Discovery Foundation Awards (DISC0): Webinar Q&A and Frequently Asked Questions

Sections

<u>Project Scope and Funding</u>

1. **Is CIRM interested in the biology of cell aging?**

   With regard to stem cell aging, yes. However, if you propose a project centered on mature immune cell aging (or aging of other terminally differentiated cell types, i.e., non-stem cells), you will need to justify how the research is responsive to CIRM's focus on either stem/progenitor cell research or genetic research related to regenerative medicine.

2. **Can preliminary results include data from animal studies, so long as the proposed studies in the Research Plan will focus on human biology?**

   Yes. Preliminary data from animal studies can be used to support the rationale for and feasibility of exploring similar phenomena in the human system. While the proposed DISC0 Research Plan should be focused on and grounded in human biology and/or human disease pathology, this requirement does not entirely preclude the use of animal models and/or systems as part of a DISC0 Research Plan. Importantly: if any studies are proposed using nonhuman stem cells or animal models, the Research Plan should also include studies using human cells to validate any discoveries made using nonhuman cells.

   Please note that if you're studying human cells transplanted into an animal model, this is considered human biology.

3. **Is my proposal weak if it incorporates preliminary data from many studies using mouse stem cells but only one or two studies using human stem cells?**

   The strength of preliminary data for a given proposal will generally depend on the scientific question(s) pursued and the scope of the three-year Research Plan. The strongest types of preliminary data tend to support the rationale for the project and/or the feasibility of executing the Research Plan in the three-year timeframe.

For example, if an applicant has no preliminary data with human pluripotent stem cells or has never worked with them before, reviewers might wonder if it is technically feasible for the project to be achieved as proposed in three years by this applicant. On the other hand, if an applicant is well versed in the proposed techniques or has an established track record of conducting similar studies (as demonstrated by preliminary data or publications), the proposal might be viewed as more achievable within three years.

4. **Is my study of stem cell biology in scope for DISC0 if it relies on animal models of human disease?**

   If human cells are studied in an animal model, for example by transplantation of human cells into a mouse or via use of a humanized mouse model, yes. However, if any studies are proposed that focus *on animal cells or models (for example, investigating the biology of endogenous stem cells in vivo in an animal)- then the Research Plan MUST also propose experiments using human cells to validate any findings made in the nonhuman model. Please be aware that reviewer enthusiasm might be diminished if a proposal is not grounded in human biology, or if it appears that human cell experiments were added to the Research Plan as an afterthought or to help an otherwise nonresponsive proposal meet eligibility requirements.*

5. **Do studies of stem cell aging in mouse models also require validation in human models or humans?**

   Yes. To be eligible for DISC0, any project proposing experiments using animal stem cells must also propose studies to validate any findings in a relevant human cell equivalent. The intent of DISC0 is to culminate in new knowledge that is grounded in human biology and/or human disease pathology.

6. **Is CIRM interested in funding studies of diseases that are not represented in the CIRM hiPSC repository? Apart from central nervous system (CNS) disorders, does CIRM have other disease priorities?**

   Yes. The [CIRM hiPSC Repository](#) comprises cell lines for 17 diagnoses for which multiple patient and familial samples were obtained and is hopefully a valuable resource for California researchers. It is not meant to promote the study of these diseases above others.

   With the passage of Prop 14 in 2020, California voters earmarked $1.5 billion of CIRM's $5 billion in funding for disease affecting the central nervous system (CNS). While we encourage submission of DISC0 proposals focused on increasing our understanding of the fundamental biology of CNS disorders, the DISC0 review process remains open and unbiased with regard to disease or system. Rather, the DISC0 review criteria ([Program Announcement](#) pgs. 9-10) speak to the overall significance and impact of what is being proposed. If you can convincingly describe the unmet need and the significance of making an impact in a given area, this could potentially be considered a strength by reviewers.

In accordance with Prop 14, CIRM may stipulate priorities for basic CNS research in future calls for Discovery applications.

7. Do studies of cancer stem cell biology fall within the scope of DISC0 awards?

Studies of the fundamental biology of cancer stem cells are considered in scope if the proposal includes convincing evidence and/or rationale that the cancer mechanism/cell type under investigation has stem/progenitor function. For instance, cancer stem cells are defined experimentally by their ability to generate and recapitulate the cellular hierarchy of a continuously growing tumor, through serial xenotransplantation into animal models. If such evidence is weak or lacking, the proposal may be viewed as less responsive or in some cases, ineligible.

8. **How does CIRM define a "key knowledge gap" in the Foundation Awards (DISC0) program?**

As stated on pg. 6 of the [Program Announcement](#) (PA), for DISC0 we require that applicants address "a key knowledge gap (including bottlenecks in the field) (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."

CIRM does not define specific knowledge gaps or bottlenecks to be addressed with DISC0 funding. It is up to an applicant to define a specific knowledge gap or bottleneck, justify its significance, and propose research to address it. Reviewers from CIRM's Grants Working Group (GWG) will consider all these factors in assessing the merit of a DISC0 proposal.

For reference, we provide general areas of need in the understanding and/or application of stem cells and genetic research as it relates to human biology, disease, and regenerative medicine in the DISC0 PA under 'What activities will CIRM fund?' (pgs. 4-5).

It is important to remember that CIRM generally receives more applications than can be reviewed in a given DISC cycle, necessitating a 'Positive Selection' screening step in which GWG reviewers select a subset of applications to move forward to full review. The Positive Selection process is described on pgs. 8-9 of the PA. An application that is not selected for review does not necessarily lack merit or fail to address a significant knowledge gap.

Applications and Resubmissions

9. **What is the historical funding success rate for DISC0?**

CIRM has only completed one DISC0 funding cycle to date (as of October 2022). A total of 11 applications were funded, reflecting a 14% success rate. Public review summaries are available in this document from the 'Public Meetings and Events' page on CIRM's website ([link here](#)) for 40 applications that were selected for full review, including the 11 that were funded. These public review summaries can provide prospective applicants with a sense of what reviewers found impactful, and what they considered to be strengths or weaknesses of a given proposal. CIRM

highly recommends prospective applicants view these public review summaries to help with framing their applications.

What are the page limits, formatting requirements for the Proposal sections described in the Program Announcement?

The full instructions (with page limits) are provided in the blank Proposal Template, which you will find within the DISC0 online application form in CIRM's Grants Management System (GMS; also called the CIRM portal). This can only be accessed by creating a CIRM login, creating a new application, navigating to the Uploads section, and downloading the Word template.

Proposal Templates can only be downloaded once applications become live in GMS, typically 4-6 weeks prior to the due date. See the [DISC0 webinar slides](#) for screenshots of the Proposal Template and templates for other required documents.

Please be sure to download and use the most current version of all CIRM templates- as they may be updated or changed in future calls.

10. **How much preliminary data are required?**

Preliminary data are required to support the rationale and establish the feasibility of a given proposal. The amount of data required will be project-specific and may depend on many factors. See related questions above (2 & 3). The strongest types of preliminary data tend to support the rationale for the project and/or the feasibility of executing the Research Plan in the three-year timeframe—including the ability of the applicant team to successfully execute the proposed research.

11. **I'm uncertain whether to apply to Foundation (DISC0) or Quest (DISC2). How can I decide?**

DISC0 and DISC2 are different with respect to expected outcome, application requirements, and review criteria. They are not interchangeable.

[DISC0 Program Announcement](#) *(9.11.22))*
[DISC2 Program Announcement](#) *(6.28.22)*

Generally speaking, the DISC0 program targets foundational or mechanistic studies that address a key knowledge gap or bottleneck in the field, whereas DISC2 awards support projects that are designed to culminate in a candidate therapeutic or prototype medical device, diagnostic or tool that is ready for translational stage activities (early development) by the end of the award period. For instance, applicants with preliminary proof-of-concept for a therapeutic approach could apply for DISC2 funding to demonstrate that their proposed therapeutic product has reproducible disease/injury modifying activity in one or more preclinical models relevant to their target indication. In contrast, a DISC0 applicant might undertake mechanistic studies of a disease process that may or may not produce a therapy in the near term but will ultimately create new avenues and/or contribute to a rigorous foundation for translational and clinical development work in the field.

It is best to consult with CIRM about a specific project if you are uncertain whether it is a better fit for DISC0 or DISC2.

12. **Will CIRM have two rounds of DISC0 grants in 2023, and will the submission dates be the same as in 2022?**

It has not yet been determined whether CIRM will have two rounds of application review for DISC0 in 2023, nor what the exact application deadlines would be. Because of the implementation of two large CIRM [Infrastructure (INFR)](#) programs, CIRM may only offer one round of DISC0 and one round of DISC2 funding in 2023.

13. **What should I prioritize when revising and resubmitting a proposal that has been scored by the Grants Working Group?**

Our advice is to be respectful of reviewer comments/feedback and address them to the best of your ability throughout your proposal, while summarizing your overall response using the Resubmission Statement page in the beginning of the Proposal Template.

14. **If I previously submitted a DISC2 application that was not funded, but think the project may be more suited to DISC0, should I submit a new application or a resubmission?**

Submitting a former DISC2 proposal under DISC0 (or vice versa) is not considered a resubmission since these two programs have distinct objectives, application requirements and review criteria. This would require an entirely new submission for DISC0.

If your prior DISC2 (or DISC0) proposal was reviewed, our advice is to consider the Grants Working Group (GWG) feedback holistically while conceiving your new DISC0 (or DISC2) application. Some of the same individual GWG reviewers may evaluate the new application, but they will use distinct review criteria. The review criteria can be found in the Program Announcements ([DISC0](#) pgs. 9-10, [DISC2](#) pg. 13).

Bear in mind that while there is minor overlap in the allowable activities for DISC0 and DISC2, applications that appear to be copy-pasted from one program to another will be considered ineligible and will not be reviewed by the GWG.

15. **Does the $1,000,000 budget cap for DISC0 awards pertain to the total award amount or the direct project costs only?**

$1,000,000 is the maximum allowed total for direct project costs. Non-profit applicants may request indirect costs in addition to direct costs, and all applicants may additionally request facilities costs. Thus, for a project with $1M direct costs, the total award amount would typically be ~$1.4-1.6M. The CIRM Funds Calculator in the online application should make this clearer. Please consult the [Grants Management FAQ](#) on CIRM's website for more information about direct and indirect project costs.

16. **Does CIRM grant extensions to the submission deadline?**

   No. CIRM does not have a mechanism for illness, bereavement, or other types of deadline extension for applicants.

17. **Basic research can take longer than anticipated; what happens if the project team doesn't meet an aim or milestone on time?**

   If project aims and timelines are delayed due to technical challenges or other unexpected issues that may arise, CIRM expects grantees to communicate promptly with their assigned Science Officer and find solutions as early as possible. A No Cost Extension (NCE) can be requested with appropriate justification.

Data Sharing and Management Plan (DSMP)

18. **Are there required qualifications for the appointed Data Project Manager?**

   This individual must have demonstrated experience in data handling and is responsible for maintaining the integrity of data during ingestion, interfacing with a data management team(s) at a repository, if applicable, and reporting data management and sharing progress to CIRM.

19. **If only a small portion of my project is generating omics data (for example, simple RNA-seq data that can quickly and easily be deposited in one of the usual repositories), am I still required to dedicate a Data Project Manager with 15% effort?**

   Yes. 15% effort for a Data Project Manager is an eligibility requirement for DISC0 projects that generate any omics data. Data Management and Sharing is a vital component of CIRM's 2022 – 2027 Strategic Plan and its commitment to fostering a collaborative regenerative medicine ecosystem. Data Project Managers are integral to a paradigm shift toward greater data sharing and broader coordination of research activities in accordance with FAIR principles (Findable, Accessible, Interoperable, Reusable). If the omics data are limited, the Data Project Manager's additional time can be spent on sharing data of other types.

   Please note that the 15% effort is time commitment that does not necessarily need to be (fully) funded by the DISC0 grant.

   For more information, visit CIRM's DSMP guidelines.

20. **How is confidentiality of the proposal and data maintained with reviewers (especially outside ones)? How are potential breaches in such confidentiality investigated?**

The most current summary of CIRM's confidentiality policies is attached as Exhibit A to this document.

Principal Investigators and Key Personnel

21. Does DISC0 allow Co-Principal Investigators?

'Co-PI' is sometimes meant to describe a Key Person who separately receives fund distributions. CIRM does not offer a 'co-PI' role nor support this type of arrangement. A DISC0 award is only given to a single PI / institution. However, collaborators, including investigators who share scientific and administrative leadership responsibilities with the PI, are allowed, and can be paid from the grant via a subcontract or as a Key Person. The specific roles and responsibilities each Key Person can be defined in the online portion of the DISC0 application.

22. Can a faculty member be a PI on one proposal and a collaborator on another proposal?

Yes. A Principal Investigator on one CIRM application can be a collaborator (subcontractor or Key Person) on another application(s), even if the applications are submitted in response to the same PA/RFA or in the same application review cycle. CIRM rules state that a PI can submit only one application per round, but this person can be a collaborator on a separate application(s) in the same round.

23. As a PI, can I commit 10% and have a Co-PI/collaborator who commits 10% to meet the 20% effort requirement?

No. The PI must commit 20% effort, salaried or not.

24. Can a postdoc be a PI on a CIRM application?

CIRM requires that a PI 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. Also, the PI must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI. There have been occasional circumstances where the applicant organization has provided a post-doc with the support and authority to act as a PI, but this not typical.

Out-of-State Collaborators

25. Can my DISC0 grant support out-of-state collaborators?

Yes, out-of-state collaborators can receive funds from a CIRM award through a subcontract. However, CIRM requires that the California Organization exercises direction and control over the subcontracted activities. The funded CA organization must retain any new intellectual property generated from the CIRM funding, and the out-of-state organization cannot retain independent publication rights in any intellectual property (e.g., invention, technology, data) arising out of the CIRM funded project.

26. **If we have a collaborator who is outside California, how should we address this in a DISC0 application?**

An out-of-state collaborator should be entered in the Consultants/Subcontracts section of the online application, along with the budget associated with the subcontract (which will be justified in the Budget Justification section). You will need to provide a name, institution, and describe the role/responsibilities for each collaboration. If the collaborator's specific expertise or resources are important components of your project, a biosketch should be included.

Reminder: Any new IP generated from the use of CIRM funds outside the State of California must either stay, via assignment if necessary, with the California applicant organization/awardee or such rights must be waived. One option is to put into place an agreement wherein the out-of-state contractor will assign rights to any new IP to the CIRM applicant/awardee that comes from the CIRM funded project if they agree to take CIRM funds and receive a license-back for research development purposes. Any commercialization with CIRM-funded intellectual property may trigger revenue requirements in the CIRM IP regulations, which are on the CIRM website ([link here](#)). This link is to CIRM's IP [FAQ](#) .

Review Process

27. **What are CIRM reviewers looking for in the Diversity, Equity, and Inclusion (DEI) section?**

CIRM provides guidance to reviewers for evaluating Diversity, Equity and Inclusion (DEI) in the [Program Announcement](#), under 'Does the project uphold principles of diversity, equity and inclusion (DEI)?' (pg. 10). This guidance is in the form of subquestions and is provided in the application critique form that reviewers fill out in advance of the review meeting.

"Does the project plan and design adequately address and account for the influence of race, ethnicity, sex, gender, and age diversity? Would the project outcomes extend or validate the applicability of regenerative medicine discoveries to underserved populations, including underserved racial/ethnic communities? Has the applicant described prior efforts or proposed plans for outreach, partnership, or educational activities to inform the development of DEI within the research project?"

Our general advice is:

- ***Focus on CIRM's Mission: Accelerating world class science to deliver transformative regenerative medicine treatments to a diverse California and world.*** *Determine how the project fits into CIRM's mission and make this very clear in the proposal.*

- *Be specific,* e.g., instead of stating that you will ensure the use of a collection of cell lines representing diverse genetic ancestries, delineate the exact cell lines you will be using, and the genetic ancestries they represent. Provide a rationale for the genetic ancestries you seek to include. Describe where you anticipate hurdles in achieving that diversity, and how you plan to overcome those hurdles – either at the DISC0 stage or, if necessary, in future work.
- *Be intentional,* e.g., instead of stating the access you may have to samples or participants from diverse backgrounds, explain how you will go about ensuring that samples / participants from diverse backgrounds are actually included / recruited into your study.
- *Convey that you understand key issues related to diversity, equity, and inclusion. If unfamiliar or inexperienced with how best to approach this subject, work with an expert to articulate and execute your DEI approach. Remember, you can propose to use CIRM funds for activities intended to promote and uphold principles of Diversity, Equity, and Inclusion (DEI) in the conduct of your study.*
- *Tap into your institution's resources, but don't rely on your institution's website text. The reviewers do not expect you to create a sea change on your own, but they are attentive to the project-specific nature of your DEI statement.*
- *Don't neglect the third subquestion (above). Even if the Research Plan fully incorporates DEI principles, your DEI statement (and the budget) should include activities intended to inform further development of DEI within the project. These, too, should be specific and intentional.*

Please note: Because CIRM is prohibited from taking race, ethnicity, national origin, and gender into account in making grant decisions, applicants should refrain from including race, ethnicity, national origin, or gender in describing the applicant team personnel.

28. **If a project proposal focuses on a research area far outside/beyond the expertise of the review panel, will external reviewers be invited?**

    The CIRM GWG currently comprises about 200 reviewers with expertise in many subject areas; a listing is here: https://www.cirm.ca.gov/board-and-meetings/grants-review-working-group-members. When necessary, CIRM's Review Office recruits Specialist reviewers to provide expertise that is not fully covered by available members of the GWG. Feel free to send general suggestions to review@cirm.ca.gov; note that an expert you refer may not be invited to review your application(s) if a potential conflict exists.

CIRM's hiPSC repository

29. **Are the primary cells from these individuals available?**

    No, the primary cells (PBMCs/fibroblasts) are not available from CIRM's hiPSC repository.

30. **Are there any isogenic iPSC repositories available to non-profit institutions through CIRM?**

    Not yet. However, this effort is underway we will update this section if/when that occurs.

31. **Does the CIRM hiPSC repository have any lines with Bulk/SC RNA Seq Data?**

   There are no single cell RNA sequencing data available via the repository for any of its hiPSC lines. However, as several of these lines have been used in published research, single cell RNA seq data may be available in association with the published articles.

CIRM Grants Management Office – Managing Your Grants FAQ

32. **I've heard that CIRM-funded researchers who don't meet aims or milestones on schedule have to self-pay for their studies using alternate funds. Is this true?**

   You may be thinking of CIRM's later stage programs (TRAN1/2/3/4, CLIN1/2), where grant payments are linked to Operational Milestone achievement. Applicants to those later stage programs are required to have access to contingency funds so their projects can continue if an Operational Milestone is significantly delayed.

   Discovery Stage programs such as DISC0 and DISC2 do not use the Operational Milestone model. Instead, grant payments are issued at scheduled intervals as defined in the Notice of Award, contingent on grantee maintaining compliance with CIRM's post-award reporting requirements. If milestones are substantially delayed, CIRM expects grantees to communicate promptly with their assigned Science Officer and find solutions as early as possible. Grantees may request a one-time no cost extension with appropriate justification.

33. **Other questions about Post Award Management: see Grants Management FAQ at link below.**

   https://www.cirm.ca.gov/researchers/managing-your-grant