CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

DISC4 (FY 2026-2027)
Frequently Asked Questions

KEY RESOURCES FOR APPLICANTS

1. The pre-submission form is available in the CIRM **Grants Management Portal**
2. **Grants Administration Policy** for Discovery, Translation, & Education Projects
3. Program Announcement, Video Guide, and Quick Guide on Guiding Principles may be found on **DISC4 Award Page**
4. **Guide for AOOs**
5. **Our Review Process**
6. To request consultations with Science Officers, email **discovery@cirm.ca.gov**

TABLE OF CONTENTS

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PROJECT SCOPE AND ELIGIBILITY

1. **What would CIRM envision as an ideal project for DISC4?**

   DISC4 awards were designed to support CIRM's strategic goal to identify novel, high-quality targets through a deliberate emphasis on disease mechanism research. The scope and structure of the DISC4 awards is flexible and intended to support teams pursuing ambitious, cross-disciplinary science across a wide range of disease areas and topics.

   Competitive DISC4 projects should articulate an ambitious scientific question with strong relevance to the understanding of human diseases. Projects should be well positioned to leverage innovations in stem cell or genetic research and meaningfully integrate different disciplines/technologies/specializations to address their core questions. The team should have a well-considered plan to accelerate translation of any new scientific insights that emerge into early therapeutic or biomarker development.

2. **What is an example of an acceptable use case for animal models?**

   We do not have examples of acceptable use cases. DISC4 proposals should be human-centered, but use of non-human models can be included if it would be highly impactful or necessary to achieve specific objectives. We invite applicants to consider relevant human tissue/models as alternatives where possible. If you believe your use case fits the scope of DISC4, be sure to provide justification in your application.

3. **Ideally, how much of the project should focus on specific disease areas? Would developing a platform technology be suitable?**

   There is no prescribed formula. Research questions do not need to be focused on a specific disease or disease area. For example, projects might focus on common biological processes that impact multiple disease types and organ systems. Technology development and other research activities and approaches can be included in DISC4 proposals, as long as the project eligibility requirements are fulfilled.

4. **Will DISC4 awards support translational development of therapeutic candidates?**

   DISC4 supports large, multidisciplinary teams pursuing foundational research to elucidate disease mechanisms and discover novel targets.

   DISC4 awards are **not** intended to support development of existing therapeutic or biomarker candidates. Major aims should not be focused on development activities, especially where study designs do not address current knowledge gaps beyond efficacy, safety and biodistribution readouts for a limited set of candidates. Proposals focused on developing a candidate risk being deemed ineligible or insufficiently aligned with program scope.

Investigators proposing to optimize or advance a therapeutic candidate are encouraged to explore CIRM's new Preclinical Development Awards program.

5. **Should the proposal be structured as a program project grant where each PI/co-I is responsible for one project, or as a single project grant where multiple PI/co-Is interact with each other for each of the aims?**

   There are no requirements or restrictions on how the project should be structured. Applicant teams should structure their proposal to maximize impact and feasibility. Regardless of the structure, the overall proposal should have significant added value as an integrated collaboration rather than as a series of independent projects.

6. **In what ways can stem cells can be incorporated into the approach? Can stem cells be considered primarily as tools, such as iPSCs for generating different cell types, or is the focus on stem cell biology and their use as therapeutics?**

   The project eligibility requirement (see "Eligibility" in Program Announcement) specifies that the "proposed project must include studies that employ human stem cells or genetic research as part of the central approach or hypothesis". Application of stem cells including patient derived stem cells as models or tools for studying biological phenomena is considered to satisfy this requirement.

7. **To what extent is CIRM is interested in understanding the mechanism of disease? Would DISC4 support purely mechanistic/discovery research, or should we include a possible route of translation?**

   The primary focus of DISC4 projects should be on generating novel foundational or mechanistic insights into disease biology as a basis for discovering new targets or biomarkers. Elucidating disease mechanisms is critical for identifying new targets and biomarkers, a key strategic goal that was defined in CIRM's Strategic Allocation Framework (See Goal 1).

   Applicants are encouraged to consider incorporating elements in their overall proposal that could facilitate the progression of potential findings into future translational efforts, for example inclusion of validating studies in disease models etc. Applicants may elaborate on their plans for facilitating progression at both the pre-submission stage as well as the full application stage.

8. **Should DISC4 applications be focused on one disease or on multiple disease?**

   DISC4 was designed to support a wide range of research questions related to disease biology that would benefit from the integration of multiple disciplines. Applicant teams may focus on common biological processes across multiple disease indications or apply a range of different techniques and tools to deeply interrogate one disease.

9. **Does this award support generating and validating patient-derived models, rather than hypothesis-driven studies?**

   A proposal does not have to be hypothesis-driven, as long as it meets the eligibility requirements to address knowledge gaps or bottlenecks in our understanding of human disease and includes studies that employ human stem cell or genetic research as part of the central approach. Creation of resources, such as new disease models, that can be useful to the broader scientific community is allowed, but the scope of the proposal should not be limited to deriving new cell lines, biobanking or model development alone.

10. **Does DISC4 support efforts for system digitalization, AI/ML collaborations?**

    Yes, AI/ML approaches or other computational components of projects are allowable, and requesting funds to support activities associated with these aims is allowed, including local data management, digitalization, and computing resources. You may also budget for funds to enable data sharing and collaboration.

11. **Are bioinformatics and genomics expected to be part of all DISC4 applications?**

    There is no requirement or expectation that all projects include genomics or bioinformatics components. However, DISC4 projects that include scalable approaches and generate significant data volume should ensure that they have expertise and capacity within the team to analyze data appropriately.

12. **Can proposals focus on aging biology as a primary target, or must aging be studied in the context of specific age-related diseases?**

    Proposals may focus on common biological processes that impact multiple diseases or organ/ systems, including the biology of aging, and do not have to be in the context of any specific disease. However, scientific reviewers will consider the potential significance and impact of the proposal in the context of advancing our understanding of human diseases. See “Pre-submission Selection and Application Review?” in Program Announcement.

13. **Is reverse translation within the scope of this award? If I already have a cell therapy target, but I would like to conduct studies to better understand the mechanism of action. Would that be within the scope of this award?**

    Reverse translation research can be a valuable and complementary approach in the study of disease biology. Reverse translation studies could be within scope if they are designed to contribute to our understanding of disease biology. However, research activities primarily intended to support the commercial or clinical success of a therapeutic candidate are not allowable (see “Unallowable Activities” in Program Announcement). CIRM supports

preclinical and clinical development efforts through other award programs, please check out our website to find the most appropriate program for your goals.

14. Is high-throughput screening (HTS) or related techniques allowed?

There are no specific requirements or restrictions on research tools or approaches. Applicants are encouraged to propose the most impactful combination of research technologies or approaches relevant to their objective. They should ensure that all other project eligibility requirements are fulfilled (stem cell, genetic research, non-human models, unallowable activities, etc.). See "Eligibility" in Program Announcement.

15. Are mechanistic clinical trials and/or prospective observational clinical/biomarker studies allowable under the DISC4 mechanism?

The DISC4 program supports foundational disease biology research that may include reverse translational studies, including those using clinical samples or data, and basic research involving human subjects, provided the study is not subject to FDA oversight or regulation. Observational clinical studies may be allowable as a component of a project if they are aimed at achieving the expected outcomes of a DISC4 award and all necessary consents and institutional approvals are obtained.

DISC4 will NOT support the conduct of clinical trials, whether interventional or mechanistic, that involve drugs, products, devices or other interventions subject to FDA oversight or regulation. Use of biosamples or data derived from such trials, however, would be allowable if all consents are in place.

DISC4 will NOT support activities aimed at preclinical or clinical development of therapeutic candidates. Those activities are targeted by CIRM's PDEV and CLIN2 programs. Please sign up to receive email notifications about those programs, if interested.

16. With regard to the "genetic" and "stem cell" requirements, does "genetic" modification have to occur in stem cells themselves?

No. Genetic research does not need to be applied to stem cells to meet the above requirement.

All projects must include studies that employ human stem cells or genetic research as part of the central approach or hypothesis.

"Stem cells" include any progenitor and precursor cells that retain the ability to divide and give rise to differentiated cells. "Genetic research" is defined as studies that alter genomic sequences of cells (edit, remove or add DNA sequences); or introduces or directly manipulates nucleic acids (e.g., coding and non-coding RNAs, antisense oligonucleotides) in human cells.

17. **Can there be overlap with a recently submitted DISC0 or DISC5?**

CIRM will not consider pre-submissions that have scientific overlap with applications pending review or active awards. If the submitted DISC0 or DISC5 application is withdrawn, you may submit a DISC4 pre-submission that includes elements from the DISC0 application.

INDIVIDUAL, TEAM, AND ORGANIZATION ELIGIBILITY

18. How many co-investigators can be from the same institution? Are there any limits on co-investigators from different institutions?

The core team must include one principal investigator (PI) and at least four co-investigators (Co-Is). There are no limits to the number of Co-Is, but all Co-Is must adhere to the requirements listed in the PA. At least one Co-I must be based outside of the PI's organization. There are no limits to the number of institutions involved with any application.

19. Is DISC4 restricted to academic labs or can startups apply?

DISC4 is not restricted to academic labs. The focus of DISC4 is on foundational and mechanistic understanding of diseases with the expectation that these will be integrated into translational pathways in the future. We encourage any academic/nonprofit and/or for-profit team to apply or consider collaborating on a DISC4 application if their research aligns with the objectives of DISC4.

20. What do you mean by multi-institutional? Can different departments from the same university be considered?

At least 1 member of the core team must be employed by a different CA organization from that of the PI. Different departments within the same institution are not considered distinct institutions for this funding mechanism.

21. Can you give examples of 'relevant translational/industry expertise'?

To encourage the integration of multiple disciplines, at least one member of the applicant team (PI, Co-I, or Key person) must possess relevant translational/industry expertise, relevant clinical expertise and relevant bioinformatic and/or computational expertise.

There are no formal requirements or definitions for any of the above expertise requirements. These requirements may be fulfilled by any member of the broader team (Core members or key personnel). Invited teams will need to identify the team member that fulfills each requirement and provide a brief explanation in their full application. **This is not required at pre-submission.**

In general, relevant translational/industry expertise should include experience that would help accelerate discoveries toward preclinical development. Examples may include experience advancing a therapeutic product, developing commercial strategies for products, or participating in discussions with regulatory bodies, etc.

22. What is CIRM looking for in a collaborative team? Do you emphasize expertise in the area of research or new perspectives and tools?

The DISC4 awards aim to support teams that integrate different disciplines, expertise, perspectives to address ambitious research questions in disease biology. We encourage proposals that include efforts to develop or optimize new approaches and tools as part of a balanced, integrated approach. Reviewers will “assess the extent to which the project cuts across silos or employs a unique synergy of technologies or disciplines to understand human disease." See “Pre-submission Selection and Application Review” in the Program Announcement.

23. Are out of state academic collaborators that would be co-inventors on IP or co-authors on publications acceptable?

An out of state collaborator can be a co-inventor, however the rights to the invention must be assigned to the Awardee Institution.

Out of state academic collaborators are encouraged to be co-authors on publications with the Award PI which will allow them to fall outside the independent publication restriction on allowable costs.

24. What are the IP obligations if a California based start-up receives part of a grant?

In general, a collaborator who receives CIRM funds and obtains ownership rights to inventions or data will be subject to CIRM IP Regulations, including, for example, revenue sharing.

25. Can 2 or more members of a Core team (PI/Co-I) be from the same lab e.g. lab head and staff scientist ?

No. Each Co-I on a CIRM application must fulfill several requirements (see Common Requirements document) to be eligible for consideration for CIRM funding:

- Must be an employee of a California-based organization and be accountable for the conduct of the proposed project to their California-based organization
- Must not currently have another application that is substantially similar or has overlapping activities pending review or approval under any CIRM opportunity
- Must meet the same institutional qualifications that would be expected of a PI

Members of the DISC4 core team CANNOT be from the same lab since only one can be accountable for the conduct of the proposed project to their CA-based organization.

26. Can the project team include investigators outside of CA or outside of the US?

Non-CA-based investigators, including those outside the US, are not eligible to serve as PI or Co-I on DISC4 awards. However, DISC4 applicants are allowed to budget grant funds to support a non-CA-based collaborator through an award subcontract, provided the out-of-state organization DOES NOT retain the intellectual property or independent publication rights of any intellectual property (e.g., invention, technology, data) arising out of the CIRM-funded project.

Optionally, collaborating non-CA investigators and organizations may contribute research activities or unique resources to the overall project at no cost to the team (in-kind contribution). If qualified as matching funds, these contributions would allow the applicant team to request additional CIRM funding. See “What are matching funds?” in Program Announcement to learn more.

27. Can the PI or a member of the core team be someone with no background in regenerative medicine?

Yes. The DISC4 program is intended to bring together different expertise and approaches to generate novel insights. There is no requirement for core team members to have a background in regenerative medicine. Applicant teams should ensure, however, that the appropriate leadership and expertise is in place to achieve stated objectives.

Note: to encourage cross-disciplinary proposals, the broader applicant team (Core Team and Key Persons) must include members with specific relevant expertise and include an experienced Data Project Manager (Full Application only).

BUDGET, AWARD DURATION, AND AWARD NUMBERS

28. How do I determine whether CIRM considers a cost allowable?

When not otherwise specified by CIRM regulations, CIRM applies the Office of Management and Budget cost allocation principles including the determination of whether costs are 1) reasonable, 2) allocable, 3) consistently treated, and 4) adhering to any other limitations set forth by the PA/RFA or Notice of Grant Award. For more information, see the NIH Cost Principles. CIRM encourages grantees to use these cost principles to make their own determinations on cost allowability given CIRM cannot make a judgment on every cost scenario.

Allowable project expenses encompass, yet are not restricted to: personnel salaries, fringe benefits, specified supplies, tuition and fees, research animal expenditures, consulting fees,

itemized clinical study outlays (encompassing research patient care costs), travel-related disbursements, project-related equipment, publication expenses, service agreements, subcontracts, and delineated administrative costs necessary for executing the endorsed project.

Please see the Grants Administration Policy and FAQ on Allowable Project Costs for more information.

29. Do indirect costs of subawards fall under the direct costs budget of the primary applicant institution?

The DISC4 awards supports up to $13,000,000 total costs. The total cost cap is inclusive of all direct, facilities, and indirect costs from the prime applicant and subcontractors.

30. Do subcontractors need to follow CIRM's Facility Cost / IDC policy, or can they apply their own indirect cost rate?

Your subcontractor would include the full amount of overhead they are eligible for under CIRM regulations as part of their subcontract budget. The full cost of the subcontract budget (direct+ indirect) is entered in the prime budget as a direct cost. Our funding calculator will automatically exclude the amount of any subcontract over $25,000 from generating F&A to the prime applicant.

31. Can matching funds be used for equipment purchase/support?

As outlined in the Program Announcement, eligible matching fund contributions must take the form of either:

(i) Unique resources that will be leveraged by the project team e.g. cell-lines, biosamples, research/computational resources, etc.; or

(ii) Independently funded activities undertaken during the award period to generate data or resources that will be leveraged by the project team during the award period.

Matching fund contributions should be provided by a non-CIRM source. Equipment or other forms of contribution may be allowed if they satisfy any of the above conditions.

PRE-SUBMISSION, APPLICATION, AND REVIEW PROCESS

32. What do new applicants need to know about the CIRM application process?

As a first-time applicant, you should look through the resources at the top of our FAQ. You should also be familiarized with Authorized Institutional Officials (AOOs), the individual with the signature authority for an institution that is submitting a full application **(not required at pre-submission stage**). The AOO must be "cleared" by our Grants Management Team before the final application is considered submitted, which can take up to a week. The submission process takes place in 2 steps: the PI will submit their application

first, which is then routed to the AOO. The approved AOO must log in and co-submit through their own interface.

There may be significant differences in application form and templates between CIRM programs and NIH or other funding agencies. First-time applicants are advised to familiarize themselves with CIRM application.

33. How binding is the pre-submission proposal?

The project described in the full application should largely reflect the project that was presented in the pre-submission proposal. During the formal eligibility assessment of full applications, CIRM will verify that this is the case. As invited teams will have the opportunity to consult with CIRM program officers during the preparation of their full applications, they will have the opportunity to discuss any changes that they anticipate and CIRM will advise whether the changes are significant enough to preclude invitation.

34. How will the pre-submissions be evaluated?

Please see “Pre-Submission Selection and Application Review” in Program Announcement. If the number of pre-submissions exceeds the volume of applications that can reasonably be discussed by the GWG panel the GWG will conduct an initial screening to identify those pre-submissions that best align with the DISC4 program objectives based on the criteria listed below. Pre-submissions will receive a composite score, which combines two measurements from the GWG reviewers, selection and rank. The two measurements are weighted 60% and 40% respectively. A composite score cut-off will be established at the closest numerical break to the target number of applications. Pre-submissions scoring above the cut-off will be invited to submit a full application.

Reviewers may provide brief comments or categorical assessments at this stage; however, detailed feedback to applicants is not guaranteed.

The selection criteria for DISC4 pre-submissions are:

- Impact of the proposed project in advancing understanding of a human disease, generating data/resources, or potential to advance novel therapeutic or biomarker targets.
- Innovation relative to the current state of research such as applying novel frameworks to study of disease, cutting across silos, employing unique synergy of technologies, or utilizing innovative approaches.
- Responsiveness to DISC4 program objective, area of focus, and scope.

35. How can prospective applicants find out page limits and formatting requirements for a DISC4 pre-submission or application?

Page limits are specified in the CIRM-provided templates, which include built in formatting that should not be changed. Prospective applicants should always download and utilize the most current templates which are found in the Uploads section of the online application, as sections are occasionally changed from previous funding cycles.