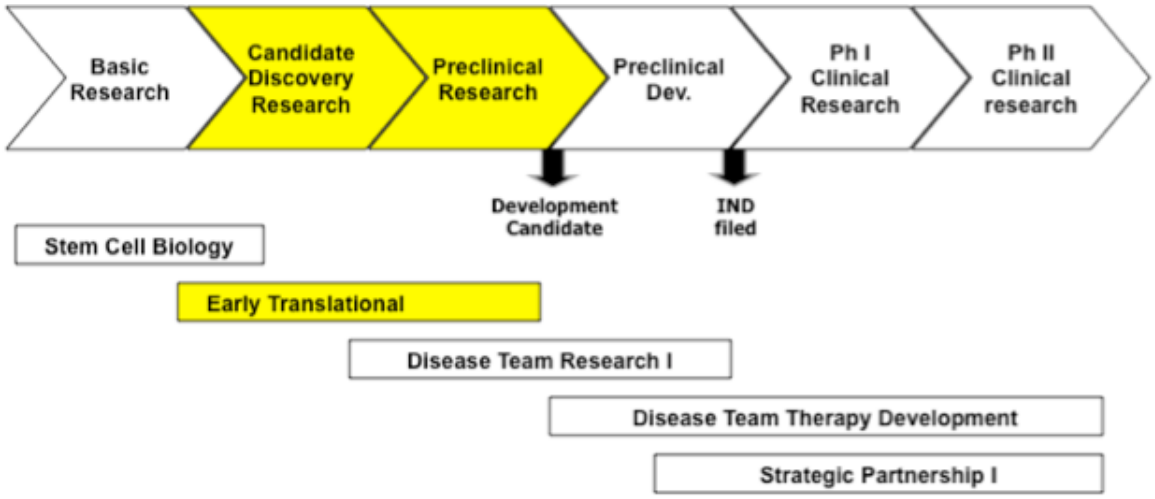
RFA 12-07 CONCEPT PROPOSAL
CIRM EARLY TRANSLATIONAL IV RESEARCH AWARDS

The objective of the CIRM Early Translational Research Awards is to fund and advance promising stem cell discoveries toward clinical development. The Governing Board (ICOC) has funded three cycles of Early Translational Research Awards, most recently in May of 2012 (21 awards). These programs cover diverse therapeutic areas such as cardiovascular diseases, neurodegenerative disease, neurologic disorders, bone/cartilage disorders, immune disorders and eye disease. The stage of research encompassed by CIRM's Early Translational Program in the context of other CIRM RFAs is highlighted below.



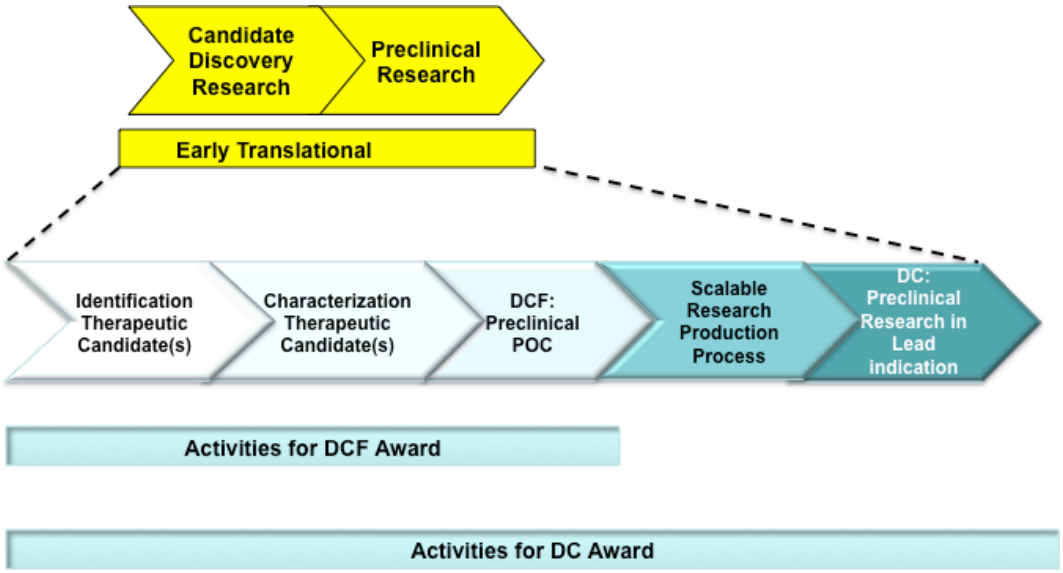
The Early Translational IV Research Awards will support two categories of human stem cell/regenerative medicine translational research projects:

1) Research that results in a stem cell-derived development candidate (DC) to treat an unmet medical need where all necessary activities to move into IND-enabling preclinical development have been completed.
   OR
2) Research conducted to identify and/or establish the feasibility of a potential stem cell-derived development candidate. The goal of these development candidate feasibility (DCF) awards is to achieve preclinical (*in vitro/in vivo*) proof of concept. CIRM is particularly interested in proposals for DCF awards that address unique new opportunities for regenerative medicine that are potentially transformative therapeutic approaches to unmet medical needs (e.g. direct reprogramming).

All proposals must meet at least one of the following criteria

- Human stem cells must be necessary or significantly advantageous to the proposed research compared to other approaches
- Targets endogenous human stem cells
- Proposes a direct reprogramming therapeutic approach

These two categories of projects and key research activities are represented below:



Research that is outside of the scope of these awards includes:

- Basic research and research with a focus on drug target discovery.
- IND-enabling preclinical development activities (e.g. GMP production, GLP toxicology and tumorigenicity studies)
- Clinical studies. Analysis of human subject samples, if directly related to the proposed research, can be funded.

CIRM will prioritize projects:

- that propose cell therapies, especially cell therapies that are differentiated derivatives of pluripotent stem cells (especially for DC awards);
- that address potentially transformative therapeutic approaches to regeneration (especially for DCF awards);
- that are ineligible for or unlikely to receive timely or sufficient federal funding.

Given that CIRM now has a significant translational portfolio, proposed projects must be compelling and novel.

CIRM Award Information

CIRM proposes to commit up to $70 million to this Early Translational Research IV Awards program for:

- Development Candidate (DC) awards, each with justifiable total direct project costs of up to $3.5 million over the three-year project period.
- Development Candidate Feasibility (DCF) awards, each with justifiable total direct project costs of up to $1.2 million over the three-year project period.

* CIRM intends to support approximately 10 DC and 10 DCF Awards.

For-profit applicant organizations will be permitted to apply for either grants or loans. Loan terms will be applicable Board-approved terms. Non-profit applicant organizations will be funded through grants.

CIRM Institutional Eligibility

- All CIRM supported research must be conducted in the state of California
- Open to all academic, non-profit and for-profit institutions in the state of California
- CIRM proposes to use its pre-application process to identify the most promising, competitive and responsive pre-application proposals, so no limits will be applied on the number of pre-applications an eligible institution can submit.

CIRM Investigator Eligibility

- A Principal Investigator (PI) with Ph.D., M.D or equivalent degree who is authorized by the applicant institution to conduct the proposed research in California.
- As a multidisciplinary team often most effectively conducts translational research, applicants for DC awards only may include up to 1 Co-Principal Investigator (Co-PI) with a Ph.D., M.D or equivalent degree who is authorized by the Co-PI institution to conduct the proposed research in California.
- PIs and Co-PIs must commit 20% and 15% effort respectively towards programs supported under this RFA.

CIRM encourages collaborative endeavors between non-profit and for-profit institutions, especially partnerships/collaborations with product development organizations committed to taking successful programs forward.

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 eligible for funding from one of CIRM's collaborative funding partners to bring important additional resources to proposed projects. 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 within its jurisdiction. Collaborative Funding Partners who currently are expected to participate in this Early Translational IV RFA include the NIH (US), the National Health and Medical Research Council (NHMRC, Australia), the Ministry of Science and Technology (MOST)/Tongji (China) and the Ministry of Science and Technology (Argentina).

Provisional Time Table*:

• Release of RFA	September	2012
• Pre-Applications due	October	2012
• Applications due	March	2013
• Grants Working Group Review of Applications	June	2013
• Earliest ICOC Approval	Summer	2013

* Assumes a Pre-Application process