

RFA 13-02: Basic Biology Awards V Grants Working Group Recommendations

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Agenda Item #8

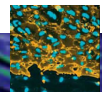
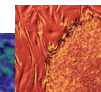
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Presentation Overview



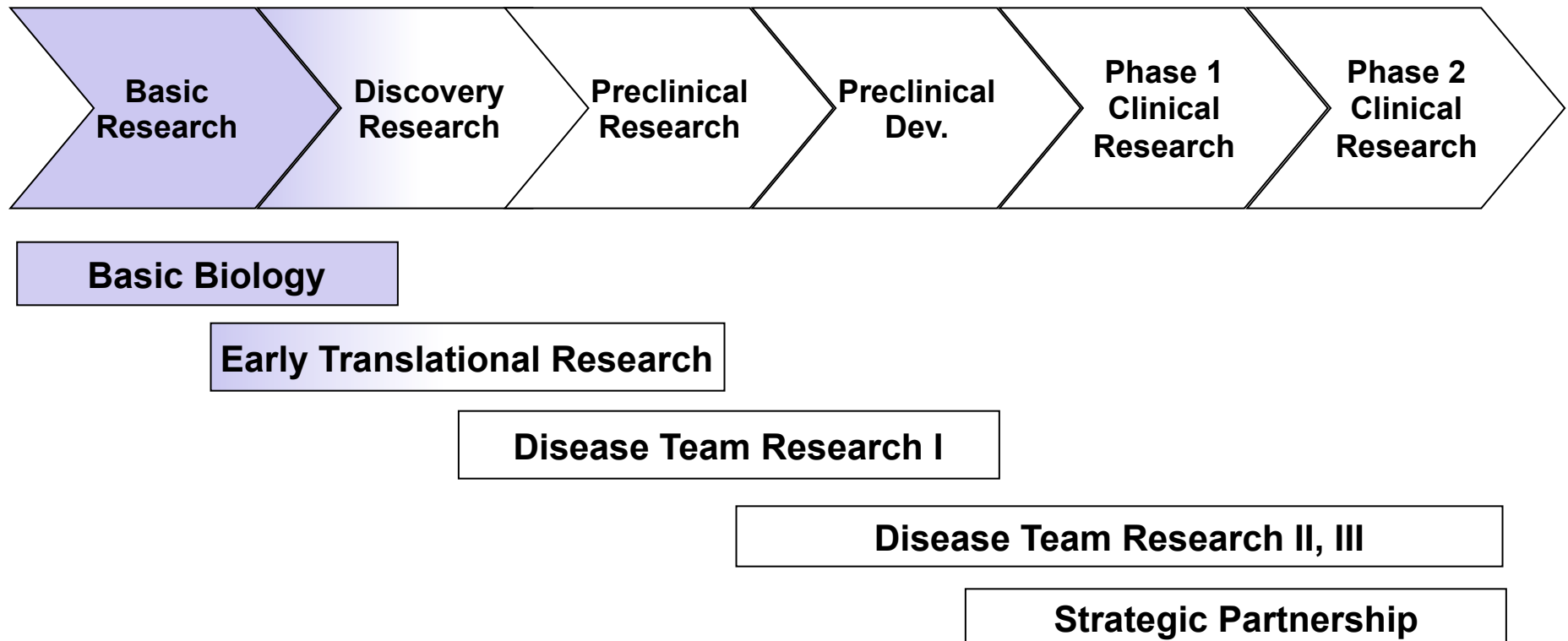
1. RFA Introduction
2. Recommendations of GWG and Staff for Fundamental Mechanisms (FM) Awards
3. Programmatic Review of Fundamental Mechanisms Awards
4. Recommendations of GWG and Staff for Exploratory Concepts (EC) Awards
5. Programmatic Review of Exploratory Concepts Awards



Basic Biology Awards



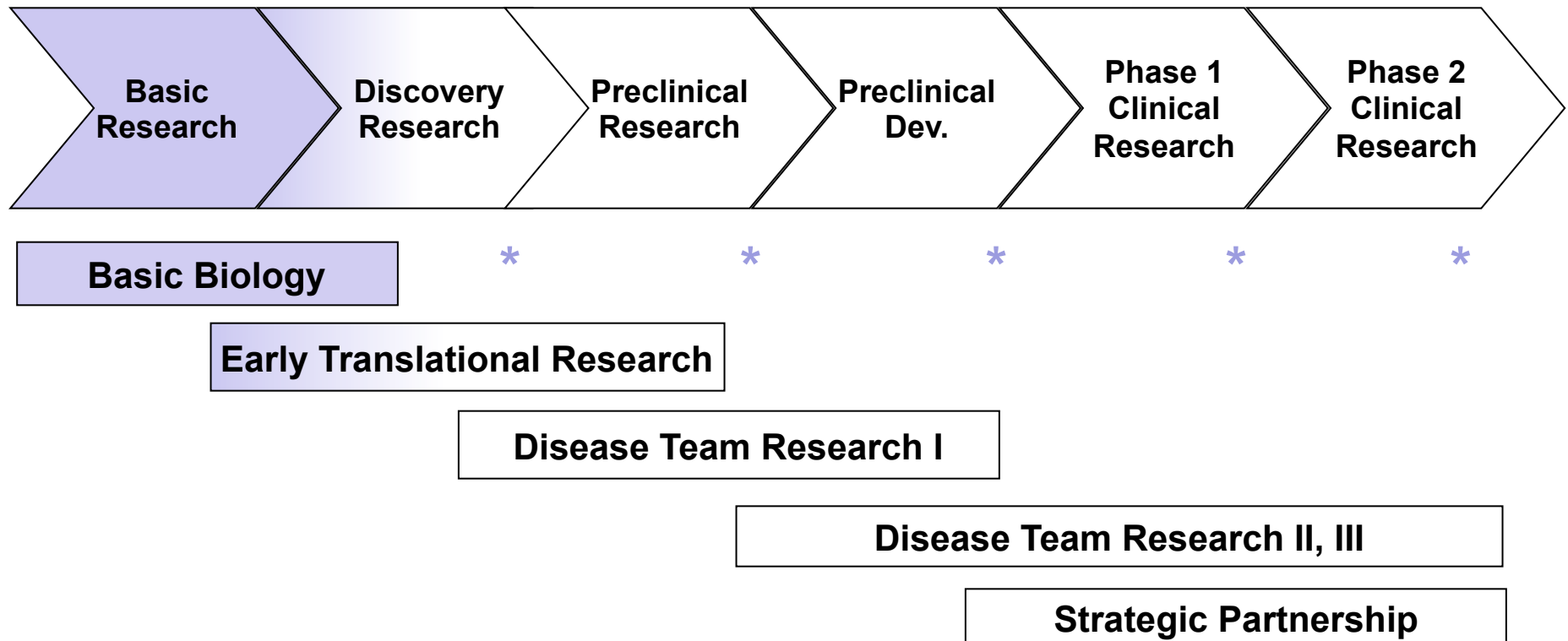
Goal: *to foster cutting-edge research tackling significant, unresolved issues in human stem cell biology, with emphasis on unraveling the key molecular and cellular mechanisms that dictate cell fate*



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Two Types of Award



Fundamental Mechanisms

- Elucidating cellular and molecular mechanisms pertinent to human stem cell biology/regenerative medicine

Exploratory Concepts

- Testing highly novel hypotheses that if proven, would challenge dogma or result in a transformative discovery for the stem cell field

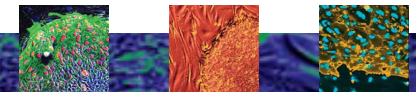


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Program Details- Fundamental Mechanisms (FM)



- Similar to projects targeted through Basic Biology I-IV
- Rigorous studies utilizing human stem cells that will significantly advance the field
- Focus on cellular and molecular mechanisms particular to stem cell function, cellular differentiation or disease mechanism
- Should be based on compelling preliminary data and strong rationale
- 3 years duration; justifiable direct project costs up to \$250,000/Year

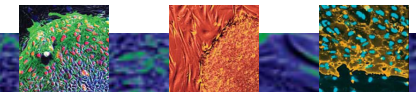


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Program Details- Exploratory Concepts (EC)



- Enabling transformative discoveries through high risk, high gain exploratory pursuits
- Studies directly related to stem cell biology, direct reprogramming or determination of cell fate and identity
- Studies may utilize human cell models and/or, with compelling justification, vertebrate animal models
- 2 years duration; justifiable direct project costs up to \$200,000/Year



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Review Process

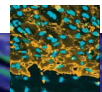
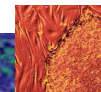


1. Preliminary Applications (PreApps)

- An eligible PI could submit to one track or the other, but not both
- Reviewed by experts from outside of California and CIIRM scientists

2) Full Applications

- Reviewed by Grants Working Group (GWG)
October 2-4, 2013



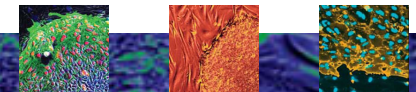
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Numbers of Applications

	FM	EC	Total
Pre Apps Received	214	127	341
Full Apps Reviewed	43	19	62
Apps to be Funded*	~20	~10	Up to 30

***TBD, based on GWG recommendations
and Programmatic Review**

Total Allocation: \$40M



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GWG Recommendations: Summary

	FM	EC	Funds
Tier 1: Score 75-100 Recommended for Funding	16	4	\$21,058,252
Tier 2: Score 65-74 Moderate Quality or No Consensus; Suitable for Programmatic Review	9	5	\$13,429,014
Tier 3: Score 1-64 Not Recommended for Funding	18	10	\$27,839,340
<i>Staff Recommendations for Funding from Tier 2</i>	3	2	\$4,801,775

Total Allocation: \$40M, up to 30 awards



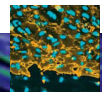
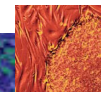
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Fundamental Mechanisms



Fundamental Mechanisms

- Elucidating cellular and molecular mechanisms pertinent to human stem cell biology/ regenerative medicine

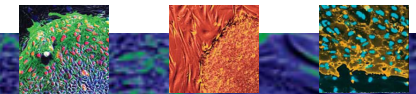


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Review Criteria- Fundamental Mechanisms



- **Significance and Innovation**
 - Innovative project; focus on mechanism; logical rationale; major impact
- **Feasibility and Experimental Design**
 - Sound approach; achievable Aims; pitfalls addressed, alternative approaches; compelling preliminary data; appropriate facilities and environment
- **Principal Investigator and Research Team**
 - PI track record and commitment; team qualifications
- **Responsiveness to the RFA**
 - Human cell focus; relevance to Track 1

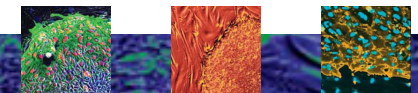


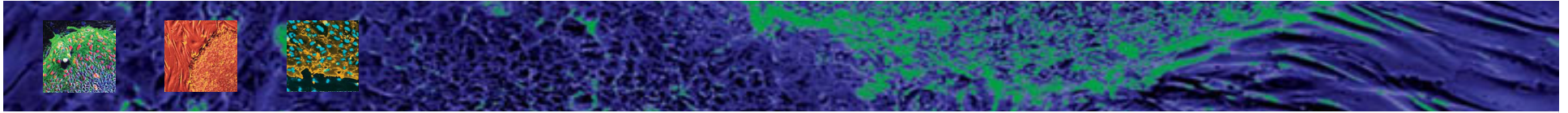
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GWG Recommendations: FM

Fundamental Mechanisms Awards		Funds
Tier 1: Score 75-100 Recommended for Funding	16	\$18,584,179
Tier 2: Score 65-74 Moderate Quality or No Consensus; Suitable for Programmatic Review	9	\$10,675,912
Tier 3: Score 1-64 Not Recommended for Funding	18	\$21,715,330
<i>Staff Recommendations for Funding from Tier 2</i>	3	\$3,785,243

Total Allocation: \$40M, up to 30 awards





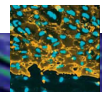
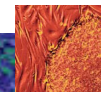
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Fundamental Mechanisms (FM)

RB5-06935: Misregulated Mitophagy in Parkinsonian Neurodegeneration (FM)

- Mechanisms linking mitochondrial dysfunction to neuronal death in Parkinson's Disease (PD) remain unclear
- CIRM is currently funding 3 iPSC-based PD modeling studies
 - do not address mitochondrial mechanisms
- Reviewers differed in opinions regarding novelty
 - findings already described in animal models
 - first attempt to validate this mechanism in diseased human neurons
- If funded, ensure commitment of contributor with required expertise
 - applicant is early-career PI, good track record
 - no direct experience with dopaminergic neuron differentiation

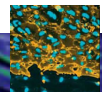
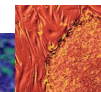
➤ **Staff Recommendation: Fund.**



RB5-07285: A Novel Druggable Mechanism to Safeguard Stem Cell Genome (FM)

- Assurance of genome stability in cell populations intended for therapy is a highly desirable goal. If successful, the findings from this effort might be transformative, i.e. could have broad impact in the field of regenerative medicine, with relevance for many different types of stem cell-derived populations considered for therapy development.
- The proposal addresses an RFA priority for Track 1 but is very high risk. as the preliminary observations from animal studies might not be relevant or reproducible in the human system.
- To mitigate this risk, CIRM staff will ensure, if funded, that a milestone be included such that the applicant must first demonstrate validity of his/her observations in the human system before expanding mechanistic explorations.

➤ **Staff Recommendation: Fund.**



RB5-07409: Biophysical Determinants of Early Embryonic Stem Cell Fate Specification (FM)



- This proposal represents a unique opportunity to investigate cell movements that are critical for early human development, utilizing human pluripotent stem cells (hPSC). There are no similar projects within CIRM's research portfolio
 - This is a high risk / high reward proposal. Risk will be managed, if funded, by implementing appropriate milestones and monitoring of progress toward generation of critical tools.
- **Staff Recommendation: Fund.**



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Exploratory Concepts



Exploratory Concepts

- Testing highly novel hypotheses that if proven, would challenge dogma or result in a transformative discovery for the stem cell field

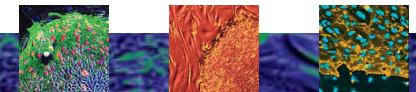


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Review Criteria- Exploratory Concepts



- **Novelty and Transformative Potential**
 - Novel hypothesis; logical rationale; transformative potential
- **Feasibility and Experimental Design**
 - Sound design; achievable Aims; appropriate facilities and environment
- **Principal Investigator and Research Team**
 - PI track record and commitment; team qualifications
- **Responsiveness to the RFA**
 - Stem cell biology, direct reprogramming or determination of cell fate/identity; human and/or vertebrate model



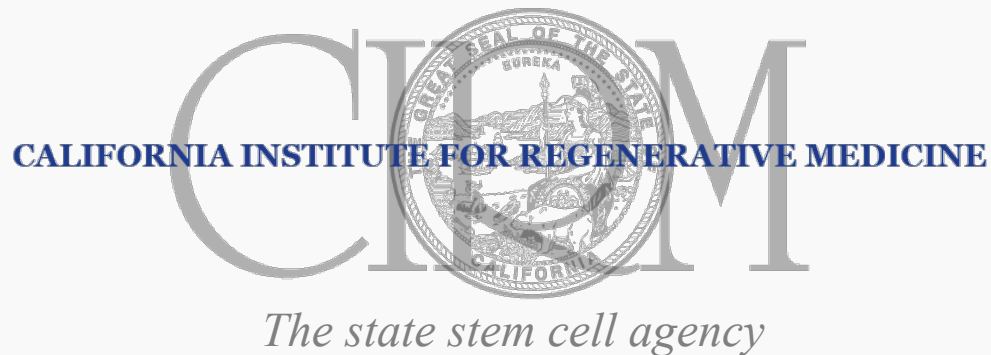
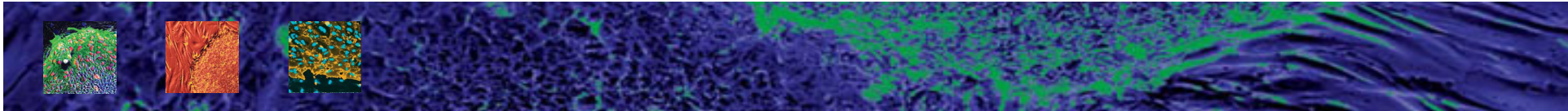
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GWG Recommendations: EC

Exploratory Concepts Awards		Funds
Tier 1: Score 75-100 Recommended for Funding	4	\$2,474,055
Tier 2: Score 65-74 Moderate Quality or No Consensus; Suitable for Programmatic Review	5	\$2,753,102
Tier 3: Score 1-64 Not Recommended for Funding	10	\$6,124,010
<i>Staff Recommendations for Funding from Tier 2</i>	2	\$1,016,532

Total Allocation: \$40M, up to 30 awards





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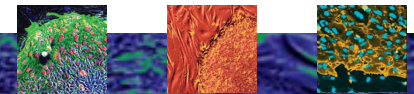
Exploratory Concepts (EC)

RB5-07414: Directed Differentiation of Specialized Endothelial Cells (EC)



- Focused on differentiation of hESCs into endothelial cells, a critical cell type for regenerative medicine applications. In particular, there is a strong emphasis on specifying arterial subtypes, an important resource for creating vascular grafts.
- The proposal addresses two areas that are not represented strongly in CIRM's research portfolio: 1) specification of endothelial cell types from pluripotent stem cells; and 2) The role of cell mechanics/mechanotransduction in differentiation of stem cells.
- The applicant is a current CIRM grantee in the New Faculty II program, whose project is nearing the end. This Basic Biology grant would allow the PI to capitalize on the initial investment CIRM has already made on the New Faculty award.

➤ **Staff Recommendation: Fund.**



RB5-7458: Non-invasive Live Imaging of Stem Cell Signature Metabolic States (EC)

- The applicant team has pioneered a unique imaging platform that enables single cells to be examined without the need for labeling or other forms of manipulation that can inadvertently impact cell behavior. This proposal tests whether this technique can be successfully applied towards investigating fundamental stem cell behaviors in ways that have not been previously possible.
- Development and use of single cell imaging techniques represent the cutting edge of the field, and are not well represented in CIRM's research portfolio.
- A successful outcome could have transformative implications for both basic and translational science.

➤ **Staff Recommendation: Fund**



