2011 Annual Report: Letter from the President

Letter from the President

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I**f the path from basic stem cell discoveries to new therapies is a freeway, then CIRM has built the on-ramps to bring new researchers into the field and a good long stretch of the scientific freeway itself.** The flow of research down that freeway produced significant results in 2011, often building on very basic discoveries to move the field closer to therapies for a variety of diseases. I believe our grantees have produced results this past year that have begun to map out new strategic routes to the clinic.

In addition to funding the science that flows along that stem cell freeway, this year CIRM began building the interchanges that allow stem cell researchers to access complementary expertise that can accelerate the field. We also started creating the off ramps that will take research projects to their final destination—the patients.

Redirecting mature cells

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Several critical advances came out of CIRM grantees this year, many of them aimed at redirecting the fate of mature cells. A team at Harvard, following up an observation from 1987, made a major breakthrough in 2010, by showing that pancreatic tissue could be directly converted into insulin-producing beta cells. Since then, CIRM-funded teams have shown that heart stromal cells could be redirected to become heart muscle and skin fibroblasts could be converted into two types of functional nerve system tissue. These were major achievements that could one day lead to drugs that induce cells in our body to change fate and repair damage.

A related advance this year came from Stanford University. Rather than turning a cell from one type to another, they simply took mature muscle cells and turned back their cellular clock in time to young rapidly multiplying tissue. This so-called de-differentiation is what happens in newts, zebra fish and many lower animals that are able to grow new limbs, eyes and even repair major heart tissue loss. When they have part of their body cut off, the local tissues at the site of injury revert to a more primitive state and regrow the missing part. Humans have generally lost this ability. Can we find ways to re-develop this regenerative ability though manipulation of these gene

pathways? If so, it would have a major impact on patient care.

We are learning many new lessons in cell biology and the way primitive cells differentiate and develop into functional tissue of the complete organism. These complex cell-fate developments are directed by gene pathways creating a complex landscape. where cells given a push will develop into the myriad types that are needed by the whole organism. Understanding the landscape of cell fate will help us to regenerate tissues destroyed by disease and injury.

Tools for speeding therapies

We introduced a new program in December to create one or two new Centers of Excellence in Stem Cells and Genomics. This will enable us to study genes and their control in the deepest possible way. We will develop the understanding necessary to enable manufacturing of cells, their manipulation to achieve the desired tissue and function and their transplantation into patients. This field can uncover the causes of complex diseases and discover new ways to create therapies to cure them. This will enable a sea change in biomedical research. (See our contribution on the field in Nature Biotechnology; Jan 2012.)

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A second initiative "CIRM Human Pluripotent Stem Cell Initiative" will similarly leverage California expertise and provide grantees with additional valuable resources. This initiative is creating and banking cells reprogrammed from adult cells of people with complex diseases. CIRM researchers have excelled at reprogramming cells from patients into so-called induced Pluripotent Stem Cells (iPSC) in order to create a model of that patient's disease in a dish. But making individual cell lines in a lab is a laborious process. It is too time consuming to make the cells needed to screen the dozens of patients needed to analyze the variety of individual differences in diseases like Alzheimer's Disease or autism. To make our researchers as efficient as possible and to deliver advances for the scores of diseases where patients have placed their hope in stem cells requires a much more automated and accelerated process. This initiative should achieve that goal by providing researchers access to these resources. (Read more about this initiative in a story in the annual report: Banking on Stem Cells.)

These two initiatives, for genomics and pluripotent stem cell lines, should go a long way to providing those interdisciplinary interchanges that make complementary technologies and expertise available to stem cells scientists. With those tools available, CIRM grantees can focus on finding cures, rather than replicating expertise that already exists.

Finding and funding partnership opportunities

In addition to the scientific advances and new resource initiatives, 2011 saw a critical increase in CIRM's commitment to forming the types of partnerships that will allow our grantees to take the off ramp from research to the clinic. Among the most important was a trio of programs we have launched under the single name of the Opportunity Fund. Collectively the three programs seek to allow California's research and biotechnology communities access to the best science anywhere, and make sure projects that are most likely to make it into clinical trials, particularly later stage trials, have sufficient capacity, expertise and financial support for this demanding work. (Read more about our efforts to speed the path to therapies in the online annual report: Smoothing the Path.)

The External Innovation component will allow CIRM to identify outstanding research taking place outside of California and fund new awards or supplement existing awards to California teams that partner with those key outside scientists. The Bridging component will provide supplemental funds to the most promising previously CIRM-funded projects to enable the research to proceed until the next applicable round of CIRM funding or receipt of other funds. The last component, the Strategic Partnership Funding Program, is designed to attract co-funding and follow-on financing by pharmaceutical industry, major biotechnology companies and the venture capital industry to support new and existing CIRM projects.

Enabling industry participation through the Opportunity Funds will be critical to many therapies navigating that "off ramp" from the research freeway to the clinic. This is particularly true for small molecule drugs found through stem cell research and for "off-the-shelf" allogeneic (donor) cell therapies. However for autologous cell therapies, those derived from a patient's own cells, the model may be more like the specialized academic clinics that perform bone marrow transplants. For that reason, we are finalizing a proposal to take to our board this year to fund a small number of what we are calling Alpha Stem Cell Clinics. These clinics would be staffed by the multidisciplinary teams of specialist clinicians, cell biologists, counselors, nurses and technicians needed to conduct clinical trials with these cell therapies and to deliver them as part of routine patient care down the road—another critical off ramp for stem cell research. We wrote about the merit of these possible clinics in the new journal Stem Cells Translational Medicine (Jan 2012).

As always, this year CIRM funded the full range of research including fundamental research. We also continued to feed the research freeway with talent. We extended the 17 research training programs and launched a new initiative at the very beginning of the onramp, the Creativity Awards. This program, which ran as a pilot last summer and was approved by the board last fall for a broader three-year

effort, selects high school students and gives them summer internships in stem cell labs.

CIRM is entering the second half of its $3 billion lifespan and we have developed a revised Strategic Plan for the organization which focuses on our need to bring transformative research discoveries to the field, proof of concept in early clinical trials, and benefit to patients and the California economy. We have an incredibly strong network of collaborating partners that include scientists and biotechnologists from Canada, Australia, Spain, Great Brittan, Germany, Japan, China, France, Brazil, Argentina, the US State of Maryland, the Juvenile Diabetes Research Foundation and NY Stem Cell Foundation, and most recently, the US National Institutes Health. In addition we have agreements with the states of Victoria, Andalucía and Scotland. Over $60 million has been contributed by these sources to CIRM collaborative grants to date with a number still in process.

With both the strategic plan in place and the capacity enabled by collaborations and solid partnerships with industry, we have the ingredients for the success envisioned by Robert Klein and the Californian voters in 2004. We look forward to delivering this extraordinary revolution in science and medicine.
