CIRM 2.0
CALIFORNIA'S STEM CELL AGENCY

Accelerating and Advancing the Discovery of Novel Stem Cell Treatments and Applications: Discovery Stage Programs

The mission of CIRM is to accelerate the development of stem cell therapies to patients with unmet medical needs. To better serve this mission, CIRM is proposing a new paradigm for promoting the discovery of promising new stem cell technologies and driving their rapid translation towards improving patient care. Through this program, CIRM will provide funding opportunities that:

- Are predictable and recur regularly

- Support exploration of new ideas

- Are responsive to emerging concepts, key bottlenecks or downstream needs

- Support stem cell discoveries that could lead to therapies, tools, diagnostic tests, and devices

- Incent progression of stem cell discoveries towards impacting patients ("passing the baton")

- Provide linkages to downstream funding opportunities

To accomplish these goals, CIRM will establish calls for three complementary types of proposal and will accept applications on a recurring basis. This concept plan further describes the three proposed Discovery Stage Research Program Announcements listed below.

- PA 15-07: Funding Opportunity for Inception Awards

- PA 15-08: Funding Opportunity for Quest Awards

- PA 15-09: Funding Opportunities for Challenge Awards

PA 15-07: DISCOVERY STAGE RESEARCH FUNDING OPPORTUNITY for INCEPTION AWARDS

OBJECTIVE

The objective of this funding opportunity is to support exploratory research on novel ideas that could lead to the discovery of promising new stem cell technologies that could be translated and ultimately, improve patient care.

AWARD INFORMATION

What is the CIRM funding allocation, project funding and project term?

- CIRM will fund direct project costs of up to $150,000 per award.

- CIRM proposes approximately $6.5M to support the issuance of about 26 Inception Awards over one annualized award cycle.

- Individual Inception Awards will be supported for the period of time it takes to test the hypothesis as proposed by the applicant. Successful applicants will act with urgency commensurate with CIRM's mission.

What activities will CIRM support?

CIRM funds will support the following activities under this opportunity:

- Exploratory research using human stem, progenitor, or directly reprogrammed cells to test novel ideas that could lead to further discovery and translation of stem cell based innovations. These activities may include supportive studies using nonhuman model systems.

CIRM funds cannot be used to support the following activities under this opportunity:

- Research that does not require stem, progenitor, or directly reprogrammed cells for achieving the project goal

- Research exclusively using nonhuman model systems

- Translational activities to develop either a Good Manufacturing Process (GMP) - compliant process, or a Clinical Laboratory Improvement Amendments (CLIA) - compliant process

- Translational activities to implement Design Control including initiation and maintenance of Design History File

- Translational activities to develop a process for commercialization for a tool or technology

- Translational activities necessary for the filing of a well-supported IND, 510(k) or IDE with the FDA, or for validation testing under CLIA or for commercialization

- Preparation for and conduct of clinical trials

2

How will applications be reviewed?

- In anticipation of high demand, members of the Grants Working Group (GWG) will review Inception Award applications in two stages. In the first stage, GWG members will conduct a pre-review of applications (called "Positive Selection", see Appendix) to advance a subset of applications to the second stage, which will involve a full review by the GWG.

How will funds be awarded?

- Awards to successful applicants will be in the form of a grant.

- CIRM will disburse funds pursuant to a Notice of Award. The first payment issued upon initiation of award will comprise 75% of allowable funds. The final 25% will be disbursed upon award closeout including receipt and CIRM approval of final progress and financial reports.

ELIGIBILITY

What types of projects are eligible for funding?

To be eligible, the proposed project must satisfy the following requirements:

(1) The applicant must propose work with human stem, progenitor, or directly reprogrammed cells

(2) The applicant must be ready to initiate work on the funded project within 120 days of approval.

Given the urgency of CIRM's mission, all approved awardees must initiate work on the funded project within 120 days of approval and authorization for funding by the Application Review Subcommittee of the Independent Citizens' Oversight Committee.

Who can apply?

California Research Organizations

California Organizations (for-profit and non-profit) may use CIRM funds for eligible project costs incurred both in California and outside California. To qualify as a California organization, the organization must have >50% of its employees located in, and paid in, the state of California, and conduct the award activities from the California location.

Non-California Research Organizations

Non-California organizations may also apply; however, CIRM funding can be used only for allowable expenditures incurred within California. The applicant must demonstrate by the application deadline a commitment of funds from other sources for project activities outside of California.

Who can serve as the Principal Investigator (PI)?

To be eligible, the PI must satisfy the following requirements:

- Must be an employee of the applicant organization

- Must commit at least 10 percent effort to working on the project.

- Must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI

- Must not currently have another application pending review or approval under this funding opportunity

SCHEDULE AND DEADLINES

Applications Due	November of each year starting in 2015. Specific dates and times will be posted on the CIRM website.
Grants Working Group (GWG) Review	Approximately 3 months post submission
ICOC Review and Approval	Approximately 5-6 months post submission
Award Start	Must start within 4 months of award approval

PA 15-08: DISCOVERY STAGE RESEARCH FUNDING OPPORTUNITY for QUEST AWARDS

OBJECTIVE

The objective of this funding opportunity is to promote the discovery of promising new stem cell-based technologies that could be translated to enable broad use and ultimately, improve patient care. Projects funded through the Quest Awards should propose technology that is uniquely enabled by human stem/progenitor cells or directly reprogrammed cells, or uniquely enabling for the advancement of stem cell-based therapies.

PROGRAM FEATURES

Promoting Discovery and Accelerating Translation

The goal of a Quest Award is to produce, within 2 years, a project deliverable that is a novel candidate therapeutic, device, diagnostic test or tool that can immediately progress to translation to enable broad use. To incent rapid advancement to translation, CIRM is implementing an Incentive Grant opportunity for Quest Award recipients who complete a "Progression Event". CIRM defines a Progression Event as the successful acquisition of funding for subsequent development of the Quest Award deliverable either by the original award recipient, if appropriate, or by a qualified team to whom the original award recipient has "passed the baton". Quest Award recipients who demonstrate to CIRM successful achievement of a Progression Event within one year of the end date of their Quest Award will receive an Incentive Grant ($150,000 in direct project costs) to utilize for stem cell research relevant to CIRM's mission. Incentive Grants will be administered post-award using the mechanism described for Inception Awards (PA 15-07).

AWARD INFORMATION

What is the CIRM funding allocation, project funding and project term?

CIRM proposes approximately $42.5M to fund one annualized award cycle (two application calls) of Quest Awards. This includes:

- Approximately $35M to support the issuance of 15-30 two year Quest Awards. CIRM will fund direct project costs of up to
  - $700,000 per award to achieve a candidate that is a diagnostic test, a device or a tool
  - $1.4M per award to achieve a candidate that is a therapeutic

- Approximately $7.5M in reserve funding for Incentive Grant awards. This assumes 100% of 30 Quest Awards achieve a Progression Event as described above.

What activities will CIRM support?

CIRM funds <u>will</u> support the following activities under this opportunity:

- Activities that will lead to selection of a novel candidate therapeutic, device, diagnostic test or tool ready for translation to enable broad use and ultimately, improve patient care including:

  o Developing and implementing assays to identify/test/characterize candidate (or prototype) therapeutic, device, diagnostic test, tool/technology

  o Feasibility and initial reproducibility assessment

  o Characterization/optimization of candidate(s)

  o Proof- of concept studies with candidate; for non stem cell-based candidates (e.g. certain devices, diagnostic tests, tools), proof of concept testing with human stem, progenitor or directly reprogrammed cells

  o Developing Target Product Profile (Product Concept Document) for candidate therapeutic, device, diagnostic test or tool

  o Preparation for and conduct of stage appropriate regulatory meetings (e.g. for stem cell based cell therapeutic candidates - a pre-pre IND meeting)

CIRM funds <u>cannot</u> be used to support the following activities under this opportunity:

- Research lacking a strong rationale for the unique necessity of human stem/progenitor cells or directly reprogrammed cells to achieve the project deliverable OR research uniquely enabling for the advancement of stem cell-based therapies that does not include testing with human stem/progenitor cells or directly reprogrammed cells to achieve the project deliverable

- Translational activities to develop either a Good Manufacturing Process (GMP) - compliant process, or a Clinical Laboratory Improvement Amendments (CLIA) - compliant process

- Translational activities to implement Design Control including initiation and maintenance of Design History File

- Translational activities to develop a process for commercialization for a tool or technology

- Translational activities necessary for the filing of a well-supported IND, 510(k) or IDE with the FDA, for validation testing under CLIA or for commercialization

- Preparation for and conduct of clinical trials

How will applications be reviewed?

- In anticipation of high demand, members of the Grants Working Group (GWG) will review Quest Award applications in two stages. In the first stage, GWG members will conduct a pre-review of applications (called "Positive Selection", see Appendix) to advance a subset of applications to the second stage, which will involve a full review by the GWG.

How will funds be awarded?

- Awards to successful applicants will be in the form of a grant.

- CIRM will disburse funds pursuant to a Notice of Award.   Except for the first payment issued upon initiation of an award, payments will be disbursed semi-annually or at CIRM's option. Continued funding is contingent upon timely progress, as outlined in the project milestones and timeline established under the Notice of Award, and, when applicable, the ongoing ability of the applicant to fund its operations and to satisfy its co-funding commitment (see below).

- Funding for Incentive Grants will be awarded only if the following conditions are met: 1) a Quest Awardee achieves a Progression Event no later than 1 year beyond the project end date; 2) A Progression Event report, including an Incentive Grant proposal and budget, has been submitted to CIRM; and 3), the CIRM President or his designee, by delegated authority of the board, determines that the Progression Event has been achieved and that the Incentive Grant proposal and budget is appropriately aligned with CIRM's mission.

ELIGIBILITY

What types of projects are eligible for funding?

To be eligible, the proposed project must satisfy the following requirements:

(1) The applicant must propose discovery research for a new technology that is uniquely enabled by human stem cells or uniquely enabling for the advancement of human stem cell based therapies including

- Discovery research for a novel therapeutic candidate:

    o where human stem, progenitor, or directly reprogrammed cells either compose the therapy or are used to manufacture the therapy

    o that stimulates, recruits or targets endogenous stem cells or cancer stem cells

    o where human stem, progenitor or directly reprogrammed cells are uniquely required for candidate identification and testing

- Discovery research for a novel human stem cell-based diagnostic test, assay or tool that can be used to discover, advance, monitor, or evaluate new therapies, OR

- Discovery research for novel technologies (a device, diagnostic test, tool) that propose proof of concept testing with human stem/progenitor cells and are uniquely enabling for the advancement of stem cell-based therapies

(2) The applicant must be ready to initiate work on the funded project within 120 days of approval

Given the urgency of CIRM's mission, all approved awardees must initiate work on the funded project within 120 days of approval and authorization for funding by the Application Review Subcommittee of CIRM's governing board, the Independent Citizens' Oversight Committee ("ICOC").

(3) Co-funding is not required. If the project requires funding over and above that which CIRM provides, documentation demonstrating the commitment of funds to cover the proposed co-funding amount must be provided at the time of application submission (e.g., copy of executed term sheet showing amount of co-funding, conditions, and source).

(4) For-profit organizations must demonstrate solvency

For-profit organizations must provide documentation that shows 180 days cash on hand from date of application submission and the financial ability to meet the co-funding and contingency requirements for the term of the project. The determination of solvency will be made at CIRM's sole discretion.

Who can apply?

California Research Organizations

California Organizations (for-profit and non-profit) may use CIRM funds for eligible project costs incurred both in California and outside California. To qualify as a California organization, the organization must have >50% of its employees located in, and paid in, the state of California, and conduct the award activities from the California location.

Non-California Research Organizations

Non-California organizations may also apply; however, CIRM funding can be used only for allowable expenditures incurred within California. The applicant must demonstrate by the application deadline a commitment of funds from other sources for project activities outside of California.

Who can serve as the Principal Investigator (PI)?

To be eligible, the PI must satisfy the following requirements:

- Must be an employee of the applicant organization

- Must commit at least 20 percent effort to working on the project.

- Must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI

- Must not currently have another application pending review or approval under this funding opportunity

SCHEDULE AND DEADLINES

Applications Due	February and July of each year starting in 2016. Specific dates and times will be posted on the CIRM website.
Grants Working Group (GWG) Review	Approximately 3 months post submission
ICOC Review and Approval	Approximately 5-6 months post submission
Award Start	Must start within 4 months of award approval

PA 15-09: DISCOVERY STAGE RESEARCH FUNDING OPPORTUNITY for CHALLENGE AWARDS

OBJECTIVE

The objective of this funding opportunity is to support research activities towards overcoming key challenges in the stem cell field that are preventing or slowing the discovery of promising new stem cell technologies that could be rapidly translated towards improving patient care. Projects funded through the Challenge Awards will address highly specific questions (HSQs) in discovery research that will be defined by CIRM on a periodic basis. These HSQs will focus on new, transformative developments in the field, long standing challenges in stem cell science, and the resolution of critical obstacles to the success of CIRM clinical stage projects.

PROGRAM FEATURES

Challenge Question Announcements

- CIRM will make calls for application submission on HSQs for the Challenge Awards through the issuance of periodic Challenge Question Announcements (CQAs).

- Details of a specific Challenge opportunity, such as the distinct questions and research goals, the total level of funds provided, the duration of the award, and eligible activities will be tailored to a given HSQ and approved by the President of CIRM, as delegated by the Board.

AWARD INFORMATION

What is the CIRM funding allocation, project funding and project term?

- CIRM proposes approximately $4M over one annualized award cycle (up to 2 application calls). The specific project funding will be defined in the Challenge Question Announcement

What activities will CIRM support?

Specific activities that are supported or not permitted under the Challenge Award program will be defined for each distinct HSQ and described when specific Challenge opportunities are announced. In general, CIRM will support research activities that directly address a specific, targeted HSQ and will not support peripheral activities or tangential studies.

How will applications be reviewed?

CIRM expects to receive a small number of highly-focused proposals addressing a particular HSQ, which will be reviewed by the Grants Working Group (GWG). In the event that CIRM receives a larger number of applications, members of the GWG will review Challenge Award proposals in two stages. In the first stage, GWG members will conduct a pre-review of applications (called "Positive Selection", see Appendix) to advance a subset of applications to the second stage, which will involve a full review by the GWG.

How will funds be awarded?

- Awards to successful applicants will be in the form of a grant.

- CIRM will disburse funds pursuant to a Notice of Award. Except for the first payment issued upon initiation of an award, payments will be disbursed as established under the Notice of Award to best facilitate successful project advancement.

ELIGIBILITY

What types of projects are eligible for funding?

To be eligible, the proposed project must satisfy the following requirements:

- Must specifically address the targeted HSQ
- Must include some work with human stem, progenitor, or directly reprogrammed cells or materials derived from such cells
- Must include a clear vision for how a successful project outcome would be put into practice for overcoming a key hurdle in regenerative medicine
- Must be ready to initiate work on the funded project within 120 days of approval of an award by the ICOC

Additional eligibility criteria specific for a given HSQ may be stipulated in the CQA.

Who can apply?

California Research Organizations

California Organizations (for-profit and non-profit) may use CIRM funds for eligible project costs incurred both in California and outside California. To qualify as a California organization, the organization must have >50% of its employees located in, and paid in, the state of California, and conduct the award activities from the California location.

Non-California Research Organizations

Non-California organizations may also apply; however, CIRM funding can be used only for allowable expenditures incurred within California. The applicant must demonstrate by the application deadline a commitment of funds from other sources for project activities outside of California.

Who can serve as the Principal Investigator (PI)?

To be eligible, the PI must satisfy the following requirements:

- Must be an employee of the applicant organization

- Must commit at least 20 percent effort to working on the project unless otherwise noted in the Challenge Question Announcement.

- Must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI

- Must not currently have another application pending review or approval under this funding opportunity

SCHEDULE AND DEADLINES

Challenge Question Announcement (CQA) Posted	Periodic. Approximately 2-3 months prior to application due date
Applications Due	February and July of each year. Specific dates and times will be posted in the CQA.
Grants Working Group (GWG) Review	Approximately 3 months post submission
ICOC Review and Approval	Approximately 5-6 months post submission
Award Start	Must start within 4 months of award approval

REQUESTED FUNDING ALLOCATION

CIRM requests up to $53M to cover issuance of awards across these three Program Announcements for one annualized award cycle, allocated as follows:

- Up to $45.5M for Inception, Quest and Challenge Award programs
- Up to $7.5M in reserve funding for Incentive Grants for Quest Award program

The indirect cost rate will be set at 20% for non-profit applicant organizations. CIRM will not fund indirect costs for for-profit applicant organizations.

REQUESTED DELEGATION OF BOARD AUTHORITY

To streamline the processes for high volume application review and awarding Incentive Grants and to enable timely calls to highly specific opportunities or challenges, CIRM is proposing process changes further described in specific programs below, that require delegation of Board Authority.

CIRM requests the Governing Board delegate to the President or his designee the authority:

- To examine those applications that are not selected for a full review and to make the final determination whether to submit such applications to the GWG for a full review or to deny funding.

- To award an Incentive Grant upon determination by the CIRM Team that a Progression Event has been achieved and that the Incentive Grant proposal and budget is appropriately aligned with CIRM's mission

- To issue periodic Challenge Question Announcements that define a specific question(s) and specific award terms unique to that question under the umbrella of the Challenge Awards Program Announcement