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INFR6.2: Shared Resources Laboratories for Stem Cell-Based Modeling

Enhancing/Expanding SRLs

REQUEST FOR APPLICATIONS

05.15.23 (revised 05.31.23)

INFR6.2: Shared Resources Laboratories for Stem Cell-Based Modeling

Enhancing/Expanding SRLs

This RFA document describes the Enhancing/Expanding Shared Resource Laboratories (E/E-SRL) program only. Please see INFR6.1 RFA for a description of the Establishing SRL (E-SRL) Program.

Objective

The mission of the California Institute for Regenerative Medicine (CIRM) is to accelerate world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world.

Stem cell-based modeling of human biology and disease is a promising approach to advance our knowledge of human disease mechanisms and to identify new therapeutic targets, biomarkers, and drug candidates. To generate such in vitro models, human pluripotent stem cells (hPSC) or adult stem cells, either derived from patients with specific diseases or engineered to represent those diseases, are differentiated into cell types that are relevant to the biological or disease-related questions under investigation. Such models can range in complexity from single layers of differentiated cell types to multidimensional systems such as organoids and bioengineered tissues/organs on chips.

There is abundant interest and expertise in the California research community to capitalize on the promise of stem cell-based modeling. Many laboratories are interested in acquiring this expertise as a core competency, while others seek to address specific research questions through collaboration. However, not all research laboratories that need these models have local access to relevant infrastructure and training, nor do all have the opportunity to collaborate with a stem cell-based modeling laboratory. Laboratories well-versed in stem cell-based modeling that share their expertise and/or provide models collaboratively cannot meet demand, as it is time consuming and costly to divert resources to educating and supporting other researchers.

In addition, to accelerate the impact of stem cell-based modeling research, the field must overcome important challenges including limited reproducibility across projects employing similar stem cell-based models, and the need to better understand these models' predictive value for elucidating human biology and disease.

CIRM intends to increase and diversify contributions to the field and help overcome some of the hurdles described above by funding dedicated Shared Resources Laboratories (SRLs) for Stem Cell-Based Modeling across the state of California. Funded SRLs will become part of a collaborative network offering infrastructure, expertise, access to stem cell-based models, training and standardization of resources and protocols, with the goals of accelerating discoveries in regenerative medicine, growing and diversifying the cohort of stem cell researchers in the state, and promoting reproducibility of stem cell-based modeling experiments within and across laboratories. CIRM expects SRLs to become self-sustaining by the end of the award period.

The concept for SRLs is grounded in CIRM's experience with 17 Shared Laboratories funded from 2007 to 2016 under Proposition 71 (Prop 71 SLs). These laboratories

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provided California researchers with dedicated research space, specialized instrumentation, cell lines, and cell culture materials free from federal restrictions on human embryonic stem cell (hESC) research that existed at the time. With CIRM funding, Prop 71 SLs also provided training in stem cell culture and related technologies, making the emerging field of human pluripotent stem cell research more accessible to California researchers. Under Prop 14, CIRM now intends to re-establish and expand this unique opportunity for California scientists, providing access to cutting edge stem cell-based modeling as a shared resource, and further advancing California as a leader in this space.

The SRL for Stem Cell-Based Modeling Awards Program represents one of several technology competency hubs programs envisioned in CIRM's 2022-2027 strategic plan. Together with a future Data Infrastructure, SRLs will broadly connect and empower California's regenerative medicine research ecosystem toward advancing world class science and therapeutic innovation.

The overall objective of this funding opportunity is to accelerate regenerative medicine research by creating a network of SRLs that will:

1. Broaden access to stem cell-based models across CA
2. Advance standards and reproducibility of stem cell-based models
3. Increase access to educational opportunities in stem cell-based techniques
4. Develop sustainable stem cell core infrastructure

Examples of how a network of SRLs for Stem Cell-Based Modeling may function to meet the goals of this funding opportunity include (but are not limited to):

Providing researchers, locally at grantee institution and regionally at nearby institutions, access to:

- Cell culture facilities to conduct stem cell-based modeling experiments
- High-cost and highly specialized technologies, needed for stem cell-based modeling

Providing researchers, locally and across California, access to:

- Well characterized, unmodified and modified hPSC collections, locally and by shipment
- Partially or fully differentiated stem cell-based models, locally and by shipment,
- Training in the creation and use of stem cell-based models, offered locally in cores through hands-on training, and via regular workshops / classes, video tutorials, etc., for broad participation

Providing educators, regionally and/or across California, access to:

- Formal techniques courses in stem cell culturing and stem cell-based modeling for student education
- Other student experiences with stem cell-based modeling, e.g., workforce development in partnership with CIRM EDUC-funded programs

Implementing sustainability plans

- Fee for service, recharge
- Alternative funding sources

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To effectively achieve the program objective, CIRM will coordinate a Steering Committee composed of SRL Program Directors and external stakeholders, to drive knowledge-sharing and standard-setting among funded SRLs and external partners, accelerating stem cell-based modeling research across California.

Award Information

How is the Program Structured?

The program intends to fund two different types of SRL:

1) Establishing (E)-SRLs to provide local access to stem cell-based models, training, specialized equipment, and educational opportunities in geographic areas/locations where access to models is limited; and
2) Enhancing / Expanding (E/E)-SRLs to enable leading experts in stem cell-based modeling to share their models and expertise locally and broadly across California.

Since the two SRL types differ in focus and scope, applications will be solicited through two separate requests for applications (RFAs), INFR 6.1 and INFR6.2. **See Appendix for a side-by-side comparison of activities and allowable costs for the two RFAs**.

This document details information about RFA INFR6.2 (E/E-SRL) only.

RFA INFR6.2 (E/E-SRL) targets California non-profit research institutions that conduct cutting edge stem cell-based modeling research and can demonstrate local, regional, and statewide interest in the expertise to be offered.

Awardees will be funded to equip an existing space as a core facility that offers stem cell-based modeling expertise to researchers not only from the grantee institution, but also broadly across California and beyond. Broad sharing of expertise should be an emphasis for E/E-SRLs. In addition to local expertise at the grantee institution, additional stem cell-based models may be established and offered at the core, in partnership with investigators from other non-profit or for-profit organizations. Successful outcomes include, but are not limited to, equipping and staffing of the SRL, implementation of stem cell-based modeling expertise, utilization of core facility, including by labs that have limited access to stem cell-based modeling expertise, establishment of and sustained enrollment in training and educational programs (if offered), broad sharing of stem cell-based models across California, success of projects utilizing core and shared models, implementation of sustainability plan, and contributions to SRL Network functions (see below).

All SRL awardees will be members of the **CIRM SRL Network.** A CIRM-coordinated Steering Committee, composed of SRL Program Directors and external stakeholders in the stem cell-based modeling field, will drive network functions and will be responsible for its outcomes. These may include, but are not limited to, establishment of processes and systems for sharing models, best practices, knowledge, and educational and other resources; standardization of cell lines, reagents, and quality control/validation across the network, where deemed feasible for improving reproducibility; and development of collaborative approaches toward improving reproducibility of stem cell-based models.

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Awardees are expected to provide and implement plans (1) for financial support of SRL facility operations through, e.g., user recharge and (2) for **sustainability of the SRL in the long term**. SRL awards will be realized in 3 phases.

E/E-SRL Awards are up to 5 years:

- Phase A – 6 months for equipping SRL core facility
- Phase B – 30 months of CIRM-supported operations
- Phase C – 24 months of tapered CIRM support (half of Phase B operational costs) during implementation of long-term sustainability plan

During Prefunding Administrative Review of funded applications, CIRM will work with awardees to make adjustments to the timing of the phases, as needed.

Pursuant to Proposition 14, Shared Resource Laboratories are intended to be operational in the first five years following the effective date of the initiative (December 2020). Therefore, applications must propose plans that are achievable within the outlined phases above.

What activities will CIRM support?

The E/E-SRLs must serve as shared resources, regionally and across California. The core facility, i.e., equipment and trained personnel, must be available not only to stem cell and regenerative medicine researchers at the grantee institution but also to those from nearby institutions without such facilities.

CIRM funds will support the following activities:

1. Creation of core facility
   - ✓ Acquisition of major equipment (e.g., incubators, hoods, freezers, liquid nitrogen containers, microscopes, cell sorters, sequencers), necessary for culturing and analyzing stem cell-based models (no co-mingling with federal funding for purchase of capital equipment)
   - ✓ Establishment of stem cell-based modeling expertise in core facility, obtained internally within grantee institution and/or externally through collaboration with partnering institutions
2. Operations
   - ✓ Supporting use of SRL by investigators from grantee and nearby institutions
   - ✓ Maintenance of SRL core
   - ✓ Providing specialized services (e.g., gene delivery, gene editing, omics, bioinformatics), necessary for manipulating and analyzing stem cell-based models
   - ✓ Broad sharing of reagents and partially or fully differentiated models across California
3. Training and Education

- ✓ Training of researchers in creation/use of models through individual training, workshops, online materials, and/or other approaches
- ✓ OPTIONAL (**if offered, additional funding provided**): Formal Stem Cell Techniques Course on general hPSC culturing techniques and creation/use of stem cell-based models, serving CIRM EDUC programs, other educational programs and/or California researchers

4. SRL Network
   - ✓ Participation in CIRM-organized SRL Network activities, including establishment of processes and systems for sharing know-how, knowledge and resources, participation in efforts to improve reproducibility

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

- ✘ Conduct of independent research studies: research projects that make use of SRLs must be funded via other sources, which may include CIRM research awards.
- ✘ Renovation/facility improvements
- ✘ Activities already budgeted or paid for under a prior, existing or future CIRM award

What is the award amount and duration?

The CIRM Governing Board has allocated $50 million for funding of the SRL program (INFR6.1 & 6.2 combined): $26M for Renovation/Facility Improvements & Equipment funds and $24M for operations.

The awards for E/E-SRLs will be up to $4.3 million (with techniques course) or up to $3.0 million (without techniques course) each in ***total*** allowable project costs over a maximum five-year period.

Total allowable cost allocation

- Equipment - up to $1.5 Million
- Operational Costs - up to $1.5 Million, **incl. 20% co-funding***
- Techniques Course (optional) - up to $1.30 Million*

**Cost allocation for operations and Techniques Course includes allowable direct facilities and indirect costs.*

Pursuant to Proposition 14, CIRM shall prioritize applications for Shared Resource Laboratories that offer matching funds or verified in-kind support, consistent with the highest medical standards, as established by the CIRM governing board.

How will funds be awarded?

CIRM will disburse funds pursuant to a Notice of Award (NOA) and based on operational milestones. Costs resulting from a delay or failure to meet an operational milestone will be the sole responsibility of the recipient. Successful applicants will

have thoughtfully accounted for foreseeable project risks and developed contingency plans that do not require additional funding from CIRM. Continued funding is contingent upon timely progress, and, when applicable, the ongoing ability of the applicant to fund its operations and to satisfy its co-funding commitment (if applicable).

Pursuant to Proposition 14, CIRM shall prioritize applications for Shared Research Laboratories that enhance the geographic distribution of resources across the state.

Eligibility

What types of projects are eligible for funding?

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

(1) Must offer expertise on in vitro models using human stem or progenitor cells

Modeling expertise offered in the proposed CIRM-funded SRL is limited to in vitro models using human stem or progenitor cells[1] (collectively, "stem cells").

(2) 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.

(3) Must include a Lab Manager

The project team must include one or more Lab Managers with experience in managing a core cell culture lab, ideally related to stem cell research, and able to devote at least a combined total of 100 percent effort to the project.

(4) Co-funding is required for E/E-SRLs

E/E-SRLs are required to co-fund at least 20% of the total "Allowable Operational Project Costs". Allowable Operational Project Costs are those costs permitted under CIRM policies and regulations and include direct and indirect costs, but not equipment costs. The sum of CIRM funds requested for operations, plus the co-funding contribution by the E/E-SRL applicant, make up the total Allowable Operational Project Costs. The co-funding may come from any funding source arranged by the applicant.

Documentation demonstrating the commitment of funds to cover the required co-funding amount must be provided at the time of application submission.

(5) Application must be accurate and complete

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

(6) Applicant must be in "good standing"

[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 or if their creation involves transfer of nucleic acids (genetic research).

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Applicants must certify that they are in good standing, as follows:

a. The applicant's Chief Executive Officer, Chief Financial Officer, and Program Director 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 Program Director 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.

Who can apply?

Only California Non-Profit Organizations are eligible to apply for this opportunity.

Non-Profit California Organizations 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.

Only one application will be accepted per institution across the SRL program, i.e., an institution can only submit a single application to either RFA INFR6.1 or RFA INFR6.2, not both.

Who can serve as the Program Director (PD)?

To be eligible, the PD 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 5 percent effort to working on the project. (Note: "project" includes CIRM-funded and applicant co-funded components and Steering Committee participation). Any effort for which salary from CIRM is claimed must be expended in California.
    - Overall Leadership must commit at least a combined 20% effort
        - Applicant PD alone, or
        - Applicant PD plus 1 additional key person
- Must be authorized by the applicant organization to conduct the proposed activities and assume the responsibilities of the PD.
- Must be authorized by the applicant organization, and be able to commit the level of effort required, to participate in the SRL Network Steering Committee
- Must not currently have another application pending review or approval under this INFR6 funding opportunity.
- Must not currently have another application that is substantially similar or has overlapping activities pending review or approval under any CIRM opportunity.

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Additional Requirements

Diversity, Equity and Inclusion

Applicants must address how the proposed activities will uphold the principles of diversity, equity and inclusion (DEI). In the DEI section of the proposal, applicants should describe

- How the proposed activities will ensure that core users and recipients of stem cell-based models and expertise represent diverse goals, approaches, perspectives and backgrounds;
- How any proposed educational activities will ensure participation by diverse and/or underserved populations;
- How the SRL team and other contributors will bring diverse and inclusive perspectives and experience to the implementation of proposed activities;
- How the SRL team and contributors demonstrate a successful track record for promoting and valuing diversity, equity and inclusion;
- How the SRL will offer stem cell lines with ancestral and sex diversity that may increase the applicability of research outcomes to diverse populations.

Knowledge Sharing Plan

The CIRM 2022-2027 Strategic Plan prioritizes knowledge sharing and collaborative approaches to the discovery, development and commercialization of regenerative medicine therapies. Applicants should describe how they will contribute to knowledge sharing in the CIRM SRL Network and are encouraged to allocate funds in their proposed budget for personnel and/or activities accordingly. Applicants should develop plans intended to establish processes and systems for advertising available models, services, and training / educational and other resources, for sharing best practices and knowledge; for standardization of cell lines, reagents, and quality control/validation across the network, vital to accelerating regenerative medicine research in California and to improving reproducibility of stem cell-based models. Proposed knowledge sharing plans of funded SRLs will be coordinated through the Steering Committee.

Data Sharing and Management Plan

The sharing of data, such as omics, FACS, imaging, and other data, produced from CIRM-funded projects is key to advancing the field of regenerative medicine and accelerating treatments to patients. CIRM requires awardees to manage and preserve raw data, processed data, and metadata, and make applicable data and metadata available to the broader scientific community.

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. To ensure data processing steps can be replicated and data can be reused by other researchers, CIRM requires sharing of data in accordance with FAIR (Findability, Accessibility, Interoperability, and Reusability) and CARE (Collective Benefit, Authority to Control, Responsibility, and Ethics) data principles, through established repositories where possible.

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A Data Sharing Overview must be included in the application, and awardees develop and execute a detailed Data Sharing and Management Plan (DSMP) for data generated during SRL operations, such as omics, FACS, imaging and other data generated for cell model quality control and validation[2]. The Data Sharing Overview is subject to evaluation by the Grants Working Group. Reviewers will be asked to comment on the quality of the Data Sharing Overview and advise CIRM on any improvements they recommend.

More information on DSMPs can be found here. The data repositories selected and other information about deposited data 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.

Sustainability Plan

In the proposal, applicants will be required to describe their plans for supporting half of operational costs during Phase C of the award period (e.g., user re-charge), and for ensuring sustainability beyond the immediate project period of any proposed operational, researcher training, and educational programs that will be developed and implemented as part of these funding opportunities.

Schedule And Deadlines

Applications Due	2:00 pm (PDT/PST), August 29, 2023
Grants Working Group (GWG) Review	Approximately 60 days post submission
ICOC Review and Approval	Approximately 120 days post submission
Award Start	Must start within 120 days of award approval (i.e., approximately 240 days post submission)

[2] Data generated by research projects, funded by CIRM or other agencies and conducted at the cores, will comply with their individual data sharing and management requirements, and should not be included in the SRL DSMP.

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Application Review Information

What is the process for evaluating an application?

Pre-submission Consultation

In accordance with CIRM's mission, the Agency is committed to helping develop promising stem cell and gene therapy-based technologies by partnering with world-class investigators. Therefore, prospective applicants are encouraged to contact CIRM before applying with questions or to discuss their project's eligibility, scientific, or budget considerations.

Eligibility Review

CIRM will assess whether the proposed project meets eligibility requirements sought under this program. If CIRM determines, in its sole discretion, that an application does not meet the eligibility requirements of the program, CIRM will notify the applicant of its decision and terminate all further action on the application.

Scientific Review

The scientific merit of each application will be assessed by the Grants Working Group (GWG), which is composed of fifteen subject matter experts from outside California, seven patient advocate and nurse members of the ICOC, and the Chair of the ICOC. The list of scientific members who may participate in the GWG review can be found at http://www.cirm.ca.gov/WorkingGroup_GrantsReview. The composition of the ICOC can be viewed at http://www.cirm.ca.gov/GoverningBoard.

The fifteen participating scientists on the GWG will evaluate the applications and score them according to scientific and technical merit, applying the review criteria described below. The GWG will score each application and make one of the following specific recommendations to the ICOC's Application Review Subcommittee: 1) fund the project based on the proposal's exceptional merit; 2) do not fund the project but may be resubmitted to address areas for improvement if the Application Review Subcommittee has not approved an application for funding following the GWG's review; or 3) do not fund the project and do not allow resubmission.

The Application Review Subcommittee will make final funding decisions giving consideration to the GWG recommendations and any CIRM team recommendations.

Consideration of Related CIRM Award Information (If Applicable)

The GWG may consider information from a previously funded and related CIRM award as part of its review. CIRM will provide the GWG with objective information regarding a related award that CIRM, in its sole discretion, deems relevant, including but not limited to achievement of specific milestones, data, and outcomes for a related CIRM award or awards.

A "related CIRM award" includes: (1) an award for which the applicant PD served as the PD/PI, a co-PD/PI, a co-investigator, or otherwise substantially participated in the conduct of the award; (2) an award involving the same research project or product; or (3) an award that includes overlapping team members.

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Confidentiality

CIRM's confidentiality and conflict screening rules apply to everyone who will have access to applications or who will attend any review meeting in which confidential information is discussed, including but not limited to CIRM team members, reviewers and members of the ICOC. Per Gov. Code §6254.5(e) non-public records may be disclosed to government agencies under confidentiality agreements.

How will the scientific merit of an application be evaluated?

Scientific members of the GWG will evaluate and score applications based on the following key questions:

1. **Does the proposed SRL offer a significant value proposition?**

Do the proposed stem cell-based models, services, and specialized technologies address critical needs of researchers across California? Do they attract researchers not currently using stem cell-based models to the field?

Are the proposed SRL outcome criteria adequate to measure the impact of the SRL core and its services?

Are the proposed Knowledge Sharing Plan and PD commitment to the Steering Committee likely to advance the success of the SRL Network as a whole, including effective sharing of knowledge and resources across the state?

2. **Is the project well planned and designed?**

Is the proposed SRL core appropriately suited for the number of anticipated users and types of research projects that will be supported?

Are the proposed stem cell-based models to be offered robust and appropriate for serving the scientific needs of the anticipated users?

Is the proposed SRL program appropriately designed to ensure effective operations and to enable access to stem cell-based modeling for researchers targeted by this program?

3. **Is the project feasible?**

Is the proposed plan to establish and begin operations of the SRL core feasible and likely to be implemented within the proposed timeline?

Does the team have access to the necessary facilities and resources to execute the project plan? Are the applicant institution's track record and commitment appropriately suited to hosting and supporting the proposed SRL core?

Is the leadership qualified to lead the project? Is the proposed SRL team appropriately staffed and qualified to execute the project plan?

Does the proposal demonstrate a commitment and the ability to sustain SRL operations beyond the project period?

4. **If proposed, is the Stem Cell Techniques Course well designed?**

Is the curriculum of the Stem Cell Techniques Course (**if proposed for educational programs**) well designed to serve the needs of CIRM EDUC programs and/or other

California educators in educating the next generation of stem cell and gene therapy researchers?

Does the curriculum of the Stem Cell Techniques Course (**if proposed for researcher training**) provide researchers with the skills needed for stem cell-based modeling research?

Are instructors of the Stem Cell Techniques Course appropriately qualified?

5. Does the project effectively uphold the principles of diversity, equity and inclusion?

Are the proposed SRL offerings designed to support researchers with diverse goals, approaches, perspectives, and backgrounds?

Are proposed training / educational offerings likely to increase participation by diverse and/or underserved populations in California, and are they likely to enable their success and retain them in the stem cell / gene therapy fields?

Does the SRL team bring diverse and inclusive perspectives and experience to the proposed SRL activities and demonstrate a successful track record for promoting and valuing diversity, equity and inclusion (DEI)?

Is ancestral and sex diversity in offered stem cell-based models scientifically well supported, and does it promote applicability of research outcomes to diverse populations?

Application Components and Submission

How does one apply?

Applications must be completed and submitted online using the CIRM Grants Management Portal at https://grants.cirm.ca.gov. Any prospective PD must create a login in the system to access application materials and apply. Applications are available in the system only to the PD. A PD may submit only a single application in a given review cycle and may not submit additional applications during the review period.

Only one application will be accepted per institution across the SRL program, i.e., an institution can only submit a single application to either RFA INFR6.1 or RFA INFR6.2, not both.

Applications are due by 2:00pm (Pacific Time) on August 29, 2023.

What components does an application include?

CIRM's online application is designed to collect information for CIRM staff to assess eligibility, for GWG reviewers to evaluate the project, and for CIRM to rapidly initiate an award if the project is approved for funding.

It includes overview sections characterizing the proposed team, the applicant institution, the proposed project, and major planned activities, a detailed budget and budget justification, and an application uploads section that includes the Project Proposal and reference documentation including Key Personnel Biosketches, Letters of Support, and Other Support.

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What are the sections of the Proposal?

Project Summary: High-level summary of the proposed SRL core and tables and/or graphics to provide easily interpretable overview of all planned SRL offerings and activities.

Value Proposition: Description of how the proposed project aligns with the objectives of this INFR6.2 RFA to enable leading experts in stem cell-based modeling to share their models and expertise locally and broadly across California, description of value proposition, knowledge sharing plan, and contributions to SRL network Steering Committee. Description of outcome criteria to measure impact of proposed SRL.

Core Offerings: Description of stem cell-based modeling area(s) of focus and services offered, high cost and highly specialized technologies offered, and research users of proposed SRL.

Stem Cell Techniques Course (OPTIONAL, extra funding provided): Description of Stem Cell Techniques Course that serves CIRM-funded EDUC programs, other educational needs in California and/or researcher training.

Core Space and Equipment: Description of the space that will be made available in the applicant institution for the proposed SRL core facility (no renovation/facilities improvement funds are available for E/E-SRLs), and an account of major equipment (to be acquired with CIRM funding and already existing) that will be housed in and utilized by the core, with justification.

Operations and Team: Description of (1) plans for development, oversight, management, and maintenance of SRL services and equipment, (2) SRL access plan, including attracting researchers not currently using stem cell-based models into the field, (3) organization and qualifications of the team that will be responsible for executing the proposed SRL project, and (4) institutional track record in operating core services.

Gantt-Like Project Timeline: Timeline for all proposed activities, within the 3-phase framework (phases A, B, C) for an E/E-SRL.

Sustainability Plan: Description of plans for supporting half of operational costs during the last 2 years of the SRL award, and for ensuring long-term sustainability beyond the immediate project period of any proposed operational programs, researcher training, and Stem Cell Techniques Course **if offered**, that will be developed and implemented as part of this funding opportunity.

Institutional Commitment and Co-Funding: Description of institutional commitment from applicant institution leadership to hosting the proposed SRL, required co-funding for at least 20% of the total "Allowable Operational Project Costs", and any additional support, if applicable. Documentation upload includes institutional support letter, documentation demonstrating the commitment of funds to cover the required co-funding amount, and documentation demonstrating the commitment of additional support, if any, from other sources.

Statement of Diversity, Equity and Inclusion (DEI): Statement describing how the proposed activities will uphold the principles of diversity, equity and inclusion. See full description under "Additional Requirements" above.

Data Sharing Overview: Description of how raw data, processed data and metadata produced during SRL operations, such as omics, FACS, imaging and other data generated for cell model quality control and validation, will be made available to the research community consistent with FAIR (Findability, Accessibility, Interoperability, and Reusability) data sharing principles.

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Plans for Risk Mitigation & Financial Contingency: Potential risks, mitigation strategies, associated costs, and non-CIRM sources of contingency funding.

References: Listing of all references used in the body of the proposal.

Who are Key Personnel?

In the application, we ask you to identify by name pertinent Key Personnel and their specific roles on the project. Key Personnel are defined as (1) the principal investigator or program director; or (2) any other person, including an independent consultant or an employee of a Subcontractor or Partner, who is expected to contribute to the scientific development or execution of the project in a substantive, measurable way *and* who is expected to: (a) receive or has been promised income, or anything else of value, of $10,000 or more per year for his or her contribution to the project or (b) contribute one percent (1%) or more effort to the proposed project. "Key Personnel" does not include a person who is expected to be involved in the proposed project but who does not satisfy conditions (1) or (2).

Individuals who do not meet the definition of Key Personnel may be supported with CIRM funds, but should not be identified by name in the application. Such unnamed personnel may be referenced indirectly by their role on the project (e.g., technician). The budget includes a line item for requesting support for unnamed personnel.

What should one know before preparing the budget?

A specific and well-justified budget must be provided that clearly outlines the total costs of the project, including those costs not proposed to be funded by CIRM. The corresponding budget justification should provide enough detail to allow budget professionals to determine the appropriateness of the costs in relation to the activities being performed. Allowable Project Costs for equipment funded by CIRM are detailed in the applicable sections of the Grants Administration Policy for Facilities and Equipment Grants and for research and training funds are detailed in the Grants Administration Policy for Discovery, Translation and Education Projects. Generally, project costs for personnel, supplies, travel, equipment, and subcontracts may be claimed. Limits for specific cost categories must be observed.

What are the rules for spending CIRM funds outside of California?

California non-profit organizations may use CIRM funds for Allowable Project Activities conducted both in California and outside of California. "Allowable Project Activities" means those activities that are conducted in California, and for activities outside of California, those activities over which the California organization exercises direction, supervision and control, including activities performed by a wholly owned subsidiary of the California organization outside of California. It does not include activities undertaken by a separate organization outside of California that retains intellectual property or publication rights in connection with the performance of those activities, including a research collaboration in which the research is conducted outside of California.

What are Direct Facilities Costs?

Direct Facilities Costs are general operating costs of the Awardee's facilities attributable to housing all elements of the CIRM-funded project or activity. Facilities costs for non-profit applicant organizations are limited to the current applicable, federally negotiated rates for the organization as defined by the Office of

Management and Budget (OMB) Circular A-21 or A-122. Facilities rates for for-profit applicant organizations are limited to 35% of the direct project costs. Facilities rates are applied to direct project costs exclusive of the costs of equipment, tuition and fees, research patient care costs, as well as the costs of each individual subcontract, consultant, and service agreement in excess of $25,000. The facilities cost rates approved and in place at the time of the application are to be applied to the entire award project period.

How much can an applicant claim for indirect costs?

Indirect costs will be limited to 20% at a non-profit institution of allowable direct costs awarded by CIRM (i.e., project costs and facilities costs), exclusive of the costs of equipment, tuition and fees, research patient care costs, as well as the costs of each individual subcontract, consultant, and service agreement in excess of $25,000. The indirect cost rate budgeted at the time of application is to be applied to the entire award project period.

Award Administration

Issuance of Award

A CIRM award is issued via a Grant Agreement, which is the formal contract that defines the terms and conditions of an award and documents the commitment of funds from CIRM.

Operational Milestones and Payment

Except for equipment funds, CIRM funds under the award will be disbursed based on achievement of specific Operational Milestones established by CIRM. An "Operational Milestone" is an objective event that is indicative of project progress occurring as proposed in the application. CIRM establishes Operational Milestones for inclusion in the Grant Agreement based upon information provided in the Application. Equipment funds are released as reimbursement upon actual costs after payment has been made.

Upon issuance of the award, funds budgeted to achieve the initial Operational Milestone will be disbursed. Upon the successful completion of the initial Operational Milestone and each successive milestone, additional funds will be disbursed. If funds allocated to a specific Operational Milestone (including both CIRM funds and the required applicant co-funds) are exhausted prior to achievement of that milestone, the Awardee will be responsible for covering any remaining costs. CIRM expects that the applicant's contingency plan will identify project timeline and budget risks and will provide details for covering such costs, including the source of funding. CIRM reserves the right to make adjustments to the timeline for inclusion in the Notice of Award to ensure that funds are appropriately dispersed across Operational Milestones.

If CIRM determines, in its sole discretion, that an awardee has failed to satisfy an Operational Milestone within a reasonable timeframe, or if the delay is not addressed to CIRM's satisfaction, CIRM may permanently cease disbursements and terminate the award.

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Suspension Events

CIRM reserves the right to hold or terminate disbursements if CIRM determines, in its sole discretion, that a Suspension Event has occurred. A "Suspension Event" means a pre-defined condition that triggers a hold of CIRM funding until the suspension event has been resolved, if resolvable. Following a Suspension Event, the Awardee is expected to provide CIRM with a plan to resolve the issue that triggered the Suspension Event. CIRM establishes Suspension Events for inclusion in the Notice of Award based on information provided in the Application.

Reporting

Grantees will be required to provide periodic written progress and financial reports to CIRM.

Other Requirements

CIRM Regulations and Grants Administration Policies

Grant or Loan awards made through this request for applications will be subject to all applicable CIRM regulations. These regulations can be found on CIRM's website at https://www.cirm.ca.gov/our-funding/cirm-stem-cell-grant-regulations. The Grants Administration Policy for Facilities and Equipment Grants shall apply to the equipment costs. The Grants Administration Policy for Discovery, Translation and Education Projects shall apply to research and training. Both shall govern for the application, review and award processes, and in the event of a conflict, the Grants Administration Policy for Facilities and Equipment Grants shall govern.

Change in Status

Applicants are required to notify CIRM of any material change in status while the application is pending review, e.g., the PD has left the applicant institution, the applicant no longer qualifies as a California Organization, etc.

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Definitions

"California organization" means: An entity, regardless of profit status, that has >50% of its employees located in, and paid in, the state of California, and conducts the award activities from the California location.

"For-profit organization" means: a sole-proprietorship, partnership, limited liability company, corporation, or other legal entity that is organized or operated for the profit or financial benefit of its shareholders or other owners. Such organizations also are referred to as "commercial organizations".

"Non-profit organization" means: (1) a governmental entity of the state of California; or (2) a legal entity that is tax exempt under Internal Revenue Code section 501(c)(3) and California Revenue and Taxation Code section 23701d.

"Operational Milestone" means an objective event that is indicative of project progress occurring as proposed in the application.

"Partner" means an organization that, in exchange for the right to the opportunity for a future financial return, has (1) agreed to provide matching funds for the proposed project or (2) entered into an agreement with the applicant organization relating to the commercialization of the proposed project.

"Subcontractor" means an organization (other than the applicant organization) that is expected to: (a) contribute to the scientific development or execution of the project in a substantive, measurable way *and* (b) receive $50,000 or more through the proposed project. "Subcontractor" does not include suppliers of widely available goods.

"Suspension Event" means a pre-defined condition that triggers a hold of CIRM funding until the suspension event has been resolved, if resolvable.

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Revisions

Revision Date	List of Changes
05/23/23	• Updated the sections, “What are Direct Facilities Costs?” and “How much can an applicant claim for indirect costs?” to clarify applicable facilities costs for the program.
05/31/23	• Removed the term “direct” from “Total allowable [direct] cost allocation” on page 6. The maximum amount allowable is inclusive of direct and indirect costs for Operational Costs and the Techniques Course categories. Indirect costs are not allowable for equipment.

Appendix

INFR6.1 & INFR6.2 comparison

Shared Resources Lab (SRL) type	INFR6.1 - Establishing SRLs		INFR6.2 - Enhancing/Expanding SRLs	
SRL type - description	Provide local access to stem cell-based models, training, specialized equipment, and educational opportunities in geographic areas/locations where access to models is limited		Enable leading experts in stem cell-based modeling to share their models and expertise locally and broadly across California.	
Renovation/facility improvement costs up to	$2.75 M	Phase A 18 months	0	Phase A 6 months
Equipment costs up to			$1.5 M	
Operational costs up to	$1.65 M	Phase B - 24 months Phase C - 18 months (half of Phase B operational costs)	$1.5 M - incl. 20% cofunding requirement	Phase B - 30 months Phase C - 24 months (half of Phase B operational costs)
Operational activities	**Research support:** Provide access to core, models, services, other resources in geographic areas/locations where access to models is limited (grantee institution, nearby institutions, remotely via cloud-based approaches)		Provide access to core, models, services, other resources locally (grantee institution, nearby institutions)	
	_____		Provide access to models, services, other resources broadly across California	
	Train researchers in creation and use of models		Train researchers in creation and use of models	
	Educational support: Courses (instead of or in addition to Stem Cells Techniques Course) and other student experiences, to attract and retain students from diverse backgrounds and from geographic areas where stem cell-based modeling research is limited, in the stem cell and gene therapy field		_____	
	Note: Relative allocation of resources to research support versus edcuational support determined by applicant			
Stem Cells Techniques Course to serve CIRM-funded EDUC programs, other educational needs in CA or train researchers (**OPTIONAL**) costs up to	$1 M		$1.3 M	
Total costs, including up to 20% indirect costs, Direct Facilities Costs	$4.4 M / $5.4 M		$3 M / $4.3 M	

Other Resources

CIRM iPSC Repository

As a resource to the regenerative medicine community, CIRM has funded the creation of an Induced Pluripotent Stem Cell Repository, a large, genetically diverse collection of stem cells produced from thousands of individuals representing various diseases of interest and healthy controls. The 2600+ lines were uniformly derived, have undergone rigorous quality control, and include demographic and clinical data. The CIRM Repository is managed by Fujifilm Cellular Dynamics, Inc., who have made the lines available for purchase at https://www.fujifilmcdi.com/search-cirm/. SNP data for 2166 CIRM lines and whole genome sequence data for 299 of the CIRM iPSC donors is available at dbGaP. A list of CIRM lines with WGS data can be found here. Applicants who are interested in using iPSCs to investigate mechanisms of disease, develop novel tools, discover therapeutic targets, or increase diversity in their experimental design are encouraged to explore the CIRM iPSC Repository or request additional information from CIRM Science Officers at discovery@cirm.ca.gov using the subject line “DISC2 application - iPSC Repository.” Please note, cells in the CIRM iPSC Repository are for research use only and are not eligible nor consented for clinical use.