

## Tools and Technologies I

### I. PURPOSE

The CIRM Tools and Technologies Awards will support the development and evaluation of innovative tools and technologies that will overcome current road blocks in basic, translational and/or clinical stem cell research. Specifically, this RFA will support two types of tool and technology development for stem cell research: (1) the discovery and evaluation of novel tools and technologies; and (2) the optimization, scale up or application of an existing tool or technology for which there is proof of concept.

### II. PROGRAM OBJECTIVES

Stem cells possess the unique ability to differentiate into multiple cell types of the adult body, and therefore have great potential to be utilized in a wide variety of diagnostic and drug discovery applications and to treat or cure various chronic diseases and injuries. However, significant technical hurdles need to be overcome before stem cell research can be effectively translated to the clinic. Development and availability of specialized tools and technologies will facilitate rapid progress in this field. CIRM proposes a new program to address these needs through Tools and Technologies grants.

While efforts to differentiate stem cells into various cell types are making considerable progress, obtaining a sufficient yield of the final functional cell product remains a challenge. Tools are needed to achieve efficient differentiation and maturation, including standardized reagents such as animal free extracellular matrices for cell culture and biomarkers for the identification, selection, purification, tracking and functional analysis of stem cells and their derivatives. It is especially critical to develop biomarkers, such as monoclonal antibodies to defined cell surface markers, and to engineer human embryonic stem cells with reporter genes targeted into key genes of developmental pathways for functional analysis and tracking. Other examples of tools and technologies that could make important contributions to discovery and application include the development and validation of better assays for pluripotency, for tumorigenicity, for genetic stability in long term culture and for functional analyses of stem cell derivatives; as well as efficient methods for homologous recombination and novel improved vectors for gene delivery in human cells.

Similarly, new tools and technologies are needed for translational research, including process and product development, and for clinical research. One of the challenges to effective translation will be the efficient production of large quantities of clinical grade cells required to develop cell-based therapies for patients. This requires the development of new scale-up and cell separation technologies that will allow rapid isolation of a given cell population in high purity and stability and with full retention of function. Also needed are sensitive imaging and molecular technologies that will allow

tracking of cell delivery, movement and activity, particularly in large animal models and potentially in patients. Other examples of technologies of practical importance to successful translation for clinical research include delivery devices (e.g., catheter/needle injection systems) for reliable and reproducible delivery of viable cells to target tissues, and encapsulation scaffolds that prevent immunological rejection while permitting release of bioactive material (e.g., insulin release from beta cells for diabetes).

To address these road blocks, CIRM proposes a new program. This program will support research proposals that fall into either of two categories: (1) the discovery and evaluation of novel tools and technologies for stem cell research or (2) the further optimization, scale -up or application of an existing tool or technology for stem cell research for which proof of concept has been achieved. Projects proposing commercial scale-up technology development and clinical testing are not appropriate for this RFA. Possible research goals include but are not limited to:

- Discovery of novel biomarkers (including monoclonal antibodies) for identification, selection, purification, tracking and functional analyses of stem cells and their derivatives
- Development of new sensitive assays for pluripotency, genetic integrity and/or for tumorigenicity of stem cells
- Development and utilization of efficient homologous recombination techniques for gene targeting in human stem cells

- Development of safer and more effective viral and non-viral vectors for gene transduction in human stem cells
- Development and analysis of human embryonic stem cell lines with reporter genes inserted into key loci
- Development and validation of stem cell scale-up technologies
- Development and optimization of new cell separation and purification technologies to effectively remove undifferentiated cells from differentiated progeny
- Development and optimization of new cryopreservation technologies
- Development of sensitive imaging and molecular techniques for tracking delivered cells in animal models
- Development of cell delivery devices and procedures

For all Tools and Technologies proposals, applicants are expected to substantiate the predicted value and role of the tool or technology in overcoming a specific road block in basic, translational or clinical stem cell research.

### III. AWARD INFORMATION

Under this RFA, CIRM intends to commit up to \$20 million to support up to 20 two-year grants with direct project costs of up to \$300,000 per year. Awards will be made to support two types of research:

- 1) Discovery and evaluation of novel tools and technologies for stem cell research; or
- 2) Further optimization, scale up or application of an existing tool or technology for stem cell research for which proof of concept has been achieved.

Research proposals utilizing pluripotent stem cells, adult stem cells or progenitor cells will be considered. Particular consideration will be given to those proposals that are ineligible for or unlikely to receive federal funding.

### IV. ELIGIBILITY INFORMATION

Applications will only be accepted from Principal Investigators (PIs) who 1) have been officially nominated on a Candidate Nomination Form (CNF, see RFA section VI.A) by their host institution and 2) have submitted a Letter of Intent (LOI, see RFA section VI.B) that is accepted by CIRM.

#### A. Institutional Eligibility

All CIRM-supported research must be conducted in California. This RFA is open to all academic and non-profit research institutions in the State of California. It is also open to for-profit organizations with research site(s) located in the State of California at the time the application is submitted. **Each eligible applicant institution may submit up to four applications.**

Non-Profit organization means either: (1) a governmental entity of the State of California; or (2) a legal entity that is tax exempt under Internal Revenue Code section 501(c)(3) and California Revenue and Taxation Code section 23701d.

For-Profit organization means: a sole-proprietorship, partnership, limited liability company, corporation, or other legal entity that is organized or operated for the profit or financial benefit of its shareholders or other owners. Such organizations also are referred to as “commercial organizations.”

## **B. Principal Investigator (PI) Eligibility**

Each Principal Investigator (PI) may submit only one application under this RFA. Candidates must have received an M.D., Ph.D. or equivalent degree and be authorized by the applicant institution to conduct the proposed research on site at the applicant institution in California. By the application deadline, the PI:

- must be an independent investigator at a non-profit applicant institution, or have an equivalent position and be an employee of a for-profit applicant institution;
- have documented authority from the applicant institution to staff the proposed project;
- have documented authority from the applicant institution for access to space and shared resources sufficient to carry out the proposed research at the applicant institution.

In addition, CIRM, mindful of the urgency of its mission, will

- • require the PI to commit a minimum of 10 percent effort;
- • instruct reviewers to give added consideration to PI qualifications where the PI commits additional percent effort to the research proposed in his/her application;
- • require all awards to be initiated within 6 months of the ICOC approval date.

## **V. REVIEW CRITERIA**

The purpose of the Tools and Technologies Awards is to support the development and evaluation of innovative tools and technologies that will overcome current road blocks in basic, translational and clinical stem cell research. Applications will be evaluated primarily in three areas: 1) impact of the research to overcome current road blocks and advance the stem cell field, 2) design and feasibility of the research plan, and 3) qualifications of the Principal Investigator and the research team.

### **1. Impact**

- • The proposed tools and/or technologies contribute to overcoming a significant road block in stem cell biology.
- The proposed tools and/or technologies research will significantly impact existing concepts or methods and drive the stem cell field forward, either scientifically or towards clinical application.

### **2. Design and Feasibility of the Research Plan**

- • The rationale for the development and testing of a novel tool and/or technology is convincing.
- The proposed research is carefully designed to give meaningful results.
- Potential difficulties are acknowledged, and alternative plans are provided should the proposed strategies fail.

- The aims of the research can be reasonably achieved within the proposed timeframe.
- The milestones stated are well described, scientifically justified and provide a quantitative assessment of research outcome(s).
- The scope of the proposed work justifies the timeline and the proposed project budget.
- For those applications addressing further development of an existing tool or technology, the preliminary data are compelling and supportive of the proposed concepts, hypotheses and approaches.

### 3. Qualifications of the Principal investigator and Research Team

- The PI and key personnel have the training and experience to conduct the proposed work.
- Evidence of prior success and track record supports the qualification of the PI to develop tools and/or technologies as proposed.
- The PI is committing the percent effort to the proposed research to maximize achievement of the aims and milestones.

## VI. APPLICATION PROCEDURE

Applicant institutions and PIs must follow these instructions for submitting a Candidate Nomination Form, Letter of Intent, and Application for the CIRM Tools and Technologies Awards. Applications will only be accepted from PIs who 1) have been officially nominated on a Candidate Nomination Form (CNF) by their host institution and 2) have submitted a Letter of Intent (LOI) that is accepted by CIRM.

### A. Candidate Nomination Form (CNF)

Applicant institutions must submit to CIRM a single Candidate Nomination Form (CNF) using the CNF template provided on the CIRM website. The CNF must list the name, degree and employment title of each of the PIs the institution wishes to nominate for these awards. CIRM will accept only one CNF from each institution; this form must be signed by an institutional official authorized to nominate candidates on behalf of the entire institution. **The signed original CNF must be received by**

**CIRM no later than 5:00 PM (PDT) on June 11, 2008. No exceptions will be made.**

Send the signed original CNF to:

Tools and Technologies Award Candidate Nomination Form California Institute for Regenerative  
Medicine

210 King Street

San Francisco, CA 94107

### B. Letter of Intent (LOI)

Each PI nominated by an applicant institution must submit a letter of intent (LOI). The LOI should describe concisely the overall goals of the proposed research and technical approaches used to achieve these goals. **Completed LOIs should be sent as an email attachment to [ToolsAndTechnologiesLOI@cirm.ca.gov](mailto:ToolsAndTechnologiesLOI@cirm.ca.gov), and must be received by CIRM no later than 5:00PM (PDT) on June 11, 2008. No exceptions will be made.** The LOI is non-binding, but CIRM will not accept an application if the LOI was not received by the stated deadline.

## C. Application Instructions

Application forms will be available online by May 9, 2008. The application for CIRM Tools and Technologies Awards consists of three parts:

### Part A: Application Information Form

Part A includes: Abstract, Public Abstract, Statement of Benefit to California, Key Personnel, and Budget (section numbers 1-5 below).

### Part B: Tools and Technologies Award Research Proposal

Part B includes: Rationale and Significance, Specific Aims, Milestones and Timeline, Research Design and Methods, Feasibility and (when applicable) Preliminary Data, References (section numbers 6-11 below).

### Part C: Biographical Sketches for Key Personnel and letters of collaboration.

The application for Tools and Technologies Awards includes the following sections:

#### 1. *Abstract (up to 3000 characters in Part A)*

State the goals of the proposal. Summarize the overall plans of the proposed research and how these will meet the stated objectives of the RFA. Describe the rationale for the studies and techniques employed to pursue these goals. If applicable, explain why this proposal cannot be or is not likely to be funded by the federal government.

#### 2. *Public Abstract (up to 3000 characters in Part A)*

Briefly describe in lay language the proposed research and how it will, directly or indirectly, contribute to the development of diagnostics, tools or therapies. This Public Abstract will become public information; therefore, do not include proprietary or confidential information or information that could identify the candidate and applicant institution.

#### 3. *Statement of Benefit to California (up to 3000 characters in Part A)*

Describe in a few sentences how the proposed research will benefit the State of California and its citizens. This Statement of Benefit will become public information; therefore, do not include proprietary or confidential information or information that could identify the candidate and applicant institution.

#### 4. *Key Personnel (included in Part A and C)*

List all key personnel and their roles on the project. Key personnel are defined as individuals who contribute to the scientific development or execution of the project in a substantive, measurable way, whether or not they receive salaries or compensation under the grant. Key personnel may include any technical staff, trainees, co-investigators (collaborators), or consultants who meet this definition. A minimum of one percent effort is required for each key person, except the PI, who is required to commit a minimum of ten percent effort. For each key personnel (except for technical staff and students) listed, provide a two-page biographical sketch using the template provided. The sketch should highlight prior research experience and/or special skills related to the proposed research. Include relevant publications and/or patent or patent applications.

Provide all budget information requested in the budget section of the Application Information Form. All allowable costs for research grants are detailed in the CIRM Grants Administration Policy (GAP, see section XI.A of this RFA). Under this RFA, allowable costs include the following:

5. *Budget (included in Part A)*

- Salaries for Key Personnel

Salaries for Key Personnel may include the Principal Investigator, Co-Investigators, Research Associates, and technical support staff (all of whom must work in California) based on percent of full time effort commensurate with the established salary structure of the applicant institution. The total salary requested by the PI must be based on a full-time, 12-month staff appointment. Institutions may request stipend, health insurance and allowable tuition and fees as costs for trainees. Administrative support salaries are expected to be covered exclusively by allowed Indirect Costs.

- Supplies

Grant funds will support supplies, including specialized reagents, reimbursement costs for human tissue donations (see section XI.D of this RFA for details), and animal costs. Minor equipment purchases (less than \$5,000 per item) are considered Supplies and may be included as direct costs in the budget.

- Travel

Recipients (PIs) of CIRM Tools and Technologies Awards are required to attend an annual CIRM-organized meeting in California and should include in the budget the travel costs for this meeting. Travel costs associated with collaborations necessary to the grant are allowable. Details of allowable travel costs can be found in the GAP (see section XI.A of this RFA).

- Equipment

Major equipment (more than \$5,000 per item) necessary for conducting the proposed research at the applicant institution should be itemized. Equipment costs should not be included as allowable direct costs in indirect cost calculations.

- Indirect Costs

Indirect costs will be limited to 20 percent of allowable direct research funding costs awarded by CIRM (i.e., project costs and facilities costs), exclusive of the costs of equipment, tuition and fees, and subcontract amounts in excess of \$25,000.

6. *Rationale and Significance (up to 1 page in Part B)*

Summarize the context and background of the present application and the specific rationale for the work proposed. Evaluate existing knowledge and technology, and specifically identify the gaps that the project is intended to fill. If the aims of the application are achieved, state how the tool or technology will make a critical contribution to the stem cell field by overcoming a specific road block in basic, translational or clinical stem cell research.

7. *Specific Aims, Milestones and Timeline (up to 2 pages in Part B)*

Explain the overall objective(s) for the development and testing of novel tools and technologies (e.g., to test a stated hypothesis, solve a specific problem, provide proof of concept for a paradigm, or address a critical barrier to progress in the field). Identify and enumerate each specific aim of the proposal in a concise and step-wise fashion. Enumerate milestones for the project, ideally for each specific aim, that are quantitative and scientifically justified. The milestones are a means of determining whether the specified objective(s) of the project have been successfully met. Milestones should be clearly stated and presented in a quantitative manner, such as numerical specifications of sensitivity and specificity for an assay or count of some newly derived monoclonal antibodies to cell surface markers that meet specific criteria for potency, specificity and utility. Provide a realistic time table for completing each proposed specific aim and for achieving the related milestones.

8. *Research Design and Methods (up to 4 pages in Part B)*

Describe concisely, but in sufficient detail to permit evaluation of the merit of the research, the experimental design, methods and techniques to be employed to achieve the aims and milestones specified in the proposal. Identify the new or risky aspects of the research, anticipated pitfalls, and plans to overcome or circumvent difficulties that may arise. Describe the methods of analysis of results including those that will determine milestone achievement.

9. *Feasibility and (when applicable) Preliminary Data (up to 3 pages in Part B)*

Provide any information that will help to establish the experience and competence of the PI and his/her team to pursue the proposed project. If collaboration is integral to the success of the project, describe how this will be achieved. When applicable, provide preliminary data to support the concepts, hypotheses and/or approaches proposed in the application.

10. *References (up to 2 pages in Part B)*

List all references used in the body of the proposal.

11. *Laboratory Facilities including Major Equipment (up to 1 page in Part B)*

Provide a short description of the facilities and environment in which the work will be done, and the major equipment and resources available for conducting the proposed research. Discuss ways in which the proposed studies will benefit from unique features of the scientific environment or employ useful collaborative arrangements where applicable.

## **VII. SUBMITTING AN APPLICATION**

Applications will only be accepted from PIs who 1) have been officially nominated on a CNF by their host institution and 2) have submitted a Letter of Intent (LOI) that was accepted by CIRM.

The application for CIRM Tools and Technologies Awards consists of three parts:

Part A: Application Information Form

Part B: Tools and Technologies Award Research Proposal

Part C: Biographical Sketches for Key Personnel

**All three parts of the application for CIRM Tools and Technologies Awards (see section VI.C of this RFA) must be submitted together and received by CIRM no later than 5:00PM on July 10, 2008, in both electronic form as well as in hard copy (signed original and five copies). No exceptions will be made.**

Candidates must use the appropriate CIRM templates to complete Parts A, B and C. These templates will be available on the CIRM website by May 9, 2008. Send electronic copies of all three parts of the application as attachments in a single email to [ToolsAndTechnologiesAwards@cirm.ca.gov](mailto:ToolsAndTechnologiesAwards@cirm.ca.gov). In addition to the electronic submittal, candidates must submit an original copy of the application (consisting of Parts A-C) signed by both the PI and the institution's Authorized Organizational Official (AOO), plus 5 copies of the full application (preferably double-sided) to:

Tools and Technologies Award Application California Institute for Regenerative Medicine  
210 King Street

San Francisco, CA 94107

**The electronic version of the application, as well as the original signed application plus the five copies must be received by CIRM no later than 5:00PM on July 10, 2008. No exceptions will be made.**

## **VIII. SCHEDULE OF RECEIPT AND ANTICIPATED REVIEW**

<b>Receipt of Candidate Nomination</b>	<b>5:00 PM (PDT) on June 11, 2008</b>
<b>Forms and Letters of Intent:</b>	
<b>Receipt of Applications:</b>	<b>5:00 PM (PDT) on July 10, 2008</b>
<b>Anticipated Review of Applications</b>	<b>September, 2008</b>
<b>by Grants Working Group (GWG):</b>	
<b>Anticipated Review and Approval by</b>	<b>December, 2008</b>
<b>ICOC:</b>	
<b>Earliest Funding of Awards:</b>	<b>March, 2009</b>

## **IX. REVIEW AND AWARD PROCESS**

CIRM Tools and Technologies Award applications will be reviewed by the CIRM Scientific and Medical Research Funding Working Group (the Grants Working Group, or GWG). The GWG consists of fifteen basic and clinical scientists from institutions outside

California, seven patient advocates who are members of the Independent Citizen's Oversight Committee (ICOC), and the Chair of the ICOC. The membership of the GWG can be found at on the GWG page. The ICOC was established by the California Stem Cell Research and Cures Act (Proposition 71) to oversee CIRM and makes all final funding decisions. The composition of the ICOC can be viewed on the governing board page.

Fifteen scientists on the GWG will review the applications and rate them according to scientific and technical merit. For Tools and Technologies Award applications, particular emphasis will be placed on: 1) the impact of the research to overcome current road blocks and advance the stem cell field, 2) the design and feasibility of the research plan; and 3) the qualifications of the Principal Investigator and the research team.

The full membership of the GWG will then review the entire portfolio of applications, taking into consideration the following criteria:

- Appropriate balance between innovation and feasibility.
- Appropriate balance between usefulness of novel tools and technologies for fundamental research, therapy development and clinical utility.
- Where relevant, the appropriate balance and range of diseases and genetic diversity addressed.
- Other considerations from the perspective of patient advocates.

The GWG's recommendations for funding will then be forwarded to the ICOC, which will make all funding decisions.



## **X. CONTACTS**

For information on this RFA: Sohel Talib, Ph.D

Scientific Officer

California Institute for Regenerative Medicine 210 King Street

San Francisco, CA 94107 Email: [stalib@cirm.ca.gov](mailto:stalib@cirm.ca.gov) Phone: (415) 396-9137 FAX: (415) 396-9141

For information about the review process: Gilberto R Sambrano, Ph.D.

Senior Officer to the Grants Working Group California Institute for Regenerative Medicine  
210 King Street

San Francisco, CA 94107 Email: [gsambrano@cirm.ca.gov](mailto:gsambrano@cirm.ca.gov) Phone: (415) 396-9103

FAX: (415) 396-9141

For information about electronic forms: Ed Dorrington

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For programmatic information: Patricia Olson, Ph.D.

Director of Scientific Activities

California Institute for Regenerative Medicine 210 King Street

San Francisco, CA 94107 Email: [polson@cirm.ca.gov](mailto:polson@cirm.ca.gov) Phone: (415) 396-9116  
FAX: (415) 396-9141

## **XI. OTHER REQUIREMENTS**

### **A. CIRM Grants Administration Policy**

CIRM's Grants Administration Policy (GAP) for Academic and Non-Profit Institutions (Non-Profit GAP) and the Interim GAP for For-Profit Institutions (For-Profit GAP) serve as the standard terms and conditions of grant awards issued by CIRM. All research conducted under this award must comply with the stated policy. The Non-Profit GAP can be found on the regulations page.

The Interim For-Profit GAP may be found on the regulations page. Funding from year to year will depend on scientific progress achieved.

## **B. Intellectual Property Regulations**

CIRM has adopted regulations governing intellectual property resulting from CIRM-funded research at Non-Profit and academic institutions (Title 17, California Code of Regulations, sections 100300-100310).

CIRM also has adopted regulations governing intellectual property for for-profit institutions. The regulations, Title 17, California Code of Regulations, Sections 100400-100410.

## **C. Sharing of Tools and Technologies**

To ensure greatest possible impact of this initiative on the advancement of stem cell research and medical therapies, and in compliance with Title 17, California Code of Regulations, section 100304, CIRM requires that immediately after publication, the tools and technologies be made available to other researchers in California for research purposes at no cost or at the actual cost of providing the material. Sharing of tools and technologies with researchers outside of California is strongly encouraged.

For-Profit organizations are also subject to sharing requirements, as set forth in Title 17, California Code of Regulations, section 100404.

## **D. Human Stem Cell and Tissue Research Regulations**

CIRM has adopted medical and ethical standards for human stem cell research (Title 17, California Code of Regulations, sections 100010 -100110). All research conducted under this award will be expected to comply with these standards. While these regulations prohibit donors of gametes, embryos, somatic cells or human tissue from receiving valuable consideration for their donation, they do allow for reimbursement for permissible expenses as determined by an Institutional Review Board (IRB) (Title 17, California Code of Regulations, section 100080). For research activities proposing to obtain gametes, embryos, somatic cells or tissue from human subjects, CIRM requires the candidate to submit, at the time of application, their reimbursement policy describing how they intend to calculate permissible expenses.

Adult stem cells are derived from various differentiated tissues, including human fetal tissue. The use of human fetal tissue in research by CIRM grantees is regulated by Title 17, California Code of Regulations, section 100085.

**ICOC approval:**

Dec 10, 2008

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**Source URL:** <https://www.cirm.ca.gov/our-funding/research-rfas/tools-and-technologies-i>