Concept Proposal for RFA 09-03: Stem Cell Transplantation Immunology

Stem cells have great potential for therapeutic benefit in the field of regenerative medicine. To fully realize this potential, the challenge of histocompatibility and rejection by the recipient immune system needs to be addressed. This is a major hurdle that is shared with the field of whole organ transplantation. Even the immune privilege of undifferentiated stem cells is fragile and dependent on a weak minor histocompatibility barrier; more differentiated hPSC derivatives are more immunogenic and more subject to rejection. Furthermore, many patients with conditions for which cell replacement therapies are anticipated will not tolerate multi-drug systemic immunosuppression, highlighting the need for new cell-based or pharmacological tolerance strategies. CIRM proposes a new program to address these needs: "Stem Cell Transplantation Immunology"

CIRM is seeking transformative research in this area with an ultimate goal of immune tolerance of allogeneic stem cell-derived cell and tissue grafts. Given this long-term goal, research in areas including the following are sought, but additional novel approaches to allogenic graft survival are encouraged:

- Development of predictive animal models of the human immune response to cell therapy; particularly in animals with immune characteristics closely aligned to the human
- Correction of autoimmunity with stem cell derived cell therapies in animal models of human diseases
- Derivation and assessment of thymic epithelial cells (TECs) from human pluripotential stem cells (hPSC) for the potential induction of tolerance
- Development of co-receptor blockade and other strategies to reprogram the immune system to accept stem cell derived grafts
- Development and optimization of tolerance induction via hematopoietic chimerism
- Assessment of hPSC-derived dendritic cells for the potential to induce donor-specific tolerance
- Development of sensitive, robust assays for monitoring stem cell derived transplant acceptance or rejection with tissue-specific resolution

CIRM Award Information

- CIRM will fund up to $ 30 million to support up to 20 three-year grants with direct project costs of up to $300,000 per year.

CIRM Institutional Eligibility

All CIRM-supported research must be conducted in California. This RFA is open to all academic, non-profit and for-profit research institutions in the state of California.

Non-profit applicant institutions with accredited medical schools will each be eligible to submit up to **four** applications. Other non-profit institutions and for-profit institutions with 250 employees or more in California will each be eligible to submit up to **two** applications. Nonprofit and for-profit applicant institutions with fewer than 250 employees in California may each submit one application.

CIRM Principal Investigator (PI) Eligibility

Each Principal Investigator (PI) may submit only one application under this RFA. The PI must have an M.D., Ph.D. or equivalent degree, and must be authorized by the applicant institution to conduct the proposed research in California. In addition, CIRM, mindful of the urgency of its mission and the scope of these awards, will require the PI to commit a minimum of **10%** effort.

Collaborative Funding Partner Participation

CIRM has established a program with several other government agencies that fund stem cell and regenerative medicine research. Through this Collaborative Funding Partner program, California-based PIs can collaborate with a Funding Partner PI from a Funding Partner applicant institution to bring important additional resources to the project. If a collaborative funding proposal is approved, CIRM will fund all project work done within the State of California and its Funding Partner will fund all project work performed within its jurisdiction. For this RFA, the **Japan Science and Technology Agency (JST) and State of Victoria (Australia)** are each participating as a Funding Partner.

Provisional Time Table:

• ICOC Concept Approval	August	2009
• RFA Release	Nov.	2009
• Grants Working Group Review of Applications	April	2010
• ICOC Approval	June	2010