

**CIRM Stem Cell Genomics Centers of Excellence Awards
Updated Concept Proposal
January 12, 2012**

Background

Genomics technologies and the data sets they yield are fast becoming the currency of biology and medicine. The cost of genome sequencing is dropping exponentially, a trend that will soon make genome-scale characterization a practical tool for fundamental studies of stem cell biology and for advancing therapeutic applications. Meanwhile, cell therapeutics are advancing toward clinical trials, and hES and hiPS cells have become the gold standard for studying human cell biology, tissue and organ development and repair, and disease. Combining genomic and associated bioinformatics technologies with stem cell research will accelerate fundamental understanding of human biology, disease mechanisms, tissue engineering and cell therapies, such as:

- Understanding how genomic and epigenomic states of cells relate to their behavior and function, in normal and diseased conditions
- Determining genetic and epigenetic pathways critical in directing differentiation to overcome current roadblocks in engineering functional cells (eg. hematopoietic bone marrow-engraftment competent stem cells) and mature tissues from stem cells for cell replacement therapies
- Leveraging CIRM's iPSC banking initiative to study how sequence variation and gene-environment interactions contribute to "disease in a dish" phenotypes
- Identifying the best stem cell lines for therapeutic use with respect to genomic integrity, immunogenic and oncogenic potential, and presence of disease-associated gene variants
- Ensuring genomic stability of stem cells during culture and expansion needed for research and for manufacturing
- Reclassification of diseases based on genomic and epigenomic determinants, stem cell phenotype and pathological mechanism. This could lead to more rapid disease therapeutics utilizing data from genetically related conditions.

Objectives

CIRM proposes funding one or two Stem Cell Genomics Centers of Excellence to advance stem cell genomics by providing pillars on which to construct a range of genomic studies focusing on the biology and therapeutic application of stem cells. The mission of these Centers will be to collaborate with stem cell scientists from throughout California on genomics, and particularly the bioinformatics components of genomics research projects, to provide advice on the design of genomics experiments, to assist with the analysis of complex data sets as well as to advance genomics technology as applied to stem cell biology, and to pursue large scale, data-intensive genomics projects that will

transformatively advance the stem cell field. The Centers will be expected to undertake projects critical to progress of stem cell research in collaboration with appropriate partners. These collaborative studies will be advanced by the Centers through guidance by an Advisory Committee agreed to as part of review by CIRM.

By spearheading fundamental studies of stem cell lines used in basic research as well as cells intended for therapeutic applications, and by developing genomic technology and standards for methodologies including data collection and sharing, these centers can provide unique leadership in both basic and translational research. Catalyzed by these Stem Cell Genomics Awards, CIRM will seek to leverage existing resources, including the present excellence and leadership in stem cell science, hiPS cell banking, powerful in-state bio-computing capacities, multiple leading genomics companies and academic centers, and CIRM's experience in facilitating multi-national projects with major international funding partners, to rapidly and efficiently build an effective stem cell genomics infrastructure that will provide a new platform for the application of genomics tools to stem cell biology and regenerative medicine.

Scope

Efforts by CIRM in this field will be directed toward:

1. Establishing advanced genomics resources for California's leading stem cell research community to advance a range of projects, from basic research to characterization of critical manufactured therapeutic cell lines
2. Enabling resource-intensive high priority stem cell genomics projects that will advance basic research and cell therapies

Funded Activities

The Center(s) will be charged with establishing global leadership in the field of stem cell genomics by advancing the development of standards and methods, facilitating data analysis and coordination, and providing expertise and collaborative opportunities for stem cell scientists throughout California. Centers will be expected to implement and engage in the activities listed below:

1. **Standardization:** developing standard operating procedures for sample and data handling which will form the basis for large scale data sharing and analysis
2. **Data Coordination and Management:** providing infrastructure and expertise for storage, transfer, assembly, and publication via web portals of the terabyte-scale amounts of data that will be generated by the Centers, to enable their analysis
3. **Data analysis:** providing advanced bioinformatics capabilities to uniformly conduct multiple types of analyses of the large data sets created by the centers and collaborators, and to develop new methods for analyzing this type of data

4. **Collaborative Resources:** providing stem cell scientists throughout the state with access to cutting-edge genomics and bioinformatics technologies, and expertise in experimental design and data analysis
5. **Center-initiated Projects:** advancing the entire stem cell field through the pursuit of large scale, coordinated projects with intensive data collection and analysis
6. **Innovative Technology Development:** leading initiatives to address major bottlenecks in stem cell genomic research including information technology (*e.g.* sample preparation, single cell analyses, bioinformatics, large scale data handling capabilities, and analysis and integration in systems biology for disease diagnostics and therapeutics.)

CIRM Stem Cell Genomics Centers of Excellence will be hosted within established California universities, research institutes or companies, and should augment existing genomics or bioinformatics resources to capitalize on expertise and infrastructure. In competing for awards, applicant institutions will be asked to address center structure, administration, policies and activities to promote collaboration and advance the program mission. A plan for sustainability beyond the period of CIRM support will be required.

Eligibility Criteria

This award is open to all California academic, non-profit and for-profit research institutions. To be eligible for funding under this RFA, Program Director(s) (PD) and up to two Co-PDs, should have a PhD, MD, or equivalent degree, and be authorized by the applicant institution to conduct research in California. The PD and Co-PDs should together possess skills, training and experience necessary to carry out Center activities rapidly and cost-effectively.

Budget

CIRM proposes to fund 1 or 2 awards for up to 5 years. Total program costs will be up to \$40 million, and we anticipate that there will be two awards of approximately \$20M each.

Provisional Timetable

- Concept proposal – January 2012
- Release of RFA - May 2012
- Letters of Intent due – June 2012
- Applications due - August 2012
- GWG Review - Fall 2012
- ICOC approval – Winter 2013

