CIRM's lifespan through another bond measure.

Establishing a coherent governance structure based on best practices will allow these conversations to take place in an environment that can enhance public trust and confidence that CIRM is furthering the goals of Californians who supported Proposition 71, not those of interested parties.

The Commission is cognizant of CIRM's institutional knowledge, the importance of continuity and CIRM's good standing in the scientific community.

The Commission also appreciates the complexities and disruption that can occur with an agency reorganization, and particularly at CIRM, with its roster of ongoing projects, many of which are international in scope. The Commission intends that its recommendations be implemented over a period of time, allowing for an appropriate transition in order to minimize disruption to CIRM's creative and ambitious agenda. Shortening the length of board terms, for example, should be introduced and phased in as current board members' terms expire. The Commissioners' observations, taken together with research, witness testimony and extensive staff interviews of ICOC board members and others have formed the basis for the study's findings and recommendations. Members of the CIRM staff and members of the ICOC have been

generous with their time and have made themselves readily available to the Commission's staff as well as to Commissioners in sharing information, ideas and reactions.

In developing its recommendations to strengthen CIRM's governance structure and improve transparency and accountability, the Commission sought to avoid the need to go back to the voters of California. These recommendations are designed to be implemented by CIRM's governing board, and where that is not possible, through legislation that can change existing statutes to, the words of Proposition 71, "enhance the ability of the institute to further the purposes of the grant and loan programs created by the measure."

Recommendation 1: The Legislature should restructure the CIRM governing board around principles of efficiency and transparency.

- The Legislature should amend the Health and Safety Code to reduce the board size, shorten terms and restructure membership.

  Decrease board size to 15 from 29. Keep diversity of membership but add independent voices to the board: five patient advocates from unspecified disease groups, two independent business leaders and two independent scientists with no ties to CIRM-funded institutions; two University of California officials, one university official (non UC); two private sector biotechnology executives, and one leader of a California research institution.

  Reduce terms to four years for all members.

- The Legislature should amend the Health and Safety Code to streamline the appointment process for CIRM board members. Allow the governor to appoint 11 of 15 board members, subject to Senate confirmation. Legislative leaders should continue to appoint two members. The UC system president should appoint two UC representatives.

- The Legislature and CIRM should realign the roles of chair and president to eliminate overlapping authority and to enhance clarity and accountability.

  The Legislature should modify all statutory references in the Health and Safety Code to the nominating process, job duties and qualifications for the chair and vice chair to invest this authority with the board.

  The CIRM board should elect a chair and a vice chair from within the existing board, subject to set terms and conditions for re-election/removal.

  The CIRM board should clarify that the president manages all day-to-day operations.

- The Legislature should amend the Health and Safety Code to rename the board to more accurately reflect its composition. The Independent Citizens Oversight Committee should be called the Board of Directors.

Recommendation 2: The Legislature and CIRM should improve efficiency and transparency for distributing grant and loan funds.

- The Legislature should amend the Health and Safety Code to remove the 50-employee cap on staffing.

- The Legislature should amend the Health and Safety Code to remove the 15-person limit on peer reviewers. CIRM should modify its triage plan to review grants internally.

- CIRM should explore options for greater disclosure of the peer review process.

  CIRM should poll CIRM's peer reviewers anonymously about their willingness to participate in the review process if their financial disclosure statements are made available to the public. The results of this poll should be made public.

  CIRM should conduct a trial grant application round that identifies all applicants.

  CIRM should provide full grant evaluations to applicants.

- CIRM should amend all meeting minutes to specify individual board members' votes and recusals, and continue the practice moving forward.

Recommendation 3: The CFAOC and the CIRM governing board should use their authority to enhance oversight.

- The Citizen's Financial Accountability Oversight Committee (CFAOC), chaired by the State Controller, should exercise its existing authority, or be statutorily authorized if necessary, to conduct performance audits and hold regular meetings to review CIRM's programmatic and strategic performance, in addition to overseeing CIRM's annual financial audits.

- The governing board should hold its members accountable by adopting removal provisions in its bylaws.

Recommendation 4: The CIRM governing board should begin planning for CIRM's future through an open process.

- The CIRM governing board should create succession plans for board leadership.

- CIRM's strategic plan should provide clear transparent direction for spending funds, with measurable benchmarks.

- CIRM should develop a transition plan for the eventual expiration of bond funding.

[Back to Appendices]

APPENDIX 14

14. Senate Bill 1064

Senate Bill No. 1064
Passed the Senate August 25, 2010

Secretary of the Senate
Passed the Assembly August 17, 2010

An act to amend Sections 125290.20, 125290.30, 125290.40, 125290.45, and 125290.60 of, and to add Sections 125290.71 and 125290.80 to, the Health and Safety Code, relating to stem cells.

Legislative counsel's digest
SB 1064, Alquist. California Stem Cell Research and Cures Act.

The California Stem Cell Research and Cures Act, an initiative measure approved by the voters at the November 2, 2004, statewide general election as Proposition 71, establishes the California Institute for Regenerative Medicine (CIRM), the purpose of which is, among other things, to make grants and loans for stem cell research, for research facilities, and for other vital research opportunities to realize therapies, protocols, and medical procedures that will result in the cure for, or substantial mitigation of, diseases and injuries. Existing law establishes the Independent Citizen's Oversight Committee (ICOC) composed of appointed members, that is required to perform various functions and duties with regard to the operation of the institute, including, but not limited to, establishing standards applicable to research funded by the institute. Existing law prohibits amendment of Proposition 71 by the Legislature unless the amendment is approved by the voters, or the amendment is accomplished by a bill introduced after the first 2 full calendar years and approved by a vote of 70% of both houses, and only if the amendment enhances the ability of the institute to further the purposes of the grant and loan programs.

Existing law specifies the appointment process for the members of the ICOC, including the chairperson and vice chairperson who are employees of the ICOC, and provides that the chairperson and vice chairperson serve 6-year terms. Existing law defines the duties of the chairperson and the president of the ICOC and limits the total number of authorized employees of the CIRM to 50.

This bill would require the CIRM, under the guidance of the ICOC, to create a succession plan addressing changes in leadership in the CIRM and ICOC, as specified. The bill would eliminate the 50-employee maximum for the CIRM.

The bill would also require the CIRM, under the guidance of the ICOC, to create, by January 31, 2012, a transition plan to address the expiration of current bond funding and to submit that plan to the Governor, the Controller, and the Legislature.

Existing law requires the CIRM to commission an independent financial audit, which is provided to the Controller for review and reported in the annual public report. Existing law establishes the Citizen's Financial Accountability Oversight Committee, chaired by the Controller, to review the annual audit and financial practices of the CIRM.

This bill would, additionally, require a performance audit to be conducted every 3 years, as specified.

Existing law contains provisions relating to the extent to which requirements relating to the disclosure of public records applied to records of the CIRM.

This bill would require the ICOC to disclose, in all meeting minutes, a summary of vote tallies, including each board member's votes and recusals.

The act provides that the ICOC shall establish standards that require that all grants and loan awards under the act shall be subject to intellectual property agreements that balance the opportunity of the state to benefit from the patents, royalties, and licenses that result from basic research, therapy development, and clinical trials with the need to ensure that essential medical research is not unreasonably hindered by the intellectual property agreements.

This bill would require that intellectual property standards that the ICOC develops include a requirement that each grantee and the exclusive licensees of the grantee submit to the CIRM a plan that will afford Californians access to any drug that is, in whole or in part, the result of research funded by the CIRM, except when the ICOC adopts a waiver, as specified. The bill would also require specified grant recipients to share a fraction of the revenue they receive from licensing or self-commercialization of an invention or technology that arises from research funded by CIRM, as specified.

Existing law establishes the procedure by which grant and loan applications are processed and scored by the 15 scientist members of the Scientific and Medical Research Funding Working Group.

This bill would remove the 15 member limit, and would instead require that a peer review panel consist of both scientists and patient advocates and require that there be 15 scientists on a peer review panel.

The people of the State of California do enact as follows:

SECTION 1. <u>The Legislature finds and declares the following</u>:

(a) The California Institute for Regenerative Medicine was established in 2004, through the passage of Proposition 71, for the purposes of implementing and managing a $3 billion investment in stem cell research on behalf of the state.
(b) Stem cell research is a promising area of research aimed at finding breakthrough cures for currently incurable diseases and injuries affecting millions of people. This investment, as stated in the proposition, would protect and benefit the California budget by funding scientific and medical research that will significantly reduce state health care costs in the future.
(c) Furthermore, the Legislative Analyst, in its official ballot information, stated that the state would "receive payments from patents, royalties, and licenses resulting from the research funded by the institute" through institute-established standards "requiring that all grants and loans be subject to agreements allowing the state to financially benefit from patents, royalties, and licenses resulting from the research activities funded under the measure."

(d) Since its inception, questions and concerns have been raised about the institute's practices, its governing board, and how the state directly and financially benefits through this sizeable investment. These criticisms divert the attention and focus of the institute to drive transformational scientific research and find cures.
(e) It is the intent of the Legislature to further enhance the ability of the institute to manage this investment made with public funds by addressing public concerns regarding oversight and transparency.
(f) It is further the intent of this act to ensure that California maximizes its receipt of revenues generated through grants or loans made through the institute and with state funds.
(g) It is in the best interests of the state that therapies that are created in whole or in part by funding from the institute be made available to Californians who have no other means of purchasing those therapies for reasons that include, but are not limited to, low income or the lack of available health insurance coverage.
(h) It is in the best interests of the state that the leadership of the institute, including the ICOC and the officers of the institute, possess the qualities necessary to serve the needs of the institute, and that the chairperson of the ICOC and the president of the institute have well defined and complementary duties.

SECTION 2. Section 125290.20 of the Health and Safety Code is amended to read:
125290.20. ICOC Membership; Appointments; Terms of Office

(a) ICOC Membership
The ICOC shall have 29 members, appointed as follows:
(1) The Chancellors of the University of California at San Francisco, Davis, San Diego, Los Angeles, and Irvine shall each appoint an executive officer from his or her campus.
(2) The Governor, the Lieutenant Governor, the Treasurer, and the Controller shall each appoint an executive officer from the following three categories:

(A) A California university, excluding the five campuses of the University of California described in paragraph (1), that has demonstrated success and leadership in stem cell research, and that has:
(i) A nationally ranked research hospital and medical school; this criteria will apply to only two of the four appointments. (ii) A recent proven history of administering scientific and/or medical research grants and contracts in an average annual range exceeding one hundred million dollars ($100,000,000). (iii) A ranking, within the past five years, in the top 10 United States universities with the highest number of life science patents
or that has research or clinical faculty who are members of the National Academy of Sciences.

(B) A California nonprofit academic and research institution that is not a part of the University of California, that has demonstrated success and leadership in stem cell research, and that has:
(i) A nationally ranked research hospital or that has research or clinical faculty who are members of the National Academy of Sciences. (ii) A proven history in the last five years of managing a research budget in the life sciences exceeding twenty million dollars ($20,000,000).

(C) A California life science commercial entity that is not actively engaged in researching or developing therapies with pluripotent or progenitor stem cells, that

has a background in implementing successful experimental medical therapies, and that has not been awarded, or applied for, funding by the institute at the time of appointment. A board member of that entity with a successful history of developing innovative medical therapies may be appointed in lieu of an executive officer.

(D) Only one member shall be appointed from a single university, institution, or entity. The executive officer of a California university, a nonprofit research institution or life science commercial entity who is appointed as a member, may from time to time delegate those duties to an executive officer of the entity or to the dean of the medical school, if applicable.

(3) The Governor, the Lieutenant Governor, the Treasurer, and the Controller shall appoint members from among California representatives of California regional, state, or national disease advocacy groups, as follows:

(A) The Governor shall appoint two members, one from each of the following disease advocacy groups: spinal cord injury and Alzheimer's disease.

(B) The Lieutenant Governor shall appoint two members, one from each of the following disease advocacy groups: type II diabetes and multiple sclerosis or amyotrophic lateral sclerosis.

(C) The Treasurer shall appoint two members, one from each of the following disease groups: type I diabetes and heart disease.

(D) The Controller shall appoint two members, one from each of the following disease groups: cancer and Parkinson's disease.

(4) The Speaker of the Assembly shall appoint a member from among California representatives of a California regional, state, or national mental health disease advocacy group.

(5) The President pro Tempore of the Senate shall appoint a member from among California representatives of a California regional, state, or national HIV/AIDS disease advocacy group.

(6) A chairperson and vice chairperson who shall be elected by the ICOC members. Each constitutional officer shall nominate a candidate for chairperson and another candidate for vice chairperson. The chairperson and vice chairperson shall each be elected for a term of six years. The chairperson and vice chairperson of ICOC shall be full- or part-time employees of the institute and shall meet the following criteria:

(A) Mandatory Chairperson Criteria (i) Documented history in successful stem cell research advocacy. (ii) Experience with state and federal legislative processes that must include some experience with medical legislative approvals of standards and/or funding. (iii) Qualified for appointment pursuant to paragraph (3), (4), or (5) of subdivision (a). (iv) Cannot be concurrently employed by or on leave from any prospective grant or loan recipient institutions in California.

(B) Additional Criteria for Consideration: (i) Experience with governmental agencies or institutions (either executive or board position). (ii) Experience with the process of establishing government standards and procedures. (iii) Legal experience with the legal review of proper governmental authority for the exercise of government agency or government institutional powers. (iv) Direct knowledge and experience in bond financing. The vice chairperson shall satisfy clauses (i), (iii), and (iv) of subparagraph (A). The vice chairperson shall be selected from among individuals who have attributes and experience complementary to those of the chairperson, preferably covering the criteria not represented by the chairperson's credentials and experience.

(b) Appointment of ICOC Members

(1) All appointments shall be made within 40 days of the effective date of this act. In the event that any of the appointments are not completed within the permitted timeframe, the ICOC shall proceed to operate with the appointments that are in place, provided that at least 60 percent of the appointments have been made.

(2) Forty-five days after the effective date of the measure adding this chapter, the Controller and the Treasurer, or if only one is available within 45 days, the other shall convene a meeting of the appointed members of the ICOC to elect a chairperson and vice chairperson from among the individuals nominated by the constitutional officers pursuant to paragraph (6) of subdivision (a)

(c) ICOC Member Terms of Office

(1) The members appointed pursuant to paragraphs (1), (3), (4), and (5) of subdivision (a) shall serve eight-year terms, and all other members shall serve six-year terms. Members shall serve a maximum of two terms.

(2) If a vacancy occurs within a term, the appointing authority shall appoint a replacement member within 30 days to serve the remainder of the term.

(3) When a term expires, the appointing authority shall appoint a member within 30 days. ICOC members shall continue to serve until their replacements are appointed.

SECTION 3. Section 125290.30 of the Health and Safety Code is amended to read:
125290.30. Public and Financial Accountability Standards

(a) Annual Public Report The institute shall issue an annual report to the public which sets forth its activities, grants awarded, grants in progress, research accomplishments, and future program directions. Each annual report shall include, but not be limited to, the following: the number and dollar amounts of research and facilities grants; the grantees for the prior year; the institute's administrative expenses; an assessment of the availability of funding for stem cell research from sources other than the institute; a summary of research findings, including promising new research areas; an assessment of the relationship between the institute's grants and the overall strategy of its research program; and a report of the institute's strategic research and financial plans.

(b) Independent Financial Audit for Review by Controller The institute shall annually commission an independent financial audit of its activities from a certified public accounting firm, which shall be provided to the Controller, who shall review the audit and annually issue a public report of that review.

(c) A performance audit shall be commissioned by the institute every three years beginning with the audit for the 2010–11 fiscal year. The performance audit, which may be performed by the Bureau of State Audits, shall examine the functions, operations, management systems, and policies and procedures of the institute to assess whether the institute is achieving economy, efficiency, and effectiveness in the employment of available resources. The performance audit shall be conducted in accordance with government auditing standards, and shall include a review of whether the institute is complying with ICOC policies and procedures. The performance audit shall not be required to include a review of scientific performance. The first performance audit shall include, but not be limited to, all of the following:

(1) Policies and procedures for the issuance of contracts and grants and a review of a representative sample of contracts, grants, and loans executed by the institute.
(2) Policies and procedures relating to the protection or treatment of intellectual property rights associated with research funded or commissioned by the institute.

(d) All administrative costs of the audits required by subdivisions (b) and (c) shall be paid by the institute.

(e) Citizen's Financial Accountability Oversight Committee There shall be a Citizen's Financial Accountability Oversight Committee chaired by the Controller. This committee shall review the annual financial audit, the Controller's report and evaluation of that audit, and the financial practices of the institute. The Controller, the Treasurer, the President pro Tempore of the Senate, the Speaker of the Assembly, and the Chairperson of the ICOC shall each appoint a public member of the committee. Committee members shall have medical backgrounds and knowledge of relevant financial matters. The committee shall provide recommendations on the institute's financial practices and performance. The Controller shall provide staff support. The
committee shall hold a public meeting, with appropriate notice, and with a formal public comment period. The committee shall evaluate public comments and include appropriate summaries in its annual report. The ICOC shall provide funds for all costs associated with the per diem expenses of the committee members and for publication of the annual report.

(f) Public Meeting Laws

(1) The ICOC shall hold at least two public meetings per year, one of which will be designated as the institute's annual meeting. The ICOC may hold additional meetings as it determines are necessary or appropriate.

(2) The Bagley-Keene Open Meeting Act, Article 9 (commencing with Section 11120) of Chapter 1 of Part 1 of Division 3 of Title 2 of the Government Code, shall apply to all meetings of the ICOC, except as otherwise provided in this section.

The ICOC shall award all grants, loans, and contracts in public meetings and shall adopt all governance, scientific, medical, and regulatory standards in public meetings.

(3) The ICOC may conduct closed sessions as permitted by the Bagley-Keene Open Meeting Act, under Section 11126 of the Government Code. In addition, the ICOC may conduct closed sessions when it meets to consider or discuss:

(A) Matters involving information relating to patients or medical subjects, the disclosure of which would constitute an unwarranted invasion of personal privacy.
(B) Matters involving confidential intellectual property or work product, whether patentable or not, including, but not limited to, any formula, plan, pattern, process, tool, mechanism, compound, procedure, production data, or compilation of information, which is not patented, which is known only to certain individuals who are using it to fabricate, produce, or compound an article of trade or a service having commercial value and which gives its user an opportunity to obtain a business advantage over competitors who do not know it or use it.
(C) Matters involving prepublication, confidential scientific research or data.
(D) Matters concerning the appointment, employment, performance, compensation, or dismissal of institute officers and employees. Action on compensation of the institute's officers and employees shall only be taken in open session.

(4) The meeting required by paragraph (2) of subdivision (b) of Section 125290.20 shall be deemed to be a special meeting for the purposes of Section 11125.4 of the Government Code.

(g) Public Records

(1) The California Public Records Act, Article 1 (commencing with Section 6250) of Chapter 3.5 of Division 7 of Title 1 of the Government Code, shall apply to all records of the institute, except as otherwise provided in this section.

(2) Nothing in this section shall be construed to require disclosure of any records that are any of the following:

(A) Personnel, medical, or similar files, the disclosure of which would constitute an unwarranted invasion of personal privacy.
(B) Records containing or reflecting confidential intellectual property or work product, whether patentable or not, including, but not limited to, any formula, plan, pattern, process, tool, mechanism, compound, procedure, production data, or compilation of information, which is not patented, which is known only to certain individuals who are using it to fabricate, produce, or compound an article of trade or a service having commercial value and which gives its user an opportunity to obtain a business advantage over competitors who do not know it or use it.

(C) Prepublication scientific working papers or research data.

(3) The institute shall include, in all meeting minutes, a summary of vote tallies and disclosure of each board member's votes and recusals on all action items.

(h) Competitive Bidding

(1) The institute shall, except as otherwise provided in this section, be governed by the competitive bidding requirements applicable to the University of California, as set forth in Article 1 (commencing with Section 10500) of Chapter 2.1 of Part 2 of Division 2 of the Public Contract Code.

(2) For all institute contracts, the ICOC shall follow the procedures required of the Regents by Article 1 (commencing with Section 10500) of Chapter 2.1 of Part 2 of Division 2 of the Public Contract Code with respect to contracts let by the University of California.

(3) The requirements of this section shall not be applicable to grants or loans approved by the ICOC.

(4) Except as provided in this section, the Public Contract Code shall not apply to contracts let by the institute.

(i) Conflicts of Interest

(1) The Political Reform Act, Title 9 (commencing with Section 81000) of the Government Code, shall apply to the institute and to the ICOC, except as provided in this section and in subdivision (e) of Section 125290.50.

(A) No member of the ICOC shall make, participate in making, or in any way attempt to use his or her official position to influence a decision to approve or award a grant, loan, or contract to his or her employer, but a member may participate in a decision to approve or award a grant, loan, or contract to a nonprofit entity in the same field as his or her employer.

(B) A member of the ICOC may participate in a decision to approve or award a grant, loan, or contract to an entity for the purpose of research involving a disease from which a member or his or her immediate family suffers or in which the member has an interest as a representative of a disease advocacy organization.

(C) The adoption of standards is not a decision subject to this section.

(2) Service as a member of the ICOC by a member of the faculty or administration of any system of the University of California shall not, by itself, be deemed to be inconsistent, incompatible, in conflict with, or inimical to the duties of the ICOC member as a member of the faculty or administration of any system of the University of California and shall not result in the automatic vacation of either such office. Service as a member of the ICOC by a representative or employee of a disease advocacy organization, a nonprofit academic and research institution, or a life science commercial entity shall not be deemed to be inconsistent, incompatible, in conflict with, or inimical to the duties of the ICOC member as a representative or employee of that organization, institution, or entity.

(3) Section 1090 of the Government Code shall not apply to any grant, loan, or contract made by the ICOC except where both of the following conditions are met:

(A) The grant, loan, or contract directly relates to services to be provided by any member of the ICOC or the entity the member represents or financially benefits the member or the entity he or she represents.

(B) The member fails to recuse himself or herself from making, participating in making, or in any way attempting to use his or her official position to influence a decision on the grant loan or contract.

(j) Patent Royalties and License Revenues Paid to the State of California

(1) The ICOC shall establish standards that require that all grants and loan awards be subject to intellectual property agreements that balance the opportunity of the State of California to benefit from the patents, royalties, and licenses that result from basic research, therapy development, and clinical trials with the need to ensure that essential medical research is not unreasonably hindered by the intellectual property agreements. All revenues received through the intellectual property agreements established pursuant to this subdivision shall be deposited into the General Fund.

(2) These standards shall include, at a minimum, a requirement that CIRM grantees, other than loan recipients and facilities grant recipients, share a fraction of the revenue they receive from licensing or self-commercializing an invention or technology that arises from research funded by CIRM, as set forth below. All revenues received pursuant to this paragraph or regulations adopted to implement this paragraph shall be deposited in the General Fund for use consistent with Section 202(c)(7) of Title 35 of the United States Code, if applicable.

(A) (i) A grantee that licenses an invention or technology that arises from research funded by CIRM shall pay 25 percent of the revenues it receives in excess of five hundred thousand dollars ($500,000), in the aggregate, to the General Fund. The threshold amount of five hundred thousand dollars ($500,000) shall be adjusted annually by a multiple of a fraction, the denominator of which is the Consumer Price Index, All Urban Consumers, All Items (San Francisco-Oakland-San Jose; 1982-84=100) as prepared by the Bureau of Labor Statistics of the United States Department of Labor and published for the month of October 2009, and the numerator of which is that index published for the month in which the grantee accepts the grant.

(ii) If funding sources other than CIRM directly contributed to the development of the invention or technology, then the return to the General Fund shall be calculated as follows: The amount of CIRM funding for the invention or technology shall be divided by the total of funding provided by all sources, and that fraction shall be multiplied by 25. That numeral is the percentage due to the General Fund.

(B) (i) A grantee that self-commercializes a product that results from an invention or technology that arises from research funded by CIRM shall pay an amount to the General Fund equal to three times the total amount of the CIRM grant or grants received by the grantee in support of the research that contributed to the creation of the product. The rate of payback of the royalty shall be at a rate of 3 percent of the annual net revenue received by the grantee from the product.

(ii) In addition to the payment required by clause (i), the first time that net commercial revenues earned by the grantee from the product exceed two hundred fifty million dollars ($250,000,000) in a calendar year, the grantee shall make a one-time payment to the General Fund equal to three times the total amount of the grant or grants awarded by CIRM to the grantee in support of the research that contributed to the creation of the product.

(iii) In addition to the payments required by clauses (i) and (ii), the first time that net commercial revenues earned by the grantee from the product exceed five hundred million dollars ($500,000,000) in a calendar year, the grantee shall make an additional one-time payment to the General Fund equal to three times the total amount of the grant or grants awarded by CIRM to the grantee in support of the research that contributed to the creation of the product.

(iv) In addition to the payments required by clauses (i), (ii), and (iii), the first time that net commercial revenues earned by the grantee from the product equal or exceed five hundred million dollars ($500,000,000) in a calendar year, the grantee shall pay the General Fund 1 percent annually of net commercial revenue in excess of five hundred million dollars ($500,000,000) for the life of any patent covering the invention or technology, if the grantee patented its invention or technology and received a CIRM grant or grants amounting to more than five million dollars ($5,000,000) in support of the research that contributed to the creation of the product.

(3) The ICOC shall have the authority to adopt regulations to implement this subdivision. The ICOC shall also have the authority to modify the formulas specified in subparagraphs (A) and (B) of paragraph (2) through regulations if the ICOC determines pursuant to paragraph (1) that a modification is required either in order to ensure that essential medical research, including, but not limited to, therapy development and the broad delivery of therapies to patients, is not unreasonably hindered, or to ensure that the State of California has an opportunity to benefit from the patents, royalties, and licenses that result from basic research, therapy development, and clinical trials. The ICOC shall notify the appropriate fiscal and policy committees of the Legislature 10 calendar days before exercising its authority to vote on the modification of the formulas specified in subparagraphs (A) and (B) of paragraph (2).

(k) Preference for California Suppliers

The ICOC shall establish standards to ensure that grantees purchase goods and services from California suppliers to the extent SB 1064 reasonably possible, in a good faith effort to achieve a goal of more than 50 percent of such purchases from California suppliers.

SECTION 4. Section 125290.40 of the Health and Safety Code is amended to read:
125290.40. ICOC Functions

The ICOC shall perform the following functions:

(a) Oversee the operations of the institute.
(b) Develop annual and long-term strategic research and financial plans for the institute.
(c) Make final decisions on research standards and grant awards in California.
(d) Ensure the completion of an annual financial audit of the institute's operations.
(e) Issue public reports on the activities of the institute.

(f) Establish policies regarding intellectual property rights arising from research funded by the institute.
(g) Establish rules and guidelines for the operation of the ICOC and its working groups.
(h) Perform all other acts necessary or appropriate in the exercise of its power, authority, and jurisdiction over the institute.
(i) Select members of the working groups.
(j) Adopt, amend, and rescind rules and regulations to carry out the purposes and provisions of this chapter, and to govern the procedures of the ICOC. Except as provided in subdivision (k), these rules and regulations shall be adopted in accordance with the Administrative Procedure Act (Government Code, Title 2, Division 3, Part 1, Chapter 4.5, Sections 11371 et seq.). (k) Notwithstanding the Administrative Procedure Act (APA), and in order to facilitate the immediate commencement of research covered by this chapter, the ICOC may adopt interim regulations without compliance with the procedures set forth in the APA. The interim regulations shall remain in effect for 270 days unless earlier superseded by regulations adopted pursuant to the APA.

(l) Request the issuance of bonds from the California Stem Cell Research and Cures Finance Committee and loans from the Pooled Money Investment Board.

(m) May annually modify its funding and finance programs to optimize the institute's ability to achieve the objective that its activities be revenue-positive for the State of California during its first five years of operation without jeopardizing the progress of its core medical and scientific research program.

(n) Notwithstanding Section 11005 of the Government Code, accept additional revenue and real and personal property, including, but not limited to, gifts, royalties, interest, and appropriations that may be used to supplement annual research grant funding and the operations of the institute.

(o) Under the guidance of the ICOC, the institute shall create a succession plan addressing changes in leadership of both the institute and the ICOC designed to minimize disruption and adverse impacts to the activities of the institute. A copy of the succession plan shall be transmitted to the Governor, Controller, and the Legislature within 30 days of its completion. The succession plan should include, but is not limited to:

(1) An assessment of leadership needs before beginning a search.
(2) An outline of succession procedures.
(3) Strategies to ensure successful knowledge transfer.

SECTION 5. Section 125290.45 of the Health and Safety Code is amended to read:
125290.45. ICOC Operations

(a) Legal Actions and Liability
(1) The institute may sue and be sued.

(2) Based upon ICOC standards, institute grantees shall indemnify or insure and hold the institute harmless against any and all losses, claims, damages, expenses, or liabilities, including attorneys' fees, arising from research conducted by the grantee pursuant to the grant, and/or, in the alternative, grantees shall name the institute as an additional insured and submit proof of such insurance.

(3) Given the scientific, medical, and technical nature of the issues facing the ICOC, and notwithstanding Section 11042 of the Government Code, the institute is authorized to retain outside counsel when the ICOC determines that the institute requires specialized services not provided by the Attorney General's office.

(4) The institute may enter into any contracts or obligations which are authorized or permitted by law.

(b) Personnel

(1) The ICOC shall from time to time determine the total number of authorized employees for the institute, excluding members of the working groups who shall not be considered institute employees. The ICOC shall select a chairperson, vice chairperson, and president who shall exercise all of the powers delegated to them by the ICOC. The following functions apply to the chairperson, vice chairperson, and president:

(A) The chairperson's primary responsibilities are to manage the ICOC agenda and workflow including all evaluations and approvals of scientific and medical working group grants, loans, facilities, and standards evaluations, and to supervise all annual reports and public accountability requirements; to manage and optimize the institute's bond financing plans and funding cashflow plan; to interface with the California Legislature, the United States Congress, the California health care system, and the California public; to optimize all financial leverage opportunities for the institute; and to lead negotiations for intellectual property agreements, policies, and contract terms. The chairperson shall also serve as a member of the Scientific and Medical Accountability Standards Working Group and the Scientific and Medical Research Facilities Working Group and as an ex officio member of the Scientific and Medical Research Funding Working Group. The vice chairperson's primary responsibilities are to support the chairperson in all duties and to carry out those duties in the chairperson's absence.

(B) The president's primary responsibilities are to serve as the chief executive of the institute; to recruit the highest scientific and medical talent in the United States to serve the institute on its working groups; to serve the institute on its working groups; to direct ICOC staff and participate in the process of supporting all working group requirements to develop recommendations on grants, loans, facilities, and standards as well as to direct and support the ICOC process of evaluating and acting on those recommendations, the implementation of all decisions on these and general matters of the ICOC; to hire, direct, and manage the staff of the institute; to develop the budgets and cost control programs of the institute; to manage compliance with all rules and regulations of the ICOC, including the performance of all grant recipients; and to manage and execute all intellectual property agreements and any other contracts pertaining to the institute or research it funds.

(2) Each member of the ICOC except, the chairperson, vice chairperson, and president, shall receive a per diem of one hundred dollars ($100) per day (adjusted annually for cost of living) for each day actually spent in the discharge

of the member's duties, plus reasonable and necessary travel and other expenses incurred in the performance of the member's duties.

(3) The ICOC shall establish daily consulting rates and expense reimbursement standards for the members of all of its working groups.

(4) Notwithstanding Section 19825 of the Government Code, the ICOC shall set compensation for the chairperson, vice chairperson, and president and other officers, and for the scientific, medical, technical, and administrative staff of the institute within the range of compensation levels for executive officers and scientific, medical, technical, and administrative staff of medical schools within the University of California system and the nonprofit academic and research institutions described in paragraph (2) of subdivision (a) of Section 125290.20.

SECTION 6. Section 125290.60 of the Health and Safety Code is amended to read:
125290.60. Scientific and Medical Research Funding Working Group

(a) Membership
The Scientific and Medical Research Funding Working Group shall have at least 23 members as follows:

(1) Seven ICOC members from the 10 disease advocacy group members described in paragraphs (3), (4), and (5) of subdivision (a) of Section 125290.20.
(2) At least 15 scientists nationally recognized in the field of stem cell research.
(3) The Chairperson of the ICOC.

(b) Functions
The Scientific and Medical Research Funding Working Group shall perform the following functions:

(1) Recommend to the ICOC interim and final criteria, standards, and requirements for considering funding applications and for awarding research grants and loans.
(2) Recommend to the ICOC standards for the scientific and medical oversight of awards.
(3) Recommend to the ICOC any modifications of the criteria, standards, and requirements described in paragraphs (1) and (2) above as needed.
(4) Review grant and loan applications based on the criteria, requirements, and standards adopted by the ICOC and make recommendations to the ICOC for the award of research, therapy development, and clinical trial grants and loans.
(5) Conduct peer group progress oversight reviews of grantees to ensure compliance with the terms of the award, and report to the ICOC any recommendations for subsequent action.
(6) Recommend to the ICOC standards for the evaluation of grantees to ensure that they comply with all applicable requirements. Such standards shall mandate periodic reporting by grantees and shall authorize the Scientific and Medical Research Funding Working Group to audit a grantee and forward any recommendations for action to the ICOC.
(7) Recommend its first grant awards within 60 days of the issuance of the interim standards.

(c) Recommendations for Awards
Award recommendations shall be based upon a competitive evaluation as follows:

A peer review panel shall consist of both scientists and patient advocates. There shall be 15 scientists on a peer review panel. Only the scientist members of the Scientific and Medical Research Funding Working Group shall score grant and loan award applications for scientific merit. Such scoring shall be based on scientific merit in three separate classifications—research, therapy development, and clinical trials, on criteria including the following:

(1) A demonstrated record of achievement in the areas of pluripotent stem cell and progenitor cell biology and medicine, unless the research is determined to be a vital research opportunity.
(2) The quality of the research proposal, the potential for achieving significant research, or clinical results, the timetable for realizing such significant results, the importance of the research objectives, and the innovativeness of the proposed research.
(3) In order to ensure that institute funding does not duplicate or supplant existing funding, a high priority shall be placed on funding pluripotent stem cell and progenitor cell research that cannot, or is unlikely to, receive timely or sufficient federal funding, unencumbered by limitations that would impede the research. In this regard, other research categories funded by the National Institutes of Health shall not be funded by the institute.
(4) Notwithstanding paragraph (3), other scientific and medical research and technologies and/or any stem cell research proposal not actually funded by the institute under paragraph (3) may be funded by the institute if at least two-thirds of a quorum of the members of the Scientific and Medical Research Funding Working Group recommend to the ICOC that such a research proposal is a vital research opportunity.

SECTION 7. Section 125290.71 is added to the Health and Safety Code, to read:

Under the guidance of the ICOC, the institute shall, by January 31, 2012, create a transition plan addressing the expiration of current bond funding. A copy of the transition plan shall be transmitted to the Governor, the Controller, and the Legislature within 30 days of its completion.

SECTION 8. Section 125290.80 is added to the Health and Safety Code, to read:

The intellectual property standards that the ICOC develops shall include:

(a) A requirement that each grantee or the exclusive licensee of the grantee submit a plan to CIRM to afford access to any drug that is, in whole or in part, the result of research funded by CIRM to Californians who have no other means to purchase the drug. The access plan must be consistent with industry standards at the time of commercialization in California, accounting for the size of the market for the drug, and the resources of the grantee or exclusive licensee.

(b) A requirement that the grantee or exclusive licensee either submit the plan required by subdivision (a), seek an extension from CIRM, or notify CIRM of its intention to seek a waiver, within 10 business days following final approval of the drug by the federal Food and Drug Administration. If the grantee seeks an extension, the plan must be submitted within 30 business days following final approval of the drug by the federal Food and Drug Administration. The plan shall be subject to the approval of CIRM, after a public hearing and opportunity for public comment.

(c) A process by which the ICOC may waive the requirement in subdivision (a) if the ICOC determines, after a public hearing, that in the absence of the waiver, development and broad delivery of the drug will be unreasonably hindered or that the waiver will provide significant benefits that equal or exceed the benefits that would otherwise flow to the state pursuant to subdivision (a). The process shall include the requirement that a request for a waiver shall be posted on CIRM's Internet Web site for a minimum of 10 business days in advance of the public hearing and that CIRM shall notify the Legislature if the ICOC grants a waiver request, including the reasons that justified the waiver request.

(d) Procedures to protect from public disclosure proprietary information submitted by grantees and exclusive licensees to CIRM pursuant to this section.

[Back to Appendices]

APPENDIX 15

15. Summary of CIRM Intellectual Property (IP) Regulations

TWO DIFFERENT FUNDING MECHANISMS

GRANTS →
- CIRM I.P. Regulations apply
- Revenue Deposited in State General Fund

LOANS →
- CIRM's I.P. Regulations apply <u>except</u> I.P. Revenue sharing requirement
- Two types of loans:
  - Product-Backed (Forgiveness)
  - Company Backed
- CIRM Retains Loan Repayments and Warrants

Development of CIRMs IP Regulations: The Balance Sought

- Prop 71 instructs Governing Board to develop IP policies that strike appropriate balance between:
  - Obtaining a financial return to citizens of California for $3 billion bond issuance while
  - assuring that essential medical research is not unreasonably hindered
- Board determined CIRM would not own IP

Intellectual Property Policy Development: Extensive Effort to Strike the Right Balance

- 15 public meetings devoted to intellectual property policy development
- 18 presentations by experts and stakeholders
- Input from biotech, VCs, traditional lenders, academics
- Best practices survey of 20+ funding entities
- More than 100 interviews
- 12 Public Comment Rounds
- Almost 100 formal comment letters responded to under the Administrative Procedure Act

FOUR MAIN OBLIGATIONS

FINANCIAL OBLIGATIONS	* License Revenue Sharing OR** * Commercial Revenue Sharing * Access / Pricing
MATERIAL SHARING	* Materials first produced in course of CIRM Funded Research and described in a published scientific paper * For research use in California only * Provide without or at actual cost
REPORTING	Report Inventions, Licensing Activities, Material Transfer, Revenue Generation
EFFORTS TO BRING INVENTIONS TO PRACTICAL APPLICATION	*Various acceptable mechanisms *Discretion left to Grantees * March-In Rights reserved to CIRM

**Assuming a single commercialization strategy

REVENUE SHARING OBLIGATIONS

LICENSE REVENUE SHARING

- After $500K earned, share 25% Royalty Revenue (net various IP costs and Inventor share)
- No Cap, but proportionality

OR*

NET COMMERCIAL REVENUE SHARING FROM A PRODUCT

- After $500K earned: owe 3X amount of Grant—paid at a rate of 3% of annual net commercial revenue
- Additional Blockbuster payments
  - Two One time payments:
    - $250M = 3x amount of Grant
    - $500M = 3x amont of Grant
  - Add'l 1% Royalty if Grant > $5M and Net Commercial Revenues > $500 M

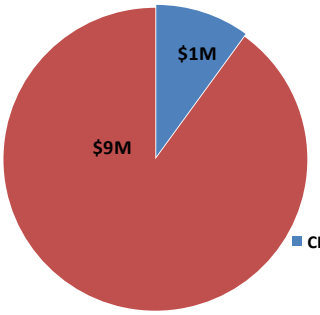
(Subject of upcoming amendment)

APPLIES ONLY TO GRANTEES AND COLLABORATORS THAT LICENSE OR SELF COMMERCIALIZE, NOT LICENSEES OR LOAN RECIPIENTS

6

REVENUE SHARING PROPORTIONALITY (Example)

Total Research Funding



Licensing Revenue Year 1 = $ 1.5 M

State's share $25,000 (to General Fund)

Grantee Collaborator's share $1,475,000

Total Funding
$10 Million

CIRM Funding
$1 Million or 10%

Calculation
$1.5 M – $0.5 M = $1 M*
$1M / $10M x 25% = 2.5%
2.5% of $1M = $25,000 to State

* Assume no amounts due to Inventor

9/14/2010 7

ACCESS AND PRICING OF DRUG/DIAGNOSTICS RESULTING IN WHOLE OR IN PART FROM CIRM FUNDED RESEARCH

ACCESS PLANS

- To uninsured California residents
- Plan must be consistent with industry standards, consider resources of Grantee/Collaborators/Exclusive Licensee at time of Commercialization
- CIRM to approve plan, public hearing

PRICING

- To eligible Californians (~ low income)
- Sales to State Agencies (eg. hospitals)
- Price = CA Discount Prescription Drug Program (not yet funded)

Burden is small – California, a small percent of overall market

Applies to Grantees, Collaborators, Loans Recipients, and Exclusive Licensees not to Non-Exclusive Licensees

Interpretation Questions

CIRM is committed to addressing questions related to interpretation of its intellectual property regulations through:

- Posting FAQ's
- Letter Opinions (Formal)
- Informal Discussions
- Workshop(s)

Summary – Top Points

1) CIRM Does Not Own Any Inventions
2) There is no obligation to publish, but if do, in some instances material must be made available for Cal. research
3) Grantees must undertake reasonable efforts to bring invention to practical use
4) Revenue sharing obligations exist – balance sought

[Back to Appendices]

APPENDIX 16

16. New Faculty Award recipients

Status	Grant #	Institution	Primary Contact	Project Title
Terminated (moved)	RN1-00525-1	Beckman Research Institute Of The City Of Hope	Dr. Tiziano Barberi	Skeletal muscle development from hESC and its in vivo applications in animal models of muscular dystrophy
Active Year 3	RN1-00527-1	Stanford University	Dr. Anne Brunet	Molecular mechanisms involved in adult neural stem cell maintenance
Active Year 3	RN1-00529-1	Stanford University	Dr. Howard Y. Chang	Noncoding RNAs in Cell Fate Determination
Active Year 3	RN1-00530-1	University of California, Santa Cruz	Dr. Bin Chen	Molecular mechanisms of neural stem cell differentiation in the developing brain
Active Year 3	RN1-00532-1	University of California, Berkeley	Dr. Irina M. Conboy	Identification of hESC-mediated molecular mechanism that positively regulates the regenerative capacity of post-natal tissues
Active Year 2	RN1-00535-1	Stanford University	Dr. Karl Deisseroth	Bioengineering technology for fast optical control of differentiation and function in stem cells and stem cell progeny
Active Year 3	RN1-00536-1	Scripps Research Institute	Dr. Sheng Ding	Reprogramming of human somatic cells back to pluripotent embryonic stem cells
Active Year 1	RN1-00538-1	Western University Of Health Sciences	Dr. Douglas W Ethell	ES-derived cells for the treatment of Alzheimer's Disease
Active Year 3	RN1-00540-1	University of California, Santa Cruz	Dr. Camilla Forsberg	Mechanisms of Stem Cell Fate Decisions
Active Year 2	RN1-00544-1	The Salk Institute for Biological Studies	Dr. Dana Jones	Characterization of mechanisms regulating de-differentiation and the re-acquisition of stem cell identity
Active Year 2	RN1-00550-1	University of California, Los Angeles	Dr. Siavash K Kurdistani	Epigenetics in cancer stem cell initiation and clinical outcome prediction
Active Year 2	RN1-00554-1	University of California, Merced	Dr. Jennifer Manilay	Enhancing Survival of Embryonic Stem Cell-Derived Grafts by Induction of Immunological Tolerance
Active Year 3	RN1-00557-1	University of California, Los Angeles	Dr. Hanna K.A. Mikkola	Mechanisms of Hematopoietic stem cell Specification and Self-Renewal

APPENDIX 16

Status	Grant #	Institution	Primary Contact	Project Title
Active Year 3	RN1-00561-1	University of California, Davis	Dr. Chong-xian Pan	Combinatorial Chemistry Approaches to Develop LIgands against Leukemia Stem Cells
Active Year 2	RN1-00562-1	University of Southern California	Dr. Mohammad Pashmforoush	Transcriptional Regulation of Cardiac Pacemaker Cell Progenitors
Active Year 2	RN1-00564-1	University of California, Los Angeles	Dr. Kathrin Plath	In vitro reprogramming of mouse and human somatic cells to an embryonic state
Terminated (moved)	RN1-00566-1	University of California, Irvine	Dr. Andrew J. Putnam	A Novel Engineered Niche to Explore the Vasculogenic Potential of Embryonic Stem Cells
Active Year 3	RN1-00572-1	University of Southern California	Dr. Songtao Shi	Oral and Craniofacial Reconstruction Using Mesenchymal Stem Cells
Active Year 2	RN1-00575-1	University of California, San Diego	Dr. David Traver	Genetic dissection of mesodermal commitment to the hematopoietic fates.
Active Year 2	RN1-00577-1	The Salk Institute for Biological Studies	Dr. Lei Wang	Genetic Encoding Novel Amino Acids in Embryonic Stem Cells for Molecular Understanding of Differentiation to Dopamine Neurons
Active Year 3	RN1-00579-1	Stanford University	Dr. Joanna Wysocka	Trithorax and Polycomb methyltransferase complexes in cell fate determination.
Active Year 3	RN1-00584-1	Scripps Research Institute	Dr. Kristin K. Baldwin	Generating pluripotent cell lines from neurons.
Active Year 2	RN2-00902-1	University of California, Los Angeles	Dr. Antoni Ribas	Stem Cells for Immune System Regeneration to Fight Cancer
Active Year 2	RN2-00903-1	The J. David Gladstone Institutes	Dr. Benoit G. Bruneau	Induction of cardiogenesis in pluripotent cells via chromatin remodeling factors
Active Year 2	RN2-00904-1	University of California, Los Angeles	Dr. Brigitte N. Gomperts	Stem Cells in Lung Cancer
Active Year 2	RN2-00905-1	Ludwig Institute for Cancer Research	Dr. Bing Ren	Mechanisms of chromatin dynamics at enhancers during ES cell differentiation
Active Year 2	RN2-00906-1	University of California, San Francisco	Dr. Robert Blelloch	Mechanisms of small RNA regulation in early embryonic development
Active Year 2	RN2-00908-1	University of California, San Diego	Dr. Benjamin D. Yu	Regulation of Adult Stem Cell Proliferation by RAS and Cell-Permeable Proteins
Active Year 2	RN2-00909-1	Stanford University	Dr. Ching-Pin Chang	VEGF signaling in adventitial stem cells in vascular physiology and disease

APPENDIX 16

Status	Grant #	Institution	Primary Contact	Project Title
Active Year 1	RN2-00910-1	University of California, San Diego	Dr. Catriona Jamieson	Derivation and Characterization of Myeloproliferative Disorder Stem Cells from Human ES Cells
Active Year 2	RN2-00915-1	University of California, Irvine	Dr. Edwin Shinichi Monuki	Mechanisms in Choroid Plexus Epithelial Development
Active Year 2	RN2-00916-1	University of Southern California	Dr. Gage DeKoeyer Crump	Skeletogenic Neural Crest Cells in Embryonic Development and Adult Regeneration of the Jaw
Active Year 2	RN2-00919-1	University of California, San Francisco	Dr. Jeremy F. Reiter	High throughput modeling of human neurodegenerative diseases in embryonic stem cells
Active Year 2	RN2-00921-1	University of California, Merced	Dr. Kara E McCloskey	Building Cardiac Tissue from Stem Cells and Natural Matrices
Active Year 2	RN2-00922-1	University of California, Davis	Dr. Paul Knoepfler	Molecular mechanisms governing hESC and iPS cell self-renewal and pluripotency
Active Year 2	RN2-00923-1	University of California, Berkeley	Dr. Lin He	The roles of non-coding RNAs in the self-renewal and differentiation of pluripotent stem cells
Active Year 1	RN2-00931-1	University of California, San Diego	Dr. Mana Parast	Molecular Mechanisms of Trophoblast Stem Cell Specification and Self-Renewal
Active Year 2	RN2-00933-1	University of California, San Francisco	Dr. Ophir David Klein	Laying the groundwork for building a tooth: analysis of dental epithelial stem cells
Active Year 2	RN2-00934-1	University of California, San Francisco	Dr. Emmanuelle Passegue	Mechanisms Underlying the Responses of Normal and Cancer Stem Cells to Environmental and Therapeutic Insults
Active Year 2	RN2-00938-1	University of Southern California	Dr. Qilong Ying	Mechanisms Underlying the Diverse Functions of STAT3 in Embryonic Stem Cell Fate Regulation
Active Year 1	RN2-00940-1	San Diego State University	Dr. Ricardo M. Zayas	The molecular basis underlying adult neurogenesis during regeneration and tissue renewal
Active Year 1	RN2-00945-1	University of California, San Diego	Dr. Shyni Varghese	A Novel Microenvironment-Mediated Functional Skeletal Muscle from Human Embryonic Stem Cells and their In Vivo Engraftment
Active Year 2	RN2-00946-1	Children's Hospital of Los Angeles	Dr. Tracy Grikscheit	Mechanism of Tissue Engineered Small Intestine Formation

APPENDIX 16

Status	Grant #	Institution	Primary Contact	Project Title
Active Year 2	RN2-00950-1	University of California, San Francisco	Dr. Holger F. Willenbring	Molecular dissection of adult liver regeneration to guide the generation of hepatocytes from pluripotent stem cells
Active Year 1	RN2-00952-1	The J. David Gladstone Institutes	Dr. Yadong Huang	Defining the Isoform-Specific Effects of Apolipoprotein E on the Development of iPS Cells into Functional Neurons in Vitro and in Vivo

[Back to Appendices]

APPENDIX 17

17. Leadership Award CV from Reya

BIOGRAPHICAL SKETCH

NAME	POSITION TITLE
Robert Wechsler-Reya, Ph.D.	Associate Professor
eRA COMMONS USER NAME WECHS001	

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Harvard College, Cambridge, MA	A.B.	1981-1986	Psychology & Biology
Univ. of Pennsylvania, Philadelphia, PA	Ph.D.	1988-1995	Immunology
Wistar Institute, Philadelphia, PA	Post-doc	1995-1996	Molecular Oncology
Stanford University, Stanford, CA	Post-doc	1997-2001	Neural Development

A. Personal Statement

My research focuses on the signals that control growth and differentiation in the developing cerebellum, and how these signals are dysregulated in the cerebellar tumor medulloblastoma. As a postdoc at Stanford, I demonstrated that Sonic hedgehog (Shh) is a critical mitogen for neuronal precursors in the cerebellum, and that mutations in the Shh pathway predispose to medulloblastoma by aberrantly activating a mitogenic pathway that normally functions only in early development. In my own lab, I have continued to study the relationship between normal development and brain tumor formation. My lab's contributions include identifying Nmyc as a key target of the Shh pathway in neuronal precursors and in medulloblastoma cells; discovering a novel population of neural stem cells in the neonatal cerebellum; demonstrating (using conditional knockout mice) that that both neuronal precursors and stem cells can serve as cells of origin for medulloblastoma; and identifying a population of cancer stem cells that is critical for propagation of tumors from *patched* mutant mice. More recently, we have begun to develop new models of medulloblastoma, and to use these models to test novel approaches to therapy. My work has garnered several awards, including a Scholar Award from the Kimmel Foundation for Cancer Research and an Award for Excellence in Pediatrics Research from the Society for Neuro-Oncology. My experience using animal models to study neural development and tumorigenesis makes me uniquely qualified to carry out the studies described in this proposal.

B. Positions and Honors

Professional Experience

Jan '86 - Jan '88 Reporter, Discover Magazine, New York, NY.
July '01 – June '08 Assistant Professor, Departments of Pharmacology & Cancer Biology and Neurobiology Duke University Medical Center, Durham, NC.

June '08 – Nov '10	Associate Professor, Departments of Pharmacology & Cancer Biology and Neurobiology Duke University Medical Center, Durham, NC.
Nov '10 – Present	Professor and Director, Tumor Development Program Sanford-Burnham Medical Research Institute, La Jolla, CA

Awards and Honors

John Harvard Scholarship for Academic Achievement of Highest Distinction, 1984-1985
Award for Excellence in Scientific Writing, American Diabetes Association, 1988
Postdoctoral Fellowship, Medical Research Council of Canada, 1995-1997
Postdoctoral Fellowship, American Cancer Society (California), 2000-2001
Children's Brain Tumor Foundation Research Award, 2002
Brain Tumor Society Research Award, 2003
Kimmel Scholar Award, Sidney Kimmel Foundation for Cancer Research, 2003
Award for Excellence in Pediatrics Research, Society for Neuro-Oncology, 2006
DukeMed Scholar, 2007
W.K. Joklik Award for Excellence in Basic Cancer Research, 2007
California Institute for Regenerative Medicine (CIRM) Leadership Award, 2010-16

Academic Service

Ad hoc reviewer for Nature, Nature Medicine, Cancer Cell, Neuron, Genes & Development, PNAS,
Cancer Research, J. Neuroscience, Oncogene, Development
Ad hoc reviewer, Neural Cell Fate (NCF) and Brain Disorders & Clinical Neuroscience (BDCN) study sections
Ad hoc reviewer for French National Cancer Institute
Molecular Cancer Biology Admissions Committee
Duke University Postdoctoral Association (DUPA) – faculty advisor
Search Committee, Director of the Office of Postdoctoral Services
External Advisory Board Member, University of Texas M.D. Anderson Brain Tumor Center
Scientific Review Board, CORD Foundation
Scientific Advisory Council, American Brain Tumor Association
Scientific Review Panel, Cancer Prevention Research Institute of Texas (CPRIT)
Editorial Board Member, Cancer Research

Invited Talks and Seminars (since 2006)

St. Jude Children's Hospital, Department of Tumor Cell Biology and Genetics, Memphis, TN, March 1, 2006
University of Queensland, Institute for Molecular Bioscience, St. Lucia, Australia, March 16, 2006
University of Oregon, Institute of Neuroscience, Eugene, OR, May 11, 2006
University College London, Institute of Child Health, London, England, June 15, 2006
CSHL Symposium on Mechanisms & Models of Cancer, Cold Spring Harbor, NY, August 16-20, 2006
St. Jude Children's Hospital Symposium: Stem Cell Biology & Therapeutics, Memphis, TN, November 10, 2006
Penn Biomedical Graduate Studies 20th Anniversary Symposium, Philadelphia, PA November 13, 2006
Sloan-Kettering Cancer Center, New York, NY, January 19, 2007
University of Michigan, Department of Cell & Developmental Biology, Ann Arbor, MI, February 21, 2007
Johns Hopkins Medical School, Program in Neuroscience, Baltimore, MD, April 12, 2007

Washington University School of Medicine, St. Louis, MO, May 7 2007
Salk Symposium on Mechanisms & Models of Cancer, La Jolla, CA, August 8-12, 2007
Symposium on Neurobiology of Disease in Children, Quebec City, Canada, October 10, 2007
Mouse Models of Human Cancer Consortium Brain Tumor Workshop, Dallas, TX November 15, 2007
Preuss Foundation Seminar on Stem Cell Biology, La Jolla, CA, November 7-9, 2007
University of Texas Health Science Center, San Antonio, TX, November 19, 2007
Texas Children's Hospital/Baylor College of Medicine, Houston, TX, January 17, 2008
Boston Children's Hospital/Harvard University Medical Center, Boston, MA, February 25, 2008
Stanford Symposium on Hedgehog Signaling in Development and Disease, Stanford, CA, June 20-22, 2008
International Neuro-Oncology Updates, Johns Hopkins Medical School, Baltimore, MD Sept. 18-19, 2008
AACR Mouse Models of Cancer Conference, San Francisco, CA, January 12-15, 2009
Division of Pediatric Oncology, Dana Farber Cancer Institute, Boston, MA, March 27, 2009
Forbeck Symposium on "Biology and Treatment of Primary Brain Tumors", Hilton Head, SC, Nov. 5-8, 2009.
Fred Hutchinson Cancer Center, Cancer Biology Seminar Series, March 30, 2010
Symposium on Medulloblastoma: Genetics and Genomics, AACR Annual Meeting, April 18, 2010
Toronto Hospital for Sick Children Seminar Series, April 28, 2010
Memorial Sloan Kettering Cancer Center Brain Tumor Seminar Series, May 17, 2010

TEACHING
Lecturer, MCB 418 – Molecular Mechanisms of Oncogenesis (Models of Cancer), 2001-Present
Lecturer, Graduate Course in Academic Integrity & Research Ethics, 2002-2010
Lecturer, PHARM/MCB 417 – Cellular Signaling, (Hedgehog Signaling), 2002-Present
Course Director, MCB 300 – Cancer as a Disease, 2004-Present
Lecturer, CSHL Course on Mechanisms of Neural Differentiation & Brain Tumors, 2008, 2010

C. Selected Peer-Review Publications (from a total of 34)

Wechsler RJ, and Monroe JG (1995). Immature B lymphocytes are deficient in expression of the src-family kinases p59fyn and p55fgr. *J. Immunol.* 154: 1919-29.
Wechsler RJ and Monroe, JG (1995). Src-family tyrosine kinase p55fgr is expressed in murine splenic B cells and is activated following antigen receptor crosslinking. *J. Immunol.* 154: 3234-44.
Sakamuro D, Elliott KJ, Wechsler-Reya R and Prendergast GC (1996) Bin1 is a novel Myc-interacting protein with features of a tumour suppressor. *Nature Genetics*. 14: 69-77.
Wechsler-Reya R, Elliott K, Herlyn M and Prendergast GC (1997) The putative tumor suppressor BIN1 is a short-lived nuclear phosphoprotein, the localization of which is altered in malignant cells. *Cancer Res.* 57:3258-63.
Wechsler-Reya RJ and Barres BA (1997). Retinal development: Communication helps you see the light. *Curr. Biol.* 7:R433-6.
Wechsler-Reya R, Sakamuro, D, Zhang, J and Prendergast, GC (1997). Structural analysis of the human BIN1 gene: Evidence for alternate splicing and tissue-specific regulation. *J. Biol Chem.* 272: 31453-31458.

Wechsler-Reya R and Prendergast GC (1997) A role for the putative tumor suppressor Bin1 in muscle cell differentiation. *Mol Cell Biol.* 18: 566-575.
Wechsler-Reya RJ and Scott MP (1999) Control of neuronal precursor proliferation in the cerebellum by sonic hedgehog. *Neuron* 22:103-114.
Wechsler-Reya RJ and Scott MP (2001) The developmental biology of brain tumors. *Annu. Rev. Neurosci.* 24:385-428.
Wechsler-Reya RJ (2001) Caught in the matrix: How vitronectin controls neuronal differentiation. *Trends Neurosci.* 24:680-2.
Oliver TG, Grasfeder LL, Carroll AL, Kaiser C, Gillingham CL, Lin SM, Wickramasinghe R, Scott MP and Wechsler-Reya RJ (2003) Transcriptional Profiling of the Hedgehog Response: A Critical Role for N-myc in Proliferation of Neuronal Precursors. *Proc. Natl. Acad. Sci.* 100:7331-6.
Oliver TG and Wechsler-Reya RJ (2004) Getting at the root and stem of brain tumors. *Neuron* 42:885-88.
Fogarty MP, Kessler, JD and Wechsler-Reya RJ (2005) Morphing into cancer: The role of developmental signaling pathways in brain tumor formation. *J. Neurobiol.* 64:458-475.
Oliver TG, Read TA, Kessler JD, Mehmeti A, Wells JF, Huynh TT, Lin, SM and Wechsler-Reya RJ (2005) Loss of patched and disruption of granule cell development in a pre-neoplastic stage of medulloblastoma. *Development* 132:2425-39.
Lee A, Kessler JD, Read TA, Kaiser C, Corbeil D, Huttner WB, Johnson JE and Wechsler-Reya RJ (2005) Isolation of neural stem cells from the postnatal cerebellum. *Nat. Neurosci.* 8:723-9
Read TA, Hegedus B, Wechsler-Reya R, Gutmann DH (2006) The neurobiology of neurooncology. *Ann Neurol*. 60:3-11.
Fogarty MP, Emmenegger BA, Grasfeder LL, Oliver TG and Wechsler-Reya, RJ (2007) Fibroblast Growth Factor Blocks Sonic Hedgehog Signaling in Neuronal Precursors and Tumor cells. *Proc. Natl. Acad. Sci.* 104:2973-8. [PMC1815291]
Yang ZJ and Wechsler-Reya RJ (2007) Hit 'em where they live: Targeting the cancer stem cell niche. *Cancer Cell* 11:3-5.
Johnson CE, Huang YY, Parrish AB, Smith MI, Vaughn AE, Zhang Q, Wright KM, Van Dyke T, Wechsler-Reya RJ, Kornbluth S, Deshmukh M (2007) Differential Apaf-1 levels allow cytochrome c to induce apoptosis in brain tumors but not in normal neural tissues. *Proc Natl Acad Sci* 104:20820-5. [PMC2409225]
Emmenegger BA and Wechsler-Reya RJ (2008) Stem Cells and the Origin and Propagation of Brain Tumors. *J. Child Neurol.* 23:1172-8.
Yang ZJ, Ellis T, Markant SL, Read, TA, Kessler JD, Bourboulas M, Schüller U, Machold R, Fishell G, Rowitch, DH, Wainwright BJ and Wechsler-Reya RJ (2008) Medulloblastoma can be Initiated by Deletion of *Patched* in Lineage-Restricted Progenitors or Stem Cells. *Cancer Cell*. 14:135-45. [PMC2538687]
Kessler JD, Hasegawa H, Brun, SN, Emmenegger BA, Yang, ZJ, Dutton JW, Wang F and Wechsler-Reya RJ (2009) N-myc Alters the Fate of Pre-Neoplastic Cells in a Mouse Model of Medulloblastoma. *Genes & Dev*. 23:157-170. [PMC2648542]
Read TA, Fogarty MP, Markant SL, McLendon RE, Wei Z, Ellison DW, Febbo PG and Wechsler-Reya RJ (2009) Identification of CD15 as a Marker for Tumor-Propagating Cells in a Mouse Model of Medulloblastoma. *Cancer Cell.* 15:135-47. [PMC2664097]

[Back to Appendices]

APPENDIX 18

18. Major Facilities leverage Chart

CIRM Major Facilities Grant Program Summary

Institutions (by CIRM category) Institutes; Centers of Excellence; & Sp. Programs	Total Project Cost	Preliminary Recommended CIRM Amount	Donor & Institutional Project Funds	Other Donor & Institutional Funds for Recruitment and Other Capital Costs	Total Project and Other Funding	Size of Facility (gross sq feet)	Size of Research Team at Capacity	Total PIs & Research-ers in Stem Cell Program Today
Stanford	$200,000,000	$47,500,000	$152,500,000	$25,450,000	$225,450,000	200,000	612	196
SD Consortium	115,202,026	43,000,000	72,202,026	46,000,000	163,202,026	101,667	247	109
UCSF	94,514,740	38,000,000	56,514,740	40,900,000	135,414,740	74,832	245	124
USC	82,610,000	29,400,000	53,210,000	60,000,000	142,610,000	87,537	234	66
UC Davis	61,770,588	21,889,791	39,880,797	37,100,000	98,870,588	54,227	132	84
UC Irvine	60,457,400	29,600,000	30,857,400	21,500,000	81,957,400	61,575	165	36
UCLA	41,834,478	21,641,780	20,192,698	40,000,000	81,834,478	34,587	68	114
UC Berkeley	78,610,000	22,000,000	56,610,000	14,000,000	92,610,000	59,600	224	28
Buck Institute	70,080,747	20,500,000	49,580,747	21,600,000	91,680,747	65,708	128	18
UCSC	12,896,500	7,191,950	5,704,550	13,400,000	26,296,500	19,829	68	18
UC Merced	7,458,000	4,359,480	3,098,520	800,000	8,258,000	8,140	36	8
UCSB	6,352,400	3,494,280	2,858,120	7,750,000	14,102,400	16,581	50	25
TOTALS	$831,786,879	$288,577,281	$543,209,598	328,500,000	1,160,286,879	784,283	2,209	826

•*Includes PIs located on campus and other locations.

[Back to Appendices]

APPENDIX 19

19. Economic analysis of impact of CIRM major facilities grants

Addendum 1: Economic Effect of CIRM Facilities and Equipment Grants on Tax Revenues and Jobs (September 10, 2008)

Addendum Objective

CIRM has now finalized the approval of the Major Facilities and Research Equipment Grants and Shared Research Lab Grants and has approval pending for Bank & Cores Grants. These grants are intended to fund facilities-related costs. CIRM has also approved grants to fund research-related costs. In total, CIRM has approved 229 grants for over $614 million. Figure 12 shows the division between CIRM's equipment-related and research-related grants approved to date.2 Since the Bank & Cores Grant program is pending final approvals, it is not included in the figure.

CIRM grantees independently raised additional funds for capital costs and new faculty lab research costs through other donor and institutional matching funds. We have been asked to evaluate the estimated economic impact on the California State Budget of CIRM facilities-related grant spending, as well as the donor and institutional matching funds for both facilities and research-related costs associated with these grants. We have also been asked to compare these results to our original estimates made in our 2003 and 2004 reports. Our 2003 report is titled Analysis of the Financial Impact on the California State Budget of the Proposed California Institute of Regenerative Medicine and our 2004 report is titled Economic Impact Analysis, Proposition 71 California Stem Cell Research and Cures Initiative. In this addendum, the reports are referred to together as the "original analyses". We have also been asked to estimate the number of additional jobs that would be generated by the facilities construction spending of CIRM and additional donor and matching funds for both facilities and research-related spending. This addendum does not include calculations on the effects of CIRM's research-related grant spending.

When considering the economic impact of CIRM's grants and other donor and institutional matching funds on the California State Budget, one should keep in mind that tax revenue is generated not only by CIRM's and the grantee institutions' direct expenditures, but also by the ripple effect of these expenditures. As a result of the CIRM-related spending, other businesses and institutions hire additional employees and increase spending on goods and services. For instance, the construction of new facilities by California institutions leads to additional in-state spending on food, rent, and other goods and services by the construction workers and suppliers.

Summary of Estimated Tax Revenue

In this analysis, we estimate the economic effect of the activities generated by CIRM's funding for construction of new research facilities and equipment from the Major New Facilities Grants and the Shared Lab Grants as described above in section 2, as well as the Bank & Core Grants, which are yet to be approved. We also estimate the impact of the grantee institutions' activities generated by matching funds they have raised or have committed to raise in addition to CIRM's grants, to fund both direct facilities costs as well as the initial funding for new faculty lab research.

APPENDIX 19

As of December 2007, CIRM budgeted $276.1 million for facility construction project grants (see Figure 13 below). The recent information from CIRM shows a somewhat increased spending level, to $320 million, including equipment spending.This includes $285 million in approved spending and $35 million in pending, but not yet finally approved, spending for Bank & Cores grants. Additionally, the grantee institutions have committed another $900.7 million through other donor or institutional matching funds.
Of these funds, $722.1 million is earmarked for facilities and equipment costs and $178.6 million for new faculty initial lab research spending. Based on the same economic impact framework described in the original analyses, we estimate the additional economic activity generated by these grants and the impact on the State Budget, and compare the results to the estimates in our original analyses. Assumptions and estimates from the original analyses were updated where new information was available, such as the current construction industry wage and spending estimates.5 Certain significant assumptions from the original analyses, such as the economic activity multiplier of 1.80 for construction of facilities and 1.93 for research spending, remain unchanged.6 The results of our analysis are presented in Figure 13 below and discussed in the following paragraphs.

The $320 million of CIRM facilities grants—which is 13 percent more than originally estimated ($282.0 million in the original analyses)—along with $900.7 million in donor and institutional matching funds for facilities and new lab research funds, are estimated to result in $99.1 million of tax revenue for the State of California over the next five years, which is 277 percent more than our original estimate of $26.3 million over five years. Of this revenue, $85.7 million is estimated to result from facilities and equipment spending, and $13.3 million is expected to result from spending on new faculty lab research facilities.

Tax revenue to California from these new lab facilities funds is based on our understanding that the facilities-related funds and the new faculty lab research funding come entirely from new funding sources that would not otherwise have been used for alternative projects during the same time period. Thus in this analysis, as in our original analyses, we assumed no offset for the economic benefits of new facility construction. In our original report, we assumed the CIRM research funding economic impact would have some offset due to researchers using some CIRM funding as a substitute for other research funding, rather than CIRM representing entirely new additional funding. This reduced the estimate of economic benefits of this funding on net new jobs and tax revenues. The research funding we consider here is different from ongoing CIRM research funds, since it represents the commitment of the institutions for initial research funding associated specifically with the new facilities. Our understanding is that this is less likely to have direct alternative uses than ongoing CIRM research funding, and thus we have not included any offsets in our primary estimate. If we were to make an assumption that there would be some offset, similar to that assumed in the original work for CIRM funding, it would decrease the portion of tax revenue and job years associated with the initial research funding in California by approximately 50 percent, or $6.6 million.

The increase of 277 percent in the tax revenue estimate is primarily attributable to a noteworthy increase in the matching funds from institutions and other donors over our original estimates. In our original analyses' base case scenario, we estimated that matching funds would be 15 percent,7 or $42 million, while in reality CIRM was able to attract commitments for facility and research-related matching funds of $901 million, or 281 percent of CIRM committed funds.

Summary of Estimated Job Creation

Spending by CIRM is expected to result not only in incremental tax revenue for California but also in the creation of new jobs for California residents. Specifically, over the first five years, CIRM facilities grants and corresponding facilities and research matching spending are projected to generate a total of 13,727 job-years (one job-year=one job for one year) or 2,745 construction and research-related jobs on average per year. The breakdown of these jobs includes 11,393 facilities and equipment related job years, equivalent to 2,279 jobs per year for five years, and 2,334 new lab research-related job years, equivalent to 467 jobs per year for five years.

As noted, we understand that the facility and lab spending from donor and matching funds is for the facilities and researchers focused on CIRM-related activities. The research matching funds were not contemplated directly or including in the financial estimates in the original analyses. Because these matching funds represent new research activities, they will not have an offset for research activities that would have occurred anyway regardless of CIRM. If one were to assume that the new facility research did have an offset for alternative uses, as was estimated for the CIRM-related research funds, the estimated matching funds lab research-related job years to California would decrease from 2,334 job-years to 1,168 job-years. Even under this assumption, the estimate of total new job-years for facilities and equipment and initial lab research spending is more than 200 percent greater than the estimate provided in the original analyses.

Submitted to:
California Institute for Regenerative Medicine (CIRM)

Submitted by:
Dr. Laurence Baker
Stanford Medical School

Mr. Bruce Deal, Managing Principal
Analysis Group, Inc.
Menlo Park, California

Contact:
Bruce Deal
Analysis Group
1010 El Camino Real, Suite 310
Menlo Park, CA 94025

September 10, 2008

[Back to Appendices]

APPENDIX 20

20. Papers in highest profile journals

Authors (CIRM-funded Bolded)	Institution	Title	Journal	Date	Grant#	Grant#	Grant#	PMID
Zovein AC, Turlo KA, Ponec RM, Lynch MR, Chen KC, Hofmann JJ, Cox TC, Gasson JC, **Iruela-Arispe ML**	UCLA	Vascular remodeling of the vitelline artery initiates extra-vascular emergence of hematopoietic clusters	Blood	8/10/2010	RB1-01328 (MLIA)	T1-00005 (ACZ)		20699440
Ieda M, Fu JD, **Delgado-Olguin P**, Vedantham V, Hayashi Y, **Bruneau BG, Srivastava D**	Gladstone	Direct reprogramming of fibroblasts into functional cardiomyocytes by defined factors	Cell	8/6/2010	RC1-00142 (DS)	RN2-00903 (BGB)	T2-00003 (PDO)	20691899
Oshima K, Shin K, Diensthuber M, Peng AW, **Ricci AJ, Heller S**	Stanford	Mechanosensitive hair cell-like cells from embryonic and induced pluripotent stem cells	Cell	5/14/2010	RC1-00119			20478259
Hansen DV, **Lui JH**, Parker PR, **Kriegstein AR**	UCSF	Neurogenic radial glia in the outer subventricular zone of human neocortex	Nature	2/14/2010	RC1-00346 (ARK)	T1-00002 (JHL)		20154730
Song H, Chung SK, Xu Y	UCSD	Modeling disease in human ESCs using an efficient BAC-based homologous recombination system	Cell Stem Cell	1/8/2010	RC1-00148			20074536
Kee K, Angeles VT, Flores M, Nguyen HN, **Reijo Pera RA**	Stanford	Human DAZL, DAZ and BOULE genes modulate primordial germ-cell and haploid gamete formation	Nature	10/28/2009	RC1-00137			19865085
Coufal NG, Garcia-Perez JL, Peng GE, Yeo GW, Mu Y, Lovci MT, Morell M, O'Shea KS, Moran JV, **Gage FH**	Salk	L1 retrotransposition in human neural progenitor cells	Nature	8/5/2009	RC1-00115			19657334
Kwon C, Qian L, Cheng P, Nigam V, Arnold J, **Srivastava D**	Gladstone	A regulatory pathway involving Notch1/beta-catenin/Isl1 determines cardiac progenitor cell fate	Nat Cell Biol	7/20/2009	RC1-00142 (DS)	T2-00003 (CK)		19620969

APPENDIX 20

Authors (CIRM-funded Bolded)	Institution	Title	Journal	Date	Grant#	Grant#	Grant#	PMID
Cordes KR, Sheehy NT, White MP, Berry EC, Morton SU, Muth AN, Lee TH, Miano JM, **Ivey KN, Srivastava D**	Gladstone	miR-145 and miR-143 regulate smooth muscle cell fate and plasticity	Nature	7/5/2009	RC1-00142 (DS)	T2-00003 (KNI)		19578358
Ieda M, Tsuchihashi T, **Ivey KN**, Ross RS, Hong TT, Shaw RM, **Srivastava D**	Gladstone	Cardiac fibroblasts regulate myocardial proliferation through beta1 integrin signaling	Dev Cell	2/17/2009	RC1-00142 (DS)	T2-00003 (KNI)		19217425
Yeo GW, **Coufal NG**, Liang TY, Peng GE, Fu XD, **Gage FH**	Salk	An RNA code for the FOX2 splicing regulator revealed by mapping RNA-protein interactions in stem cells	Nat Struct Mol Biol	1/11/2009	RC1-00115			19136955
Marchetto MC, **Muotri AR**, Mu Y, Smith AM, Cezar GG, **Gage FH**	Salk	Non-cell-autonomous effect of human SOD1 G37R astrocytes on motor neurons derived from human embryonic stem cells	Cell Stem Cell	12/3/2008	RC1-00115			19041781
ten Berge D, Koole W, Fuerer C, Fish M, Eroglu E, **Nusse R**	Stanford	Wnt signaling mediates self-organization and axis formation in embryoid bodies	Cell Stem Cell	11/5/2008	RC1-00133			18983966
Fish JE, Santoro MM, Morton SU, Yu S, Yeh RF, Wythe JD, **Ivey KN**, Bruneau BG, Stainier DY, **Srivastava D**	Gladstone	miR-126 regulates angiogenic signaling and vascular integrity	Dev Cell	8/11/2008	RC1-00142 (DS)	T2-00003 (KNI)		18694566
Ivey KN, Muth A, Arnold J, King FW, Yeh RF, Fish JE, **Hsiao EC**, Schwartz RJ, Conklin BR, Bernstein HS, **Srivastava D**	Gladstone	MicroRNA regulation of cell lineages in mouse and human embryonic stem cells	Cell Stem Cell	3/5/2008	RC1-00142 (DS)	T2-00003 (KNI,ECH)		18371447
Fouse SD, **Shen Y**, Pellegrini M, Cole S, Meissner A, Van Neste L, Jaenisch R, **Fan G**	UCLA	Promoter CpG methylation contributes to ES cell gene regulation in parallel with Oct4/Nanog, PcG complex, and histone H3 K4/K27 trimethylation	Cell Stem Cell	2/7/2008	RC1-0111 (GF)	T1-00005 (YS)		18371437

APPENDIX 20

Authors (CIRM-funded Bolded)	Institution	Title	Journal	Date	Grant#	Grant#	Grant#	PMID
Mohrin M, Bourke E, Alexander D, Warr MR, Barry-Holson K, Le Beau MM, Morrison CG, **Passegué E**	UCSF	Hematopoietic stem cell quiescence promotes error-prone DNA repair and mutagenesis	Cell Stem Cell	7/8/2010	RN2-00934 (EP)	T1-00002 (MM)		20619762
Hang CT, Yang J, Han P, Cheng HL, Shang C, Ashley E, Zhou B, **Chang CP**	Stanford	Chromatin regulation by Brg1 underlies heart muscle development and disease	Nature	7/1/2010	RN2-00909			20596014
Lee JH, Durand R, Gradinaru V, Zhang F, Goshen I, Kim DS, Fenno LE, Ramakrishnan C, **Deisseroth K**	Stanford	Global and local fMRI signals driven by neurons defined optogenetically by type and wiring	Nature	5/16/2010	RN1-00535			20473285
Hawkins RD, Hon GC, Lee LK, Ngo Q, Lister R, Pelizzola M, Edsall LE, Kuan S, Luu Y, Klugman S, Antosiewicz-Bourget J, Ye Z, Espinoza C, Agarwahl S, Shen L, Ruotti V, Wang W, Stewart R, Thomson JA, Ecker JR, **Ren B**	Ludwig	Distinct epigenomic landscapes of pluripotent and lineage-committed human cells	Cell Stem Cell	5/7/2010	RN2-00905			20452322
Gradinaru V, Zhang F, Ramakrishnan C, Mattis J, Prakash R, Diester I, Goshen I, Thompson KR, **Deisseroth K**	Stanford	Molecular and cellular approaches for diversifying and extending optogenetics	Cell	3/18/2010	RN1-00535			20303157
Singla V, Romaguera-Ros M, Garcia-Verdugo JM, **Reiter JF**	UCSF	Ofd1, a human disease gene, regulates the length and distal structure of centrioles	Dev Cell	3/16/2010	RN2-00919			20230748
Bertrand JY, Chi NC, Santoso B, Teng S, Stainier DY, **Traver D**	UCSD	Haematopoietic stem cells derive directly from aortic endothelium during development	Nature	2/14/2010	RN1-00575 (DT)	T1-00003 (JYB)		20154733
Wang JK, **Tsai MC**, Poulin G, Adler AS, Chen S, Liu H, Shi Y, **Chang HY**	Stanford	The histone demethylase UTX enables RB-dependent cell fate control	Genes Dev	2/1/2010	RN1-00529			20123895

APPENDIX 20

Authors (CIRM-funded Bolded)	Institution	Title	Journal	Date	Grant#	Grant#	Grant#	PMID
Suh N, Baehner L, Moltzahn F, Melton C, Shenoy A, Chen J, **Blelloch R**	UCSF	MicroRNA function is globally suppressed in mouse oocytes and early embryos	Curr Biol	1/28/2010	RN2-00906			20116247
Bertrand JY, Cisson JL, Stachura DL, **Traver D**	UCSD	Notch signaling distinguishes 2 waves of definitive hematopoiesis in the zebrafish embryo	Blood	1/27/2010	RN1-00575 (DT)	T1-00003 (JYB)		20107232
Peng JC, Valouev A, Swigut T, Zhang J, Zhao Y, Sidow A, **Wysocka J**	Stanford	Jarid2/Jumonji coordinates control of PRC2 enzymatic activity and target gene occupancy in pluripotent cells	Cell	12/24/2009	RN1-00579			20064375
Olive V, Bennett MJ, Walker JC, Ma C, Jiang I, Cordon-Cardo C, Li QJ, Lowe SW, Hannon GJ, **He L**	UC Berkeley	miR-19 is a key oncogenic component of mir-17-92	Genes Dev	12/15/2009	RN2-00923			20008935
Li G, Bien-Ly N, Andrews-Zwilling Y, Xu Q, Bernardo A, Ring K, Halabisky B, Deng C, Mahley RW, **Huang Y**	Gladstone	GABAergic interneuron dysfunction impairs hippocampal neurogenesis in adult apolipoprotein e4 knockin mice	Cell Stem Cell	12/4/2009	RN2-00952 (YH)	T2-00003 (GL)		19951691
Renault VM, Rafalski VA, Morgan AA, Salih DA, Brett JO, Webb AE, Villeda SA, Thekkat PU, Guillerey C, Denko NC, Palmer TD, Butte AJ, **Brunet A**	Stanford	FoxO3 regulates neural stem cell homeostasis	Cell Stem Cell	11/6/2009	RN1-00527			19896443
Boland MJ, Hazen JL, Nazor KL, Rodriguez AR, Gifford W, Martin G, Kupriyanov S, **Baldwin KK**	Scripps	Adult mice generated from induced pluripotent stem cells	Nature	8/2/2009	RN1-00584			19672243
Sohal VS, Zhang F, Yizhar O, **Deisseroth K**	Stanford	Parvalbumin neurons and gamma rhythms enhance cortical circuit performance	Nature	4/16/2009	RN1-00535			19396159
Airan RD, Thompson KR, Fenno LE, Bernstein H, **Deisseroth K**	Stanford	Temporally precise in vivo control of intracellular signalling	Nature	3/18/2009	RN1-00535			19295515

APPENDIX 20

Authors (CIRM-funded Bolded)	Institution	Title	Journal	Date	Grant#	Grant#	Grant#	PMID
Yamaza T, Miura Y, **Akiyama K**, Bi Y, Sonoyama W, Gronthos S, Chen W, **Le A, Shi S**	USC	Mesenchymal stem cell-mediated ectopic hematopoiesis alleviates aging-related phenotype in immunocompromised mice	Blood	3/12/2009	RN1-00572			19074727
Sridharan R, Tchieu J, Mason MJ, Yachechko R, Kuoy E, Horvath S, Zhou Q, **Plath K**	UCLA	Role of the murine reprogramming factors in the induction of pluripotency	Cell	1/23/2009	RN1-00564 (KP)	T1-00005 (RS)		19167336
Wang G, Chen HW, Oktay Y, Zhang J, Allen EL, Smith GM, Fan KC, Hong JS, French SW, McCaffery JM, Lightowlers RN, Morse HC 3rd, Koehler CM, **Teitell MA**	UCLA	PNPASE regulates RNA import into mitochondria	Cell	8/6/2010	RS1-00313	RB1-01397		20691904
Gilbert PM, Mouw JK, Unger MA, Lakins JN, Gbegnon MK, Clemmer VB, Benezra M, Licht JD, Boudreau NJ, Tsai KK, Welm AL, Feldman MD, Weber BL, **Weaver VM**	UCSF	HOXA9 regulates BRCA1 expression to modulate human breast tumor phenotype	J Clin Invest	4/12/2010	RS1-00449			20389018
Delaloy C, Liu L, **Lee JA**, Su H, Shen F, Yang GY, Young WL, Ivey KN, **Gao FB**	Gladstone	MicroRNA-9 coordinates proliferation and migration of human embryonic stem cell-derived neural progenitors	Cell Stem Cell	4/2/2010	RS1-00462 (FBG)	TG2-01160 (CD)	T2-00003 (JAL)	20362537
Bajpai R, Chen DA, Rada-Iglesias A, Zhang J, Xiong Y, Helms J, Chang CP, Zhao Y, Swigut T, **Wysocka J**	Stanford	CHD7 cooperates with PBAF to control multipotent neural crest formation	Nature	2/3/2010	RS1-00323			20130577
Melton C, Judson RL, **Blelloch R**	UCSF	Opposing microRNA families regulate self-renewal in mouse embryonic stem cells	Nature	1/6/2010	RS1-00161	RN2-00906		20054295

APPENDIX 20

Authors (CIRM-funded Bolded)	Institution	Title	Journal	Date	Grant#	Grant#	Grant#	PMID
Gaspar-Maia A, Alajem A, **Polesso F**, **Sridharan R**, Mason MJ, Heidersbach A, Ramalho-Santos J, McManus MT, **Plath K**, Meshorer E, **Ramalho-Santos M**	UCSF	Chd1 regulates open chromatin and pluripotency of embryonic stem cells	Nature	7/8/2009	RS1-00434 (AGM,FP,MRS)	RN1-00564 (KP)	T1-00005 (RS)	19587682
Chin MH, Mason MJ, Xie W, Volinia S, Singer M, Peterson C, Ambartsumyan G, Aimiuwu O, Richter L, Zhang J, Khvorostov I, Ott V, Grunstein M, Lavon N, Benvenisty N, Croce CM, Clark AT, Baxter T, Pyle AD, **Teitell MA**, Pelegrini M, **Plath K, Lowry WE**	UCLA	Induced pluripotent stem cells and embryonic stem cells are distinguished by gene expression signatures	Cell Stem Cell	7/2/2009	RS1-00259 (WEL), RS1-00313 (MAT)	RN1-00564 (KP)	RL1-00681 (KP & WEL)	19570518
Ootani A, Li X, Sangiorgi E, Ho QT, Ueno H, Toda S, Sugihara H, Fujimoto K, Weissman IL, Capecchi MR, **Kuo CJ**	Stanford	Sustained in vitro intestinal epithelial culture within a Wnt-dependent stem cell niche	Nat Med	4/27/2009	RS1-00243 (CJK)	T1-00001 (AO)		19398967
Judson RL, **Babiarz JE**, Venere M, **Blelloch R**	UCSF	Embryonic stem cell–specific microRNAs promote induced pluripotency	Nat Biotechnol	4/12/2009	RS1-00161			19363475
Heintzman ND, Hon GC, Hawkins RD, Kheradpour P, Stark A, Harp LF, Ye Z, Lee LK, Stuart RK, Ching CW, Ching KA, Antosiewicz-Bourget JE, Liu H, Zhang X, Green RD, Lobanenkov VV, Stewart R, Thomson JA, Crawford GE, Kellis M, **Ren B**	Ludwig	Histone modifications at human enhancers reflect global cell-type-specific gene expression	Nature	3/18/2009	RS1-00292			19295514

APPENDIX 20

Authors (CIRM-funded Bolded)	Institution	Title	Journal	Date	Grant#	Grant#	Grant#	PMID
Xiong H, Wang D, Chen L, Choo YS, Ma H, Tang C, Xia K, Jiang W, Ronai Z, Zhuang X, **Zhang Z**	Burnham	Parkin, PINK1, and DJ-1 form a ubiquitin E3 ligase complex promoting unfolded protein degradation	J Clin Invest	2/23/2009	RS1-00331	RL1-00682		19229105
Gekas C, Rhodes KE, Gereige LM, Helgadottir H, Ferrari R, Kurdistani SK, Montecino-Rodriguez E, Bassel-Duby R, Olson E, Krivtsov AV, Armstrong S, Orkin SH, Pellegrini M, **Mikkola HK**	UCLA	Mef2C is a lineage-restricted target of Scl/Tal1 and regulates megakaryopoiesis and B-cell homeostasis	Blood	2/11/2009	RS1-00420			19211936
Li P, Tong C, Mehrian-Shai R, Jia L, Wu N, Yan Y, Maxson RE, **Schulze EN**, Song H, Hsieh CL, Pera MF, **Ying QL**	USC	Germline competent embryonic stem cells derived from rat blastocysts	Cell	12/26/2008	RS1-00327 (QLY)	T1-00004 (ENS)		19109898
Geron I, Abrahamsson AE, **Barroga CF**, **Kavalerchik E**, Gotlib J, Hood JD, Durocher J, Mak CC, Noronha G, Soll RM, Tefferi A, Kaushansky K, **Jamieson CH**	UCSD	Selective inhibition of JAK2-driven erythroid differentiation of polycythemia vera progenitors	Cancer Cell	4/1/2008	RS1-00228 (CFB,CHJ)	T1-00003 (EK)		18394555
Pajcini KV, Corbel SY, Sage J, Pomerantz JH, **Blau HM**	Stanford	Transient inactivation of Rb and ARF yields regenerative cells from postmitotic mammalian muscle	Cell Stem Cell	8/6/2010	RT1-01001			20682446
Gilbert PM, Havenstrite KL, Magnusson KE, Sacco A, Leonardi NA, Kraft P, Nguyen NK, Thrun S, Lutolf MP, **Blau HM**	Stanford	Substrate elasticity regulates skeletal muscle stem cell self-renewal in culture	Science	7/15/2010	RT1-01001 (HMB)	TG2-01159 (PMG)		20647425
Laurent LC, Nievergelt CM, Lynch C, Fakunle E, Harness JV, Schmidt U, Galat V, Laslett AL, Otonkoski T,	Scripps	Restricted ethnic diversity in human embryonic stem cell lines	Nat Methods	1/1/2010	RT1-01108 (JFL)	RN2-00931 (LCL)		20038950

APPENDIX 20

Authors (CIRM-funded Bolded)	Institution	Title	Journal	Date	Grant#	Grant#	Grant#	PMID
Keirstead HS, Schork A, Park HS, **Loring JF**								
Eguchi A, Meade BR, Chang YC, Fredrickson CT, Willert K, Puri N, **Dowdy SF**	UCSD	Efficient siRNA delivery into primary cells by a peptide transduction domain-dsRNA binding domain fusion protein	Nat Biotechnol	5/17/2009	RT1-01063			19448630
Minear S, Leucht P, **Jiang J**, Liu B, Zeng A, Fuerer C, **Nusse R, Helms JA**	Stanford	Wnt proteins promote bone regeneration	Sci Transl Med	4/28/2010	TR1-01249			20427820

[Back to Appendices]

21. Collaborative Funding Partner sample MOU

Alliance Memorandum of Understanding between the California Institute for Regenerative Medicine and the State of Victoria

WHEREAS, the California Institute for Regenerative Medicine ("CIRM"), an agency of the State of California, was established, inter alia, to make grants and loans for stem cell research, for research facilities and for other vital research opportunities in California to realize therapies and/or medical procedures that will result in the cure for, or substantial mitigation of, major diseases and injuries;

WHEREAS, the State of Victoria ("Victoria") is working, together with the Victorian stakeholder group of stem cell scientists and related scientists and staff in the academic, medical and research organizations of Victoria, to facilitate a process to enable Victorian and Californian researchers to undertake joint stem cell research projects;

WHEREAS, for the purposes of this Memorandum of Understanding (MOU), the Department of Innovation, Industry and Regional Development (DIIRD) is acting on behalf of the State of Victoria;

WHEREAS, CIRM and Victoria each desire to explore an alliance ("the Alliance") for possible collaborative funding of stem cell research projects by:

- combining respective Californian and Victorian expertise to achieve scientific and medical goals;
- developing specialized knowledge and effective use of facilities;
- increasing cooperation and mutual support;

WHEREAS, The Parties agree that this MOU is not legally binding but reflects a spirit of cooperation and shared intent between them;

Now, Therefore, CIRM and Victoria enter into the following MOU effective on the date of signature.

Introduction:

1. **PARTIES:** The Parties to this Memorandum of Understanding ("MOU") are the California Institute for Regenerative Medicine ("CIRM") and the State of Victoria ("Victoria").

2. **PURPOSE:** The purpose of this MOU is to confirm the Parties' mutual interest in exploring opportunities for collaborative evaluation, funding and monitoring of applications for stem cell research.

Confirmation of Interest:

CIRM and Victoria each hereby confirm their interest in the Alliance to explore collaborative approaches to evaluate, fund and monitor stem cell research projects. This interest is motivated by a shared understanding that the cure and treatment of chronic diseases and injury may potentially be accomplished through the use of regenerative medical therapies, including stem cells. The Parties further understand that medical breakthroughs in this area

will most likely happen only if adequate funding is made available to advance stem cell research, develop therapies and conduct clinical trials.

Development of the Alliance:

Both Parties recognize that, as a result of their different legal and stakeholder criteria, different operational arrangements will be required to service the Alliance as proposed in this MOU. Each Party also recognizes that further planning work is required in each jurisdiction in order to ensure the smooth running of the Alliance.

The Parties agree to continue to hold discussions seeking agreement on operational arrangements for this MOU during 2008.

Proposed Program Evaluation:

CIRM and Victoria will explore joint definition of funding concepts relating to areas of common collaborative interest. CIRM and Victoria shall work towards development of a process for evaluating proposed projects. The process may include the following:

Participation by Victoria in CIRM planned and approved Requests For Applications ("RFA").

Issuance of Joint Requests for Application which will specify objectives and requirements, eligible costs and the review criteria that will be applied to evaluate the merits of applications submitted in response to the RFA.

Disclosure to one another by CIRM and Victoria of actual and potential conflicts of interest which may be presented by any RFA or application.

Review of each proposed project for both scientific and collaborative merit, including due diligence evaluation of management and financial aspects.

Approval of funding by CIRM to be assessed by CIRM's Independent Citizens' Oversight Committee, as required.

Program Funding:

Subject to the provisions of this MOU, CIRM and Victoria shall work towards the development of guidelines for a funding process applicable to jointly funded research programs, as follows:

CIRM shall only fund research performed in the State of California.

Funds provided by Victoria shall only fund research performed in the State of Victoria.

CIRM grantees, to the extent reasonably possible, shall be encouraged to purchase goods and services related to the approved programs from California suppliers in proportion to the percent of funding provided by CIRM.

CIRM Funding shall be by grant, loan or a hybrid of both, in California.

No funds awarded pursuant to collaborative arrangements under this MOU shall be used for research involving human reproductive cloning or any other matter that is prohibited by Australian or Californian law or CIRM regulation.

For each approved project, funding and administration shall be managed by either CIRM or Victoria, or a combination of both, as determined on a case by case basis.

Post Award Monitoring and Reporting:

Subject to the provisions of this MOU, CIRM and Victoria shall work towards the development of reporting requirements to ensure that all grantees provide timely and adequate information ("Progress Information") concerning project performance and progress, which may include the following:

Both CIRM and Victoria shall receive Progress Information for all aspects of each approved project, notwithstanding the fact that specific activities may have been funded by only one or the other funder.

Progress Information shall include at a minimum, the information that is currently required by CIRM and Victoria respectively.

Grantees shall be subject to audit on terms established by CIRM and Victoria as applicable to each jurisdiction respectively.

Either CIRM or Victoria may suspend or cancel funding in the event progress towards approved objectives is unsatisfactory or milestones are not met.

No party shall withdraw or cancel funding without first having consulted the other.

Intellectual Property: All CIRM grantees shall agree to be bound by the intellectual property regulations of CIRM. Applicants will be required to explain how they propose to comply with CIRM intellectual property regulations in the collaborative context. Victoria will consider intellectual property issues in its funding of grantees as indicated in Section VIII of this MOU.

Sharing of Research Data: All CIRM grantees shall agree to be bound by CIRM regulations concerning sharing research data, biomedical materials and publications. Victoria will consider these issues under the operational arrangements to be made as indicated in Section VIII of this MOU.

Miscellaneous Provisions:

LIMITATIONS ON PARTICIPATION: Notwithstanding anything herein to the contrary, CIRM's participation hereunder is subject to, and must be in conformance with, statutory and policy requirements. California Constitution Section XXXV, California Health and Safety Code Section 125290.10 et seq. and applicable regulations, see title 17 Cal. Code of Regs., section 100000 et seq., all of which are incorporated herein by this reference. Nothing herein requires CIRM or Victoria to approve or fund any proposed project, nor does execution of this MOU constitute a commitment of funds.

CIRM and Victoria shall each absorb 100% of their internal expenses related to performance under this MOU.

CIRM and Victoria shall each designate a point person to manage their performance under this MOU, to coordinate performance and to facilitate communication hereunder. From time to time, but not less than once per calendar year, CIRM and Victoria shall meet to review activities being performed by grantees, processes and other matters relating to the viability of this MOU.

This MOU shall remain in effect for a period of three (3) years from the date the last Party hereto signs it and shall be extended thereafter upon mutual written agreement of the Parties. However, either Party may terminate the MOU upon 30 days written notice. Termination shall operate prospectively only: commitments to fund any specific programs made by either Party prior to termination shall remain in effect notwithstanding termination.

Operational arrangements within Victoria:
The development of the operational arrangements in Victoria will be based on discussion amongst the Victorian stakeholders and reaching a Victorian stakeholders cooperation arrangement. This would set out clear directions and opportunities for their cooperation (and participation in) the operational management, in Victoria, of the Alliance. This would cover:

- Governance
- Stakeholder Involvement
- Promotion
- Collaborative Activities and Project Selection
- Scientific Results and Intellectual Property
- Funding Commitments
- Cost Distribution and Financial Processes

CIRM	**Victoria**
_____	_____
Alan TROUNSON President	John BRUMBY MP Premier
Witnesses –	
_____	_____
Robert N. KLEIN Chairman	Gavin JENNINGS MLC Minister for Innovation

Dated: _____

[Back to Appendices]

APPENDIX 22

22. Science Office activity per grant

Review with PreApplication			
COMPLETION DATES		Check	
Ideal	Planned	✓	EVENTS AND TASKS
			TOP OF PAGE
1/1/2010	1/1/2010		RFA DEVELOPMENT AND APPROVAL
1/1/2010	1/1/2010	✓	Concept approval by ICOC
1/8/2010	1/8/2010	✓	Finalize RFA
1/8/2010	1/8/2010	✓	Review criteria in final form (match to reviewer guidelines)
1/8/2010	1/8/2010	✓	Submission deadlines (Pre-App, App, Review, ICOC)
1/8/2010	1/8/2010	✓	Create specific submission emails (e.g., SEED@cirm.ca.gov)
	1/8/2010	✓	Finalize funding partner (CFP) participation and requirements
1/15/2010	1/15/2010	✓	Acquire RFA approvals (i.e., DSA, CSO, GC, President)
1/21/2010	1/21/2010	✓	Acquire meeting venue
2/1/2010	2/1/2010		RFA AND PRE-APPLICATION POSTING
1/26/2010	1/26/2010	✓	Complete pre-application template
1/26/2010	1/26/2010	✓	Information page with proposal elements
1/26/2010	1/26/2010	✓	Related Business Entities Disclosure Form
1/30/2010	1/30/2010	✓	Test and fix any issues on pre-application forms
1/30/2010	1/30/2010	✓	Create review guidelines (criteria)
1/30/2010	1/30/2010	✓	Create mailbox for pre-application receipt (and auto reply message)
1/30/2010	1/30/2010	✓	Create web page with RFA and pre-application information
2/1/2010	2/1/2010	✓	Post RFA and pre-applicaiton on web site
2/1/2010	2/1/2010	✓	Send email announcement to RFA subscribers
2/1/2010	2/1/2010	✓	Invite/confirm reviewers to participate in pre-app review
			PRE-APPLICATION WEB MODULE POSTING
3/5/2010	3/5/2010	✓	Finalize reviewers expected to participate in pre-application review
3/5/2010	3/5/2010	✓	Finalize web module for pre-application review and COI check
3/5/2010	3/5/2010	✓	Post RFA and COI policy in web module

APPENDIX 22

Review with PreApplication			
COMPLETION DATES		Check	
Ideal	Planned	✓	EVENTS AND TASKS
3/5/2010	3/5/2010	✓	Post financial disclosure/ COI certification forms
3/5/2010	3/5/2010	✓	Input list of known reviewers
3/5/2010	3/5/2010	✓	Create and assign login/passwords
3/5/2010	3/5/2010	✓	Guidelines for pre-application review (based on RFA review criteria)
3/5/2010	3/5/2010	✓	Test and fix any issues with web module
			PRE-APPLICATION PROCESSING
3/12/2010	**3/12/2010**		**Due date for pre-applications**
		☐	**Check submission**
3/12/2010	3/12/2010	✓	Check for on-time receipt of electronic submission
3/12/2010	3/12/2010	✓	Check for on-time receipt of signed hard copy and cross check with e-form
3/13/2010	3/13/2010	✓	Meet to review flags and any issues with pre-applications
3/13/2010	3/13/2010	✓	Send "regret" email notice to PI of any incomplete, unqualified or late submissions
3/14/2010	3/14/2010	✓	Finalize list of allowable applications
3/17/2010	3/17/2010	✓	File and extract data from pre-applications
3/17/2010	3/17/2010	✓	File electronic pre-applications in RFA folder in Science drive
3/17/2010	3/17/2010	✓	Create XML files from each pre-application PDF
3/17/2010	3/17/2010	✓	Create XML files from each RBE PDF
3/17/2010	3/17/2010	✓	Import pre-application data into web module
3/17/2010	3/17/2010	✓	Export expertise requirements from pre-application (Excel file)
3/17/2010	3/17/2010	✓	Export table of pre-applications (PI name, Institution) vs. reviewers
3/17/2010	3/17/2010	✓	Generate application numbers
3/17/2010	3/17/2010	✓	Send list of applicant for-profit companies and RBEs to legal counsel for COI check
3/17/2010	3/17/2010	✓	Inform and reconcile with funding partner about collaborative PreApps received
			PRE-APPLICATION REVIEW
		☐	**Introduce reviewers to web review module**
3/19/2010	3/19/2010	✓	Post final list of COI names and institutions

APPENDIX 22

Review with PreApplication			
COMPLETION DATES		Check	
Ideal	Planned	✓	EVENTS AND TASKS
3/19/2010	3/19/2010	✓	Email notice to reviewers to complete COI and forms on web
3/19/2010	3/19/2010	✓	Email notice to CIRM staff to report COIs on web
		☐	**Collect COI and expertise information**
3/22/2010	3/22/2010	✓	Generate a master COI template (i.e., reviewers vs. applications)
3/26/2010	3/26/2010	✓	Compile signed COI and financial disclosure forms, review, and file
3/26/2010	3/26/2010	✓	Send reminders as necessary about completing COIs and forms
		☐	**Make final reviewer assignments**
3/27/2010	3/27/2010	✓	Make final assignments based on reported/identified COIs/expertise
3/27/2010	3/27/2010	✓	Post final assignments on web review module
3/27/2010	3/27/2010	✓	Email assignment notice to reviewers
4/12/2010	4/12/2010	✓	Send reminders as necessary to complete reviews
		☐	**Collect rankings from reviewers**
4/16/2010	4/16/2010	✓	Export ranking data to Excel file and sort in rank order
4/16/2010	4/16/2010	✓	Identify any missing reviews or rankings
4/16/2010	4/16/2010	✓	Determine scope of SO review
4/16/2010	4/16/2010	✓	Assign pre-applications to Science Officer reviewers
		☐	**Preparation for staff review meeting**
4/17/2010	4/17/2010	✓	Schedule meeting with Science Officers
4/17/2010	4/17/2010	✓	Prepare sign-in sheet
4/17/2010	4/17/2010	✓	Prepare scientific staff COI list
4/17/2010	4/17/2010	✓	Prepare PreApp books for SO
		☐	**Staff review meeting**
5/1/2010	4/28/2010	✓	Present rules regarding confidentiality and non-disclosure and procedures for review
5/1/2010	4/28/2010	✓	Present objectives of RFA
5/1/2010	4/28/2010	✓	Monitor motions and recusals

APPENDIX 22

Review with PreApplication			
COMPLETION DATES		Check	
Ideal	Planned	✓	EVENTS AND TASKS
5/1/2010	4/28/2010	✓	Finalize rankings and determine pre-applications to invite
		☐	**Invitationsto apply**
5/2/2010	4/29/2010	✓	Inform funding partner of invited/deferred pre-applications
5/2/2010	5/1/2010	✓	Send email with application number to PIs with invited pre-application
5/2/2010	5/1/2010	✓	Send defferal email to PIs with deferred pre-application
			INVITED APPLICATION REVIEW
		☐	**Review expertise of invited applications**
5/2/2010	5/2/2010	✓	Identify and recruit specialists for unmet expertise
5/2/2010	5/2/2010	✓	Generate template for pre-assigments and COI tracking
5/2/2010	**5/2/2010**	✓	**APPLICATION POSTING**
4/25/2010	4/25/2010	✓	Complete all application parts
4/25/2010	4/25/2010	✓	Part A - Information Form (applicant info, budget pages)
4/25/2010	4/25/2010	✓	Part B - Project Proposal
4/25/2010	4/25/2010	✓	Part C - Biosketches
4/25/2010	4/25/2010	✓	Related Business Entities Disclosure Form
4/25/2010	4/25/2010	✓	Additional parts (any lists, forms, letters of support)
	4/25/2010	✓	Consolidate any requirements/suggestions from CFP
4/29/2010	4/29/2010	✓	Test and fix any issues with application forms
4/29/2010	4/29/2010	✓	Create mailbox for application receipt (and auto reply message)
4/29/2010	4/29/2010	✓	Create web page with application instructions
5/2/2010	5/2/2010	✓	Post application and instructions on CIRM web site
			REVIEW WEB MODULE POSTING
6/6/2010	6/6/2010	✓	Finalize GWG member attendence for meeting
6/6/2010	6/6/2010	✓	Complete meeting fact sheet
6/6/2010	6/6/2010	✓	Post meeting fact sheet, RFA, and COI policy in reviewer module

Review with PreApplication			
COMPLETION DATES		Check	
Ideal	Planned	✓	EVENTS AND TASKS
6/6/2010	6/6/2010	✓	Post financial disclosure/ COI certification forms (should already be in system)
6/6/2010	6/6/2010	✓	Input list of attending GWG members and assign login/passwords
6/6/2010	6/6/2010	✓	Reviewer critique interface (based on review criteria)
6/6/2010	6/6/2010	✓	Guidelines for review (based on review criteria)
6/6/2010	6/6/2010	✓	Create module versions for GWG scientists, specialists, and ICOC GWG
			APPLICATIONS PROCESSING
6/13/2010	**6/13/2010**		**Due date for full applications**
		☐	**Check receipt and finalize allowable applications**
6/13/2010	6/13/2010	✓	Check for on time receipt of electronic and hardcopy versions (basis for disqualification)
6/13/2010	6/13/2010	✓	Check for signatures from PI and AOO on hardcopy (basis for disqualification)
6/14/2010	6/14/2010	✓	Check for basic qualifications (e.g., PI, institution), flag as necessary
6/14/2010	6/14/2010	✓	Check for submission of LOI, if required (basis for disqualification)
6/14/2010	6/14/2010	✓	Check for correct number of copies
6/14/2010	6/14/2010	✓	Check for unallowable materials (e.g., appendices); flag and remove as needed
6/16/2010	6/16/2010	✓	Meet to review flags and any issues with applications
6/16/2010	6/16/2010	✓	Finalize list of allowable applications (confer with SRO)
6/16/2010	6/16/2010	✓	Send "regret" email notice to PIs of incomplete, unqualified or late applications
6/16/2010	6/16/2010	✓	File hard copy applications
		☐	**Prepare applications for review and finalize pre-assignments**
6/20/2010	6/20/2010	✓	Organize electronic application materials in RFA folder in Science drive
6/20/2010	6/20/2010	✓	File and extract data from applications (PDF data)
6/20/2010	6/20/2010	✓	File electronic pre-applications in RFA folder in Science drive
6/20/2010	6/20/2010	✓	Create XML files from each application PDF and RBE PDF
6/20/2010	6/20/2010	✓	Export table of applications (App#, PI name, Institution) vs. reviewers
6/20/2010	6/20/2010	✓	Create flattened and combined PDF application files for web

Review with PreApplication			
COMPLETION DATES		Check	
Ideal	Planned	✓	EVENTS AND TASKS
			viewing
6/20/2010	6/20/2010	✓	Review application for additional collaborators/COIs (i.e., not listed with key personnel)
6/20/2010	6/20/2010	✓	Check for names that might constitute a 1090 COI
6/20/2010	6/20/2010	✓	Generate COI list from accepted applications
6/20/2010	6/20/2010	✓	Send list of applicant for-profit companies and RBEs to GC for COI check
6/20/2010	6/20/2010	✓	Finalize pre-assignments for reviewers
			ASSIGNMENTS AND COIs
		☐	**Web review module**
6/20/2010	6/20/2010	✓	Post final list of COI names and institutions
6/20/2010	6/20/2010	✓	Post pre-assignments for each scientific reviewer
6/23/2010	6/23/2010	✓	Email notice to Scientific WG members to complete COI, expertise, and forms on web
6/23/2010	6/23/2010	✓	Email notice to CIRM staff to report COIs on web
6/23/2010	6/23/2010	✓	Email notice to ICOC WG members to complete COI, and pre-review COI form on web
		☐	**Specialists (as needed)**
6/20/2010	6/20/2010	✓	Collect availability and schedule times for review call-in
6/20/2010	6/20/2010	✓	Email notice to Specialists to complete COI, expertise, and forms on web
6/27/2010	6/27/2010	✓	Confirm time window and phone number for specialists conference call
		☐	**Collect COI and expertise information**
6/27/2010	6/27/2010	✓	Compile signed forms (fax and mail) including financial disclosure, review, and file
6/27/2010	6/27/2010	✓	Send reminders as necessary about completing COIs and forms
6/27/2010	6/27/2010	✓	Review reported COIs and disclosure statements
6/27/2010	6/27/2010	✓	Generate Master COI Template
		☐	**Make final reviewer assignments**
6/27/2010	6/27/2010	✓	Make final assignments based on reported/identified COIs
6/27/2010	6/27/2010	✓	Post final assignments on web review module

APPENDIX 22

Review with PreApplication			
COMPLETION DATES		Check	
Ideal	Planned	✓	EVENTS AND TASKS
6/27/2010	6/27/2010	✓	Email assignment notice to GWG and Specialists
		☐	**Prepare hardcopies for mail-out**
6/27/2010	6/27/2010	✓	Write cover letter for mail-out
6/27/2010	6/27/2010	✓	Include guidelines for review and RFA in mailout to reviewers
6/27/2010	6/27/2010	✓	Create individual list of review assignments for mail-out package
6/27/2010	6/27/2010	✓	Prepare mail-out package for Scientific WG members (i.e., cover letter, guidelines for review)
6/27/2010	6/27/2010	✓	Prepare mail-out package for Specialists (i.e., cover letter, guidelines for review)
6/27/2010	6/27/2010	✓	Prepare abstract books for ICOC WG members as requested
6/27/2010	6/27/2010	✓	**Mail out packages with final hardcopy assignments to GWG and Specialists**
6/27/2010	6/27/2010	✓	Mail out packages for ICOC GWG members as needed
			PREPARATION FOR REVIEW MEETING
		☐	**Reviewers**
6/27/2010	6/27/2010	✓	GWG travel and accomodations
6/27/2010	6/27/2010	✓	Set up travel itinerary for reviewers (flag any late arrivals/early departures)
		☐	**Review logistics**
7/4/2010	7/4/2010	✓	Set up order of review schedule based on call times and GWG travel itinerary
7/4/2010	7/4/2010	✓	Establish assignments for CIRM staff and set up meeting to review roles
7/4/2010	7/4/2010	✓	Assign notetakers for meeting and summary writing
7/4/2010	7/4/2010	✓	Set up meeting with Vice-Chair to prepare for programmatic review
7/4/2010	7/4/2010	✓	Set up meeting with Chair to prepare for scientific review
		☐	**Prepare documents for review meeting**
7/18/2010	7/18/2010	✓	Generate scoring booklets for each GWG scientific reviewer with recusals
7/18/2010	7/18/2010	✓	Prepare individual programmatic vote/recommendations document (all WG members)
7/18/2010	7/18/2010	✓	Prepare sign-in sheet

Review with PreApplication			
COMPLETION DATES		Check	
Ideal	Planned	✓	EVENTS AND TASKS
7/18/2010	7/18/2010	✓	Prepare confidentiality and non-disclosure (sign-out) sheet
7/18/2010	7/18/2010	✓	Prepare roster for recording motions and initial roll call
7/18/2010	7/18/2010	✓	Initiate preparation of critique books for staff and GWG (generate after critique deadline)
7/18/2010	7/18/2010	✓	Generate abstract books for staff (two copies)
7/18/2010	7/18/2010	✓	Generate seating chart
7/18/2010	7/18/2010	✓	Generate Master Order of Review with Recusals (GWG version) and assignments (staff only)
7/18/2010	7/18/2010	✓	General Counsel cross-check recusals on Master spreadsheet
7/18/2010	7/18/2010	✓	Prepare reviewer folders (e.g., agenda, order of review, seating chart)
7/18/2010	7/18/2010	✓	Create display of applications during review meeting
7/18/2010	7/18/2010	✓	Create display for programmatic review
7/18/2010	7/18/2010	✓	Prepare slides for meeting
		☐	**Public agenda**
7/29/2010	7/29/2010	✓	Post public agenda for GWG meeting
8/1/2010	**8/1/2010**		**PATIENT ADVOCATE PREP MEETING**
7/18/2010	7/18/2010	✓	Schedule Meeting
8/1/2010	8/1/2010	✓	Present RFA overview and address questions
8/6/2010	**8/6/2010**		**REVIEWER CRITIQUE SUBMISSION DEADLINE**
7/30/2010	7/30/2010	✓	Remind reviewers about critique submission deadline
8/7/2010	8/7/2010	✓	Finialize critique books for staff and GWG with recusals
8/8/2010	**8/8/2010**		**REVIEW MEETING**
8/7/2010	8/7/2010	✓	Site visit to review venue (ensure all requirements are in place and working)
8/8/2010	8/8/2010	✓	Transport materials to meeting venue
8/8/2010	8/8/2010	✓	Ensure all present at meeting sign the sign-in sheet (at start of meeting)
8/8/2010	8/8/2010	✓	Present rules regarding confidentiality and non-disclosure and procedures for review
8/8/2010	8/8/2010	✓	Present objectives of RFA

APPENDIX 22

Review with PreApplication			
COMPLETION DATES		Check	
Ideal	Planned	✓	EVENTS AND TASKS
8/8/2010	8/8/2010	✓	Ensure that all Scientific Reviewers sign each page of the scoring booklet
8/8/2010	8/8/2010	✓	Ensure that all present at meeting sign the confidentiality and non-disclosure (sign-out) sheet
8/8/2010	8/8/2010	✓	Ensure that all SMRFWG members present sign the programmatic vote/recommendations document
8/8/2010	8/8/2010	✓	If video conference, GRS to manage remote site and ensure all of above
8/8/2010	8/8/2010	✓	Pre-calls to Specialists (ensure participation and timing)
8/8/2010	8/8/2010	✓	Monitor and run getner for Specialist calls
8/8/2010	8/8/2010	✓	Monitor motions and recusals
8/8/2010	8/8/2010	✓	Venue, lodging, travel logistics
8/8/2010	8/8/2010	✓	Score tabulation
8/8/2010	8/8/2010	✓	Public meeting agenda items and roll call
8/8/2010	8/8/2010	✓	Collect all confidetial materials and tear-down
			Prepare review reports
8/9/2010	8/9/2010	✓	Set up schedule for summary write up
8/9/2010	8/9/2010	✓	Summary assignments and backups
8/18/2010	8/18/2010	✓	Post notes from meeting (all scientists in attendance)
9/1/2010	9/1/2010	✓	Compile summary drafts/copy editing/ summary formatting
9/9/2010	9/9/2010	✓	Check for applicant identifiers in public summaries
9/9/2010	9/9/2010	✓	Executive Summary draft due
9/20/2010	9/20/2010	✓	Executive Summary final due
			REVIEW SUMMARIES
9/11/2010	9/11/2010	✓	Prep time for printing and posting
9/11/2010	9/11/2010	✓	Prepare email letter and merge template for emailing summaries to PI
9/11/2010	9/11/2010	✓	Prepare merge template and pdf for printing summaries for ICOC
9/11/2010	9/11/2010	✓	Prepare CIRM web page for posting summaries/recommendations
9/11/2010	9/11/2010	✓	Export summary and abstract data from web system
9/13/2010	9/13/2010	✓	Confidential summaries emailed to PI
9/13/2010	9/13/2010	✓	Public summaries mailed to ICOC

APPENDIX 22

Review with PreApplication			
COMPLETION DATES		Check	
Ideal	Planned	✓	EVENTS AND TASKS
9/15/2010	9/15/2010	✓	Public summaries posted on web
			PREPARE FOR ICOC MEETING
9/11/2010	9/11/2010	✓	Prepare slides for presenting GWG recommendations and send to Vice-Chair
9/11/2010	9/11/2010	✓	Meeting with SO/SA to discuss possible questions from ICOC
9/11/2010	9/11/2010	✓	Generate notebooks for SO with assigned applications and summary sheet
9/11/2010	9/11/2010	✓	Generate COI list for board members
9/20/2010	9/20/2010	✓	Identification of COIs by board members
9/20/2010	9/20/2010	✓	Staff review of SEIs for additional conflicts
9/20/2010	9/20/2010	✓	Preparation of final COI lists for board
9/20/2010	9/20/2010	✓	Create Master spreadsheet of COIs
9/24/2010	9/24/2010	✓	Collect, respond and file any communications regarding review including appeal requests
9/24/2010	9/24/2010	✓	Collect, respond and process (including web posting) any Extraordinary Petitions
9/25/2010	**9/25/2010**		**ICOC MEETING**
9/25/2010	9/25/2010	✓	Provide each board member with a list of applications from which member is recused
9/25/2010	9/25/2010	✓	Announce recusals at meeting before consideration of each application
9/25/2010	9/25/2010	✓	Counsel monitors recusals based on Master speadsheet
9/25/2010	9/25/2010	✓	Board members sign COI certification
9/25/2010	9/25/2010	✓	Present objectives and recommendations from GWG
9/25/2010	9/25/2010	✓	Science Officers prepared to address questions from board
9/25/2010	9/25/2010	✓	Display applications/recommendations and monitor approvals
9/25/2010	9/25/2010	✓	Present any requested Extraordinary Petitions to ICOC
			ICOC MEETING FOLLOW UP
9/26/2010	9/26/2010	✓	Send ICOC decision to applicant
10/2/2010	10/2/2010	✓	Create official review file
10/2/2010	10/2/2010	✓	Review close-out
			ADMINISTRATIVE REVIEW

APPENDIX 22

Review with PreApplication			
COMPLETION DATES		Check	
Ideal	Planned	✓	EVENTS AND TASKS
10/2/2010	10/2/2010	✓	JIT and Budget Amendment requests mailed out
10/23/2010	10/23/2010	✓	Full Administrative Review (GMO-SPO-GMO)
10/30/2010	10/30/2010	✓	NGA Preparation
10/30/2010	10/30/2010	✓	NGA Mail-out
11/13/2010	11/13/2010	✓	Signed NGAs returned
11/20/2010	11/20/2010	✓	Pay Memo to SCO
11/27/2010	11/27/2010	✓	Warrants to Grantees

[Back to Appendices]

APPENDIX 23

23. Workshops organized by CIRM

2005

- Stem Cell Research: Charting New Directions for California Conference - Oct 2005

2006

- Funding Mechanisms – May 25, 2006
- From Basic Research to the Clinic - July 13, 2006
- Industry Roundtable – July 25, 2006

2007

- Advancing Effective Research Oversight: CIRM's Evaluation Initiative Regional Workshop – Feb & April 2007
- Disease Team Workshop: Information Gathering Session Workshop - July 25-26, 2007

2008

- Cancer Stem Cell Workshop – April 17, 2008
- CIRM Predictive Toxicology Workshop – July 7-8, 2008
- Cancer Stem Cells Workshop Canada/California Collaboration – Aug 26, 2008
- IP Information Sessions & Q&A on CIRM For-Profit Grant Applications – Sept 11 & 12, 2008
- CIRM GMP Workshop – Nov 3, 2008
- CIRM/German Institute for Regenerative Medicine Workshop – Dec 8, 2008

2009

- CIRM/Medical Research Council (UK) Workshop – January 12-13, 2009
- Immunology Workshop – Feb 4, 2009
- Achieving our Mission through Funding Industry: Update to CIRM Strategic Plan – Feb 3 & 20, 2009
- Preparing for the Clinic: Policy Considerations for the Use of Cell Based Therapies – Feb 17-18, 2009
- Achieving our Mission: Update to CIRM Strategic Plan – March 5 & 11, 2009
- CIRM Autism Workshop – May 28-29, 2009
- CIRM/Japan Science & Technology – Basic Biology Workshop – June 8-9, 2009
- Advancing the Field: Institutional Approaches Supporting Ethics in Stem Cell Research – June 30 & 31 2009
- CIRM/Japan Science and Technology Immunology Workshop– Kyoto, Japan – Sept 1, 2009

2010

- The Role of CIRM in Enhancing Diversity– February 2010
- Grant Writing Workshop for Industry – March 3, 2010
- How to Talk to the Media: Grantee Workshop – March 3, 2010
- CIRM-Federal Ministry of Education and Research, Germany Workshop – March 6, 2010
- Maryland/Tedco/ California Workshop – March 11-1, 2010
- CIRM/Regenerative Medicine Consortium Webinar - Characterization and Its Critical Role in Manufacturing – Better, Faster and Cost Effective Approaches for the Stem Cell and Regenerative Medicine Industry -- April 15, 2010

APPENDIX 23

- Ethical & Policy Considerations for a Pluripotent Cell Resource Center – May 26, 2010
- CIRM/Medical Research Council(UK) – SCNT/Parthenogenesis – June 13-14th, 2010
- ISSCR/CIRM/ISCT – Clinical Trials Regulatory Harmonization – June 15, 2010
- CIRM/The Netherlands Science Collaboration – June 16, 2010
- Advancing Effective Research Oversight: 2010 Regional Workshops on Regulatory Compliance – March & April, 2010
- CIRM / Regenerative Medicine Consortium Webinar: Preclinical Considerations for Stem Cell Therapies -- Sept 28, 2010
- CIRM-iPSC Banking Workshop – Nov 17-18, 2010

[Back to Appendices]

APPENDIX 24

24. Conference developed by grantees with CIRM conference grants

Proposed # Attendees	Expected Attendees	Application #	Institution	Title	Start Date	End Date	Field
141 final	Clinical Researchers	CG1-99000	Children's Hospital of Orange County	Stem Cell Therapies for Pediatric Diseases and Injuries: A Critical Evaluation	March 12, 2009	March 12, 2009	
300	slet biologists, stem cell and gene transfer scientists, transplant scientists, immunologists, cell biologists, endocrinologists, diabetologists, and other health care professionals	CG1-99001	City of Hope National Medical Center	2009 Rachmiel Levine Diabetes and Obesity Symposium: Advances in Diabetes Biology, Immunology and Cell Biology	March 18, 2009	March 21, 2009	
100 Final	educational needs of investigators and teams involved in these translational initiatives	CG1-99002	Blood Systems Research Institute	Translation of Stem Cell Therapies: Best Practices and Regulatory Considerations	May 2, 2009	May 2, 2009	
275-350	clinicians, engineers, geneticists, cell biologists, and molecular biologists working in cardiovascular development and stem cell/progenitor biology.	CG1-99003	University of California, San Francisco	Weinstein Cardiovascular Development Conference	May 7, 2009	May 10, 2009	
60-75 teachers	academia, industry, high school education and the media	CG1-99005	University of California, San Diego	San Diego Stem Cell Science Education Symposium at UCSD	April 25, 2009	April 25, 2009	
300 invited	clinicians and scientists studying neural stem cell biology and brain developmen	CG1-99004	University of California, San Francisco	UCSF Frontiers of Neural Stem Cells Symposium	Oct. 1, 2009	Oct. 2, 2009	
200 approx	200 students and faculty from UC Campuses	CG1-99006	University of California, San Diego	10th Annual UC Systemwide Bioengineering Symposium	June 19, 2009	June 21, 2009	

APPENDIX 24

Proposed # Attendees	Expected Attendees	Application #	Institution	Title	Start Date	End Date	Field
300 max	California clinical and scientific investigators, students and patient advocates.	CG1-99008	City of Hope	Innovation and Translational Stem Cell Therapy for Diabetes and Neurological Diseases:Paving the way for real life solutions	September 29, 2009	September 30, 2009	Type I Dabetes and Neurological disease
200 approx	Law and science students and faculty from Bay Area research institutions and representatives from Bay Area SC research companies.	CG1-99009	Stanford University	Stem Cell Policy: Understanding the Scientific and Legal Challenges Ahead	October 2, 2009	October 3, 2009	Policy
350	The target audience includes researchers, industry executives, thought leaders, student and the general public from California and beyond.	CG1-99010	Sanford Consortium for Regenerative Medicine	Stem Cell Meeting on the Mesa	November 11, 2009	November 11, 2009	Epigenetics, RNA, Clinical applications of Stem Cell Research and iPSC
120	Students, postdoctoral fellows, and reseachers in California.	CG1-99011	University of California, Irvine	Systems Biology of Stem Cells	May 24, 2010	May 25, 2010	Systems Biology
200	Scientists, clinical investigators, technical/regulatory personnel from academia, industry and government engaged in tranlsational medicine	CG1-99013	Blood Systems Research Institute	Translation of Stem Cell Therapies: Strategies and Best Practices for Preclinical Development	September 27, 2010	September 28, 2010	IND Development
40	leading stem cell junior investigators from CA and Harvard	CG1-99015	University of California,San Francisco	CA-HSCI 1st Generation Stem Cell PI Meeting	September 24, 2010	September 25, 2010	

[Back to Appendices]

25. First Clinical trial fostered by CIRM funding

Media contact:
Debra Kain
ddkain@ucsd.edu
619-543-6163

April 7, 2008

From Bench to Bedside in One Year: Stem Cell Research Leads to Potential New Therapy for Rare Blood Disorder

A unique partnership between industry and academia has led to human clinical trials of a new drug for a rare class of blood diseases called myeloproliferative disorders (MPD), which are all driven by the same genetic mutation and can evolve into leukemia. In just one year, collaborative discoveries by stem cell researchers from the University of California, San Diego, Dana-Farber Cancer Institute, the Mayo Clinic and a San Diego pharmaceutical company, TargeGen, moved from identification of the most promising drug candidate to clinical trials for a new drug to fight this degenerative blood disorder, which affects more than 100,000 Americans.

A study headed by Catriona H.M. Jamieson, M.D. Ph.D., assistant professor of medicine at the University of California, San Diego and Director for Stem Cell Research at Moores UCSD Cancer Center, found an inhibitor that can stop the over-proliferation of blood cells that results in problems with blood clotting, heart attacks and, in some cases, leukemia. Funded in part by a grant from the California Institute for Regenerative Medicine (CIRM), the study will be published in *Cancer Cell* on April 8, 2008. A parallel study at Harvard Medical School, headed by D. Gary Gilliland, Ph.D., M.D., yielded similar results which will appear in the same issue of *Cancer Cell*.

“As a clinician, I asked myself who is going to get this disease, and what can we do to stop its progression, instead of waiting until it evolves into a deadly cancer?” said Jamieson. “This project has been so extraordinary, because a small pharmaceutical company took a big chance on a rare disease.”

With major contributions from collaborators Jason Gotlib at Stanford University and Ayalew Tefferi at the Mayo Clinic, the research findings led to development of the inhibitor by TargeGen. That drug is currently being tested in human clinical trials at the UC San Diego School of Medicine, the Mayo Clinic, M.D. Anderson Cancer Center, and the University of Michigan, Stanford and Harvard University Schools of Medicine.

A patient with MPD makes too many blood cells, caused by a mutation expressed in the stem cell, the early stage cell that goes on to differentiate to become either red or white blood cells. In 2006, Jamieson was first author on a paper published in *PNAS*, outlining the discovery that a mutation in the JAK2 signaling pathway in patients with a type of MPD called *polycythemia vera* (PV) allows cells to bypass the process which would normally regulate the production of red blood cells. As a result of this defect, the bone marrow produces excessive numbers of red blood cells.

In the current research described in *Cancer Cell*, the UCSD School of Medicine researchers and collaborators transferred human cord blood stem cells, engineered to contain the mutant JAK2 gene, into mouse models with a suppressed immune system to find whether over-expression of

a single gene could drive, or initiate, the disease. These stem cells were introduced directly into the liver, the main site of blood development in the newborn mouse. As a result, the stem cells over-expressing the mutant gene led to overproduction of human red blood cells, and the mice developed a disease that looked like PV.

The researchers corroborated these results by injecting actual stem cells from patients with PV into the same mouse model, achieving similar results. "We found that the JAK2 mutation was necessary and sufficient, by itself, to drive the disease," Jamieson said.

Theorizing that blocking this mutation would prevent overproduction of red blood cells, TargeGen developed a selective JAK2 inhibitor called TG101348. This therapy was shown in animal studies to halt over-expression of the gene and reverse excessive production of red blood cells. Because TG101348 selectively targets the JAK2 protein that causes the disease, side effects have been minimized.

"Pre-clinical testing at the UCSD and Harvard University Schools of Medicine confirmed the therapeutic potential of TG101348. The compound was rapidly advanced into the current, ongoing human clinical trials being conducted at major research institutions across the country," said John Hood, Ph.D., Director of Research for TargeGen. "This unique industry-academia collaboration has helped guide a new drug from bench to bedside, from evaluating the compound's efficacy on cancer stem cells to its evaluation in patients bearing a disease which otherwise has very limited treatment options."

Under the auspices of Jamieson, co-first authors Ifat Geron, M.S., and Annelie Abrahamsson, M.S., worked in close collaboration with Kenneth Kaushansky, M.D., chair of the UCSD Department of Medicine; Jason Gotlib, M.D., M.S., at Stanford University School of Medicine; and Ayalew Tefferi, M.D., Department of Medicine at the Mayo Clinic in Minnesota.

Additional contributors to this study include Charlene Barroga, Ph.D. and Edward Kavalerchik, M.D., UCSD Department of Medicine; John Hood, Ph.D., Chi Ching Mak, Glenn Noronha and Richard Soll, Ph.D., TargeGen Inc., San Diego; and Jeffrey Durocher, PH.D., Transgenomic Inc., Gaithersberg, MD. The study was funded in part by the California Institute for Regenerative Medicine and the Mizrahi Family Foundation, the National Institutes of Health (K23HL04409) and an unrestricted gift from TargeGen Inc.

[Back to Appendices]

APPENDIX 26

This table includes all training appointments funded on CIRM grants. This list includes some individuals who served as trainees on more than one grant and therefore appear multiple times on this list.

Contact	Grant Number	Organization Name	Role	TBAppoint Type	TGAPPTTYPE
Leah Hutnick	RC1-00111-1	University of California, Los Angeles	Graduate-Predoc		
Shaun Fouse	RC1-00111-1	University of California, Los Angeles	Graduate-Predoc		
Simone Joers	RC1-00119-1	Stanford University	Graduate-Predoc		
Lori Phillips	RC1-00134-1	Stanford University	Graduate-Predoc		
Karina Nakayama	RC1-00144-1	University of California, Davis	Graduate-Predoc		
Ms. Melissa Freedenberg	RC1-00144-1	University of California, Davis	Graduate-Predoc		
Yun Choi	RC1-00347-1	University of California, San Francisco	Graduate-Predoc		
Mr. Antonio Davila	RC1-00353-1	University of California, Irvine	Graduate-Predoc		
Chad Tang	RC1-00354-1	Stanford University	Graduate-Predoc		
Jenny Ross	RM1-01732	University of California, Berkeley	Graduate-Predoc		
Ritchie Ho	RN1-00564-1	University of California, Los Angeles	Graduate-Predoc		
Dr. David Brafman	RS1-00173-1	University of California, San Diego	Graduate-Predoc		
Dayu Teng	RS1-00173-1	University of California, San Diego	Graduate-Predoc		
Hua Wang	RS1-00173-1	University of California, San Diego	Graduate-Predoc		
Anthony Daggett	RS1-00205-1	University of California, San Diego	Graduate-Predoc		
Emily Sylwestrak	RS1-00205-1	University of California, San Diego	Graduate-Predoc		
Matthew O'Sullivan	RS1-00205-1	University of California, San Diego	Graduate-Predoc		
Diep Nguyen	RS1-00239-1.2	University of California, Irvine	Graduate-Predoc		
Silin Sa	RS1-00239-1.2	University of California, Irvine	Graduate-Predoc		
Mr. Michael Quay Chen	RS1-00242-1	Stanford University	Graduate-Predoc		
Andrew Tran	RS1-00247-1	University of California, Irvine	Graduate-Predoc		
Nicholas Castello	RS1-00247-1	University of California, Irvine	Graduate-Predoc		
Michaela Patterson	RS1-00259-1	University of California, Los Angeles	Graduate-Predoc		
Elinore Mercer	RS1-00280-1	University of California, San Diego	Graduate-Predoc		
Dr. Jamie Conklin	RS1-00298-1	Stanford University	Graduate-Predoc		
Ms. Stacey Wirt	RS1-00298-1	Stanford University	Graduate-Predoc		
Carolyn Richard	RS1-00428-1	Beckman Research Institute Of The City Of Hope	Graduate-Predoc		
Dustin Wakeman	TR1-01267	Sanford-Burnham Medical Research Institute	Graduate-Predoc		
Andrew Burch	TB1-01175	California Polytechnic State University, San Luis Obispo	Intern	Graduate	
Anna McCann	TB1-01175	California Polytechnic State University, San Luis Obispo	Intern	Graduate	
Ashley Russell	TB1-01175	California Polytechnic State University, San Luis Obispo	Intern	Graduate	
Aubrey Smith	TB1-01175	California Polytechnic State University, San Luis Obispo	Intern	Graduate	
Blake Warbington	TB1-01175	California Polytechnic State University, San Luis Obispo	Intern	Graduate	
Gabrielle Winters	TB1-01175	California Polytechnic State University, San Luis Obispo	Intern	Graduate	
Kaitlyn Kirk	TB1-01175	California Polytechnic State University, San Luis Obispo	Intern	Graduate	
Kyla Thoele	TB1-01175	California Polytechnic State University, San Luis Obispo	Intern	Graduate	
Christopher Miracle	TB1-01175	California Polytechnic State University, San Luis Obispo	Intern	Undergraduate	
Thomas Harper	TB1-01175	California Polytechnic State University, San Luis Obispo	Intern	Undergraduate	
Julie Kim	TB1-01176	California State Polytechnic University, Pomona	Intern	Graduate	
Omar Snoussi	TB1-01176	California State Polytechnic University, Pomona	Intern	Graduate	
Xian Chen	TB1-01176	California State Polytechnic University, Pomona	Intern	Graduate	
Yuan Han Teh	TB1-01176	California State Polytechnic University, Pomona	Intern	Graduate	
Kanomi Sasaki-Capela	TB1-01176	California State Polytechnic University, Pomona	Intern	Undergraduate	
Matthew Parkhurst	TB1-01176	California State Polytechnic University, Pomona	Intern	Undergraduate	
Nadine Morgan	TB1-01176	California State Polytechnic University, Pomona	Intern	Undergraduate	
Raha Shirkhani	TB1-01176	California State Polytechnic University, Pomona	Intern	Undergraduate	
Revathiswari Tirughana-Sambadan	TB1-01176	California State Polytechnic University, Pomona	Intern	Undergraduate	
Chelsea Presbrey	TB1-01177	California State University, Channel Islands	Intern	Graduate	
Drew Shami	TB1-01177	California State University, Channel Islands	Intern	Graduate	
Francesca Boscolo	TB1-01177	California State University, Channel Islands	Intern	Graduate	
Jesus Olvera	TB1-01177	California State University, Channel Islands	Intern	Graduate	
Kartheek Dokka	TB1-01177	California State University, Channel Islands	Intern	Graduate	
Rohit Gehani	TB1-01177	California State University, Channel Islands	Intern	Graduate	
Sara Abdelrahman	TB1-01177	California State University, Channel Islands	Intern	Graduate	
Sidney Pehrson	TB1-01177	California State University, Channel Islands	Intern	Graduate	
Tyler Holt	TB1-01177	California State University, Channel Islands	Intern	Graduate	
Yuejia Wu	TB1-01177	California State University, Channel Islands	Intern	Graduate	
Arjuna Ugarte	TB1-01182	California State University, Long Beach	Intern	Graduate	
Carl Van Ness	TB1-01182	California State University, Long Beach	Intern	Graduate	
Denisse Moreno	TB1-01182	California State University, Long Beach	Intern	Graduate	
Eileen Do	TB1-01182	California State University, Long Beach	Intern	Graduate	
Estibaliz Alvarado	TB1-01182	California State University, Long Beach	Intern	Graduate	
Gayani Batugedara	TB1-01182	California State University, Long Beach	Intern	Graduate	
Harvey Perez	TB1-01182	California State University, Long Beach	Intern	Graduate	
Ricardo Ramirez	TB1-01182	California State University, Long Beach	Intern	Graduate	
Siranush Argalian	TB1-01182	California State University, Long Beach	Intern	Graduate	
Thach-Vu Ho	TB1-01182	California State University, Long Beach	Intern	Graduate	
Tien Vo	TB1-01182	California State University, Long Beach	Intern	Graduate	
Melissa Jones	TB1-01182	California State University, Long Beach	Intern	Undergraduate	
Alex Lindsay	TB1-01184	California State University, Sacramento	Intern	Graduate	
Brian Fury	TB1-01184	California State University, Sacramento	Intern	Graduate	
Elaina Kenney	TB1-01184	California State University, Sacramento	Intern	Graduate	

APPENDIX 26

Contact	Grant Number	Organization Name	Role	TBAppoint Type	TGAPPTTYPE
Heather Stewart	TB1-01184	California State University, Sacramento	Intern	Graduate	
Michelle Ohlson	TB1-01184	California State University, Sacramento	Intern	Graduate	
Nataly Lessa	TB1-01184	California State University, Sacramento	Intern	Graduate	
Ninnie Abrahamsson	TB1-01184	California State University, Sacramento	Intern	Graduate	
Ryan Lim	TB1-01184	California State University, Sacramento	Intern	Graduate	
Sean Roenspie	TB1-01184	California State University, Sacramento	Intern	Graduate	
Steve Tobin	TB1-01184	California State University, Sacramento	Intern	Graduate	
Brandon Mack	TB1-01186	California State University, San Marcos	Intern	Graduate	
Cari Cox	TB1-01186	California State University, San Marcos	Intern	Graduate	
Kristin Rauscher	TB1-01186	California State University, San Marcos	Intern	Graduate	
Naomi Guyette	TB1-01186	California State University, San Marcos	Intern	Graduate	
Nastaran Afari	TB1-01186	California State University, San Marcos	Intern	Graduate	
Shira Geller	TB1-01186	California State University, San Marcos	Intern	Graduate	
Susanne Montague	TB1-01186	California State University, San Marcos	Intern	Graduate	
Veronica Modesto	TB1-01186	California State University, San Marcos	Intern	Graduate	
Amanda Phillips	TB1-01186	California State University, San Marcos	Intern	Undergraduate	
Andrew Segina	TB1-01186	California State University, San Marcos	Intern	Undergraduate	
Irene Catalan	TB1-01186	California State University, San Marcos	Intern	Undergraduate	
Jordan Seldeen	TB1-01186	California State University, San Marcos	Intern	Undergraduate	
Krystal Sousley	TB1-01186	California State University, San Marcos	Intern	Undergraduate	
Lisa Johnson	TB1-01186	California State University, San Marcos	Intern	Undergraduate	
Mary Spinharney	TB1-01186	California State University, San Marcos	Intern	Undergraduate	
Sujata Godbole	TB1-01186	California State University, San Marcos	Intern	Undergraduate	
Terrence Messmer	TB1-01186	California State University, San Marcos	Intern	Undergraduate	
Victoria Glenn	TB1-01186	California State University, San Marcos	Intern	Undergraduate	
Wallace Wong	TB1-01186	California State University, San Marcos	Intern	Undergraduate	
Deborah Ann Lamm	TB1-01188	City College Of San Francisco	Intern	Graduate	
Kyounghee Seo	TB1-01188	City College Of San Francisco	Intern	Graduate	
Sahar Taheri	TB1-01188	City College Of San Francisco	Intern	Graduate	
Cuong Lieu	TB1-01188	City College Of San Francisco	Intern	Undergraduate	
Robert Keith Lodes	TB1-01188	City College Of San Francisco	Intern	Undergraduate	
Jennifer Hampton	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern	Graduate	
Julia Morgaine Freewoman	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern	Graduate	
Katherine Steeper	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern	Graduate	
Peter Din	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern	Graduate	
Robert Wagner	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern	Graduate	
Andrew Chin	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern	Undergraduate	
Elizabeth Gould	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern	Undergraduate	
Humberto Contreras	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern	Undergraduate	
Logan Linthicum	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern	Undergraduate	
Robin Martin	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern	Undergraduate	
Sara Downey	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern	Undergraduate	
Spencer Falor-Ward	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern	Undergraduate	
Timothy Laurent	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern	Undergraduate	
Daniel Hunter	TB1-01190	Humboldt State University Sponsored Programs Foundation	Intern		
Angelie Nguyen	TB1-01192	Pasadena City College	Intern	Graduate	
Anu Cherian	TB1-01192	Pasadena City College	Intern	Graduate	
Athena Arias	TB1-01192	Pasadena City College	Intern	Graduate	
Christopher Chung	TB1-01192	Pasadena City College	Intern	Graduate	
Doreen Rhee	TB1-01192	Pasadena City College	Intern	Graduate	
Ibrahim Hajjali	TB1-01192	Pasadena City College	Intern	Graduate	
Mimi Sadoshima	TB1-01192	Pasadena City College	Intern	Graduate	
Monica Lui	TB1-01192	Pasadena City College	Intern	Graduate	
Nandini Girish	TB1-01192	Pasadena City College	Intern	Graduate	
Piers Pravdo	TB1-01192	Pasadena City College	Intern	Graduate	
Ragini Pandita	TB1-01192	Pasadena City College	Intern	Graduate	
Rudy Tieu	TB1-01192	Pasadena City College	Intern	Graduate	
Rushil Shah	TB1-01192	Pasadena City College	Intern	Graduate	
Tassja Spindler	TB1-01192	Pasadena City College	Intern	Graduate	
Thu Zan Tun Thein	TB1-01192	Pasadena City College	Intern	Graduate	
Va Si	TB1-01192	Pasadena City College	Intern	Graduate	
Vincent Mateus	TB1-01192	Pasadena City College	Intern	Graduate	
Yeu-Fen Wu	TB1-01192	Pasadena City College	Intern	Graduate	
Yi-Jen Chen	TB1-01192	Pasadena City College	Intern	Graduate	
Russell Lund	TB1-01192	Pasadena City College	Intern	Undergraduate	
Christine Thornton	TB1-01193	San Diego State University	Intern	Graduate	
Melissa Carrillo	TB1-01193	San Diego State University	Intern	Graduate	
Trevor Gale	TB1-01193	San Diego State University	Intern	Graduate	
Aryan Zarrabi	TB1-01193	San Diego State University	Intern	Undergraduate	
Chelsea Kidwell	TB1-01193	San Diego State University	Intern	Undergraduate	
Chiara Leroy	TB1-01193	San Diego State University	Intern	Undergraduate	
Daniel Williams	TB1-01193	San Diego State University	Intern	Undergraduate	
Erica Campau	TB1-01193	San Diego State University	Intern	Undergraduate	
Jeff Bernitz	TB1-01193	San Diego State University	Intern	Undergraduate	
Kelley Fracchia	TB1-01193	San Diego State University	Intern	Undergraduate	
Lydia Rojas	TB1-01193	San Diego State University	Intern	Undergraduate	

APPENDIX 26

Contact	Grant Number	Organization Name	Role	TBAppoint Type	TGAPPTTYPE
Nicholas Glembotski	TB1-01193	San Diego State University	Intern	Undergraduate	
Nima Dolatabadi	TB1-01193	San Diego State University	Intern	Undergraduate	
Robert Lacharite	TB1-01193	San Diego State University	Intern	Undergraduate	
Sam Sances	TB1-01193	San Diego State University	Intern	Undergraduate	
Seema Patel	TB1-01193	San Diego State University	Intern	Undergraduate	
Shannon Waltz	TB1-01193	San Diego State University	Intern	Undergraduate	
Warren Plaisted	TB1-01193	San Diego State University	Intern	Undergraduate	
Yanelli Nunez	TB1-01193	San Diego State University	Intern	Undergraduate	
Ashley Sanders	TB1-01194	San Francisco State University	Intern	Graduate	
Chanawan (Joy) Chananukul	TB1-01194	San Francisco State University	Intern	Graduate	
Claudia Tomas Miranda	TB1-01194	San Francisco State University	Intern	Graduate	
David Newstrom	TB1-01194	San Francisco State University	Intern	Graduate	
Gaelen Smith	TB1-01194	San Francisco State University	Intern	Graduate	
Jason Liu	TB1-01194	San Francisco State University	Intern	Graduate	
Jerome Kahiapo	TB1-01194	San Francisco State University	Intern	Graduate	
KitMan Yeung	TB1-01194	San Francisco State University	Intern	Graduate	
Lidia Tekie	TB1-01194	San Francisco State University	Intern	Graduate	
Marisa Leal	TB1-01194	San Francisco State University	Intern	Graduate	
Masae Ahmann	TB1-01194	San Francisco State University	Intern	Graduate	
Nicole Haste	TB1-01194	San Francisco State University	Intern	Graduate	
Nicole Slusher	TB1-01194	San Francisco State University	Intern	Graduate	
Philbert Lee	TB1-01194	San Francisco State University	Intern	Graduate	
Rachel Nitta	TB1-01194	San Francisco State University	Intern	Graduate	
Saeed Azimi	TB1-01194	San Francisco State University	Intern	Graduate	
Sompob Cholsiripunlert	TB1-01194	San Francisco State University	Intern	Graduate	
Tatiane Russo Varys	TB1-01194	San Francisco State University	Intern	Graduate	
Vanessa Aguilera	TB1-01194	San Francisco State University	Intern	Graduate	
Vikash Jethwani	TB1-01194	San Francisco State University	Intern	Graduate	
Akshi Goyal	TB1-01195	San Jose State University	Intern	Graduate	
Anna Babakhanyhan	TB1-01195	San Jose State University	Intern	Graduate	
Anne Robaczewska	TB1-01195	San Jose State University	Intern	Graduate	
Anthony Parenti	TB1-01195	San Jose State University	Intern	Graduate	
Apexa Trivedi	TB1-01195	San Jose State University	Intern	Graduate	
Bhamini Purandare	TB1-01195	San Jose State University	Intern	Graduate	
Christopher Nye	TB1-01195	San Jose State University	Intern	Graduate	
Deepika Tewari	TB1-01195	San Jose State University	Intern	Graduate	
Erica Anderson	TB1-01195	San Jose State University	Intern	Graduate	
James Wright	TB1-01195	San Jose State University	Intern	Graduate	
Maja Zukic	TB1-01195	San Jose State University	Intern	Graduate	
Malini Vangipuram	TB1-01195	San Jose State University	Intern	Graduate	
Prachi Gujar	TB1-01195	San Jose State University	Intern	Graduate	
Shaun Teacher	TB1-01195	San Jose State University	Intern	Graduate	
Shelly Nigam	TB1-01195	San Jose State University	Intern	Graduate	
Shifteh Iranmanesh	TB1-01195	San Jose State University	Intern	Graduate	
Sylvia Do	TB1-01195	San Jose State University	Intern	Graduate	
Takele Teklemariam	TB1-01195	San Jose State University	Intern	Graduate	
Yuanying Huang	TB1-01195	San Jose State University	Intern	Graduate	
Benjamin Parcher	TB1-01197	Berkeley City College	Intern	Graduate	
Ranjani Lakshmin	TB1-01197	Berkeley City College	Intern	Graduate	
Robin Wong	TB1-01197	Berkeley City College	Intern	Graduate	
Yingzhan Li	TB1-01197	Berkeley City College	Intern	Graduate	
Alexandria Lee-Goldman	TB1-01197	Berkeley City College	Intern	Undergraduate	
Ashley Ginbey	TB1-01186	California State University, San Marcos	Intern	Undergraduate	
Dr. David Brafman	RB1-01406	University of California, San Diego	Postdoctoral		
Dr. Jason Nathanson	RB1-01413	University of California, San Diego	Postdoctoral		
Dr. Kasey Hutt	RB1-01413	University of California, San Diego	Postdoctoral		
Dr. Se Jin Yoon	RC1-00100-1	Stanford University	Postdoctoral		
Yuquiong Pan	RC1-00100-1	Stanford University	Postdoctoral		
Jian Feng	RC1-00111-1	University of California, Los Angeles	Postdoctoral		
Jin Zhong	RC1-00111-1	University of California, Los Angeles	Postdoctoral		
Tamar Dvash	RC1-00111-1	University of California, Los Angeles	Postdoctoral		
Zhigang Xue	RC1-00111-1	University of California, Los Angeles	Postdoctoral		
Dr. Kristen Brennand	RC1-00115-1	The Salk Institute for Biological Studies	Postdoctoral		
Kunyoo Shin	RC1-00119-1	Stanford University	Postdoctoral		
Jiashing Yu	RC1-00124-1	University of California, San Francisco	Postdoctoral		
Eun-Gyun Cho	RC1-00125-1	Sanford-Burnham Medical Research Institute	Postdoctoral		
Hyojin Lee	RC1-00125-1	Sanford-Burnham Medical Research Institute	Postdoctoral		
Jimmy Elliott	RC1-00125-1	Sanford-Burnham Medical Research Institute	Postdoctoral		
Dr. Scott R. McKercher	RC1-00125-1	Sanford-Burnham Medical Research Institute	Postdoctoral		
Jan Strnadel	RC1-00131-1	University of California, San Diego	Postdoctoral		
Jan Struckelova	RC1-00131-1	University of California, San Diego	Postdoctoral		
Derk ten Berge	RC1-00133-1	Stanford University	Postdoctoral		
Timothy Blauwkamp	RC1-00133-1	Stanford University	Postdoctoral		
Yuquiong Pan	RC1-00133-1	Stanford University	Postdoctoral		
Harish Babu	RC1-00134-1	Stanford University	Postdoctoral		
Makoto Ideguchi	RC1-00134-1	Stanford University	Postdoctoral		

APPENDIX 26

Contact	Grant Number	Organization Name	Role	TBAppoint Type	TGAPPTTYPE
Guangnan Li	RC1-00135-1	University of California, San Francisco	Postdoctoral		
Seonok Lee	RC1-00135-1	University of California, San Francisco	Postdoctoral		
Youngshik Choe	RC1-00135-1	University of California, San Francisco	Postdoctoral		
Fanny Polesso	RC1-00137-1	Stanford University	Postdoctoral		
Dr. James Byrne	RC1-00137-1	Stanford University	Postdoctoral		
Dr. Jing Li	RC1-00137-1	Stanford University	Postdoctoral		
Sohyun Lee McElroy	RC1-00137-1	Stanford University	Postdoctoral		
Sonya Schuh-Huerta	RC1-00137-1	Stanford University	Postdoctoral		
Dr. Kathryn N. Ivey	RC1-00142-1	The J. David Gladstone Institutes	Postdoctoral		
Dr. Cynthia A. Batchelder	RC1-00144-1	University of California, Davis	Postdoctoral		
Sun-Ku Chung	RC1-00148-1	University of California, San Diego	Postdoctoral		
Zhili Rong	RC1-00148-1	University of California, San Diego	Postdoctoral		
Margaret Coutts	RC1-00345-1	University of California, Irvine	Postdoctoral		
David Hansen	RC1-00346-1	University of California, San Francisco	Postdoctoral		
Jasmine Ying-Jiun Chen	RC1-00346-1	University of California, San Francisco	Postdoctoral		
Joy Sebe	RC1-00346-1	University of California, San Francisco	Postdoctoral		
Kim Insil	RC1-00353-1	University of California, Irvine	Postdoctoral		
Mark Sharpley	RC1-00353-1	University of California, Irvine	Postdoctoral		
Wei Fan	RC1-00353-1	University of California, Irvine	Postdoctoral		
Matt Inlay	RC1-00354-1	Stanford University	Postdoctoral		
Dr. Micha Drukker	RC1-00354-1	Stanford University	Postdoctoral		
Reza Ardehali	RC1-00354-1	Stanford University	Postdoctoral		
Thomas Serwold	RC1-00354-1	Stanford University	Postdoctoral		
Aliye Sarmasik	RN1-00540-1	University of California, Santa Cruz	Postdoctoral		
Dr. Chao Zhang	RN2-00945-1	University of California, San Diego	Postdoctoral		
Dr. David Madden	RS1-00163-1	Buck Institute for Age Research	Postdoctoral		
Dr. Masakazu Kamata	RS1-00172-1	University of California, Los Angeles	Postdoctoral		
Sanggu Kim	RS1-00172-1	University of California, Los Angeles	Postdoctoral		
Concepcion Esteban	RS1-00174-1	The Salk Institute for Biological Studies	Postdoctoral		
Elvira Martin	RS1-00174-1	The Salk Institute for Biological Studies	Postdoctoral		
Mr. George Allendorph	RS1-00174-1	The Salk Institute for Biological Studies	Postdoctoral		
Yohannes Ghebremariam	RS1-00183-1	Stanford University	Postdoctoral		
Christina Chatzi	RS1-00193-1	Sanford-Burnham Medical Research Institute	Postdoctoral		
Li Cui	RS1-00198-1	University of California, San Diego	Postdoctoral		
Maretoshi Hirai	RS1-00198-1	University of California, San Diego	Postdoctoral		
Michico Muraki	RS1-00198-1	University of California, San Diego	Postdoctoral		
Ralf Dirschiger	RS1-00198-1	University of California, San Diego	Postdoctoral		
Dr. Dimitrios Vatakis	RS1-00203-1	University of California, Los Angeles	Postdoctoral		
Jieun Kim	RS1-00205-1	University of California, San Diego	Postdoctoral		
Dr. Karl H. Willert	RS1-00205-1	University of California, San Diego	Postdoctoral		
Stephanie Otto	RS1-00205-1	University of California, San Diego	Postdoctoral		
Dr. Zilong Qiu	RS1-00205-1	University of California, San Diego	Postdoctoral		
Chengzhong Wang	RS1-00215-1	University of California, San Francisco	Postdoctoral		
Hui Chen	RS1-00215-1	University of California, San Francisco	Postdoctoral		
Julio Ramirez	RS1-00215-1	University of California, San Francisco	Postdoctoral		
Dan Hong Zhu	RS1-00222-1	University of Southern California	Postdoctoral		
Jessica Rusert	RS1-00228-1	University of California, San Diego	Postdoctoral		
Kim-Hien Dao	RS1-00228-1	University of California, San Diego	Postdoctoral		
Ning Sun	RS1-00242-1	Stanford University	Postdoctoral		
Dr. Akifumi Ootani	RS1-00243-1	Stanford University	Postdoctoral		
Lee Xingnan	RS1-00243-1	Stanford University	Postdoctoral		
Dr. Jingyu Li	RS1-00245-1	University of California, Los Angeles	Postdoctoral		
Kristine Karla Freude	RS1-00247-1	University of California, Irvine	Postdoctoral		
Dr. Mathew M. Blurton-Jones	RS1-00247-1	University of California, Irvine	Postdoctoral		
Cornelia von Levetzow	RS1-00249-1	Children's Hospital of Los Angeles	Postdoctoral		
Craig Semerad	RS1-00280-1	University of California, San Diego	Postdoctoral		
Suzanna Diel	RS1-00280-1	University of California, San Diego	Postdoctoral		
Dr. Ivan Khvorostov	RS1-00313-1	University of California, Los Angeles	Postdoctoral		
Dr. Brile Chung	RS1-00321-1	Stanford University	Postdoctoral		
Dr. Dullei Min	RS1-00321-1	Stanford University	Postdoctoral		
Li Zonjgin	RS1-00322-1	Stanford University	Postdoctoral		
Ning Sun	RS1-00322-1	Stanford University	Postdoctoral		
Rutger Swijnenburg	RS1-00322-1	Stanford University	Postdoctoral		
Ruchi Bajpai	RS1-00323-1	Stanford University	Postdoctoral		
Jaehoon Chung	RS1-00326-1	Stanford University	Postdoctoral		
Jane Pappas	RS1-00326-1	Stanford University	Postdoctoral		
Olga Shcherbakova	RS1-00326-1	Stanford University	Postdoctoral		
Hongjun Zhang	RS1-00327-1	University of Southern California	Postdoctoral		
Dr. Dong-Hyun Lee, Ph.D.	RS1-00428-1	Beckman Research Institute Of The City Of Hope	Postdoctoral		
Dr. Li Luo, Ph.D.	RS1-00428-1	Beckman Research Institute Of The City Of Hope	Postdoctoral		
Christian Frantz	RS1-00449-1	University of California, San Francisco	Postdoctoral		
Jose Lopez	RS1-00449-1	University of California, San Francisco	Postdoctoral		
Sylvia Espejel Carbajal	RS1-00452-1	University of California, San Francisco	Postdoctoral		
Celine Delaloy	RS1-00462-1	The J. David Gladstone Institutes	Postdoctoral		
Ms. Jennifer J. Brady	RB1-01292	Stanford University	Trainee		
Ms. Hoangkim Nguyen	RB1-01328	University of California, Los Angeles	Trainee		

APPENDIX 26

Contact	Grant Number	Organization Name	Role	TBAppoint Type	TGAPPTTYPE
Dr. Rana Abou-Khalil	RB1-01328	University of California, Los Angeles	Trainee		
Ms. Katrina L. Adams	RB1-01367	University of California, Los Angeles	Trainee		
Ms. Crystal Sengstaken	RB1-01372	University of Southern California	Trainee		
Dr. Jun Wu	RB1-01372	University of Southern California	Trainee		
Dr. Han Qin	RB1-01385	Stanford University	Trainee		
Dr. Laura Gorges	RB1-01385	Stanford University	Trainee		
Dr. Geng Wang	RB1-01397	University of California, Los Angeles	Trainee		
Dr. Ivan Khvorostov	RB1-01397	University of California, Los Angeles	Trainee		
Mr. Jin Zhang	RB1-01397	University of California, Los Angeles	Trainee		
Mr. Wei-Siang Liau	RB1-01397	University of California, Los Angeles	Trainee		
Dr. Lin Cao	RB1-01417	University of California, Davis	Trainee		
Amanda Tencza	RB2-01494	University of California, San Francisco	Trainee		
Jessica Orr	RB2-01494	University of California, San Francisco	Trainee		
Margaret Cooke	RB2-01494	University of California, San Francisco	Trainee		
Dr. Luis Batista	RB2-01497	Stanford University	Trainee		
Dr. Dadi Jiang	RB2-01498	Stanford University	Trainee		
Dr. Daniela Kenzelman-Broz	RB2-01498	Stanford University	Trainee		
Ms. Chelsea Gloria Gordon	RB2-01500	University of California, Berkeley	Trainee		
Ms. Lissette Andres	RB2-01500	University of California, Berkeley	Trainee		
Dr. Michael Scott Boyce	RB2-01500	University of California, Berkeley	Trainee		
Mr. Anthony Linares	RB2-01502	University of California, Los Angeles	Trainee		
Ms. Areum Han	RB2-01502	University of California, Los Angeles	Trainee		
Dr. Niroshika M Keppetipola	RB2-01502	University of California, Los Angeles	Trainee		
Dr. Sika Zheng	RB2-01502	University of California, Los Angeles	Trainee		
Angel Leu	RB2-01504	University of California, San Diego	Trainee		
Dr. Maheswaran Mani	RB2-01507	Stanford University	Trainee		
Dr. Shivkumar Venkatasubrahmanyam	RB2-01507	Stanford University	Trainee		
Dr. Changsung Kim	RB2-01512	Sanford-Burnham Medical Research Institute	Trainee		
Dr. Maryam Majdi	RB2-01512	Sanford-Burnham Medical Research Institute	Trainee		
Dr. Tongyin Yi	RB2-01512	Sanford-Burnham Medical Research Institute	Trainee		
Dr. Kim Ly	RB2-01514	University of California, San Diego	Trainee		
Dr. Kunfu Ouyang	RB2-01514	University of California, San Diego	Trainee		
Dr. Tom Moore-Morris	RB2-01514	University of California, San Diego	Trainee		
Dr. Francisco J. Morera	RB2-01523	University of California, Los Angeles	Trainee		
Dr. Lori Hartnett	RB2-01523	University of California, Los Angeles	Trainee		
Ms. Peggy Vorwald	RB2-01523	University of California, Los Angeles	Trainee		
Dr. Philipp Vick	RB2-01523	University of California, Los Angeles	Trainee		
Dr. Masayo Yumoto	RB2-01526	University of California, San Francisco	Trainee		
Dr. Ningzhe Zhang	RB2-01527	Buck Institute for Age Research	Trainee		
Dr. Theodora Papanikolaou	RB2-01527	Buck Institute for Age Research	Trainee		
Dr. Jamison Nourse	RB2-01534	University of California, Irvine	Trainee		
Mr. Jente Lu	RB2-01534	University of California, Irvine	Trainee		
Noelle Huskey	RB2-01540	University of California, San Francisco	Trainee		
Elisabetta Soragni	RB2-01542	Scripps Research Institute	Trainee		
Jintang Du	RB2-01542	Scripps Research Institute	Trainee		
Dr. Ian Lian	RB2-01547	University of California, San Diego	Trainee		
Ms. Karen Tumaneng	RB2-01547	University of California, San Diego	Trainee		
Peter Shepard	RB2-01550	University of California, Irvine	Trainee		
Dr. Shu-Ning Hsu	RB2-01550	University of California, Irvine	Trainee		
Ms. Tara Crabb	RB2-01550	University of California, Irvine	Trainee		
Dr. Yuan Cheng	RB2-01553	Stanford University	Trainee		
Dr. Lincoln Nadauld	RB2-01566	Stanford University	Trainee		
Luis Alberto Chia	RB2-01566	Stanford University	Trainee		
Dr. Jackelyn Alva	RB2-01571	University of California, Los Angeles	Trainee		
Ms. Karina Palomares	RB2-01571	University of California, Los Angeles	Trainee		
Dr. Saki Shimizu	RB2-01571	University of California, Los Angeles	Trainee		
Dr. Chao Liu	RB2-01580	Stanford University	Trainee		
Dr. Song Liu	RB2-01580	Stanford University	Trainee		
Dr. Stephan Gehrke	RB2-01580	Stanford University	Trainee		
Dr. Suzanne Angeli	RB2-01580	Stanford University	Trainee		
Dr. Wendou Yu	RB2-01580	Stanford University	Trainee		
Sabrina Spencer	RB2-01581	Stanford University	Trainee		
Samuele Marro	RB2-01581	Stanford University	Trainee		
Elinore Mercer	RB2-01585	University of California, San Diego	Trainee		
Kasoku Miyasaki	RB2-01585	University of California, San Diego	Trainee		
Andrew Harmon	RB2-01588	University of California, Los Angeles	Trainee		
Anna Beaudin	RB2-01588	University of California, Los Angeles	Trainee		
Eli R Zunder	RB2-01592	Stanford University	Trainee		
Samuele Marro	RB2-01592	Stanford University	Trainee		
Sean Bendall	RB2-01592	Stanford University	Trainee		
Dr. Brian Biehs	RB2-01597	University of California, San Francisco	Trainee		
Lorenzo Giordani	RB2-01598	Sanford-Burnham Medical Research Institute	Trainee		
Luca Cignolo	RB2-01598	Sanford-Burnham Medical Research Institute	Trainee		
Sonia Albini	RB2-01598	Sanford-Burnham Medical Research Institute	Trainee		
Sonia Forcales	RB2-01598	Sanford-Burnham Medical Research Institute	Trainee		
Mr. Aaron Prussin	RB2-01600	University of California, Santa Barbara	Trainee		

APPENDIX 26

Contact	Grant Number	Organization Name	Role	TBAppoint Type	TGAPPTTYPE
Celeste Holz	RB2-01600	University of California, Santa Barbara	Trainee		
Deyra Rodgriquez	RB2-01600	University of California, Santa Barbara	Trainee		
Cory R. Nicholas	RB2-01602	University of California, San Francisco	Trainee		
Daniel Vogt	RB2-01602	University of California, San Francisco	Trainee		
Se Hoon Choi	RB2-01602	University of California, San Francisco	Trainee		
Dr. Hua Su	RB2-01603	University of California, Riverside	Trainee		
Dr. Fabian Zanella de Sa	RB2-01608	University of California, San Diego	Trainee		
Dr. Valeria Mezzano	RB2-01608	University of California, San Diego	Trainee		
Mr. Justin Langerman	RB2-01609	University of California, Los Angeles	Trainee		
Mr. Miguel Edwards	RB2-01609	University of California, Los Angeles	Trainee		
Ms. Kimberlee Fischer	RB2-01615	San Diego State University	Trainee		
Dr. Natalie Gude	RB2-01615	San Diego State University	Trainee		
Ms. Shabana Din	RB2-01615	San Diego State University	Trainee		
Dr. Dinorah Friedmann-Morvinski	RB2-01622	The Salk Institute for Biological Studies	Trainee		
Dr. Yasushi Soda	RB2-01622	The Salk Institute for Biological Studies	Trainee		
Mr. John J Yang	RB2-01627	University of California, Irvine	Trainee		
Mr. Robert Sierra	RB2-01629	University of California, Irvine	Trainee		
Dr. Shivkumar Venkatasubrahmanyam	RB2-01630	Stanford University	Trainee		
Dr. Takeshi Fukuhara	RB2-01637	Palo Alto Institute for Research and Education, Inc.	Trainee		
Mr. Athurva Gore	RB2-01646	University of California, San Diego	Trainee		
Dr. Hsin-I Chiang	RB2-01646	University of California, San Diego	Trainee		
Dr. Jie Deng	RB2-01646	University of California, San Diego	Trainee		
Mr. Chuba Oyola	RC1-00100-1	Stanford University	Trainee		
Mr. Si Wan Kim	RC1-00100-1	Stanford University	Trainee		
Dr. Frank King	RC1-00104-1	University of California, San Francisco	Trainee		
Ms. Helen Hwang	RC1-00104-1	University of California, San Francisco	Trainee		
Dr. Gautam Dravid	RC1-00108-1.1	Children's Hospital of Los Angeles	Trainee		
Duncan Lieuw	RC1-00110-1	University of California, Irvine	Trainee		
Kristi Hohenstein	RC1-00110-1	University of California, Irvine	Trainee		
Raymond Wong	RC1-00110-1	University of California, Irvine	Trainee		
Yin Shen	RC1-00111-1	University of California, Los Angeles	Trainee		
Mr. Zhicheng Ma	RC1-00111-1	University of California, Los Angeles	Trainee		
Dr. Tal Imbar	RC1-00113-1	University of California, San Francisco	Trainee		
Dr. Ahmet M. Denli	RC1-00115-1	The Salk Institute for Biological Studies	Trainee		
Professor Alysson Muotri	RC1-00115-1	The Salk Institute for Biological Studies	Trainee		
Dr. Christian Carson	RC1-00115-1	The Salk Institute for Biological Studies	Trainee		
Dr. Gene Yeo	RC1-00115-1	The Salk Institute for Biological Studies	Trainee		
Ms. Nicole G. Coufal	RC1-00115-1	The Salk Institute for Biological Studies	Trainee		
Ms. Emily Davis	RC1-00116-1	University of California, San Diego	Trainee		
Ms. Jessica Novak	RC1-00116-1	University of California, San Diego	Trainee		
Mr. Mason Israel	RC1-00116-1	University of California, San Diego	Trainee		
Ms. Rhiannon L. Nolan	RC1-00116-1	University of California, San Diego	Trainee		
Dr. Shauna Yuan	RC1-00116-1	University of California, San Diego	Trainee		
Dr. Tomas Falzone	RC1-00116-1	University of California, San Diego	Trainee		
Dr. Zhigang Xu	RC1-00119-1	Stanford University	Trainee		
Dr. Christian Heiss	RC1-00124-1	University of California, San Francisco	Trainee		
Dr. Atsushi Nanohara	RC1-00131-1	University of California, San Diego	Trainee		
Dr. Pei Wang	RC1-00133-1	Stanford University	Trainee		
Dr. Takuya Sugiyama	RC1-00133-1	Stanford University	Trainee		
Albrecht Stroh	RC1-00134-1	Stanford University	Trainee		
Dr. Katrin L Schrenk-Seimens	RC1-00134-1	Stanford University	Trainee		
Dr. Michelle L Monje	RC1-00134-1	Stanford University	Trainee		
Dr. Pamela Carpentier	RC1-00134-1	Stanford University	Trainee		
Dr. Ursula Haditsch	RC1-00134-1	Stanford University	Trainee		
Dr. Christine Pozniak	RC1-00135-1	University of California, San Francisco	Trainee		
Dr. Marcus D. Schonemann	RC1-00135-1	University of California, San Francisco	Trainee		
Dr. Connie Wong	RC1-00137-1	Stanford University	Trainee		
Dr. Shawn Chavez	RC1-00137-1	Stanford University	Trainee		
Dr. Chulan Kwon	RC1-00142-1	The J. David Gladstone Institutes	Trainee		
Dr. Jason Fish	RC1-00142-1	The J. David Gladstone Institutes	Trainee		
Dr. Li Qian	RC1-00142-1	The J. David Gladstone Institutes	Trainee		
Ho Seok Song	RC1-00148-1	University of California, San Diego	Trainee		
Jin Liu	RC1-00148-1	University of California, San Diego	Trainee		
Li Jin Feng	RC1-00148-1	University of California, San Diego	Trainee		
Tongxiang Lin	RC1-00148-1	University of California, San Diego	Trainee		
Dr. Aparna Subramanian	RC1-00149-1	University of California, Los Angeles	Trainee		
Miss Sylvie Inkindi	RC1-00149-1	University of California, Los Angeles	Trainee		
Dr. James J Norman	RC1-00151-1	Stanford University	Trainee		
Ms. Jennifer T. Blundo	RC1-00151-1	Stanford University	Trainee		
Dr. Mei Huang	RC1-00151-1	Stanford University	Trainee		
Dr. Oscar J. Abilez	RC1-00151-1	Stanford University	Trainee		
Dr. Gabriel Nistor	RC1-00345-1	University of California, Irvine	Trainee		
Ms. Maya Hatch	RC1-00345-1	University of California, Irvine	Trainee		
Dr. Vicky Sung	RC1-00345-1	University of California, Irvine	Trainee		
Dr. Corey Harwell	RC1-00346-1	University of California, San Francisco	Trainee		
Dr. Dorothy Jones-Davis	RC1-00346-1	University of California, San Francisco	Trainee		

APPENDIX 26

Contact	Grant Number	Organization Name	Role	TBAppoint Type	TGAPPTTYPE
Dr. Leon Huang	RC1-00347-1	University of California, San Francisco	Trainee		
Dr. Robert J. Lebbink	RC1-00347-1	University of California, San Francisco	Trainee		
Dr. Jason Poole	RC1-00353-1	University of California, Irvine	Trainee		
Dr. Olga Derbeneva	RC1-00353-1	University of California, Irvine	Trainee		
Ms. Christine Jung	RC1-00359-1	University of California, Davis	Trainee		
Dr. Se Jin Yoon	RL1-00630-1	Stanford University	Trainee		
Dr. Annahita Keravala	RL1-00634-1	Stanford University	Trainee		
Dr. Christopher L. Chavez	RL1-00634-1	Stanford University	Trainee		
Ms. Lauren E. Woodard	RL1-00634-1	Stanford University	Trainee		
Ms. Hengameh K Zahed	RL1-00639-1	The J. David Gladstone Institutes	Trainee		
Dr. Jennifer K Ng	RL1-00639-1	The J. David Gladstone Institutes	Trainee		
Dr. Katriina Aalto-Set	RL1-00639-1	The J. David Gladstone Institutes	Trainee		
Dr. Kiichiro Tomoda	RL1-00639-1	The J. David Gladstone Institutes	Trainee		
Mr. Matthew Spindler	RL1-00639-1	The J. David Gladstone Institutes	Trainee		
Dr. Vasanth Z Vedantham	RL1-00639-1	The J. David Gladstone Institutes	Trainee		
Dr. Jem Efe	RL1-00642-1	Scripps Research Institute	Trainee		
Dr. Rajesh Ambasudhan	RL1-00642-1	Scripps Research Institute	Trainee		
Dr. Tongxiang Lin	RL1-00642-1	Scripps Research Institute	Trainee		
Dr. Wenlin Li	RL1-00642-1	Scripps Research Institute	Trainee		
Dr. Naohisa Yoshioka	RL1-00644-1	University of California, San Diego	Trainee		
Dr. Tomomi Kogiso	RL1-00644-1	University of California, San Diego	Trainee		
Dr. Alysson Renato Muotri	RL1-00649-1	The Salk Institute for Biological Studies	Trainee		
Dr. Gerald M. Pao	RL1-00649-1	The Salk Institute for Biological Studies	Trainee		
Dr. Karl-Dimiter Bissig	RL1-00649-1	The Salk Institute for Biological Studies	Trainee		
Dr. Kristen Brennand	RL1-00649-1	The Salk Institute for Biological Studies	Trainee		
Dr. Maria Carolina Marchetto	RL1-00649-1	The Salk Institute for Biological Studies	Trainee		
Dr. Oded Singer	RL1-00649-1	The Salk Institute for Biological Studies	Trainee		
Ms. Karen Ring	RL1-00650-1	The J. David Gladstone Institutes	Trainee		
Dr. Deepa Subramanyam	RL1-00660-1	University of California, San Francisco	Trainee		
Dr. Ji Wang	RL1-00660-1	University of California, San Francisco	Trainee		
Ms. Kathryn Blaschke	RL1-00669-1	University of California, San Francisco	Trainee		
Dr. Yuki Ohi	RL1-00669-1	University of California, San Francisco	Trainee		
Dr. Connie Wong	RL1-00670-1	Stanford University	Trainee		
Dr. James Byrne	RL1-00670-1	Stanford University	Trainee		
Dr. Micha Drukker	RL1-00670-1	Stanford University	Trainee		
Ms. Nina Kossack	RL1-00670-1	Stanford University	Trainee		
Dr. Danling Wang	RL1-00682-1	Sanford-Burnham Medical Research Institute	Trainee		
Dr. Haiyan Fang	RL1-00682-1	Sanford-Burnham Medical Research Institute	Trainee		
Dr. Rachel Hill	RL1-00682-1	Sanford-Burnham Medical Research Institute	Trainee		
Dr. Tingxia Guo	RM1-01703	University of California, San Francisco	Trainee		
Dr. Todd M. Brusko	RM1-01703	University of California, San Francisco	Trainee		
Dr. Magali Noval Rivas	RM1-01707	University of California, Los Angeles	Trainee		
Dr. Antonio Mueller	RM1-01710	Palo Alto Institute for Research and Education, Inc.	Trainee		
Dr. Gulsah Altun	RM1-01717	Scripps Research Institute	Trainee		
Dr. Jason Weinger	RM1-01717	Scripps Research Institute	Trainee		
Maite Alvarez	RM1-01724	University of California, Davis	Trainee		
Mr. Andrew Stephen Lee	RM1-01725	Stanford University	Trainee		
Dr. Dennis Brian Leveson-Gower	RM1-01725	Stanford University	Trainee		
Dr. Emanuela Ionela Sega	RM1-01725	Stanford University	Trainee		
Dr. Abdur Rub	RM1-01729	La Jolla Institute for Allergy and Immunology	Trainee		
Dr. Kian Peng Koh	RM1-01729	La Jolla Institute for Allergy and Immunology	Trainee		
William Pastor	RM1-01729	La Jolla Institute for Allergy and Immunology	Trainee		
Dr. Lucas H Horan	RM1-01730	University of California, Berkeley	Trainee		
Ms. Nataliya Shifrin	RM1-01730	University of California, Berkeley	Trainee		
Dr. Heather Melichar	RM1-01732	University of California, Berkeley	Trainee		
Ms. Agnieszka Dorota Czechowicz	RM1-01733	Stanford University	Trainee		
Ms. Agnieszka Dorota Czechowicz	RM1-01733	Stanford University	Trainee		
Mr. Andrew Stephen Lee	RM1-01739	Stanford University	Trainee		
Dr. Dullei Min	RM1-01739	Stanford University	Trainee		
Dr. Valarie M Renault	RN1-00527-1	Stanford University	Trainee		
Ms. Victoria Antonina Rafalski	RN1-00527-1	Stanford University	Trainee		
Dr. John L. Rinn	RN1-00529-1	Stanford University	Trainee		
Mr. Jordon K. Wang	RN1-00529-1	Stanford University	Trainee		
Kevin C. Wang	RN1-00529-1	Stanford University	Trainee		
Miao-Chih Tsai	RN1-00529-1	Stanford University	Trainee		
Dr. Rajnish A Gupta	RN1-00529-1	Stanford University	Trainee		
Tiffany Hung	RN1-00529-1	Stanford University	Trainee		
Han Ly	RN1-00530-1	University of California, Santa Cruz	Trainee		
Dr. Hui Yang	RN1-00530-1	University of California, Santa Cruz	Trainee		
Matthew Eckler	RN1-00530-1	University of California, Santa Cruz	Trainee		
Mr. Will McKenna	RN1-00530-1	University of California, Santa Cruz	Trainee		
Haroldo Souza Silva	RN1-00532-1	University of California, Berkeley	Trainee		
Morgan Erik Carlson	RN1-00532-1	University of California, Berkeley	Trainee		
Charu Ramarkrishnan	RN1-00535-1	Stanford University	Trainee		
Hsing-chen Tsai	RN1-00535-1	Stanford University	Trainee		
Dr. Kim Thompson	RN1-00535-1	Stanford University	Trainee		

APPENDIX 26

Contact	Grant Number	Organization Name	Role	TBAppoint Type	TGAPPTTYPE
Leslie Meltzer	RN1-00535-1	Stanford University	Trainee		
Raagq Airan	RN1-00535-1	Stanford University	Trainee		
Viviana Gradinaru	RN1-00535-1	Stanford University	Trainee		
Dr. Caroline Desponts	RN1-00536-1	Scripps Research Institute	Trainee		
Dr. Wan-Guo Wei	RN1-00536-1	Scripps Research Institute	Trainee		
Dr. Wenlin Li	RN1-00536-1	Scripps Research Institute	Trainee		
Dr. Yan Shi	RN1-00536-1	Scripps Research Institute	Trainee		
Dr. Yue Xu	RN1-00536-1	Scripps Research Institute	Trainee		
Arash Adami	RN1-00538-1.1	University of California, Riverside	Trainee		
Arvin Tahami	RN1-00538-1.1	University of California, Riverside	Trainee		
Darice McClelland	RN1-00538-1.1	University of California, Riverside	Trainee		
Veronica Gusti	RN1-00538-1.1	University of California, Riverside	Trainee		
Garrett C. Heffner	RN1-00540-1	University of California, Santa Cruz	Trainee		
Martina Koeva	RN1-00540-1	University of California, Santa Cruz	Trainee		
Ms. Chihunt Wong	RN1-00544-1	The Salk Institute for Biological Studies	Trainee		
Severine Landais	RN1-00544-1	The Salk Institute for Biological Studies	Trainee		
Dr. Bing Li	RN1-00550-1	University of California, Los Angeles	Trainee		
Dr. Jingyu Li	RN1-00550-1	University of California, Los Angeles	Trainee		
Matthew McBrian	RN1-00550-1	University of California, Los Angeles	Trainee		
Dr. Omar Habeeb	RN1-00550-1	University of California, Los Angeles	Trainee		
Dr. Roberto Ferrari	RN1-00550-1	University of California, Los Angeles	Trainee		
Mr. Corey Cain	RN1-00554-1	University of California, Merced	Trainee		
Mr. David Gravano	RN1-00554-1	University of California, Merced	Trainee		
Heather Thompson	RN1-00554-1	University of California, Merced	Trainee		
Benjamin Joseph Van Handel	RN1-00557-1	University of California, Los Angeles	Trainee		
Mr. Christos Gekas	RN1-00557-1	University of California, Los Angeles	Trainee		
Ms. Katrin Elisabeth Rhodes	RN1-00557-1	University of California, Los Angeles	Trainee		
Laurraine Gereige	RN1-00557-1	University of California, Los Angeles	Trainee		
Dr. Mattias Magnusson	RN1-00557-1	University of California, Los Angeles	Trainee		
Dr. Roberto Ferrari	RN1-00557-1	University of California, Los Angeles	Trainee		
Bin Li	RN1-00561-1	University of California, Davis	Trainee		
Dr. Hong-yong Zhang	RN1-00561-1	University of California, Davis	Trainee		
Li Huang	RN1-00562-1	University of Southern California	Trainee		
Liguo Chen	RN1-00562-1	University of Southern California	Trainee		
Markus Plate	RN1-00562-1	University of Southern California	Trainee		
Dr. Penelope Thomas	RN1-00562-1	University of Southern California	Trainee		
Dr. Sina Tavakoli	RN1-00562-1	University of Southern California	Trainee		
Yuchang Li	RN1-00562-1	University of Southern California	Trainee		
Mr. Jason Tchieu	RN1-00564-1	University of California, Los Angeles	Trainee		
Mark Chin	RN1-00564-1	University of California, Los Angeles	Trainee		
Matthew Denholtz	RN1-00564-1	University of California, Los Angeles	Trainee		
Mike Mason	RN1-00564-1	University of California, Los Angeles	Trainee		
Dr. Rupa Sridharan	RN1-00564-1	University of California, Los Angeles	Trainee		
Mr. Carlos Huang	RN1-00566-1	University of California, Irvine	Trainee		
Mr. Cyrus Ghajar	RN1-00566-1	University of California, Irvine	Trainee		
Mrs. Ekaterina Kniazeva	RN1-00566-1	University of California, Irvine	Trainee		
Mr. Albert D. Kim	RN1-00575-1	University of California, San Diego	Trainee		
Jennifer Cisson	RN1-00575-1	University of California, San Diego	Trainee		
Dr. Julien Y. Bertrand	RN1-00575-1	University of California, San Diego	Trainee		
Dr. Wilson K. Clements	RN1-00575-1	University of California, San Diego	Trainee		
Bin Shen	RN1-00577-1	The Salk Institute for Biological Studies	Trainee		
David Johnson	RN1-00577-1	The Salk Institute for Biological Studies	Trainee		
Jeffrey Takimoto	RN1-00577-1	The Salk Institute for Biological Studies	Trainee		
Wenyuan Wang	RN1-00577-1	The Salk Institute for Biological Studies	Trainee		
Zheng Xiang	RN1-00577-1	The Salk Institute for Biological Studies	Trainee		
Dr. Jamy Peng	RN1-00579-1	Stanford University	Trainee		
Dr. Ziyang Ma	RN1-00579-1	Stanford University	Trainee		
Jennifer Hazen	RN1-00584-1	Scripps Research Institute	Trainee		
Ms. Kiely Martinez	RN1-00584-1	Scripps Research Institute	Trainee		
Dr. Bartosz Chmielowski	RN2-00902-1	University of California, Los Angeles	Trainee		
Mr. Jeffrey M Alexander	RN2-00903-1	The J. David Gladstone Institutes	Trainee		
Dr. Kiyonori Togi	RN2-00903-1	The J. David Gladstone Institutes	Trainee		
Dr. Aik T. Ooi	RN2-00904-1	University of California, Los Angeles	Trainee		
Dr. Andrea Smallwood	RN2-00905-1	Ludwig Institute for Cancer Research	Trainee		
Celso Espinoza, PhD	RN2-00905-1	Ludwig Institute for Cancer Research	Trainee		
Fulai Jin, PhD	RN2-00905-1	Ludwig Institute for Cancer Research	Trainee		
Dr. Joshua E Babiarz	RN2-00906-1	University of California, San Francisco	Trainee		
Dr. Nayoung Suh	RN2-00906-1	University of California, San Francisco	Trainee		
Dr. Anandaroop Mukhopadhya	RN2-00908-1	University of California, San Diego	Trainee		
Ms. Suguna Krishnaswami	RN2-00908-1	University of California, San Diego	Trainee		
Dr. Ying Crystal Wang	RN2-00908-1	University of California, San Diego	Trainee		
Mr. Calvin T. Hang	RN2-00909-1	Stanford University	Trainee		
Dr. Joshua Lehrer-Graiwer	RN2-00909-1	Stanford University	Trainee		
Dr. Yiqin Xiong	RN2-00909-1	Stanford University	Trainee		
Daniel Goff	RN2-00910-1	University of California, San Diego	Trainee		
Dr. Edward Kavalerchik	RN2-00910-1	University of California, San Diego	Trainee		

APPENDIX 26

Contact	Grant Number	Organization Name	Role	TBAppoint Type	TGAPPTTYPE
Dr. Isabel Newton	RN2-00910-1	University of California, San Diego	Trainee		
Kim-Hien Dao	RN2-00910-1	University of California, San Diego	Trainee		
Mr. Gregory Chinn	RN2-00915-1	University of California, Irvine	Trainee		
Ms. Linda Doan	RN2-00915-1	University of California, Irvine	Trainee		
Momoko Watanabe	RN2-00915-1	University of California, Irvine	Trainee		
Miss Ankita Das	RN2-00916-1	University of Southern California	Trainee		
Dr. Samuel Cox	RN2-00916-1	University of Southern California	Trainee		
Dr. Francesc R. Garcia-Gonzalo	RN2-00919-1	University of California, San Francisco	Trainee		
Ms. Julie Gaulden	RN2-00919-1	University of California, San Francisco	Trainee		
Dr. Kevin Corbit	RN2-00919-1	University of California, San Francisco	Trainee		
Agnieszka Laskowski	RN2-00922-1	University of California, Davis	Trainee		
Natasha Varlakhanova	RN2-00922-1	University of California, Davis	Trainee		
Ms. Alice Goodwin	RN2-00933-1	University of California, San Francisco	Trainee		
Ms. Kerstin Seidel	RN2-00933-1	University of California, San Francisco	Trainee		
Miss Mary Mohrin	RN2-00934-1	University of California, San Francisco	Trainee		
Eric Schulze	RN2-00938-1	University of Southern California	Trainee		
YongSung Hwang	RN2-00945-1	University of California, San Diego	Trainee		
Dr. Frederic Sala	RN2-00946-1	Children's Hospital of Los Angeles	Trainee		
Amar Sharma	RN2-00950-1	University of California, San Francisco	Trainee		
Mr. Collin Melton	RS1-00161-1	University of California, San Francisco	Trainee		
Dr. Yangming Wang	RS1-00161-1	University of California, San Francisco	Trainee		
Dr. Senait Ghirmai	RS1-00169-1	Human BioMolecular Research Institute	Trainee		
Craig Fredrickson	RS1-00173-1	University of California, San Diego	Trainee		
Mr. Michael Isaacs	RS1-00174-1	The Salk Institute for Biological Studies	Trainee		
Dr. Taylor I Liu	RS1-00198-1	University of California, San Diego	Trainee		
Dr. Lusine Aghajanova	RS1-00207-1	University of California, San Francisco	Trainee		
Mr. Brian Webster	RS1-00210-1	The J. David Gladstone Institutes	Trainee		
Ms. Priya Mathur	RS1-00215-1	University of California, San Francisco	Trainee		
Dr. Zhiqiang Dong	RS1-00215-1	University of California, San Francisco	Trainee		
Daniel Goff	RS1-00228-1	University of California, San Diego	Trainee		
Dr. Yosuke Minami	RS1-00228-1	University of California, San Diego	Trainee		
Chuba Oyula	RS1-00236-1	Stanford University	Trainee		
Dr. Dirk Grimm	RS1-00236-1	Stanford University	Trainee		
Laura Wang	RS1-00236-1	Stanford University	Trainee		
Dr. Xiaoyan Xie	RS1-00242-1	Stanford University	Trainee		
Miss Caroline Sham	RS1-00245-1	University of California, Los Angeles	Trainee		
Dr. Roberto Ferrari	RS1-00245-1	University of California, Los Angeles	Trainee		
Dr. Cynthia Jiang	RS1-00249-1	Children's Hospital of Los Angeles	Trainee		
Dr. Diana Abdueva	RS1-00249-1	Children's Hospital of Los Angeles	Trainee		
Dr. Hyoung-Tai Kim	RS1-00262-1	University of Southern California	Trainee		
Dr. Jungmook Lyu	RS1-00262-1	University of Southern California	Trainee		
Miss Vicky N. Yamamoto	RS1-00262-1	University of Southern California	Trainee		
Dr. Yin C Lin	RS1-00280-1	University of California, San Diego	Trainee		
Dr. Mi-Ryoung Song	RS1-00288-1	The Salk Institute for Biological Studies	Trainee		
Dr. Todd Macfarlan	RS1-00288-1	The Salk Institute for Biological Studies	Trainee		
Dr. Yan (Jessie) Zhang	RS1-00288-1	The Salk Institute for Biological Studies	Trainee		
Gary Chung Hon	RS1-00292-1	Ludwig Institute for Cancer Research	Trainee		
R David Hawkins	RS1-00292-1	Ludwig Institute for Cancer Research	Trainee		
Dr. Ou Li	RS1-00295-1	University of California, Berkeley	Trainee		
Dr. Sue Sohn	RS1-00295-1	University of California, Berkeley	Trainee		
Ms. Deborah Burkhart	RS1-00298-1	Stanford University	Trainee		
Shoutian Zhu	RS1-00302-1	Scripps Research Institute	Trainee		
Tae-gyu Nam	RS1-00302-1	Scripps Research Institute	Trainee		
Dr. Ying Peng	RS1-00308-1	University of California, San Francisco	Trainee		
Dr. Yoshiko Kametani	RS1-00308-1	University of California, San Francisco	Trainee		
Dr. Christine Bonzon	RS1-00313-1	University of California, Los Angeles	Trainee		
Ms. Heather Tienson	RS1-00313-1	University of California, Los Angeles	Trainee		
Ms. Vivian Liao	RS1-00313-1	University of California, Los Angeles	Trainee		
Dr. Dwayne Bisgrove	RS1-00317-1	The J. David Gladstone Institutes	Trainee		
Dr. Esther Xie	RS1-00322-1	Stanford University	Trainee		
Dr. Feng Cao	RS1-00322-1	Stanford University	Trainee		
Dr. Hyung Chun	RS1-00322-1	Stanford University	Trainee		
Dr. Esther Xie	RS1-00326-1	Stanford University	Trainee		
Dr. Mayumi Yamada	RS1-00326-1	Stanford University	Trainee		
Chengyuan Tang	RS1-00331-1	Sanford-Burnham Medical Research Institute	Trainee		
Dr. Hui Xiong	RS1-00331-1	Sanford-Burnham Medical Research Institute	Trainee		
Dr. Danling Wang	RS1-00333-1	University of California, San Diego	Trainee		
Dr. Julia Herrmann	RS1-00333-1	University of California, San Diego	Trainee		
Ms. Katherine Ruby	RS1-00333-1	University of California, San Diego	Trainee		
Ms. Phung T Gip	RS1-00365-1	University of California, Berkeley	Trainee		
Ms. Sarah Gilmore	RS1-00365-1	University of California, Berkeley	Trainee		
Dr. Hal Nguyen	RS1-00377-1	University of California, Irvine	Trainee		
Dr. Reinhard Meier	RS1-00381-1	University of California, San Francisco	Trainee		
Dr. Tobias Henning	RS1-00381-1	University of California, San Francisco	Trainee		
Nathan Lemp	RS1-00402-1	University of California, Los Angeles	Trainee		
Dr. Myungjin Kim	RS1-00408-1	University of Southern California	Trainee		

APPENDIX 26

Contact	Grant Number	Organization Name	Role	TBAppoint Type	TGAPPTTYPE
Dr. Christopher Schaumburg	RS1-00409-1	University of California, Irvine	Trainee		
Andy Huang	RS1-00420-1	University of California, Los Angeles	Trainee		
Dr. Mattias Magnusson	RS1-00420-1	University of California, Los Angeles	Trainee		
Christina Chaivorapol	RS1-00434-1	University of California, San Francisco	Trainee		
Dr. Marica Grskovic	RS1-00434-1	University of California, San Francisco	Trainee		
Dr. Matthew B. Wilson	RS1-00444-1	University of California, San Francisco	Trainee		
Dr. Janna K Mouw	RS1-00449-1	University of California, San Francisco	Trainee		
Dr. Dongguang Wei	RS1-00453-1	University of California, Davis	Trainee		
Dr. Liping Nie	RS1-00453-1	University of California, Davis	Trainee		
Dr. Snezana Levic	RS1-00453-1	University of California, Davis	Trainee		
Dr. Yan Li	RS1-00462-1	The J. David Gladstone Institutes	Trainee		
Dr. Hari A Reddi	RS1-00464-1	University of California, Davis	Trainee		
Dr. Penney Gilbert	RT1-01001-1	Stanford University	Trainee		
Ms. Melissa Freedenberg	RT1-01019-1	University of California, Davis	Trainee		
Dr. Francisco Herrera	RT1-01021-1	University of California, Berkeley	Trainee		
Dr. Jae Hyung Jang	RT1-01021-1	University of California, Berkeley	Trainee		
Ms. Kaushali Thakore-Shah	RT1-01022-1	University of California, Los Angeles	Trainee		
Dr. Mark A. Eddings	RT1-01022-1	University of California, Los Angeles	Trainee		
Mr. Alex Lei	RT1-01028-1	University of Southern California	Trainee		
Ms. Bingbing Dai	RT1-01028-1	University of Southern California	Trainee		
Ms. Poornima Kolhar	RT1-01053-1	University of California, Santa Barbara	Trainee		
Miss Teisha Rowland	RT1-01053-1	University of California, Santa Barbara	Trainee		
Mr. Javier Lopez-Prieto	RT1-01074-1	University of California, Irvine	Trainee		
Mr. Jente Lu	RT1-01074-1	University of California, Irvine	Trainee		
Mr. Oscar Azucena	RT1-01095-1	University of California, Santa Cruz	Trainee		
Ji-Dong Fu	RT1-01097-1	University of California, Davis	Trainee		
Dr. Charles A. Gersbach	RT1-01103-1	Scripps Research Institute	Trainee		
Dr. Franz-Joseph Mueller	RT1-01108-1	Scripps Research Institute	Trainee		
Dr. Ibon Garitaonandia	RT1-01108-1	Scripps Research Institute	Trainee		
Mr. Seung H Ha	RT1-01120-1	University of California, Irvine	Trainee		
Ms. Katelyn McCabe	RT1-01126-1	University of California, Los Angeles	Trainee		
Dr. Matthias Benz	RT1-01126-1	University of California, Los Angeles	Trainee		
Ms. Rachel Laing	RT1-01126-1	University of California, Los Angeles	Trainee		
Dr. Changsung Kim	RT1-01143-1	Vala Sciences Inc.	Trainee		
Dr. Maryam Majdi	RT1-01143-1	Vala Sciences Inc.	Trainee		
Dr. Nejmi Dilmac	RT1-01143-1	Vala Sciences Inc.	Trainee		
Eric Dec	TG2-01152	University of California, Irvine	Trainee		Clinical Fellow
Amar Nijagal	TG2-01153	University of California, San Francisco	Trainee		Clinical Fellow
Jose Otero	TG2-01153	University of California, San Francisco	Trainee		Clinical Fellow
Nam Tran	TG2-01153	University of California, San Francisco	Trainee		Clinical Fellow
Theodore Nicolaides	TG2-01153	University of California, San Francisco	Trainee		Clinical Fellow
Jennifer Black	TG2-01154	University of California, San Diego	Trainee		Clinical Fellow
Maria Cecilia Scimia	TG2-01154	University of California, San Diego	Trainee		Clinical Fellow
Neha Trivedi	TG2-01154	University of California, San Diego	Trainee		Clinical Fellow
Ralf Dirschinger	TG2-01154	University of California, San Diego	Trainee		Clinical Fellow
Veronique Tache	TG2-01154	University of California, San Diego	Trainee		Clinical Fellow
Jaehoon Chung	TG2-01159	Stanford University	Trainee		Clinical Fellow
James Lue	TG2-01159	Stanford University	Trainee		Clinical Fellow
Jun Seita	TG2-01159	Stanford University	Trainee		Clinical Fellow
Kelley Yan	TG2-01159	Stanford University	Trainee		Clinical Fellow
Reza Ardehali	TG2-01159	Stanford University	Trainee		Clinical Fellow
Mr. Baba Shiro	TG2-01160	The J. David Gladstone Institutes	Trainee		Clinical Fellow
Tim Rand	TG2-01160	The J. David Gladstone Institutes	Trainee		Clinical Fellow
Walter Devine	TG2-01160	The J. David Gladstone Institutes	Trainee		Clinical Fellow
Alexander Ring	TG2-01161	University of Southern California	Trainee		Clinical Fellow
Hsin Yi, Grace Huang	TG2-01161	University of Southern California	Trainee		Clinical Fellow
Joyce Lee	TG2-01163	University of California, Davis	Trainee		Clinical Fellow
Nanette Joyce	TG2-01163	University of California, Davis	Trainee		Clinical Fellow
Bindu Kanathezhath	TG2-01164	University of California, Berkeley	Trainee		Clinical Fellow
Joanna Halkias	TG2-01164	University of California, Berkeley	Trainee		Clinical Fellow
Kenneth Loh	TG2-01164	University of California, Berkeley	Trainee		Clinical Fellow
Caterina Tiozzo	TG2-01168	Children's Hospital of Los Angeles	Trainee		Clinical Fellow
Dr. Jun Wu	TG2-01168	Children's Hospital of Los Angeles	Trainee		Clinical Fellow
Sha-Ron Jackson	TG2-01168	Children's Hospital of Los Angeles	Trainee		Clinical Fellow
Diana Katsman	TG2-01169	University of California, Los Angeles	Trainee		Clinical Fellow
Gayane Ambartsumyan	TG2-01169	University of California, Los Angeles	Trainee		Clinical Fellow
Jeremy Reid	TG2-01169	University of California, Los Angeles	Trainee		Clinical Fellow
Lydia Lee	TG2-01169	University of California, Los Angeles	Trainee		Clinical Fellow
Michael Dorsi	TG2-01169	University of California, Los Angeles	Trainee		Clinical Fellow
Peiyee Lee	TG2-01169	University of California, Los Angeles	Trainee		Clinical Fellow
Sanjeet Patel	TG2-01169	University of California, Los Angeles	Trainee		Clinical Fellow
Yuluia Linhares	TG2-01169	University of California, Los Angeles	Trainee		Clinical Fellow
Lipi Singh	TG2-01150	Beckman Research Institute Of The City Of Hope	Trainee		Post-doc
Rachael Namba	TG2-01150	Beckman Research Institute Of The City Of Hope	Trainee		Post-doc
Robin Jeannet	TG2-01150	Beckman Research Institute Of The City Of Hope	Trainee		Post-doc
Wendong Li	TG2-01150	Beckman Research Institute Of The City Of Hope	Trainee		Post-doc

APPENDIX 26

Contact	Grant Number	Organization Name	Role	TBAppoint Type	TGAPPTTYPE
Eun Joo Lee	TG2-01151	University of California, Santa Barbara	Trainee		Post-doc
Minseon Cho	TG2-01151	University of California, Santa Barbara	Trainee		Post-doc
Oren Erster	TG2-01151	University of California, Santa Barbara	Trainee		Post-doc
Alvin King	TG2-01152	University of California, Irvine	Trainee		Post-doc
Ippei Nagamori	TG2-01152	University of California, Irvine	Trainee		Post-doc
Katja Pilitti	TG2-01152	University of California, Irvine	Trainee		Post-doc
Munjal Acharya	TG2-01152	University of California, Irvine	Trainee		Post-doc
Christine Fritz	TG2-01153	University of California, San Francisco	Trainee		Post-doc
Kevin Ebata	TG2-01153	University of California, San Francisco	Trainee		Post-doc
Markus Bussen	TG2-01153	University of California, San Francisco	Trainee		Post-doc
Michael Housley	TG2-01153	University of California, San Francisco	Trainee		Post-doc
Muluye Liku	TG2-01153	University of California, San Francisco	Trainee		Post-doc
Sijun Zhu	TG2-01153	University of California, San Francisco	Trainee		Post-doc
Apua Paquola	TG2-01154	University of California, San Diego	Trainee		Post-doc
Chien-Wen Chang	TG2-01154	University of California, San Diego	Trainee		Post-doc
Jessica Young	TG2-01154	University of California, San Diego	Trainee		Post-doc
Dr. Jie Deng	TG2-01154	University of California, San Diego	Trainee		Post-doc
Sandra Klein	TG2-01154	University of California, San Diego	Trainee		Post-doc
Bryan Haines	TG2-01155	Buck Institute for Age Research	Trainee		Post-doc
Dr. Jun Peng	TG2-01155	Buck Institute for Age Research	Trainee		Post-doc
Olga Momcilovic	TG2-01155	Buck Institute for Age Research	Trainee		Post-doc
Qiuyue, QL Liu	TG2-01155	Buck Institute for Age Research	Trainee		Post-doc
Rammohan Rao	TG2-01155	Buck Institute for Age Research	Trainee		Post-doc
Shona Mookerjee	TG2-01155	Buck Institute for Age Research	Trainee		Post-doc
Chao Guo	TG2-01157	University of California, Santa Cruz	Trainee		Post-doc
Fernando Ugarte	TG2-01157	University of California, Santa Cruz	Trainee		Post-doc
Frank Jacobs	TG2-01157	University of California, Santa Cruz	Trainee		Post-doc
Gwyndolen Harburg	TG2-01157	University of California, Santa Cruz	Trainee		Post-doc
Michael Halbisen	TG2-01157	University of California, Santa Cruz	Trainee		Post-doc
Neal Sweeney	TG2-01157	University of California, Santa Cruz	Trainee		Post-doc
Guanghui Lui	TG2-01158	The Salk Institute for Biological Studies	Trainee		Post-doc
Dr. Kristen Brennand	TG2-01158	The Salk Institute for Biological Studies	Trainee		Post-doc
Leo Kurian	TG2-01158	The Salk Institute for Biological Studies	Trainee		Post-doc
Quan Zhu	TG2-01158	The Salk Institute for Biological Studies	Trainee		Post-doc
Ryan Lister	TG2-01158	The Salk Institute for Biological Studies	Trainee		Post-doc
Sungtae Kim	TG2-01158	The Salk Institute for Biological Studies	Trainee		Post-doc
Xinde Zheng	TG2-01158	The Salk Institute for Biological Studies	Trainee		Post-doc
Oleksandr Shcheglovitov	TG2-01159	Stanford University	Trainee		Post-doc
Dr. Penney Gilbert	TG2-01159	Stanford University	Trainee		Post-doc
Rong Lu	TG2-01159	Stanford University	Trainee		Post-doc
Sohyun McElroy	TG2-01159	Stanford University	Trainee		Post-doc
Vittorio Sebastiano	TG2-01159	Stanford University	Trainee		Post-doc
Celine Delaloy	TG2-01160	The J. David Gladstone Institutes	Trainee		Post-doc
ChengZhong Wang	TG2-01160	The J. David Gladstone Institutes	Trainee		Post-doc
Juan Fung	TG2-01160	The J. David Gladstone Institutes	Trainee		Post-doc
Dr. Kiichiro Tomoda	TG2-01160	The J. David Gladstone Institutes	Trainee		Post-doc
Dr. Li Qian	TG2-01160	The J. David Gladstone Institutes	Trainee		Post-doc
Silke Wissing	TG2-01160	The J. David Gladstone Institutes	Trainee		Post-doc
Ms Yaisa Andrews-Zwilling	TG2-01160	The J. David Gladstone Institutes	Trainee		Post-doc
Dr. Zhiyuan Yang	TG2-01160	The J. David Gladstone Institutes	Trainee		Post-doc
Chong Pyo Choe	TG2-01161	University of Southern California	Trainee		Post-doc
Danielle Bittencourt	TG2-01161	University of Southern California	Trainee		Post-doc
Douglas Feldman	TG2-01161	University of Southern California	Trainee		Post-doc
Eve Kandyba	TG2-01161	University of Southern California	Trainee		Post-doc
Rachel Britt	TG2-01161	University of Southern California	Trainee		Post-doc
Si Ho Choi	TG2-01161	University of Southern California	Trainee		Post-doc
Xiaoying Zhou	TG2-01161	University of Southern California	Trainee		Post-doc
Bonnie Barrilleux	TG2-01163	University of California, Davis	Trainee		Post-doc
Fernando Fierro	TG2-01163	University of California, Davis	Trainee		Post-doc
Fuzheng Guo	TG2-01163	University of California, Davis	Trainee		Post-doc
Jesus Ciriza	TG2-01163	University of California, Davis	Trainee		Post-doc
Qini Gan	TG2-01163	University of California, Davis	Trainee		Post-doc
Aijun Wang	TG2-01164	University of California, Berkeley	Trainee		Post-doc
Elizabeth Irwin	TG2-01164	University of California, Berkeley	Trainee		Post-doc
Paul Hauser	TG2-01164	University of California, Berkeley	Trainee		Post-doc
Swomitra Mohanty	TG2-01164	University of California, Berkeley	Trainee		Post-doc
Tandis Vazin	TG2-01164	University of California, Berkeley	Trainee		Post-doc
Virginie Olive	TG2-01164	University of California, Berkeley	Trainee		Post-doc
Dr. Ibon Garitaonandia	TG2-01165	Scripps Research Institute	Trainee		Post-doc
Isabel Martinez Garay	TG2-01165	Scripps Research Institute	Trainee		Post-doc
Punita Sharma	TG2-01165	Scripps Research Institute	Trainee		Post-doc
Rodolfo Gonzalez	TG2-01165	Scripps Research Institute	Trainee		Post-doc
Yoshitake Cho	TG2-01165	Scripps Research Institute	Trainee		Post-doc
Ahmed El-Hashash	TG2-01168	Children's Hospital of Los Angeles	Trainee		Post-doc
Cornelia von Levetzow	TG2-01168	Children's Hospital of Los Angeles	Trainee		Post-doc
Dr. Frederic Sala	TG2-01168	Children's Hospital of Los Angeles	Trainee		Post-doc

APPENDIX 26

Contact	Grant Number	Organization Name	Role	TBAppoint Type	TGAPPTTYPE
Gianni Carraro	TG2-01168	Children's Hospital of Los Angeles	Trainee		Post-doc
Jieun Kim	TG2-01168	Children's Hospital of Los Angeles	Trainee		Post-doc
Katie Wiens	TG2-01168	Children's Hospital of Los Angeles	Trainee		Post-doc
Nicolas Plachta	TG2-01168	Children's Hospital of Los Angeles	Trainee		Post-doc
Andrew White	TG2-01169	University of California, Los Angeles	Trainee		Post-doc
Anne Lindgren	TG2-01169	University of California, Los Angeles	Trainee		Post-doc
David Mulholland	TG2-01169	University of California, Los Angeles	Trainee		Post-doc
Dr. Jingyu Li	TG2-01169	University of California, Los Angeles	Trainee		Post-doc
Konstantinos Chronis	TG2-01169	University of California, Los Angeles	Trainee		Post-doc
Mirko Corselli	TG2-01169	University of California, Los Angeles	Trainee		Post-doc
Dr. Rupa Sridharan	TG2-01169	University of California, Los Angeles	Trainee		Post-doc
Tamar Dvash	TG2-01169	University of California, Los Angeles	Trainee		Post-doc
Tanya, Ivanova Stoyanova	TG2-01169	University of California, Los Angeles	Trainee		Post-doc
Gregory Cherryholmes	TG2-01150	Beckman Research Institute Of The City Of Hope	Trainee		Pre-doc
Marisa Bowers	TG2-01150	Beckman Research Institute Of The City Of Hope	Trainee		Pre-doc
Kolhar Poornima	TG2-01151	University of California, Santa Barbara	Trainee		Pre-doc
Misty Riddle	TG2-01151	University of California, Santa Barbara	Trainee		Pre-doc
Miss Teisha Rowland	TG2-01151	University of California, Santa Barbara	Trainee		Pre-doc
Ellen Smith	TG2-01152	University of California, Irvine	Trainee		Pre-doc
Mr. Jente Lu	TG2-01152	University of California, Irvine	Trainee		Pre-doc
Lee Keumsil	TG2-01152	University of California, Irvine	Trainee		Pre-doc
Leonardo Scherer Alves	TG2-01152	University of California, Irvine	Trainee		Pre-doc
Lucia Whitman	TG2-01152	University of California, Irvine	Trainee		Pre-doc
Michelle Wedemeyer	TG2-01152	University of California, Irvine	Trainee		Pre-doc
Momoko Watanabe	TG2-01152	University of California, Irvine	Trainee		Pre-doc
Noelle Thompson	TG2-01152	University of California, Irvine	Trainee		Pre-doc
Archana Shenoy	TG2-01153	University of California, San Francisco	Trainee		Pre-doc
Jan Lui	TG2-01153	University of California, San Francisco	Trainee		Pre-doc
Jason Park	TG2-01153	University of California, San Francisco	Trainee		Pre-doc
Jessica Orr	TG2-01153	University of California, San Francisco	Trainee		Pre-doc
Julie Hunkapiller	TG2-01153	University of California, San Francisco	Trainee		Pre-doc
Miss Mary Mohrin	TG2-01153	University of California, San Francisco	Trainee		Pre-doc
Bethany Sotak	TG2-01154	University of California, San Diego	Trainee		Pre-doc
Jessica DeQuach	TG2-01154	University of California, San Diego	Trainee		Pre-doc
Leah Boyer	TG2-01154	University of California, San Diego	Trainee		Pre-doc
Mr. Mason Israel	TG2-01154	University of California, San Diego	Trainee		Pre-doc
Vipul Bhargava	TG2-01154	University of California, San Diego	Trainee		Pre-doc
Wesley Gifford	TG2-01154	University of California, San Diego	Trainee		Pre-doc
Andrew Nguyen	TG2-01157	University of California, Santa Cruz	Trainee		Pre-doc
Daniel Carlin	TG2-01157	University of California, Santa Cruz	Trainee		Pre-doc
David Greenberg	TG2-01157	University of California, Santa Cruz	Trainee		Pre-doc
Ms. Muriel M Kmet	TG2-01157	University of California, Santa Cruz	Trainee		Pre-doc
Alisa Mueller	TG2-01159	Stanford University	Trainee		Pre-doc
Eric Teasley	TG2-01159	Stanford University	Trainee		Pre-doc
Ernesto Lujan	TG2-01159	Stanford University	Trainee		Pre-doc
Ilya Shestopalov	TG2-01159	Stanford University	Trainee		Pre-doc
Richard Chiu	TG2-01159	Stanford University	Trainee		Pre-doc
Zhengqing Ouyang	TG2-01159	Stanford University	Trainee		Pre-doc
Amanda Crow	TG2-01161	University of Southern California	Trainee		Pre-doc
Ang Li	TG2-01161	University of Southern California	Trainee		Pre-doc
Dasgupta Krishnakali	TG2-01161	University of Southern California	Trainee		Pre-doc
Guanyi Huang	TG2-01161	University of Southern California	Trainee		Pre-doc
Vivian Medina	TG2-01161	University of Southern California	Trainee		Pre-doc
Wing Yan Yik	TG2-01161	University of Southern California	Trainee		Pre-doc
Ms. Christine Jung	TG2-01163	University of California, Davis	Trainee		Pre-doc
Christy Kim	TG2-01163	University of California, Davis	Trainee		Pre-doc
Heather Thompson	TG2-01163	University of California, Davis	Trainee		Pre-doc
Karina Nakayama	TG2-01163	University of California, Davis	Trainee		Pre-doc
Martin Decaris	TG2-01163	University of California, Davis	Trainee		Pre-doc
Rebecca Beer	TG2-01163	University of California, Davis	Trainee		Pre-doc
Elizabeth Kirby	TG2-01164	University of California, Berkeley	Trainee		Pre-doc
Jenny Ross	TG2-01164	University of California, Berkeley	Trainee		Pre-doc
Lingyan Jin	TG2-01164	University of California, Berkeley	Trainee		Pre-doc
Melanie Worley	TG2-01164	University of California, Berkeley	Trainee		Pre-doc
Zhe (James) Liu	TG2-01164	University of California, Berkeley	Trainee		Pre-doc
Bradley Charette	TG2-01165	Scripps Research Institute	Trainee		Pre-doc
Jennifer Hazen	TG2-01165	Scripps Research Institute	Trainee		Pre-doc
Kristopher Nazor	TG2-01165	Scripps Research Institute	Trainee		Pre-doc
Stuart Webb	TG2-01165	Scripps Research Institute	Trainee		Pre-doc
Weiwei Li	TG2-01165	Scripps Research Institute	Trainee		Pre-doc
Akanksha Chhabra	TG2-01169	University of California, Los Angeles	Trainee		Pre-doc
David Chan	TG2-01169	University of California, Los Angeles	Trainee		Pre-doc
Evan Nair-Gill	TG2-01169	University of California, Los Angeles	Trainee		Pre-doc
Mr. Jin Zhang	TG2-01169	University of California, Los Angeles	Trainee		Pre-doc
John Vincent	TG2-01169	University of California, Los Angeles	Trainee		Pre-doc
Jonathan Nakashima	TG2-01169	University of California, Los Angeles	Trainee		Pre-doc

APPENDIX 26

Contact	Grant Number	Organization Name	Role	TBAppoint Type	TGAPPTTYPE
Michaela Patterson	TG2-01169	University of California, Los Angeles	Trainee		Pre-doc
Rita Lukacs	TG2-01169	University of California, Los Angeles	Trainee		Pre-doc
Sean Sherman	TG2-01169	University of California, Los Angeles	Trainee		Pre-doc
Anna Denise Garcia	TG2-01157	University of California, Santa Cruz	Trainee		Post-doc
Christian Elabd	TG2-01164	University of California, Berkeley	Trainee		Post-doc
Keiko Takahashi	TG2-01164	University of California, Berkeley	Trainee		Post-doc
Dr. Monica Zhou	TR1-01219	Scripps Research Institute	Trainee		
Dr. Steffie Krohne	TR1-01219	Scripps Research Institute	Trainee		
Dr. Sunia A. Trauger	TR1-01219	Scripps Research Institute	Trainee		
Dr. Tim Krohne	TR1-01219	Scripps Research Institute	Trainee		
Dr. Wan-Guo Wei	TR1-01219	Scripps Research Institute	Trainee		
Dr. Wenlin Li	TR1-01219	Scripps Research Institute	Trainee		
Dr. Zhiyuan Yang	TR1-01227	The J. David Gladstone Institutes	Trainee		
Dr. Daniel Layton	TR1-01245	University of California, Irvine	Trainee		
Nicholas Castello	TR1-01245	University of California, Irvine	Trainee		
Mr. Blake Byers	TR1-01246	The Parkinson's Institute	Trainee		
Mr. Branden Cord	TR1-01246	The Parkinson's Institute	Trainee		
Dr. Gozde Yucel	TR1-01249	Stanford University	Trainee		
Dr. Jay Jiang	TR1-01249	Stanford University	Trainee		
Dr. Nicholas Evans	TR1-01249	Stanford University	Trainee		
Dr. Rajnish A Gupta	TR1-01249	Stanford University	Trainee		
Dr. Shijun Hu	TR1-01249	Stanford University	Trainee		
Astra Chang	TR1-01257	University of California, Davis	Trainee		
Mr. Matthew Lindsey	TR1-01257	University of California, Davis	Trainee		
Dr. Scott Olson	TR1-01257	University of California, Davis	Trainee		
Dr. David L. Boucher	TR1-01269	University of California, Davis	Trainee		
Ms. Melissa Freedenberg	TR1-01269	University of California, Davis	Trainee		
Dr. Amy Tien	TR1-01272	University of California, Los Angeles	Trainee		
Dr. Chinatsu Tosha	TR1-01272	University of California, Los Angeles	Trainee		
Dr. Joanna J Kaylor	TR1-01272	University of California, Los Angeles	Trainee		
Dr. Maren Engelhardt	TR1-01272	University of California, Los Angeles	Trainee		
Miss Michelle Lee	TR1-01272	University of California, Los Angeles	Trainee		
Dr. Vanda S. Lopes	TR1-01272	University of California, Los Angeles	Trainee		
Dr. Gerald M. Pao	TR1-01273	The Salk Institute for Biological Studies	Trainee		
Dr. Maria Jose Barrero NÃºÃ±ez	TR1-01273	The Salk Institute for Biological Studies	Trainee		
Dr. Niels-Bjarne Woods	TR1-01273	The Salk Institute for Biological Studies	Trainee		
Dr. Trond Aasen	TR1-01273	The Salk Institute for Biological Studies	Trainee		
Miss Izorte Santin	TR1-01277	University of California, San Diego	Trainee		
Ning-Yuan Su	TR1-01277	University of California, San Diego	Trainee		
Tongbiao Zhao	TR1-01277	University of California, San Diego	Trainee		
Zhili Rong	TR1-01277	University of California, San Diego	Trainee		
Ha Nam Nguyen	RC1-00137-1	Stanford University	Undergraduate		
Deena Hassanein	RN1-00540-1	University of California, Santa Cruz	Undergraduate		

APPENDIX 27

27. Collaborative Funding Partner sample funding agreement

COLLABORATIVE FUNDING AGREEMENT BETWEEN CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE AND THE STATE OF VICTORIA FOR EARLY TRANSLATIONAL RFA (Draft no. 8)(April 20, 2009)

This is an Agreement between the California Institute for Regenerative Medicine, an agency of the State of California, ("CIRM") and the Crown in Right in the State of Victoria of 121 Exhibition Street, Melbourne, Victoria, Australia ("Victoria") entered and effective as of April 23, 2009.

WHEREAS, CIRM and Victoria (collectively, the "Parties") have a common interest in collaboratively funding and monitoring stem cell research projects motivated by their common understanding that the cure and treatment of chronic diseases may be accomplished through the use of regenerative medical therapies and that medical breakthroughs in this area are more likely to happen only if adequate funding is made available to advance stem cell research, develop therapies and conduct clinical trials;

WHEREAS, in 2008, the Parties executed an Alliance Memorandum of Understanding ("Alliance MOU") confirming their collective interest in exploring opportunities for collaboratively evaluating and funding stem cell research projects;

WHEREAS, CIRM issued a Request for Applications titled Early Translational Research Awards in September 2008 seeking research project proposals relating to translational medicine (the "Translational RFA"). The Translational RFA announced that teams comprised of California and Victoria researchers ("Joint Teams") could apply and compete for funding under the terms set forth therein. Thereafter, several Joint Teams submitted applications (the "Eligible Collaborative Projects");

WHEREAS, in February 2009, CIRM's Grants Working Group ("GWG") considered and evaluated the applications received in response to the Translational RFA, including several Eligible Collaborative Projects. A Victoria representative was an official observer of the GWG evaluation process;

WHEREAS, in April, 2009, the GWG evaluations and funding recommendations will be formally considered by CIRM's Governing Board, the Independent Citizen's Oversight Committee ("ICOC") and the ICOC will make its final determination concerning which Early Translational Research projects to fund;.

WHEREAS, the ICOC will not approve funding for the California Portion of any Eligible Collaborative Project unless and until Victoria agrees that it is prepared to fund the Victorian Portion of said Project; and

WHEREAS, Victoria and CIRM want to collaboratively fund certain Eligible Collaborative Projects responsive to the Translational RFA under the terms and conditions stated herein;

NOW, THEREFORE, CIRM and Victoria agree as follows:

1. Victoria Consideration and Approval of Eligible Collaborative Projects

2. At the conclusion of the GWG Translational RFA analysis, the ranking assigned by the GWG to each Eligible Collaborative Project and the basis for the ranking was, or will be, shared by CIRM with Victoria.

3. Victoria shall determine, at its sole discretion, whether it is willing to pay for work done in Victoria (the "Victoria Portion") of proposed research for any of the Eligible Collaborative Projects. Victoria shall make and communicate that determination to CIRM at least one week before the ICOC meeting at which the Translational RFA will be evaluated. Said determination will be communicated to CIRM in writing, will include financial details of the Victoria Portion for the Eligible Collaborative Projects, and will be legally binding on Victoria, subject only to: the relevant Victorian recipient entering into a Grant Agreement with Victoria; an administrative review by Victoria concerning appropriateness of the proposed budget; and agreement by the ICOC/CIRM to pay for work done in California on each such Project (the "California Portion").
4. **ICOC Consideration And Approval of Eligible Collaborative Projects**
5. The ICOC will not consider funding the California Portion of any Eligible Collaborative Project for which Victoria has not agreed to pay for the Victoria Portion of said Project in accordance with Paragraph 3 above. The fact that Victoria is willing, and has agreed, to fund the Victoria Portion of any Eligible Collaborative Project does not in any way bind CIRM or the ICOC to fund the California Portion of said Project. Nothing herein diminishes the power, authority, jurisdiction or discretion of the ICOC.
6. Victoria may have a representative present at the ICOC meeting at which the Translational RFA funding is considered.
7. If and only if the ICOC determines to fund the California Portion of any Eligible Collaborative Project for which Victoria already has agreed to fund the Victoria Portion, as described in paragraph 3 above, then said Project shall be awarded a grant by CIRM, subject only to: an administrative review by CIRM concerning appropriateness of the proposed budget; and execution of an acceptable Notice of Grant Award.
8. **Funding Approved Collaborative Projects**
9. Eligible Collaborative Projects that are approved for funding by both Victoria and the ICOC shall be referred to herein as "Approved Collaborative Project or Projects".
10. For each Approved Collaborative Project, CIRM agrees to pay for the California Portion an amount not to exceed U.S. $6,000,000 over a three year period. CIRM shall pay the California Portion for each Approved Collaborative Project only in accordance with its applicable Policies, including, but not limited to its Grants Administration Policy, http://www.cirm.ca.gov/reg., as may be amended from time to time.
11. For each Approved Collaborative Project, Victoria agrees to pay for the Victorian Portion in an amount not to exceed U.S. $1,000,000 over a three year period. Victoria shall pay the Victoria Portion for each Approved Collaborative Project in accordance with its Grant Agreement and applicable Policies and Guidelines.
12. CIRM is responsible for monitoring and ensuring that the California Portion of any Approved Collaborative Project is used appropriately by California recipients. Victoria is responsible for monitoring and ensuring that the Victoria Portion of any Approved Collaborative Project is used appropriately by Victoria recipients. Nothing herein obligates, or creates any responsibility for either Victoria or CIRM to monitor or assure proper use of funds paid by the other Party.
13. The Parties agree to pay for their agreed upon Portions of each Approved Collaborative Project subject to adequate performance and progress by the relevant Joint Team members. In the event that a Joint Team fails to perform the work contemplated by an Approved Collaborative Project, or fails to make satisfactory progress toward meeting approved objectives or milestones or otherwise materially breaches a term of the relevant Grant Agreement, then either Party hereto may suspend or cancel the remaining payments of its Portion. Each Party hereto shall give written notice to the other Party at least sixty days before discontinuing or suspending funding. Thereafter, and before discontinuing or suspending funding, the Parties shall meet and confer

concerning the basis for the proposed funding disruption, with a view to resolving the relevant issues within a reasonable time.

14. Except as provided in Paragraph 13 above, both Victoria and CIRM agree to fund their respective Portions of each Approved Collaborative Project in accordance with paragraphs 11 and 10 above, respectively.

15. In the event that only one Party hereto seeks to discontinue funding of its Portion of an Approved Collaborative Project, that Party shall undertake reasonable efforts to mitigate any resulting negative impact such discontinuance may have on the other Party hereto, on the remaining member(s) of the Joint Team and on the subject research.

Monitoring Performance of Approved Collaborative Projects

16. Grantees from both Victoria and California on each Approved Collaborative Project shall be required to regularly submit to the Parties various reports sufficient to allow the Parties to evaluate the financial and scientific progress of each such Project including but not limited to reports required by CIRM's Grants Administration Policies for Academic and Non-Profit Institutions and For-Profit Institutions as applicable. The standard CIRM reporting format and templates are to be used for all reporting by both California and Victoria Grantees.
17. Both Victoria and CIRM shall have full access to all progress, performance and financial reports generated by each Approved Collaborative Project team, regardless of whether the reports reflect research done as part of the California or Victoria Portion of the Project. Both Parties shall require their Grantees to allow disclosure of all such reports to both Parties hereunder. The Parties agree to maintain these reports in confidence to the fullest extent permitted by law.
18. Periodically, but not less than once per calendar year, representatives of Victoria and CIRM shall confer, preferably in person, to review the status, progress and performance of each Approved Collaborative Project. CIRM and Victoria each shall designate a point person acceptable to the other to serve as a primary liaison concerning their interactions relating to Approved Collaborative Projects.

Intellectual Property Issues

19. CIRM Grantees who receive CIRM funds in connection with an Approved Collaborative Project shall be subject to all applicable portions of the CIRM Intellectual Property Requirements for Non-Profit Organizations and the Intellectual Property and Revenue Sharing Requirements for For-Profit Organizations (http://www.cirm.ca.gov/reg)(collectively, "CIRM IP Regulations"), as each may be amended from time to time.
20. Victoria Grantees will be required to adhere to an intellectual property policy approved by their governing bodies that is congruent with the document "National Principles of Intellectual Property Management for Publicly Funded Research" (as amended) released September 2001.
21. Each Joint Team approved for funding hereunder shall be required to negotiate agreements amongst themselves addressing intellectual property issues including ownership, revenue sharing, licensing and associated costs relating to their Approved Collaborative Project ("Grantee IP Agreements"). The Grantee IP Agreements must be submitted for review to the Parties hereto to ensure consistency with the terms of this Agreement. Grantee IP Agreements will be held in confidence by the Parties hereto, to the fullest extent permitted by law. Neither CIRM nor Victoria will actually disperse funds to any Grantee that has not entered into a Grantee IP Agreement consistent with the terms of this Agreement.

22. All Victorian Grantees shall be subject to, and must comply with, the following CIRM IP Regulations with respect to their efforts on any Approved Collaborative Project. Said obligations must be reflected in the Grantee IP Agreement submitted for each Approved Collaborative Project:
    a. Access Requirements (CIRM IP Regulations, Secs. 100306, 100406 and 100407): These requirements are mandatory for Victoria Grantees only to the extent that said Grantees commercialize or exclusively license others to commercialize inventions which were funded in whole or in part by CIRM hereunder ("Products") in the State of California;
    b. Pricing Requirements (CIRM IP regulations, Secs. 100306, 100406 and 100407): These requirements are mandatory for Victoria Grantees only to the extent that said Grantees commercialize or exclusively license others to commercialize Products in the State of California;
    c. Biomedical Materials Sharing Requirements (CIRM IP Regulations, Secs. 100304 and 100404): These requirements are mandatory for Victoria Grantees only for purposes of research in California; and
    d. Reporting Requirements: (CIRM IP Regulations, Secs. 100302, 100402, 100303, 100403, 100309 and 100409) Victoria shall require its Grantees to provide reports in accordance with these requirements.
23. All Grantees shall be subject to, and must comply with, relevant Australian legislative requirements detailed in the Australian National Health Act 1953 (as amended), Part VII concerning operations of the Pharmaceutical Benefits Scheme together with the National Health Pharmaceutical Benefits Regulations 1960 made under the Act and the Therapeutic Goods Act 1989 (as amended) only to the extent that said Grantees commercialize inventions in Australia which were funded in whole or in part by Victoria hereunder. Said obligations must be reflected in the Grantee IP Agreement submitted for each Approved Collaborative Project.
24. Victoria shall retain the right to require its Grantees and their exclusive licensees to grant non-exclusive, partially exclusive or exclusive license in any field of use to a responsible applicant or applicants upon reasonable terms in the event that a Victoria Grantee does not reach the minimum commercialization requirements outlined in their funding agreement and does not have an alternative approved commercialization scheme in place or a satisfactory explanation for failure to encourage or facilitate commercialization of the funded research intellectual property.

Compliance with Law

25. Notwithstanding anything herein to the contrary, CIRM's participation hereunder is subject to, and must be in conformance with, all relevant statutory and policy requirements including but not necessarily limited to California Constitution Section XXXV, California Health and Safety Code Section 125290.10 et seq. and applicable regulations, see title 17 Cal. Code of Regulations., section 100000 et seq., all of which are incorporated herein by this reference.
26. CIRM Grantees who participate in an Approved Collaborative Project must comply with all applicable laws, regulations and CIRM policies.
27. No funds awarded under this Agreement shall be used for research involving human reproductive cloning or any other matter that is prohibited by California law or CIRM regulations for CIRM Grantees, or Australian and Victoria law and regulations for Victorian Grantees.
28. The Parties understand and agree that if any of them are required or become compelled, pursuant to any applicable law, regulation or legal process with whose rules the Party is

required to comply, to disclose any matters involving confidential intellectual property or work product, whether patentable or not, including but not limited to any formula, data, plan, pattern, process, tool, mechanism, compound, procedure, production data, financial information or compilation of information which is not patented and which is known only to certain individuals who are using it to fabricate, produce, engage in or compound an article of trade or a service having commercial value and which gives its user an opportunity to obtain a business advantage over competitors who do not know or use it ("Confidential Information") which said Party acquired in connection with this Agreement, the Party will, prior to any such disclosure, promptly, before complying with any such requirement, use best endeavours to notify the other Party in writing of same and of the action which is proposed to be taken in response. Further, the compelled Party will cooperate fully with the other Party in taking legally available steps to resist or limit the disclosure and to obtain an appropriate protective order or other assurance that confidential treatment will be afforded the Confidential Information required to be disclosed. If no such protective order or other remedy is obtained or the other Party does not waive compliance with the terms of this Agreement, the compelled Party agrees and understands that it:

A) will furnish only that portion of the Confidential Information which the compelled Party is advised by counsel is legally required to be disclosed; and

B) will exercise all reasonable efforts to obtain reliable assurances that confidential treatment will be accorded such Confidential Information.

Dispute Resolution

29. Each Party hereto enters into this Agreement in its governmental capacity and agrees that the subject matter hereof is not a "commercial transaction" for purposes of the Australian Foreign States Immunities Act 1985 nor a "commercial activity" for purposes of the United States Foreign Sovereign Immunities Act. Except as agreed hereafter in Paragraph 30 -32, nothing herein is intended to nor should be construed as waiving whatever immunity from suit that each Party enjoys as a consequence of its sovereign or governmental status.

30. The Parties recognize that the work done by Victoria and California scientists contemplated by the Early Translational Research projects which may be funded hereunder is fully integrated. As such, it will be important for CIRM and Victoria, as co-funders, to communicate fully and regularly concerning funded projects. In the event a dispute arises between the Parties relating in any way to this Agreement, the Parties' representatives (as nominated in accordance with paragraph 18) agree to promptly meet and confer in a good faith effort to resolve it in accordance with the spirit underlying the Agreement.

31. If a dispute is not resolved by the Parties' representatives within fifteen days or such other reasonable time frame as may be agreed in writing, the dispute will be referred to CIRM 's President as CIRM's representative, and the Deputy Secretary Innovation and Technology as Victoria's representative for further efforts at resolution.

32. Should the meet and confer process described in Paragraph 31 above fail to resolve the Parties' differences within thirty days of referral, or within such other time as may be agreed by the Parties in writing, then the Parties agree to refer the dispute to formal mediation. Any mediation will be conducted in accordance with guidelines to be agreed by the Parties. In the event that neither negotiation nor mediation resolves a dispute, the Parties agree to refer any remaining disputes arising hereunder between them to binding arbitration pursuant to the auspices and procedures of the International Chamber of

Commerce. Notwithstanding the existence of a dispute, the Parties will continue to perform their obligations under this Agreement.

Miscellaneous Provisions

33. The Parties may publicise the funding and outcomes of the Approved Collaborative Projects, subject to the confidentiality requirements set forth above. The Parties agree, subject to such obligations as may be imposed by law, to mutually consult with each other prior to publicising matters pertaining to the Approved Collaborative Projects.

34. This Agreement may be executed in any number of counterparts (including by electronic communication) and those counterparts taken together are one agreement. The Parties acknowledge and agree that signature by electronic communication will constitute both writing and signing of this Agreement under the *Electronic Transactions (Victoria) Act 2000* and related Acts.

35. In the event of a dispute among the Parties, this Agreement shall be governed by and construed in accordance with:

The laws of The State of California if CIRM is the Party initially acting therein as defendant; or

The applicable laws of Victoria if Victoria is the Party initially acting therein as defendant.

36. If any clause or provision of the terms and conditions of this Agreement is adjudged to be invalid, the remaining terms and conditions shall remain in full force and effect.

37. This Agreement and its schedules constitute the entire agreement between the parties relating to CIRM's Early Translational RFA and sets forth all the covenants, promises, warranties, representations, conditions, understandings, and agreements between the Parties pertaining to the subject matter of this Agreement and supersede all prior agreements, understandings, negotiations and discussions, whether oral or written, including the Alliance MOU. The Alliance MOU, however, survives in so far as it relates to other CIRM RFAs and other projects that the Parties may jointly sponsor.

38. Unless otherwise extended or terminated earlier by mutual agreement of the Parties, this Agreement shall become effective as of April 23, 2009 and shall continue in full force and effect until all aspects of performance, monitoring and performance of any Approved Collaborative Project are concluded. However, the provisions, covenants and conditions contained in paragraphs 28, and 30 -32, shall be and remain in force notwithstanding such expiration or other termination of the Agreement for any reason whatsoever**.**

39. Each Party agrees to execute, acknowledge and deliver such further instruments and to do all such other acts as may be reasonably necessary or appropriate to effectuate the terms of this Agreement.

40. Except as otherwise permitted hereunder, none of the rights or obligations of this Agreement may be assigned by any Party without the prior written consent of the other Party. This Agreement shall be binding upon and inure to the benefit of each Party and its permitted successors and assigns. Each Party shall be responsible for the compliance by its permitted successors and assigns with the terms and conditions of this Agreement.

41. This Agreement creates no third party beneficiary rights in Approved Collaborative Project Grantees or in any other person, or entity that contracts with said Approved Collaborative Project Grantees, whose contracts will be funded by grant funds, against either CIRM or Victoria. Similarly, nothing herein creates any obligation or other right in the Grantee of one Party hereto as against the other Party hereto.

42. This Agreement may be amended, supplemented, or otherwise modified only by means of a written instrument executed by the Parties. Any waiver of any rights or failure to act

in a specific instance shall relate only to such instance and shall not be construed as an agreement to waive any rights or fail to act in any other instance, whether or not similar.

43. CIRM and Victoria shall each absorb 100% of their internal and external expenses related to performance under this Agreement.

44. Performance of a Party's obligations hereunder may be excused or delayed where such failure to perform or delay in performance is due to circumstances beyond that Party's control, including, without limitation, fires, labor disputes, severe weather, natural disasters or other acts of God (a "Force Majeur Event"). Each Party shall give the other Party prompt notice of the occurrence of a Force Majeur Event and use its best efforts to minimize the duration and consequences of any failure of or delay in performance resulting from a Force Majeur Event.

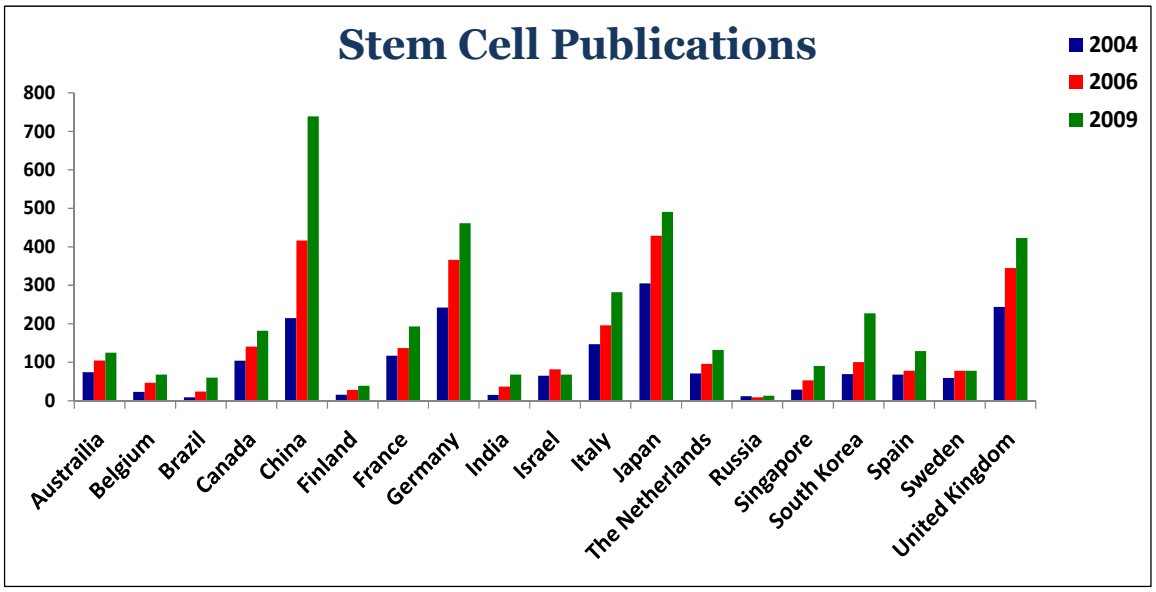
45. Each Party hereto and its counsel have reviewed and revised (or requested revisions of) this Agreement, and the rule of construction that any ambiguities are to be resolved against the drafting party shall not be applicable in the construction and interpretation of this Agreement.

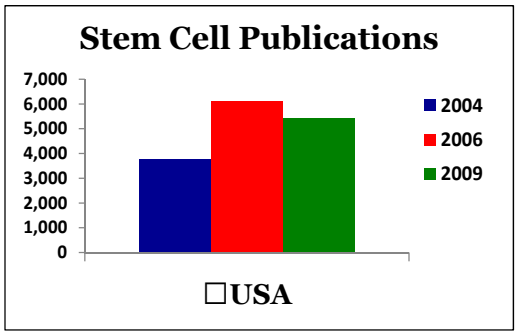
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE (CIRM)	**VICTORIA**
by: _____	**by:** _____
Title: _____	**Title:** _____
Dated: _____	**Dated:** _____

[Back to Appendices]

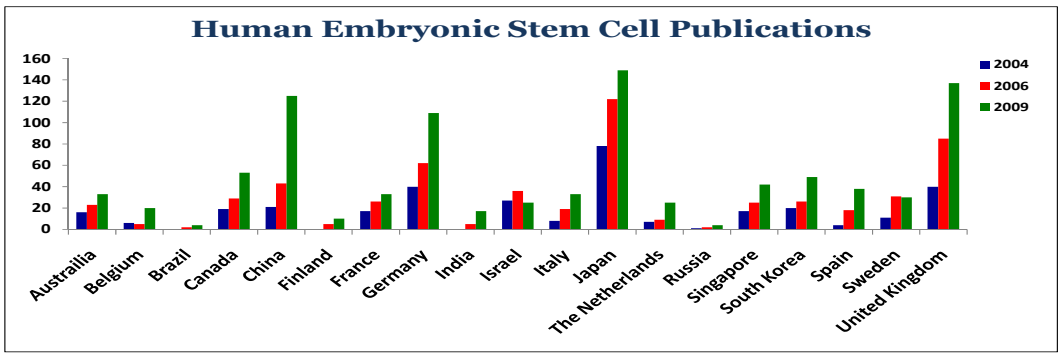
APPENDIX 28

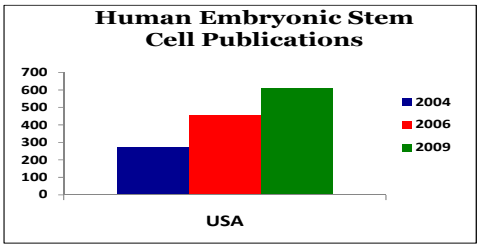
28. Pub Med data by country over time

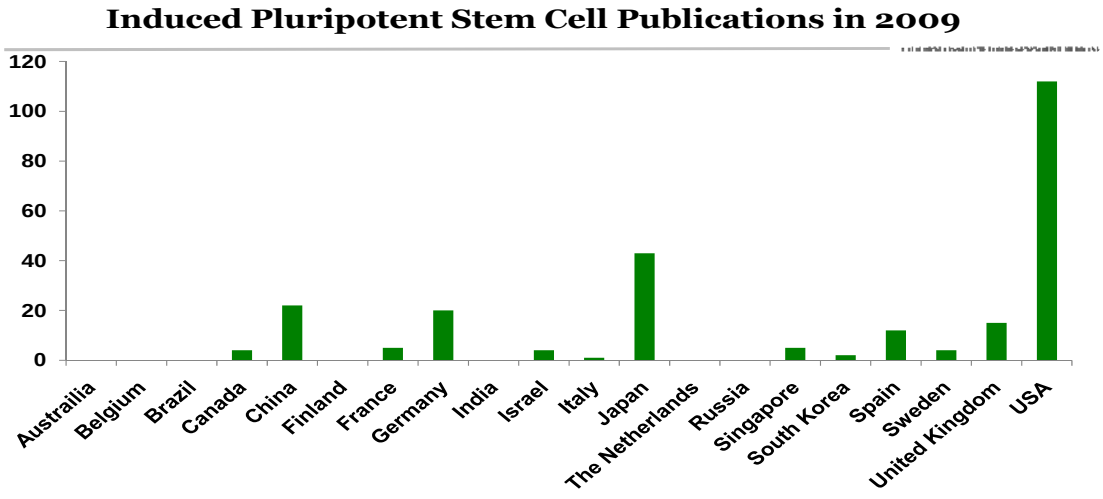




APPENDIX 28



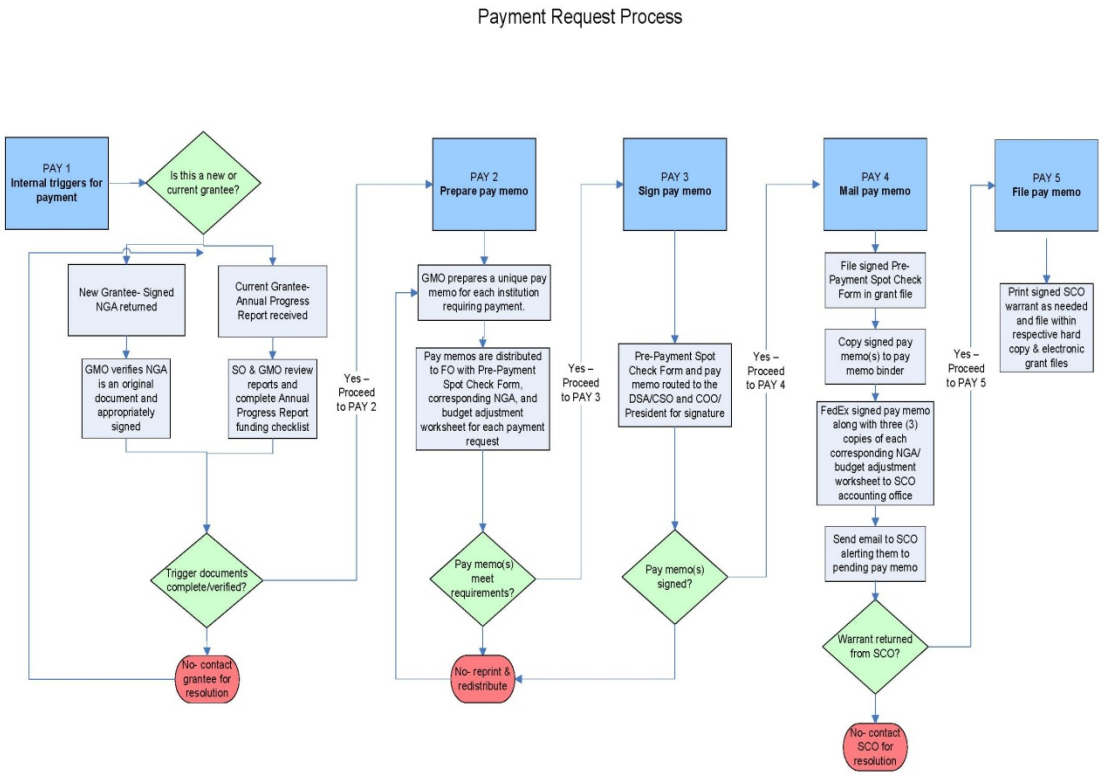




[Back to Appendices]

APPENDIX 29

29. Grants Management Office activity/grant list



[Back to Appendices]

APPENDIX 30

30. Duties of the Board, the Board Chair and the President

Proposition 71 Sections Dealing with Duties of the Board and Its Chair

The ICOC shall perform the following functions:

(a) Oversee the operations of the institute.
(b) Develop annual and long-term strategic research and financial plans for the institute.
(c) Make final decisions on research standards and grant awards in California.
(d) Ensure the completion of an annual financial audit of the institute's operations.
(e) Issue public reports on the activities of the institute.
(f) Establish policies regarding intellectual property rights arising from research funded by the institute.
(g) Establish rules and guidelines for the operation of the ICOC and its working groups.
(h) Perform all other acts necessary or appropriate in the exercise of its power, authority, and jurisdiction over the institute.
(i) Select members of the working groups.
(j) Adopt, amend, and rescind rules and regulations to carry out the purposes and provisions of this chapter, and to govern the procedures of the ICOC. Except as provided in subdivision (k), these rules and regulations shall be adopted in accordance with the Administrative Procedure Act (Government Code, Title 2, Division 3, Part 1, Chapter 4.5, Sections 11371 et seq.).
(k) Notwithstanding the Administrative Procedure Act (APA), and in order to facilitate the immediate commencement of research covered by this chapter, the ICOC may adopt interim regulations without compliance with the procedures set forth in the APA. The interim regulations shall remain in effect for 270 days unless earlier superseded by regulations adopted pursuant to the APA.
(l) Request the issuance of bonds from the California Stem Cell Research and Cures Finance Committee and loans from the Pooled Money Investment Board.
(m) May annually modify its funding and finance programs to optimize the institute's ability to achieve the objective that its activities be revenue-positive for the State of California during its first five years of operation without jeopardizing the progress of its core medical and scientific research program.
(n) Notwithstanding Section 11005 of the Government Code, accept additional revenue and real and personal property, including, but not limited to, gifts, royalties, interest, and appropriations that may be used to supplement annual research grant funding and the operations of the institute.

125290.45. ICOC Operations

(a) Legal Actions and Liability
(1) The institute may sue and be sued.
(2) Based upon ICOC standards, institute grantees shall indemnify or insure and hold the institute harmless against any and all losses, claims, damages, expenses, or liabilities, including attorneys' fees, arising from research conducted by the grantee pursuant to the grant, and/or, in the alternative, grantees shall name the institute as an additional insured and submit proof of such insurance.
(3) Given the scientific, medical, and technical nature of the issues facing the ICOC, and notwithstanding Section 11042 of the Government Code, the institute is authorized to retain outside counsel when the ICOC determines that the institute requires specialized services

not provided by the Attorney General's office.

(4) The institute may enter into any contracts or obligations which are authorized or permitted by law.

(b) Personnel

(1) The ICOC shall from time to time determine the total number of authorized employees for the institute, up to a maximum of 50 employees, excluding members of the working groups, who shall not be considered institute employees. The ICOC shall select a chairperson, vice chairperson and president who shall exercise all of the powers delegated to them by the ICOC. The following functions apply to the chairperson, vice chairperson, and president:

(A) The chairperson's primary responsibilities are to manage the ICOC agenda and work flow including all evaluations and approvals of scientific and medical working group grants, loans, facilities, and standards evaluations, and to supervise all annual reports and public accountability requirements; to manage and optimize the institute's bond financing plans and funding cash flow plan; to interface with the California Legislature, the United States Congress, the California health care system, and the California public; to optimize all financial leverage opportunities for the institute; and to lead negotiations for intellectual property agreements, policies, and contract terms. The chairperson shall also serve as a member of the Scientific and Medical Accountability Standards Working Group and the Scientific and Medical Research Facilities Working Group and as an ex-officio member of the Scientific and Medical Research Funding Working Group. The vice chairperson's primary responsibilities are to support the chairperson in all duties and to carry out those duties in the chairperson's absence.

(B) The president's primary responsibilities are to serve as the chief executive of the institute; to recruit the highest scientific and medical talent in the United States to serve the institute on its working groups; to serve the institute on its working groups; to direct ICOC staff and participate in the process of supporting all working group requirements to develop recommendations on grants, loans, facilities, and standards as well as to direct and support the ICOC process of evaluating and acting on those recommendations, the implementation of all decisions on these and general matters of the ICOC; to hire, direct, and manage the staff of the institute; to develop the budgets and cost control programs of the institute; to manage compliance with all rules and regulations on the ICOC, including the performance of all grant recipients; and to manage and execute all intellectual property agreements and any other contracts pertaining to the institute or research it funds.

(2) Each member of the ICOC except, the chairperson, vice chairperson, and president, shall receive a per diem of one hundred dollars ($100) per day (adjusted annually for cost of living) for each day actually spent in the discharge of the member's duties, plus reasonable and necessary travel and other expenses incurred in the performance of the member's duties.

(3) The ICOC shall establish daily consulting rates and expense reimbursement standards for the non-ICOC members of all of its working groups.

(4) Notwithstanding Section 19825 of the Government Code, the ICOC shall set compensation for the chairperson, vice chairperson, and president and other officers, and for the scientific, medical, technical, and administrative staff of the institute within the range of compensation levels for executive officers and scientific, medical and technical.

[Back to Appendices]

APPENDIX 31

31. Office of State Controller Audit

CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE (CIRM)

Review Report

REVIEW OF CONFLICT-OF-INTEREST

POLICIES, GRANT ADMINISTRATION, ADMINISTRATIVE EXPENSES, AND EXPENDITURES

July 1, 2006, through December 31, 2007

JOHN CHIANG, California State Controller

May 1, 2008

Alan O. Trounson, Ph.D., President
California Institute for Regenerative Medicine
210 King Street
San Francisco, CA 94107

Dear Dr. Trounson:

The State Controller's Office completed a review of the California Institute for Regenerative Medicine (CIRM) for the period of July 1, 2006, through December 31, 2007. The objectives of our review were to determine whether CIRM complied with the requirements of Proposition 71, the voter-approved initiative that created CIRM, as it relates to CIRM's conflict-of-interest policies, grant administration, administrative expenses, and expenditures.
Except for the issue concerning specialists' failure to sign post-review conflict-of-interest certification forms, we found that CIRM's conflict-of-interest policies and procedures are adequate, and that they were properly followed.
A draft report was issued on April 1, 2008. Your response to the draft report is included in our final report.
If you have any questions, please contact Casandra Moore-Hudnall, Chief, Financial Audits Bureau, at (916) 322-4846.

Sincerely,

Original signed by
JEFFREY V. BROWNFIELD
Chief, Division of Audits
JVB/sk
cc:

Independent Citizen's Oversight Committee
California Institute for Regenerative Medicine
Financial Accountability Oversight Committee
California Institute for Regenerative Medicine

APPENDIX 31

Contents

Review Report

Specialists failed to sign post-review conflict-of-interest certification forms.

In our review of the California Institute of Regenerative Medicine's conflict-of-interest processes, we noted that, although the specialists working with the grants working group signed pre-review conflict-of-interest statements and confidential financial disclosure forms, they did not sign post-review certification forms regarding conflicts-of-interest, confidentiality, and non-disclosure of information as required. The specialists participate in meetings via teleconference to provide their scientific expertise on specific items; however, they do not have voting privileges and they are not counted towards a quorum.

Recommendation: We recommend that the specialists also sign a post-review certification form regarding conflicts of interest, confidentiality, and non-disclosure of information for each meeting in which they participate.

This report presents the results of the State Controller's Office (SCO) review of the California Institute for Regenerative Medicine (CIRM) for the period of July 1, 2006, through December 31, 2007. The objectives of our review were to determine whether CIRM complied with the requirements of Proposition 71, the voter-approved initiative that created CIRM, relative to CIRM's conflict-of-interest policies, grant administration, administrative expenses, and expenditures.

Our review found that CIRM has extensive conflict-of-interest policies and processes that are modeled after and, in some instances, go beyond National Institute of Health requirements. Our conclusion is consistent with the Bureau of State Audits in its audit report of CIRM issued in February 2007. Our review also found that CIRM and its associated committees and working groups adhered to these policies and processes. The specialists used by the grants working group signed pre-review conflict-of-interest statements and confidential financial disclosure

forms. However, contrary to CIRM's policy, the specialists used by the grants working group do not sign post-review certification forms
regarding conflicts of interest, confidentiality and non-disclosure of
information. CIRM uses specialists when specific scientific expertise is
needed in evaluating a grant application. The specialists review and
participate in discussion on applications but do not have voting privileges; their presence is not counted towards a quorum. The specialists participate in these meetings via teleconference to provide their scientific expertise on specific grants of research fields.

Exhibit 1 provides a detailed description of CIRM's policies and procedures relative to conflicts of interest and the audit procedures that we performed to determine compliance.

Results in Brief

Summary

We found that CIRM has developed its grants administration policies based on Proposition 71 requirements and industry best practices. Our review disclosed that CIRM is administering its grants in compliance with Proposition 71 requirements and CIRM's policies and procedures. Exhibit 2 provides a detailed description of CIRM's policies and procedures governing grant administration and the audit procedures that we performed to determine compliance.

We also found that CIRM has administrative processes and procedures in place to ensure that its administrative expenses are properly approved, authorized, and in compliance with Proposition 71 requirements. CIRM expenditures also receive additional state oversight, as they are reviewed by the SCO Departmental Accounting Office and the SCO Claims Audit Unit before payments are made.

Our review disclosed that CIRM's expenditures are in compliance with Proposition 71 requirements and CIRM's policies and procedures. Exhibit 3 provides a detailed description of CIRM's policies and procedures governing administrative expense, as well as the audit procedures that we performed to determine compliance.

On November 27, 2007, the State Controller directed his office to conduct a review of CIRM in order to determine how grants are allocated and whether CIRM provides adequate oversight once the grants are awarded. In addition, the Controller requested that we review CIRM's expenditure practices, its conflicts of interest standards, and its compliance with State law. Pursuant to Government Code section 12410, the State Controller is to "superintend the fiscal concerns of the state. The Controller shall audit all claims against the state, and may audit the disbursement of any state money, for correctness, legality, and for sufficient provisions of law for payment."

In addition, under Proposition 71, the State Controller appoints members to the Independent Citizen's Oversight Committee (ICOC), which oversees CIRM, and chairs CIRM's Citizen's Financial Accountability and Oversight Committee (CFAOC). CFAOC reviews the annual financial audit, the State Controller's report and evaluation of the audit, and the financial practices of CIRM.

Background

APPENDIX 31

The CIRM is a California state agency formed pursuant to the provisions of Proposition 71, the California Stem Cell Research and Cures Act, approved by voters in November 2004. Although CIRM is a state agency, Proposition 71 allowed it to adopt travel and procurement policies based on University of California policies, which are more liberal than other California state agency travel and procurement policies. Proposition 71 also authorized the issuance of $3 billion in bonds over ten years to provide funding for stem cell research.

Introduction

The purpose of the legislation was the formation of an institute to:

- Make grants and loans for stem cell research, for research facilities, and for other vital research opportunities to realize therapies, protocols, and/or medical procedures that will result in, as speedily as possible, the diagnosis, treatment, and cure for, and/or substantial mitigation of, major diseases, injuries, and orphan diseases.
- Support all stages of the process of developing treatments and cures, from basic research and discovery through preclinical and translational research to the conduct of successful clinical trials.
- Establish the appropriate regulatory standards and oversight bodies for research and facilities development.

Independent Citizen's Oversight Committee

Proposition 71 required the creation of the Independent Citizen's Oversight Committee (ICOC) that governs CIRM and has full power, authority, and jurisdiction over the CIRM. The ICOC has 29 members who are appointed in accordance with specific parameters set forth in Health and Safety Code section 125290.20. The 29 ICOC members elect a chairperson and vice chairperson, who serve six-year terms and meet certain criteria also specified in the code.

The ICOC is required to perform the following functions as they relate to our audit of CIRM:

- Oversee CIRM's operations.
- Develop annual long-term strategic research and financial plans for CIRM.
- Make financial decisions on research standards and grant awards in California.
- Ensure completion of an annual financial audit of CIRM's operations.
- Establish policies regarding intellectual property rights arising from research funded by CIRM.
- Establish rules and guidelines for the operation of the ICOC and its working groups.
- Adopt, amend, and rescind rules and regulations to carry out the purposes and provisions of Health and Safety Code section 125290.20 and to govern the procedures of the ICOC.

Scientific and Medical Working Groups

CIRM is also required to establish three separate scientific and medical working groups as follows: Scientific and Medical Accountability Standards Working Group, Scientific and Medical Research Funding Working Group, and Scientific and Medical Research Facilities Working Group.

Appointments of scientific and medical working group members are made by a majority vote of a quorum of the ICOC. The working group members may serve a maximum of two consecutive terms; working group members' terms are limited to six years. Each working group's recommendations may be forwarded to the ICOC only by a majority vote of a quorum of the members of each working group. If 35% of the members of any working group join in a minority position, a minority report may be submitted to the ICOC.

The primary functions of the scientific and medical working groups are described below:

Scientific and Medical Accountability Standards Working Group

1) Makes recommendations to the ICOC regarding:
- Scientific, medical, and ethical standards.
- Standards for all medical, socioeconomic, and financial aspects of clinical trials and therapy delivery to patients including, among others, standards for safe and ethical procedures for obtaining materials and cells for research and clinical efforts for the appropriate treatment of human subjects in medical research and to ensure compliance with patient privacy laws.
- Oversight of funded research to ensure compliance with the above standards.

2) Provides advice to the ICOC, the Scientific and Medical Research Funding Working Group, and the Scientific and Medical Research Facilities Working Group, on an ongoing basis, on relevant ethical and regulatory issues.

Scientific and Medical Research Funding Working Group (also referred to by CIRM as the Grants Working Group)

1) Makes recommendations to the ICOC regarding:
- Interim and final criteria, standards, and requirements for considering funding applications and for awarding research grants and loans.
- Standards for the scientific and medical oversight of awards.
- Any needed modifications of criteria, standards, and requirements described above.

2) Reviews grant and loan applications based on the criteria, requirements, and standards adopted by the ICOC, and makes recommendations to the ICOC for awards regarding research, therapy, development, and clinical trial grants and loans.
- Conducts peer group progress oversight reviews of grantees to ensure their compliance with the terms of the award, and reports to the ICOC any recommendations for subsequent action.
- Recommends to the ICOC standards for the evaluation of grantees to ensure that they comply with all applicable requirements. Such standards mandate periodic reporting by grantees and authorize the Scientific and Medical Research Funding Working Group to audit a grantee and forward any recommendations for action to the ICOC.

Scientific and Medical Facilities Working Group

1) Makes recommendations to the ICOC on interim and final criteria, requirements, and standards for applications for, and the awarding of, grants and loans for buildings, building leases, and capital equipment.

Those standards and requirements include:

- Facility milestones and timetables for achieving such milestones.
- Priority for applications that provide for facilities available no more than two years after the grant award.
- All funded facilities and equipment are to be located solely in California.
- Grantees are to be not-for-profit entities.
- Awards are made on a competitive basis, requiring the grantee secure matching funds from sources other than CIRM equal to at least 20% of the award and that capital equipment costs/loans be allocated when equipment costs can be recovered in part by the grantee or other users of the equipment. The matching fund requirement can be waived by the Working Group in extraordinary cases of high merit or urgency.

2) Makes recommendations to the ICOC on oversight procedures to ensure grantees' compliance with the terms of the award.

Proposition 71 required that a Citizen's Financial Accountability Oversight Committee (CFAOC) be created and chaired by the State Controller. This committee reviews the annual financial audit, the State Controller's report and evaluation of the audit, and the financial practices of the Institute.

The CFAOC consists of public members appointed by the State Controller, the State Treasurer, the President pro Tempore of the Senate, the Speaker of the Assembly, and the ICOC chairperson. Committee members must have medical backgrounds and knowledge of relevant financial matters and provide recommendations on CIRM's financial practices and performance.

Exhibit 4 provides a detailed description of the composition of the working group members.

Our review encompassed the period from July 1, 2006, through December 31, 2007, and was performed in accordance with auditing standards generally accepted in the United States of America, and Government Auditing Standards issued by the Comptroller General of the United States.

Through interagency agreements, the SCO has provided non-audit services to CIRM since its inception. The SCO's Departmental Accounting Office and Human Resources Office provide accounting and payroll services to CIRM. In addition, beginning January 1, 2008, the SCO's Departmental Accounting Officer was appointed as CIRM's acting Finance Officer. The appointment was made outside the time period of the scope of this audit. In accordance with generally accepted government auditing standards, the performance of the aforementioned non-audit services and the appointment of the acting Finance Officer do not impair our independence with respect to our review of conflict of interest and grant administration. As an organization, the SCO is not considered independent with respect to expenditure testing because the accounting services provided by the SCO to CIRM included preparing and processing of claims for payment.

Under California's Constitution and statutes, the State Controller is responsible for ensuring the legality and propriety of state disbursements. Consistent with this responsibility, the SCO performs pre-payment audits and, when deemed necessary, post-payment field audits of claims filed against the State Treasury. The expenditure testing in this review was performed pursuant to the State Controller's constitutional and statutory audit authority and responsibility. Within the

SCO, the Division of Audits is functionally independent from the units that performed non-audit services to CIRM.

We did not review expenditures for the period of July 1, 2006, through June 30, 2007, because these expenditures were reviewed by an independent auditor as part of CIRM's annual financial audit. Consistent with the State Controller's responsibility under Proposition 71, the SCO reviews the report and working papers of the independent auditor and reports the results of the evaluation to the Citizen's Financial Accountability Oversight Committee. This report was issued on March 14, 2008.

We limited our scope to planning and performing review procedures necessary to obtain reasonable assurance that CIRM complied with the requirements of Proposition 71 relative to its conflict-of-interest policies, grant administration, and administrative expenses and expenditures. We limited our review of CIRM's internal controls to gaining an understanding of the transaction flows and processes necessary to develop appropriate procedures. Government auditing standards require that we plan and perform our review to obtain sufficient, appropriate evidence to provide a reasonable basis for our finding and conclusions based on our review objectives. We believe that the evidence obtained during our review provides a reasonable basis for our finding and conclusions based on our review objectives.

Objectives, Scope, and Methodology

Prior to the commencement of our review, a situation surfaced that raised questions concerning a possible conflict of interest involving members of the Independent Citizen's Oversight Committee (ICOC). The State Controller referred the matter to the Fair Political Practices Commission (FPPC) for investigation on November 27, 2007. The FPPC investigatory procedures may disclose additional issues, facts, and circumstances beyond the matters noted in our review, as our review was not an investigation.

Our review objectives were to:

- Determine the adequacy of CIRM's policies and procedures for grants administration.
- Determine compliance with conflict-of-interest rules and best practices.
- Determine compliance with Proposition 71 requirements related to grants administration.
- Determine the adequacy of the mandated grantee reporting requirements.
- Determine whether CIRM's administrative expenses are in line with Proposition 71 requirements.
- Determine whether CIRM's expenditures were properly approved and authorized.

To accomplish our review objectives, we performed the following procedures:

- Reviewed pertinent laws and regulations, including all documents related to the Proposition 71 initiative.
- Reviewed CIRM's written policies and procedures documents, including: Grants Administration Policies, Conflict of Interest Policies, Expenditure and Travel Policies, Internal Governance Policy, and Hiring Procedures.
- Reviewed the previous audit report, issued in February 2007 by the Bureau of State Audits (BSA), as well as the status of CIRM's corrective actions to determine the scope and findings and to build upon the work the BSA performed. Refer to Exhibit 5 for CIRM's corrective actions in response to the BSA audit.

- Interviewed key personnel to gain an understanding of CIRM's procedures, processes, and control structures related to expenditures, grant administration, and hiring.
- Sampled, on a limited basis, CIRM's expenditures and grant awards to determine whether payments and grants were awarded in accordance with applicable laws, regulations, and policies.
- Reviewed meeting files for the Scientific and Medical Research Facilities (Grants Working Group [GWG]) and ICOC to evaluate the effectiveness of controls over conflicts of interest and to determine whether CIRM's processes were effective.

Except for the issue concerning specialists' failure to sign post-review conflict-of-interest certification forms, we found that CIRM's conflict-of-interest policies and procedures are adequate and that they were properly followed.

We reviewed 49 grants, totaling $74.26 million, of 159 grants totaling $233.6 million. Our review covered approximately 31% of grants awarded. We did not note any exceptions in our testing. Schedule 1 provides a summary of the grants tested.

For the period of July 1, 2007, through December 31, 2007, we reviewed 25 expenditures totaling $27.23 million, of a total of $44.04 million; our review covers approximately 62% of expenditures. We did not note any exceptions in our testing. Schedule 2 provides a summary of the expenditures tested.

We discussed our audit results with CIRM's representatives and issued a draft audit report during an exit conference conducted on April 1, 2008. Tamar Pachter, General Council; Robert Klein, Chairman, Independent Citizen's Oversight Committee; and other CIRM representatives agreed with the audit results. Alan O. Trounson, Ph.D., President of CIRM, responded by letter dated April 14, 2008 (Attachment), agreeing with the audit results. This final audit report includes CIRM's response.

This report is intended for the information and use of the California Institute for Regenerative Medicine, its governing board, and the SCO; it is not intended to be and should not be used by anyone other than these specified parties. This restriction is not intended to limit distribution of the final report, which is a matter of public record.

Original signed by

JEFFREY V. BROWNFIELD, CPA
Chief, Division of Audits

May 1, 2008

Conclusion

Restricted Use

Views of
Responsible
Officials

Finding and Recommendation

In our review of CIRM's conflict-of-interest processes, we noted that, although the specialists working with the Grants Working Group signed pre-review conflict-of-interest statements and confidential financial disclosure forms, they did not sign post-review certification forms regarding conflicts of interest, confidentiality, and non-disclosure of information as required. CIRM uses specialists when specific scientific expertise is needed in evaluating a grant application. In our discussion with CIRM staff, they explained that although CIRM's policy states that the post-review certification must be signed, they did not have the specialists sign the forms because the specialists participated in the meetings via teleconference and thus were not physically present to sign the form. Even though the specialists are not physically present, because they do participate in the meeting, they should sign the post-review meeting certifications and either e-mail, fax, or mail the certifications to CIRM.

Recommendation

In accordance with CIRM's Grants Working Group conflict-of-interest policy and processes, we recommend that the specialists also sign a post-review certification form regarding conflicts of interest, confidentiality, and non-disclosure of information for each meeting in which they participate.

CIRM's Response

CIRM agrees with the recommendation and implemented it beginning with the most recent meeting of the Grants Working Group on April 9-11, 2008.

CIRM's Policy

CIRM has adopted a conflict-of-interest code as required by the Political Reform Act. Additionally, CIRM has adopted a conflict of interest (COI) policy for its ICOC members, CIRM employees, and three working groups (Grants Working Group, Facilities Working Group, and Standards Working Group).

CIRM's COI code for ICOC members is consistent with the Political Reform Act. CIRM's COI policy for members of the Grants Review Working Group and Facilities Working Group is closely modeled on the policies of the National Institute of Health. The working group members are required to disclose any financial, personal, or professional COI. All reviewers must sign a pre-review statement indicating any possible conflicts of interest that they have, and must also sign a post-review statement that they did not participate in the discussion or review of any application for which they might have a conflict of interest.

The Bureau of State Audits (BSA) conducted an audit of CIRM, including its COI code and policies, and published its audit report in February 2007. To accomplish our audit objective, we reviewed the BSA's audit report and recommendations to CIRM for corrective actions regarding CIRM's COI policies, as well as CIRM's corrective actions.

We found that CIRM incorporated the BSA's recommendations in its revised COI policies.

The BSA audit noted that the ICOC COI policy restates stipulations of the Political Reform Act and further limits its members' decision-making opportunities. An example noted in the report is

that according to CIRM's policy, committee members cannot receive gifts from entities doing, or seeking to
do, business with CIRM if it could reasonably be substantiated that the gift was intended to influence a
future official action or reward a past one. In comparison, the report notes that the Political Reform Act permits state officials to receive annually up to $360 of gifts from a single source for a two-year period.

The BSA audit also noted that the COI policies of the Grants Review and Facilities Working Groups are
modeled on the NIH policy but are at times stricter than NIH policy. An example noted in the report is that the NIH considers a reviewer to have a conflict of interest if the reviewer received or could receive from the applicant institution a financial benefit exceeding $10,000 per year. In comparison, CIRM sets the limit at $5,000.

Scientific and Medical Research Funding Working Group/Grants Working Group (GWG)

CIRM staff generates a list of all applicant institutions and key personnel from all of the applications submitted for a particular request for application (RFA). That list is made available to all GWG members online. Members must review the list, identify any institution or key personnel with which they have a COI, and sign off on the result. Each member must complete this process before he or she is given access to any application. Once completed, reviewers are given access only to those applications with which they have no COI. In addition, each GWG member must sign a pre-review certification form that identifies all applications with which the reviewer has a COI. These COI forms are compiled and kept in the working group meeting files.

CIRM staff generates a Conflict of Interest Tracking Form that shows a grid of each application and each member and highlights any COI. This tracking form is used during the working group meetings to record that members left the meeting when applicants with which they had a conflict of interest were discussed. The tracking form with the notations becomes part of the permanent file for each RFA review meeting.

At the beginning of each GWG review meeting, CIRM provides an overview reminder of the COI policy and the objectives of the RFA. Because the meetings are "closed," individuals who have a COI with a particular application must leave the room during discussion of that application.

CIRM staff members maintain a meeting file/binder that has the "sign in" sheet for the meeting as well as the "sign out" sheet. The sign out sheet also serves as a certification form for non-disclosure of information and confidentiality. The COI certificate form (for all participants in the meeting) and the financial disclosure form (for the GWG members) are also maintained in the meeting file.

SCO Review Procedures and Results

To test for compliance with CIRM's conflict-of-interest policy and reliability of the summary COI Tracking form for the GWG, we:

- Selected a meeting file for the GWG.
- Verified that the file contained, for each member attending the meeting, signed conflict-of-interest statements; confidential financial disclosure forms; funding recommendation

letters; and post-review certification forms regarding conflicts of interest, confidentiality, and non-disclosure of information.
- Verified that that file contained a COI Tracking Form.
- Traced information from each members' detailed COI statement, funding recommendation letters, and post-review certification forms to the COI Tracking Form.

Based on the results of our testing, we determined that CIRM is following its COI policies and procedures, with the exception of the post-review certification related to specialists. We also determined that the Conflict of Interest Tracking Form was complete and, thus, the form's information could be relied upon during our testing of grants administration.

The GWG uses specialists in reviewing grant applications. Specialists are used if the GWG needs scientific expertise on a particular issue. The specialists review and participate in discussions on applications but do not have voting privileges; their presence is not counted towards a quorum. The specialists participate in these meetings via teleconference to provide their scientific expertise on specific grants or research fields.

We noted in our testing that, although the specialists signed pre-review conflict of interest statements and confidential financial disclosure forms, they did not sign post-review certification forms regarding conflicts of interest, confidentiality, and non-disclosure of information as required. In accordance with CIRM's grants working group COI policy, the specialists should also sign a post-review certifications for each meeting in which they participate. Therefore, we recommend that CIRM require specialists to sign a post-review certification form regarding conflicts of interest, confidentiality, and non-disclosure of information for reviewers of grant applications.

Independent Citizen's Oversight Committee

CIRM's Policy

In advance of an ICOC meeting, all ICOC members must review the online list of applicant institutions and key personnel to identify any conflicts of interest and must sign off on their review. CIRM's legal office also reviews the members' form 7001 and disclosures to make sure there is no conflict of interest. CIRM staff compiles these lists and generates for each ICOC member a list that shows which applications for which members have a COI. Because the ICOC meeting is a public meeting, the members are not required to leave the meeting when the applications for which they have a COI are discussed, but they are prohibited from commenting or voting on those applications. CIRM staff members also prepare a listing by application that shows all ICOC members with COIs who are disqualified from participating. Throughout the meeting, CIRM staff members monitor this list, as well as the discussion, motions, and voting, to ensure that all members adhere to CIRM's COI policies.

SCO Review Procedures and Results

To test for compliance with CIRM's conflict-of-interest policy, and to test the reliability of the ICOC summary COI form, we:

- Selected an ICOC meeting file.

- Verified that the file contained, for each member attending the meeting, conflict-of-interest forms for each ICOC member, individual conflict-of-interest recusal forms, and a copy of a signed certification of ICOC conflict-of-interest recusal form.
- Verified that that file contained a summary COI form.
- Traced information from each member's detailed COI statement and post-review certification forms to members' recusal form and to the summary COI form.

We noted that for the ICOC members and CIRM staff, the COI forms were complete and were supported with collaborating original documentation from each person. Based on the results of our testing, we determined that CIRM is following its COI policies and procedures. We also determined that the summary COI form was complete and, thus, the form's information could be relied upon during our testing of grants administration.

1 Form 700 is the Fair Political Practices Commission's "Statement of Economic Interests" form.

Exhibit 2—

Grants Administration Review

July 1, 2006, through December 31, 2007

The objective of our review was to determine the adequacy of CIRM's policies and procedures for grants administration, compliance with Proposition 71 requirements related to grants administration, compliance with conflict-of-interest policies, and adequacy of grantee reporting requirements.

CIRM's Policy

Proposition 71 grants administration requirements include the following:

1) The ICOC shall:
- Make final decisions on research standards and grant awards.
- Award all grants, loans, and contracts in public meetings.

2) The Scientific and Medical Research Funding Working Group shall:
- Review grant and loan applications based on the criteria, requirements, and standards adopted by the ICOC, and make recommendations to the ICOC for awards regarding research, therapy, development, and clinical trial grants and loans.
- Recommend to the ICOC standards for the evaluation of grantees to ensure that they comply with all applicable requirements. Such standards shall mandate periodic reporting by grantees and shall authorize the Scientific and Medical Research Funding Working Group to audit a grantee and forward any recommendations for action to the ICOC.
- Base award recommendations upon competitive evaluations. Only the 15 scientist members of the Scientific and Medical Research Funding Working Group shall score grant and loan award applications for scientific merit. The scoring shall be based upon scientific merit in three separate classifications: research, therapy development, and clinical trials and criteria.

The CIRM grants administration process consists of the following six processes:

1. Pre-Review
   - CIRM scientific staff members develop a concept for a grant, based on the initiatives in CIRM's strategic plan. The concept describes the proposed Request for Application (RFA), including a description of the objective, high-level eligibility requirements, and the pool of money required for the concept.
   - CIRM staff present the written concept to the ICOC for approval. The ICOC discusses the concept and votes to approve or deny the concept.
   - If the ICOC approves the concept, CIRM scientific staff members develop the RFA. The RFA is an official solicitation by CIRM for applications directed to a particular funding opportunity. Each RFA specifies the objectives and requirements that apply, eligible costs, and the review criteria that will be used to evaluate the merits of applications submitted in response to the RFA.

2. Review by Grants Working Group (GWG)
   - The GWG completes its Conflict of Interest (COI) process for the application review.
   - Each application submitted in response to the RFA is reviewed by two to three reviewers.
   - Reviewers submit via secure intranet written critiques of each application to CIRM for all GWG members to review. The reviewers comment on the overall scientific merit of the application and the specific review criteria for the RFA. The comments may address the feasibility of the proposal and whether or not it meets the objectives of the strategic plan.
   - The GWG has a review meeting to discuss the applications. The GWG review meeting comprises two parts – a scientific review and a programmatic review.
   - During the scientific review, the GWG members discuss the merits of each application and score the applications on a scale from 1 to 100. Members who have a conflict of interest with an application under consideration during scientific review must leave the room during this discussion. CIRM staff members create a histogram displaying the distribution of scores for all applications (the histogram does not identify the applications by name or number; it simply shows a score for anonymity). The GWG uses the histogram to break the list of applications into three different categories. The three categories are: rank 1–recommended for funding, rank 2–recommended, if funds are available, and rank 3–not recommended for funding. CIRM staff members then create a listing of all applications by rank order showing the budget for each application.
   - During the programmatic review, the GWG members take into account programmatic issues and any other issues that are outside the pure scientific score. During this time, they will also consider how each application fits into the CIRM's overall strategic plan. Working group members may also make a motion to move a particular application from one category to another. Members who have a conflict of interest with an application under consideration during programmatic review must leave the room during this discussion. A vote is taken on the motion, and if it carries, the application is moved pursuant to the vote from one category to another, although the scientific score remains the same. When there are no more motions to move applications between categories, the members vote to make their recommendations to the ICOC by category: recommended for funding; recommended if funds are available; and not recommended for funding. CIRM staff members then create a table of applications identifying three categories of recommendation.

3. ICOC Approval
   - After the GWG review meeting, the CIRM science office takes the initial critiques and notes from the meeting and creates summary reports for each application. They prepare two different types of summary reports; one is confidential and the other is non-confidential. The confidential summary is provided to the applicant so that it can understand the score that its application received. The non-confidential summary is provided to the ICOC members and is also available to the public. The summaries are posted on CIRM's Web site prior to the ICOC meeting ("Summaries of Review for Application to RFA"). This public summary shows only the score for applications that are being recommended for funding. It also shows which GWG members had a conflict of interest, so that the public will know those members did not participate in the discussion or scoring of that particular application.
   - Prior to the ICOC meeting, the ICOC completes its COI process for the meeting.
   - At the meeting, the ICOC is presented with the table of applications identifying the three categories of recommendations and a list of the application summaries. The ICOC chairman asks whether anyone has a comment on any particular application and/or wants to move any application from one recommended category to another. During this discussion, a screen shows the ICOC the real-time funding impact of any changes. When all discussions are completed, the chairman extends a motion to approve all applications in the category "recommended to fund." A roll call vote is taken and the members vote to either fund or not fund the entire block of applications (excluding any applications for which they have a COI).
   - When approved, the ICOC commits to funding the block of applications. CIRM then issues a press release.

4. Pre-Funding Administrative Review
   - After the applications are approved by the ICOC, CIRM staff members create a grant file for the approved applications.
   - CIRM's Grants Management Officer (GMO) and Scientific Program Officer (SPO) perform a pre-funding administrative review prior to funding an approved application. Both the GMO and SPO have a pre-funding checklist that details what they must review. Contact with the applicant and any notes regarding the pre-funding review are noted on the checklists.

5. Award Acceptance and Funding
   - After the SPO and the GMO have completed and signed off on their checklists, CIRM grants management staff prepares the Notice of Grant Award (NGA). The NGA includes any special terms and/or any budget adjustments noted on the checklists.
   - The NGA is reviewed and signed off on by the CIRM's General Counsel, Chief Operating Officer, and Chief Scientific Officer. Once these staff members have signed off on the NGA, it goes to the CIRM President for approval and signature.
   - The grants management staff then mail the NGA to the applicant/grantee. The grantee signs the NGA and returns it to CIRM. When CIRM receives the signed NGA, grants management staff members prepare a pay memo.
   - The pay memo is reviewed and signed off on by the Chief Financial Officer and the Chief Scientific Officer. Once signed/approved, the pay memo is sent to the SCO to request issuance of a warrant and release of funds to the grantee.
   - The SCO sends a warrant to the grantee. The SCO keeps the original pay memo and sends a copy of it back to CIRM with the warrant information listed on the pay memo. The pay memo is then filed in the grants file.

6. Post-Award Follow-Up

- The grantee must provide CIRM with various progress reports after the grant has been awarded. CIRM's grant administration policy lists everything that grantees must report.
- As listed in Chapter 6 of the policy, training grant grantees must report the following:

a. Estimated Budget Overview: The grantee lists the amount of the grant award, actual expenditures and any anticipated expenditures for the next budget period, and any anticipated carry forward amounts. The grantee must explain and justify any changes or any anticipated carry forward amounts. Any changes greater than 25% require prior CIRM approval.

b. Trainee Overview and Roster: The grantee institution appoints the specific trainees that will receive the training funds. In the progress report, the institution must list the number of approved trainees, the number of trainees appointed for the budget period, the number of trainees appointed for the next budget period, and the number of new trainees expected. The institution must also list each trainee, along with the appointment start and stop dates and type as well as their mentor.

c. Training Program Overview: The grantee describes the trainee selection process, the program activities (such as any seminars or workshops), the training courses implemented, any course developments or changes, any changes in program administration and staffing, and any plans or changes for the upcoming year.

d. Trainee Appointment Form: In addition to the annual programmatic report, when the institution appoints a trainee, they complete a trainee appointment form and submit it to CIRM. These forms are kept in the grant file.

e. Trainee Progress Report: The trainee also completes a progress report form, which is submitted to CIRM. This report lists what the trainee has been doing during the reporting period, including any coursework, the trainee must also include an updated Curriculum Vitae and a list of any publications they publish using CIRM support. These items are also kept in the grant file.

f. Financial Report: Financial reports are due CIRM from the grantee 90 days after the anniversary of the grant award date. CIRM sends the grantees a progress report template to use. The annual financial report must include all actual costs incurred under the CIRM grant during the expired budget period and any carry forward amounts. The report must also include any adjustments made to the grant as a result of prior approval requests or budgetary changes. Additionally, all CIRM grantees must report on interest earned on CIRM grant funds and must use those funds in support of the CIRM grant before grant close-out.

g. Annual Progress Report Funding Checklist: A subsequent year of funding for a grant is not approved until all annual progress reports are received by CIRM. The grants management staff use an Annual Progress Report Funding Checklist to check for any scope, budget, or outcome changes. A checklist is completed and signed off on by both the Scientific Program Officer and the Grants Management Officer. If any budgetary discrepancies or changes are noted, they are taken out of the next year's funding amount. For example, if the second year funding was originally approved at $100,000 but the year one progress report shows a $10,000 discrepancy, the $10,000 will be taken out of the year two funding, making the adjusted year two funding $90,000. Any funding adjustments are noted in the grants file.

APPENDIX 31

SCO Review Procedures and Results

We obtained a listing of all of the grants awarded by CIRM. From this list of 158 grants totaling $233,595,002, we selected 49 grants totaling $74,257,101 to review. The grants selected for testing covered 31% of the total number of grants and 32% of the total dollar amount of all grants.

For each grant selected, we performed the following procedures to determine whether the grant was administered in compliance with Proposition 71 and CIRM's policies and procedures.

1. Pre-Review
   - Verified that the ICOC voted on and approved a grant concept.
   - Reviewed the Request for Application (RFA) for each grant.

2. Review by Grants Working Group
   - Verified that the application and all other documents required by the RFA were maintained by CIRM.
   - Verified that the application was reviewed by two to three reviewers who do not have a conflict of interest.
   - Verified that the application is in rank 1 on the listing of recommendations to the ICOC from the GWG (and Facilities Working Group, where applicable).
   - Verified that any conflicts noted on the GWG COI Summary Sheet are included in the Public Application Summary written by CIRM staff, so that the public is made aware of members with conflicts of interest. Also verified that the Summary Sheet shows that members were recused when the application was discussed.

3. ICOC Approval
   - Verified that the COI Summary lists members who must be and were recused during discussion and voting on given applications.
   - Verified that the ICOC approved the application and the grant amount.

4. Pre-Funding Administrative Review
   - Verified that the Grants Management Officer (GMO) Review checklist is completed and signed by the GMO.
   - Verified that the Scientific Program Officer (SPO) Review checklist is completed and signed by the SPO.
   - Verified that the GMO has explained and reconciled any differences between the ICOC approved amount and the funded amount. Funding differences are noted by the GMO in instances where the applicant included ineligible costs or used incorrect or non-approved indirect cost rates. Verified that the GMO adjusted the funding amount. Also verified that the adjusted funded amount was not greater than the ICOC approved amount (any adjustments above the ICOC-approved amount would require ICOC approval).

5. Award Acceptance and Funding
   - Reviewed terms on the Notice of Grant Award (NGA).
   - Verified that the NGA is approved and signed by appropriate CIRM staff.
   - Verified that the NGA is signed by grantee.
   - Verified that the amount on the pay memo from CIRM to the SCO requesting payment on grant agrees to NGA and budget worksheet.

- Verified that the pay memo was approved by appropriate CIRM staff members.

6. Post-Award Follow-Up
   - Verified that various progress reports due CIRM from the grantee are submitted and in the grant file.
   - Verified that grants management staff complete an Annual Progress Report Funding Checklist (signed by the Scientific Program Officer and Grants Management Officer).
   - Verified that any budgetary discrepancies or changes noted on the Annual Progress Report Funding Checklist are taken out of the grantee's next-year funding amount.

Based on the grants reviewed, we determined that CIRM is allocating and administering its grants in compliance with Proposition 71 and CIRM's policies and procedures.

Exhibit 3—

Administrative Expense Review and Expenditure Testing

July 1, 2006, through December 31, 2007

The objective of our review was to determine whether CIRM's administrative expenses are in line with Proposition 71 requirements and whether CIRM expenditures were properly approved and authorized.

We designed our testing to review administrative expenses and expenditures in response to concerns brought to the SCO regarding CIRM's compliance with administrative expense limits set forth in Proposition 71, as well as concerns regarding CIRM's adherence to proper procedures, authorizations, and approval for expenditures.

Proposition 71 restricts how CIRM moneys can be spent. It limits the amount that CIRM can spend on administrative costs as follows:

• No less than 97% may be used for grants and grant oversight.
• No more than 3% may be used for general administration of the institute.
• No more than 3% may be used for research facilities implementation costs, including the development, administration, and oversight of the grant-making process and the operations of the working groups.

SCO Review procedures and results

We verified that CIRM properly categorized expenditures. SCO Departmental Accounting has a system in place to monitor expenditure categorization and to ensure that expenditure percentages are in accordance with Proposition 71 limitations.

We also obtained an expenditure summary for two time frames (July 1, 2006, through June 30, 2007) and (July 1, 2007, through December 31, 2007) and reconciled them against the detail ledger. Because the expenditures during July 1, 2006, through June 30, 2007, were reviewed during CIRM's annual financial audit, we reviewed expenditures between July 1, 2007, and December 31, 2007. The annual financial audit did not disclose any findings relating to expenditure testing.

We selected 25 expenditures for testing. The selected expenditures covered 62% ($27,230,875 out of $44,039,447) of the total expenditures for July 1, 2007, through December 31, 2007.

We verified that each expenditure was within the allowable activities of the CIRM program by determining whether:

- Adequate documentation is maintained to support all expenditures;
- Expenditures are properly authorized and put out for bid (if applicable);
- Expenditures are related to the CIRM program and salary rates are correct; and
- Contracts and personnel records (if applicable) are maintained.

We reviewed Proposition 71 in regards to the eligibility of expenditures for certain legal counsel. Proposition 71 states that given the scientific, medical, and technical nature of the issues facing the ICOC, CIRM is authorized to retain outside counsel when the ICOC determines that CIRM requires specialized services not provided by the Attorney General's Office. Therefore, CIRM is legally authorized to retain outside counsel when the ICOC deems it to be necessary.

We also reviewed CIRM's Internal Governance Policy to determine whether salary expenditures were allowable and within CIRM's administrative expense limits. We verified that the current organizational structure and number of employees were properly authorized by the ICOC and that CIRM is paying its employees in accordance with Proposition 71.

In accordance with the Internal Governance Policy, CIRM's president recommends to the Governance Subcommittee for its consideration organizational structure. The policy further states that the ICOC shall approve CIRM's organizational structure based on the recommendation of the Governance Subcommittee. The Subcommittee approved the current organizational chart and proposed it to the ICOC at the January 16-17, 2008, ICOC meeting. The ICOC voted on and approved the current Internal Governance Policy.

This policy provides the organization and administrative structure of CIRM. It stipulates that CIRM's staff, other than the President, shall be organized into four offices: Office of the President, Office of the Chair, Office of the Chief Scientific Officer, and Office of the Chief Operating Officer. It states that the Office of the Chair shall be limited to no more than six employees whose primary duties are to support the Chairperson and two employees whose primary duties are to support the Vice-Chairperson. The President may assign additional CIRM staff members to assist the Chairperson or Vice-Chairperson as necessary, consistent with CIRM's priorities. The Governance Subcommittee may review these staff allocations on a periodic basis and recommend any adjustments to the ICOC. The policy also sets forth how salaries will be set for all employees.

With regard to CIRM staff salary, the BSA audit noted that there were deficiencies with CIRM's initial salary survey and recommended that CIRM proceed with its plan to obtain another salary survey. In response, CIRM issued a request for proposal (RFP) to contract with an experienced firm for the review and survey of all CIRM salaries. CIRM subsequently contracted with Mercer Human Resources Consulting (Mercer). Mercer completed the survey and delivered the results to CIRM in 2007. We reviewed the Mercer survey results against CIRM's current salary ranges and determined that CIRM's salary ranges are within or below the Mercer results. Based on our review, CIRM's salary ranges are in accordance with Proposition 71.
Proposition 71 states that the ICOC shall, from time to time, determine the total number of authorized employees for CIRM, up to a maximum of 50 employees—excluding members of the working groups—who shall not be considered institute employees. In our review, we noted that

CIRM is operating within its 50-employee limitation and also within its administrative costs restrictions.

Exhibit 4—

Composition of Scientific and Medical Working Groups
July 1, 2006, through December 31, 2007

Appointments of scientific and medical working group members are made by a majority vote of a quorum of the ICOC. The working group members may serve a maximum of two consecutive terms; working group members' terms are limited to six years. Each working group's recommendations may be forwarded to the ICOC only by a majority vote of a quorum of the members of each working group. If 35% of the members of any working group join in a minority position, a minority report may be submitted to the ICOC.

The Scientific and Medical Accountability Standards Working Group (SMASWG) has 19 members:

- Five ICOC members from the ten disease advocacy groups described in Health and Safety Code section 125290.20;
- Nine scientists and clinicians nationally recognized in the field of pluripotent and progenitor cell research;
- Four medical ethicists; and
- The ICOC chairperson.

The Scientific and Medical Research Funding Working Group (SMRFWG), also referred to by CIRM as the Grants Working Group (GWG), has 23 members:

- Seven ICOC members from the ten disease advocacy groups;
- Fifteen scientists nationally recognized in the field of stem cell research; and
- The ICOC chairperson.

The Scientific and Medical Facilities Working Group (SMFWG) has eleven members:

- Six members of the Scientific and Medical Research Funding Working Group;
- Four real estate specialists who must be residents of California, are prohibited from receiving compensation from any construction or development entity providing services to the research facilities, cannot provide brokerage services to any research facility applicant, and shall not receive compensation from any grant recipient awarded by CIRM; and
- The ICOC chairperson.

We reviewed the BSA findings related to our review objectives and CIRM's corrective actions.

Exhibit 5—

CIRM's Corrective Actions for

Bureau of State Audits' Findings2

July 1, 2006, through December 31, 2007

Bureau of State Audits' Recommendation
CIRM's Corrective Action Noted During SCO's Review
CIRM should complete the development of its grants administration policy targeted toward for-profit organizations. At its December 12, 2007, meeting, the ICOC approved the Interim CIRM Grants Administration Policy for For-Profit Organizations to go forward to the Office of Administrative Law (OAL). OAL's notice of proposed regulation adoption states a deadline for submission of written comment of March 24, 2008.

To provide increased accountability over the grants award process, the institute should ensure that the grants review working group follows the new procedures to record its votes to recommend funding for stem cell research grants, and maintains those records.

CIRM is applying its new procedures. CIRM maintains records of the Grants Working Group (GWG) meeting. These records show members participating in a given meeting, the members recused from discussing or voting on applications due to conflicts of interest, and the members' votes. Additionally, the names of the recused members are publicly disclosed on the summary review of each application, which is given to the ICOC and posted on CIRM's Web site.

To effectively monitor the performance of the grantees, the institute should complete the implementation of a grants monitoring process, including audits, and the development of related procedures.

CIRM's grants administration process (GAP) includes a pre-funding administrative review by both the Scientific Program Officer and the Grants Management Officer prior to issuing a Notice of Grant Award. The grant is not funded until the grantees submit all required documentation as requested by CIRM.

CIRM's current GAP requires grantees to submit various progress reports to CIRM after the grant has been awarded. For CIRM's training grants (the only grants that have gone beyond the initial year of funding), the GAP lists, in Chapter 6, the reports that the grantee must submit (see Attachment B for more detail on required reporting and CIRM's Post Awards Follow-up).

The institute should follow its plans to amend its conflict-of-interest policies to include any specialists it might invite to participate in stem cell research program activities, such as grant application review.

In March 2007, the ICOC adopted a conflict-of-interest policy for the Grants Working Group (GWG) that specifically includes specialists. The GWG is currently using this policy.

Bureau of State Audits' Recommendation

CIRM's Corrective Action Noted during SCO's Review

The institute should develop the necessary procedures to ensure that its employees are aware of the companies that apply for funding to provide employees with the information they need to disclose all potential conflicts of interests.

APPENDIX 31

CIRM's current conflict-of-interest policies and procedures include a process in which all entities that have applied for funding are identified and require CIRM employees to review a listing of the entities and to note any conflicts. Employees who identify a conflict of interest with any given application are disqualified from reviewing or participating in discussions on that application. Any employee conflicts of interest are also noted and maintained in CIRM's meeting files of the GWG meeting.

To ensure compliance with its conflict-of-interest policies, the institute should revise its procedure for reviewing grants to include a review of the Statements of Economic Interest for committee members of the working groups before every grants review meeting. Moreover, it should revise its procedures for grants review meetings to ensure that it retains documentation regarding conflicts of interest of the working groups, including information that it took appropriate recusal actions.

CIRM's current procedures to identify conflicts of interest of members of the Grants Working Group include a staff review of conflict-of-interest disclosures prior to each grant review meeting. In addition, CIRM now documents the recusal actions of each member (including any specialists) with respect to each application reviewed to ensure that no one participating in the review of a particular application has a conflict of interest. CIRM maintains these records.

The committee should adopt a travel reimbursement policy for its members that will result in the reimbursement of reasonable and necessary expenses, as stated in the act, and that address the concerns we raised in the report.

The ICOC approved CIRM's Policy Governing Travel. This policy applies to all official CIRM travel and was adopted on January 18, 2008. This policy can be found on CIRM's Web site.

To ensure that the methodology to set their salary ranges complies with the act, the institute should follow through with its plan to resurvey any position whose ranges were affected by the errors, omissions, and inconsistencies in its initial salary survey and salary setting activities.

CIRM issued a request for proposal (RFP) to contract with an experienced firm for the review and survey of all CIRM salaries and subsequently contracted with Mercer Human Resources Consulting (Mercer). Mercer completed the survey and delivered the results to CIRM in 2007.

[Back to Appendices]

APPENDIX 32

32. Analysis of duration of CIRM expenditures

Matching the Expenditure of CIRM's Authorized $3 Billion to its Strategic Goals

This document follows internal discussions at CIRM about the pace at which CIRM is funding its research. It began as an effort to estimate the longevity of the $3 billion but evolved into an analysis of whether CIRM's funding programs are best targeted to achieve the goals laid out in the 2006 Strategic Plan.

Progress toward many of these goals is quite impressive. As CIRM approaches five years of research funding, its grantees are on target to accomplish most, if not all, of the 5-year benchmark goals listed in the 2006 Strategic Plan. Some, like increasing the stem cell research work force, have already been achieved. Similarly, many of the 10-year goals appear to be within reach. Thus this document will focus on the most ambitious and difficult 10-year goals, related to moving stem cell therapies into the clinic.

Initial assumptions

Over the past year CIRM has been developing a schedule of core RFAs that will repeat on a regular basis. There are several advantages to such a schedule. It provides predictability for our grantees and co-funding partners; it allows the staff to plan well in advance; and it creates a basis for projecting the expenditure of CIRM's funds. However, it is also clear that not all RFAs should repeat regularly and not all future programmatic needs can be anticipated now. Therefore, in planning future RFAs to carry through the entire $3 billion, it is important to allow for some one-time offerings and provide flexibility to meet new challenges as they arise.

With these requirements in mind a plan for future RFAs was constructed with input from the President and the Science Office. That plan is summarized in Table 1. It includes three core RFAs that repeat regularly – Basic Stem Cell Biology, Early Translational and Diseases Teams. Each addresses different stages in the research pipeline and the dollar amounts assigned to each are based on previous rounds of funding by the ICOC. Also included are two RFAs that are planned for the near future - Tools and Technologies 2 and Clinical Development - which have already received concept approval from the ICOC; four one-time programs; and an additional round of Tools and Technology (3). Finally one additional RFA is included on an annual basis beginning in 2013 but the focus is "To Be Determined". It is intended to provide flexibility for addressing unanticipated needs. A complete list of all RFAs, including those that have already been approved and funded is provided as Appendix 1.

Table 1 – Currently Planned RFA Schedule

Program	Frequency	Next ICOC Decision	Total/RFA
Early Translational	Every 15 months	October 2010	$80M
Basic Stem Cell Biology	Every 12 months	May 2011	$45M
Disease Teams	Every 24 months	June 2012	$240M
To Be Determined	Every 12 months	January 2013	$30M
Tools and Technology 2	Not regular	January 2011	$40M
Clinical Development	One time	May 2011	$50M
iPS Cell Banking	One time	TBD 2011-12	$25M
Shared Labs 2	One time	December 2011	$30M

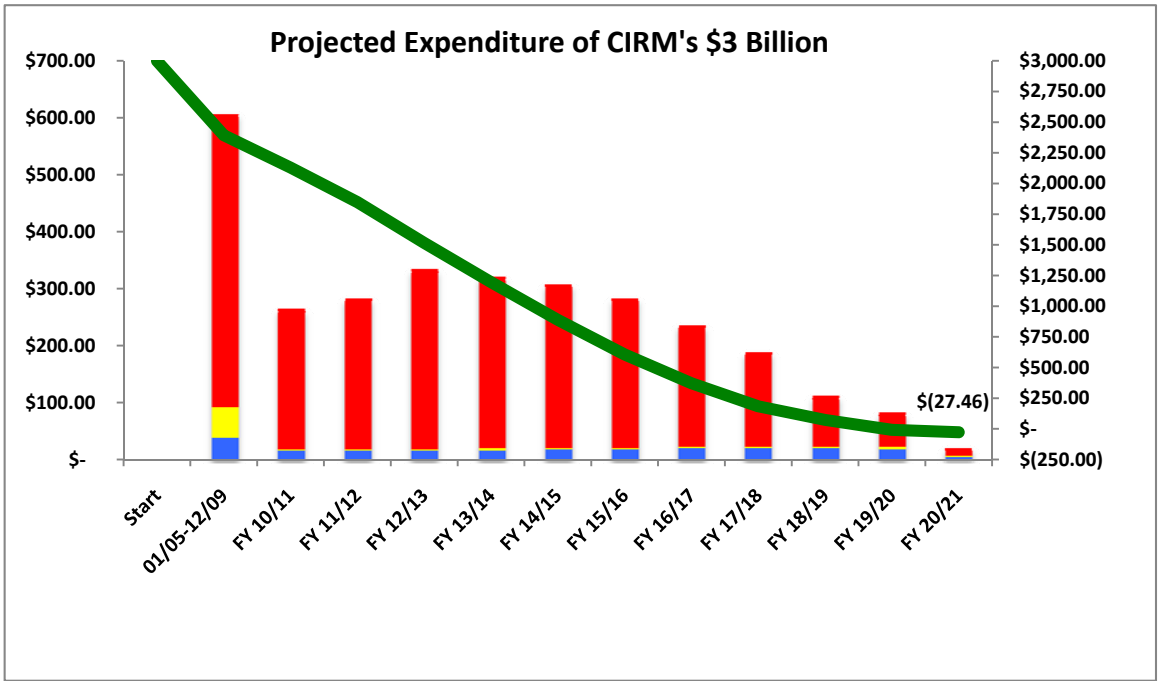
Training 3	One time	June 2012	$45M
Bridges 2	One time	June 2012	$20M
Tools and Technology 3	Not regular	October 2012	$30M

Before projecting forward to the full expenditure of CIRM's $3 billion, it is important to first explain the assumptions used in addition to the RFA schedule described above. These assumptions include the following:

1. All of the money targeted for each RFA will be committed by the ICOC. It is not unusual for the ICOC to approve projects that total more or less than the amount originally targeted for any given RFA. In this analysis it is assumed that those variances will balance.
2. It is assumed that all funds that are committed will be expended. For some RFA programs (Early Translational and Disease Teams) go-no-go decision points could result in the early termination of projects. Similarly, awards could be terminated early if the PI moves out of state or fails to make progress on the project. In those cases the amount ultimately expended would be less than the amount committed. However, CIRM is not able to predict when such savings might occur or how much they might total, so no dollar value has been assigned. See below (4 on page 7) for additional discussion of this issue.
3. No new funds will come to CIRM from revenue sharing from grantees whose CIRM-funding research is commercialized. Those funds will go to the General Fund of the State.
4. No new funds will come to CIRM from its Loan Program prior to 2020. Funds resulting from the repayment of loans or the sale of warrants will return to CIRM to support additional research. However, only one loan has been issued to date ($20 million) and it is not scheduled for repayment until 2020. Additional funds could be generated from the sale of warrants received as part of this loan, but CIRM's expectation is that this will not occur prior to 2020. As shown below it is likely that CIRM's $3 billion will be fully committed long before that date.
5. California will not approve additional funding for CIRM beyond the current authorization of $3 billion. It is likely that an effort will be made to extend CIRM's authorization beyond $3 billion. However, it is too early to gauge the likelihood of that effort succeeding. It will depend on the future economic status of California and the success of CIRM's programs in producing health and economic benefits to Californians.

With these assumptions and the RFA schedule described above and listed in Appendix 1, it is possible to project the full expenditure of CIRM's $3 billion. This is illustrated in Figure 1. Under this scenario the final RFA would be Disease Teams 4. It would be presented to the ICOC in the summer of 2016 and would terminate by the end of 2020. If any of the assumptions described above change, the projection would have to be adjusted accordingly.

Figure 1 – The columns in this graph show the annual expenditures for research and facilities (red), operations (blue) and other expenses (yellow – capitalized interest, bond issuance) based on the RFA schedule outlined in Table 1 and the assumptions listed above. The first column on the left (Jan 05-Dec 09) is based on actual expenditures and the others are projections. For each column, the values are indicated by the numbers along the vertical axis on the left (in $millions). The green line indicates the total amount of CIRM's $3 billion authorization remaining to be expended with the amounts indicated along the vertical axis on the right (in $millions). Thus the line begins at $3 billion (upper left) and declines to zero in FY 18/19 (lower right).



Is this an appropriate plan and rate for expending CIRM's $3 billion? Stem cell science is a rapidly progressing, fast moving field. However, it is still a young discipline. The next big advances to come out of basic research can only be imagined (direct re-programming; de-differentiation?) but it is not unreasonable to expect additional paradigm-shifting results in the next couple of years that will rival the impact of iPS technologies. CIRM will likely be in position to contribute to those breakthroughs but will it have enough money and time remaining to push them into the clinic? Currently, there are programs in the pipeline with potential for significant clinical benefits but, given the early stage of stem cell research and the well-documented studies of success rates in drug development, it is difficult to predict how many, if any, of them will fulfill that promise. However, as the field matures there will surely be many more therapeutic candidates and it is reasonable to predict that some of the later ones will have a greater chance of success because they will be able to take advantage of more advanced technologies.

This is a difficult issue that requires some crystal ball gazing. One could argue that the future directions of the field are unknown, so CIRM should invest as much funding as possible now to push it along and assume that other funding sources will be available in the future to develop CIRM-funded discoveries.

Alternatively, one could make the case that the greatest benefits (health-related and economic) from CIRM's investments will come from clinically proven therapies, so funds should be reserved to support those efforts when the field is more advanced. This could be accomplished by reducing the frequency of RFAs or by reducing their targeted budgets. Either (or a combination) approach would spread out CIRM's funds; permit additional cycles of funding; and allow the field to mature an additional year or two before starting the last clinical programs.

APPENDIX 32

CIRM's Strategic Plan

One instructive way to evaluate CIRM's funding strategies is to benchmark CIRM's RFA schedule against its strategic aims and industry standards for developing new therapeutics. In CIRM's strategic plan, the first, and most ambitious, of its 10-year goals states that "CIRM grantees will have clinical proof-of-principle that transplanted cells derived from pluripotent stem cells can be used to restore function in at least one disease." (i.e. will have completed a Phase 2 trial for a pluripotent-derived cellular therapy that shows safety and efficacy). What must CIRM do to be confident that it can achieve that goal? How long will it take?

In many cases, research into potential therapeutics in the early stages of development (e.g. Early Translational 1 and most Disease Team 1 projects) does not result in submission of an IND that is accepted by the FDA. Further, a number of studies show that only about 20% of drugs that enter Phase 1, first–in-man clinical trials succeed in demonstrating safety and efficacy in Phase 2 trials. Of that 20%, only about half eventually succeed in Phase 3 and make it to clinical practice. These statistics are based on small molecule drugs and biologics, such as monoclonal antibodies, and not on novel cellular therapeutics for which there are very limited data and regulatory history. Nevertheless, these odds indicate that CIRM should plan to have at least 5 pluripotent cellular therapies accepted by the FDA for Phase 1 clinical trials in order to be confident that at least one will show effectiveness in a Phase 2 study. Based on reported probabilities, *twice* that many may be required for development of a useful therapy. Further, it takes 5-10 years for a drug to get from Phase 1 through Phase 3 and to patients, but it is likely that this process will take longer for the initial pluripotent stem cell therapies because of the novelty of the therapeutic strategy, the lack of a well defined regulatory framework and, most importantly, safety concerns inherent with pluripotent cell-derived cellular therapeutics.

Currently, five of CIRM's Disease Team awards support research programs that will use pluripotent stem cells to develop therapies. They are slated to submit INDs to the FDA by 2014. While some are likely to make or, perhaps, even beat that target, others probably will not. The next round of disease team applications is scheduled to go to the ICOC for approval in June 2012 and a Clinical Development RFA is being planned that could fund up to two projects using pluripotent stem cells for Phase 1-2 trials beginning in mid-2011.

To determine the number of INDs, the time and the investment required to reach the above stated goal of developing a pluripotent cell-based therapy through Phase 2 trials, the following assumptions were used:

1. A minimum of 5 FDA-accepted INDs will be required.
2. Half of the Disease Team awards that fund projects using pluripotent stem cells will lead to FDA-accepted INDs in 4 years.
3. In 2011 CIRM will provide support for clinical trials for 2 pluripotent cellular therapies with FDA authorization to initiate testing in humans.
4. The time period from IND approval to the completion of a Phase 2 trial (not Phase 3) will be 5 years.
5. Each project with an accepted IND will require $15-25 million (mean $20 million) from CIRM to proceed through a Phase 2 trial (if additional funds are required, they would have to come from other sources).

Table 2 summarizes these assumptions and projected timelines.

Table 2 – In column 3 (Pluripotent SC projects) all numbers are estimates except for Disease Team 1. It is assumed that the RFAs for Disease Teams 2 and 3 will both be valued at $240 million and each will include 6 projects with pluripotent stem cells. In column 4 (INDs in 4 years) the numbers are estimated. However applicants for Clinical Development funding in 2011 must already have an FDA-accepted IND by the time of funding.

RFA	Start Date	Pluripotent SC projects	INDs in 4 years	Clinical trial funding date ($20M each)	Phase 2 - completion date
Disease Teams 1	2010	5	2	2014	2019
Clinical Development	2011	2	2 (obtained)	2011	2016
Disease Teams 2	2012	6	3	2016	2021
Disease Teams 3	2014	6	3	2018	2023

Based on the assumptions used to create Table 2, it seems unlikely that the goal - "…clinical proof-of-principle that transplanted cells derived from pluripotent stem cells can be used to restore function in at least one disease" – can be reached in the original 10-year time frame (by 2016) unless a recipient of a Clinical Development Award proceeds quickly and successfully through Phase 2. It is more reasonable to anticipate that this milestone can be achievable by 2021, but for that to happen it is likely that CIRM would have to make clinical trial funding commitments between 2014 and 2017. This would require a reassignment of funds from RFAs planned for those years since, under the current schedule, no funds are earmarked for clinical trials beyond the two Clinical Development Awards planned for next year. Further, all funds will be committed by the end of 2016 (except for those that are returned from previously approved projects that did not meet key milestones or successfully pass go-no-go decisions - see assumption #2, page 2, above; and #4, page 7, below).

Alternatively the level of grant funding over the next 2-3 years could be reduced in an effort to reserve more funds for projects later in CIRM's lifespan. This could include projects that take advantage of future technologies and projects that are ready for testing in humans but need additional financial support. For example, if the budgets for the next 3 rounds of Disease Team RFAs (Disease Teams 2-4) were reduced from $240 million to $180 million it would preserve an additional $180 million that could fund new research initiatives or up to 9 clinical trials at the later stages of CIRM's lifespan. This would likely reduce the number of candidate cellular therapeutics with IND approval by 2017 but it would reserve funds to help push the most successful ones into the clinic.

There are other important issues to consider in evaluating these plans.

1. This analysis of CIRM's RFA schedule has focused on one specific goal listed in the strategic plan of 2006. However, programs were also retained (e.g. Basic Biology, Early Translational and Disease Teams) that would continue supporting projects at all stages along the research pipeline until the end of the Institute's lifespan, even though CIRM would not be able to deliver many of those projects to the clinic. This approach was supported in the 2006 Scientific Strategic Plan and it ensures that CIRM will always be funding research at the leading edge of the stem cell field. Assigning proportionality in this funding approach is an important strategic decision that the External Review Panel should consider.

2. This plan focuses only on the first of the Ten-Year Goals listed in CIRM's Strategic Plan and there are nine others (see Attachment 2). For example, the second Goal states – "CIRM grantees will have therapies based on stem cell research in Phase 1 or Phase 2 clinical trials for 2-4 additional diseases." Given the breadth of this goal, it is quite reasonable to expect that it will be achieved. In fact, one clinical study of polycythemia vera already meets this standard. However, future projects in this category may need support from CIRM in order to initiate Phase 1 and/or Phase 2 trials. Therefore, reserving more funds for later in CIRM's lifespan could certainly benefit these projects too.

3. There are eight additional Ten-Year Goals listed in the 2006 Strategic Plan. Many of them will rely heavily on basic research, if they are to be achieved, so CIRM cannot stop investing in the early phases of the research pipeline.

4. CIRM makes its research funding predictions based on the expectation that the approved research programs will be successful. However, it is likely that some research investments will be returned and the amounts could be significant if large projects (Early Translation or Disease Teams) fail to meet go-no-go milestones or if they are terminated for other reasons. However, the amount that might be retained by CIRM is very difficult to predict, as is the timing, especially since the first projects with go-no-go decision points are just beginning. If it is assumed that 10% of all research investments made from this point forward will be returned to CIRM to be used for future RFAs, the total would be less than $200 million (10% of the remaining, uncommitted $1.9 billion). Such funds could be used to increase the amounts of future RFAs or to support additional RFAs, including clinical trials. However, CIRM's management is not comfortable making strategic decisions about future research funding based on projects that might fail. It seems more appropriate to assume that all projects will succeed and then readjust later, if additional funds become available.

5. Should the 2006 Strategic Plan be modified? This is a core question and challenge for the external review panel. Should some of the goals be changed or should their timelines be adjusted? Should others be deleted and replaced by new goals. How should CIRM invest its remaining funds to maximize the chances that it will meet its mission to bring health and economic benefits to the citizens of California?

APPENDIX1 - This table is a full list of RFAs based on Table 1.

RFA	RFA Number	Amount	Stage	Start Date
Training 1	RFA 05-01	37,253,385	Current Program	
Seed	RFA 06-01	42,233,826	Current Program	
Comprehensive Research	RFA 06-02	67,313,412	Current Program	
Shard Labs	RFA 07-01	49,047,039	Current Program	
New Faculty 1	RFA 07-02	53,720,258	Current Program	
Major Facilities	RFA 07-03	270,946,931	Current Program	

APPENDIX 32

RFA	RFA Number	Amount	Stage	Start Date
Disease Team Planning	RFA 07-04	1,175,368	Current Program	
New Cell Lines	RFA 07-05	24,449,174	Current Program	
New Faculty 2	RFA 08-01	59,292,558	Current Program	
Tools and Technology 1	RFA 08-02	19,253,974	Current Program	
Bridges to Stem Cell Research 1	RFA 08-04	23,873,044	Current Program	
Training 2	RFA 08-03	44,988,409	Current Program	
Basic Biology 1	RFA 08-07	16,288,581	Current Program	
Early Translational 1	RFA 08-05	70,401,825	Current Program	
Conference Grants	RFA 08-06		Current Program	
Disease Team 1	RFA 09-01	224,984,899	Current Program	
CIRM Leadership Award	RFA 09-04	44,800,000	Review Stage	April - June 2010
Basic Biology 2	RFA 09-02	30,000,000	PFAR Stage	July - September 2010
Immunology	RFA 09-03	30,000,000	PFAR Stage	July - September 2010
Early Translational 2	RFA 10-01	80,000,000	Review Stage	January - March 2011
Tools and Technology 2	RFA 10-02	40,000,000	Review Stage	April - June 2011
Clinical Trials		50,000,000	Concept Approved	July - September 2011
Basic Biology 3		45,000,000	Future Program	July - September 2011
Disease Team 2 Planning		3,300,000	Future Program	October - December 2011
Shared Labs 2		30,000,000	Future Program	January - March 2012
IPS - banking		25,000,000	Future Program	April - June 2012
Early Translational 3		80,000,000	Future Program	April - June 2012
Bridges 2		25,000,000	Future Program	July - September 2012

RFA	RFA Number	Amount	Stage	Start Date
Training 3		45,000,000	Future Program	July - September 2012
Basic Biology 4		45,000,000	Future Program	October - December 2012
Disease Team 2 Award		240,000,000	Future Program	October - December 2012
Tools and Technology 3		30,000,000	Future Program	January - March 2013
To Be Determined 1		30,000,000	Future Program	April – June 2013
Early Translational 4		80,000,000	Future Program	July/September 2013
Basic Biology 5		45,000,000	Future Program	October - December 2013
Disease Team 3 Planning		3,300,000	Future Program	October - December 2013
To Be Determined 2		30,000,000	Future Program	April – June 2014
Disease Team 3 Award		240,000,000	Future Program	October - December 2014
Early Translational 5		80,000,000	Future Program	October - December 2014
Basic Biology 6		45,000,000	Future Program	October - December 2014
TO Be Determined 3		30,000,000	Future Program	April – June 2015
Disease Team 4 Planning		3,300,000	Future Program	October – December 2015
Early Translational 6		80,000,000	Future Program	January - March 2016
Disease Team 4 Award		240,000,000	Future Program	October – December 2016

* Start Date is about 3 months after ICOC approval

APPENDIX 2

Ten-Year Goals (from "CIRM Scientific Strategic Plan" - December, 2006 – pp 34-36)

CIRM commits to the following 10-year goals:

- Goal I: CIRM grantees will have clinical proof-of-principle that transplanted cells derived from pluripotent cells can be used to restore function for at least one disease.
- Goal II: CIRM-sponsored research will have generated therapies based on stem cell research in Phase I or Phase II clinical trials for two to four additional diseases.
- Goal III: CIRM-funded projects will have achieved sufficient success to attract private capital for funding further clinical development of stem cell therapies.

- Goal IV: CIRM will have funded new approaches for achieving immune tolerance for transplantation that are in pre-clinical development.
- Goal V: Using stem cell research, CIRM-funded investigators will have established proof of principle in preclinical animal models for the treatment of six to eight diseases.
- Goal VI: CIRM-funded investigators will have created disease-specific cell lines for 20 to 30 diseases and used them to gain new information about pathogenesis, to identify new drug targets and to discover new therapeutics.
- Goal VII: CIRM will have enabled development of new procedures for the production of a variety of stem and/or progenitor cells that meet GMP requirements.
- Goal VIII: Through research sponsored by CIRM and others, a thorough description of the steps of differentiation leading to the production of the various cells of the body will have been achieved.
- Goal IX: Through research sponsored by CIRM and others, the mechanisms regulating the self-renewal and oncogenic potential of embryonic stem cells and their derivatives will have been identified and characterized
- Goal X: CIRM will have enabled development of new methods for tissue replacement based on stem cell research.

[Back to Appendices]

33. Proposed new loan terms

CIRM LOAN TERMS

Type of Loans: CIRM offers *Company-backed* and *Product-backed* loans. The recipient of a Company-backed loan is required to repay CIRM, regardless of the success of the CIRM-funded project while the obligation of a recipient of a Product-backed loan to repay CIRM may be suspended or forgiven based on the status of the CIRM-funded project.

Term of Loan: 5 years, extendable at the option of the loan recipient up to a maximum of 10 years provided that, each year following the 5th year, the loan recipient shall repay 25% of unpaid, accrued interest and the interest rate shall increase 1%.

Collateral/Personal Guarantee: Not required.

Repayment: Principle and accrued interest are payable on last day of loan term, unless repayment obligation has been suspended, forgiven, or accelerated.

Interest: Compound interest set at LIBOR plus 2% for the 5-year term; interest rate increases by 1% in each year following the 5th year.

Warrant Coverage: Company-backed loan: lesser of 20% of Loan Recipient's shares, fully diluted and: (1) 10% of the Loan Amount if Loan Recipient shows a profit for previous 2 years; (2) 25% of the Loan Amount if Loan Recipient has: (a) raised in prior financings since its inception 3x the total amount of the loan; AND (b) entered into a contractual arrangement (still in effect) with a biotechnology or pharmaceutical company which requires the payment of licensing revenues or milestone payments predicated on the success of a funded project (regardless of whether it is a CIRM Funded Project); or (3) 50% of the Loan Amount if Loan Recipient has met only one of the two requirements set forth above in (2); 75% of the Loan Amount if none of the criteria set forth in (2) are satisfied.

Product-backed loan: lesser of 20% of Loan Recipient's shares, fully diluted and: (1) 50% of the Loan Amount if the Loan Amount is less than 50% of the total funds required to complete the CIRM-Funded Project as defined in the activities based budget attached to the Notice of Loan Award; (2) 60% of the Loan Amount if the Loan Amount is less than 75% of the total funds required to complete the CIRM-Funded Project as defined in the activities based budget attached to the Notice of Loan Award; or (3) 100% of the Loan Amount if the Loan Amount represents more than 75% of the total funds required to complete the CIRM-Funded Project as defined in the activities based budget attached to the Notice of Loan Award.

Price of Warrants: Public companies = closing price of the loan recipient's common stock on the business day immediately before CIRM disburses funds; private companies = the share price from the most recent round of equity financing prior to disbursement; if no previous round, the warrants are floated until next round.

Expiration of Warrants: 10 years from date of issuance.

Transfer of Warrants: Warrants are transferrable.

Intellectual Property: Loan recipient owns IP; revenue sharing provisions of CIRM's IP regulations do not apply.

[Back to Appendices]

34. Cell Stem Cell Article

Cell Stem Cell
Forum

Developing a Case Study Model for Successful Translation of Stem Cell Therapies

Alan Trounson,[1,*] Elona Baum,[1] Don Gibbons,[1] and Patricia Tekamp-Olson[1]
[1]California Institute for Regenerative Medicine, 210 King Street, San Francisco, CA 94107, USA
*Correspondence: atrounson@cirm.ca.gov
DOI 10.1016/j.stem.2010.05.008

Cell therapies derived from pluripotent stem cells are entering the preclinical and early clinical development phase, but eventual translation faces many challenges. We describe a new approach by California to form global public-private "disease team" partnerships to enable new clinical opportunities to be evaluated in the complex regulatory environment.

There are three key elements that must be present to ensure the clinical translation of candidate stem cell therapies. The first two are obvious. There needs to be adequate funding, and the therapies need to be shown to be safe and efficacious in accordance with regulatory requirements. Third, and perhaps less obvious, is in order to accelerate and perhaps even succeed in demonstrating safety and efficacy of these novel therapies, researchers need to work in multidisciplinary, collaborative teams (U.S. Department of Health and Human Services, 2005).

The opportunity for stem cell science to lead to therapeutic benefit is increasing as evidenced by rapid advances and reproducible results in so many parts of the field from self-renewal and differentiation to reprogramming pluripotentiality. There are also challenges to realizing this opportunity. The business climate is presently difficult, but it seems to be particularly challenging for therapies originating from pluripotent stem cells or genetically manipulated adult stem cells. Venture capital is increasingly risk-averse and intolerant of waiting for long-term payouts. Product regulatory bodies are acting with caution, and insurers and healthcare payers have yet to determine whether health-care reform will allow them to benefit from regenerative therapies that are likely to require many years to accrue sufficient savings to cover upfront costs.

Sustained funding will be critical because the complex nature of the delivery and monitoring of stem cell treatments will result in an extended time frame for development of many therapies. Candidate small molecule and protein therapeutics arising from stem cell research would be expected to reach the clinic more quickly than pluripotential stem cell treatments or even genetically modified adult cells. Yet, with the field promising to significantly alter healthcare by delivering not just incremental improvements but potentially cures, this is an area that warrants investment and, even in these difficult economic times, public financial support.

With most funding sources pressuring research to increase speed to the market at the same time the Food and Drug Administration (FDA) and other regulators are showing caution with some new avenues to therapy, industry publications and conferences have started to discuss the theory that the best way to increase speed to market without increasing risk is via industry-industry collaboration and cooperation to solve the common preclinical chalenges in the precompetitive space (Brainloop, Inc., 2010; Cambridge Health Institute, 2010). We postulate that while this aspect of collaboration can help, a broader, more effective way to accelerate the path from research bench to clinic is to foster academic-industry collaborations that are structured in a manner that is more focused than these relationships have been in the past. Academic stem cell biologists and those clinicians who will be responsible for testing these treatments can answer questions that are blocking a particular path to the clinic and may be able to take advantage of more favorable licensing and Material Transfer Agreements (MTAs) offered to academia. A discussion on risk involving regulators, industry and academic team members, patient advocates, and clinicians who will be involved in delivery of the candidate therapy may be more productive in looking at new measures of risk. Also, since existing cell-based therapies, largely from bone marrow, have generally relied on academic-based clinical trials and early roll-out, creating those partnerships that include clinical staff at the beginning can cut steps and time to a marketable product.

A test case of this hypothesis is now underway. In October 2009, the California Institute for Regenerative Medicine (CIRM) awarded 14 Disease Team Awards (CIRM, 2009), averaging over U.S. $16 million each, and involved some level of academic-industry partnerships to achieve the team goal of filing an Investigational New Drug (IND) application within 4 years to begin a clinical trial. Four of the five awards for pluripotent-derived therapies have industry participation, as do three of the five genetically manipulated adult stem cell therapies. Two of the three targeting cancer stem cells have industry participants. In these first awards, the grants were awarded based on scientific merit and the potential to achieve an IND filing. Hence, several grants targeted the same disease. Given the probability of success for any of the awards is far from assured, CIRM decided not to restrict the awards programmatically on this occasion.

Incentives for Translational Research

As Dr. Susan Desmond-Hellmann, Chancellor of UCSF and former President of Product Development at Genentech, stated at CIRM's recent grantee conference, "what matters to patients is not that these therapies get into a clinic, but rather that they ultimately get approved

Cell PRESS

Cell Stem Cell
Forum

for wide use in patients." It is not getting into clinical trials that matters; it's getting commercial approval for use in all patients that could benefit. This requires funding of the complete program from preclinical translational studies to the safety and proof of concept of benefit to patients, commonly referred to as Phase I and IIA/B clinical trials. There is very little funding available from investment financing or pharmaceutical company support for this component of the development chain.

It is necessary for private foundations and public funding initiatives, such as NIH's expenditures on Clinical and Translation Science Centers, to fill the void left by the virtual exit of angel funders (investors interested for simply programmatic reasons) and venture capital from the translational phases of stem cell research. In the present difficult economic environment, it is challenging to persuade government to contribute to funding medical research despite the acknowledged economic return of such investments because the benefits are long term and budget shortfalls are acute (Murphy and Topel, 2003; Health Economics Research Group, 2008). The long-term benefits for the economy and for health require funding that is reliably sustained for decades. This enables the discovery process to mature and the translational phase to support proof of concept. Few public agencies adequately support the translation phase, and even those that do require multiple grant application rounds to enable a new product, such as stem cells, to reach a mature stage attractive for private investment.

CIRM has decided to invest significantly in preclinical and clinical research with grants of up to U.S. $25 million for pluripotent-derived stem cell candidate clinical trials, up to U.S. $20 million for each "Disease Team" research award and up to U.S. $6 million each for "Early Translational" research awards. These awards are large enough to support multiple phases of preclinical-clinical development through a single grant application and have been supplemented with additional funding by collaborative funding partners in other nations and, in some instances, further leveraged by funds from the grantee.

The size of the grants available and the potential to collaborate within California and with overseas and interstate researchers has dramatically incentivized the research community. There are a very large number of applications submitted to CIRM in response to calls for applications, many with merit for support.

Global Collaborations Accelerate Research Benefits

Team research is effective in achieving high impact developments because of its speed of producing innovative high quality data. This is true on a national scale and an international scale, but there are relatively few funding bodies that support international collaborations between multiple public and private teams. The European Framework Programme and NIH have such collaborative initiatives, but they are limited in number and in the level of funding available for translational research. While some countries have some private-public funding mechanisms, they are still relatively rare and don't provide comprehensive funding for the full translational process, particularly for stem cell research. One partial exception is seen in Spain, in the form of the Andalusian Initiative for Advanced Therapies (Cuende and Izeta, 2010, this issue). Klein and Trounson have argued that state or international bond funded initiatives for such purposes can be a very effective approach to stimulate these arrangements with little direct influence on public debt repayments before substantial economic returns are generated (Klein and Trounson, 2010). They argue returns to California on the bond sales are likely to be substantial as debt repayments are offset for 5 years in the capital raising, and taxation benefits accrue as buildings are erected and academic and biotechnology components expand. Clinical trials have already been initiated with potentially large savings on the state's healthcare budget expected.

CIRM has taken a very proactive role in creating international collaborative agreements to cofund stem cell research. These agreements enable scientists to jointly submit research team applications for review by CIRM's international review panels (excludes Californian reviewers) and the collaborating national or state review panels if necessary. The agreements include the State of Victoria, Australia, the Canadian Cancer Stem Cell Consortium, the UK Medical Research Council, the Japanese Science and Technology (JST) organization, the Chinese Ministry of Science and Technology, Spanish Ministry of Science and Innovation, German Ministry of Education and Research, and the U.S. State of Maryland and the New York Stem Cell Foundation.

Globalizing collaborations provides opportunities for different communities to participate in the development of a new area of research and to ensure that the priorities of these communities are included in determining the direction of the research. Consequently the emphasis on cancer stem cells is driven by both Californian and Canadian researchers as a priority for their communities. Certain diseases that may dominate in one community may be less frequent in another but collaborative research tends to be inclusive of these needs. For example, the need for affordable cures for diseases such as HIV/AIDS and malaria becomes evident when global health priorities are considered.

Regulatory Approval: Drugs and Biologics versus Cell Therapies

While CIRM's funding of the translational phases of the research pipeline will provide the critical financial support needed to meet the first condition laid out above for success in this field, the second element, proving safety and efficacy, will be more challenging. Unlike for biologics and small molecules, the regulatory pathway for stem cell-derived therapeutics is not well defined and, hence, not well understood. While the biologic and small molecule industries benefit from a well-defined regulatory pathway and commonly accepted best practices for preclinical safety testing, product characterization, and measures of purity and potency, the same cannot be said for product development for the stem cell industry. Certainly, there are a number of autologous stem cell therapies in clinical trial as well as some allogenic adult cell therapies, but pluripotent and genetically manipulated stem cell therapies are experiencing significant delays in entering into the clinic (Plagnol et al., 2009). While it may be argued that companies need to address significant concerns of the regulators, the

Cell Stem Cell
Forum

burn rate of capital while waiting for additional data and approval to proceed makes survival particularly difficult for any corporate entity with limited financial flexibility (McKernan et al., 2010, this issue). While the FDA is not insensitive to the situation, many unknowns remain in this new field that can delay approvals, despite the best intentions of all parties.

The US federal government has taken steps to address the issue. The FDA is in active discussion with industry, in part through the Regenerative Medicine Consortium, which was convened by CIRM and has a mix of industry and academic participants. FDA Commissioner Margaret Hamburg's emphasis in regulatory science may ultimately provide more tools and regulatory certainty to the field. Likewise, NIH has declared its intention to work with the FDA as well.

There are concerns that the relative ease of obtaining regulatory approval for clinical studies for transient cell therapies, such as those based on autologous bone marrow implantations for a wide variety of disorders without solid scientific rationale, may be counterproductive for regulatory support of regenerative therapies involving pluripotent stem cell derivatives. Others see these as a logical order for the relative risk versus benefit.

Developing a Symbiotic Team Approach

In the absence of well-defined regulatory requirements for the development and approval of pluripotential and genetically manipulated stem cell therapeutics, it is necessary to have sufficient innovative expertise on the team to address the concerns of regulators. The knowledge base for new developments in stem cell biology generally resides in the academic research community and in biotechnology companies with a substantial research capacity or those well connected to academic research groups. The academic community is, however, generally less well prepared for the highly regulated aspects of product development, particularly those relating to toxicological testing, consistency, and source of product as required for cGMP (current Good Manufacturing Practices) manufacturing, etc. Academic scientists are, in many instances, less familiar with the timeline and milestone demands of industry, where delays in product development are very costly, not only to the funder but potentially to the patient. There is clearly a potential symbiotic relationship between academic research talent and the know-how of the biotechnology industry. In fact, it is difficult for one to make major advances without the other in the present relative absence of significant venture capital.

The depth of research resources in the university sector and the considerable infrastructure there is of immense value to biotechnology companies that have limited capital. The companies, in turn, can keep academic scientists focused on the critical developments needed for regulatory filing. Hence, merging the resources provided by companies and academic research institutions can create the ideal team.

CIRM has implemented an active team management approach for its multidisciplinary Disease Teams. The approach is based on best practices following discussion with individuals whose expertise and relevant experience derives from academia, the biotechnology and pharmaceutical industries, and from private foundations (CIRM, 2007).

Challenges to translational research teams include maintaining focus, ensuring that the scope of the research conducted best addresses the project goal, and maintaining good communication among team members and with funders. For Disease Team projects, each team is required to have a project team leader(s) and a project manager with development experience to ensure team direction, focus, energy, and communication. Prior to the start of funding, to further facilitate successful project outcomes, each team, together with CIRM, develops mutually agreed upon timelines for key project activities and determines milestones that reflect critical measures of project progress and go/no go decision points. These, in conjunction with an activity based budget, help teams to refine project plans to ensure that all necessary research is conducted, and that the time and funding allowed for the conduct of the research activities are sufficient and reasonable.

The response of the Disease Team investigators to the new funding format opportunity has been exceptional, given that academics are rarely organized in such a targeted and highly focused manner. These academic-industry partnerships could provide ongoing benefit in future steps as well. It is anticipated that, like bone marrow and organ transplantation, many new cell therapies are likely to be delivered in tertiary clinical settings that will involve academic and community clinicians and networked stem cell clinics that may be partnered with companies supplying specific reagents and cell products.

Public-Private Partnerships for Translation Established by CIRM Funding

In the area of human embryonic stem cells (hESCs), the studies on dry macular degeneration at the University of Southern California, University of California (UC) Santa Barbara, and University College London are further enhanced through collaboration with the company Geron and the Center for Applied Technology Development (CATD) at City of Hope, which serves as a national academic biologics manufacturing resource. Geron and CATD provide cell banks, cGMP manufacturing, and expertise for regulatory requirements. A study on ESCs derivatives for treatment of stroke at Stanford University has a collaboration with Progenitor Cell Therapy, a company that provides the expertise in product and assay development and cGMP manufacturing for the therapeutic candidate. This team is also working with SRI whose expertise in toxicological testing and their successful record in medical product development are major assets. Progenitor Cell Therapy will also be participating in the development and manufacture of neural stem cells on behalf of a team at UC San Francisco in support of their efforts to leverage the homing ability of these cells to deliver drugs to treat glioblastoma. The team from UC San Diego and the Salk Institute are working with Life Technologies Inc. for the scale-up, differentiation, and purification of ESCs to astrocyte precursors and cGMP manufacturing for treatment of Amyotrophic Lateral Sclerosis (ALS). For diabetes, the company ViaCyte Inc. has several associations with academia, including a critical collaboration on immune modulation with UC San Francisco.

For genetically modified adult stem cells, the team at the City of Hope that

is devising permanent resistance to HIV/AIDS is using Sangamo Biosciences' novel zinc-finger nuclease (ZFN) technology to disrupt the gene CCR5 in hematopoietic stem cells (HSCs), which encodes a critical HIV coreceptor in blood cells. The team at UC Los Angeles is mimicking a naturally occurring mutation in CCR5 by transducing the patient's HSCs using a shRNA. They are partnered with City of Hope's CATD and with Calimmune Inc., who provide expertise in preclinical development and product commercialization. According to the Principal investigator Dr. Chen, "traditionally, research, drug development, and clinical medicine were three virtually separate endeavors…CIRM created a funding mechanism that breaks down the barriers to this critical interaction." (Atchison, 2010).

Connecting to the End User

While organizations like CIRM are unable to maintain financial support beyond Phase II studies of proof of concept for human efficacy, it can provide the data that make the project more attractive for Phase III partnerships involving venture funding and major pharmaceutical company support. However, with the costs of clinical trials spiraling out of control with estimates now approaching U.S. $4 billion per drug (Munos, 2009), it seems unlikely that the present model is sustainable, particularly for smaller market diseases. It is apparent that government may need to coinvest and to persuade the health insurance companies to also join in supporting biotech and pharma in the clinical trials. Government and health insurance companies are beneficiaries of cures and improvement in the quality of life of patients with serious diseases. With the increasing number of clinical trials proposed for cell therapies, there is an urgent need to address this issue.

WEB RESOURCES

Atchison K.A. (2010). Inventor Spotlight: Professor Irvin Chen and Calimmune, Inc. The Inventor (http://oip.ucla.edu/publications/Newsletter_Winter_Quarter_09_10.pdf).

CIRM (California Institute for Regenerative Medicine) (2007). The California Institute for Regenerative Medicine Disease Team Workshop Report. (http://www.cirm.ca.gov/pub/pdf/DTW_Report.pdf).

CIRM (California Institute for Regenerative Medicine) (2009). CIRM, the UK and Canada Award more than $250 Million to Accelerate the Pace of Bringing Stem Cell Therapies to the Clinic. (http://www.cirm.ca.gov/PressRelease_102809).

U.S. Department of Health and Human Services (2005). 2020: A New Vision: A Future for Regenerative Medicine. (http://www.hhs.gov/reference/newfuture.shtml).

REFERENCES

Brainloop, Inc.. (2010). White Paper: Seamless life sciences collaboration (Boston, MA: Brainloop, Inc.).

Cambridge Health Institute. (2010). Conference: Second Annual Collaborative Innovation in Biomedicine, Strategies and Best Practices for Pre-Competitive Sharing of Data, Results and Costs.

Cuende, N., and Izeta, A. (2010). Cell Stem Cell *6*, this issue, 508–512.

Health Economics Research Group. (2008). Medical Research: What's it worth? Estimating the economic benefits from medical research in the UK (London: UK Evaluation Forum).

Klein, R.N., and Trounson, A. (2010). A New Political-Financial Paradigm for Medical Research: The California Model. In The Delivery of Regenerative Medicines and Their Impact on Healthcare, C. Prescott and J. Polak, eds. (Boca Raton: Taylor & Francis), in press. 978-1-4398360-6-4.

McKernan, R., McNeish, J., and Smith, D. (2010). Cell Stem Cell *6*, this issue, 517–520.

Munos, B. (2009). Nat. Rev. Drug Discov. *8*, 959–968.

Murphy, K.M., and Topel, R.H. (2003). The Economic Value of Medical Research. In Measuring the Gains from Medical Research: An Economic Approach, K.M. Murphy and R.H. Topel, eds. (Chicago: University of Chicago Press), pp. 41–73.

Plagnol, A.C., Rowley, E., Martin, P., and Livesey, F. (2009). Regen. Med. *4*, 549–559.

[Back to Appendices]

APPENDIX 35

35. Alpha Clinic model for therapy roll-out

The Alpha Stem Cell Clinic Model for Application of Stem Cell Therapies

Alan Trounson
California Institute for Regenerative Medicine

Summary
Cellular therapies will involve the careful preparation, expansion, characterization and delivery of cells in a clinical environment that has GMP or near equivalent facilities. The delivery systems will be specialized and require well-trained cell culture biologists. Nursing staff and patient counselors experienced in clinical trails will be needed as well as specialist medical staff. The model proposed for Alpha Clinics utilizes the capacities that exist in the most advanced tertiary medical clinics for delivery of established bone marrow stem cell therapies and for introducing improved procedures and cell preparations as the research evolves. This model enables commercialization of medical devices, reagents and other products required for cell therapies but avoids the high-cost drug model that involves the pharmaceutical industry.

Introduction
The average cost of delivery of a new drug into medical practice has blown out to more than $3.9 billion including capital costs and the costs of failed drugs (1). It will be difficult for the new generation of cell therapies to generate sufficient revenue to offset the present well-defined but very expensive drug regulatory pathway to the clinic. There are simply insufficient investors and pharmaceutical or biotechnology companies with interest in cell therapies to enable this to occur. The use of stem cell derivatives as a product is not well understood nor does their use for treatments as cures fit into the business approach that benefits from ongoing use of a product to generate significant long-term profits.
In the absence of venture capital and major company interest it is likely that the academic-biotechnology partnerships that are forming (2.) will find an alternative system to enable the clinical trials and progress to clinical acceptance. In many respects this is already happening with bone marrow and umbilical cord blood transplants. The major cancer clinics and hospitals with hematologists provide these services to patients. The very successful Assisted Conception Clinics that provided wide-spread in vitro fertilization (IVF) also evolved through major clinics attached to Universities and clinical research organizations (3, 4).

The Alpha Stem Cell Clinic
The concept that primary stem clinics be identified in association with major medical centers that have the clinical infrastructure and are presently involved in clinical phase I-III studies for cell therapeutics is relatively straight forward. These clinics would need to have access to GMP facilities to enable the preparation of cell products, and where appropriate their purification, expansion and characterization, as well as cryostorage. While hematopoietic stem cells (HSCs) cannot be expanded, mesenchymal and adipose stem cells can. New cells such as cardiomyocytes can also be expanded for use in autologous transplants for myocardiopathy (5). The cost for cell biologists to properly manage the cell products is not unlike the necessity for embryologists at in vitro fertilization (IVF) clinics. The possibility of genetically modifying autologous HSCs for a range of applications such as targeting inoperable glioma (6) or gene therapy (7) are an additional complexity normally provided by Bone Marrow Transplant Units attached to tertiary medical centers. The need to prepare hematopoietic stem cells (HSCs) from mobilized marrow cells induced by specific growth factors, to purify those cells, and often, to genetically modify them will require cell biology expertise that will be very specialized and demanding. As an example, the

gene therapy associated with targeted interruption of genes that could be a cure for HIV/AIDS relies on the isolation of HSCs and disruption or interference in the CCR5 gene – a critical co-receptor for HIV binding to blood cells (8).

The clinical environment will need to include specially trained support staff, including those with the essential role for counseling patients, as is needed in the IVF clinics and Bone Marrow Transplant Units (9). The clinic will also need advanced cell separation equipment, cell culture facilities, molecular biology technology, cell monitoring equipment and access to a GMP laboratory.

These capacities already exist in some advanced medical facilities such as City of Hope and Cedars Sinai Medical Center in Los Angeles, and some University of California Medical Centers. These may well evolve to become the Alpha Stem Cell Clinics and there are good reasons to encourage them to be recognized as CIRM Alpha Stem Cell Clinics – providing cutting edge stem cell therapies for conditions where there is evidence of safety and efficacy from recognized clinical trials. This model would strongly attract patients who are seeking therapeutic intervention for otherwise intractable disease and serious injury. The proper counseling of potential benefit and risk would be enabled by well-informed professional counselors.

This model deviates from the drug model of small molecules and biologics that the pharmaceutical industry is required to follow and creates a paradigm that would place responsibility for treatment quality assurance with major tertiary clinics and their Research and Ethics Oversight Committees. Possibly significant savings could accrue for the stem cell therapies, when compared with new drug candidates, if they follow the standards set by the Bone Marrow Transplant Service Units.

CIRM should explore this concept and be prepared to endorse and assist the development of the Alpha Stem Clinic concept in cities in California. It is also important to consider seeding a few of these clinics in under-resourced environments where there is high quality clinical capacity in order to enable the widest possible access of all Californians to evolving stem cell therapies.

References

1. Munos, B. (2009). Nat. Rev. Drug Discov. 8, 959–968. CrossRef | PubMed)
2. Trounson A, Baum E, Gibbons D, Tekamo-Olson P (2010) Developing a model for successful translation of stem cell therapies. Cell Stem Cell 6(6):513-6.
3. J Cohen, A Trounson, K Dawson, H Jones, J Hazekamp, K-G Nygren, L Hamberger (2005) The early days of IVF outside the UK. Human Reprod Update, 11: 439-459.
4. Ziebe S, Devroey P (2008); Assisted reproductive technologies are an integrated part of national strategies addressing demographic and reproductive challenges. State of ART 2007 Workshop Group. Hum Reprod Update. 14(6):583-92.
5. Marbán E, Cheng K. (2010) Heart to heart: The elusive mechanism of cell therapy. Circulation. 2010 May 11;121(18):1981-4
6. Frank RT, Edmiston M, Kendall SE, Najbauer J, Cheung CW, Kassa T, Metz MZ, Kim SU, Glackin CA, Wu AM, Yazaki PJ, Aboody KS. (2009) Neural stem cells as a novel platform for tumor-specific delivery of therapeutic antibodies. PLoS One. 2009 Dec 15;4(12):e8314.
7. Perumbeti A, Malik P.(2010) Genetic correction of sickle cell anemia and beta-thalassemia: progress and new perspective. ScientificWorldJournal. 2010 Apr 13;10:644-54

8. Holt N, Wang J, Kim K, Friedman G, Wang X, Taupin V, Crooks GM, Kohn DB, Gregory PD, Holmes MC, Cannon PM (2010) Human hematopoietic stem/progenitor cells modified by zinc-finger nucleases targeted to CCR5 control HIV-1 in vivo. Nat Biotechnol. 2010 Jul 2.
9. Hendrick SS, Cobos E (2010) Practical model for psychosocial care. J Oncol Pract. 2010 Jan;6(1):34-6.

[Back to Appendices]

36. Brief Staff Bios

President, Alan Trounson

Alan Trounson, Ph.D., is currently President of the California Institute for Regenerative Medicine. Prior to joining CIRM, Dr. Trounson was Professor of Stem Cell Sciences and Director of the Monash Immunology and Stem Cell Laboratories at Monash University. Dr. Trounson founded the National Biotechnology Centre of Excellence – 'Australian Stem Cell Centre'.
Professor Trounson graduated from the University of New South Wales in 1971 with an M.Sc. in Wool and Pastoral Sciences. In 1974 he was awarded a Ph.D. in animal embryology by Sydney University. From 1974-1976 he was awarded the Dalgety Research Fellow at the ARC Institute of Animal Physiology and Biochemistry at Cambridge University. In 1977 he was appointed Senior Research Fellow at Monash University, and by 1984 was a Reader in the Department of Obstetrics and Gynaecology. He was appointed Director of the Centre for Early Human Development in 1985, was awarded a Personal Chair in Obstetrics and Gynaecology/Paediatrics in 1991 at Monash University, and in 2003 was awarded a Personal Chair as Professor of Stem Cell Sciences, also at Monash University. The Faculties of Medical Sciences and Physical Education and Physiotherapy, Vrije Universiteit Brussel, Brussels, Belgium, awarded Professor Trounson a Doctor Honoris Causa in 2003. In 2005, Professor Trounson was made an Honorary Fellow of the Australian and New Zealand College of Obstetricians and Gynaecologists, and in 2007 he was made a Fellow ad eundem of the Royal College of Obstetricians and Gynaecologists.
His scientific accomplishments include; the pioneering of human in vitro fertilisation (IVF) and associated reproductive technologies; the diagnosis of inherited genetic disease in preimplantation embryos; the discovery and production of human embryonic stem cells and their ability to be directed into neurones, prostate tissue and respiratory tissue. He is on the Victorian Government's Innovation Economy Advisory Board, and is a Director of the Victorian Endowment for Science, Knowledge and Innovation (VESKI). His present research interests are focused on the formation of human embryonic stem cells and stem cell biology; reprogramming pluripotentiality by cytoplasmic and nuclear transfer; embryonic stem cell differentiation into respiratory, thymic, prostate and gametic lineages; and adult and embryonic stem cell utilization in cell therapy for inflammatory lung disease and cystic fibrosis.

Science Office:

- *Arie Abo*

Arie is a member of the Science Office, which is responsible for developing, organizing, and facilitating CIRM's scientific programs. As part of the science officers' team, Arie is involved in planning and developing Requests for Applications (RFAs), organizing scientific meetings to facilitate the review process and management of a portfolio of grants.
Arie has over 15 years experience in the Pharmaceutical and biotechnology area, with 10 years in a drug discovery and development. Arie worked in several biotech companies including Onyx Pharmaceutical, PPD Discovery, and Nuvelo. At Onyx pharmaceuticals, as the head of the inflammation group, Arie managed and directed all aspects of drug discovery and development to advance leads to clinical development. At PPD Discovery, he held a vice president of research and led a genomic organization to discover and develop therapeutics in cancer, HIV and inflammation. At his most recent position at Nuvelo, Arie managed and directed the research and preclinical groups focused on mAb development for leukemia and Wnt pathway. His group advanced a therapeutic agent that modulates stem cells expansion for the use for

tissue repair in bone and inflammatory bowl diseases.
Arie received a BSc. Degree in Biochemistry from UCLA and MSc and Ph.D from the department of Microbiology at Tel Aviv University. Arie completed his postdoctoral training at University College London (UCL), London

- *Bettina Steffen*

Bettina is responsible for the Disease Team Initiative at CIRM, and manages a portfolio of cardiovascular disease, transplantation, and translational awards. Along with the Science Team, Bettina supports grant application and review processes.
Bettina joined CIRM in 2007. Prior to that, Bettina spent ten years in business development and account management in the pharmaceutical industry and healthcare-related fields. Her last position was as Vice President of Market Development at ProSanos Corporation, where she was accountable for scientific program and account management.
Bettina graduated from Stanford Medical School where she also trained in general surgery. She holds a Physicians and Surgeons License from the state of California.

- *Gil Sambrano*

Gil is responsible for managing and coordinating the process of grant application peer-review. He acts as the primary liaison with the Grants Working Group members, scientific specialists as well as the chair and co-chair of the working group to facilitate the review of applications. Gil is also Program Officer for the CIRM Training Grant Program and monitors the progress of both the program and trainees.
Gil joined CIRM in 2005 as the first Scientific Officer. Prior to CIRM, he was an assistant professor in the department of Cellular and Molecular Pharmacology at UCSF. In 2001, Gil took on a notable position to coordinate efforts of the Alliance for Cellular Signaling, a multi-institutional and multi-disciplinary consortium of scientists whose goal is to understand the basic principles that regulate signal transduction in cells.
His scientific education includes a B.S. in biology from the University of Texas at El Paso and a Ph.D. in biomedical sciences from the University of California, San Diego. Gil trained as a postdoctoral fellow with the Cardiovascular Research Institute at the University of California San Francisco.

- *Ingrid Caras*

Ingrid is a member of the Science Office, which is responsible for developing, organizing, and facilitating CIRM's scientific programs. Together with other science officers, Ingrid is involved in planning and developing Requests for Applications (RFAs), organizing scientific meetings, assisting with the review process and managing a portfolio of grants, in particular, those involving Disease Team or Early Translation awards.
Ingrid has more than 20 years of experience in the biotech industry. Prior to joining CIRM she spent six years at PDL Biopharma where she held the positions of Executive Director of Preclinical and Clinical Development Sciences and Senior Director of Bioanalytical Sciences. In this role she oversaw a multi-functional department that included Toxicology, Bioanalytical Sciences, Immunogenicity, Pharmacokinetics and Translational Sciences. In addition, she contributed to multiple IND filings and managed the non-clinical portions of clinical trials. Before joining PDL, Ingrid spent 5-years as Director of Cell Biology and Development Sciences at Eos Biotechnology, and 14-years at Genentech, initially as a Scientist and later as a Senior Scientist. Ingrid has extensive experience in both basic research as well as drug development and has worked in a number of diverse areas that include immunology, cell and molecular biology, cancer and neuroscience.

She was principal consultant at IWC Bioscience and provided consulting services to the pharmaceutical industry, particularly in the area of immunogenicity of biologics.
Ingrid has a B.Sc (Hons) degree from the University of the Witwatersrand in Johannesburg, South Africa and a Ph.D. from the Hebrew University of Jerusalem in Israel. She did post-doctoral training at Harvard University and at the University of California, San Francisco.

- *Karen Berry*

Karen is a member of the Science Office, which is responsible for developing and managing science and technology objectives of CIRM. Along with her Science Officer colleagues, Karen participates in planning and developing Requests for Applications (RFAs), assisting with the review process and managing a portfolio of Early Translational and Disease Team awards.
Prior to joining CIRM in 2009, Karen spent 15 years in the pharmaceutical and biotechnology industry in Research and Development. Karen established and managed groups in preclinical pharmacology for inflammatory and autoimmune diseases at Bristol-Myers Squibb, Tularik, and Amgen working with biological and small molecule drug candidates. Karen's last position was Senior Scientist at Genentech where she directed the Immunology Pharmacodynamic Biomarker group in Development Sciences. She has extensive experience in authoring IND sections, Investigator Brochures, Phase 1 and 2 clinical protocols, and in managing Phase 1/2 clinical studies and GLP toxicology studies.
Karen received a D.V.M. (Doctor of Veterinary Medicine) degree from the University of Tennessee and a Ph.D. from Vanderbilt University. She did post-doctoral training at M.D. Anderson Cancer Center.

- *Kelly Shepard*

Kelly collaborates with members of the scientific team to realize CIRM's strategic research and development objectives. While assisting with the development and implementation of grants and research applications, she also helps to organize and conduct meetings in support of the scientific review of these efforts.
Prior to joining CIRM in 2009, Kelly used multidisciplinary approaches to investigate biological mechanisms that underlie cell behavior and function. As a graduate student, she identified and characterized several proteins required for mitochondrial function and maintenance. As a postdoctoral scholar, she utilized microarrays and other high throughput screening methodologies to identify novel targets of gene regulation. After leaving academia, Kelly led an effort at Parallel Synthesis Technologies, Inc. to adapt a new optical encoding platform for addressing questions in genomics. She has also acted as an independent contractor and biotechnology consultant.
Kelly graduated from the University of Utah with a B.S. in Biology. After receiving her Ph.D. at UCSD, she completed a postdoctoral fellowship at UCSF.

- *Lila Collins*

Lila manages a portfolio of grants focused on cardiovascular development, cardiovascular disease and novel technologies. In collaboration with other members of CIRM's science team, Lila also helps develop internal processes, supports grant reviews and plans and develops Requests for Applications focused on stem cell research translation.
Prior to joining CIRM, Lila spent over 10 years in the Biotechnology Industry. She served as a Senior Scientist at Geron Corporation, a biotechnology company focused on Regenerative Medicine and Cancer. Lila's work focused on characterizing human cardiac progenitors as well as the development of cell-based assays for human embryonic stem cell-derived therapies. Lila was also the High Content Screening group leader at Collateral Therapeutics in San Diego, CA,

a biotechnology company specializing in cardiovascular gene therapies, where her group developed assays for the company's functional genomics initiative.
Lila's academic training includes postdoctoral research in angiogenesis and cell migration at The Scripps Research Institute. Lila earned her PhD from the University of California at San Diego in G-protein coupled receptor signal transduction and her Bachelors in Human Biology at Stanford University.

- *Mani Vessal*

Mani is a member of the science office and together with other science officers helps to realize CIRM's objectives. He manages a portfolio of grants, with a focus on neurological diseases and basic neuroscience research. Additionally, he participates in organizing meetings, grant applications and review processes.
Following a four year postdoctoral fellowship, Mani accepted a senior staff scientist position at the Department of Comparative Medicine at Stanford. During this time, he followed up on his previous research in the field of spinal cord injury where he investigated neuronal plasticity, adult neurogenesis in the primate and rodent spinal cord, as well as the brain. In addition to his research, Mani has served as a reviewer for Faculty of 1000 (Biology) and a number of scientific journals. At the same time, he founded a think tank in Toronto, a company where novel educational concepts were designed and implemented with an aim to improve and expand on the science education system at both the high school and the University level. In Fall of 2009, the company was acquired by a large policy institute in Toronto.
After completing his undergraduate degree in Biology and Anthropology, Mani earned a Masters degree in Medical Anthropology in Ottawa, Canada, where his research focused on the role of cannibalism in the transmission of Kuru (a member of the prion family diseases) among the Fore people of Papua New Guinea. Mani then earned his doctorate in Neurological Sciences at the University of Toronto School of Medicine. He investigated the possible role(s) of glial cells in contributing to seizures in animal models of epilepsy. He then completed a postdoctorate at Stanford, where he proposed and implemented studies that examined the extent to which neuronal plasticity occurs in primate and rodent models of spinal cord injury.

- *Michael Yaffe*

Michael works in collaboration with others in the Science Office to develop, organize, and facilitate CIRM's scientific programs. He is responsible for planning and developing Requests for Applications (RFAs) and organizing scientific reviews of grant applications. He also manages a portfolio of grants, communicates with principle investigators, and evaluates progress towards CIRM's strategic objectives.
Michael was a Professor of Biology at the University of California, San Diego for 23 years. His laboratory studied cell growth and subcellular structure, with particular focus on the mitochondria, the cellular power plants. He also taught both undergraduates and graduate students and served for three years as Associate Dean for Education in Biological Sciences. Michael served on grant review panels for the National Institutes of Health and the American Cancer Society and as an organizer for a number of international scientific conferences. Prior to joining UCSD he carried out postdoctoral research at the Biozentrum, University of Basel in Basel, Switzerland.
Michael attended the University of California, Davis and received a B.S. degree in Biochemistry. He earned the Ph.D. degree in Biochemistry from Harvard University.

- *Patricia Olson*

Patricia plans and devises the research and development programs, policies and procedures in consultation and collaboration with the executive officers of the organization and key

stakeholders to implement and monitor the organization's overall research and development strategy. She participates in determining scientific direction and in science policy development. She represents the organization's interests internally and externally on science and science-related matters.
Patricia joined CIRM in 2006 as a Scientific Officer where her first responsibility was directing the development of CIRM's Scientific Strategic Plan. Prior to that Patricia held a number of key positions of increasing responsibility with Chiron Corporation including Vice President of R&D strategic planning and Portfolio Management, and then, Vice President of Proteins Therapeutics Research.
Patricia graduated from University of Michigan, Ann Arbor, magna cum laude with a B.S in Cell Biology. She received her Ph.D. in Biochemistry from the University of California, Berkeley and did post-doctoral training at the University of California, San Francisco.

- *Rahul Thakar*

Rahul is part of the Science Team responsible for identifying and realizing scientific and development objectives at CIRM. Specifically, he participates in review meetings of the Grants Working Group, documents reviewers' discussion, helps organize and conducts review meetings in collaboration with the Senior Review Officer and other members of review team. In addition, he prepares written summaries of applications that convey the Grants Working Group's findings and recommendations for CIRM's governing board, the Independent Citizens Oversight Committee (ICOC), the public and the applicant and conducts scientific administrative review for approved awards prior to issuance. Finally, he assists with the implementation of Requests for Application (RFAs) or Requests for Proposal (RFPs) to address strategic scientific priorities and needs in collaboration with the Science team and other CIRM staff.
Rahul joined CIRM in 2009. Prior to that, he was a postdoctoral scholar at the University of California, San Francisco's Laboratory of Therapeutic Micro and Nanotechnology, where he studied cell mechanics in microfabricated cardiac/vascular tissue engineered constructs and helped incorporate drug delivery strategies into these constructs.
Rahul graduated with a B.S. in chemical engineering from The University of Texas at Austin and earned a Ph.D. in bioengineering from the University of California, San Francisco/University of California, Berkeley Joint Graduate Group in Bioengineering.

- *Rebecca Jorgenson*

Rebecca is a Science Officer and integral part of the scientific review team. Her primary responsibilities include organizing and coordinating the grant application review process and recruitment and management of the scientific reviewers in the Grants Working Group. She also manages a portfolio of grants, and, in collaboration with other members of the Science Team, participates in the development, implementation, and organization of internal processes and Requests for Applications (RFA).
Prior to joining CIRM in 2009, Rebecca was a Scientific Review Officer at the National Institutes of Health for the National Institute of Allergy and Infectious Disease where she was responsible for managing and organizing grants review. As a post-doctoral fellow, she studied the molecular biology of retroviruses and cellular biology of retrovirus infected cells utilizing electron microscopy and biochemical techniques. Prior to that, she received training as a graduate student studying mucosal immune responses to pathogen.
Rebecca graduated from Centre College with a B.S. in Biochemistry and Molecular Biology. She earned her PhD in Molecular Microbiology & Immunology and completed her post-doctoral training at the University of Missouri-Columbia.

- *Rosa Canet-Aviles*

Rosa works in collaboration with the other members of the scientific team at CIRM with the goal of implementing CIRM's strategic research and development objectives. She is responsible for planning and developing Requests for Applications (RFAs), organizing scientific meetings and reviews of grant applications and managing a portfolio of grants.
Previously, Rosa led some of the neurodegeneration projects at Amgen Inc., a leading human therapeutics biotechnology company. Rosa's group was responsible for the discovery and validation of therapeutic targets for Parkinson's and Alzheimer's diseases. Prior to that, she held post-doctoral fellowships at Elan Inc., a neuroscience-based biotechnology company; at the laboratory of Neurogenetics at the National Insititutes of Health (NIH, Bethesda), and at the laboratory of Cell Biology at Mayo Clinic (Jacksonville, Florida).
Rosa earned her Ph.D. in Neuroscience from the School of Medicine at Leeds University, UK. She also holds a B.S. in Organic Chemistry from the Central University of Barcelona, Spain and a Masters in Quality management from the Catalan Institute of Technology of Barcelona, Spain.

- *Sohel Talib*

Sohel is part of the Science Team responsible for developing and managing science and technology objectives of CIRM.He is responsible for planning and developing Requests for Applications (RFAs), organizing scientific reviews of grant applications and managing a portfolio of grants.
Sohel served as a Director of Product development at Geron Corporation, a pharmaceutical company developing and commercializing cell-based therapies derived from embryonic stem cells platform for applications in multiple chronic diseases. His group was responsible for the process development and technology transfer. He has previously served as the Director of Immunology at Cerus Corporation, where he utilized adult stem cells and donor T cells for allogeneic stem transplantation for the treatment of hematological malignancies and Director of Molecular Biology at Applied Immune Sciences/RPR-Gen Cell. Prior to joining biopharmaceutical industry he carried out post doctoral research at Stanford University, UC Berkeley and Roche Institute of Molecular Biology.
Sohel earned Ph D degree in Biochemistry from Aligarh University, India and DANIDA international fellowship at Danish Institute of Protein Chemistry, Horsholm, Denmark

- *Tricia Chavira*

Tricia joined CIRM in its earliest days, serving as the administrative assistant to the interim president and coordinating the recruitment of the Scientific and Medical Research Funding Working Group (the "Grants Working Group"). Later that year, she joined the Institute's scientific team, and assisted with the implementation of the scientific grant review process. She continues to coordinate meetings of the Grants Working Group as well as providing administrative support to the Chief Scientific Officer and the Director of Scientific Activities.
Tricia comes to CIRM with nearly a decade's experience in the private and public sectors, in marketing, administration, staff recruiting, and client management.
Tricia holds a BA in anthropology from Rice University.

- *Uta Grieshammer*

Uta is part of a team that is responsible for realizing the scientific and development objectives of CIRM. She develops Requests for Application (RFA), participates in organizing and conducting meetings to support the scientific review of the applications received in response to the RFAs, conducts pre-approval activities, and manages a portfolio of grants.
Prior to joining CIRM in October 2007, Uta was a research scientist investigating the mechanisms underlying organ formation during embryonic development. As a graduate student,

Uta was interested in transcriptional regulation, specifically during skeletal muscle differentiation. During her post-doctoral work, she then focused on the study of organ formation using chick and mouse model systems, with an emphasis on limb development and formation of specialized cell types during early embryogenesis. As a staff scientist at UCSF, she continued to explore cellular and molecular mechanisms involved in organ formation, focusing on kidney development, and using advanced mouse genetics tools. Uta also has experience in the biotechnology industry, where she was involved in cancer target identification research.
After completing her initial education in Germany, with a Vordiplom from Christian Albrecht's University in Kiel in Agricultural Sciences, Uta received a Masters degree in Crop Science from North Carolina State University, followed by a Ph.D. in Biochemistry from Boston University.

- *Zachary Scheiner*

Zach works in the Science Office which is responsible for developing and implementing CIRM's research objectives. Zach's primary responsibilities include preparing written summaries of grant review decisions made by CIRM's Grants Working Group, conducting pre-funding administrative review of awarded grants and monitoring and assessing scientific progress made by CIRM grantees. Zach also works with other members of the Science Office in developing Requests for Applications (RFAs), organizing scientific review meetings and evaluating CIRM's progress towards strategic scientific goals.
Prior to joining CIRM in January 2009, Zach studied the molecular basis of learning, memory and drug addiction, utilizing biochemical, imaging and behavioral approaches. Prior to that, he taught middle school science and math for three years at The Harrisburg Academy, in Pennsylvania.
Zach attended Yale University and received a B.S. degree in Molecular Biophysics and Biochemistry. He earned a Ph.D. in Neurobiology and Behavior from the University of Washington.

Administration

- *Alexandra Campe Degg*

Alexandra is responsible for all human resources functions for the CIRM including but not limited to recruitment, compensation, benefit administration and performance management. In addition, Alexandra provides support in contract and interagency agreements and other administrative functions as needed.
Alexandra spent ten years with UCSF in Human Resources handling recruitment and compensation needs for the entire campus. Her last position was as Staffing Manager overseeing five Staffing and Compensation Analysts. Prior to UCSF Alexandra worked for ten years in the private sector for employment service firms placing people in temporary, temp to hire and permanent administrative positions.
Alexandra graduated from Central Michigan University and earned a B.S in Interpersonal and Public Communication. She also is certified as a Senior Professional in Human Resources from the Society of Human Resource Management.

- *Amy Adams*

Amy explains advances in stem cell research to the public. This includes video interviews with grantees, stories about significant advances, and background material about the science. She also works with institution news offices and the media to promote media attention for CIRM-funded research.
Amy spent the past seven years as a science writer at Stanford University where she wrote press releases, magazine articles and news stories about research in genetics, cancer,

developmental biology and stem cells. Prior to that she worked for an online health information site and for biotech companies writing stories for print and web. Amy has also freelanced extensively for publications including The Scientist, Science, Astronomy and New Scientist. Amy earned her BA in biology from Whitman College then earned an MS in developmental biology from Cornell University. She later went through the UCSC science communication program.

- *Amy Cheung*

Amy is responsible for providing administrative support to the Executive Director of the ICOC and the 27 Member board of the ICOC board. She also provides support to the Office of the Chair staff when needed. She assists with board meeting preparation, provides oniste support to the ICOC Board Members and additional support where needed.

- *Amy Lewis*

Amy is responsible for developing and supervising the Grants Management Office within CIRM. She oversees, directs and facilitates the business-related and financial grants management functions of the institute to ensure an overall high quality of grants administration across all CIRM programs. In addition, Amy is the primary advisor on grants policy matters for CIRM institute staff, grantees and others interested in the business management aspects of the granting process.
Amy has worked in the not for profit sector since 2000 with experience in development, patient advocacy, and administration/finance. She previously served as Deputy Chief of Staff to the Chairman at CIRM and as the lead development staffer for Northern California for the Proposition 71 campaign.
Amy earned an MBA from the University of San Francisco with an emphasis in Finance and holds a B.A. in Communication Studies from the University of California, Los Angeles.

- *Chila Silva-Martin*

In collaboration with the Finance Officer, Chila Silva-Martin provides fiscal support for the CIRM. CIRM Finance staff work closely with various State departments to ensure the Accounting and Budgeting functions are performed in accordance with CIRM's approved policies and the State of California's rules and regulations.
Chila has worked for the State for more than 33 years. She has experience managing and directing administrative and program functions of several state agencies. Most recently, Chila served as Chief of the State Personnel Board's Administrative Services Division. Chila oversaw the State Personnel Board's administrative support functions, including Accounting, Business Services, Contracting, Equal Employment Opportunity, Fiscal, Human Resources, and Information Technology.
Chila received a Bachelor of Science degree from California State University, Sacramento (CSUS). She majored in Business Administration with an emphasis in strategic planning. In 2007, Chila received a certificate for participation in CSUS' Leadership for the Government Executive program.

- *Cynthia Schaffer*

Cynthia is responsible for Contracts Administration and works in close coordination with CIRM's Legal and Finance Departments to manage existing vendors, new Requests for Proposals and Amendments to existing Consulting Agreements and Purchase Orders. Cynthia also works as a Compliance Officer and manages the program of financial oversight visits to CIRM Grantees. Cynthia also supports CIRM's General Counsel on various projects including the activities of CIRM's Regenerative Medicine Consortium.

Over the past twenty years Cynthia has worked as in-house counsel in a number of industries dealing with contracts and compliance issues for software, financial services and real estate companies.
Cynthia earned her Juris Doctor from University of California, Hastings College of the Law and her B.S. in Management and Marketing is from New York University.

- *Don Gibbons*

Don fosters communication with CIRM's many audiences, from the ICOC and the general public to grantees and their institutions. He uses many tools to do this, but the primary conduits are the Media and the Web. He also gives counsel to senior leadership and other colleagues on issues and message development.
Don came to CIRM after 12 years as Associate Dean for Public Affairs at Harvard Medical School where he tried to foster some sense of unity among its 10,000 faculty scattered at 18 hospitals and research institutes. He also did extensive work on message development for lobbying for NIH funding and stem cell initiatives in the state. Prior to that, he spent five years as Director of Communication for Stanford University Medical Center having come to that career change after 14 years in commercial publishing. Most of that time was with Medical World News, sort of a doctor's Newsweek. His final years there were as Editor in Chief.
Don graduated from Indiana University with a BS degree in biology and minors in chemistry and journalism.

- *Douglas J. Guillen, Jr.*

Douglas is responsible for the overall business service functions of CIRM to ensure a smooth running and efficient office and work environment. Among his many other responsibilities, Douglas also provides IT support for all staff and guests at the CIRM. Douglas is also responsible for the procurement of equipment and provides support in other administrative functions as needed.
Douglas spent the last few years managing two family businesses. His last two positions were as office manager for a family equipment service and repair business and marketing director for his family real estate company.
In 2004, Douglas graduated from the University of San Francisco and earned a B.S. in Business Administration.

- *Elona Baum*

Elona Baum is the General Counsel of the California Institute for Regenerative Medicine and a member of CIRM's executive team. In this capacity, she is responsible for oversight of the legal functions of the agency and for strategic initiatives. She frequently interfaces with the agency's grantee institutions, the FDA, industry and patient advocacy groups.
From 1996 to 2009, Ms. Baum held the positions of Associate General Counsel, and later Director of Regulatory Policy and Strategy at Genentech, Inc. While at Genentech, Ms. Baum also served as the Secretary of Genentech's Spanish subsidiary, Genentech España, and was the lead attorney for strategic acquisitions including manufacturing plants in Spain and in San Diego. She managed a team of attorneys responsible for research collaboration, manufacturing and supply agreements and counseled on matters relating to clinical trial practice, and FDA regulatory compliance matters.
Prior to Genentech, Ms. Baum practice law at private firms where she had an environmental litigation and real estate transactions practice. Ms. Baum received her B.A. in Economics from the University of California, Los Angeles, and her J.D. from the University of San Francisco School of Law. She was selected and served as an extern for Justice John A. Arguelles, California Supreme Court.

- *Gabriel Thompson*

Gabe is responsible for implementing the grants management functions of the institute to ensure that all activities are in compliance with applicable laws, regulations and policies. He ensures the proper reporting of all CIRM financial and programmatic activities through grant and loan funding mechanisms and he advises CIRM staff and grantees on various policy issues.
Gabe has worked in university research administration and finance since 2001. He worked for the University of Chicago as a Senior Budget Analyst counseling departments, education areas and administrative units in the preparation and presentation of appropriate budgets. He also worked at the UCSF Center for Reproductive Sciences as an Administrative Director helping to double the size of their research portfolio.
Gabe received his BS in economics from the University of Chicago and has taken continuing education classes in financial modeling and business statistics at the University of Chicago Booth School of Business.

- *Geoff Lomax*

Geoff provides ongoing facilitation of CIRM's Scientific and Medical Accountability Standards Working Group. In this capacity, he performs scientific and policy research, provides outreach to research institutions and represents the institute at conferences, workshops and public events.
For over 15 years Geoff has continually worked to bridge issues of scientific, policy and ethics in the development of state-based public health programs and research. With the California Environmental Health Investigations Branch he published a strategic plan for the development of an Environmental Health Surveillance System. Previously, he performed occupational health research and education and worked to implement the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65).
Geoff received his Dr. PH and M.P.H. from the Division of Environmental Health Sciences at the University of California at Berkeley. His BS in Environmental Toxicology was conferred by the University of California at Davis.

- *Ian Sweedler*

Ian works with CIRM's General Counsel to advise CIRM's administration and staff on a wide range of legal issues, with a particular emphasis on state agency law. He has been involved with the development and application of CIRM's policies and regulations, and with issues that arise in the grantmaking process.
From 2000-2008, Ian was a Deputy Attorney General in the California Department of Justice, prosecuting violations of consumer protection, privacy and charitable trust laws. Before that he was in private practice for nine years, with law firms in Washington, D.C. and San Francisco, primarily in the area of attorney professional liability.
Ian received his law degree with high honors from George Washington University in 1991, and a bachelor's degree in philosophy from the University of Chicago in 1986.

- *Jennifer Pryne*

Jenna is the primary liaison and administrator for the activities of the Chairman. She is responsible for providing information to the Chairman on global stem cell research activity, for the logistical management of all ICOC meetings and press conferences, as well as the administration of the Office of the Chair. She has worked for CIRM since October 2005.
A Bay Area native, Jenna spent fifteen years working in Silicon Valley for a variety of corporate and venture capital firms, supporting high-level executives. Her last position was with CommerceNet, a non-profit technology incubator, where she provided administrative support to

the Chairman and the President, as well as managed their global conferences and acted as office administrator. She also served eight years in the US Army, primarily as a military intelligence analyst and Russian Linguist stationed in Europe.
Jenna graduated from San Jose State University earning a B.A in Economics. She also is a member of the Phi Theta Kappa International Honor Society.

- *Jenny Lam*

Jenny works in collaboration with the other members of the Grants Management Office to help facilitate and implement the financial, compliance, and operational aspects of grants administration. She is responsible for ensuring due diligence around awards, financial reports and programmatic reports in accordance with required laws and established policies.
Prior to joining CIRM, Jenny has worked at UCLA and UCSF in the contracts and grants research administration since 2001. In addition, she has also worked for Kaiser Permanente as a Contracts & Grants Administrator for the Kaiser Foundation Research Institute.
Jenny has a B.A. in Anthropology from University of California, Los Angeles and will receive her M.P.A. in Public Administration with special emphasis in Health Care Administration from California State University, East Bay in June 2010.

- *John Robson*

John is CIRM's Vice President of Operations. The Vice President of Operations is a key member of CIRM's senior management team who reports to and partners with the President to lead CIRM and meet the scientific and administrative goals of the Institute. John focuses on identifying strategic opportunities and developing action plans for the Institute to fulfill its mission. John is responsible for the administrative and operations component of CIRM including but not limited to legal, communications, human resources, finance, facilities and information technology. He partners with the Chief Scientific Officer (CSO) and President to identify strategic opportunities and develops action plans to advance CIRM's mission and strategic goals.
John's last position was Associate Dean for Faculty Affairs in the Faculty of Medicine at McGill University in Montreal, Canada. John was responsible for overseeing all academic activities related to the professional lives of the members of the Faculty, including recruitment, promotions and retention. His other duties included, but were not limited to strategic planning and capital campaign planning. Prior to being the Associate Dean, John was the Associate Director for Scientific Affairs at the Montreal Neurological Institute at McGill where he was responsible for overseeing academic and research programs.
John went to Trinity College, Hartford, Connecticut for his B.S. in Biology. He earned his Ph.D. in Anatomy at Duke University, Durham, North Carolina. His research interests have been in the field of Neuroscience.

- *Lynn Wood Harwell*

Lynn works in the Office of the Chair and primarily manages financing activities, public outreach, and policy issues. This includes the general obligation bond financing, the BioTech/Product Loan Task Force, economic impact analysis, as well as outreach activities including the ICOC Spotlight on Disease, CIRM Annual Report, and other policy and regulatory functions within the Chair's Office.
Lynn has worked in a number of industries including government, professional services, high technology, and media & entertainment. Lynn previously worked in tax consulting and business advisory at Arthur Andersen LLP consulting to organizations regarding finance and accounting functions including determining infrastructure and technology for entrepreneurial clients in the hi-tech, internet strategy and chemical and plastics logistical supplier industries. Most recently,

Lynn was a manager in corporate business development and strategy at Warner Bros. Entertainment and engaged in research and analysis of business and legal matters of new media, wireless, broadband, intellectual property, and general corporate oversight. Lynn worked to develop relationships with potential content and technology companies to license and facilitate launch of new business/consumer offerings.
Lynn received her MBA from Harvard Business School and her JD from Harvard Law School. Lynn has a B.S. in Business Administration/ Accounting from Boston University and is a Certified Public Accountant (CPA). Lynn is married to Dr. Corey Harwell, a neuroscientist, who is currently a post-doctorate fellow at the University of California, San Francisco's (UCSF) Institute for Regeneration Medicine. Lynn and Corey have a daughter Noor.

- *Melissa King*

Melissa is responsible for management of the ICOC, the 29-member governing board of the CIRM. Working closely with the ICOC Chair, she manages the agenda and workflow of the board, the development of board policies, and the ongoing operations of the board and all its subcommittees. She serves as the chief liaison between the ICOC and the CIRM, facilitating CIRM communications with the board and serving as the main point of contact at the agency for ICOC members and their alternates, along with supporting all ICOC members and alternates in their roles as state officials and volunteer board members.
Melissa's experience in management and communications spans more than 15 years and includes specific experience in public affairs, public relations, corporate communications, investor relations and internal communications. Prior to joining CIRM in January 2005 as a founding staff member, Melissa served in Vice President and Account Director roles at public relations agencies, where she managed communications programs and teams for clients ranging from publicly traded Fortune 500 companies to start-ups heading into IPOs. As Director of Corporate Communications, she launched a software company in Bangalore and Chennai, India in 2000, directing press conferences and related events in both cities. Melissa has also worked on both congressional and ballot initiative campaigns in California.
Melissa has a Bachelor of Arts degree in Philosophy from Wellesley College, and serves on the Board of Directors of the Wellesley College Alumnae Association.

- *Meybel Cortez*

Meybel is support personnel to the Science Office. She assists in meeting and review planning and logistics; she is the hotel liaison for review meetings in San Francisco. She arranges for travel and reimbursement of Science Staff as well as the Grants Review Working Group. She is also responsible for other administrative support functions as needed.
Meybel spent four years with Kaiser Permanente in San Francisco as a unit coordinator. At Kaiser she helped facilitate communication between patients, hospital staff and families. She coordinated on-site meetings, trainings, and outreach for staff attendance as required. She was also the point person for a wide range of needs; including Doctor's orders for consultations and calling for medical supply services.
Meybel graduated from City College of San Francisco and earned an A.S. in Human Biology. She then transferred to San Francisco State University (SFSU) and in 2006 obtained a B.S. in Health Education. Currently she is enrolled in SFSU's College of Extended Learning to obtain a certificate in Clinical Research Management and Design where policy & regulation are a point of focus.

- *Nick Warshaw*

Nick is responsible for providing administrative support to *CIRM* Vice Chairman, Senator Art Torres (Ret.). He also assists Senator Torres with governmental relations work at both the state

and federal levels. In addition, Nick works with the Office of the Chair on various tasks pertaining to the ICOC.
Prior to joining CIRM, Nick held various political and governmental positions. Most recently, he worked as a communications staffer on the Obama Campaign in Missouri. Before working on the presidential campaign, Nick interned for Speaker Nancy Pelosi in Washington DC, and for Senator Barbara Boxer in Los Angeles. For the past two years, Nick was also the President of the California College Democrats.
Nick recently graduated with a B.A. in Government and a minor in Leadership Studies from Claremont McKenna College.

- *Nini Gabra*

Nini provides administrative support to the Vice President of Operations, Executive Director of Scientific Affairs and the General Counsel.
Prior to joining CIRM, Nini worked for three years at Stanford Institute for Stem Cell Biology and Regenerative Medicine as the Director's Travel Coordinator and the Associate Director's Executive assistant. Before moving to the States, Nini worked at the American Embassy/US Agency for International Development (USAID) in Cairo as a Human Resources Specialist in charge of the transfer of US Diplomats to Egypt post and the hiring of local employees.
Nini earned her Bachelor degree in Economics and Political Science from Cairo University, Egypt. She is currently pursuing her law degree.

- *Pat Becker*

Pat is responsible for administrative support and coordination for the Office of the President. In addition, Pat supports the Science team with logistics for review and scientific meetings and serves as staff coordinator for the Facilities and Standards Working Groups.
Pat's last position was as Executive Assistant to the communications officer at VaxGen, a biotech company that completed the world's first HIV /Aids vaccine clinical trial. Prior to that she worked as Executive Assistant to the executive team at BioSpace, a biotechnology information and career portal. Pat worked for 10 years as an Executive Assistant in a small law firm in San Francisco. Earlier in her career Pat worked in film and theater. Her film credit of note was as assistant location manager on Alan Parker's ***Mississippi Burning***.
Pat graduated from Marymount Manhattan College in New York City and earned a B.F.A., with an emphasis in theater arts.

- *Scott Tocher*

Responsible for advising the Vice Chair of the ICOC, Dr. Ed Penhoet, on legal matters affecting the CIRM and ICOC, including assisting the Vice Chair and the Intellectual Property Task Force in drafting and shepherding IP regulations through the adoption process. In addition, Scott provides assistance to ICOC counsel James Harrison and CIRM General Counsel on regulatory and state legal compliance issues, such as the Political Reform Act, the Administrative Procedure Act, Bagley-Keene Act, Public Records Act and Government Code section 1090. Scott will be assisting the ICOC's Loan Task Force in development of its policies regarding loans to for-profit and non-profit entities.
Scott graduated from law school and practiced complex litigation and appellate work in Sacramento for three years following graduation in 1995. He left the private law firm to join the Fair Political Practices Commission as a legislative coordinator and eventually became a Senior Counsel to the Commission, representing the agency in federal and state courts and draft Commission opinions and regulations; and present legal and policy matters to the Commission as well as legislative committees, agencies of the state and meetings of interested groups.

Scott graduated from CSU Sacramento with a degree in Government and earned his Juris Doctor with honors from McGeorge School of Law, where he was a member of both law reviews. In his last year of law school he prosecuted misdemeanors on behalf of the United States Attorney for the Eastern District of California and earned the Solicitor General's Integrity Award.

- *Susan Marton*

Susan is responsible for obtaining and tracking all scientific assurances for grants that have been approved for funding, including IRB, IACUC, and ESCRO documentation, as part of the pre-funding process for all scientific RFAs. She is responsible for updating spreadsheets and files to reflect RFA document status and to ensure compliance with CIRM regulations. As a member of the Grants Management Office, she is a liaison to the grantees and works to facilitate the issuance of NGAs (Notice of Grant Awards) to funded organizations.
Susan spent the last four years at Stanford University in the roles of Assistant to the Director and then Records Specialist in the Department of Public Safety where she was responsible for functions including data documentation, report writing, and records tracking. Prior to this, and also at Stanford, she similarly assisted the directors of the Sexual Harassment Policy Office, and Ombudsman Office. Her background also includes work for Thermo Fisher Scientific Inc. at Dartmouth College where she was the campus account manager for scientific equipment purchases for the college and medical school.
Susan graduated from Vanderbilt University with a B.A. degree in Psychology.
She received her Masters degree (M.S.) from San Francisco State University in Industrial / Organizational Psychology.

- *Todd Dubnicoff*

Todd collaborates with the Communication team to create multimedia content that aims to educate and inform the public and scientific community about new developments in CIRM-funded stem cell research. His main role is shooting and editing video content, which he posts onto CIRM TV, the agency's very own YouTube channel.
Before joining CIRM in December 2008, Todd produced laboratory techniques videos for the web-based Journal of Visualized Experiments (www.JoVE.com). Prior to JoVE, he spent eight years as a research scientist at Entelos, Inc., where he applied mathematical models of rheumatoid arthritis and obesity to support drug development projects of various pharmaceutical companies. During his early days at Entelos, Todd was also a scientific trainer and taught customer scientists how to use PhysioLabs, Entelos' propriety biosimulation modeling platform.
Todd graduated with a B.A. in cell biology from UCSD and earned a Ph.D. in molecular biology from UCLA's Molecular Biology Institute. He did post-doctoral training at Tularik, Inc.

[Back to Appendices]

APPENDIX 36 A

36 A: Senior Staff duties and responsibilities

Vice President - Operations

- Reports to and supports the President of CIRM in carrying out CIRM's scientific and administrative mission.
- Acts in the President's absence as the decision maker for CIRM.
- Is the first point of contact at CIRM with community and stakeholder requests, complaints and questions.
- Responsible for the administrative and operations component of CIRM including but not limited to legal, communications, human resources, finance, facilities and information technology. Has signatory capacity in these areas of CIRM operations.
- Liaison role to the Office of the Chairman to ensure strategic conformity, consensus communication and alignment of agreed priorities are in accordance with science and administrative and presidential components of CIRM management.
- Partners with Chief Scientific Officer (CSO) and President to identify strategic opportunities and develops action plans to advance CIRM's mission and strategic goals.
- Represents and speaks for the President and the Institute before the Governance Subcommittee, the ICOC, and represents CIRM externally at applicable conferences, public meetings, with patient advocacy groups and in other venues as required.
- Consults with the General Counsel on all legal matters to ensure that CIRM complies with all applicable laws, regulations and policies.
- Participates with the ICOC Chair, Vice Chair, President and other senior staff in strategic planning, policy development and problem resolution pertaining to CIRM.
- In coordination with the CSO and Director Scientific Activities, oversees grants management and short and long term budget planning and financial analyses for grant awards and operational expenses for CIRM.
- Works with Chief Communications Officer to address and expand the educational outreach component of CIRM.
- Collaborates with the Chief Human Resources Officer to ensure a total compensation program and other employee policies are implemented to effectively recruit, retain and motivate highly qualified staff. In addition, responsible for overseeing any internal grievances and matters of occupational health and safety.
- Serves as the primary liaison, with the finance and legal departments, between CIRM and various state control agencies, including the Departments of Finance and Department of General Services, the Office of the Controller and the state legislature regarding CIRM's budget and other financial and administrative matters, including testimony before legislative committees.
- Monitors the financial aspects of the CIRM budget and reporting to Finance Committee and audit representatives, to ensure that the organization complies with Proposition 71 and all State of California laws and regulations.
- Works with the CSO and Grants Management Officer to ensure grants and funds awarded by the Independent Citizen's Oversight Committee (ICOC) are in compliance with award requirements and of appropriate provisions in Proposition 71.
- Participates with the President, CSO and Senior Officer for Scientific and Medical Research Facilities to oversee grants administration for capital projects to ensure compliance.

- Collaborates with the President, Senior Officer for Scientific and Medical Research Facilities and the Facilities Working Group in implementing policies approved by the ICOC.
- Collaborates with the Chair of the ICOC on all matters pertaining to the issuance of bonds authorized by Proposition 71 and the receipt, accountability and disbursement of the proceeds.
- Prepares reports and information needed to meet the requirements of Proposition 71 and other legislative and administrative requirements and to assist the CIRM and ICOC in carrying out its respective responsibilities.
- Other duties as assigned.

General Counsel to the President

- Acts as legal counsel to the President and confers with and advises the Vice President-Operations, Chief Scientific Officer, Chief Communications Officer and other senior staff of the Institute,
- Confers with and advises with members of the public and officials of the State, City and Federal Government with respect to legal rights and obligations in connection with CIRM's regulations.
- Serves as member of executive leadership team of the Institute and on committees of the Institute as required.
- Participates in the identification and development of Institute policies, procedures and programs and provides continuing counsel and guidance on all legal matters and on legal implications.
- Serves as key legal advisor on all major business transactions of CIRM administration.
- Advises on all corporate, legal, compliance, and regulatory matters including but not limited to general contracts, third party agreements, vendor/supplier relationships, employment laws, contracts, employment policies, conflict of interest issues and intellectual property.
- Advises the President and Executive Officers on matters that relate to the working relationship of CIRM to the Independent Citizens Oversight Committee (ICOC) and works in conjunction with legal advisors of the ICOC to enable a smooth and productive relationship
- Advises the President on international relationships with CIRM
- Works with the CIRM legal advisors responsible for business and IP to ensure a smooth and productive relationship with grantees and the commercial sector
- Ensures that the Institute conducts business in compliance with applicable state and federal laws and regulations.
- Oversees, manages and coordinates the work of Paralegal and outside counsel and coordinates with other Institute legal officers.
- Manages the Institute internal legal function; prepares legal budget requests and executes approved budget; responsible for the conduct of all litigation.

Chief Communications Officer

- Create, develop, and direct a comprehensive communications plan for CIRM, including media relations, public information, website development and ongoing management and publication management in coordination with CIRM leadership and the ICOC.

- Direct a public information program that drives and maintains effective communication with several audiences, including the lay public, the patient advocacy community, the legislature and the scientific community and that responds to local, national and international news that directly impacts the mission of the Institute.
- Evaluate and develop opportunities to generate positive publicity for the Institute.
- Answer inquiries from the press, individuals and other outside requests.
- Prepare and supervise the production of publicity brochures, handouts, direct mail leaflets, educational videos, photographs and reports.
- Develop and maintain effective working relations with the media, including local and national newspapers, magazines, online reporters and bloggers, radio and television.
- Foster community relations, through events such as open days and involvement in community initiatives.
- Work collaboratively with CIRM staff and outside collaborators who will aid in the communications effort.
- Direct the development and enhancement of CIRM's web-based communications.
- Develop CIRM as a key source of information about stem cell research and its relations to specific diseases.
- Write and edit press releases, in-house newsletters, speeches and articles.
- Develop communications procedures and policies for CIRM.
- Perform other duties as may be required to further the goals of the ICOC/CIRM.

Executive Director, Scientific Activities

- Works in collaboration with VP-R&D to design and develop an effective research and development program that addresses CIRM's scientific mission.
- In collaboration with VP-R&D drafts initiatives to target funding of biomedical research.
- Works closely with the VP R&D to design, implement and manage teams involved in preclinical and clinical studies.
- Manage day-to-day grants management activities for Science office.
- Formulates, writes and issues Requests for Applications and/or Requests for Proposals for scientific grants and loans.
- Prepares and presents materials supporting the recommendations of the scientific staff and Grants Working Group to the ICOC at its regular meetings.
- With the financial and ethics management of the CIRM, monitors compliance with fiscal and programmatic requirements by applicants that receive funding. Initiates corrective action under the terms of the agreement when appropriate.
- Stays informed about the progress of research in the stem cell field and biomedical applications within the United States as well as abroad.
- Participates in the strategic planning and prioritization of CIRM activities.
- Craft initiatives to target the funding of specific areas of biomedical research.
- Write, review and edit scientific, technical and medical reports.
- Participates in policy making relevant to the development of programs.
- Recruits, hires and directs the scientific, technical and support staff of the Science sub groupings described above.
- Oversees the scientific review of applications for funding. This includes, organizing the meetings of the statutory Working Groups for Review, assembling materials for these meetings and preparing written statements summarizing the review of each application.
- Documents the ICOC decisions in responses to applicants, including any modifications deemed necessary and enters into negotiation with applicants approved for funding. Issues

grant or loan award notifications and executes agreements with the applicants approved for funding.
- Ensures Grants Management Officer tracks and documents final results of all awards and loans.
- Representing the CIRM at scientific meetings and in discussions with representatives of other public and private scientific and granting institutions.
- Supervises workshops and conferences directed at exploring the state of the science of stem cell technology and to identify results, gaps and opportunities in the field.
- Develop meaningful tracking systems to review and evaluate progress in grants and loans approved by the ICOC and administered through the CIRM.

Chief Human Resources Officer

- Initiates, directs, manages, and supervises all aspects of human resource issues, programs and policies of the California Institute for Regenerative Medicine.
- Develops and makes recommendations to senior management for improvement of CIRM's policies, procedures, and practices on personnel matters.
- Responsible for implementing the President's new policy of creating a compensation committee that will be responsible for updating all position description documents, meeting with supervisors to assess the annual performance of all employees, making recommendations to the COO and compensation committee (on which he/she sits) on merit awards, annual raises, and change in responsibilities for all positions.
- Responsible for writing and issuing position descriptions for all recruitments, advertising, arranging interview schedules, scheduling meetings and summing up meetings, and dealing with all Institute recruitment follow-ups.
- Responsible to work with supervisors, the COO, and CEO for writing and maintaining records dealing with employee disciplinary actions.
- Advises the President, Chief Operating Officer and other senior staff to address long term workforce planning and problem resolution for CIRM to maximize the organization's recruitment and retention of high performing staff.
- Partners with senior staff and managers to implement effective management strategies.
- Communicates changes in CIRM personnel policies and procedures and insures proper compliance is followed.
- Responsible for ensuring all payroll and benefit changes and issues are dealt with efficiently and effectively with the State Controller's Office.
- Interfaces with all staff on related human resources issues.
- Consults with internal and external legal counsel when appropriate.
- Manages relationships with all staff to create a supportive work environment.
- Participates on committees and special projects, as appropriate.
- Performs other duties as may be required to further the goals of the ICOC/CIRM.

[Back to Appendices]

APPENDIX 37

37. Staff patents

Alan Trounson, Ph.D.

1. Alan Trounson, Title: Embryonic Stem Cells, Patent Application No: PP7009, Filing Date: 9 November 1998
2. Alan Trounson, Title: Method of Nuclear Transfer, Patent Application No: PCT/AU99/00275, Filing Date: 15 April 1999
3. Alan Trounson, Title: A Method of Cryopreservation and Compositions for Use Therein, Patent Application No: 60/136560, Filing Date: 28 May 1999
4. Alan Trounson, Title: Methods of Inducing Differentiation of Stem Cells Into A Specific Cell Lineage, Patent Application No: PCT/AU03/00310, Filing Date: 14 March 2002
5. Alan Trounson, Title: Treatment of Chronic Lung Disease, Prov. Patent Application No 2007902844, Filing Date: 28 May 2007

Arie Abo, Ph.D.

1. Abo & Martin (1997) Six US Patents: 5605825 5698428, 6048706, 6013464, 5698445, 5518911. A novel human serine protein kinase, human p21-protein activated serine kinase p65 protein, referred to as hPAK65, and methods for its preparation and use are provided. Nucleic acids encoding hPAK65 and methods for their use in preparing hPAK65 as well.
2. Abo & Aronheim (2003) Two US Patents: 6500653, 7442534. Nucleic acids and polypeptides which resemble RHO and which interact with cell signaling pathways and proteins
3. Abo et al. (2005) US Patent Application 20060094046.Compositions and methods relating to angiogenesis and tumorigenesis.
4. Abo et al. (2005) US Patent Application 20060127919. Compositions and methods relating to cell adhesion molecule L1.
5. Abo & Korver (2007) Antibodies to NTB-A, currently pending US, PCT and Taiwan applications – filed 8/17/2007 (provisional application filed 8/28/2006). Only the PCT application is published (No. WO 2008/027739).
6. Abo & Korver (2008) Antibodies to IREM-1, currently pending PCT application (not yet published) – filed 10/1/2008 (provisional application filed 10/16/2007).
7. Abo & Korver (2008) Antibodies to CLL-1, currently pending PCT application (not yet published) – filed 10/3/2008 (provisional application filed 10/17/2007).
8. Abo & Binnerts (2007) Antibodies to LRP6, currently pending PCT application (not yet published) – filed 11/14/2008 (provisional application filed 11/16/2007).
9. Abo & Binnerts (2008) Antibodies to DKK1," 2, currently pending US provisional applications – filed 8/12/2008 and 11/18/2008.

Karen Berry, Ph.D.

1. Alejandro A. Aruffo, Diane Hollenbaugh, Anthony W. Siadak, Karen K. Berry, Linda Harris, Barbara A. Thorne, and Jurgen Bajorath. Antibodies against human CD40.

Ingrid Caras, Ph.D.

APPENDIX 37

1. Caras; Ingrid W. (Issued 1991) AU612572(B2) : Decay Accelerating Factor compositions
2. Caras; Ingrid W. , Davitz; Michael A. Nussenzweig; Victor Martin, Jr.; David W. (Issued 1992) US 5,109,113: Membrane anchor fusion polypeptides: Novel fusions of a phospholipid anchor domain and a polypeptide heterologous to the anchor domain donor polypeptide are provided for industrial use. Therapeutic administration of the fusions enables the targeting of biological activity to cell membrane surface
3. Caras; Ingrid W. , Davitz; Michael A. Nussenzweig; Victor; Martin, Jr.; David W. (Issued 1993) US 5,264,357: Nucleic acids, vectors and cells for the synthesis of membrane anchor fusion polypeptides
4. Caras; Ingrid W. (Issued 1994) US 5,374,548: Methods and compositions for the attachment of proteins to liposomes using a glycophospholipid anchor
5. Ingrid W. Caras, John W. Winslow (Issued 1996) WO/1996/013518: AL-1 NEUROTROPHIC FACTOR, A LIGAND FOR AN EPH-RELATED TYROSINE KINASE RECEPTOR
6. Ingrid W. Caras, John W. Winslow (Issued 1998) US 5,759,775: Methods for detecting nucleic acids encoding AL-1 neurotrophic factor
7. Ingrid W. Caras, John W. Winslow (Issued 1998) US 5,798,448 AL-1 neurotrophic factor antibodies
8. Ingrid W. Caras, John W. Winslow (Issued 2001) US 6,280,732: Methods of using an AL-1 neurotrophic factor immunoadhesin
9. Caras; Ingrid W. , Davitz; Michael A. Nussenzweig; Victor; Martin, Jr.; David W. (Issued 2003) US 6,632,634: Decay accelerating factor (DAF) and nucleic acids encoding it
10. Caras; Ingrid W. , Davitz; Michael A. Nussenzweig; Victor; Martin, Jr.; David W. European Patent EP-B-0244267: Nucleic acid and methods for the synthesis of novel DAF compositions
11. Ingrid W. Caras, John W. Winslow (Issued 2003) US 6,610,296: Methods of enhancing cognitive function using an AL-1 neurotrophic factor immunoadhesin
12. Ingrid W. Caras (Issued 2004) US 6,696,557: AL-2 neurotrophic factor nucleic acid. The present invention provides nucleic acids encoding AL-2 protein, host cells and vectors containing these nucleic acids, and methods for their use to produce AL-2 protein by recombinant DNA methods.
13. Caras; Ingrid W. , Davitz; Michael A. Nussenzweig; Victor; Martin, Jr.; David (Issued 2005) **CA 1341485**: Fusion proteins utilizing the Decay Accelerating Factor membrane binding domain
14. Ingrid W. Caras, John W. Winslow (Issued 2006) US 7,067,484 B1 AL-1 Neurotrophic Factor Treatments
15. Ingrid Caras, Vinay Bhaskar, Agustin de la Calle, Debbie Law, Vanitha Ramakrishnan, Richard Murray, Daniel Afar (Issued 2010) US 7288248 and WO/2003/075855: Antibodies against cancer antigen TMEFF2 and uses thereof.
16. Caras, Ingrid W., Murray, Richard, Hevezi, Peter, Wilson, Keith. **CA 2376798** (Canadian) : NOVEL METHODS OF DIAGNOSING MACROPHAGE DEVELOPMENT RELATED DISORDERS, COMPOSITIONS, AND METHODS OF SCREENING FOR MACROPHAGE DEVELOPMENT MODULATORS

APPENDIX 37

Patricia Olson, Ph.D.

1. United States Patent 4,751,180, Expression Using Fused Genes for Protein Product, Inventors: Lawrence S. Cousens, Patricia Tekamp-Olson, Jeffrey R. Shuster, James P. Merryweather, June 14, 1988.

2. United States Patent 4,876,197, Eukaryotic Regulatable Transcription, Inventors: Rae Lyn Burke, Steven Rosenberg, Jeffrey R. Shuster, Patricia Tekamp-Olson, Pablo D. Valenzeula, October 24, 1989.
3. United States Patent 4,880,734, Eucaryotic Regulatable Transcription, Inventors: Rae L. Burke, Steven Rosenberg, Jeffrey R. Shuster, Patricia Tekamp-Olson, Pablo D. Valenzeula, Philip J. Barr, November 14, 1989.
4. United States Patent 5,089,398, Enhanced Yeast Transcription Employing Hybrid GAPDH Promoter Region Constructs, Inventors: Steven Rosenberg, Patricia Tekamp-Olson, February 18, 1992.
5. United States Patent 5,342,921, Superoxide Dismutase Fusion Polypeptides for Expression of Mammalian Proteins, Inventors: Lawrence S. Cousens, Patricia Tekamp-Olson, Jeffrey R. Shuster, James P. Merryweather, August 30, 1994.
6. United States Patent 5,349,059, Hybrid Promoter Constructs of Glyceraldehyde-3-Phosphate Dehydrogenase Promoter, Inventors: Steven Rosenberg, Patricia Tekamp-Olson, September 20, 1994.
7. United States Patent 5,460,950, Expression of PACE in Host Cells and Methods of Use Thereof, Inventors: Philip J. Barr, Anthony J. Brake, Randal J. Kaufman, Patricia Tekamp-Olson, Louise Walsey, Polly A. Wong, October 24, 1995.
8. United States Patent 5,523,215, Enhanced Purification and Expression of Insoluble Recombinant Proteins, Inventors: Lawrence S. Cousens, Patricia Tekamp-Olson, June 4, 1996.
9. United States Patent 5,602,034, Expression and Secretion of Heterologous Proteins in Yeast Employing Truncated Alpha Factor Leader Sequences, Inventor: Patricia Tekamp-Olson, February 11, 1997.
10. United States Patent RE35,749, Constructs of Glyceraldehyde-3-Phosphate Dehydrogenase Promoter and Methods for Expressing Genes Using Said Constructs , Inventors: Steven Rosenberg, Patricia Tekamp-Olson, March 17, 1998.
11. United States Patent 5,814,484, Expression of Macrophage Inducible Proteins (MIPs) in Yeast Cells, Inventors: Patricia Tekamp-Olson, Carol Ann Gallegos, September 29, 1998.
12. United States Patent 5,866,362, Enhanced Purification and Expression of Insoluble Recombinant Proteins, Inventors: Lawrence S. Cousens, Patricia Tekamp-Olson, February 2, 1999.
13. United States Patent 5,965,425, Expression of PACE in Host Cells and Methods of Use Thereof, Inventors: Philip J. Barr, Anthony J. Brake, Randal J. Kaufman, Patricia Tekamp-Olson, Louise Walsey, Polly A. Wong, October 12, 1999.
14. United States Patent 5,986,079, Expression of PACE in Host Cells and Methods of Use Thereof, Inventors: Philip J. Barr, Anthony J. Brake, Randal J. Kaufman, Patricia Tekamp-Olson, Louise Walsey, Polly A. Wong, November 16, 1999.
15. United States Patent 6,017,731, Method for Expression of Heterologous Proteins in Yeast, Inventors: Patricia Tekamp-Olson, James P. Merryweather, January 25, 2000
16. United States Patent 6,083,723, Method for Expression of Heterologous Proteins in Yeast, Inventor: Patricia Tekamp-Olson, July 4, 2000.
17. United States Patent 6,103,234, Composition Comprising an antibody to macrophage-derived inflammatory mediator (MIP-2), Inventors: Stephen D. Wolpe, Anthony Cerami, Barbara Sherry, Patricia Tekamp-Olson, August 15, 2000.

18. United States Patent RE37,343, Expression and Secretion of Heterologous Proteins in Yeast Employing Truncated Alpha Factor Leader Sequences, Inventor: Patricia Tekamp-Olson, August 28, 2001.
19. United States Patent 6,312,923, Method for Expression of Heterologous Proteins in Yeast, Inventor: Patricia Tekamp-Olson, November 6, 2001.
20. United States Patent 6,436,390, IL8 Inhibitors, Inventors: Patricia Tekamp-Olson, Guy Mullenbach, Mary Ellen Wernette-Hammond, August 20, 2002.
21. United States Patent 6,448,379, IL8 Inhibitors, Inventors: Patricia Tekamp-Olson, Guy Mullenbach, Mary Ellen Wernette-Hammond, September 10, 2002.
22. United States Patent 6,706,496, Method for Expression of Heterologous Proteins in Yeast, Inventor: Patricia Tekamp-Olson, March 16, 2004.

Rahul Thakar, Ph.D.

1. Rahul G. Thakar & Song Li, US Pat No. 7,744,914; Issued: Jun 29, 2010, Ser No. 11/103,916; Filed: Apr 11, 2005; Conf No. 8205, Title: Vascular Implant Device

Uta Grieshammer, Ph.D.

1. Cen H, Garcia PD, Grieshammer U, Kassam A, Lee PP, Pot D, Gospodarowicz D, Martin K WO/1999/046381, Chiron Corporation, “Human FGF Gene and Gene Expression Products” 1999, World Intellectual Property Organization.

[Back to Appendices]

38. Book Chapter on a new paradigm for funding research

The California Model?

Robert N. Klein and Alan Trounson

The Delivery of Regenerative Medicines and Their Impact on Healthcare

Introduction: evaluatIon of PotentIalofCalifornia Model

The California Model is an extraordinarily promising new paradigm for government funding of stem cell research and therapy development. It is structured to carry research project funding all the way to a Phase II human trial efficacy demonstration. While this model demonstrates numerous strategic advantages, its ultimate optimization in safely and expeditiously advancing stem cell therapies to patients is currently being tested in programs to integrate private capital and biotechnology enterprises with non-profit research institutions. All the performance milestones of the California agency and its scientific portfolio are extremely positive.

Over $1 billion (U.S.) in donor and institutional matching funds provide a strong external validation for the agency's programs and capital structure. Its seven international collaborative funding partners offer an independent international validation of its scientific quality and importance in contributing to the advancement of the translational frontier for stem cell research. Although the final verdict will take a number of years, there is strategic value in examining the strength of the California Model's capital structure and organizational independence—all subject to executive branch and legislative oversight and audits.

At its conclusion, a recent study funded by the National Science Foundation (NSF) stated, "California has established itself as a major center for stem cell research. Recruitment of world-class stem cell scientists from across the globe has been a direct result of CIRM** funding." (Adelson and Weinberg 2010). The study summarizes Proposition 71's impact†** by stating: "In its short history, the CIRM has taken on a vigorous life of its own. It is apparent that the shift of a major focus for stem cell research to California will have a significant effect into the future on the geographic distribution of biological science and biotechnology infrastructure in the United States; on the location of university, biotechnology, and pharmaceutical research and start-up firms; and on the investment of venture capital. Evidence for this is the $300million the CIRM has invested in stem cell facilities, already leveraged to more than $1 billion in linked donations."

Fundamental Concepts driving Public Funding of Medical Research

The scientific mission and its discoveries to reduce human suffering from disease and injury produce the intellectual capital of a society needed to enable and protect the right of the individual to live a healthy life. With a highly mobile world population, a society must organize to protect human health aggressively or face:

- A rapid and continuous series of pandemics and health disasters
- Rising levels of chronic disease
- Widespread impacts of environmentally induced disease from industrial pollution

The current system for funding society's intellectual capital for healthcare is based upon an industrial capital system that is inefficient, frequently counterproductive and inappropriate to deliver on the fundamental intellectual capital requirements and opportunities of 21st century medicine. Industrial capital values direct financial returns; this system is not designed to capture the societal benefits of longer productive lives or reduced governmental healthcare costs.

Nor is it organized to capture the benefits to individuals of reduced pain, a broader spectrum of physical activity, or a healthier more vibrant life unless the individual has an unlimited ability to pay. Even then, with an unlimited financial capacity, the capital system for medical research is not producing the breadth of medical options that would be available under alternative financial structures that support research and therapy development.

The intent of the public financial funding model described in this chapter is not to replace the existing system, but rather to supplement it with a series of financial structures that align the interests of society and the individual with the financial systems driving the direction and breadth of medical research.

U.S. History of Public Funding of Medical Research through Appropriation Process

While primary U.S. medical research public funding has come through the federal government's annual or biannual appropriations process, states have also followed this model. A reliance on the appropriations process for funding has historically led to major swings in research funding. Negative economic cycles, wars, and other financial stresses that force an intense competition for annual appropriations generate an extremely high level of uncertainty in the funding patterns for U.S. medical research.

Predictably, massive federal deficits, trade imbalances and constraints on global financing of governmental needs will soon re-establish severe restrictions on U.S. government funding of medical research. For current appropriations, the "pay–go" system (Wikipedia 2009) that requires revenue increases or spending cuts to authorize any supplemental expenditures by the U.S. Congress will necessarily severely constrain any future increases in U.S. medical research funding and/or any renewal of the 2009 stimulus-driven increases to the budget of the National Institutes of Health (NIH; Adelson and Weinberg 2010).

The fundamental question is whether current government appropriations are the best approach to future medical research funding—in any country.Should and can the burden of medical research funding be carried by current taxpayers? Should medical research compete for funding against critical current needs for operating costs of public clinics and public hospitals and/or medical reimbursements under Medicare or other national healthcare systems? Is medical research an operating cost of the country or society?

Medical Research Produces Intellectual Capital Infrastructure for Healthcare

The public funding premise of this chapter is founded on the concept that medical research produces a vital intellectual capital infrastructure that determines the advances on the frontiers of healthcare for any nation and/or the world.

Indeed, biotech and pharma industries have their core financial values organized around a system of patents and licenses of intellectual capital. In the 20th century, states and nations that invested heavily and early in their physical infrastructures propelled their societies to great prosperity. These infrastructure investments—roads, railways, bridges, harbors—were major determinants of the speed of economic development and the sustained competitive capacity of these states and nations. It is the thesis of this chapter that the intellectual capital infrastructures of the core areas of society's development sectors—specifically including healthcare—will be the primary determinants of economic and social prosperity in the 21st century.

Intellectual capital is not an annual disposable good or expense like operating costs normally funded through annual appropriations. When capital expenditures compete directly against critical operating costs within the healthcare system, the capital options can generally be

expected to fare poorly because of the urgent and non negotiable nature of current care demands of patients with life threatening conditions. Medical research should not compete against healthcare operating costs for scarce, current operating appropriations of the government. Intellectual capital investments in medical research represent a long-term capital asset of society that should be funded under a separate system from critical, current healthcare.

Aligning Payments for Medical Research with Benefit Groups

Any process of appropriations or funding that draws down current funding resources to pay for intellectual medical research capital creates a misalignment between the intended medical benefit group and the group paying for the investment. Consider the Salk vaccine as an example: it created massive improvements in health and cost savings through the avoidance of broad scale polio over the last 50 years (Thompson and Duintjer Tebbens 2006). For the U.S. alone, in the late 1950s, it was estimated that by 2005 it would cost $100 billion per year just to maintain polio victims in iron lungs housed in hotels specifically developed to meet the scale of victims anticipated (Thompson and Duintjer Tebbens 2006). Clearly, American society has benefited over a number of generations from the successful research investment in intellectual capital made in the 1950s; yet the cost of developing the vaccine was borne solely by the generation of that time.

Cost of Transformative Long-term Research should be spread over benefitting generations

To accomplish this, the research investment should be funded through long-term capital financing structures such as state, national, or international bonds that amortize the cost over the benefitting generations. By utilizing bonds that spread the cost over 30 to 50 years, the critical mass of financial assets that can be marshaled in the near-term increases enormously.

As discussed below, California's Proposition 71, a $6 billion initiative approved by the voters in 2004, demonstrates the power of this concept, even at a state level, to lift an entirely new field of medical intellectual capital—stem cell research—from an exploratory phase into an intense medical revolution. Proposition 71 also demonstrates the positive ripple effect that can occur when one jurisdiction undertakes to align the research cost structure with the benefitting group. Once a major state or nation demonstrates a commitment to raise vast sums of capital through long-term bonds, other states and nations will be encouraged, if not compelled, to raise their investments in intellectual capital to remain competitive in the future research advances and commercialization of this broad-based intellectual capital asset: the development of stem cell therapies for chronic diseases and injuries.

EmpowerIng a new Political and Funding Paradigm for Medical Research

By changing the political and economic structures for medical research funding to align the medical benefit group with the payer group, through the utilization of long-term capital funding bonds, the politics of medical research funding profoundly changes. Healthcare constituencies have historically been deeply fractured by the competitive conflict between funding of current medical care and long-term medical research. In the competition for funding of current medical care, hospital suppliers and the medical and nursing professions, along with advocates for low-income, underserved groups, are aligned together. In competing for the same funds, scientific and medical researchers, along with a portion of the patient advocacy organizations will vie politically for specific research agendas and targets. Patient advocacy organizations are further fractured into specific advocacy initiatives focused around their own specific disease interests.

When the funding structure changes to long-term bonds authorized through the state initiative process or other state bond approval political processes presented to voters, the healthcare constituencies are united in support and the historical fractures are healed for these specific efforts. When the cost of the medical research is to be funded by long-term bonds, the hospitals and medical professionals no longer have their direct operating cost budgets threatened competitively in the appropriation process. It is in their collective interest that the voters approve the bonds, by a direct ballot process, so that this capital resource demand is separately satisfied.

The healthcare constituencies know that if the bonds fail, the capital demands for research will fall back upon the appropriations process.

When the funding mechanism for medical research requires a public vote for a bond authorization and an objective, balanced peer review process to award and fund the best medical science across the entire spectrum of disease, patient advocacy groups can be united behind a singular unified effort (Health.org) rather than dissipating their individual strength in fighting for a medical appropriations program that addresses a particular disease. Even when the appropriation process, as with NIH funding for research, claims to fairly cover the entire spectrum of medical research, embedded institutional resource allocation prejudices reflected in the historical allocation of funds may play a distorting role.

Unless there are informal agreements to reallocate resources among the individual institutes of the NIH, for example, the congressional appropriation process carries grossly different benefits for competing disease advocacy organizations. This results in supplementary appropriation “set-aside” or “earmarking” competitions between intensely competitive disease advocacy organizations. These politically costly struggles consume substantial political capital that otherwise could be used to increase the overall scientific medical funding for research, therapy development and clinical trials to implement new discoveries. Until the appropriation funding process for medical research is substantially supplemented by a long-term bond-type funding program through an independent agency preferably with a separate governing board, the intense battles for earmarked appropriations will not be significantly mitigated.

There are endless examples of these battles for special medical research appropriations for cancer, heart disease, Alzheimer’s disease, and every other major and/or orphan disease. The examination of even a single example demonstrates clearly how harnessing this intense effort by patient advocacy organizations into a unified effort can empower a new scientific medical funding paradigm for stem cell research.

One such example occurred in 2002. President Bush had instructed the Republican leadership in the House of Representatives and the Senate to shut down all of the appropriation committees of both Houses of Congress as to any appropriation increases or renewals. No new appropriations were to be approved by committees outside of the core budget to run the U.S. government and huge special appropriations to fund the new Homeland Security Agency, and the prospective war in Iraq. By blocking the committee approval of several bills that would have renewed the supplemental mandatory NIH appropriation for type I juvenile diabetes research, the NIH type I research appropriations would have been reduced for this disease by over 30%. These deep cuts would have shut down vital research to mitigate complications and/or funding to advance pending clinical trials. Concurrently, the expiring typeII diabetes appropriation funding of diabetes clinics for Native Americans, where over 50% of the resident population of many reservations was experiencing TypeII Diabetes, would have led to tragic complications

and unnecessary deaths among those disease victims. Without this funding, these Native American clinics on reservations would have been closed.

To remedy this crisis, a combined, stand-alone supplemental mandatory appropriations bill for $1.5 billion was created at the 11th hour to renew these special targeted medical appropriations. To pass such an appropriations bill that does not go through any congressional committee, a unanimous vote of the House of Representatives and the Senate is required. No current congressional members or staff could ever recall this occurring; however, this bill passed both houses unanimously after extra ordinary legislative advocacy of the National Juvenile Diabetes Research Foundation in key congressional districts across the nation.

Through the personal contacts of individual advocate families, the last Senate holdout, the incoming Republican Senate Budget Chairman, Senator Nichols of Oklahoma, experienced a flood of calls from corporate leaders (from his home state) that rose to such an extreme level that the switch boards in his state Senate Office and in his Washington Senate Office were at times shut down due to an overload for two days before the final vote. When combined with the bipartisan Senate leadership that supported the bill—Democratic Senators Harry Reid and Max Baucus, and Republican Senators Orrin Hatch and Arlen Specter (then Republican)—Congress demonstrated a rare bipartisan unity behind medical research funding by unanimously passing this stand-alone legislation, even in the face of a major new war. Patient advocacy had again demonstrated its tremendous strength. This example shows that when the nation's patient advocacy groups unite behind a single bond funding program that must be approved by the voters within a state or nation, the unifying power of their advocacy, combined with reuniting the entire healthcare constituency, presents a powerful and effective voting and advocacy force to empower a new funding paradigm.

Creating State Paradigm to complement Federal Research Funding

California's Proposition 71 was designed to create a paradigm change in governance and funding structures, to launch a new field of medical research—stem cell therapies—and to provide the funding platform to carry that research safely at an unprecedented speed through the 5- to 15-year development process to initial human efficacy trials. The voters of California approved $6 billion ($3 billion in the principal amount of bonds and $3 billion to pay the interest over approximately 35 years. This funding model was not designed as an interim replacement for the NIH. In fact, it contemplates the NIH as a long-term funding partner. Although Proposition 71 filled a critical gap and continues to fund embryonic stem cell research outside the funding authority of the NIH, one of its core purposes is to establish a funding system for medical research that is within the governmental powers of some states and/or foreign states, provinces, and/or nations via collaborative funding agreements. The U.S. Congress and Executive Branch cannot readily duplicate the California Model under the federal governmental system.

The primary and complementary role of the California funding agency is to drive discoveries from stem cell research to the clinic (Trounson, Klein & Murphy 2008). Funding from the NIH generally is not targeted or designed to carry discoveries through the entire development pipeline to the clinic. At the end of 2009, CIRM, the California agency, had allocated approximately $1 billion to research and facilities. The distribution of these funds was as follows:

- $320 million for facilities and equipment ($50 million for shared laboratory grants and $270 million for major facilities grants)
- $388 million for basic research, training grants, research development and tools projects, and research faculty funding

- $310 million for translational medicine to take discoveries to the clinic

The California agency was able to financially leverage the building of the 12 new stem cell research facilities in California with US$540 million from private donors, and a further sum of about US$340 million in institutional support in commitments for facilities construction, initial faculty hiring and equipment funding for the institutes . Combined with the state agency funding, the 12 California facilities have therefore been supported with approximately $1.1 billion for facilities, faculty and equipment alone. Table 2.1 summarizes the major facilities grants.

California Model

The California Model is intended to change the nature, the structure, and the speed at which scientific discoveries can be made and delivered to patients. The six key components of the model are described below.

1. Creating an Independent agency—The initiative, through a state constitutional and statutory amendment, created within the state government an independent agency governed by a 29-member board (Cal. Health & Saf. Code §125290.20(a)) composed of medical school eans (6) (principally appointed by their University of California chancellors); executive officers of scientific research institutions, research hospitals, and universities (7); patient advocates (10); and biotech industry representatives (4). All board members must be appointed by California's state constitutional executive officers and/or legislative leaders, according to detailed specifications cover ing expertise and scientific and/or medical experience and leadership. These members serve for 6- to 8-year terms (Cal. Health & Saf. Code §125290.20(c)) and they are not subject to removal, except for statutory violations . The board elects its chairman and two vice chairmen from additional patient advocates nominated by the governor, lieutenant governor, treasurer, and controller (Cal. Health & Saf. Code §125290.20(a)).
2. Funding derived from bonds—The initiative's funding for research and facilities is derived from general obligation bonds of the state of California, not from appropriations of the state's general fund. Constitutionally, bonds of the state have their debt service paid from general fund revenues immediately after the state's commitments to education are met from the top 40% of state revenues (Cal. Const. Art. XVI, §8(a); §1). This constitutional priority provides extraordinary stability to the state's bond debt service payments, enabling the state to issue bonds even during difficult economic cycles. The initiative directs the state to "capitalize" the first five years of interest payments in the initial bond issues, thereby relieving the general fund of debt service payments for five years (Cal. Health & Saf. Code §125291.45(c)).
3. Large-scale, long-term portfolios—The $3 billion in bond principal authorized by the public in the 2004 election created a minimum critical port folio funding scale intended to generate a national-scale research program for stem cell scientists and clinicians within California. Historically, large-scale, long-term portfolios of medical research have high statistical opportunities for success because of broad risk diversification—a critical strategic requirement for innovative new fields of medical research. Additionally, with $3billion , even if spread over 10 to 12 years, the annual funding portfolio could realistically engage scientists across the entire state; and, with other states and countries engaged through collaborative funding agreements, the agency could provide a broad platform for synergy and real-time, iterative scientific advances that would reinforce research momentum.
4. Unlimited term—The term of the California initiative is unlimited (Cal. Const. Art. XXXV). The initiative is established within the California Constitution as a state agency with no time limitation. Before considering loan repayments, including principal, interest, and stock

warrant revenue, the original general obligation bond funding for the agency would be exhausted around 2017 unless the California public viewed the performance of the agency's funded research to merit approval for an additional bond authority.

5. Horizontally integrated pipeline from basic science through Phase II trials—The agency has an authorized staff of 52, including the chairman and the statutory vice chairman. The president of the agency creates a strategic plan, subject to the governing board's approval, which evolves with the progress of scientific and clinical discovery. The intent is to create a horizontally integrated pipeline from basic science through FDA-approved Phase IIA or IIB clinical trials to verify efficacy. All grants and loans under this strategic plan must obtain recommendations from a confidential peer review of the Grants Working Group (GWG) populated by panels composed of 15 U.S. scientists and clinicians from other states and 7 patient advocates from the governing board. Recommendations then must be submitted to the governing board for discussion of confidential or proprietary information in executive session followed by a final debate and approval in public session.
6. Collaborative Funding Agreements to Enable Globalization of Effort—In order to facilitate the globalization of the Californian research endeavors in stem cell research, CIRM has linked together with many of the world leading researchers in collaborative research with California colleagues. Agreements with public funding agencies in Great Britain, Spain, Japan, Canada, Germany, China, and the state of Victoria Australia enable scientists from these countries to submit joint applications for funding with those selected and then supported by CIRM and the country involved. These joint project grants effectively break down scientific barriers between countries and enable the world's premier scientists and clinicians to work together for the common good. CIRM has a similar arrangement with the state of Maryland and the Juvenile Diabetes Research Foundation. These arrangements further leverage the Californian public investment in achieving goals for new clinical treatments and cures.

Basic Rational of California Model

The California Model assumes that with outstanding scientific talent and facilities, the character of the capital funding source becomes a primary determinant in the potential for medical discovery and advances in implementing such discoveries. In designing a capital funding structure to fund medical research, the initiative's five central structural features were organized to meet the following five strategic objectives:

1. Structure must protect funding—The organizational structure must protect the source of the funding from real and perceived potential pressures and distortions to the scientific discovery process.
2. Critical long-term funding—A long-term commitment of the funding source is critical to provide adequate assurances to attract the best scientific talent and to permit complex long-term scientific challenges to be undertaken.
3. Stability of funding critical—The stability of the funding—its insulation from interruption—is critical to provide the security to embark on challenging, innovative research with a long development path and attract major philanthropic, biotechnology, and institutional matching fund commitments.
4. Financial scale—The capital must reach a financial scale sufficient to drive a critical mass of core research in the field into a portfolio of translational therapies that result in a number of novel and efficacious treatments.
5. Objective resource allocation—The resource allocations system for the capital must be based on objective scientific and medical criteria that permit research to be funded for a horizontally integrated pipeline through Phase II human proof of concept trials, rather

than an allocation system that funds only discrete increments of discovery, preclinical development, and human trial processes.

After these criteria are met, the California Model proposes that scientific and medical advances can be driven from basic concept discovery grants through (1) preclinical proof of concept; (2) evidence of safety; and (3) early indications of benefit and efficacy (Phase I/II A human clinical trials). A high level of predictability of a continuing chain of funding is essential, as is a development program that requires the research to meet robust peer review milestones and standards. This generates a continuous funding stream up to proof of human efficacy for consideration of venture capital and/or commercial support. This capacity to fund proof of human efficacy represents a critical advantage rarely available through public funding models for scientific research.

Optimizing Governmental Cashflow of California Research Funding Model

To strengthen governmental support for the California funding model through bonds, the cash flow costs and benefits should be organized in the original financial structure to minimize or offset general fund payments of bond debt service in the years before net state medical costs savings become available to offset general obligation bond debt service payments. Generally, in the first five to seven years of a major medical research program in a broad-based field of high potential, the only state governmental revenue flows from state income and sales taxes generated by the research expenditures and the normal economic multipliers on those expenditures.

In the United States, because of the strength of private philanthropy, these revenue benefits are multiplied by matching funds donated by individuals and institutions.

In California, for example, $100 million in new state tax revenue is projected to be received by the end of the fifth year of the agency's full strength funding operations that started in 2006 due to funding delays arising from constitutional litigation (California Family Bioethics Council v. California Institute for Regenerative Medicine). These revenues represent economic activity driven only by $320 million in Proposition 71 funding advanced under the first$1 billion in agency funding commitments. The revenues are, however, enhanced by private donor and institutional matching funds of $800 million for facilities construction, equipment, and new faculty hiring that will be expended during this period under matching fund commitments contractually pledged in exchange for funding from the CIRM (2008 Annual Report).

The cash flow impact on California's general fund is also mitigated by the initiative's requirement that all interest payments on the bonds during the first 5 years will be capitalized in the bonds (paid by bond proceeds). The new state tax revenues are therefore available to pay debt service on the bonds arising in years 6 and later (Cal.Health & Saf. Code §125291.45(c)). Current projections through year 10 suggest that bond payments by the general fund to the middle of year 9 will be almost completely offset by the initial $100 million in tax revenue generated by the end of year5 plus supplemental tax revenue in years 6 through 8. If matching funds continue to be committed, at even 25% of the rate to date, general fund expenditures for debt service could actually be offset for several additional years, before considering actual medical services cost savings for California.

The design of the Proposition 71 initial cash flow plan did not project any intellectual property revenue share collections from royalties or licensing fee participations until the end of year 14. However, some initial medical savings from research advances and therapy developments were

anticipated by year 10 at the minimal level necessary to offset bond debt service payments at that point. In fact, an FDA-approved
Phase I human trial of a therapy developed in part with CIRM funding has recently been concluded successfully and demonstrated strong initial efficacy, even as a Phase I trial. If efficacy continues to be demonstrated for treating polycythemia vera and primary myelofibrosis, the economic savings for California residents alone are expected to reach $100 million (CIRM Statement 2008).

An analysis is currently in progress to project the potential savings and the portion of that savings that will reduce California's government healthcare costs. In addition, because the therapy allows patients to return to work full time, additional state tax revenues will be generated by the therapeutic results. These savings, if realized, would already substantially exceed the original projections for this stage of Proposition 71 funding, even though these conditions affect only approximately 12,000 Californians. Intellectual property state revenue participations would be in addition to the numbers cited above. Furthermore, the second clinical trial, arising from CIRM-funded research started in 2010 and it is expected that a third human trial may receive FDA approval in 2011.

Apart from these initial indications of potential revenue and/or medical savings (from avoided costs) for California, more than 400 scientific papers were published during the first 36 months of research funding (CIRM Announcement 2009). The discoveries and knowledge represented in those papers creates a portfolio of work that provides substantial promise of improvements in the current treatment of chronic disease along with as new therapies. While the actual cash flows generated by therapy development and new discoveries for California will not be definitive— even preliminarily—for 4 to 5 years at the earliest, the current research portfolio includes 14 disease teams that have provided "compelling and reproducible evidence" that "demonstrates that the proposed therapeutic has disease- (or injury-) modifying activity" and that "there is reasonable expectation that an IND filing" for a Phase I human trial "can be achieved within 4 years [48 months] of the project start date." (CIRM Press Release, October 28, 2009; CIRM Request for Application 09-01, Disease Research Team Award).

In short, the research portfolio of CIRM is on track or ahead of schedule in demonstrating a credible case that new tax revenues and initial governmental medical savings can reach the minimum levels during the first 10 years of a bond-funded program, to offset a substantial portion, if not all, of the early debt service payments. This approach, again, relies upon the initial five years being structured on an interest-only basis, with this debt service capitalized within the original bond issues.

<u>Models providing enhanced opportunities</u>
By supporting the biotechnology industry with grants and loans (when a company budget request is in excess of $3 million), CIRM is further leveraging public funds to enhance the ability of the for-profit sector to develop new instrumentation, methods , and reagents and to more effectively chaperone translational and clinical programs through regulatory agencies such as the FDA for clinical trials. CIRM looks forward to developing constructive partnerships with other major stakeholders in the pharmaceutical and finance industries.

The California CIRM model has not been functional long enough to determine the success of the integrated academic and biotechnology team approach to translational research. However, it is clear that scientists who have engaged with CIRM and are building impressive inter-institutional and international teams that include one or several biotechnology partners and

companies are also seeking academic and medical partnership expertise to enhance their intellectual competiveness.
This is well demonstrated in the successful CIRM Disease Team Program of preclinical research awarded in October 2009 (Press Release, April 8, 2008). The spillover benefits include support for growth of the biotech industry, jobs associated with the new research facilities, and increased competitiveness of CIRM-supported scientists for national grants.

It is not uncommon that major grants are awarded to institutions by pharmaceutical companies for first right of access to research developments and discoveries, particularly those with intellectual property rights attached. These awards are useful in underwriting work that otherwise cannot be adequately funded by public agency granting. These may be seen at times to be very successful but more frequently do not deliver constant source of new discoveries that are useful to the companies.

Organizations that fund a wide variety of research projects, particularly those that fund the translation, preclinical, and early clinical phases of research, are attractive to major pharmaceutical companies because they source a larger population of scientists and hence ideas; the research is further down the pipeline of application and hence closer to a potential product for application. Also the work has been comprehensively reviewed and managed for success and hence more likely to lead to a successful product.

As a result many of these companies are looking at some kind of partnership arrangements with publically funded organizations such as CIRM. The object is for the companies to access high value clinical opportunities, and the interest of the funding body is to connect end-users to the teams that have made progress toward the clinic but still require substantial financing to undertake the expensive phase IIB/IV trials needed to finally enable the community to access these new developments.

The possible development of reinsurance funds under which health plans contribute from healthcare savings as a result of progress to cures of disease brought about by stem cell research warrants further examination. Such funds should attract government contributions and could be used to offset some of the development costs of clinical trials or to contribute to cost claims of new stem cell therapies. It seems unlikely that all the potential clinical developments will be able to attract the large quantum of finance necessary for completion of late stage clinical trials. At risk are orphan diseases, conditions that have low cost recovery because they are rare, or be a simple cell therapeutic cure that can be delivered as an outpatient's procedure. While the costs of clinical trials remain extremely high there will be many examples of insufficient return to attract private investment. Solutions for these problems are needed in the near future.

Relationship of Research Complexity to Capital

The California Model was designed to empower greater levels of research complexity than would normally be feasible through governmental or private industry funding. As a starting point for analysis by private capital, there is an inverse relationship between the complexity of scientific research and the tolerance of private capital for risk. Particularly in a new medical research field like stem cell medicine, government capital must normally fund research until early Phase II human trial efficacy is demonstrated. That governmental funding role is especially critical during a downturn in the global financial cycle. Despite While a few notable exceptions to this position, the private biotech companies funding major preclinical research and PhaseI clinical trials for cellular therapies (especially those derived from human embryonic stem cells) obtained their primary capital bases prior to 2005.

In the current economic climate and for the foreseeable future, the complex development paths for cellular therapies will rely upon governmental sources to carry them through preclinical and early stage clinical trials. To optimize the research potential through this difficult developmental period, governmental funding sources can provide large-scale grants that permit and/or encourage multi-institutional teams that will often include private companies. By building multi-institutional teams that target Phase I and/or Phase II clinical trials, from the starting point of an identified Phase I IND (investigational new drug) clinical target, the scope of the skill set and experience level of the entire team can increase significantly, but the complexity of the management challenge and the scale of the financial investment are substantially increased.

Under the California Model, the portfolio size is significant enough to tolerate risk increments in the range of $20 million to $40 million because that range represents less than 10% of the loan portfolio before counting matching funds or loan repayments. This permits optimization of the team composition and tolerates a risk scale that the private sector would infrequently embrace at the IND definition point, even with preliminary preclinical evidence that an IND approval by the FDA could be achieved within 48 months. The California agency created a specific funding model to match this risk spectrum, with the justification that the higher level of integrated expertise early in the preclinical process will expedite therapy development and reduce long-term risk. Few private companies have been established in this risk-profiled space over the past 2 years; and this is not expected to change until significant commercial product successes occur.

International scientific collaboration is an important goal of the California Model. The creation of disease team program grants in the $20 million range (the California team portion) for preclinical and therapy development research in pursuit of a Phase I IND approval builds an attractive scale for international scientific collaboration.

As a validation of this concept, CIRM has signed bilateral agreements with seven nations to advance international scientific collaboration and accelerate potential stem cell therapy development. Active programs have been launched or are in process of initial funding rounds with six of the seven governments. Agreements are in place with scientific funding organizations in the United Kingdom, Spain, Japan, Canada, Germany, China, and the state of Victoria, Australia. Scientists in these nations that lead world stem cell research can file team applications with their California counterparts; research grant awards approved for a jurisdiction are funded by that jurisdiction. The scale of the portfolio that permits large-scale grants and the broad-based developments of scientific capacity in California, with the assurance of long-term stable funding, incentivizes and enables a level of international collaboration on translational medicine that has rarely been achieved. After the threshold transactional costs of building a funding relationship have been invested, additional collaborative relationships to perform complementary research in immunology and/or basic science can also be advanced with smaller scale grants.

When nations can verify a stable, long-term funding source on a major scale, there is a strategic value in building a scientific collaboration, especially where the funding jurisdiction represents a global center of outstanding scientific capacity. Proposition71 and the California Model permitted the California agency to meet these strategic utility criteria. In the first year of this program of international collaboration, over $58 million in international funding and leverage have been obtained. Dissolving the artificial national geographic funding boundaries (that have historically prevented the world's best scientists and clinicians from building international teams to advance critical therapy development for chronic disease) represents an additional strategic advantage of the financial funding structure under the California Model.

Interface of Governmental Funding with Private Capital Markets

If governmental funding is to maximally leverage its impact on stem cell research, it must create a capital framework that recruits private capital into shared risk relationships at the earliest possible stage of research. While private capital will not generally undertake early stage development projects, on cellular therapies in particular, prior to a positive Phase IIA or Phase IIB human efficacy trial, private capital can be induced to participate in early stage stem cell therapy preclinical risks, if there is a credible funding access to government capital that can leverage their private capital assets. To the extent that private capital can predictably evaluate the opportunity to diversify its portfolio risks with substantial government leverage, private capital can justify spreading significant funding into a number of early stage stem cell investments, with a reasonable expectation that some small percentage of a large portfolio will be successful.

Government funding leverage for private capital also provides a major benefit in averaging down the capital carrying costs on complex, long-term therapy development projects. If the entire cost had to be carried at venture capital internal rates of return, a complex project with a long development horizon would, as a general rule, immediately be eliminated from the eligible investment list (see Chapter 5 by Prescott). Given the high risk premiums assigned to even real property mortgage securities, starting with the 2008 economic cycle, novel stem cell therapies will predictably need to be funded by social capital (public financing) by governmental units that can internalize and capture medical savings across a broad cross-section of their populations.

California Model for Funding Large-scal Biotech Research

For major funding opportunities with biotech companies, the California Model of Proposition 71 employs a loan structure rather than a grant approach. The intent of the loan model is to recycle state research funding to drive a broader and longer-term portfolio. Two types of loans are provided: (1) recourse (company-backed) loans, and (2) non-recourse (product-backed) loans with payback requirements conditioned on producing a commercial product.

Recource Loans

Under a recourse loan, principal and interest accrue for 5 to 10 year, unless an acceleration liquidity event (e.g., cash sale of the company) triggers an accelerated payment. The recourse loan carries a repayment obligation regardless of whether the research project financed is successful. This type of loan allows recourse to the company as a general obligation and it carries a 10 to 75% stock warrant obligation adjusted for the financial strength and track record of the company.

Non-Recource Loans

A non-recourse loan must be repaid only if the project financed is successfully commercialized by the company and/or sold and commercialized by a successor in interest. The non-recourse loan attaches only to revenues of the company's research product funded by the loan and derivative products from that research. This loan carries a stock warrant obligation from 50 to 100%, adjusted based on the company's co-investment in the research. Again, if the product is not successful, neither principal nor interest of the non-recourse loan needs to be repaid, but the retains the contract right to the stock warrants. All interest and principal payments accrue for 5 years, unless a repayment major liquidity event triggers acceleration of repayment.

The loan with interim payments can be extended up to a 10-year total term.

While the CIRM loan program is in its start-up phase, the long-term benefits of recycling any substantial portion of state government funding would provide a major strategic value in funding a broader disease portfolio and permitting larger scale funding for any specific project. The commitment to any individual project can reach sizable proportions when a Phase I preclinical therapeutic research project leading to a Phase I human trial approval is followed by Phase I and Phase IIA or IIB clinical trial funding.

A loan task force of the governing board, with substantial lender and venture capital public testimony along with a PricewaterhouseCoopers independent study, found that even with a very high percentage of non-performance on the loan portfolio, the interest and stock warrant revenue on the minority performing share of the portfolio could result in doubling of the portfolio from payback revenues every Au: Add study to ten years (PricewaterhouseCoopers 2008). Even if the program were half as success ful as projected, the recycling benefits would be significant.

Biotechnology Full Engagement as Strategic Goal

Ultimately, to engage the best scientific minds in California with the greatest therapy development experience, private sector biotech companies must be fully engaged as central participants in the California Model. While private sector capital risk sharing is important strategically, the experiences of private sector personnel in managing therapeutic products through the FDA process to the patient and commercialization is a critical human resource asset necessary to successfully develop a portfolio of stem cell therapies for chronic disease and injury. Beyond participating with CIRM as principal investigators (PIs) through the loan model, for larger scale CIRM requests for applications (RFAs), private companies can also participate on teams with non-profit research institutions as co-PIs or as contractual collaborators. Private companies can also apply directly as PIs for smaller scale grants.

Governmental Validation of Private Company Research

As CIRM seeks to recruit greater private company participation, it becomes clear that as private companies receive public grant approvals or loan approvals from CIRM, the “validation value” of CIRM’s peer review and board approval is substantial. After a public approval, companies often receive significant new expressions of private capital interests and/or their stock valuations or stock values are expected to increase.

At this point, information to prove this theory is merely anecdotal, because neither a large enough pool of companies nor a long enough validation period for verification yet exist. The anecdotal evidence is, however, promising.

Global Funding Priorities for Medical Research

Chronic disease is a global burden. In 2004, the Priority Medicines Project of the World Health Organization (WHO) outlined priorities for future public funding for research and development of new drugs and vaccines. Using burden-of-disease rankings, the project identified 20 major diseases that account for 60% of the total disease burden worldwide, measured in disability-adjusted life years (DALYs). After adjusting with information on the most vulnerable groups—women, children, and the elderly—and neglected (mostly tropical) diseases, a list of the 10 highest priorities was developed (WHO 2004):

- Infections caused by antibacterial-resistant pathogens
- Pandemic influenza
- Cardiovascular disease
- Diabetes types 1 and 2
- Cancer
- Acute stroke
- HIV/AIDS
- Tuberculosis
- Neglected diseases (including but not limited to sleeping sickness (trypanosomiasis), Buruli ulcer, leishmaniasis, and Chagas disease
- Malaria

It is important to note that 5 of these were included in the first 14 CIRM disease team stem cell grants and loans. IND applications seeking approval from the FDA to start Phase I clinical trials are represented by the priority research areas listed including:

- Glioblastoma, brain tumor, cancer (two grants)
- Type I diabetes
- Leukemia and cancer (two grants)
- HIV/AIDS (two grants)
- Acute stroke
- Cancer stem cells
- Cardiovascular disease

Additionally, in the most advanced economies, up to 75% of healthcare costs are consumed by chronic diseases, dominantly represented above. Certainly, there is a global consensus on the severity of the human and financial burdens imposed by these chronic diseases, but funding for research to cure or substantially mitigate these diseases remains largely segregated along national and/or regional jurisdictional lines. This territorial, fractured approach to medical research funding is dysfunctional if our goal is to build the finest global teams to advance medical research in these critical areas of patient suffering and massive governmental cost burdens.

Financing to Research Millennium Development Goals for Medical Objectives

One of the most promising new sources of funding for addressing the millennium development goals to eliminate chronic disease has followed the bond financing model. To front-end load the financial resources available for immunization efforts against infectious disease in the developing world, bond financing against a chain of future government financial pledges has emerged as one of the most effective new financial tools.

While remarkable, innovative examples of donations and creative approaches have been devised by individual countries, achieving an effective global funding scale quickly may best be served by studying the International Finance Facility for Immunization (IFFIm). The creation of this financing authority was announced in 2005 by Gordon Brown, then British Chancellor of the Exchequer, and Bill Gates, then Chairman of Microsoft. As of 2008, IFFIm benefitted from more than $5 billion in pledges from at least eight nations. This model relies on international bonds backed by the pledges of the participating nations; bond payments are spread over a period of 20 years, matching the principal amortization payment schedule on the bonds.

The bond funding structure for the IFFIm is worthy of immediate focus as a model for it could certainly be brought to a much higher scale quickly. Although the funds are utilized for immunizations, the goal is to eliminate the diseases, just as smallpox was eradicated globally in 1979. These expenditures for immunization are therefore more of a capital investment in international health, with a goal of permanently securing global health by providing long-term protection against the risks and costs of infectious disease. In that context, the cost of the program could properly be amortized by bonds over the cost of the program for the groups that benefit globally. The current funding structure does not align the contributing nations and the direct beneficiary nations, but the funding structure arguably leverages the foreign aid structures of the major nations, capturing a human health capital asset—the permanent freedom of the world's peoples from these deadly diseases.

Blending IFFIM and Proposition 71 Models

The current global financial crisis and the resulting national and international debt burdens arising from recovery stimulus programs and financial bailouts will constrain many national and regional government medical research funding options over the next several decades. The United States and European governments in particular will face ever increasing and tighter financial discipline in funding medical research. The U.S. Congress should expect a "pay–go" system under which no appropriation can be increased or renewed without cutting another competing government program an equal amount or increasing taxes in an offsetting amount. Many European Union countries may arrive at similar difficult budgetary tradeoffs.

Based on the crushing weight of rising national medical costs, the global challenge will be how to fund a quantum increase in medical research as the best hope to reduce the future health burden while meeting the extraordinary current demands of rising healthcare costs. This conflict over resource choices should be expected to be especially severe in the United States.

If the leading nations that contribute to the World Bank were to recognize the value of the California Model and agree to finance substantial increases in global medical research via bonding, a major supplementary funding source for stem cell research—indeed all medical research—could be mobilized rapidly. The World Bank currently acts as the financial advisor and the treasury manager to IFFIm. Rather than having the bonds backed by a pool of nations' credits or the individual credit of a pledging nation, a World Bank guarantee would clearly enhance the efficiency of the borrowing structure. An international peer review panel could allocate the research funding derived from the bonds, with a recusal of the scientists from judging any applicant of a nation in which they had a professional, financial, personal, or institutional relationship within the past 3 to 5 years.

For California, these rules, while stricter than NIH guidelines for conflict, have worked well to protect the quality and preserve the integrity of the peer review. An additional board requirement excludes any scientist from California from participating in peer review. A high sensitivity to conflicts of interest is a recommended feature of any peer review system; and, it should enhance efforts to recruit a large number of nations as financial contributors to a research funding mechanism of this type.

For countries in the European Union, this program should be highly attractive, since Eurostat ruled in the fall of 2005 that each country would bear only a budgetary charge for the current year's pledge to IFFIm instead of the following 15 to 19 years of their commitments encumbered by the financing. It is doubtful that budgetary funding in the U.S. would follow this model, but deferred start dates and long-term funding commitments spread over 20 to 40 years should be easier to obtain than major upfront appropriations spread over 5 years.

For example, setting the starting contribution at year 7 with a stream of continuing pledges running through year 30 could substantially enhance the potential for a country to commit to the program.

Like California's plan, the first 5 years might feature a capitalized interest structure and deferred principal payments to better align the start of the benefit period of medical savings and new tax revenue with the beginning of interest and principal payments. A stable 15- to 20-year funding stream for the international funding agency would have to be established and highly defined governing board selection criteria would need to separate expertise and mission commitment from political office seekers.

A prototype program of $5 billion to $10 billion might test this translation of the California and/or IFFIm Models on an international application for stem cell research. If successful, the stem cell research prototype could reasonably be transformed into a general medical research funding model with a global commitment at the $50 billion to $100 billion level. If a country's scientists could participate only when the nation made a financial commitment to the common effort based on a proportion of its gross domestic product (GDP), the participation level might include a broad array of nations. The best scientists of the world funded adequately on effective global teams could conceivably shorten the WHO's list of the planet's most deadly diseases. A historic reduction in the future of human suffering is possible, perhaps even predictable, if novel financial structures permit concentrated major medical research funding up front. On November 7, 2006, when the first $1 billion in IFFIm bonds were sold, Gordon Brown and Bill Gates said, "We need more minds devoted to finding creative solutions. By matching the power of medical advance with innovative finance we can fill the gap between what we are capable of and what we are willing to do- and unleash the power of human ingenuity and goodness to save millions of lives." (Independent 2006). They also quoted Mahatma Gandhi, "The difference between what we do and what we are capable of doing would suffice to solve most of the world's problems."

[Back to Appendices]

APPENDIX 39

39. Folder for Media Highlights and CIRM Web information

CIRM's communications office has to serve very disparate audiences ranging from the California stem cell research community to patients and general California taxpayers.

All these audiences are recognized in some aspect of the CIRM web home page http://www.cirm.ca.gov/ and the major groups have specific landing pages for their interests, including one for researchers http://www.cirm.ca.gov/for-researchers and one for our Board and working groups and policy oriented individuals http://www.cirm.ca.gov/node/9 and one geared for patients and the general public http://www.cirm.ca.gov/for-the-public

This "About Stem Cell" page has links to our blog on current research, "Stem Cell Basics" that provides a primer in words and video about all aspects of stem cell research, and links to all of CIRM's social media, including the agency's YouTube channel http://www.youtube.com/cirmtv and 18 landing pages for specific diseases listing all CIRM grants relevant to the disease along with any consumer friendly content the agency has on the topic.
http://www.cirm.ca.gov/Disease_facts

A Small Sample of some Major Media Outlet Stories about CIRM

Postdocs Reap Stem-Cell Funding Benefits
Nature, 06/09/2010
http://www.nature.com/naturejobs/2010/100610/full/nj7299-831a.html

With the California Institute for Regenerative Medicine (CIRM) in its third year of doling out research grants, stem-cell scientists are starting to see the benefits of the 2004 ballot measure that gave the state a stem-cell research windfall. These advantages have not been limited to established researchers: the money is also giving postdocs rare opportunities, not only in terms of funding but also by providing avenues to independence.

The San Francisco-based institute, which was set up by the 2004 vote, announced on 29 April that it would give US$28 million to support 17 basic stem-cell-biology grants. Other grants awaiting disbursal this year focus on transplantation immunology and clinical development. Voters approved stem-cell funding of $3 billion over 10 years; to date, the CIRM has disbursed about $1 billion.

Grants from the CIRM, including two training grants for graduate students, postdocs and clinical fellows, have given some early carer researchers quicker grant turnaround times and sought-after routes to independence. Aileen Anderson, an associate professor at the Sue and Bill Gross Stem Cell Research Center at the University of California, Irvine, says that her lab will soon hire two new postdocs as a direct result of her $1.28 million, three-year CIRM grant. More significantly, she says, the grant has allowed her to create a co-investigator position for her most senior postdoc, Hal Nguyen. "A lot of postdocs are stuck — they can't move on because of the hiring freezes at many universities," says Anderson, noting that Nguyen wants his own lab. "Now he has a glimmer of hope," she says. The grants require that recipients work in California, but collaborators can be anywhere.

The CIRM's quick turnaround is important for postdocs, grant recipients say. Postdocs who apply to the US National Institutes of Health often endure long waiting times, and grants may not come through until the postdoc has moved on to a new position. "Here, a postdoc can

develop an idea and see it funded in a rapid way. I've never seen that before," says Garry Nolan, professor of microbiology and immunology at the Baxter Laboratory in Stem Cell Biology at Stanford University, Palo Alto, California. Nolan and his colleague Marius Wernig received a $1.45-million four-year grant, for which Nolan's postdoc, Eli Zunder, co-wrote the application. Zunder had thought of and developed the study idea — to examine pathway structures in specialized cells dedifferentiating into stem cells — on his own. "It grew directly out of his project," says Nolan. At Stanford, postdocs are not allowed to apply for grants, but Nolan says that Zunder's grant-writing experience will prove useful in future.

Such benefits for postdocs are unlikely to slow for the next five years, according to a CIRM-funded economic-impact study conducted in 2008 by The Analysis Group,an economic and financial consulting agency headquartered in Boston, Massachusetts. The study authors analysed the 229 CIRM grants awarded up to September 2008 and found that each recipient, including 45 senior researchers recruited from outside California, had hired or planned to hire about 10 researchers, including postdocs. A new economic impact study commissioned by the CIRM has not yet been released.

$62 million UC Davis center puts Sacramento at hub of stem cell research
Modesto Bee, 03/10/10
http://www.modbee.com/2010/03/10/1081484_p2/62-million-uc-davis-center-puts.html

A hub for regenerative medical research opens today in Sacramento, putting the University of California, Davis, in the forefront of stem cell research.

UC Davis already is testing dozens of therapies in the laboratory, such as HIV treatments and organ regeneration, and is even using stem cells to repair injuries in horses.

The new $62 million UC Davis Institute for Regenerative Cures will consolidate those efforts, which are scattered in various locations in the region. The center will bring 200 scientists and laboratory personnel together under one roof.

Experts say the new center reflects where medical advances are heading.

"Regenerative medicine will take us into a whole new era of medicine, especially personalized medicine, because we can make a cell line for each patient," said Jan Nolta, director of the UC Davis stem cell institute.

The red brick building a few blocks south of UC Davis Medical Center in Sacramento will be the first of a dozen major laboratories to open in California, funded in part by Proposition 71 of 2004. The initiative, the California Stem Cell Research and Cures Act, authorized $3 billion in bonds.

The new institute, housed in a former California State Fair exhibit hall on Stockton Boulevard, received $20 million from the state's agency in charge of stem cell funding – the California Institute for Regenerative Medicine.

Outside, the 1940s structure has arches and Corinthian columns. Inside, it sports 90,000 square feet of hallways and pure-white state-of-the-art research facilities.

Giant tanks of liquid nitrogen store stem cells, and the researchers will work at rows and rows of laboratory benches.

Powerful filters hum and change the air every minute to discourage contamination. A normal cubic foot of air has 35 million dirt particles. This lab has fewer than 10,000.

"When we start working here in a month, we're going to have to wear all sorts of coverings and masks," said Nolta, one of America's top stem cell researchers with more than 20 years of research experience.

A year ago, President Barack Obama lifted a ban on embryonic stem cell research that was imposed by former President George W. Bush.

But UC Davis now is moving away from using embryonic stem cells, Nolta said. Instead, researchers have found that skin cells have the ability to function much like embryonic stem cells.

Lab designer Gerhard Bauer said skin cells can produce a more favorable outcome.

"With skin cells we can make a personalized stem cell line, so there is no chance the patient would reject the stem cells," he said.

Bauer hopes to get the skin cell technique to clinical trials within five years.

The opening of California's first major center comes as national policy and public acceptance of stem cell research has shifted, observers said Tuesday.

Robert Klein, who conceived, wrote and led the campaign for Prop. 71, said the change has been sweeping. He cited three examples:

• First, the scientific community has identified new therapies it believes will be successful in treating a number of chronic diseases. The therapies are expected to reach human trials within 48 months.

• Second, $270 million in bond funds combined with another $880 million of donor, institutional and matching funds are financing the new stem cell centers, most attached to the UC system.

• Third, he said, there has been a "broad-based global validation" of California's leadership in the field, with more than a half dozen nations seeking collaboration and bilateral funding of some projects.

Judy Roberson, president of the Northern California chapter of the Huntington's Disease Society of America, said stem cell research is more accepted. Her husband died from Huntington's in 2003 at age 51.

"Before, people used to think of stem cells only as embryonic," she said. "Now there are a lot more types of cells. And people are starting to listen."

Acceptance grew, too, with the personal stories of well-known public figures who sought the benefits that stem cell research could bring.

The late Christopher Reeve, who became a quadriplegic after he was thrown from a horse, was perhaps the best known advocate for research to treat spinal injuries.

Actor Michael J. Fox has promoted stem cell research to aid those with Parkinson's disease, a degenerative disorder of the central nervous system.

Lisa Hughes, president of the Coalition for the Advancement of Medical Research in Washington, D.C., said both have been powerful persuaders of public opinion.

She said Obama's decision to reverse Bush's policy on embryonic stem cell research was pivotal.

"Just lifting that policy alone has breathed new life into the research community, and there is a sense they can move forward now, supported by the federal government," Hughes said.

California isn't the only state paying for stem cell research. New York is spending $600 million, said John Robson of the California Institute for Regenerative Medicine.

The California institute reports that it has funded more than 425 discoveries being published in scientific journals, each discovery moving closer to new therapies.

At UC Davis, dozens of therapies are being tested. Nolta, the stem cell institute director, described the process of using bone marrow cells for damaged hearts with a bit of awe.

"We put the stem cells into the bloodstream through an IV bag, and the stem cells find the injured area and repair it," she said. "It's really amazing."

Leukemia Under The Microscope
San Diego Union-Tribune, 02/01/2010
http://www.signonsandiego.com/news/2010/feb/01/leukemia-under-microscope

Leukemia is a maddening disease.

This family of blood cancers afflicts more than 250,000 adults and children in the United States, with almost 45,000 new cases diagnosed each year. Though much-studied, its cause or causes remain unknown. There are effective therapies, but none that works for everyone or in every case.

The disease often goes into remission with treatment, only to return with a vengeance.

A novel effort by scientists at the University of California San Diego aims to fundamentally alter that reality — and do so with surprising speed.

Researchers at the UCSD Moores Cancer Center, along with colleagues in Canada and elsewhere, have received a $20 million grant from the California Institute for Regenerative Medicine to pursue rapid development of six stem-cell-based leukemia drugs. The goal is to have at least one medication ready for clinical trials within four years.

“We want researchers to take on massive, game-changing projects,” said Bettina Steffen, a science officer for the institute, which was created in 2005 after voters approved a statewide ballot measure providing $3 billion for stem cell work.

“We want their work to go forward all of the way to approvable clinical trials, to not fall short, which is what often happens now.”

Steffen said the institute’s substantial funding sets the leukemia project and 13 others that received similar grants apart from past efforts to find new treatments against diabetes, AIDS and other diseases.

Scientists in the leukemia initiative are targeting cancer stem cells, which spawn and perpetuate the disease, because they have defied remedy so far. Leukemia disrupts and displaces normal bone-marrow tissues responsible for generating the trillions of red and white blood cells needed for life.

Though different types of leukemia likely have different origins, the disease is essentially the result of DNA mutations that create cancer stem cells.

No one knew such cells existed until the mid-1990s. Then, Dr. John Dick, a pioneering researcher at the University of Toronto who is collaborating with UCSD on the new project, identified cancer stem cells in some forms of human leukemia. Other scientists have since found these cells in some types of solid-tumor cancers.

While they have been studied the longest and are relatively easy to analyze in some ways, leukemia cancer stem cells continue to be an enigma, said Dr. Catriona Jamieson, director of the Cancer Stem Cell Research Program at the UCSD Moores Cancer Center.

Researchers are unclear on how they form or how they can be stopped from creating other leukemia cells.

In some variations of leukemia, state-of-the-art therapies kill virtually all ordinary cancer cells. Patients experience fairly rapid remission, but the cancer eventually returns because the treatments failed to kill the cancer stem cells.

Several factors have made these cells especially hardy, Jamieson said.

First, they are comparatively rare and thus difficult to find. Second, they hole up in bone marrow, which shields them more from therapeutic drugs. Third, they don’t constantly divide and replicate — a classic indicator of a cancer cell.

“They can go to sleep,” Jamieson said. “We need to get them out of their niche and find a way to wake them up so that drugs will attack them.”

The grant from the California Institute for Regenerative Medicine may help Jamieson and her colleagues fulfill that quest more quickly than traditional drug research and development programs because it brings together researchers, clinicians and industry professionals from the start.

The ultimate objective is more effective clinical trials that involve smaller numbers of participants and shorter durations.

The project isn’t starting from scratch. It will focus on six drug candidates — three monoclonal antibodies and three small molecules — that have undergone extensive testing and development.

“These are solid leads,” Jamieson said. “These are potential drugs that are close to clinical testing.”

Such trials, needed to fully prove that a drug works effectively and safely, can’t begin soon enough for patients like Clifford Northway, 57, a former middle-school teacher in Oceanside. Northway was diagnosed in 2002 with myelofibrosis, a debilitating bone-marrow disorder that evolves into full-blown leukemia.

“My doctor said the disease probably would run its course in 10 years, but hopefully a cure would be found before then,” said Northway, a gaunt man with dark eyes and thinning hair but also a bright and frequent smile.

He has tried to enroll in two clinical trials for new leukemia drugs, but was rejected both times as too risky. He struggles to remain optimistic even through great pain. Parts of his body are breaking down, and he hates being a burden to his wife and family.

“The bottom line is that I don’t know if I’m running out of time, if one of these trials will happen in time to help me,” Northway said. “It’s an odd disease. It might go on like this for years or shift into leukemia tomorrow. Obviously, I’m hoping for progress sooner than later.”

Grant Money Could Speed Stem Cell Cures
Los Angeles Times, 01/10/2010
http://www.latimes.com/news/nationworld/nation/la-sci-stem-cells10-2010jan10,0,2536499.story

Dr. Karen Aboody estimates that she has cured several hundred mice of a cancer of the central nervous system called neuroblastoma.

First she injected them with specialized neural stem cells that naturally zero in on the tumors and surround them. Then she administered an anti-cancer agent that the cells converted into a highly toxic drug.

In her tests, 90% of the animals were rid of their tumors while healthy brain tissue remained undamaged.

To hear Aboody tell it, that was the easy part.

"People are curing mice right and left," said the City of Hope neuroscientist. The real challenge is convincing the Food and Drug Administration to let her try this on people with brain tumors.

Reams of safety data must be amassed to satisfy the FDA. Scientists struggle to navigate all that red tape. Many don't even try.

Now the California Institute for Regenerative Medicine has stepped in -- with an $18-million grant financed by state taxpayers, courtesy of 2004's Proposition 71, which created the state agency.

Aboody's windfall is just one manifestation of the agency's changing mission, galvanized by the 2008 hire of a director with a track record of moving discoveries from lab to clinic.

For 3 1/2 years, the agency focused on the basic groundwork needed to someday use human embryonic stem cells to replace body parts damaged by injury or disease. Such cures are still far in the future.

Now the institute has a more immediate goal: boosting therapies that are much further along in development and more often rely on less glamorous adult stem cells. It is concentrating its vast financial resources on projects that could cure conditions such as age-related macular degeneration, AIDS, sickle cell disease and various types of cancer.

In shifting its focus, the agency is moving to fill a void known as the "valley of death" -- a point at which projects are typically too commercial to vie for federal funds, yet too risky to entice private investors.

This is how the agency -- with its constitutional mandate to invest $3 billion in stem cell research over 10 years -- plans to stay relevant as the state slashes billions from education, public safety, health and welfare programs to close a gargantuan budget hole.

"If we went 10 years and had no clinical treatments, it would be a failure," said the institute's director, Alan Trounson, a stem cell pioneer from Australia. "We need to demonstrate that we are starting a whole new medical revolution."

Other changes helped spur this new direction. In March, President Obama said he would expand federal funding for research on embryonic stem cells beyond the narrow limits set in 2001 by President Bush, making state funding less crucial.

And since Proposition 71 was passed, scientists have created new kinds of stem cells -- known as induced pluripotent stem cells -- that can be coaxed to form many different types of tissues but are made without harming embryos and thus are eligible for federal funding.

When the institute handed out nearly $230 million in October to 14 research teams, including Aboody's at City of Hope, it was its largest scientific investment by far. But it came with strings attached: In four years, recipients should have a clinical trial request ready to file with the FDA. Only four of the projects involve embryonic stem cells.

A new emphasis

It is a significant change in direction for an effort originally designed to bolster research on human embryonic stem cells.

Proposition 71 was set in motion in August 2001, when Bush announced that federal funds could be used to study stem cell lines derived from human embryos. It marked the first time money from the National Institutes of Health and other government agencies was made available to the growing cadre of biologists who believed the cells could be transformed into replacement tissues that would cure a range of diseases.

But there was a catch. Like many Americans, Bush was opposed to the idea of destroying human embryos for any reason, including medical research. So he restricted federal funding to about 20 embryonic stem cell lines that had already been created.

Scientists were soon complaining that the Bush policy was unworkable. Many of the lines had chromosomal abnormalities or were contaminated with animal products, rendering them

unsuitable for use in humans. Newer lines developed with private money could only be used in separate labs built without federal money.

The situation was also frustrating to patients who stood to benefit from the research. Bay Area real estate developer Robert Klein, whose son has Type 1 diabetes, proposed a radical solution: raise $3 billion through the sale of state bonds to fund stem cell research in California.

Backers of the California Stem Cell Research and Cures Initiative, better known as Proposition 71, emphasized the potential for these flexible cells to reverse paralysis from spinal cord injuries and cure intractable diseases such as Parkinson's, diabetes and Alzheimer's. Scientists, not normally known for grandstanding, rallied voters across the state. Californians approved Proposition 71 in November 2004 with 59% of the vote.

The first grants went out in April 2006, after fighting off legal challenges. Hundreds of millions of additional dollars followed.

Money put to work

USC, for example, used a grant to build its Center for Regenerative Medicine and Stem Cell Research essentially from scratch.

The university hired Martin Pera, a colleague of Trounson's, to lead the effort. It was quite a coup: In Australia, Trounson and Pera's team was the first to show that human embryonic stem cells could grow into mature cells in laboratory dishes.

Within three months of his arrival, USC received a $600,000 grant to support graduate students and postdocs working on stem cell projects. The following year, the university racked up nearly $4 million in state funding for scientists to study basic properties of human embryonic stem cells.

An additional $2.2 million from the agency allowed USC to set up its Stem Cell Core Facility, where staffers can derive, grow and maintain stem cell lines for researchers. And $27 million more helped finance a new stem cell research building. By the time construction wraps up this summer, Pera said he hopes to recruit two additional research groups using more state grants.

It may seem extravagant, especially in light of California's broken budget. But Pera sees stem cell science as a sound long-term investment.

"This is going to be a key area of scientific research," he said. "What's wrong with making this state a national and worldwide leader in this technology?"

Until a few months ago, these types of grants were the institute's bread and butter. The agency has financed 29 new labs and more than 350 researchers at 51 California institutes, from UC San Diego to Humboldt State. Scientists funded by the California Institute for Regenerative Medicine have produced 412 publications describing heart muscle cells, liver cells, retinal cells and others grown from human embryonic stem cells, among other experiments.

But those academic achievements don't matter much to average taxpayers, Trounson said. People who voted for Proposition 71 "want to see some clinical treatments happen."

A better therapy?

Count Karen Aboody among the impatient masses.

Watching her sister-in-law struggle with breast cancer that spread to the brain, she saw up close how the side effects of treatment can be as devastating as cancer itself. Aboody is convinced that stem cells can provide more effective, less debilitating therapies.

It all hinges on her discovery that neural stem cells flock to a chemical that cells make when they need new blood vessels. Tumors, which need blood to grow, release that chemical in abundance. And so stem cells flock to tumors.

Now she is using her Proposition 71 money to engineer human neural stem cells that produce a key enzyme. The cells are injected into a patient's brain, and a drug called CPT-11 is administered. As the enzyme and drug interact, they produce a powerful chemotherapy agent that kills tumor cells as they divide but leaves surrounding tissues intact.

The team will spend the next few years honing the process while regulatory specialists compile toxicology data, details on the cell manufacturing process and other safety information that the FDA will need when it considers granting permission for a clinical trial in patients with recurring malignant brain tumors.

The institute grants also went to 13 other research teams that believe they are on the verge of bringing stem-cell-based therapies to patients.

Among them is a group from UCLA and Childrens Hospital Los Angeles that hopes to cure patients with sickle cell disease by genetically modifying their blood-forming stem cells so that they produce healthy red blood cells; and researchers at Cedars-Sinai Medical Center who want to inject heart-attack patients with concentrated amounts of their own cardiac stem cells, which naturally repair heart tissue.

Some scientists who study basic stem cell biology say the new emphasis on clinical trials is premature. They say many fundamental questions about stem cells still need to be answered, and diverting money from basic science means that revolutionary therapies -- still many years away -- will take even longer to materialize.

Trounson acknowledged that the shift has elicited "a bit of a reaction from scientists" despite the institute's commitment to continue steering millions of dollars to basic biology. But, he said, the investments will have to produce actual therapies "if we're going to be relevant to the community."

Even under the best of circumstances, Aboody's brain tumor therapy wouldn't win FDA approval for general use for at least a decade, she said.

But, she added, the Proposition 71 money will shave at least four years off the process.

"We can cure mice forever in our labs," she said, "but moving this from the lab to the patient is the ultimate goal."

Stem cell agency awards $230 million in grants
San Francisco Chronicle, 01/11/2010
http://www.sfgate.com/cgi-bin/article.cgi?f=/c/a/2009/10/29/MNSU1AC1MP.DTL

California's stem cell agency announced Wednesday $230 million in grants for research into treating cancer, diabetes and a host of other devastating diseases that scientists hope will be ready to test in human subjects in the next four years.

Among the grants are two to UCSF, $20 million for research into stem cell "missiles" that attack brain tumors, and $19 million to scientists studying implantable sacs of stem cells that make insulin. Stanford University is receiving $52 million in grants for stem cell research involving leukemia, stroke and epidermolysis bullosa, a deadly skin-blistering disease.

The four-year grants, funded by the California Institute for Regenerative Medicine, are the first to demand that scientists be prepared to start human clinical trials, with approval from the Food and Drug Administration, in the relatively near future. Previous grants were focused on building labs or studying the nature of stem cells and how they operated in animals.

"These are not well-placed bets. These are carefully considered projects," said Jeff Sheehy, a member of the agency's governing board that approved the grants. "We are not casually throwing away money hoping we'll get a cure at the end of the day. We're moving forward aggressively but with a rigorous review of science."
Grants to 14 teams

Meeting in Los Angeles, the governing board approved grants, ranging from $5 million to $20 million, to 14 research teams in California. Including these most recent grants, the institute has awarded more than $1 billion in funding to 321 projects statewide. Stanford has won the most grants, totaling $163 million, and UCSF has received $103 million.

The Institute for Regenerative Medicine was created in 2004, when voters approved legislation to provide funding for stem cell research. The legislation was in response to Bush administration restrictions on funding studies involving embryonic stem cells.

Most of the projects approved Wednesday do not involve embryonic stem cells, but researchers said that even now, after years of study and under a new administration, funding for all kinds of stem cell research is difficult to secure.

"There is a very serious shortage for all stem cell research," said Dr. Irving Weissman, director of Stanford University's Institute for Stem Cell Biology and Regenerative Medicine. The state agency "allows us to do research that the federal government won't fund."

Weissman is the lead researcher on a project studying acute myeloid leukemia stem cells that was granted $20 million. The leukemia stem cells, Weissman said, send "don't eat me" signals that protect them from the body's immune system. Researchers are developing antibodies that would block those "don't eat me" signals and make the body fight and kill the leukemia cells.

At UCSF, Dr. Mitch Berger, head of neurosurgery and director of the university's Brain Tumor Center, is studying stem cells that hone in on brain tumors. Scientists are hoping to attach drugs to the stem cells so that when they hit the tumors, "they drop the bomb and deliver the payload," Berger said.

UCSF scientists also are studying a novel diabetes treatment involving stem cells. Dr. Jeff Bluestone, director of the UCSF Diabetes Center, is working with researchers in Southern California to develop sacks of beta cells - the cells responsible for producing insulin - that are grown from stem cells. The sacks would be implanted in diabetics whose beta cells have died off, leaving them reliant on insulin injections.

Bluestone, an immunologist, is focusing on ways to keep the body from attacking the newly grown beta cells. Placing them in a type of porous sack or tube and implanting that under the skin would keep the beta cells safe, but allow the insulin to seep into the body.
Testing is next step

Researchers have the basic mechanics of the beta-cell sacks figured out, Bluestone said. The next step is to manufacture them in large quantities and test them in primates, to make sure they're safe and do their job. Bluestone said his team hopes to be ready to test their research in humans in three years.

"We're on an aggressive timeline," Bluestone said. "Grants are great. But when we can actually treat people, that will be a lot nicer."
Stem cell grants

Fourteen projects were funded by the California Institute for Regenerative Medicine:

-- $18 million for stem cells that would target and kill brain tumors. City of Hope National Medical Center in San Francisco.

-- $20 million for research into insulin-producing cells grown from embryonic stem cells. UCSF and Novocell Inc. in San Diego.

-- $19 million for stem cells that would target and kill brain tumors. UCSF, Ludwig Institute for Cancer Research in San Diego and Burnham Institute for Medical Research in La Jolla.

-- $20 million for developing drugs to destroy leukemia stem cells. UC San Diego.

-- $20 million to modify stem cells so they create T cells that are resistant to HIV infection. UCLA and Calimmune Inc. in Los Angeles.

-- $16 million to treat macular degeneration using transplanted retinal cells made from embryonic stem cells. University of Southern California and UC Santa Barbara.

-- $9 million to treat sickle cell disease by modifying patients' blood-forming stem cells so they produce normal red blood cells. UCLA and Children's Hospital of Los Angeles.

-- $12 million to treat the skin disease epidermolysis bullosa by genetically modifying skin cells. Stanford University.

-- $5.5 million to repair heart tissue damaged in a heart attack using stem cells from a patient's own heart. Cedars-Sinai Medical Center in Los Angeles.

-- $16 million to treat amyotrophic lateral sclerosis by implanting cells made from embryonic stem cells. The Salk Institute for Biological Studies in San Diego, UC San Diego, and Ludwig Institute for Cancer Research.

-- $20 million to develop drugs that destroy cancer stem cells in solid tumors. UCLA, Stanford and the University of Southern California.

-- $20 million to treat stroke using implanted neural stem cells made from embryonic stem cells. Stanford and UCLA.

-- $20 million to create an antibody that helps destroy leukemia stem cells. Stanford.

-- $15 million to modify stem cells so they create T cells that are resistant to HIV infection. City of Hope National Medical Center, University of Southern California and Beckman Research Institute of City of Hope.

Stem Cell's New Sugar Daddy
Wall Street Journal, 08/07/2008
http://online.wsj.com/article/SB121814080611321763.html?mod=todays_us_page_one

SAN FRANCISCO -- Alan Trounson, a pioneering Australian embryologist, is conducting what may be the world's most ambitious experiment in public funding for science: California's voter-approved $3 billion speculative venture in human stem-cell research.

California is the first state in the U.S. to use public bonds to fund such critical experiments. Whether or not researchers can deliver hoped-for treatments of several chronic diseases, they have already transformed how controversial biomedical research is sustained.

Aiming to shape the future of medicine, Dr. Trounson and his colleagues at the California Institute of Regenerative Medicine here struggle daily with the ethical and political challenge of funding human-embryo research the federal government has largely shunned.

There is an air of urgency. The scientists and patient activists persuaded seven million state voters in 2004 to approve Proposition 71, the ballot measure authorizing the state funding, with promises to deliver clinical stem-cell treatments for intractable medical disorders within a decade.

Now, it is up to Dr. Trounson, the institute's third president in two years, to make good on those promises. An early leader in human-embryo research, Dr. Trounson developed the key techniques of commercial in vitro fertilization, which have been responsible so far for the birth of four million or so healthy children to infertile couples world-wide.

If things work out, this could be his second medical revolution. "Most people think it is impossible," Dr. Trounson says. "Ten years, by anybody's framework in this business, is incredibly short."

Even so, he is keeping California's research options open, allocating $23 million in June to create not just human embryonic stem cells but also new iPS adult stem-cell lines, to stay abreast of shifts in a field moving more swiftly than many had anticipated.

On Thursday, federally funded Harvard University researchers announced that they had produced human iPS stem-cell lines for 10 diseases by cultivating skin cells from patients suffering conditions ranging from diabetes and muscular dystrophy to Parkinson's disease. Last week, a team of privately financed Harvard and Columbia university scientists announced they

had produced stem cells for the first time from the skin of patients with a genetically based disease called ALS (amyotrophic lateral sclerosis, or Lou Gehrig's disease).

These new stem-cell lines can be used to study the diseases and to screen potential medical compounds, but all are considered too risky to transplant into people because they -- unlike embryonic cells -- could cause cancer.

"Serendipity plays such a big role in science, always has," Dr. Trounson says. "I'd rather not pick winners at this stage. Some things are going to happen that, I think, are going to be astonishing. Some things will come out as real disappointments."

Until now, intensive drives like the war on cancer and the Human Genome Project were efforts that only the National Institutes of Health and other federal agencies could afford. In California, though, this intellectual infrastructure is being funded just like a new highway bridge or harbor improvements, with 30-year general obligation bonds.

California inspired nine other states to circumvent federal restrictions on human-embryo research via local funding initiatives. Earlier this year, New York awarded its first state stem-cell grants from $600 million pledged over the next decade. State bond funding is spreading to other research endeavors. In November, Texas voters approved a $3 billion cancer-research bond measure.

Until last year, though, California's bond issue was blocked in court challenges by groups opposed to human-embryo research. To keep the institute alive, Robert Klein, an influential real-estate investment banker who led the original ballot initiative, raised $45 million in bond anticipation notes from nine foundations and private philanthropists, including Intel co-founder Gordon Moore and his family's Gordon and Betty Moore Foundation, and the David and Lucille Packard Foundation. Mr. Klein, chairman of the institute's governing board, also secured a $150 million state loan from Gov. Arnold Schwarzenegger.

"The litigation from the far right cost us two years," Mr. Klein says.

In October, the state started selling general obligation bonds to fund the research. By June, Dr. Trounson and his colleagues had committed $554 million in 206 peer-reviewed grants to scientists and research centers across the state. Of that, the institute awarded $241 million to build 12 new stem-cell research centers that, by terms of the grants, must be finished in two years. Private donors and universities added an additional $880 million, bringing the total for the state's new research facilities to almost $1.2 billion, according to an internal audit.

"That commitment was inspiring," says Mr. Klein. By the institute's own accounting, the prospect of steady state funding for stem-cell research so far has lured 24 leading scientists in the field to the state and 33 younger researchers.

Dr. Trounson hopes that is just the beginning of the migration. When finished in 2010, the new labs are expected to employ up to 2,200 researchers, roughly equal to the entire membership of the International Society for Stem Cell Research, which represents experts from 44 countries.

"You can see this is going to unbalance the international equilibrium quite substantially," Dr. Trounson says.

His next step is the creation of disease teams -- funded at about $20 million each -- to develop a range of stem-cell therapies that can be ready for clinical trials within five years. Next week, the institute's board expects to consider creating a $500 million loan fund, that would give the state a stake in any successful commercial stem-cell ventures it funds.

Success is far from guaranteed. Of every 5,000 medicines tested, only five on average make it to clinical trials, and only one of those is eventually approved for patient use, Tufts University analysts say.

California can't go it alone in shepherding new stem-cell therapies through clinical trials, Dr. Trounson says. He must harness the commercial skills of pharmaceutical and biotech companies to the discoveries of academic researchers -- all under the eye of a state legislature with its own ideas about intellectual property and profit-sharing.

That may be his biggest challenge.

"They don't really like one another. They mix like oil and water," he says of the drug companies and university researchers. "But if this is all going to happen, they will have to be paired. That will be our role. Costs and deals will have to be worked out."

Bay Area bids for stem cell bonanza
San Francisco Chronicle, 05/07/2008
http://articles.sfgate.com/2008-05-07/news/17156458_1_cell-research-cell-agency-stem

California voters who raised $3 billion for stem cell research in 2004 finally will see their tax dollars at work - not yet in the form of diseases cured, but in the rise of vast laboratories built of concrete, glass and steel.

The governing board of the California Institute for Regenerative Medicine is expected to give final approval today to a package of grants that will prompt a construction boom at academic campuses throughout the state.

More than three-quarters of a billion dollars in laboratory construction will get under way as early as next month, seeded by $271 million in facilities grants made possible by the passage of Proposition 71.

Stem cells are specialized, primal cells that circulate in the bloodstream or lodge within organs and have the potential to transform into virtually any cell in the human body. Scientists hope to build lines of stem cells that can be coaxed into replacing tissues that have been damaged by trauma or disease, or worn out by old age.

The state grants to be awarded today are designed to spur construction of laboratories dedicated to stem cell science. Projects approved by the state stem cell board will receive grants covering between one-quarter and two-thirds of projected costs. Private fundraising efforts by each grant recipient will make up the difference.

"This is an incredibly unusual opportunity that may never happen again, anywhere," said Ralph O'Rear, vice president for facilities and planning at Buck Institute for Age Research in Novato.

The institute is one of four Bay Area research centers awaiting approval for a facilities grant. If it wins the $20.5 million award it is seeking, the institute will have to raise an equal amount to

cover the costs of the proposed lab. "We're looking at every possible way we can make this work," said O'Rear.

A dozen applications

Grant applications from a dozen institutions are up for approval by the Independent Citizens' Oversight Committee, the 28-member governing board for the state stem cell agency. If all four Bay Area proposals are approved, it would launch construction of new stem cell labs valued at $443 million. Statewide, the total is $832 million.

The largest proposal in the state was made by Stanford University, which intends to build a four-story headquarters for its Stem Cell Biology and Regenerative Medicine Institute on campus.

Inside, 24 teams of researchers will explore different facets of stem cell science, investigating how cells derived from human embryos might be coaxed to regenerate tissues damaged by trauma, disease or aging. In a joint project with the Stanford Cancer Center, researchers in the building will study how some stem cells go haywire, possibly causing recurrent bouts of malignancies.

At UCSF, planners had to figure out a way to shoehorn a stem cell research center into the space-constrained confines of their hilltop Parnassus Heights campus. So they tapped one of the world's top design firms, Rafael Viñoly Architects, which delivered a striking plan.

The Institute for Regeneration Medicine will be housed in a silver, terraced structure that snakes uphill along the winding curves of Medical Center Way - tucked behind the 16-story towers housing the campus' major research labs.

Dr. Arnold Kriegstein, director of the UCSF stem cell institute, said the unusual design was chosen not only to fit the available space but to foster easy interaction among laboratory scientists from different disciplines and the doctors who will be treating patients in the buildings nearby.

"We're very excited about the design, because it perfectly captures the spirit of the stem cell program here," said Kriegstein.

Stem cell research laboratories are little different from the molecular biology labs found in universities and pharmaceutical companies around the world. However, because the goal is to manipulate human cells, they do need special equipment to assure that the cells and tissues grown are not contaminated by lab personnel or the variety of microbes that naturally inhabit the laboratory environment.

Melding disciplines

Most of the designs, like UCSF's, stress the interdisciplinary nature of stem cell science. "When you have key scientists coming from different places to a single environment, you can expect something very special," said Alan Trounson, president of the state-run stem cell agency, based in San Francisco.

Molecular biologists are encouraged to work side by side with engineers who might be inventing the next generation of laboratory equipment and among doctors who are treating the patients who could benefit from these new therapies.

Trounson hopes these new buildings will help draw more young scientists into the stem cell field. "Research students, the Ph.D.s, the early postdocs - they'll all want to get into this field because they can see it's a growth area," he said.

Most proposals call for stand-alone construction of stem cell labs, but UC Berkeley is applying for funds to put stem cell labs in two floors of its new five-story Li Ka Shing Center for Biomedical and Health Sciences. Ground has already been broken for the $256 million research laboratory, located at the former site of Warren Hall, which housed the Berkeley School of Public Health.

Li Ka Shing never attended UC Berkeley, but the Hong Kong businessman, one the world's richest men and a leading philanthropist, donated $40 million toward construction of the building that will bear his name.

"Prop. 71 came at almost a perfect time. We had intended to do the stem cell work anyway," said Robert Tijian, director of the Berkeley Stem Cell Center.

The Berkeley laboratory will feature a sod roof, sunshades and rely on lots of natural light to save energy. It will more than double the square footage of Warren Hall, but retain the old building's footprint.

The 12 proposals before the stem cell board were winnowed from a list of 17 a month ago. Before a decision can be made, however, board members must pare $18 million from the total requested to keep the combined awards under the ceiling set for facilities construction grants by Prop. 71.

A quick way to save money would be to reject one or more of the proposals. A less painful alternative, favored by Trounson and governing board chairman Robert Klein, would be to reduce grant offers to the biggest institutions by about 9 percent, but provide the entire amount to the grantees immediately. That would save enough money to fund all projects, and allow the bigger institutions to invest their reduced grant money during the course of construction, using the proceeds to make up the difference.

"We definitely want to fund all 12 proposals," said stem cell agency spokesman Don Gibbons.

[Back to Appendices]