



Funding Opportunity Concept Plan

DISC0: Foundation Awards

BACKGROUND

The mission of CIRM is to accelerate world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world.

Despite unquestionable progress in regenerative medicine, there remain critical gaps in our understanding of fundamental human cell biology and disease that hinder the pace and prevent the potential of this research from being fully realized as a basis for new therapies and as tools for biomedical innovation. At the same time, technological innovation in gene editing, single cell profiling, data science, and engineering is presenting new opportunities for addressing questions of biology that have remained elusive. CIRM seeks to harness these and other synergies through the DISC0 Foundation Awards mechanism to foster a robust discovery engine that will not only open new doors to treatments, but also accelerate and increase the likelihood of bringing regenerative medicine treatments to patients in need. By incorporating principles and practices of diversity, equity and inclusion within the science, this program strives to foster discoveries that will equitably impact patients in all our communities.

While CIRM seeks basic exploratory research projects related to stem cells, gene therapy, and regenerative medicine under this opportunity, the focus is on the biology of *human* cells. This provides a critical opportunity to California scientists for foundational discovery research with relevance to CIRM's therapeutic development pipeline. Furthermore, DISC0 Foundation Awards focus on unique research priorities since existing federal funding opportunities for discovery stage activities are primarily driven by the internal priorities and interests of the administering body and, therefore, are unpredictable and limited in both scope and focus. CIRM therefore provides this unique opportunity to California scientists to support discovery research projects that are unlikely to receive timely or sufficient funding from other sources.

OBJECTIVE

The objective of the DISC0 Foundation Awards is to support rigorous studies addressing critical basic knowledge gaps in the biology of stem cells and regenerative medicine approaches and to advance stem cell-based tools. Projects funded through the Foundation Awards should propose impactful or innovative research that culminates in a discovery or technology that would:

- Advance our understanding of the biology of stem or progenitor cells¹ (collectively, “stem cells”) that is relevant to human biology and disease; or
- Advance the application of genetic research² that is relevant to human biology and disease and pertains to stem cells and regenerative medicine³; or
- Advance the development or use of human stem cells as tools for biomedical innovation; or
- Lead to the greater applicability of regenerative medicine discoveries to communities representing the full spectrum of diversity.

Beyond the unique contributions of individual innovators, CIRM recognizes the value of team science in making scientific breakthroughs that would not be achievable by individual investigators within an award period. The DISC0 Foundation Awards program capitalizes on both approaches by supporting two types of programs. The Single PI Track supports projects with discrete objectives that are achievable under the leadership of a single investigator, and the Team Track supports multidisciplinary collaborations of 2-3 investigators that bring specific knowledge and skills to a project to create a unique advantage or synergy, where diverse perspectives drive innovation and creativity in the regenerative medicine field.

Since Proposition 14 dedicates more than a quarter of funds to support of research and the development of treatments for diseases and conditions of the brain and central nervous system (CNS), CIRM encourages the submission of proposals focused on increasing our understanding of the fundamental biology of CNS disorders.

¹ Under Proposition 14, progenitor cells are “multipotent or precursor cells that are partially differentiated, but retain the ability to divide and give rise to differentiated cells.” Progenitor cells may include directly reprogrammed cells if they meet the criteria in the above definition.

² For the scope of this solicitation, CIRM considers genetic research to mean research that alters genomic sequences of cells (edit, remove, or add DNA sequences) or introduces or directly manipulates nucleic acids (such as mRNAs, antisense oligonucleotides) in cells.

³ For the scope of this solicitation, CIRM considers regenerative medicine to mean therapeutic approaches that are intended to replace, regenerate or repair the function of aged, diseased, damaged or defective cells, tissues, and/or organs.

AWARD INFORMATION

The DISCO Foundation Awards will support responsive basic research projects via two tracks:

- 1) Single PI Track: projects led by a single principal investigator.
- 2) Team Track: projects led by a team of 2-3 co-investigators where synergistic, multidisciplinary collaboration justifies larger scale projects of critical or unique value.

What activities will CIRM fund?

CIRM funds will support the following activities under this opportunity:

- Basic research into stem cell mechanisms as they relate to human biology.
- Investigating stem cells or their derivatives as tools for discovering and enabling therapeutic or other innovations, e.g., for studying or modeling disease.
- Basic genetic research relevant to human biology and as it pertains to stem cells or regenerative medicine.
- Research and tools related to diversity, equity and inclusion in science, i.e., extending or validating the applicability of regenerative medicine discoveries to underserved populations (e.g., use of human induced pluripotent stem cell (hiPSC) lines or omics analyses from diverse groups of individuals, target diseases or disease subtypes more frequently experienced by underserved groups).
- Basic research and tool discovery to address bottlenecks in the development of cell and gene therapies, such as cell/tissue targeting, immunogenicity and toxicity, in vivo gene therapy delivery, engineering human pluripotent stem cells (hPSC) to evade the immune system.
- Studies of primary-to better understand human ~~cells and~~ tissues (healthy and/or diseased) to obtain ground truth knowledge that is critical for validating be modeled in vitro stem cell-based models or to improve targeted with regenerative medicine approaches (e.g., omics and other profiling for, human cell/~~+~~tissue atlases). Aa), a human stem cell/~~+~~regenerative medicine component (wet lab and/or data-related) must be included in the project.
- Auxiliary research activities that support regenerative medicine science (e.g., biomarker discovery, genome and epigenome editing tools, imaging tools, mechanism of disease to enable rational design of stem cell- or gene therapy-based treatments, data science and computational approaches), a

human stem cell / regenerative medicine component (wet lab and/or data-related) must be included in the project.

- Reverse translation studies related to stem cell- or gene therapy-based regenerative medicine therapies.

Activities should focus on human cells but may include supportive studies using nonhuman cells provided that human cells are also investigated, or activities may focus on nonhuman cells if a strong justification is provided that the proposed research is of immediate relevance to human biology / disease but cannot be conducted using human cells.

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

- Projects targeted by DISC2, TRAN and CLIN programs
- Projects that propose solely or mainly to derive new pluripotent stem cell lines from somatic cells or embryos

What is the award amount and duration?

Single PI Track awards CIRM will fund direct project costs of up to ~~\$1.5M~~4M per award for up to three years duration. If the project period is less than three years with an annual proposed budget above ~~\$600,000~~400,000 for the Innovator Track Single PI Track, a strong justification needs to be provided, and the GWG will be instructed to consider that budget rationale in their scoring.

Team Track awards will fund direct project costs of up to \$3M per award for up to three years duration. If the project period is less than three years with an annual proposed budget above \$1.2M, a strong justification needs to be provided, and the GWG will be instructed to consider that budget rationale in their scoring.

How will funds be awarded?

Awards will be made in the form of a grant. Funds will be disbursed pursuant to a CIRM Notice of Award. The first payment will be issued upon initiation of an award and subsequent payments will be disbursed on a regular interval at CIRM's option. Continued funding is contingent upon timely progress, as outlined in the project specific aims 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.

ELIGIBILITY

What types of projects are eligible for funding?

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

(1) The applicant must

- a) ~~Define~~define a key knowledge gap (i) in our understanding of the biology or application of stem cells, or (ii) in the application of genetic research as it pertains to stem cells or regenerative medicine;
- b) ~~Propose~~propose research that addresses this knowledge gap; and
- c) ~~Validate~~validate any discoveries made in nonhuman cells with a relevant human cell equivalent.

(2) Projects that generate molecular omics data must include an experienced Data Project Manager on the team

To ensure effective ~~and collaborative sharing and management~~contribution of data, ~~to selected data platforms (see Data Sharing Plan),~~ a dedicated Data Project Manager must be part of the team (minimum 15% effort) in projects that collect substantial omics data, such as genomics, transcriptomics, epigenomics, proteomics, metabolomics, lipidomics, etc. This individual must have demonstrated experience in data handling and is responsible for interfacing with a data management team(s), interfacing with CIRM's planned Data Coordination and Management Center (see DCMC section below), ~~and~~ reporting ~~data~~-progress on data management and sharing as well as maintaining the integrity of data during ingestion.

(3) Must be ready to initiate work on the funded project within 90 days of approval

Given the urgency of CIRM's mission, all approved awardees must initiate work on the funded project within 90 days of approval and authorization for funding by the Application Review Subcommittee of the Independent Citizens' Oversight Committee.

(4) Co-funding is not required

If the project does, however, require 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).

(5) 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 proposed co-funding, if applicable, for the term of the project. The determination of solvency will be made at CIRM's sole discretion.

(6) Application must be accurate and complete

All required components of the application must be completed and may not contain false or inaccurate information.

(7) Applicant must be in “good standing”

In order to be eligible to apply for CIRM funding, an applicant must certify that it is in good standing, as follows:

- a. The applicant's Chief Executive Officer, Chief Financial Officer, and Principal Investigator must not have been convicted of, or currently under investigation for, crimes involving fraud/misappropriation;
- b. The applicant must have accounting systems in place that are capable of tracking CIRM funds; and
- c. The Principal Investigator or key personnel named in the application must not be currently under investigation for research misconduct by the applicant institution or a funding agency and must not be currently debarred by HHS Office of Research Integrity.

~~a. Non-Profit (in existence for less than five years):~~

- ~~(i) The applicant's Chief Executive Officer, Chief Financial Officer, and Principal Investigator must not have been convicted of, or currently under investigation for, crimes involving fraud/misappropriation; and~~
- ~~(ii) The applicant must have accounting systems in place that are capable of tracking CIRM funds.~~

- ~~b. The Principal Investigator and key personnel must not be currently under investigation for research misconduct by the applicant institution or a funding agency, and must not be currently debarred by HHS Office of Research Integrity.~~

Who can apply?

Only California Organizations are eligible to apply for this opportunity.

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 must direct and control the award activities from the California location.

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 or be accountable for the conduct of the proposed project to the applicant organization through a formal contract.
- Must commit at least ~~1520~~ percent effort to working on the project. Any effort for which salary from CIRM is claimed must be expended in California.
- 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.
- Must not currently have another application that is substantially similar or has overlapping activities pending review or approval under any CIRM opportunity.

Who can serve as a Co-Investigator (Co-I) on a Team Track Award?

To be eligible, the Co-I must satisfy the following requirements:

- Must be an employee of a California-based organization or be accountable for the conduct of the proposed project to their California-based organization through a formal contract.;
- Must commit at least 10 percent effort to working on the project. Any effort for which salary from CIRM is claimed must be expended in California.;
- Must not currently have another application that is substantially similar or has overlapping activities pending review or approval under any CIRM opportunity.; and
- Must not currently be part of the same lab as the PI.

ADDITIONAL REQUIREMENTS

Positive Selection

CIRM anticipates that the number of applications submitted will be very high for this competition. When the number of applications received in a cycle is significantly in excess of the number that can be reviewed by the GWG panel, the GWG members conduct the review in two stages. In the first stage, GWG members (including scientific members and patient advocate and nurse members of the Governing Board) will conduct a pre-review of applications (called “Positive Selection”) to identify applications that the panel believes are most responsive to the funding opportunity and hold the most potential for impact. Applications that are not selected are examined by the CIRM scientific team and CIRM President to determine whether any additional applications merit a full GWG review. The remaining non-selected applications are deemed to be denied. Since the selection process is focused on quickly identifying promising proposals rather than identifying deficiencies in applications, no reviewer comments are collected at this stage. Positively selected applications advance to the second stage of review, which involves assignment to specific reviewers on the panel, a full discussion at review meeting, and scoring by the GWG.

Diversity, Equity and Inclusion in CIRM-Funded Projects

All applicants for the DISCO Foundation Awards program will be required to provide a statement describing how their overall study plan and design has considered the influence of race, ethnicity, sex, gender, and age diversity. Applicants should discuss the limitations, advantages and/or challenges of their research proposal as it relates to the diverse California population, including underserved racial/ethnic communities. Examples include use of models and tools that account for population diversity (e.g. HLA types, gender, genomics data, cell models). Applicants should also address how the research team has or will incorporate diverse and inclusive perspectives and experience in the implementation of the research project, including, for example, developing partnerships with patient organizations, acquiring training in cultural competence and/or DEI, utilizing institutional resources for DEI, and allocating funds and/or personnel to address DEI

The GWG and CIRM’s governing board will evaluate these statements as a review criterion in making funding recommendations. Priority will be given to projects with the highest quality plans in this regard.

Data Sharing and Management Plan

The sharing of data and knowledge produced from CIRM-funded projects is key to advancing the field of regenerative medicine and accelerating treatments to patients. A general overview (Data Sharing Overview) of a plan for sharing data produced in the proposed project must be included in the application and is subject to evaluation by the Grants Working Group (GWG). Applicants must allocate funds in their proposed budget for personnel and/or activities related to managing and sharing data produced from the funded project. CIRM requires

~~awardees CIRM requires applicants~~ to develop and execute a Data Sharing Plan that includes management and preservation of raw data, processed data and metadata and making applicable data and metadata available to the broader scientific community. To ensure data processing steps can be replicated and data can be reused by other researchers, CIRM also requires applicants to allocate funds in their proposed budget for personnel and/or activities related to managing and sharing data produced from the funded project. CIRM requires sharing of data in accordance with FAIR data principles (Findability, Accessibility, Interoperability, and Reusability) through established repositories where possible. The data including, but not limited to, specialized NIH-supported repositories selected, and summary of the data shared must be reported to CIRM during and after the project period. To promote FAIR data sharing and open science, CIRM may publicly share information about CIRM-funded data, including what types of data were generated and where data are deposited., generalist repositories, cloud platforms and institutional repositories. The Data Sharing Plan must be included in the application and the plan is subject to evaluation by the Grants Working Group.

Data Coordination and Management Center

Subject to board approval, CIRM has preliminary plans to fund the development and implementation/creation of a Data Coordination and Management Center (DCMC) through a separate funding opportunity. At such time, CIRM will require awarded teams to coordinate activities related to data sharing with the DCMC.

SCHEDULE AND DEADLINES

Frequency of Opportunity	One or two cycles per year
Grants Working Group (GWG) Review	Approximately 90 days post submission
ICOC Review and Approval	Approximately 120 days post submission

Award Start	Must start within 90 days of award approval (i.e., approximately 210 days post submission)
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REQUESTED FUNDING ALLOCATION

On an annual basis, CIRM will present for the Board’s consideration a calendar-year budget for each of its on-going research programs, including the DISCO Foundation Awards 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 to enable timely calls to highly specific opportunities or challenges, CIRM requests the Governing Board delegate to the President or his/her 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.