

**RFA 08-05 CONCEPT PROPOSAL
CIRM TRANSLATIONAL I RESEARCH AWARDS**

A major challenge in the development of therapies is translating basic science discoveries into preclinical and clinical programs. The purpose of the CIRM Translational Research Initiative will be to provide funding to ensure that promising discoveries in stem cell research can be translated into potential stem cell-based cures, therapies and diagnostics for the benefit of patients. This initiative will support at least two Translational Research awards, for early and for later-stage programs.

The CIRM Translational I Research Award will support research that enables the initial stage of translation of basic stem cell research to potential clinical application. This award will support two types of early translational research including research that:

- 1) Results in a development candidate that meets an unmet medical need
- 2) Addresses a significant bottleneck that, if overcome, would advance effective translation of discoveries towards testing in patients.

A key objective of the Translational I Research Awards will be the identification of a development candidate that has the necessary supportive data, including activity in relevant in vitro and in vivo models of disease, to be considered for further funding (under a separate RFA) for activities to enable a regulatory filing for clinical testing. The applicant for this type of Translational I Research Award must have strong supportive evidence for a disease target for therapeutic intervention and a scientifically justifiable hypothesis for a proposed therapeutic approach. Examples of development candidates include a stem cell or stem cell-derived progenitor candidate, or a small molecule or protein therapeutic derived with stem cells. In this RFA, use of human stem cells must offer an advantage over other approaches in obtaining a development candidate.

Activities designed to result in a development candidate that will be supported include but are not limited to:

- Assay development and testing for potency, identity and purity;
- Expansion, purification, and characterization of cells appropriate for therapy or screening;
- Determination of in vitro and in vivo biological activity in appropriate model systems;
- Demonstration of in vitro and in vivo safety and disease modifying activity in generally accepted models of disease;
- Definition of pharmacokinetic/pharmacodynamic and drug metabolism profiles (as relevant in appropriate models).

A second key objective of this RFA will be to find solutions to bottlenecks to effective translation that, if overcome, would allow the more rapid advancement of discoveries in stem cell biology to the identification of better development candidates for clinical testing. Goals for research on bottlenecks that will be supported include but are not limited to:

- Development of improved disease models that would overcome limitations of current models and be more predictive of efficacy in humans;

- Development of animal models that would more clearly predict safety, tolerance, including local tolerance, and immune response in humans than present strategies;
- Development of methods to induce tolerance;
- Development of stem cell-derived in vitro systems that would be more predictive of toxicity in humans than present strategies;
- Development of methods to non-invasively track the migration, integration and/or fate of in vivo transplanted stem cells including teratoma or cancer formation;
- Development of cell differentiation and selection/purification methods that result in higher and more consistent yield of cells of the desired phenotype and are scalable and/or more cost effective.

Research utilizing pluripotent stem cells, adult stem cells or progenitor cells will be considered. Particular consideration will be given to those proposals that are ineligible for or unlikely to receive federal funding.

The CIRM Translational I Research Awards program will be open to Principal Investigators with a Ph.D., a M.D. or an equivalent degree who are authorized by the applicant institution to conduct the research. CIRM, mindful of the urgency of its mission and the scope of these awards, will require Principal investigators to commit a minimum of 10% effort. Translational research is often most effectively conducted by a multidisciplinary team and CIRM encourages PIs to form such collaborative endeavors, including collaboration between non-profit and for-profit institutions.

Non-profit and for-profit institutions will be eligible to apply for this award. Non-profit applicant institutions with accredited medical schools will be eligible to submit up to three applications. Other non-profit institutions and for-profit institutions with over 500 employees will be eligible to submit up to two applications. Non-profit and for-profit applicant institutions with fewer than 500 employees may submit one application. CIRM proposes to fund up to 10 three year awards with justifiable project costs of up to \$1.2 million per year for a total program cost of up to \$60 million.

Provisional time table

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| • Release of RFA | August 2008 |
| • Applications due | November 2008 |
| • Review | Winter 2009 |
| • ICOC approval | Winter/Spring 2009 |