CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

RFA 10-04: CIRM Basic Biology Awards III

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. Program Objectives

The objective of the CIRM Basic Biology Awards III is to provide funding for cutting-edge stem cell research and to support studies tackling significant, unresolved issues pertinent to understanding the biology of human stem cells and the control of cell fate. CIRM also seeks to explore the potential for stem cell-based approaches to yield novel mechanistic insights into pathological processes by supporting innovative, hypothesis-driven research towards understanding the molecular and cellular basis of disease. 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 studies that necessitate the use of animal systems.

CIRM is specifically seeking projects in the following areas and will place special emphasis on those exploring new avenues of research with the potential to yield insights that are transformative in nature.

- Elucidating the determinants of stem cell fate decisions during differentiation
  - Molecular characterization of specific precursor populations at intermediate stages of differentiation
  - Molecular basis of lineage specification towards mature adult, metabolically functional cell types, tissues and mini-organs
  - Role of the cellular and extracellular microenvironment in regulation of stem cell fate and behavior

- Molecular basis of human pluripotent stem cell self-renewal and expansion

- Molecular basis of pluripotency or the developmental potential of stem cells to specific lineages

- Mechanisms of cellular reprogramming
  - Molecular basis for induction of multipotency or pluripotency
  - Mechanisms of direct reprogramming to other cell types (trans-differentiation)

- Genetic, epigenetic and genomic instability of stem cells and the effects of such instability on their differentiation and tumorigenicity

- Epigenetic and/or other regulatory mechanisms (e.g. retrotransposon activity) underlying the developmental potential/plasticity of stem cells and their derivatives, including those mechanisms that generate diversity within an individual cell type

- Molecular mechanisms by which endogenous or engineered multidimensional microenvironments influence stem cell fate and behavior

- Molecular basis of disease: elucidating/validating human disease mechanisms with *in vitro*, human stem cell-based models

III. Award Information

Under this Request for Applications (RFA), CIRM intends to commit up to $45 million to support up to 30 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 of approval and authorization for funding by the Independent Citizen's Oversight Committee.

IV. Eligibility

A. 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 Preliminary 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".

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 Preliminary 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 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 who are already PIs or Co-PIs on 3 or more active CIRM awards[1] as of January 19, 2011, the deadline for submission of the full application. In addition, mindful of the urgency of its mission, CIRM will only fund PIs who are willing to commit a minimum of 20% effort to the proposed project. During review of the full Application, CIRM will instruct reviewers to give added consideration to the PI's qualifications when the PI commits more than 20% effort to the proposed research.

In extraordinary circumstances, the President of CIRM shall have the discretion to permit exceptions to the above eligibility requirements if the President determines, in his sole 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 requirements of Proposition 71 as well as California state regulations, including the Grants Administration Policy (see section XI.A of this RFA) or they will not be considered. Such exceptions **must** be requested prior to December 29, 2010 (see contact information, section X of this RFA) to allow the President of CIRM adequate time to review and to approve or deny the request prior to January 19, 2011, the deadline for submission of a full Application.

V. 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

[1] The limit includes all CIRM awards that have been approved but not yet closed out, with the exception of the following RFAs: Shared Labs, Major Facilities, Training I & II, Bridges, Disease Team Planning, or CIRM Conference Grants.

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 **Japan Science and Technology Agency (JST) and Federal Ministry for Education and Research, Germany (BMBF)** are each participating as CFPs.

To apply for a collaboratively funded project, applicants must satisfy both the CIRM requirements (Section VIII below) and any additional requirements put forth by the CFP. For more details on these requirements, please see Appendices A (JST) or B (BMBF).

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.

VI. Application and Evaluation Process

Submission of an application for the CIRM Basic Biology Awards III RFA involves a two-step process. Any qualified applicant may submit a brief Preliminary Application (Pre-Application, or 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 in the latter half of 2011.

PreApps should emphasize the significance of the proposed work and explain how the proposed research will lead to important advances in stem cell biology or regenerative medicine. 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 VII below. Applicants whose projects are judged as most promising, competitive, and responsive to the RFA will be invited to submit a full Application. **The research project proposed in the full Application must be the same as that described in the PreApp; otherwise, the full Application will be deemed ineligible**.

Full Applications will be evaluated by the CIRM Grants Working Group using the criteria described in the RFA. CIRM's confidentiality and conflict screening rules will apply to everyone who will have access to the applications or attend the review meeting, including CIRM staff, external reviewers, and representatives of Collaborative Funding Partner Agencies. (Disclosure to collaborative funding agencies is protected by inter-governmental agreement, per Gov. Code § 6245.2(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 (the Independent Citizen's Oversight Committee, or ICOC) 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 Governing Board 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 VII 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 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 Governing Board, which will make final funding decisions.

VII. 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 renewal, normal or aberrant cell differentiation, cellular reprogramming, or disease mechanism *in vitro*.
- 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 including use of nonhuman cells or models, the proposed research is groundbreaking or transformative in nature and necessitates the use of a nonhuman cell or model.

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 XI.A of this RFA).

1. Significance and Innovation

- Major Unsolved Problem: The project addresses a major unsolved problem in stem cell renewal, normal or aberrant cell differentiation, cellular reprogramming, or disease mechanism *in vitro*.
- 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.

4. Responsiveness to the RFA

- The proposed research adequately and appropriately addresses the goals and objectives of the RFA. For studies including use of

nonhuman cells or models, the proposed research is groundbreaking or transformative in nature and necessitates the use of a nonhuman cell or model.

VIII. Application Procedure

Applicants must follow these instructions for submission of a PreApp and, if invited, a full Application for the CIRM Basic Biology Award III. 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 Pre-Application (PreApp) using the forms and instructions provided at http://www.cirm.ca.gov/RFAs. The PreApp should emphasize the significance of the work for the field and describe how the proposed research will lead to important advances in stem cell biology and regenerative medicine.

When describing aims and experimental approaches, applicants must clearly designate the species of origin for all cells and tissues to be studied. For example, use human ESC or hESC for human embryonic stem cells; mouse ESC or mESC for mouse embryonic stem cells.

The PreApp for the Basic Biology Awards III consists of the following sections:

1. *Principal Investigator*

   Identification information about the PI and Institutional Official. For CIRM/CFP collaborations, include the name of the Partner PI and the Partner applicant institution.

2. *Title of Proposed Project (limited to 100 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. 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.

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 nonhuman cells or systems are proposed, explain a) how 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.

In addition to the PreApp form, **an Applicant (PI) must submit a Related Business Entities Disclosure Form (RBE) if either of the following apply:** 1) the applicant PI (and/or Partner PI to be funded by a CFP) is from a for-profit institution; 2) PreApp proposes funding for one or more for-profit organizations identified by name (see instructions at http://www.cirm.ca.gov/RFA_10-04).

B. Preliminary Application Submission Instructions

Please follow the specific, most up-to-date submission instructions for RFA 10-04 on the CIRM Funding Opportunities web page (http://www.cirm.ca.gov/RFA_10-04). **A PI may submit only a single PreApp for this RFA. The PreApp, as well as an appropriately signed copy of the signature page, must be received by CIRM no later than 5:00 pm (PDT) on October 7, 2010. No exceptions to this deadline will be made.**

C. Full Application Forms

Full Applications for the CIRM Basic Biology Awards III 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 on the CIRM website (http://www.cirm.ca.gov/RFA_10-04_Application_Instructions) in the latter half of December 2010.

The full Application for the CIRM Basic Biology Awards III consists of four parts:

Part A: Application Information Form (Adobe PDF template provided at

http://www.cirm.ca.gov/RFA_10-04_Application_Instructions). Part A includes: Abstract, Public Abstract, Statement of Benefit to California, Key Personnel, and Budget (section numbers 1-5 below).

Part B: Basic Biology Award Research Proposal (MS Word template provided at http://www.cirm.ca.gov/RFA_10-04_Application_Instructions). Part B includes: Rationale and Significance, Specific Aims, Preliminary Data, Research Design and Methods, Project Timeline, References, and Environment including Laboratory Facilities and Major Equipment (section numbers 6-12 below).

Part C: Biographical Sketches for Key Personnel (MS Word template provided at http://www.cirm.ca.gov/RFA_10-04_Application_Instructions) and letters of collaboration.

Part D: Related Business Entities (Adobe PDF template provided at http://www.cirm.ca.gov/RFA_10-04_Application_Instructions). In order to comply with the Conflict of Interest policies under which CIRM operates, Part D must be submitted to indicate whether the application would, if awarded, provide funding from CIRM or (if applicable) from a Funding Partner to a for-profit organization that is either: 1) the applicant organization; 2) a subcontractor; or 3) the employer of a co-investigator, consultant or subcontractor (section number 13 below).

The application for Basic Biology Awards III 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. Summarize 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 contribute to the advancement of stem cell biology and regenerative medicine. This Public Abstract will become public information and will be available online; therefore, do not include proprietary or confidential information or information that could identify the PI 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 and will be available online; therefore, do not include proprietary or confidential information or information that

could identify the PI 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, their contributions to and percent effort towards the project must also be listed in the corresponding section of Part A, Subpart II.

For CIRM funded key personnel, 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, unless the President of CIRM approves an exception pursuant to Section IV.B, above.

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, accomplishment and/or special skills related to the proposed research. Include relevant publications and/or patents or patent applications. Following biosketches for the PI and, if applicable, the Partner PI, include all remaining biosketches in alphabetical order.

5. Budget (included in Part A)

Provide all budget information requested in the budget section of the Application Information Form. For CIRM/CFP teams, the funding requested from the Funding Partner (total requested and per year) must be indicated and justified in sufficient detail (under “Budget Justification” in Part A, Subpart II) 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 XI.A of this RFA). For CIRM/CFP teams, allowable costs for research funded by the Funding Partner may differ. Guidance will be provided separately by JST (see Appendix A) or BMBF (Appendix 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 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 and animal costs. Small 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 III are strongly 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 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 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.

See Appendices A/B 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.

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.

The full Application consists of four parts: Part A: Application Information Form, Part B: Basic Biology Award Research Proposal, Part C: Biographical Sketches for Key Personnel, and Part D: Related Business Entities. **All four parts of the full Application for CIRM Basic Biology Awards III must be submitted together and received by CIRM no later than 5:00 pm (PST) on January 19, 2011, in both electronic form and in hard copy (a signed original and five copies)**. **No exceptions will be made.**

Submit electronic copies of all 4 parts of the application online via the CIRM Grants Management Portal, at https://grants.cirm.ca.gov/.

In addition**, submit an original hard copy** of the application (consisting of Parts A-D) signed by both the applicant and the institution's Authorized Organizational Official (AOO), **plus 5 hard copies** of the full Application (preferably double-sided) via express mail or courier service to:

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

E. Submission of Supplemental Information

If desired, 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 February 24, 2011**. 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, Dr. Gilberto R. Sambrano and sent via Email to** gsambrano@cirm.ca.gov (**see section X).** 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 letter.

2. Within the one-page letter, provide 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, provide 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.

IX. Schedule of Deadlines and Reviews

Pre-Applications due	5:00 pm (PDT), Thursday, October 7, 2010.
Invitations for full Applications sent out by CIRM	December 17, 2010
Full Applications due	5:00 pm (PST), Wednesday, January 19, 2011
Review of full Applications by Grants Working Group (GWG)	March 2011.
Review and Approval by ICOC	May 2011.
Earliest Funding of Awards	Summer 2011.

X. 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

XI. 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.

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

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.