CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

Memorandum

To: Members of the Application Review Subcommittee
From: CIRM Leadership Team
Re: CIRM Team Recommendations: DISC5
Date: September 24, 2026

Executive Summary

This memo summarizes the CIRM program staff funding recommendations for applications submitted to the DISC5 Program for consideration by the Application Review Subcommittee (ARS) on September 24, 2026.

CIRM received 275 applications for this first cycle of the DISC5 program. Of these applications, 51 were selected by the Grants Working Group (GWG) to move forward to full review and discussion. Following full review, 21 applications were recommended for funding by the GWG, receiving median scores of 85 or greater. Four additional applications, with median scores ranging from 82 to 84, include a minority report. The available program budget is $52.5 M, which provides sufficient funds to support those applications recommended for funding by the GWG. Following programmatic review, assessing potential portfolio value and synergy with former and existing CIRM investments, the CIRM Team concurs with the GWG, recommending the top 21 scoring applications for funding.

The Appendix contains detailed application assessments, including portfolio and programmatic considerations where relevant, and the basis for the CIRM funding recommendations.

I. Background

Introduction

The role of CIRM staff during the Application Review Subcommittee (ARS) meetings is to assist the ARS in making well-informed funding decisions by providing programmatic context alongside the outcomes of the Grants Working Group (GWG) recommendations. In developing these recommendations to ARS, CIRM evaluated all applications consistent with the following CIRM funding recommendation framework presented to the ICOC (March 2026):

1. Available program budget
2. GWG score & comments
3. Programmatic factors
4. Prior awardee performance
5. New information available to CIRM after GWG review

Summary of Program Budget Considerations

Available Program Budget (Annual)	$ 52,500,000
Budget Utilization – GWG Recommended	$ 52,425,400
Budget Utilization – CIRM Recommended	$ 52,425,400
Remaining Program Budget	$ 74,600

II. Proposal

After a review of all applications with a score tied with or higher than the lowest scoring application with a minority report, the CIRM team recommends, in accordance with the GWG,

1. To **fund** DISC5-19989, DISC5-20068, DISC5-20026, DISC5-20172, DISC5-19908, DISC5-19839, DISC5-20195, DISC5-20158, DISC5-19638, DISC5-19747, DISC5-19949, DISC5-19810, DISC5-19686, DISC5-20061, DISC5-19811, DISC5-19893, DISC5-19870, DISC5-19807, DISC5-19957, DISC5-19950, and DISC5-19900.
2. To ***not*** **fund** DISC5-20142, DISC5-19775, DISC5-19843, and DISC5-19705.

Summary of Funding Recommendations

Application	Median Score	Scores to fund	Scores not to fund	CIRM Recommendation
DISC5-19989	92	15	0	Fund
DISC5-20068	91	14	1	Fund
DISC5-20026	90	14	0	Fund
DISC5-20172	90	13	2	Fund
DISC5-19908	88	14	0	Fund
DISC5-19839	88	12	3	Fund
DISC5-20195	88	11	4	Fund
DISC5-20158	87	13	2	Fund
DISC5-19638	86	14	0	Fund
DISC5-19747	86	13	2	Fund
DISC5-19949	85	13	2	Fund
DISC5-19810	85	12	3	Fund
DISC5-19686	85	13	2	Fund
DISC5-20061	85	13	2	Fund
DISC5-19811	85	10	4	Fund
DISC5-19893	85	13	2	Fund
DISC5-19870	85	8	7	Fund
DISC5-19807	85	7	6	Fund
DISC5-19957	85	9	6	Fund
DISC5-19950	85	8	7	Fund
DISC5-19900	85	7	7	Fund
DISC5-20142*	84	5	8	Do not fund
DISC5-19775*	83	7	8	Do not fund
DISC5-19843*	83	6	9	Do not fund
DISC5-19705*	82	6	9	Do not fund

*Application includes a minority report.

The CIRM team provides assessments for any applications with a GWG score above or tied with the lowest scoring application where the CIRM recommendation differs from the GWG recommendation or for which there is a minority report.

III. Appendix: Application Assessments

1. Application number: DISC5-19989

Title: Advancing next-generation models for the development of thymoregenerative medicines

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
92	92	95	89	15	0

CIRM Team Recommendation: Fund

DISC5-19989 proposes the development and utilization of human-based models of the thymus, including hiPSC-derived thymic epithelial progenitors (TEPs) and primary TEPs from human organoids, to better characterize thymic dysfunction. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Unique model system, addressing bottleneck in fundamental understanding of thymic biology (regulators of TEP differentiation), an area of research not currently represented in the DISC portfolio. • Utilization of a unique human thymic RNAseq dataset • Applicant would be a first-time CIRM PI
Synergy with former or existing CIRM investments	• Directly builds upon prior CIRM-funded research (Basic Biology Award) to develop TEC differentiation protocol • Potential synergy with future DISC4 cohort focused on immune-tissue interactions • Generation of knowledge and in vitro platforms that could impact other CIRM-supported research in domains including cancer, immunodeficiencies, autoimmune disorders, and other conditions related to thymic dysfunction.

2. Application number: DISC5-20068

Title: Decoding regulatory sequence function during human brain organoid development

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
91	88	92	50	14	1

CIRM Team Recommendation: Fund

DISC5-20068 proposes to utilize stem cell-derived organoids to study genetic variants of cis-regulatory elements (CREs) and the cell-specific effects of CRE function in development to ultimately inform the design of stem-cell based therapies. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Addresses a novel bottleneck in the DISC portfolio • Novel application of high throughput massively parallel reporter assays to single-cell samples, incorporated with functional genomics • Applicant would be a first-time CIRM PI
Synergy with former or existing CIRM investments	• Knowledge generated from this work has the potential to inform fundamental understanding of developmental disorders as well as discovery and preclinical development of stem-cell based therapies of interest to CIRM

3. Application number: DISC5-20026

Title: Leveraging iPSCs and a deep learning-based virtual cell model to identify therapeutic targets for ALS

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
90	90	95	85	14	0

CIRM Team Recommendation: Fund

DISC5-20026 proposes to use a deep learning-based virtual cell model and iPSCs to identify and validate new therapeutic targets with broad efficacy in ALS patient neurons. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery	• This project employs a novel AI cell state model designed to predict the transcriptomic trajectory of a

portfolio through novel approaches or attributes	cell when subject to perturbations to evaluate potential therapeutic targets for ALS.
Synergy with former or existing CIRM investments	• Strong potential to integrate with active DISC4 network teams focusing on ALS mechanistic discovery and target identification. • Model was trained on data generated with a previous CIRM investment (DISC2 Award)

4. Application number: DISC5-20172

Title: Phoenix WNTears: A Platform for Selectivity Expanding Adult Stem Cell Potency and Plasticity

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
90	88	90	82	13	2

CIRM Team Recommendation: Fund

DISC5-20172 proposes to understand the mechanisms by which the WNT/FZD7 pathway regulates adult epithelial stem cell plasticity and promotes regenerative repair. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• There are currently no active Discovery stage grants in the area of wound repair or skin tissue stem cell biology. • Team employs an engineered Wnt signaling antibody mimetic to interrogate basic biology, potentially accelerating the transition to future translation. • Applicant would be a first-time CIRM PI
Synergy with former or existing CIRM investments	• Team member serves on institutional program committee for a CIRM Bridges grant

5. Application number: DISC5-19908

Title: Generating biological age in a stem cell-based complex disease model of osteoarthritis

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
88	88	92	85	14	0

CIRM Team Recommendation: Fund

DISC5-19908 proposes to develop a protocol for inducing rapid aging in a hiPSC-based organ-on-a-chip model of osteoarthritis (OA), consisting of fat, bone, cartilage, and macrophages, and use it to determine how biological age changes inter-tissue communication function in OA. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Addresses two subjects not well represented in the CIRM Discovery portfolio: modeling aging and modeling osteoarthritis using hPSC-based models. • Includes access to clinical samples to benchmark stem-cell driven OA models vs. patient derived data. • Applicant would be a first-time CIRM PI.
Synergy with former or existing CIRM investments	• If successful, a protocol to rapidly age stem cell-based models would be applicable to many other projects that aim to study age-related diseases • Participating labs are mentoring students through the CIRM Bridges and COMPASS programs

6. Application number: DISC5-19839

Title: Uncovering disease and cell-type-specific constraints on therapeutic delivery using a human CNS tissue discovery platform

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
88	87	94	80	12	3

CIRM Team Recommendation: Fund

DISC5-19839 proposes to establish a human CNS tissue research platform to identify mechanisms of cell-specific lipid nanoparticle (LNP) uptake for gene editing therapies, which is largely unknown. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Novel platform utilizing reperfused human CNS tissues obtained from donors to study LNP delivery mechanisms, a unique and underdeveloped approach • Addresses gap in knowledge of LNP delivery principles that affect successful therapeutic access • Applicant would be a first-time CIRM PI.
Synergy with former or existing CIRM investments	• Leverages previous CIRM investment (DISC2 Award), that established feasibility of CNS genome editing, with insights that will be used to define delivery principles in this proposal • If successful, will generate a scalable platform that will support translational research

7. Application number: DISC5-20195

Title: Decoding Human Pancreatic Progenitor Biology to Enable Next-Generation Stem Cell-based Therapies for Type 1 Diabetes

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
88	86	90	75	11	4

CIRM Team Recommendation: Fund

DISC5-20195 proposes to elucidate how pancreatic endocrine progenitors execute cell fate decisions in developing human tissue, generating knowledge to inform strategies for improved function, efficiency and yield of beta cells derived from hPSCs. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• The team leverages unique insights, tools and datasets from developing human pancreata to tackle longstanding challenges through a lens of human biology • The project will enrich CIRM's early-stage diabetes portfolio that is currently limited to 3 active awards: two exploring diabetes from an immune perspective and one focused on postnatal lineage pathways
Synergy with former or existing CIRM investments	• Resources and knowledge generated would benefit programs pursuing PSC-derived beta cell replacement therapy or endogenous beta cell regeneration

	• Potential to lead to less expensive/more efficient manufacture of PSC-beta cell therapy candidates such as those supported though previous CIRM investments • Intentional support and mentoring planned for CIRM EDUC trainees and those from similar programs

8. Application number: DISC5-20158

Title: Engineering Nephron Connectivity in Human Kidney Tissue Using Synthetic Signaling Centers

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
87	86	88	81	13	2

CIRM Team Recommendation: Fund

DISC5-20158 aims to advance kidney tissue engineering through use of synthetic morphogenic organizers to control the development and connectivity of nephrons in vitro. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Kidney research is currently underrepresented in the CIRM Discovery portfolio. This application proposes a novel approach to in vitro modeling of kidney tissue that could have broad applications beyond this initial study. • Applicant would be a first-time CIRM PI
Synergy with former or existing CIRM investments	• This application leverages preliminary data arising from a CIRM SRL to the applicant institution • Multiple laboratories associated with this application currently support CIRM Scholars trainees (EDUC4 grant)

9. Application number: DISC5-19638

Title: Systematic cell-type-resolved single-base resolution functional characterization of neurodevelopmental risk genes

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
86	86	88	85	14	0

CIRM Team Recommendation: Fund

DISC5-19638 proposes to systematically interrogate the functional impact of rare single-nucleotide variants associated with neuropsychiatric disorders across multiple central nervous system cell types. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Project applies a newly developed screening tool that enables interrogation of single-nucleotide disease-associated variants at single-cell resolution. • This capacity would have significant utility across basic research in multiple areas and overcomes significant technical hurdles to achieve.
Synergy with former or existing CIRM investments	• Strong potential to complement DISC4 ReMIND network due to its focus on molecular and genetic underpinning of neurodevelopmental disorders. • Demonstration of novel scalable variant profiling tool that may have strong use case in many research projects

10. Application number: DISC5-19747

Title: Leveraging lessons from normal development to overcome barriers to efficient transplantation of stem cell derived cortical neurons.

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
86	86	90	80	13	2

CIRM Team Recommendation: Fund

DISC5-19747 proposes to improve the ability of human pluripotent stem cell-derived cortical neurons to anatomically and functionally integrate into the adult brain, by deriving specific subtypes of cortical projection neurons and enhancing their axon outgrowth and cell migration. The CIRM team recommendation concurs with the GWG. In addition, the

CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Uses cutting edge molecular analyses to address a translationally relevant hurdle for cell replacement therapies in movement disorders. • Makes use of single cell RNA sequencing data from developing human brain
Synergy with former or existing CIRM investments	• Leverages CRISPR screening strategy established with prior support from CIRM (DISC0 award). • If successful, approach may be generally applicable to the development of a broad range of cell replacement therapies in the nervous system.

11. Application number: DISC5-19949

Title: Neurovascular control of follicle growth using stem-cell derived ovary assembloids

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	86	90	80	13	2

CIRM Team Recommendation: Fund

DISC5-19949 proposes to study ovarian follicle function, focusing on the coupled neurovasculature microenvironment to understand how this interplay can influence therapeutic strategies for ovarian aging, polycystic ovarian syndrome (PCOS), and other infertility-relevant conditions. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Research in ovarian aging and reproductive health, underrepresented in portfolio • Applicant would be a first time CIRM PI • Unique focus on neurovascular-ovarian network • Novel first creation of ovarian assembloids • Applicant would be a first-time CIRM PI.
Synergy with former or existing CIRM investments	• Potential synergy with DISC4 network, team includes co-I on DISC4 award with expertise in assembloids

	• Incorporation of vascular components into organoids, if successful, could be useful technique for organoid-relevant research

12. Application number: DISC5-19810

Title: Impact of Sex-Differences on Intestinal Stem Cell Function in Pediatric Inflammatory Bowel Disease

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	86	90	80	12	3

CIRM Team Recommendation: Fund

DISC5-19810 proposes to understand how sex and puberty contribute to inflammatory bowel disease pathology by exploring the effects of sex-specific signaling on intestinal stem and epithelial cell states. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Significantly enriches CIRM's portfolio of programs targeting intestinal diseases, which is currently limited to a couple of DISC programs focused on nervous system aspects of intestinal function • Exploring the role of sex-specific hormones on intestinal pathology is novel to CIRM portfolio and may establish a conceptual framework for investigating sexually dimorphic stem cell regulation in other tissues and disease contexts • Makes use of pediatric patient-derived samples across pre- and post-pubertal developmental stages, a unique and understudied resource • The PI, a practicing pediatric gastroenterologist, brings a specialized clinical perspective to CIRM's portfolio and would be a first-time CIRM PI
Synergy with former or existing CIRM investments	• Omics datasets will complement those from other CIRM teams exploring effects of inflammatory states on tissue microenvironments

13. Application number: DISC5-19686

Title: Allelic Expression States as Determinants of Neurodevelopmental Disorder Risk

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	85	90	80	13	2

CIRM Team Recommendation: Fund

DISC5-19686 proposes to define how monoallelic and biallelic expression states arise, are maintained, and influence neurodevelopmental disorder risk during human cortical development. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• This project's focus on allelic expression states represents a novel perspective that complements CIRM's broader neurodevelopmental disorder research portfolio.
Synergy with former or existing CIRM investments	• Strong potential to integrate with existing DISC4 ReMIND network awards focused on neurodevelopmental disease. • The human iPSC neural platforms and experimental infrastructure proposed in this study were enabled via a prior CIRM Early Translational award. • PI and Co-I support CIRM Scholars trainees (EDUC4 grant)

14. Application number: DISC5-20061

Title: Characterizing how neurons from human stem cell transplants integrate into spinal neural circuits following injury

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	85	86	83	13	2

CIRM Team Recommendation: Fund

DISC5-20061 proposes to characterize the mechanisms and properties of neural circuit formation and network activity in the context of neural stem cell transplantation for the treatment of spinal cord injury. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Application of novel tools, including spatial transcriptomics and in-vivo microelectrode recordings, to dissect circuit formation in spinal cord grafts to improve graft efficiency.
Synergy with former or existing CIRM investments	• Innovative tools deployed in this project to understand circuit function may find synergy amongst ReMIND networks and with other neuroscience focused projects through protocol and data sharing • Insights will inform current and future translational efforts employing neural stem cell based regenerative therapies in multiple injury and degenerative conditions

15. Application number: DISC5-19811

Title: Mapping Human Retinal Niches to Improve Stem-Cell Therapy for Geographic Atrophy

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	85	90	75	10	4

CIRM Team Recommendation: Fund

DISC5-19811 proposes to define the cellular, molecular and extracellular features of retinal regions affected by geographic atrophy and their effects on transplanted stem cell-derived retinal grafts to enable rational, niche-aware therapeutic design. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Applicant would be a first time CIRM-PI, a physician scientist engaging in stem cell-based discovery research • Uses micron-scale robotic system that enables spatial tissue harvesting and cell placement not achievable manually.

Synergy with former or existing CIRM investments	• CIRM has invested in stem cell-based therapies for blinding eye diseases, and this research has the potential to help overcome the bottleneck of poor transplanted cell survival. • Generates a resource of imaging and omics atlases of the retina affected by geographic atrophy.

16. Application number: DISC5-19893

Title: Revealing the Mechanistic Architecture Governing CAR-T Cell Potency and Failure at Single-Cell Resolution

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	84	85	75	13	2

CIRM Team Recommendation: Fund

DISC5-19893 proposes to define how cell-cell interactions can be shaped by chimeric antigen receptor (CAR) design and intrinsic immune states, aiming to establish a mechanistic framework to address bottleneck of patient-specific therapeutic failure. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Novel atlas that will address how CAR engineering designs affect cellular immune states and functional outcomes at the single-cell level
Synergy with former or existing CIRM investments	• Partnering with a CIRM Community Centers of Excellence grantee for donor samples • PI partners with an academic GMP facility supported by a CIRM INFR program, which helped establish the non-viral CAR-T engineering platform described in this proposal • Generating unique atlas with biologically diverse patient-derived material, which will be a community resource

17. Application number: DISC5-19870

Title: Foundational Mapping of Splicing-Derived Neoantigen Recognition in Human Sarcoma Using Stem Cell-Enabled Immune Platforms

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	84	93	75	8	7

DISC-19870 proposes to develop and validate an automation-enabled platform for discovering neoantigens associated with sarcoma that can meaningfully activate T cells. If successful, this platform could be utilized to develop new and more broadly effective immunotherapies for sarcoma and other solid tumors. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Investigating tumor-specific RNA splicing events to identify neoantigens is a unique approach within CIRM's portfolio • Enriches CIRM's portfolio in sarcoma which is currently limited to one active clinical trial-stage award, focused on singular previously studied antigen • Applicant would be a first-time CIRM PI.
Synergy with former or existing CIRM investments	• Project leverages CIRM's INFR6 program (Shared Resources Lab) to ensure rigor

18. Application number: DISC5-19807

Title: A precision organoid platform to investigate APOE4 dependent cerebrovascular impairments

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	84	90	75	7	6

CIRM Team Recommendation: Fund

DISC5-19807 proposes to develop functional vascularized brain organoids to interrogate the role of APOE4 in neurovascular organization and function. The CIRM team

recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• The successful establishment of a human vascularized brain organoid platform modeling the blood brain barrier (BBB) would address a major bottleneck in drug discovery and development. • Applicant would be a first-time CIRM PI.
Synergy with former or existing CIRM investments	• Strong potential to integrate with ReMIND network teams focused on neurodevelopmental and neurodegenerative disorders. • This BBB organoid system, if successful, would be of great utility to many investigators in the CIRM Discovery and Preclinical portfolio.

19. Application number: DISC5-19957

Title: Spatiotemporal Control of Human Primordial Germ Cell Fate by the Embryonic Niche

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	83	85	75	9	6

CIRM Team Recommendation: Fund

DISC5-19957 proposes to apply stem cell-based embryo models to understand the cues that drive specification of primordial germ cells, which give rise to all eggs and sperm cells. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• The topic of reproduction and fertility has been historically under-represented in the CIRM portfolio; currently no active awards focused on developmental biology of germ cells. • This project applies novel human embryoid models and unique approaches like 4D live-imaging to study key processes at the very early stages of embryonic development.
Synergy with former or existing CIRM investments	• Comprehensive multimodal approach and analytical tools to map niche dynamics and interactions may have relevance to the study of other complex

	cellular interactions as proposed in other DISC awards

20. Application number: DISC5-19950

Title: Temporal AI models for programming therapeutic cell state transitions

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	82	90	60	8	7

CIRM Team Recommendation: Fund

DISC5-19950 proposes to develop temporal, not static, AI models, based on stem cell-based modeling and CRISPR engineering, to enable the prediction of effective interventions in Alzheimer disease (AD). The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• PI is early-career investigator and would be first-time CIRM awardee. • Utilizes novel foundational AI model developed by the team for predicting the impact of perturbations on cells. • Shared code will be accompanied by tutorials for ease of access.
Synergy with former or existing CIRM investments	• New findings relevant to potential AD targets may be complementary to other CIRM-funded AD findings. • PI and Co-I mentor current CIRM Scholars and Bridges students (EDUC4, EDUC2), respectively

21. Application number: DISC5-19900

Title: Validating Safety and Efficacy of Extremeophile Stress Tolerance Transgenes in Stem Cells

GWG Outcome: Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
85	82	95	60	7	7

CIRM Team Recommendation: Fund

DISC5-19900 proposes to engineer stem cells that express tardigrade stress tolerance genes to address the bottleneck of delivery and grafting-related damage in stem cell therapy. The CIRM team recommendation concurs with the GWG. In addition, the CIRM team believes that this project would enhance the value of the discovery portfolio by addressing the following:

Potential to enhance the value of CIRM's Discovery portfolio through novel approaches or attributes	• Applicant would be a first-time CIRM PI • Novel to CIRM portfolio and underrepresented area using extremophile biology (tardigrades) to discover potential in therapeutic use
Synergy with former or existing CIRM investments	• PI has strong track record of mentoring CIRM trainees through COMPASS and Scholars programs

22. Application number: DISC5-20142

Title: APOE4 compromises BBB integrity through pericyte-microglia cross talk

GWG Outcome: Do not fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
84	84	90	81	5	8

CIRM Team Recommendation: Do not fund

DISC5-20142 proposes to investigate how the APOE4 genotype drives early cerebrovascular dysfunction through cell-cell interactions at the blood-brain barrier. The CIRM team recommendation concurs with the GWG.

23. Application number: DISC5-19775

Title: Mechanisms driving the tempo of life in human cells

GWG Outcome: Do Not Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
83	83	88	75	7	8

CIRM Team Recommendation: Do Not Fund

DISC5-19775 proposes to understand how glycogen metabolism regulates the tempo of maturation and regenerative potential in human stem cells, and how these processes deteriorate with aging and disease. The CIRM team recommendation concurs with the GWG.

24. Application number: DISC5-19843

Title: Causes and consequences of age-related myeloid bias

GWG Outcome: Do Not Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
83	82	85	70	6	9

CIRM Team Recommendation: Do Not Fund

DISC5-19843 proposes to study the genetic basis, disease associations, and mechanisms of age-related myeloid-bias in hematopoietic stem cells (HSCs) and the effect of that myeloid bias on immune function and disease susceptibility. The CIRM team recommendation concurs with the GWG.

25. Application number: DISC5-19705

Title: Leveraging natural and engineered hematopoietic surface receptor variation for non-toxic stem cell transplantation

GWG Outcome: Do Not Fund

Median	Mean	High	Low	Scores to fund	Scores not to fund
82	82	88	74	6	9

CIRM Team Recommendation: Do Not Fund

DISC5-19705 proposes to enhance human hematopoietic stem cell engraftment during transplantation by studying surface receptor biology to advance non-toxic HSCT. The CIRM team recommendation concurs with the GWG.