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Funding Opportunity to Manage a Symposium on Pluripotent Stem Cell Manufacturing

REQUEST FOR APPLICATIONS
6/30/17

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Objective

The mission of the California Institute for Regenerative Medicine (CIRM) is to accelerate stem cell treatments to patients with unmet medical needs.

The objective of this request for applications (RFA) is to solicit a highly qualified applicant to organize and implement a symposium on clinical pluripotent stem cell manufacturing. The emphasis of the symposium is on final product characterization & standardization to harmonize with the regulatory processes for expedited programs available to regenerative medicine including the newly established regenerative medicine products regulatory provisions program: the Regenerative Medicine Advanced Therapy (RMAT) designation.

Award Information

Rationale

Cell therapy activities using pluripotent stem cells (PSCs) have been growing rapidly in recent years and hold promise for the treatment of many diseases, yet manufacturing of these cells is costly, complicated, and largely unstandardized. Ongoing advances and innovation in this area together with the near-term potential of approval and commercialization of such therapies have heightened the need and desire for standardization around these products. Because of the unique considerations involving PSC therapy, especially induced PSCs, CIRM is issuing a request for applications to host a symposium on PSC therapy manufacturing systems and characterization.The main portion of the symposium will cover one to two days of presentations delineating the state of the art in PSC manufacturing and related topics. As part of the symposium, workshops will be organized to facilitate in-depth deliberation around a focused topic in PSC manufacturing.

Symposium Aims and Themes

The aim of the symposium is to catalyze discussion of the technical and economic aspects of PSC therapy manufacturing, as well as establishment of characterization and standardization methodologies to facilitate the expedited development and ultimate approval of such products.

Symposium organizers are required to recruit participants from organizations involved in PSC manufacturing, and especially those directly involved with CIRM-funded projects, to participate in presentations and discussions and to share their relevant experience.

The symposium organizers should convene a scientific steering committee composed of content and subject-area experts to propose central and innovative topics consistent with the aim of the symposium. The steering committee should identify and address topics with the greatest potential to advance development of PSC therapies. Particular weight should be given to topics where consensus on standardization of approaches that to conform with regulatory policy and guidance is desired and needed in the field.

Topics for the main portion of the symposium may include all or a subset of the following:

- Cell source selection
    - Autologous vs. allogeneic vs. HLA-matching approaches
    - Donor considerations – regulatory issues, donor-to-donor variability, genetic screening
- Manufacturing processes
    - Raw materials selection and regulatory issues
    - Differentiation process variability – strategies to address
    - Scale-up vs. scale-out – technologies and impact on commercialization
- Quality control testing
    - Identification and characterization of off-target cells
    - Assays for residual undifferentiated cells and teratoma formation potential
    - Potential transformation events and tumorigenicity – in vitro methods
    - Genetic changes – karyotype, CNV analysis, WGS vs targeted sequencing
- Preservation and clinical logistics, transportation and administration/delivery methods
- Non-clinical testing programs
    - Testing plans to address safety toxicology, biodistribution, and tumorigencity
    - Substrate (e.g., patch, gel) evaluation for cell-device combination products
    - Delivery device evaluation

Up to two days should be devoted for these presentations. Additional or alternative topics relevant to PSC manufacturing may be proposed.

Workshop

A single or multiple small group workshops should be convened the day after the symposium to review and discuss **selected** focus topics. Focus topics address immediate needs for the field where standardization and harmonization could serve to expedite process/product development. Workshop deliberations must be documented and summarized in the final symposium report for publication, with the aim of follow up activity in coordination with regulatory agencies to facilitate guideline development.

As a requirement for the award, one of the focused workshops will cover *in vitro* strategies to assess tumorigenicity in PSCs. *In vivo* tumorigenicity tests are critically important for the development of clinical PSCs, but create significant costly bottlenecks for cell therapy development programs. Several methods have been used to examine genetic changes in PSCs, and the importance and advantage of these types of *in vitro* evaluation methods is becoming more apparent. However, there is no consensus on the value of genetic data as an assay for safety release and no standardization of methodology. Participation of regulatory representatives is highly recommended for the workshop(s) and encouraged to provide guidance for

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key focus areas to allow achievement of the meeting goals in harmonizing and advancing manufacturing, characterization, and testing standards for PSC-derived cell therapies.

CIRM resources will support the following required core activites under this opportunity:

✓ Direct meeting logistics:

- Overall management of the symposium including, but not limited to, site selection, food and beverage planning, meeting agenda, speaker and symposium attendees, symposium materials, and other symposium related tasks
- Onsite symposium registration and services

✓ Pre-conference logistics:

- Website management including website design, online symposium registration, capture of poster abstracts from attendees during online registration
- Preparation of program book with speaker bios and poster titles
- Develop contracts/service agreements with vendors and service providers as needed
- Participate in regular conference calls with CIRM team
- Floor plan and site map preparation including diagrams for break out rooms, food and beverage spaces, event spaces, and poster room
- Coordinate food and beverage services and stay within the California state per diem requirements
- Travel and housing coordination as needed
- Discuss and arrange for appropriate signage/map for posters and other conference related events

✓ Symposium / Workshop day requirements:

- Venue set up
- Symposium registration
- Work with hotel contact onsite to coordinate food and beverage and meeting logistics
- Manage all AV requirements as needed during the symposium
- Symposium break down
- Security management

✓ Symposium / Workshop follow up requirements:

Facilitate the documentation of major findings from the symposium for publication and advance focused topics of immediate need for regenerative medicine therapeutics, including documentation of workshop conclusions to inform guideline development.

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Meeting Information

For purposes of this RFA, CIRM anticipates the Symposium (including Workshop(s)) will be conducted up to 3 days (at the discretion of the applicant) sometime during the first half of 2018. The conference should be hosted in a metropolitan area of California containing a major international airport. Solicitation of outside sponsorship is allowed and encouraged, but not required. A strategic plan to follow up from workshop recommendations post-symposium by coordination with subsequent conferences and/or regulatory agencies in order to drive towards final product characterization and standardization is required for the application, although this award cannot fund additional conferences or meetings.

Eligibility

Who is eligible to apply?

(1) To be eligible, the applicant or applicant organization must satisfy the following requirements:

- Applicant organization has at least five years of experience in hosting scientific or education events
- Program Director and one additional staff member each have at least five years of experience organizing scientific/educational events
- The applicant has a track record that includes organizing events that have required working with individuals and institutions not connected to the applicant organization in the field of stem cell manufacturing.

(2) Meetings must be held in California by an eligible applicant and have a qualified Program Director (PD)

The conferences must be conducted at locations in California. California-based and non-California-based organizations (for-profit and non-profit) may apply for and use CIRM funds for eligible conference costs. Foreign institutions are not eligible to apply for conference grant support.

A qualified Program Director (PD) is any individual with the skills necessary to direct the planning and execution of the proposed conference. The applicant must provide the PD's qualifications at time of application submission.

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Schedule, Deadlines, and Budget

Applications Due	2:00 pm (PDT/PST) on Aug. 11, 2017
Presidential Review and Approval	Approximately 10 days post-submission
Meeting Budget	Up to $100,000 for all eligible costs
Award Start Date	September or October 2017
Meeting Scheduling Window	January-June 2018
Meeting Length	Up to 3 days covering main symposium and workshop(s)

Application Review Information

What is the process for evaluating an application?

Pre-submission Consultation

In accordance with CIRM's mission through this funding mechanism, the Institute is committed to funding scientific conferences that focus on regenerative medicine research and educational programs to train future scientists. Prospective applicants are encouraged, but not required, to contact CIRM with questions to discuss their proposal, including its eligibility, before applying for a Conference Grant.

Eligibility Review

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

Application Review

CIRM's governing board, the Independent Citizens Oversight Committee (ICOC), has delegated to the President of CIRM authority to review and make funding decisions for CIRM-initiated conferences.

The following criteria will be considered in the review of applications and funding decisions:

1. Experience and Track Record

Do the applicant organization and Program Director have the appropriate experience to manage and perform the proposed activities? Does the applicant organization have a proven commitment to stem cell manufacturing?

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2. Resources
Does the applicant organization have the necessary resources to adequately manage the meeting and carry out all the required core activities in a timely fashion? Has the applicant organization appointed an appropriate team that will collaborate effectively with CIRM to understand needs, implement tasks, and manage the process?

3. Overall Value
Does the proposal offer a good value to CIRM by providing quality event management services for a reasonable price that is commensurate with use of California public funds? Are proposed costs appropriately justified?

Confidentiality
CIRM's confidentiality and conflict screening rules apply to everyone who will have access to applications or who will attend any review conference 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.)

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.

Applications are due by 2:00pm (Pacific Daylight Time) on Friday, August 11, 2017.

What components does an application include?
The Grants Management Portal provides instructions for completing all the necessary components and submitting a final application. The application is designed to collect information necessary to appropriately evaluate the proposal and for CIRM to rapidly initiate an award if approved for funding. Applicants are required to indicate key personnel involved in the project, describe how the proposal addresses the objective of the funding opportunity, provide a detailed plan of proposed activities, and provide a budget estimates.

The application for CIRM Conference Grants consists of an Application Information and Proposal Form (Web-based document) and can be found at https://grants.cirm.ca.gov.

The application for CIRM Conference Grant includes the following sections:
1. **Key Personnel**. "Key Personnel" means (i) the principal investigator or program director; or (ii) any other person, including an independent consultant or an employee of a Subcontractor or Partner, who is expected to contribute to the 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 through the proposed project or (b) contribute one percent (1%) or more of their 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 paragraphs (i) or (ii).

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2. **Budget.** Provide budget approximations requested in the budget section of the Application Information Form. Highlight previous experience and quote requests that justify budget estimates. Final budgets will be coordinated with CIRM staff post-award. All allowable costs for research grants are detailed in the CIRM Grants Administration Policy.

Allowable Costs for CIRM-Initiated Conference Grants include:

- Conference facility and equipment rental (including easels, poster display boards, tables/chairs and associated taxes and service fees)
- Transportation, parking, lodging and per diem or subsistence allowances for the organizers, attendees and speakers and other costs
- Hotel room charges and fees (overnight accomodations for CIRM staff and speakers)
- AV equipment rental and planning costs (e.g., audio/visual and internet connectivity) (and associated taxes and service fees)
- Meeting planning and management costs that include up to 10% justified salary support for the Program Director for time spent conducting conference-specific activities; reasonable salary support for administrative staff time conducting conference-specific activities; and meeting planner costs
- Production, publicity and supply costs (website development, program printing, name tags, etc.) needed for conduct of the conference (only if received for use during the budget period)
- Meals (food and non-alcoholic beverages) not related to travel conference services
- Other items as described in the the CIRM Grants Administration Policy available here: https://www.cirm.ca.gov/sites/default/files/files/funding_page/CIRM_Interim_Grants_Administration_Policy_for_Discovery,_Translation,_and_Education_Projects.pdf

These costs are allowable whether incurred by the applicant or by contracted vendors providing the above services needed to conduct the conference. Please note all meal costs must comply with the maximum per-person expenditures for meals and light refreshments according to CIRM's Business Meeting Expenditure policy and may not exceed the following amounts:

Breakfast $27.00
Lunch $47.00
Dinner $81.00
Light refreshments $18.00

The maximum per-person expenditures listed above include the cost of the food and beverages, labor, sales tax, delivery charges, and other service fees. CIRM's full Business Meeting Expenditure policy can be found at https://www.cirm.ca.gov/sites/default/files/files/about_cirm/Business_Policy.pdf

Non-allowable costs for CIRM-Initiated Conference Grants include:

Purchase of equipment; visas; passports; entertainment; alcoholic beverages; personal telephone calls; laundry charges; dues; honoraria for

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speakers; cash awards; facilities alterations or renovations. The CIRM Grants Administration Policy also indicates unallowable costs. Indirect Costs are not allowable on this award.

3. Conference Planning, Coordination and Logistics Plan. Describe your proposed plan: how you will coordinate with CIRM and the scientific organizing committee to develop the agenda for the symposium. While a final agenda with speakers is not required for the application, include a detailed outline of proposed symposium sessions and focused workshops with implementation strategy. Include contacts and communication with academic, industry, and regulatory organizations that would add value to symposium aims. For focused workshops, include a plan to follow up on recommendations post-symposium.

4. Experience and Track Record. Describe the relevant experience and track record of the Program Director and team to manage and successfully produce the symposium. Describe the track record of the Program Director in managing conferences in stem cell manufacturing.

5. Available Resources. Describe the resources available to ensure that the symposium is adequately managed and that all required core activities will be carried out in a timely fashion. Describe the composition of the team including each individual's experience and qualifications. Describe how the team will collaborate with CIRM to plan and organize the symposium.

Award Administration

Issuance of Award

A CIRM Conference Award is issued via a Notice of Award, which is the formal contract that defines the terms and conditions of an award and documents the commitment of funds from CIRM. The Awardee will be subject to CIRM's Grants Administration Policy, including the insurance requirements specified therein.

Reporting
Awardees will be required to provide written financial reports to CIRM upon completion of the conference. Awardees should include the final conference agenda or program.

Contacts

For information about this RFA:

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For information about the review process:

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Definitions

"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.

"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 $25,000 or more through the proposed project. "Subcontractor" does not include suppliers of widely available goods.

Appendix

CIRM Regulations

Grant or Loan awards made through this RFA will be subject to all applicable CIRM regulations. These regulations can be found on CIRM's website at http://www.cirm.ca.gov/reg/default.asp.