

---

**RFA 09-03: CIRM Stem Cell Transplantation Immunology**

---

## **I. Purpose**

The potential for stem cells to replace or restore tissues lost to injury or disease represents one of the most promising outcomes of regenerative medicine. As is the case with whole organ transplantation, these stem cell grafts are often not host derived. The grafts possess major and minor histocompatibility antigen (MHC, mHA) differences that, when recognized by the host immune system as foreign, can ultimately lead to their rejection. Thus, it will be necessary to overcome significant challenges related to immune rejection before such therapies can be made practical and effective. The purpose of the CIRM Stem Cell Transplantation Immunology initiative is to support transformative research leading to the development of immune tolerance of pluripotent stem cell derivatives and the potential correction of autoimmunity.

## **II. Objectives**

The introduction of novel immunosuppressive therapies has led to significant improvement in the short-term survival of solid organ allografts. However, these immunosuppressants are non-specific and increase the risks of both opportunistic infection and cancer. Therefore, novel approaches for inducing robust, sustained, tolerance of allogeneic transplants would be of major benefit not only for stem cell replacement therapies, but also for solid organ transplants. Current animal models and immunological assays are of limited utility in predicting graft acceptance or rejection in allogeneic human hosts. The development of more predictive tools will be critical for preclinical assessment of progress towards graft acceptance.

Based on recent advancements in the stem cell field, several approaches have potential to improve the acceptance of transplanted stem cells and their differentiated derivatives. For example, the derivation of hematopoietic stem cells (HSC) from human embryonic stem cells (hESC) opens the possibility of donor specific tolerance induction via hematopoietic chimerism. The recipient immune system is reconstituted with ES-derived HSC followed by transplantation of therapeutic tissue derived from the same hESC line. However, while research to differentiate hESC into HSC is making considerable progress, the efficiency of engraftment of HSC in the recipient remains a challenge. Similarly, because of their immunomodulatory properties, dendritic cells (DCs) and regulatory T (Treg) cells could also induce donor specific tolerance and graft acceptance in allogeneic hosts. Methods for efficient derivation of tolerogenic DCs and Tregs

are needed to enable clinical application of these strategies. The thymus plays a primary role in the generation of thymocytes as well as the deletion of potentially self-reacting thymocytes. Rejuvenation of the thymus is therefore an important strategy to induce and sustain donor specific tolerance to hESC-derived grafts. The mirror image of tolerance is autoimmunity where reinitiating self-tolerance is needed and critical for the successful cell therapy of a variety of diseases such as Type 1 diabetes and multiple sclerosis.

To address these areas of stem cell transplantation immunology, CIRM proposes a new program. This program is specifically directed towards the goal of inducing tolerance to stem cell grafts. Potential strategies include means to manipulate the host immune system or engineer allogeneic grafts to promote their acceptance. This Request For Application (“RFA”) will also support the development and verification of animal models to predict the human immune response to allogeneic transplantation as well as the development of sensitive immunological assays to monitor graft acceptance or rejection.

CIRM will only consider research proposals utilizing human or mammalian stem cells, or tissues or cells derived from them in culture. Particular consideration will be given to those proposals that are ineligible for or unlikely to receive funding from the United States Federal government.

### **III. Award Information**

Under this RFA, CIRM intends to commit up to \$30 million to support about 20 awards. Projects will be funded for up to three years, with justifiable direct project costs of up to \$300,000 per year. Given the urgency of CIRM’s mission, all approved applications must be initiated (grant start date in issued and signed Notice of Grant Award) within 6 months (preferentially within 3 months) of approval and authorization for funding by the CIRM’s governing board, the Independent Citizen’s Oversight Committee (“ICOC”), unless CIRM’s President grants an extension.

### **IV. Collaborative Funding Partners**

CIRM has established a program with several other government agencies that fund stem cell and regenerative medicine research. Through this Collaborative Funding Partner program, California-based Principal Investigators (PIs) can collaborate with a Funding Partner PI (“Partner PI”) from a Funding Partner applicant institution (“partner applicant institution”) eligible for funding from one of CIRM’s collaborative funding partners to bring important additional resources to proposed projects. If a collaborative funding proposal is approved (a “CIRM/Funding Partner Award”) CIRM will fund all project work done within the State of California and its Funding Partner will fund all project work within its jurisdiction. For this RFA, the State of Victoria, Australia and the Federal Ministry for Education and Research, Germany (BMBF) are each participating as a Collaborative Funding Partner (CFP). To apply for a collaboratively funded project involving CIRM and one of its CFPs, applicants must satisfy both the

CIRM processes and requirements (Section VI below) and any additional requirements put forth by the applicable CFP. Please see Appendices A and B for information and requirements of BMBF and Victoria, respectively.

Before funding contracts are signed, successful CIRM/CFP applicant teams must have signed written agreements addressing Intellectual Property (IP) and other issues relating to their collaborative project and must provide CIRM and its applicable CFP with copies. These applicant team Agreements must be consistent with CIRM's applicable IP regulations, with the IP requirements of the applicable CFP and with the provisions of all Agreements between the co-funders.

Successfully funded applicants for this RFA whose projects are specifically relevant to therapy for type 1 diabetes and that require research outside the State of California are encouraged to contact the Juvenile Diabetes Research Foundation International ("JDRF") (<http://www.jdrf.org/>), which may provide funding for the portion of these projects conducted outside the State of California. Contact: Adrienne L. Wong, Ph.D. at [awong@jdrf.org](mailto:awong@jdrf.org) or at +1 212-479-7642.

## **V. Notification Regarding Disclosure of Information**

All applicants, including those not applying with a Partner PI, are hereby notified that CIRM may share LOI's, applications and related information submitted by applicants with Victoria, and/or BMBF in order to facilitate their participation in the Immunology RFA program. Information concerning approved CIRM/Funding Partner Awards may also be shared with Victoria and/or BMBF. Before receiving any such material, Victoria and BMBF will undertake in writing to hold the materials in strict confidence and to use them solely for purposes directly related to the Immunology RFA.

## **VI. Eligibility**

### **A. Project Eligibility**

Under this RFA, CIRM will not limit the number of applications from each eligible institution. However, CIRM will not accept a Letter of Intent (LOI) for any project that does not meet the following Eligibility Criteria.

1. The project must use human or mammalian stem cells or stem cell-derived tissues or cells.
2. All aims of the proposed project must have applicability to the development of tolerance to stem cell grafts. The proposed research aims must directly address one or more of the following:
  - a) Reprogramming of the host immune system to accept stem cell grafts

- b) Engineering stem cell derivatives to facilitate graft acceptance in allogeneic hosts
  - c) Development of predictive animal models of the human immune response to stem cell transplantation
  - d) Development and optimization of tolerance induction to stem cell derived grafts via hematopoietic and/or thymic chimerism
  - e) Development and assessment of cell based strategies utilizing hPSC-derived dendritic cells and/or tolerogenic T cells (Tregs) that have the potential to induce donor-specific tolerance and/or lead to the correction of autoimmune diseases
  - f) Development of sensitive, robust, assays for monitoring or predicting stem derived graft acceptance or rejection that can be adapted for clinical use.
3. The Principal Investigator (PI), Co-Investigator and or Partner PI, either individually or collectively, must have published expertise in both transplantation immunology and stem cell research. **The PI must have published expertise in at least one of these two areas.**
4. CIRM funding under this RFA may not be used for studies involving non-mammalian cells or models, immunology studies not directly related to items a-f above, clinical studies or commercial scale up technology development. Analysis of human subject samples, if directly related to the proposed research, can be funded.

## **B. Institutional Eligibility**

All CIRM-supported research must be conducted in California. Principal Investigators may apply from non-profit and for-profit research organizations that are, at the time the application is submitted, conducting research at a site in California.

“Non-profit organization” means: (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”.

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

A Principal Investigator (PI) may submit only one application under this RFA. The PI must have an M.D., Ph.D. or equivalent degree, and must be authorized by the applicant institution to conduct the proposed research 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; and
- have documented commitment from the applicant institution to provide laboratory space and shared resources sufficient to carry out the proposed research.

#### **D. Percent Effort Requirements**

CIRM, mindful of the urgency of its mission, will only fund PIs who are willing and able to commit a minimum of 10% effort to the proposed project. In addition the Co-Investigator or Partner PI providing complimentary stem cell or immunology expertise must also commit 10% effort towards the project. During review of the application, CIRM will instruct reviewers to give added consideration to applications where the PI, the Co-Investigator or Partner PI providing complimentary stem cell or immunology expertise commits effort in excess of the stated minimum.

### **VII. Application and Evaluation Process**

Submission of an application for the Stem Cell Transplantation Immunology RFA involves a two-step process. Any qualified applicant may submit a Letter of Intent (LOI). Unless notified by CIRM that they do not meet the eligibility criteria (as defined in section VI) based on information provided in the LOI, all applicants that submitted a LOI that was accepted by CIRM may submit an application. The PI, Co-Investigator and Partner PI (if applicable) providing complementary expertise (see section VI) and the research project proposed in the application must be the same as those described in the Letter of Intent; otherwise, the application is deemed ineligible.

Applications will be evaluated by the CIRM Grants Working Group (GWG), which is composed of fifteen scientific experts from outside California, seven patient advocate members of CIRM's governing board, the Independent Citizen's Oversight committee (ICOC), and the Chair of the ICOC. The membership of the GWG can be found at <http://www.cirm.ca.gov/GrantsWkgGrpMembers>. The composition of the ICOC can be viewed at <http://www.cirm.ca.gov/ICOCMembers>. The fifteen scientists on the GWG will review the applications and score them according to scientific and technical merit applying the review criteria described in section VIII below. The full membership of the GWG will then review the entire portfolio of applications, taking into consideration the following criteria:

- Appropriate balance among applications addressing focus areas of stem cell transplantation immunology research.
- Appropriate balance between innovation, risk and feasibility.
- Other considerations from the perspective of patient advocates.

The GWG will make funding recommendations to the ICOC, which will make final funding decisions.

## VIII. Review Criteria

Applications will be evaluated in three key areas: (1) innovation and impact of the proposed research, (2) scientific rationale, design and feasibility of the research plan and (3) the qualifications and track record of the PI, Co-Investigator and Partner PI (if applicable). As CIRM is particularly interested in transformative research, reviewers will be asked to consider innovative proposals where there is strong scientific rationale even if preliminary data is limited or lacking. Moreover, reviewers will be asked to evaluate whether the PI, Co-Investigator and, or Partner PI (if applicable), either individually or collectively, have experience in the both immunology and stem cell fields as required by this RFA. The specific criteria for review of applications (below) are elaborated from the standard review criteria described in the CIRM Grants Administration Policy (GAP, see section XIII of this RFA).

### 1. Innovation and Impact

- A. Innovative Project: The research is innovative in proposing novel ways to induce central or peripheral tolerance to a stem cell allogeneic graft.
- B. Creative Approach: The project utilizes a creative approach to the research.
- C. Major Impact: If successful, the proposed research will have major impact on the RFA's focus areas of research (see section VI A.). It will significantly advance the broader clinical applicability of stem cell derived therapies rather than incrementally advancing the field.

### 2. Rationale, Design and Feasibility of the Research Plan

- A. Scientific Rationale: The rationale for the development and testing of tolerance strategies is logical, convincing and based on strong scientific evidence.
- B. Sound Approach: The proposed research is carefully designed to give meaningful results.
- C. Logical and Achievable Aims: The specific aims are logical and the research proposal well organized, with achievable milestones and timelines provided over 3-year timeframe.
- D. Alternative Plans: Potential difficulties are acknowledged and alternative plans are provided should the proposed strategies fail.
- E. Preliminary data: The preliminary data, if available, are compelling and supportive of the proposed concepts, hypotheses and approaches.

### 3. Qualifications of the Principal Investigator (PI) and Research Team

- A. Qualifications: Evidence of prior success and track record supports the qualification of the PI to lead and conduct the proposed research. The PI, Co-Investigator, and/or Partner PI (if applicable) among them, have the training and experience in immunology and or stem cell research to conduct the proposed project. There is cited published work supporting the required expertise and experience. The PI has developed an appropriate budget.
- B. Commitment: The PI is committing a minimum of 10% effort to the proposed research to maximize timely achievement of the research goals. The Co-Investigator or Partner PI providing complimentary expertise is committing a minimum of 10% effort towards the proposed project. Reviewers are requested to give special consideration to applications where the PI, Co-Investigator or Partner PI providing complimentary stem cell or immunology expertise commits effort in excess of the stated minimum above.
- C. Research Team: The research team has the appropriate expertise and commitment to conduct the proposed research. Any proposed collaboration is integral to the success of the project.

## IX. Application Procedure

Applicant institutions and PIs must follow these instructions for submitting a Letter of Intent and Application for the CIRM Stem Cell Transplantation Immunology Awards. Applications will only be accepted from PIs who have submitted a Letter of Intent that was accepted by CIRM. The PI, Co-Investigator and Partner PI (if applicable) providing complementary expertise (see section VI) and the research project proposed in the application must be the same as those described in the Letter of Intent; otherwise, the application is deemed ineligible.

### A. Letter of Intent (LOI)

Each PI must submit a LOI using the LOI template provided at <http://www.cirm.ca.gov/grants/default.asp>. The LOI should concisely describe the proposed project including the overall goals, technical approaches and how it will specifically address the development of tolerance to stem cell grafts. Applicants must answer the questions included in the LOI template provided. **The completed LOI should be sent as an email attachment to [immunologyLOI@cirm.ca.gov](mailto:immunologyLOI@cirm.ca.gov) and must be received by CIRM no later than 5:00PM (PST) on December 15, 2009. No exceptions will be made.**

### B. Application Submission Instructions

Application forms will be available on the CIRM website (<http://www.cirm.ca.gov/grants/default.asp>) by December 1, 2009. Only those applicants that submitted a LOI that was accepted by CIRM



may submit an application. The Application for the CIRM Stem Cell Transplantation Immunology Awards consists of four parts:

Part A: Application Information Form, (Adobe PDF template provided at <http://www.cirm.ca.gov/grants/default.asp>). Part A includes: Abstract, Public Abstract, Statement of Benefit to California, Key Personnel, and Budget (sections 1- 5 below). Part A consists of the following subparts:

Part A – PI Application Information Form

Part A subpart II – Partner PI Information Form (if applicable)

Part B: Stem Cell Transplantation Immunology Awards Research Proposal (MS Word template provided at <http://www.cirm.ca.gov/grants/default.asp>). Part B includes: Scientific Rationale and Impact; Project Objective, Success Criteria, Specific Aims, Milestones and Timeline; Research Design and Methods; Feasibility and (when applicable) Preliminary Data; Collaborations, Resources and Environment; and References (section numbers 6-11).

Part C: Biographical Sketches for the Key Personnel (MS Word template provided at <http://www.cirm.ca.gov/grants/default.asp>) and letters of collaboration.

Part D: Related Business Entities (Adobe PDF template provided at <http://www.cirm.ca.gov/grants/default.asp>). In order to comply with the conflict of interest policies under which CIRM operates, Part D must be submitted by the applicant organization to indicate whether the application would, if awarded, provide funding from CIRM or (if applicable) from a Collaborative Funding Partner to a for-profit organization that is either: 1) the applicant organization; 2) a subcontractor; or 3) the employer of the Co-Investigator, consultant or subcontractor (section number 12 below).

The application for Stem Cell Transplantation Immunology Awards includes the following:

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.
2. *Public Abstract (up to 3000 characters in Part A)*  
In lay language, briefly describe the proposed research and how it will, directly or indirectly, contribute to the development of stem cell transplantation tolerance. This Public Abstract will become public information; do not include proprietary or confidential information or



information that could identify the candidate and applicant institution or, if applicable, the Partner PI and his/her 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; do not include proprietary or confidential information or information that could identify the candidate and applicant institution or, if applicable, the Partner PI and his/her 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. For CIRM/CFP applications, key personnel sponsored by the CFP must also be listed in the corresponding section of Part A subpart II. A minimum of one percent effort is required for each key person, except for the PI and the Co-Investigator or Partner PI (if applicable) providing complimentary expertise (see section VI D), who are 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 relevant research experience, accomplishments and/or special skills related to the proposed research. Include relevant publications and/or patent or patent applications and regulatory filings.
5. *Budget (included in Part A)*  
Provide all budget information requested in the budget section of the Application Information Form. For CIRM/CFP collaborations, the funding requested from the CFP (total and per year requested) must be indicated and justified in sufficient detail (in Part A subpart II section "Budget Justification") for reviewers to assess the appropriateness of the non-California research budget.

All allowable costs for research funded by CIRM are detailed in the CIRM Grants Administration Policy (GAP, see section XIII of this RFA). For CIRM/CFP collaborations, allowable costs for research funded by the CFP may differ. Guidance will be provided separately by the CFP (see Appendices A and B).

Under this RFA, CIRM-funded allowable costs include the following:

- 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 perform the subject 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 may be used for supplies, including specialized reagents, 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 Stem Cell Transplantation Immunology 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 XIII 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 and justified. 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. *Scientific Rationale and Impact (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 proposed approach will make a critical contribution to the stem cell field by overcoming the immunological barrier to translation of stem cell therapies to the clinic.

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

State the objective(s) of the specific research proposed. Define success criteria to assess whether the objective of the proposed research has been achieved. Success criteria must be well described, meaningful and scientifically justifiable. List each specific aim of the proposal in a concise and step-wise fashion, and describe how each aim will support the objective of this research. Enumerate milestones for the project, ideally for each specific aim, which provide a measure of progress toward achieving the aim. Provide a realistic timetable 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.

For applications from CIRM/CFP collaborators, applicants must clearly delineate the research that will be performed in California and funded by CIRM from the research that will be funded by the CFP. This delineation is essential for review of the research plan and the appropriateness of the budget.

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, Partner PI (where applicable) and the team(s) to pursue the proposed project. 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. *Collaboration, Resources and Environment (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. If collaboration (including CIRM/CFP collaborations) is integral to the success of the project, describe how the collaboration will be managed.

#### 12. *Related Business Entities (Part D)*

All applicants (including, if applicable, a Funding Partner applicant) must provide information on related business entities for any application that, if awarded, would fund a for-profit organization either as: 1) the applicant organization; 2) a subcontractor or 3) the employer of a Co-Investigator, consultant or subcontractor. If the application does not seek funding for any such for-profit organizations, indicate that on Part D and submit the form. If for-profit funding is sought, include the following for each such for-profit organization to be funded:

- A list of any parent organization that owns 50% or more of the for-profit's voting shares;
- A list of all subsidiaries in which the for-profit owns 50% or more of the voting shares; and
- A list of all other related business entities (i.e., entities with which the for-profit shares management and control, or shares a controlling owner).

## **X. Submitting an Application**

Applications will only be accepted from PIs who have submitted a Letter of Intent that was accepted by CIRM.

The Application for CIRM Stem Cell Transplantation Immunology Awards consists of four parts:

Part A: Application Information Form (Adobe PDF template provided at <http://www.cirm.ca.gov/grants/default.asp>.)

Part B: Stem Cell Transplantation Immunology Award Research Proposal (MS Word template provided at <http://www.cirm.ca.gov/grants/default.asp>.)

Part C: Biographical Sketches for Key Personnel (MS Word template provided at <http://www.cirm.ca.gov/grants/default.asp>.)

Part D: Related Business Entities (Adobe PDF template provided at <http://www.cirm.ca.gov/grants/default.asp>.)

For this RFA, all four parts of the Application (see section IX.B) must be submitted together and received by CIRM no later than **5:00PM PST on January 26, 2010 in both electronic forms well as in hard copy (signed original and five copies). No exceptions will be made.** Send electronic copies of all parts of the Application as attachments in a single email to [immunology@cirm.ca.gov](mailto:immunology@cirm.ca.gov). In addition to the electronic submission, candidates must submit an original copy of the Application (consisting of Parts A-D) signed

by both the applicant and the institution's Authorized Organizational Official (AOO), plus 5 copies of the Application (preferably double-sided) to:

Stem Cell Transplantation Immunology Application  
California Institute for Regenerative Medicine  
210 King Street  
San Francisco, CA 94107

## **XI. Schedule of Deadlines and Reviews**

Receipt of Letter of Intent	5:00 pm (PST), Tuesday, December 15, 2009
Receipt of Applications	5:00 pm (PST), Tuesday, January 26, 2010
Anticipated Review of Applications by Grants Working Group (GWG)	April 2010
Review and Approval by ICOC	June 2010
Earliest Funding of Awards	Summer, 2010

## **XII. Contacts**

### For information on this RFA:

Sohel Talib, Ph.D.  
Scientific Officer II  
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 Review Officer  
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

## **XIII. CIRM Regulations**

Grant awards made through this RFA will be subject to CIRM regulations. These regulations can be found on CIRM's website at <http://www.cirm.ca.gov/req/default.asp>.

## **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. Progress reports of research, as required by the GAP, are important to CIRM: Funding from year to year will depend on adequate scientific progress as outlined in the grant application timeline.

## **B. Intellectual Property Regulations**

CIRM has adopted intellectual property and revenue sharing regulations for non-profit and for-profit organizations (see <http://www.cirm.ca.gov/Regulations>). By accepting a CIRM Grant, the Grantee agrees to comply with all such applicable regulations.

## **C. Human Stem Cell 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). "Permissible Expenses" means necessary and reasonable costs directly incurred as a result of donor participation in research activities and may include costs such as those associated with travel, housing, child care, medical care, health insurance and actual lost wages. For research activities proposing to obtain gametes, embryos, somatic cell 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.

## **Appendix A: National eligibility criteria for partner-PIs from Germany**

This first participation of the Federal Ministry for Education and Research (BMBF) in a research call of the California Institute for Regenerative Medicine (CIRM) is a pilot project. Eligible for funding under this pilot are all BMBF grantees supported by BMBF grants in the field of translational and regenerative medicine. Under this pilot, BMBF grantees may reallocate an appropriate sum of granted BMBF funds to collaborative activities under CIRM's RFA 09-03, CIRM Stem Cell Transplantation Immunology.

The applicants (partner-Principal Investigators, partner-PIs) have to form consortia with their respective Californian partners and follow CIRM's application procedure as outlined in CIRM's RFA 09-03.

To participate in CIRM's RFA 09-03, the German partner-PIs have to provide an informal request in writing to the Project Management Jülich, PtJ (Projekträger Jülich), delineating

- i.) under which grant the reallocation is intended to be performed
- ii.) the added value of the international cooperation over the existing grant
- iii.) the impact of the reallocation of funds upon the existing grant and the following utilization.

This request has to be submitted to PtJ in parallel to the submission of the LOI to CIRM (December 15, 2009 deadline).

All requests will be subjected to an eligibility check. Positively evaluated requests from BMBF Grantees will enter CIRM's evaluation procedure.

Additional German application documents (AZA/AZK) are not required for the pilot activity.

It is recommended that potential German applicants contact PtJ prior to an application for further advice.

### Contact point:

Dr. Marion Wehner  
Projekträger Jülich, BIO 4  
Tel.: ++49 2461/ 61 4809  
E-mail: [m.wehner@fz-juelich.de](mailto:m.wehner@fz-juelich.de)

The funding regulations, the follow up and reporting of publicly funded projects are regulated according to ANBest (Allgemeine Nebenbestimmungen), BNBest (Besondere Nebenbestimmungen) and NKBF 98 (Nebenbestimmungen für Zuwendungen auf Kostenbasis des Bundesministeriums für Bildung und Forschung an Unternehmen der gewerblichen Wirtschaft für Forschungs- und Entwicklungsvorhaben).



## **Appendix B: Key Points for joint Victorian-Californian applicants to the Stem Cell Transplantation Immunology RFA.**

The Victoria-California Stem Cell Alliance Program will be jointly administered by the Victorian Department of Innovation, Industry and Regional Development (DIIRD) and the California Institute for Regenerative Medicine (CIRM). CIRM will fund the Californian aspects of joint projects and the Department of Innovation, Industry and Regional Development (DIIRD) will fund the Victorian aspects of joint projects.

### **Full Guidelines:**

The Victoria-California Stem Cell Alliance Grant Program Guidelines for the Stem Cell Transplantation Immunology RFA will be available from the contact point below from 10 November. It is essential that joint applicants request, read and understand these guidelines.

### **Funding Available in Victoria:**

The Victorian Government will commit up to Au\$2 million to support approximately 3 - 4 joint project awards with a maximum grant of up to Au\$500,000 to Au\$600,000 over a period up to three years. This funding must be used to support the Victorian research components, in Victorian institutions, for joint teams that are successful in the CIRM selection process and awarded CIRM funding. The Victorian grant award will be in addition to the CIRM award.

DIIRD will only fund direct research costs, no indirect costs will be eligible for funding. DIIRD is not seeking matched funds from Victorian applicants but applicant teams and their institutions are expected to bring in-kind resources to projects and detail these contributions clearly in the application.

### **Project Budget Allowables:**

To simplify comparisons, your joint application documents should be stated in US\$ but the Victorian-only budget details will also need to be supplied to DIIRD in Au\$.

Victorian Government project funds awarded under this Program will not include indirect costs - including the salary for the Principal Investigator (PI).

Project Funds in Victoria may include or typically be used for supplies & equipment; salaries (proportionately to % effort) and training costs; and travel.

### **Contact Point for further information in Victoria:**

Enquiries about the Victoria-California Stem Cell Alliance Grant Program and this RFA may be addressed to:

Mr. Roland Diggins, Science and Technology Programs  
Department of Innovation Industry and Regional Development (DIIRD)  
E-mail: [roland.diggins@diird.vic.gov.au](mailto:roland.diggins@diird.vic.gov.au) Telephone: (+ 61 3) 9651 8102

*The following pages provide simplified information on the application process and eligibility requirements - aimed at Victorians intending on jointly applying with a Californian collaborator. (Please review the full guidelines for detailed information.)*

### **Overview of the Application Format and Process:**

A single application, jointly prepared by the two collaborating applicants, and using the standard CIRM Letter of Intent and Application Documents (meeting the two separate deadlines) is the minimum requirement for CIRM in California.

However, further detail is required of applicants in Victoria and the information below indicates both the requirement in California and the additional minimum requirement for DIIRD in Victoria.

For clarity and to limit unnecessary duplication in preparing applications, DIIRD has sought to adopt the standard CIRM application and selection process when possible and CIRM has included options for collaborative partnerships within the RFA documentation. The application will be judged on the basis of the standard CIRM Grant Working Group process which includes both a scientific and programmatic review.

### **STAGE 1 – the Letter of Intent**

#### **In California - Letter of Intent document.**

All Californian and Victorian Principal Investigators planning to apply for an award must notify CIRM and DIIRD in a Letter of Intent (LOI) (please see section IX A in RFA 09-03, Stem Cell Transplantation Immunology Awards (pdf). The LOI Form contains options which allow joint applicants to provide information for both the Californian and Victorian collaborators. To be eligible, information must be completed for both.

**The LOI must be received by CIRM (and copied by email to DIIRD in Victoria) no later than 5:00PM (PST) on 15 December 2009 - as an email attachment to: [immunologyLOI@cirm.ca.gov](mailto:immunologyLOI@cirm.ca.gov) (and copied to [roland.diggens@iird.vic.gov.au](mailto:roland.diggens@iird.vic.gov.au)). No exceptions will be made.**

**In addition, In Victoria - A requirement of all Victorian participants is that they also submit the following additional information documents to DIIRD three working days prior to lodgment of the LOI – by 9 Dec 2009:**

- A copy of the signed Candidate Nomination Letter (CNL). (See below and Guidelines).
- A Table / List, countersigned by their Department or Faculty Head, of the Victorian PIs (referred to in CIRM documents as “Partner PIs”) current grants / research projects and their respective % Effort Expended on these existing commitments. (Note: At least 10% Victorian PI effort required.)
- A Table / List, countersigned by their Department or Faculty Head, of the existing grant / research commitments and their respective % Effort Expended by the Victorian PIs proposed staff on this project. (10% + effort will be expected from senior staff.)

**Candidate Nomination Letter:**

Each Victorian PI must be an independent investigator at a non-profit administering institution, or have an equivalent position and be an employee of a for-profit applicant institution. DIIRD requires each administering or applicant institution in Victoria to provide a CNL which indicates the institution supports up to a maximum of four Victorian PI candidates.

This letter should also clearly indicate that each candidate Victorian PI:

1. is employed / salaried by the administering institution;
2. holds an M.D., Ph.D. or equivalent degree;
3. is authorised by the administering institution to conduct the proposed research in Victoria;
4. has authority from the applicant institution to staff the proposed project; and
5. has commitment from the applicant institution to provide laboratory space and shared resources sufficient to carry out the proposed research as an in-kind contribution.

**Please send these documents, by email, to [roland.diggens@iird.vic.gov.au](mailto:roland.diggens@iird.vic.gov.au) by 9 December 2009 (followed by scanned hard copies of the signed originals in the post.) Format templates for these additional documents are provided for your use within the full Guidelines.**

These documents will inform DIIRD's first screening of the Victorian aspects of joint applications and are a requirement for all Victorian applicants.

**STAGE 2 – the Application Documents**

Joint Applications will only be accepted from Victorian PIs who 1) have been officially nominated on a CNL from their home institution in Victoria and 2) have previously submitted, with their partner, a LOI on or before 15 December 2009 that was accepted by CIRM and DIIRD.

- A single, joint application is required, using the CIRM Forms. Application forms will be available on the CIRM website ([www.cirm.ca.gov/grants/default.asp](http://www.cirm.ca.gov/grants/default.asp)) by 1 December 2009. Please see section IX B in RFA 09-03, CIRM Stem Cell Transplantation Immunology Awards (pdf) for instructions for the application procedure.
- Electronic and hard copies of the final joint application must be lodged to CIRM on behalf of all research workers and collaborating organisations as described in section X, "Application Submission" of RFA 09-03, CIRM Stem Cell Transplantation Immunology.
- For each application there must be a single Principal Investigator and administering institution responsible for the project within each state.
- A single project plan with detail of the work aspects from each partner is required.
- A total project budget, in Au\$ and covering the Victorian research components of the collaborative research project, should also be provided direct to DIIRD.

**Final Application documents must be received by CIRM no later than 5:00pm PST on 26 January 2010. (A soft copy must also be provided at the same time to DIIRD to [roland.diggens@iird.vic.gov.au](mailto:roland.diggens@iird.vic.gov.au) ) No exceptions will be made.**

Victorian applications will only be accepted from Victorian PIs that: 1) have been officially nominated by their host institution on a CNL; and 2) have submitted a LOI that was accepted by CIRM and DIIRD.

**Stem Cell Transplantation Immunology RFA Timeline:**

Schedule of Receipt / Anticipated Review	Date
Receipt of Additional Information including the Candidate Nomination Letter in Victoria	5:00 PM on 9 Dec 2009
Receipt of Letter of Intent in California and Victoria	5:00 PM (PST) on 15 Dec 2009
Receipt of Application Documents in California and Victoria	5:00 PM (PST) on 26 Jan 2010
Anticipated Review of Applications by Grants Working Group (GWG)	April 2010
Anticipated Review and Approval by ICOC	June 2010
Earliest Funding of Awards	July / August 2010

**Minimum Eligibility Criteria:**

Minimum eligibility criteria apply to the program of research, the research organisation(s) and the PIs and their research team. Before discussing a collaboration or completing the joint application form, the applicant PI and their administering institution should confirm their eligibility to apply for the Victoria-California Stem Cell Alliance Grant Program by checking the Victorian Guidelines to ensure they meet all of the minimum eligibility criteria. Some key criteria are listed below -

The Program of Research:

- Is to be undertaken in the jurisdictions of California and Victoria, has been agreed between the research workers and the research organisation(s) and includes a mature research plan; and
- Includes details of the partner organisation(s) based in the other state; a research project plan and timetable which identifies activities in each state; and a research project budget which identifies where the components of the project budget are to be spent.

The Victorian Research Organisation or Organisations and Administering Institution:

- Are publicly funded non-profit research organisations, cooperative research centres or private, for-profit organisations or companies – located in Victoria;
- Must provide a Candidate Nomination Letter (see Victorian Guidelines) which nominates no more than 4 applications / PIs from their institution;
- Have given a firm commitment to provide the facilities and services necessary for the efficient conduct of the research; and
- Agree to meet the normal overhead expenses and normal institutional charges.

The Research Team Workers:

The Victorian Principal Investigator must:

- Have demonstrated expertise, including a publication record, in either one of transplantation immunology or stem cell research (which is complemented by the Californian PI having published expertise in stem cell research or transplantation immunology);

- commit at least 10% effort to the proposed project (More than 10% is expected from the other Victorian listed key personnel - excepting technical staff);
- hold a salaried appointment at the applicant, administering or partner institution;
- and not be named as a PI on more than 1 application to the Stem Cell Transplantation Immunology RFA.
  
- Please note that Victorian PIs and their senior research team members who hold a current award from the Early Translation RFA are not eligible to apply as PIs or lead staff in this Stem Cell Transplantation Immunology RFA. However, they may be named participants within an applicant research team and may, for example, act as advisers to / within an applicant research team. (Please see full Victorian Guidelines. In such cases, existing awarded PIs and the intending PIs should contact DIIRD for further guidance prior to 20 November 2009.)

Additional Review Criteria:

The review criteria are set out in CIRM's guidance on each RFA. DIIRD has no formal additional criteria but reserves the right to consider other aspects of an application when considering funding a project.