RFA 11-03: CIRM Basic Biology Awards IV

I. Purpose

Investigations of the basic mechanisms underlying stem cell biology, cellular plasticity, and cellular differentiation form the foundation of future translational and clinical advances. Despite considerable recent progress, many fundamental issues related to the control of stem cell fate and cellular reprogramming, especially with regard to human cells, remain to be resolved. The purpose of the CIRM Basic Biology Initiative is to support basic research that enables the realization of the full potential of human stem cells and reprogrammed cells for therapies and as tools for biomedical innovation.

II. Objectives

The objective of this RFA is to foster cutting-edge research tackling significant, unresolved issues in human stem cell biology. Studies should focus on elucidating basic molecular and cellular mechanisms and should utilize pluripotent stem cells, adult stem cells, and/or their differentiated derivatives. The CIRM Basic Biology Awards IV will support efforts towards characterizing the molecular and cellular basis of self-renewal, differentiation, and maturation into metabolically functional cell types, as well as mechanistic studies on cell reprogramming, such as induction of pluripotency, trans-differentiation and induced de-differentiation. These awards will also support studies utilizing human stem cell-based in vitro models to gain novel insights about disease mechanisms and other medically relevant processes. With CIRM's overall mission in mind, **funding under this initiative will be prioritized towards studies utilizing human cells**, except for groundbreaking and highly innovative approaches that require the use of an animal model system. Specifically, CIRM is seeking proposals in the following areas of focus:

- Cellular and molecular basis of disease or injury: use of *in vitro*, human stem cell-based models to elucidate and/or validate pathological or regenerative mechanisms related to injury or disease; investigators studying childhood-related neurological disorders are particularly encouraged to apply

- Studies to understand and address immunogenicity of human stem cell derivatives in transplantation; mechanisms by which immune suppression and tolerance approaches affect human stem cells and their derivatives

- Systems biology approaches using stem cell, genomics and phenotype data to elucidate the basis of complex disease and/or inform potential strategies for regeneration

- Characterization of molecular determinants of human stem cell fate decisions during differentiation
  - Cellular and molecular characterization of specific cell populations that emerge during differentiation, from precursors and lineage intermediates to mature, terminally differentiated cell types
  - Molecular basis of lineage specification towards mature adult, metabolically functional cell types, tissues and mini-organs
  - Role of the endogenous microenvironment in the regulation of stem cell fate, behavior, and the properties of stem cell derivatives
  - Mechanisms underlying cellular diversity in stem cell-derived populations

- Molecular basis of self-renewal and expansion in human pluripotent stem cells (hPSC) or human adult stem cells

- Molecular basis of pluripotency, multipotency, senescence and aging of human stem cells

- Understanding human stem cell mechanisms using tissue engineering approaches, including use of natural and/or artificial scaffolds that recruit endogenous stem cell populations or are seeded with stem cells, appropriate support cells, growth factors and/or matrix molecules

- Mechanisms of cellular reprogramming
  - Molecular basis for induction of multipotency or pluripotency
  - Molecular induction of de-differentiation or trans-differentiation of cells for tissue regeneration

- Genomic and epigenetic instability (single cell and related populations) of hPSCs and progenitor cells, and the effects of such instability on differentiation, tumorigenicity or function

III. Award Information

Under this Request for Applications (RFA), CIRM intends to commit up to $35 million to support up to 25 awards. Projects will be funded for up to 3 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 of approval and authorization for funding by the Independent Citizen's Oversight Committee (ICOC), CIRM's Governing Board.

IV. Award Mechanism

CIRM expects to fund approved proposals from non-profit and for-profit institutions (separately or in collaborations) through grants. Institutions will receive funding in quarterly disbursements and be subject to all terms of CIRM's Intellectual Property and Revenue Sharing Requirements for Non-Profit and For-Profit Grantees (17 Cal. Code Regs. § 100600 et seq.).

V. Eligibility

A. Institutional Eligibility

Both non-profit and for-profit organizations are welcome to apply. At the time of the Preliminary Application (PreApp) deadline, the applicant organization must be located in California (that is, the organization must have employees who are conducting business or operations at a location in California). At the time of funding, the applicant organization must be conducting or managing research that is taking place in California. If these requirements are not met, CIRM may terminate all further action on the application.

"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".

CIRM encourages collaborative endeavors between non-profit and for-profit organizations.

B. Principal Investigator (PI) Eligibility

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 PreApp deadline, the PI must:

- Be an independent investigator in California at a Non-profit applicant institution, or have an equivalent position and be an employee in California (at least 50-percent time) of a For-profit applicant institution
- Have documented authority from the applicant institution to staff the proposed project
- Have documented commitment from the applicant institution to provide laboratory space and shared resources sufficient to carry out the proposed research

In order to broaden the pool of applicants engaged in stem cell research and to encourage leveraging of CIRM's investment, CIRM is limiting the number of active CIRM research awards in which an investigator may participate as PI or Co-PI. This RFA is not open to investigators as a PI who are already a PI or Co-PI on 3 or more active CIRM awards as of the deadline for submission of the full application.

The limit includes all CIRM awards that have been approved but not yet closed out, with the exception of the following CIRM RFAs/PAs: Shared Research Labs, Major Facilities, Research Training Awards I & II, Bridges to Stem Cell Research, Disease Team Therapy Development Part I Planning Awards, or Conference Grants.

C. Co-Principal Investigator (Co-PI) Eligibility

This RFA does not allow designation of a Co-Principal Investigator (Co-PI).

D. Percent Effort Requirements

CIRM, mindful of the urgency of its mission, will only fund PIs who are willing to devote substantial, focused attention to the project. For this RFA, PIs must be willing and able to commit a minimum 20% effort.

E. Extraordinary Exceptions

The President of CIRM has the discretion to permit exceptions to any eligibility requirement specified in this Section V. Permission is also required to submit a full Application with a PI or project that do not match the Preliminary Application. The President may permit an exception if he determines, in his individual discretion, that the applicant has demonstrated that the exception would preserve an important research opportunity or make a critical contribution to one of CIRM's mission objectives. Exceptions must be consistent with the objectives of this RFA and the requirements of Proposition 71 as well as California state regulations, including the Grants Administration Policy (see Section XIII of this RFA.)

If CIRM determines that an application does not meet the eligibility requirements, CIRM may terminate all further action on the application. Applicants who will need an exception are strongly encouraged to request it at least 30 days before the relevant application deadline. To request an exception, or for assistance in determining whether one is necessary, contact the CIRM staff listed in Section XII.

VI. Collaborative Funding Partners

CIRM has established a program with several other agencies that fund stem cell and regenerative medicine research. Through this Collaborative Funding Partner (CFP) 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 CFPs to bring

important additional resources to the project. If a collaboratively funded proposal is approved (a "CIRM/CFP Award") CIRM will fund all project work done within the State of California and the CFP will fund all project work within its jurisdiction. For this RFA, the Federal Ministry for Education and Research, Germany (BMBF), the Institute for Stem Cell Biology and Regenerative Medicine, India (inSTEM), the Chinese Ministry of Science and Technology (MOST), and the National Research Agency of France (ANR) are each participating as a CFP.

To apply for a collaboratively funded project involving CIRM and a CFP, applicants must satisfy both the CIRM requirements and any additional requirements put forth by the CFP. For more details on these requirements, please see Appendices A, B, C or D.

Before funding contracts are signed, successful CIRM/CFP applicant teams must have a signed written agreement adequately addressing Intellectual Property (IP) issues relating to the collaborative project and must provide CIRM and the CFP with copies. These IP Agreements will be reviewed by both CIRM and the respective CFP to ensure that they are consistent with CIRM's applicable IP regulations and with the Agreement between the co-funders.

Before funding contracts are signed, successful CIRM/CFP applicant teams must obtain all necessary approvals for animal protection, human subject protection, and use of human embryonic stem cells, unless the approval is not required to initiate the award. CIRM and the CFP will monitor compliance with approval procedures required in their respective jurisdictions.

Both CIRM and the CFP may be involved in the management/oversight of the CIRM/CFP Award by participating in mutually agreed upon joint award administration activities. These activities may include but are not limited to participation in progress monitoring via progress reports.

VII. Notification Regarding Disclosure Information

All applicants, including those not applying with a Partner PI are hereby notified that CIRM may share Preliminary Applications, full Applications and related information submitted by applicants with a CFP in order to facilitate their participation in this RFA. Information concerning approved CIRM/CFP Awards may also be shared with a CFP. Before receiving any such material, the CFP will agree in writing to hold the materials in strict confidence and to use them solely for purposes directly related to this RFA.

VIII. Application and Evaluation Process

Submission of an application for this RFA involves a two-step process. Any qualified applicant may submit a single, brief Preliminary Application (PreApp). Applicants submitting the most promising, competitive and responsive PreApp proposals will be

invited to submit a detailed, full Application. All other applicants will be deferred with the opportunity to apply in response to a future RFA. CIRM expects to reissue a Basic Biology Awards RFA within the next 12 months.

PreApps should emphasize the overall impact of the proposed work and address the review criteria for the PreApp described in Section IX. PreApps will be evaluated by scientific specialists from outside California who are experts in specific areas of research described in the PreApp and by CIRM scientific staff, based on the scientific review criteria described in Section IX below. **The research project and PI proposed in the full Application must be the same as those described in the PreApp; otherwise, the full Application will be deemed ineligible unless the applicant requests and receives an "Extraordinary Exception" as described in Section V.E.**

Full 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, and the Chair of the Governing Board. The list of scientific members who may participate in the GWG review can be found at http://www.cirm.ca.gov/GrantsWkgGrpMembers. The composition of the ICOC can be viewed at http://www.cirm.ca.gov/GoverningBoard. The fifteen participating scientists on the GWG will review the applications and score them according to scientific and technical merit applying the review criteria described in Section IX below. The GWG (scientists and patient advocates) will then review the entire portfolio of applications, taking into consideration the following criteria:

- Appropriate balance among applications addressing various key problems of stem cell biology and cellular plasticity
- Appropriate balance between 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.

CIRM's confidentiality and conflict screening rules will apply to everyone who will have access to applications or who will attend the review meeting, including CIRM staff, external reviewers, and representatives of Collaborative Funding Partner Agencies. (Per Gov. Code §6254.5(e), non-public records may be disclosed to government agencies under confidentiality agreements.)

IX. Review Criteria

A. Preliminary Application

The goal of the PreApp review process is to identify the most promising, competitive, and responsive proposals. The PreApp will be evaluated in three key areas: 1) Significance and Innovation; 2) Feasibility and Experimental Design; and 3)

Responsiveness to the RFA. The quality of appropriate preliminary results is an important factor in assessing feasibility of the proposals.

1. Significance and Innovation

    - Major Unsolved Problem: The project addresses a major unsolved problem in stem cell biology or regenerative medicine.
    - Innovative Project: The research explores novel mechanisms, pathways or cellular events with potential to significantly advance the field. The applicant employs innovative or creative approaches.
    - Focus on Mechanism: The project is focused on elucidating basic molecular or cellular mechanisms.
    - Logical Rationale: The rationale is logical and scientifically sound.
    - Major Impact: If successful, the project would have a major impact on potential applications of stem cell research and regenerative medicine, rather than incrementally advancing the field.

2. Feasibility and Experimental Design

    - Sound Approach: The overall experimental approach is sound and likely to produce meaningful results.
    - Logical and Achievable Aims: The specific aims are logical and well organized with achievable milestones or timeline provided for the 3-year timeframe.
    - Compelling Preliminary Results: The scientific evidence and preliminary results (as summarized by the applicant) are well understood, substantive, compelling and supportive of the proposed concepts, hypotheses, and approaches.

3. Responsiveness to the RFA

    - The proposed research adequately and appropriately addresses the goals and objectives of the RFA. For studies outside the areas of focus specifically designated in this RFA, the proposal is compelling. For studies focused on nonhuman cells or animal model systems, the proposed research is groundbreaking or transformative in nature and necessitates the use of a nonhuman cell or animal system. (Use of animal models as an assay to test or evaluate human cells is considered within scope of this RFA).

B. Full Application

The full Application will be evaluated in four key areas: 1) Significance and Innovation; 2) Feasibility and Experimental Design; 3) Qualifications of the Principal

Investigator and Research Team; and 4) Responsiveness to the RFA. A key component for assessing feasibility will be the quality of the preliminary data. 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.A of this RFA).

1. Significance and Innovation

   - Major Unsolved Problem: The project addresses a major unsolved problem in stem cell biology or regenerative medicine.
   - Innovative Project: The research explores novel mechanisms, pathways or cellular events with potential to significantly advance the field. The applicant employs innovative or creative approaches.
   - Focus on Mechanism: The project is focused on elucidating basic molecular or cellular mechanisms.
   - Logical Rationale: The rationale is logical and scientifically sound.
   - Major Impact: If successful, the project would have a major impact on potential applications of stem cell research and regenerative medicine, rather than incrementally advancing the field.

2. Feasibility and Experimental Design

   - Sound Approach: The proposed research is carefully designed to give meaningful results.
   - Logical and Achievable Aims: The specific aims are logical and the research proposal well organized with achievable milestones and timeline provided over the 3-year timeframe.
   - Alternative Plans: Potential difficulties are acknowledged, and alternative plans are provided should the proposed strategies fail.
   - Research Facilities & Environment: Appropriate facilities are available to conduct the proposed research. The scientific environment is beneficial and conducive to project success.
   - Compelling Preliminary Data: The scientific evidence and preliminary data are well understood, substantive, compelling and supportive of the proposed concepts, hypotheses, and approaches.

3. Principal Investigator (PI) and Research Team

   - Track Record: Evidence of prior success and track record supports the qualification of the PI to conduct the proposed research.
   - PI Commitment: The PI's level of commitment heightens the probability for success of the project.

- Appropriate Team: The research team has appropriate expertise to conduct the proposed research. Any proposed collaboration(s) is critical and integral to the success of the research, and there is a reasonable plan to ensure communication amongst collaborators.

4. Responsiveness to the RFA

- The proposed research adequately and appropriately addresses the goals and objectives of the RFA. For studies outside the areas of focus specifically designated in this RFA, the proposal is compelling. For studies focused on nonhuman cells or animal model systems, the proposed research is groundbreaking or transformative in nature and necessitates the use of a nonhuman cell or animal system. (Use of animal models as an assay to test or evaluate human cells is considered within scope of this RFA).

X. Application Procedure

Applicants must follow these instructions for submission of a PreApp and, if invited, a full Application for the Basic Biology Awards IV. Full applications will only be accepted from applicants who 1) submitted a PreApp and 2) are invited by CIRM to submit a full application.

A. Preliminary Application Forms

Each applicant must submit a PreApp using the forms and instructions provided at https://grants.cirm.ca.gov.

The PreApp consists of the following sections:

1. Principal Investigator
Provide identification information about the PI and Authorized Organizational Official. For CIRM/CFP collaborations, include the name of the Partner PI and the Partner applicant institution.

2. Title of Proposed Project (limited to 90 characters)

3. Specific Aims of Proposed Research (limited to 1500 characters)
Describe concisely the goal and specific aims to be achieved by the proposed project.

4. Preliminary Results (limited to 3500 characters)
Summarize concisely the preliminary data that support the proposed study. Clearly indicate results generated by the applicant PI and, if applicable, by the Partner PI. Figures or Tables cannot be included in the PreApp.

5. Experimental Approach and Design (limited to 3500 characters)
Describe concisely the experimental approaches proposed for accomplishing the project goals within 3 years including appropriate milestones or timeline. Highlight novelty or creative use of approaches and methods. For proposals including a Partner PI, clearly indicate proposed activities to be conducted by the applicant PI and by the Partner PI.

6. Significance of Proposed Research (limited to 3000 characters)
Describe the importance of the proposed research for stem cell biology and regenerative medicine. Identify the major unsolved problem addressed by the proposed research and, most importantly, describe how proposed experiments will overcome existing hurdles and significantly advance the field. If experiments on non-human cells or systems are proposed, explain how a) the overall goals of the project necessitate their use; b) how they will inform human biology; and c) why they are considered groundbreaking.

7. Project Keywords
Select one keyword in each category (from the list provided) that best describes the proposed research. If appropriate, supply additional keywords that are central to the proposed project.

8. Collaborative Funding Partner Requested Information (limited to ~3000 characters)
A Partner PI may use this section, in addition to those above, in order to comply with the specific Funding Partner's requirements. Please see relevant Funding Partner Appendix.

In addition to the PreApp form, all applicants must submit a Related Business Entities Disclosure Form (see instructions at https://grants.cirm.ca.gov). Applicants (PIs) from a for-profit institution (including Partner PIs from a for-profit institution to be funded by the Funding Partner) must complete the form by listing all related business entities. Applicants who do not have any related business entities to declare must so certify and submit the form. The information in this form is required for compliance with the Conflict of Interest policy under which CIRM operates.

B. Preliminary Application Submission Instructions

PreApps must be submitted online using the CIRM Grants Management Portal at https://grants.cirm.ca.gov. A PI may submit only a single PreApp for this RFA, which must be received by CIRM no later than 5:00 pm (PST) on January 10, 2012.

C. Full Application Forms

Full Applications for this RFA may be submitted only by applicants who 1) submitted a PreApp (as described above) and 2) are invited by CIRM to submit a full

Application. Application forms will be available via the Grants Management Portal at https://grants.cirm.ca.gov on March 23, 2012.

The application for the CIRM Basic Biology Awards IV consists of **four parts**:

Part A: Application Information Form (Web-based form)
Part B: Proposal (MS Word template)
Part C: Biographical Sketches and Letters of Support (MS Word template)
Part D: Related Business Entities Disclosure Form (Adobe PDF template)

The full Application includes the following sections:

1. Abstract (up to 1500 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. Summarize the rationale for the studies and techniques employed to pursue these goals.

2. Public Abstract (up to 1500 characters in Part A)
In lay language, briefly describe the proposed research and how it will contribute to the advancement of stem cell biology and regenerative medicine. This Public Abstract will become public information and will be posted online; therefore, do not include proprietary or confidential information or information that could identify the applicant (e.g., PI name, applicant institution name or location).

3. Statement of Benefit to California (up to 1500 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 and will be posted online; therefore, do not include proprietary or confidential information or information that could identify applicant (e.g., PI name, applicant institution name or location).

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 twenty percent (20%) effort.

For each key person listed, provide a two-page biographical sketch using the template provided under Part C. The sketch should highlight prior relevant research experience, accomplishments and/or special skills related to the proposed research. Include relevant publications and/or patents or patent applications.

5. Budget (included in Part A)
Provide all budget information requested in the budget section of Part A. Budgets must be justified in detail, including all subcontracts and consulting fees.

If, to achieve the objective of the project described in Part B, the applicant will require funding from sources other than CIRM and, if applicable, its Funding Partner, then the applicant must specify and justify the added cost and identify funding sources that will enable conduct of the project (in the Part A section "Budget Justification").

All allowable costs for research funded by CIRM are detailed in the CIRM Grants Administration Policy (GAP, see Section XIII.A of this RFA). For CIRM/CFP teams, allowable costs for research funded by the Collaborative Funding Partner may differ. Guidance will be provided separately by the Federal Ministry for Education and Research, Germany (BMBF, Appendix A), the Institute for Stem Cell Biology and Regenerative Medicine, India (inSTEM, Appendix B), the Chinese Ministry of Science and Technology (MOST, Appendix C), and the National Research Agency of France (ANR, Appendix D).

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

- ***Salaries for Key Personnel***
  Salaries for Key Personnel (e.g., Principal Investigator, Co-Investigators, Research Associates) and any Additional Personnel (e.g., unnamed technical support staff), each 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 must be based on a full-time, 12-month staff appointment or the full time annual salary for employees of a for-profit institution. Institutions may request stipend, health insurance and allowable tuition and fees as costs for trainees. Administrative support salaries should be covered exclusively by allowed Indirect Costs.

- ***Supplies***
  Grant funds will support 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 Basic Biology Awards IV are encouraged to attend a CIRM-organized grantee meeting in California and should include travel costs for this meeting in the budget. 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.

• Consultants/Subcontracts
Grantees that subcontract CIRM-funded work should note that CIRM-funded **research** must generally be conducted in California.

Aside from small consulting contracts, Grantees may not use CIRM funds to contract for research to be performed outside of California. Consulting contracts for out-of-state research are limited to $15,000 per year for a single contract, and $25,000 per year in aggregate. (CIRM may allow modest increases to these limits in exceptional circumstances.)

For support services **other than research**, Grantees may subcontract outside California, but must make a good faith effort to use California suppliers for more than half of their contracts and purchases in accordance with CIRM's California Supplier regulation (Cal. Code Regs. tit. 17, § 100502).

• 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. See Appendices A-D for details concerning CFP allowable costs.

6. Rationale and Significance (up to 1 page in Part B)
Summarize the context and background of the application and the specific rationale for the work proposed. Specifically identify the gaps in the current knowledge base that the project is intended to fill. If the aims of the application are achieved, state how the findings will make a critical contribution to the field of stem cell biology or regenerative medicine. If experiments on nonhuman cells or systems are proposed, explain how the overall goals of the proposed project necessitate their use and how they will inform human biology.

7. Specific Aims (up to 1 page in Part B)
Explain the goal of the specific research proposed. Identify and enumerate each specific aim of the proposal in a concise and step-wise fashion, and describe how each aim will support the goal of this research.

8. Preliminary Data (up to 4 pages in Part B)
Provide preliminary data to support the concepts, hypotheses and/or approaches proposed in the application. Clearly indicate data generated by the applicant PI and, if applicable, by the Partner PI.

9. 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 goals specified in the proposal. Use clear and consistent terminology to identify the species of origin for various cell types that may be employed throughout the project. 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. Describe specific criteria for success including meaningful quantitative measures to determine if the objective of the proposed studies has been achieved.

For applications from CIRM/CFP teams, the proposed research must be presented as an integrated project. However, 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.

10. Project Timeline (up to 1/2 page in Part B)
Provide a realistic timetable for completing each proposed specific aim of the project; where appropriate, provide specific milestones for evaluating the achievement of each specific aim.

11. References (up to 2 pages in Part B)
List all references used in the body of the proposal.

12. Collaboration and Environment, Including Laboratory Facilities and 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. If collaboration (including CIRM/CFP collaborations) is integral to the success of the project, describe how the collaboration will be managed.

13. Related Business Entities (Part D)
All applicants (including, if applicable, a Funding Partner applicant institution) 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 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).

D. Full Application Submission Instructions

Full Applications will only be accepted from applicants who 1) submitted a PreApp and 2) are invited by CIRM to submit a full Application.

All four parts of the Basic Biology Awards IV application must be submitted together and received by CIRM no later than 5:00PM PDT on April 25, 2012, in both electronic form (via the Grants Management Portal) and in hard copy (a signed original plus five copies). It is the applicant's responsibility to meet this deadline; no exceptions will be made. The electronic copy of all four parts of the Basic Biology Awards IV application must be submitted online as instructed on the CIRM Grants Management Portal (**https://grants.cirm.ca.gov**). Both the PI and the applicant institution's Authorized Organizational Official (AOO) must sign the original hard copy of the application (consisting of Parts A-D). The original application plus 5 hard copies (preferably double-sided) should be sent via express mail or courier service to:

Basic Biology Awards IV Applications
California Institute for Regenerative Medicine
210 King Street
San Francisco, CA 94107

E. Submission of Supplemental Information

If necessary, the PI may submit limited supplemental materials that provide critical new information related to their research proposal after the application deadline but not later than 5:00pm PDT on May 22, 2012. Supplementary materials will not be accepted after this deadline. CIRM will accept a one-time-only submission of materials from the PI only if it meets the submission deadline and conforms to the requirements described herein. Accepted submissions will be forwarded to reviewers for their consideration.

The submission should be in the form of a one-page letter addressed to the Senior Review Officer and submitted via email to gsambrano@cirm.ca.gov. The body of the letter may not exceed 500 words and should briefly describe the type of information submitted and when the information became available. The following materials qualify for submissions of supplemental materials:

1. Within the one-page letter, provide specific citation(s) to journal publications related to the proposed project that were published or accepted for publication

since the application submission deadline. You may briefly describe the significance of the publication(s) to the proposal in the cover letter.

2. Within the one-page letter, confirmation of funding secured from other sources or regulatory (e.g., IND, IDE) filings or approvals acquired since the application submission deadline.

3. Within the one-page letter, notice of patent application(s) filed, notice of allowance received or patent(s) issued, or notice of license(s) to relevant intellectual property (granted or received) since the application submission deadline.

The letter may not be used to describe any additional data or experiments. Changes in scope, experimental approach, or research design are not allowed.

XI. Schedule of Deadlines and Reviews

Preliminary Applications due	5:00 pm (PST), January 10, 2012
Invitations for full Applications sent out by CIRM	March 23, 2012
Full Applications due	5:00 pm (PDT), April 25, 2012
Review of full Applications by Grants Working Group (GWG)	June, 2012
Review and Approval by ICOC	September, 2012
Earliest Funding of Awards	November, 2012

XII. Contacts

For information about this RFA or the review process:

Gilberto R. Sambrano, Ph.D.
Senior Review Officer
California Institute for Regenerative Medicine
Email: gsambrano@cirm.ca.gov
Phone: (415) 396-9103

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/reg/default.asp.

A. CIRM Grants Administration Policy

CIRM's Grants Administration Policy (GAP) for Academic and Non-Profit Institutions (Non-Profit GAP) and the 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. CIRM's GAP is available at http://www.cirm.ca.gov/our-funding/our-regulations/stem-cell-regulations-governing-cirm-grants#GAP

B. Intellectual Property Regulations

CIRM has adopted intellectual property and revenue sharing regulations for non-profit and for-profit organizations. By accepting a CIRM Grant, the Grantee agrees to comply with all such applicable regulations.

C. Human Stem Cell Research Regulations

As reflected in CIRM's GAP, CIRM has adopted medical and ethical standards for human stem cell research (Title 17, California Code of Regulations, sections 100010-100110 available at http://www.cirm.ca.gov/our-funding/our-regulations/stem-cell-regulations-governing-cirm-grants#standards). All research conducted under this award will be expected to comply with these standards. This information can be found on the CIRM website.

D. California Supplier Regulation

CIRM has adopted a regulation to implement the requirement in Proposition 71 that grant and loan recipients make a good faith effort to achieve a goal of purchasing more than 50% of their goods and services from California suppliers (Title 17, California Code of Regulations, section 100502). Grant and loan recipients are required to comply with this standard.