# Real Life™

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Grants Working Group DISC0 Recommendations

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CIRM
CALIFORNIA'S STEM CELL AGENCY

# Mission Statement

## OUR MISSION

Accelerating world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world

# DISC0 Foundation Awards

## CIRM's DISC0 Purpose & Objectives

- Broadly re-initiate funding of basic stem/progenitor ("stem") cell science and genetic research.
- Support rigorous studies addressing critical *basic knowledge gaps* or *bottlenecks* in regenerative medicine research.
- Advance the development of stem cell-based tools for innovation.

# DISC0 Foundation Awards

## DISC0 Proposal Objective

Projects should culminate in a discovery or technology that would advance (1 or more):

- Understanding of biology of stem cells that is relevant to human biology and disease,
- Genetic research relevant to human biology or disease that pertains to stem cells or regenerative medicine,
- The development of human stem cells as tools for biomedical innovation, and/or
- Greater applicability of regenerative medicine discoveries to communities representing the full spectrum of diversity.

# DISC0 Foundation Awards

## DISC0 funds can support the following EXAMPLE activities

- Basic research into stem cell or genetic research mechanisms as they relate to human biology.
- Basic research to address bottlenecks - such as tissue targeting, immunogenicity or toxicity - in the development of stem cell-based therapies.
- Studies to better understand healthy and/or diseased human cells and tissues – such as omics profiling or human cell / tissue atlases.
- Mechanistic studies of disease to enable rational design of stem cell-based treatments.
- Investigation of stem cells or their derivatives as tools for therapeutic or other innovation, e.g., for modeling disease.
- Generation of omics data that will extend or validate the applicability of regenerative medicine discoveries to underserved racial or ethnic groups.

# DISC0 Foundation Awards

- Applications must address a *knowledge gap* or a *bottleneck* in regenerative medicine research.
- Awards are for 3 years and up to $1 million in direct project costs
- Next opportunity not yet scheduled. Likely to be in a year.

# Positive Selection (Two-Stage) Review Process

- Performed when the total number of applications exceeds the capacity of the GWG to review in a single session.
- In the first stage, GWG members including patient advocates and nurse Board Members conduct a pre-review of applications and select which ones to advance to a full review.
- The CIRM President and CIRM will examine non-selected applications to determine if any merit a full review. The remainder are not considered further.
- A total of 93 eligible applications were submitted and a total of 48 advanced to the full discussion stage by GWG.

# GWG Composition and Roles

| | |
|---|---|
| Scientific GWG Members | Positive selection<br>Scientific evaluation based on broad subject area or methods expertise<br>Enter final scores for **every** application |
| GWG Board Members | Positive selection<br>Patient perspective on significance and potential impact, oversight on process |
| Specialists | Scientific evaluation based on specialized expertise<br>Provide recommended scores in the discussion |

# Scoring System for DISC0 Applications

- **Score of "85-100"**

  *Recommended for funding, if funds are available*

- **Score of "80-84"**

  *Not recommended for funding*

  *Applications receiving a score of **80-84** in this review cycle were deemed by the GWG to have sufficient merit to bypass the positive selection process and advance to full scientific review if resubmitted in the next review cycle*

- **Score of "1-79"**

  *Not recommended for funding*

Applications are scored by all scientific members of the GWG with no conflict.

The **median** of all individual GWG scores determines final score.

# Review Criteria

1. Does the project hold the necessary significance and potential for impact? (i.e., what value does it offer; is it worth doing?)
2. Is the rationale sound? (i.e., does it make sense?)
3. Is the project well planned and designed?
4. Is the project feasible? (i.e., can they do it?)
5. Does the project uphold the principles of diversity, equity and inclusion (DEI)?

# GWG Recommendations Summary

| | Number of Apps | Total Applicant Request | Funds Available |
|---|---|---|---|
| **Recommended for funding** Score 85-100 | 16 | $24,568,033 | $73,007,735 |
| **Not recommended for funding** Score 1-84 | 32 | | |

For each award, the final award amount shall not exceed the amount approved by the ICOC Application Review Subcommittee and may be reduced contingent on CIRM's assessment of allowable costs and activities.

# Process for CIRM Team Recommendations

To better serve the Application Review Subcommittee in its duty of making final funding decisions, we are developing (with your input) a formal process for making and presenting CIRM Team Recommendations.

- Generally, the CIRM Team will support the GWG recommendation unless the team identifies clear and compelling grounds to make a specific recommendation otherwise.
- The CIRM Team will examine applications that qualify for a Minority Report to determine if a recommendation contrary to the majority GWG recommendation is warranted.
- We encourage the ARS to consider programmatic factors (e.g., portfolio, unmet need, strategic plan) in making a funding decision (whether in agreement or not with GWG or CIRM Team recommendations). The CIRM Team will provide available background information to assist the ARS as needed.

# Minority Reports

- Under Prop 14, any application that is not recommended for funding by the GWG, but which had 35% or more members score to fund the application must include a minority report.

- The minority report is included in the review summary and provides a brief synopsis of the opinion of reviewers that scored the application 85 or above.

# Applications with a Minority Report

| App Number | Title | Funds Requested | Score |
|---|---|---|---|
| **DISC0-14514** | An interactive data resource for hypothesis testing in stem cell single-cell gene expression and validation of the results with brain organoids | **$1,160,126** | 83 |
| DISC0-14499 | Exploring pregnancy-associated systemic factors to rejuvenate aged stem cells - a new frontier in regeneration | **$1,543,645** | 82 |
| DISC2-14566 | Immune cloaking of human stem cell-derived insulin producing cells for curative cell therapy without immunosuppression | **$1,192,586** | 80 |

The CIRM Team supports the minority position for application **DISC0-14514** and recommends funding of this application.

# Minority Report for DISC0-14514

| Score | Num ≥85 (Fund) | Num <85 (Do not fund) | Range | Funds Requested |
|---|---|---|---|---|
| 83 | 6 | 9 | 79-100 | $1,160,126 |

TITLE: An interactive data resource for hypothesis testing in stem cell single-cell gene expression and validation of the results with brain organoids

AREA OF IMPACT: Creates a user friendly, “virtual microscope” by which any scientist, without special training, can investigate the role of their favorite gene in human cerebral cortex development in the context of high-dimensional single-cell assay data

# Minority Report for DISC0-14499

| Score | Num ≥85 (Fund) | Num <85 (Do not fund) | Range | Funds Requested |
|---|---|---|---|---|
| 82 | 7 | 8 | 45-89 | $1,543,645 |

TITLE: Exploring pregnancy-associated systemic factors to rejuvenate aged stem cells - a new frontier in regeneration

AREA OF IMPACT: Seeks to identify molecular features that differentiate old vs. young female pelvic floor muscle tissue, and to determine whether any systemic factors associated with pregnancy promote regeneration of the aged niche.

# Minority Report for DISC0-14566

| Score | Num ≥85 (Fund) | Num <85 (Do not fund) | Range | Funds Requested |
|---|---|---|---|---|
| 80 | 6 | 9 | 75-90 | $1,192,586 |

TITLE: Immune cloaking of human stem cell-derived insulin producing cells for curative cell therapy without immunosuppression

AREA OF IMPACT: Explores a new, gene engineering approach for the goal of shielding human stem cell-derived insulin producing cells from the immune system upon therapeutic transplantation for diabetes.

# Board members with Conflicts of Interest

| Board members with Conflicts of Interest for DISC0 applications | |
|---|---|
| Haifaa Abdulhaq | Larry Goldstein |
| Kim Barrett | Pat Levitt |
| Linda Boxer | Shlomo Melmed |
| Michael Botchan | Christine Miaskowski |
| George Blumenthal | Michael Stamos |
| Ysabel Duron | Karol Watson |
| Elena Flowers | Keith Yamamoto |
| Judy Gasson | |