Shared Resources Labs for Stem Cell-Based Modeling
INFR 6.1 and 6.2: Webinar Q&A

Topics:

Submitted Questions

INFR 6.1 vs INFR 6.2

What is the difference between INFR 6.1 and INFR 6.2?
INFR 6.1 aims 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. INFR 6.2 aims to enable leading experts in stem cell-based modeling to share their models and expertise locally and broadly across California.

In the proposal, you are asked to discuss the value proposition of your proposed SRL and how it aligns with the objectives of the relevant RFA, as described above. Reviewers are asked to evaluate this value proposition.

Can my institute apply to both INFR 6.1 and INFR 6.2?
No, only one application per institution is permitted. An institution may submit an application to either INFR 6.1 or INFR 6.2 but not both.

My university has received CIRM funding for shared facilities in the past. Does that exclude us from INFR 6.1?
No, it does not. Regardless of prior CIRM funding for Shared Labs, to be a good fit for INFR 6.1, the SRL must focus on increasing access to stem cell-based models, training, specialized equipment, and educational opportunities in California regions where access to models is limited.

Core Services

How should potential research projects that the SRL would support be characterized in the application?
Your application should convey (1) the need in the research community the core will address, (2) how the core will contribute to advancing world class, innovative science, and (3) how the core will enable basic and / or clinical researchers not currently using stem cell-based models into the field. Please include letters of support from potential core users, describing their need and interest in using your future SRL core.

How important are innovative cores vs. more traditional technologies to this mechanism?
Your application should consider the needs in the research community that your core would help support. Sometimes innovative research can be supported by simpler models. When considering this balance, it is important to address feasibility.

How do you see the priority between generating a service that enables and educates the research community vs. a core that performs specific end-point assays for a user? In other words, should a core perform specific physiological assays with readouts or facilitate users to do these themselves?
This depends on your likely users. Once you have an idea of who your interested clientele would be, determine whether they want to learn how to perform stem cell-based modeling experiments in their own labs, or whether they are interested in someone performing specific experiments for them. For example, some researchers working with animal models or with patients may be more interested in a core performing assays with human cells for them to test a specific hypothesis, rather than developing the expertise in their own lab. Depending on the interests of your likely users, you may focus on one type of offering or offer both types of offerings.

Can we offer services involving model organisms? What if the model organisms are used to demonstrate functionality of stem cells?
The SRL cores must be dedicated to human stem cell and progenitor-based models. Models based on directly reprogrammed cells are also allowed, if they meet the definition of progenitor cells, or if their creation involves transfer of nucleic acids (genetic research). Modeling based on non-human systems is not eligible under this opportunity.

However, if a non-human system (e.g., mice) is needed to test the functionality of human stem cell-derived cell types, such as testing engraftment of hPSC-derived HSC, inclusion of the non-human system is an allowed SRL core activity, as part of QC/validation of the differentiation process. If proposed, make sure to provide a strong rationale for the inclusion of a non-human system as part of the validation process.

Could the core facility provide its stem cell-based modeling services to a user while also participating in that research?
It is very important for the proposal to convey how the core access plan will assure access is provided to as large and diverse a group of users as possible. However, one

strength of a core could be enabling and fostering new collaborations, which could include collaborations among core users or among a core user and the core provider. SRL team members with their own laboratories can collaborate through the core as long as it is not at the expense of serving a broad range of other users.

Can we propose a modeling facility that has an R&D side that helps users create their own model systems and then offer a service using that model (e.g., to run screens)?
As a general response, this opportunity is **not** meant to support the **development of new human stem cell-based models**, i.e., the development of new differentiation protocols or new organoid systems, etc. This opportunity aims to **create competency hubs that enable researchers to share their existing models.** On the other hand, we understand the stem cell-based modeling field is continuously developing, and adjustments to existing models will have to occur during the course of an SRL award. In addition, as part of the Steering Committee's goals, we will consider how reproducibility of stem cell-based models may be improved, and we may coordinate as a group to see how we can improve on certain aspects of these models.

Depending on the exact intent regarding 'help users create their own model systems', this could fall under 'high cost and highly specialized technologies' offered in the core, where the core supports, e.g., genome editing of existing stem cell-based models offered in the core. It is also possible the core may offer or teach, e.g., genome editing to a core user who wants to improve or expand on their own model that may not itself be offered in the core.

Screening capabilities may also be part of 'high cost and highly specialized technologies' offered in a proposed core.

Educational Opportunities

We have put on a stem cell techniques course for many years and have ideas for additional training that is specific to cutting-edge technologies. Would it be appropriate to include the new training in the stem cell techniques course? Can we add modules from our advanced core offerings as add-ons to our base course?
Absolutely, you may update your stem cell techniques course to include advanced culturing technologies, especially as they relate to stem cell-based modeling, either as part of a single stem cell techniques course that teaches both basic and advanced technologies, or as separate optional modules or courses.

For INFR 6.2, how are you defining "increase access to educational opportunities in stem cell-based techniques?" Should access be increased to people who would not have access otherwise (e.g., via partnerships with community colleges)?
One of the objectives of the overall INFR6 program is to "increase access to educational opportunities in stem cell-based techniques".

For INFR6.2, offering educational opportunities is not required. However, educational opportunities may be offered through the stem cell technique course, if proposed. If so, the INFR6.2 applicant may use this opportunity to increase access to trainees from diverse and/or underserved populations. For example, you may include letters of support from community colleges who can testify to the diversity of student populations who may participate. To be clear, though, the stem cell techniques course may also be offered solely to train researchers.

For INFR6.1 applications, it is expected that as part of the overall operations of the core, educational opportunities are provided. However, the relative allocation of resources to research support versus educational support is determined by the applicant. In addition, INFR6.1 applicants can propose to offer a stem cell techniques course, which may serve educational needs and / or researcher training for stem cell-based modeling.

Co-funding and Sustainability

Is there any restriction on the source of the 20% co-funding requirement for INFR 6.2?
The required co-funding for INFR6.2 applications applies to operational costs, so there are no restrictions on sources. Federal funding is permitted.

To clarify, while co-mingling with federal funding is not allowed for the CIRM-funded purchase of capital equipment, capital equipment purchased with federal funds may be included as in-kind contribution to the proposed SRL core.

Can we mix CA state funds with CIRM funds for equipment purchases? For example, our institution has received significant state funding, and some of those dollars will be allocated to launching our new Cellular/Molecular Biotechnology training program. Would using some of those dollars for equipment purchases and/or the facility be allowed?
Yes, this is allowable, and we are prioritizing applications with this kind of "in kind" support.

What happens if the core is unable to reach 50% funding through recharges in Phase C?
Your application will propose a way to cover 50% of operations in Phase C, which will be evaluated by the GWG. As part of your proposal, in the "Plans for Risk Mitigation &

Financial Contingency" section, you have an opportunity to describe this risk, any mitigation plans you may have, and you may include financial contingency plans for this risk. If an Awardee is unable to reach 50% funding during Phase C, then this contingency funding plan would be activated or operational activities may have to be decreased.

Are we considering charging investigators using core resources as we enter phase C? Core facilities are rarely independently sustainable, so I'm curious about potential models for this.
Yes, fees for service are one approach toward sustainability. Core users would use the funding they have for a project to pay for your core's services, or educational programs may have funds to pay for the stem cells techniques course. For instance, the CIRM EDUC2 program includes techniques course fees as part of trainee funds (please go here for details).

At the discretion of the applicant, and as justified for the value and feasibility of the proposed SRL core, fees for service may already be implemented during Phase B of the SRL award, and then may be increased during the CIRM ramp-down in Phase C and for long-term sustainability.

Can you provide more information regarding the "Financial Contingency Fund"?
There is a section in the proposal template where we ask applicants to identify project risks and how you plan to mitigate those risks. Risks could be related to timeline delays, equipment failures, costs exceeding the budget, reagents shortage, variable interest in the use of the core, and other risks you may identify. Some of these risks may incur extra costs and for those we expect you to have access to contingency funds.

Use of Funds

Operational Budget for Establishing SRLs is limited. Can Plastic or Cell culture reagents be purchased with funds for equipping the E-SRL?
Consumables cannot be charged under equipment funds. However, applicants do have the choice to budget equipment maintenance, which is normally charged under operations, to the equipment budget.

The Review Process

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 effectively uphold the principles of diversity, equity and inclusion?' This guidance is in the form of

subquestions and is provided in the preliminary critique form that reviewers fill out in advance of the review meeting.

1. Are the proposed SRL offerings designed to support researchers with diverse goals, approaches, perspectives, and backgrounds?
2. 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?
3. 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)?
4. 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?

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.
- **Be intentional**, e.g., instead of stating the access you may have to a researcher or student population from a particular underserved background, explain how you will go about ensuring that researchers or students from that background will be engaged and recruited as users of your core.
- **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. 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.

Please note: Based on Proposition 209, CIRM is prohibited from taking race, ethnicity, national origin, and gender into account in making grant decisions. Therefore, applicants should refrain from including race, ethnicity, national origin, or gender **in describing the applicant team personnel.**