SHARED RESOURCES LABS

APP #	TITLE	TOTAL BUDGET REQ	GWG SCORE	1	2	3	FWG SCORE	1	2	3	CIRM Recommendation
INFR6.1-15363	Stem cell-based Partnership Resource for Investigating Human Diseases and Training (SPRINT)	**$5,400,000**	**1**	10	5	0	**1**	8	0	0	FUND
INFR6.1-15366	Shared Research and Training Facility for Bio-Fabrication of Organs for Regenerative Medicine (Bio-FORM) in Underserved Areas	**$5,400,000**	**1**	13	2	0	**3**	0	0	8	DO NOT FUND
INFR6.1-15413	Resources for Expanding Stem cell-derived Tissues and Organs for Regenerative Engineering (RESTORE)	**$5,396,133**	**1**	8	4	0	**1**	8	0	0	FUND
INFR6.1-15478	The Live Cell Biotechnology Discovery Lab	**$5,399,996**	**3**	0	0	13	**1**	5	4	0	DO NOT FUND
INFR6.1-15517	Shared Resource Laboratory for Human Stem Cell-Based Modeling (SRL-hSC)	**$4,399,888**	**1**	13	0	0	**1**	9	1	0	FUND
INFR6.2-15440	Shared Resource Laboratory for Stem Cell-Based Modeling: Resources for Exploring the Biological Underpinnings of Aging and Age-Associated Pathologies	**$3,641,064**	**1**	12	1	0	N/A				FUND
INFR6.2-15416	Expanding and enhancing molecular, cell biological and bioengineering resources for stem cell-based models	**$4,000,000**	**2**	1	11	1	N/A				DO NOT FUND
INFR6.2-15475	Shared Resource Laboratory for Advanced Stem Cell-Based Modeling	**$3,991,879**	**1**	12	0	0	N/A				FUND

APP #	TITLE	TOTAL BUDGET REQ		GWG SCORE	1	2	3		FWG SCORE	1	2	3		CIRM Recommendation
INFR6.2-15403	Enhancing/Expanding Stem Cell-Based Modeling at a Shared Research and Training Facility	**$3,760,466**		**2**	2	10	0		N/A					DO NOT FUND
INFR6.2-15457	Shared Resources Laboratory for Stem Cell-Based Modeling in Stem Cell Biology and Engineering	**$3,999,995**		**1**	13	0	0		N/A					FUND
INFR6.2-15513	A Comprehensive Biorepository of Human Induced Pluripotent Stem Cells and Their Cardiovascular Derivatives	**$3,994,062**		**2**	2	10	1		N/A					DO NOT FUND

Application #	INFR6.1-15363 #2
Title (as written by the applicant)	Stem Cell-based Parternship Resource for Investigating Human Diseases and Training (SPRINT)
Project Objective (as written by the applicant)	Use of stem cells in human disease modeling has reached a broader scientific audience of underserved, marginalized communities. Researchers/scholars have comprehensive training in iPSC generation, genetic modification, and differentiation techniques to model human diseases successfully.
Summary (as written by the applicant)	The centralized facility is designed to advance the use of human pluripotent stem cells (hPSC) for human disease modeling among researchers from partner institutions with limited access to stem cell laboratory resources, expertise, training, and services. Structurally, it consists of two arms: - A research arm will: 1) provide a shared stem cell laboratory to researchers and scholars from minority, underserved, and diverse community services; and 2) partner with research institutions that engage in health disparities and minority health research. - An educational arm will focus on comprehensive training in: 1) generating patient-derived iPSC lines, 2) generating genetically modified ESC/iPSC lines, and 3) differentiation into neural cell types. The core has three objectives: 1. Provide users access to equipment and expertise for the generation, reprogramming, and genetic modification of hPSCs, to address human diseases, especially those suffered by minority and marginalized communities. 2. Provide directed differentiation of hPSCs into organ and lineage-specific cell types allowing the modeling of human diseases in 2D and/or 3D (e.g., organoids) cultures for comprehensive disease research. 3. Provide comprehensive online and hands-on training in iPSC generation, genetic modification, and differentiation techniques to model human diseases successfully.
Statement of Benefit to California (as written by the applicant)	The core fills a gap for the scientific community, particularly those studying underserved populations where access to resources, training, expertise, and services for hPSCs is limited and distance and transportation costs are deterrents to stem cell research participation. The patient population, particularly those who lack equitable medical services, will benefit from the support of regenerative or modeling tools of human diseases that may have delayed diagnosis and that often lack treatments.
Funds Requested	$5,400,000
FWG Recommendation	**Tier 1: warrants funding**
Process Vote	All FWG members unanimously affirmed that “The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the FWG.” Patient advocate members unanimously affirmed that “The review was carried out in a fair manner and was free from undue bias.”

SCORING DATA

Final Score: 1

Up to 11 members of the FWG score each application. The final score for an application is the majority score of all of the individual member scores. Additional parameters related to the score are shown below.

Highest	1
Lowest	1

Count	8
Votes for Tier 1	8
Votes for Tier 2	0
Votes for Tier 3	0

- A score of "1" means that the application has exceptional merit and warrants funding.
- A score of "2" means that the application needs improvement and does not warrant funding but, at the applicant's option, may be resubmitted to address areas for improvement if the Application Review Subcommittee has not approved an application for funding following the Grants and Facilities Working Group's review.
- A score of "3" means that the application is sufficiently flawed that it does not warrant funding.

KEY QUESTIONS AND COMMENTS

Proposals were evaluated and scored based on the key questions shown below, which are also described in the PA/RFA. Following the panel's discussion and scoring of the application, the members of the FWG were asked to indicate whether the application addressed the key question and provide brief comments assessing the application in the context of each key question. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

FWG Votes	Does the proposed renovation/facilities improvement project support the applicant's proposed SRL core research and educational activities?
Yes: 3 **No:** 0	• The revised proposal does an exceptional job of clearly defining the scope of work. The revised design and related narrative are demonstrative of a highly efficient and functional layout. • Yes; the applicant takes a very thorough approach, and has made impressive updates to the application. • The grant applicant has responded to reviewer feedback, thus improving the application to a fundable level. • This is a very thorough revision, with detailed back-up information.
FWG Votes	**Are the SRL renovations/facility improvements feasible as proposed?**
Yes: 3 **No:** 0	• Yes. The drawings are well developed, equipment is identified as back up, and a GC budget is provided. All detail needed to determine feasibility is provided. • The revised proposal has done an excellent job of clearly describing the existing conditions and adjacent uses and the appropriate scope of work to support the intended design. • Yes. The revised proposal illustrates an ideal arrangement that mitigates issues related to chemical storage, building vibration, and placement of vibration-sensitive equipment. • The revised proposal includes a realistic and adequate project schedule, with key milestones and activities. • Detailed plans/blueprints make clear the scope, the nature of the buildings, and exactly where the costs go. This is very nice work for pre-construction level scope and drawings. • The project managers have extensive experience in lab renovations.
FWG Votes	**Does the proposed SRL facility include the appropriate research equipment and laboratory configuration in support of the proposed SRL activities?**
Yes: 3 **No:** 0	• Yes, all back up for equipment plus the as-builts and how to modify the MEP systems to accommodate are provided in the revised submission. • The revised proposal, including both drawings and narratives, includes the appropriate MEP services and utility connections. • Yes, the applicant did a great job describing existing systems and equipment as well as appropriate addition/placement of new equipment. • Yes, the revised layout and increased square footage are ideal for the intended scope of functions. • The applicant took into consideration the comments of the first review and was able to secure additional space to support the proposed functions. • The application seems very well put together, by what appears to be an experienced crew that understands facilities construction and work-flow.

FWG Votes	Are the renovation/facility improvement costs appropriate?
Yes: 3 **No:** 0	• Yes, costs are appropriate and back-up has been provided. • The revised budget estimate clearly includes appropriate allowances for a project of this type. • A major strength is the completeness of planning.
FWG Votes	**Does the applicant ensure diversity, equity and inclusion goals for design and construction?**
Yes: 3 **No:** 0	• A very detailed plan to address DEI is provided. • In the revised application, both budget and narrative clearly demonstrate adequate compliance with the requirements of Prop 14. • In the original application, the applicant did not fully understand the DEI question. In the revised application, the applicant did an exceptional job of clearly addressing DEI compliance. • This is a very good application that is much improved. • DEI for the overall proposal is very strong.

Application #	INFR6.1-15366 #2
Title (as written by the applicant)	Shared Research and Training Facility for Bio-Fabrication of Organs for Regenerative Medicine (Bio-FORM) in Underserved Areas
Project Objective (as written by the applicant)	The shared Bio-FORM Core will introduce organoid models to the research community in underserved areas and provide a knowledge-sharing platform and ecosystem for hands-on training and developing advanced organoid technologies and 3D organs toward regenerative medicine applications.
Summary (as written by the applicant)	This proposal aims to develop a "Shared Research and Training Facility for Bio-Fabrication of Organs for Regenerative Medicine (Bio-FORM) in Underserved Areas." A diverse group of researchers, students, and start-up companies in the Inland Empire have voiced strong interest in working with organoids and have identified a critical need for essential training and facilities. The Bio-FORM Core will establish a critical platform for researchers in underserved areas to enter organoid work and create advanced 3D organs with cutting-edge engineering technologies. The Bio-FORM Core aims to support both research and educational programs and create vital linkages between them for diverse students and researchers. This Core will support a rich ecosystem of interdisciplinary regenerative medicine research, grounded in organoid culture methodologies and advanced engineering technologies in 3D printing. The shared Bio-FORM Core will enable researchers, educators, trainees, and medical professionals in the Inland Empire to gain direct access to a state-of-art research and training facility. The Bio-FORM Core will offer nine hands-on training courses for key techniques. Videos of course materials will be published and be accessible online by anyone in California. The Core will provide easy and low-cost access for making cutting-edge scientific discoveries in Stem Cells and Regenerative Medicine, share research and training opportunities, disseminate knowledge, raise awareness among under-resourced communities, and break the infrastructural and technical barriers for adoption of new technologies and therapies in underserved areas. Such facilities and the attendant training would be unique in the Inland Empire. Inland Empire is a geographically, socioeconomically, medically, and educationally underserved region with a diverse population. By providing a critical entry point for training and access to major instruments, the shared Bio-FORM Core will enable researchers to: (1) work with organoid models, (2) create stem cell-based 3D models of organoids, tissues and organs to be more like those in vivo, and (3) produce complex, 3D tissue structures and organs for regenerative therapies. This Core will transform regenerative medicine research beyond current organoid culture by providing training and access to state-of-the-art 3D to 4D printing technologies and other major analytical instruments. The Bio-FORM core will enhance the efficiency, accuracy, and creativity in stem cell and regenerative medicine research, enabling groundbreaking discoveries and fostering collaborations beyond Inland Empire. The users of Bio-FORM Core will be diverse, including students and researchers in the Inland Empire, from startup companies, from California State University (CSU) partners, and institutions of Inland Empire and greater Los Angeles Regenerative Medicine Consortium.
Statement of Benefit to California (as written by the applicant)	Located in the Inland Empire, the Bio-FORM Core will provide researchers, educators, trainees, and regional medical professionals with access to a state-of-the-art research & training facility. Bio-FORM will support fundamental science and translational research. For California and the Inland region (a medically underserved area), this Core will raise stem cell awareness, reduce infrastructural barriers to scholarship, and enable clinical translation of new therapies for underserved populations.
Funds Requested	$5,400,000
FWG Recommendation	**Tier 3: sufficiently flawed, cannot be resubmitted**
Process Vote	All FWG members unanimously affirmed that "The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the FWG."

	Patient advocate members unanimously affirmed that "The review was carried out in a fair manner and was free from undue bias."

SCORING DATA

Final Score: 3

Up to 11 members of the FWG score each application. The final score for an application is the majority score of all of the individual member scores. Additional parameters related to the score are shown below.

Highest	3
Lowest	3
Count	8
Votes for Tier 1	0
Votes for Tier 2	0
Votes for Tier 3	8

- A score of "1" means that the application has exceptional merit and warrants funding.
- A score of "2" means that the application needs improvement and does not warrant funding but, at the applicant's option, may be resubmitted to address areas for improvement if the Application Review Subcommittee has not approved an application for funding following the Grants and Facilities Working Group's review.
- A score of "3" means that the application is sufficiently flawed that it does not warrant funding.

KEY QUESTIONS AND COMMENTS

Proposals were evaluated and scored based on the key questions shown below, which are also described in the PA/RFA. Following the panel's discussion and scoring of the application, the members of the FWG were asked to indicate whether the application addressed the key question and provide brief comments assessing the application in the context of each key question. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

FWG Votes	Does the proposed renovation/facilities improvement project support the applicant's proposed SRL core research and educational activities?
Yes: 0 **No:** 3	• The revised proposal material presents a general high-level concept that effectively illustrates the functional adjacencies and separation of processes. However, it lacks several crucial baseline details, both graphically and narratively, which are necessary for a comprehensive evaluation. Specifically, the proposal does not address the following 7 concerns. Due to the absence of the critical information above, it is currently impossible to determine whether the proposed project can adequately support the intended research and education activities. More comprehensive information is required to ensure all aspects of the project are thoroughly evaluated and planned. 1. Existing Conditions: Information on the current state of the building, including structural integrity and any existing limitations, is missing. 2. Available Capacity of Building Utility Infrastructure: The proposal does not provide details on the current capacity of the building's utility infrastructure (e.g., HVAC, water supply, waste management) and whether it can support the proposed additions or modifications. 3. Electrical Requirements: There is no detailed assessment of the electrical needs of the new project, including power consumption estimates and distribution plans. 4. Emergency Power System Remaining Capacity: The proposal does not include an analysis of the emergency power system's current capacity and its ability to handle additional load from the new project. 5. Plumbing Requirements: The document lacks information on the plumbing requirements for the proposed project, including water supply, drainage, and waste disposal needs. 6. ADA Compliance: There is no mention of how the proposed project will meet the standards set by the Americans with Disabilities Act (ADA) to ensure accessibility for all users.

	7. Other Critical Details: Additional essential elements, such as safety protocols, environmental impact assessments, and compliance with local building codes, are not covered in the resubmission. ● The biggest concern is that application did not address the real concerns from the original application (time/unknown cost/realistic feasibility/security of the facility in the future) and in fact provided updates that made less logistical sense overall and clouded real (and potential) costs even further. The additional concern related to their high laboratory equipment costs (in some cases easily up to 2x) means all costs are questionable. ● Drawings have not been developed enough to support the budget and back-up provided. ● Did not respond sufficiently to the previous (1st) review of this application.
FWG Votes	**Are the SRL renovations/facility improvements feasible as proposed?**
Yes: 0 **No:** 3	● The proposal has an unrealistic schedule. Many questions or concerns from the prior review were addressed as to be dealt with in the future. ● The revised proposal lacks sufficient information to determine its feasibility. Specifically, the following two critical elements are missing. Without addressing these issues and providing the necessary supporting information, it is not possible to accurately assess the feasibility of the proposed project. More detailed and justified financial planning is required to ensure that the project can be completed within budget and without compromising quality or functionality. 1. Justification for Low Construction Allowances: The proposal does not include any backup information or rationale to support the unusually low construction allowances. This raises concerns about the accuracy and realism of the projected budget. 2. Low Construction Contingency: Considering the extensive number of unknown conditions and the uncertain capacities of existing utilities, the construction contingency appears to be inadequate. This low contingency does not provide a sufficient buffer for unforeseen issues that may arise during the project. ● Feasibility is difficult to evaluate, given the inadequate information on timeline/costs. ● Too many problems with the architectural scheme were identified: extent of bringing a very old building up to modern standards, issues with scale; uncertainty as to how long the lab would be able to occupy the space (and not be dislodged), addressing ADA-related issues; capacity of generators; and a low contingency cost %.
FWG Votes	**Does the proposed SRL facility include the appropriate research equipment and laboratory configuration in support of the proposed SRL activities?**
Yes: 1 **No:** 2	● The proposal seems to include the right equipment, but not in a layout that makes sense or is usable given ADA/path-of-travel. ● This seems to have a very high equipment budget or duplicative equipment, plus quotes were expired. ● Major issues were raised as to the cost of many pieces on the inventory request list, even with allowances for maintenance contract costs. ● The equipment outlined in the proposal appears to be adequate to support the SRL activities. However, there are several major concerns about the adequacy of the laboratory configurations, including the list below. These concerns highlight significant gaps in the proposal that need to be addressed to ensure the laboratory configurations are adequate to support the intended SRL activities effectively and safely. 1. Spacing and Clearances: The proposal does not provide detailed information on the spacing and clearances within the laboratory, which are critical for safe and efficient operation. 2. Personnel Pathways: There is a lack of clarity on the pathways for personnel movement within the laboratory. Well-defined pathways are essential to ensure smooth workflow and safety. 3. ADA Accommodations: The proposal does not adequately address accommodations required to comply with the Americans with Disabilities Act (ADA), ensuring accessibility for all individuals. 4. IT Network: There is no mention of an IT network infrastructure to support the laboratory's digital and data needs. A robust IT network is essential for modern laboratory operations. 5. Equipment Monitoring Systems: The proposal does not include information about systems for monitoring equipment, which are crucial for maintaining operational efficiency and preventing equipment failures. 6. Security Systems: There is a lack of detail on the scope of security systems, which are necessary to protect sensitive data and equipment within the laboratory.

FWG Votes	Are the renovation/facility improvement costs appropriate?
Yes: 1 **No:** 2	● The budget might be appropriate; however, the drawings are not sufficiently developed to support the budget provided. ● The revised budget for construction-related work lacks critical details, raising several concerns: 1. Lump Sum Allowances: The budget does not break down the lump sum allowances for major categories of work, making it difficult to understand the allocation of funds and the feasibility of the estimates provided. 2. Deferred Assessments: Numerous deferred conditions and building systems assessments are not addressed, adding uncertainty to the project's overall cost and timeline. 3. Low Construction Contingency: The construction contingency is unusually low, especially given the number of unknown conditions and potential issues with utility capacities. This poses a significant risk of budget overruns. 4. Missing Internal Fees: The renovation budget omits standard internal fees for services typically provided by the applicant institution's design and construction departments. These include fees for plan reviews, project management services, inspections, and shutdowns. The omission of these fees is atypical for an institution of this type. 5. Missing Fees for External Consultants: Similarly, fees for external consultants are not included, which is unusual and problematic, as these services are essential for a comprehensive and accurate project plan. 6. Expired Vendor Quotes: All vendor quotes included in the revised submittal expired in 2023, rendering them invalid. Updated quotes should have been secured prior to resubmitting the application to ensure budget accuracy. 7. Inflated Vendor Estimates: Several vendor estimates for equipment appear substantially higher than the retail list prices and do not reflect any discounts, especially those that the institution has negotiated with numerous vendors. ● Costs of equipment does not reflect actual costs of such equipment - makes estimate as reported in the application unreliable. ● No, given what has been supplied by the applicant.
FWG Votes	Does the applicant ensure diversity, equity and inclusion goals for design and construction?
Yes: 3 **No:** 0	● DEI has been thoroughly addressed. ● The application appropriately includes information based on institutional policies related to Diversity, Equity, and Inclusion (DEI), which they are mandated to comply with. ● This is the strongest part of the application. ● DEI is mostly OK and deserved some merit as written, but overall it is not up to the highest possible standard.

Application #	INFR6.1-15413 #2
Title (as written by the applicant)	Resources for Expanding Stem cell-derived Tissues and Organs for Regenerative Engineering (RESTORE)
Project Objective (as written by the applicant)	The areas of focus for our SRL will include induced pluripotent stem cell generation and characterization, cell differentiation and generation of a microvascular tissue model and in vivo models.
Summary (as written by the applicant)	This SRL aims to broadly support research and educational needs in human stem cell culture, stem cell differentiation, cell and tissue characterization, transplantation, small-animal imaging, and vascular modeling. The specific stem cell models, chosen based on expertise of the faculty, will focus on using human embryonic stem cells (ESCs) and human induced pluripotent stem cells (iPSCs) to direct vascular stem cell fates and vascular tissue development. The SRL will also generate and offer new human stem cell products: genetically diverse iPSC lines and differentiated endothelial cells (ECs). We will also offer an online introductory stem cell course plus three weeks of intensive in-person summer Stem Cells Techniques Courses with lessons in Human Stem Cell Culture, Stem Cell Differentiation, Cell and Tissue Characterization, Microfluidic Device Design and Fabrication, Cell-Material Hydrogel Assemblies, Image Analysis, Animal Handling, Human Stem Cell Transplantation, Tracking and Quantifying Stem Cell Transplantation using a Variety of Imaging Scanners.
Statement of Benefit to California (as written by the applicant)	Our stem cell-based models will provide diverse iPSCs and hands-on trainings to California's Central Valley where access to these models is limited and populations are diverse. The core offerings will be shared using protocol booklets and video tutorials posted on our SRL website and through hands-on mentoring within the facility and through multiple techniques courses focused on iPSC culture, characterization, vascular cell differentiation and tissue models, transplantation, and imaging.
Funds Requested	$5,396,133
GWG Recommendation	**Tier 1: warrants funding**
Process Vote	All GWG members unanimously affirmed that “The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the GWG.” Patient advocate members unanimously affirmed that “The review was carried out in a fair manner and was free from undue bias.”

SCORING DATA

Final Score: 1

Up to 15 scientific members of the GWG score each application. The final score for an application is the majority score of all of the individual member scores. Additional parameters related to the score are shown below.

Highest	1
Lowest	2
Count	12
Votes for Tier 1	8
Votes for Tier 2	4
Votes for Tier 3	0

- A score of “1” means that the application has exceptional merit and warrants funding.
- A score of “2” means that the application needs improvement and does not warrant funding but, at the applicant’s option, may be resubmitted to address areas for improvement if the Application Review Subcommittee has not approved an application for funding following the Grants and Facilities Working Group’s review.
- A score of “3” means that the application is sufficiently flawed that it does not warrant funding.

KEY QUESTIONS AND COMMENTS

Proposals were evaluated and scored based on the key questions shown below, which are also described in the PA/RFA. Following the panel's discussion and scoring of the application, the members of the GWG were asked to indicate whether the application addressed the key question and provide brief comments assessing the application in the context of each key question. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

GWG Votes	Does the proposed SRL offer a significant value proposition?
Yes: 12 **No:** 0	• This SRL proposal aims to build a new core facility and aims to provide access to shared resource to support research in human stem cell culture, stem cell differentiation, cell and tissue characterization, transplantation, small-animal imaging. The Stem Cell Transplantation Techniques training in proposed SRL is especially useful, which currently very few stem cell cores provide. • The revised version of the proposal has adequately addressed the open questions and recommendations of the reviewers. Hence, the significant improvements and clarifications make the proposed stem cell models, services, technologies, and training courses adequate and fill critical needs in California and particularly the underserved Central Valley area. • This is an underserved area with high potential for impact. While there will be bumps along the way, the team is committed to this project and will be able to drive it forward. • In the revised proposal, they have included additional letters of support from potential users. However, the interest in the proposed service of iPSC-derived endothelial cell models are not identified. The Technical Director lacks experience in iPSC generation and the iPSC-derived endothelial cell model which would be necessary to guide the proposed services.
GWG Votes	**Is the project well planned and designed?**
Yes: 10 **No:** 2	• Yes, the outcome criteria as it relates to impact and services will be measured in quarterly meetings held by the leadership team. Furthermore, success criteria will be measured by assessing learning outcomes, participation of underserved scientists, and sustainability. • The presented knowledge sharing plan is realistic, well-developed, and will have a significant impact on connecting the underserved Central Valley scientists to other stem cell centers in California. • While there is some question about specifics of users and projects, once built, researchers and students will find ways to use the facilities. • In the revision, addition of anticipated users that are interested in iPSC generation and cell culture are identified. The interest in the proposed service of iPSC-derived endothelial cell models are not identified. • The Technical Director's expertise in SRL organization, equipment repair, and other laboratory day-to-day operations is well suited. However, they lack experience in iPSC generation and the iPSC-derived endothelial cell model that is proposed. It is important that the Technical Director has extensive experience to guide the daily projects, services and troubleshooting of the proposed services.
GWG Votes	**Is the project feasible?**
Yes: 10 **No:** 2	• The proposed plan is feasible: Lab space is provided. Instruments and trainings can be established based on the experience of the personnel. • The models are well-developed and the decision of the applicants to focus on vascular progenitors and endothelial cells in the revised proposal is an advantage. • The available technologies and the planned acquisition of new instruments are appropriate. • The rooms are built and ready to be filled with equipment. • Yes. The team led by the Program Director is experienced and qualified and staffed to execute the project plan. Both the Program Director and co-Director were recipients of CIRM New Faculty awards. The revised proposal clarified that three faculty members and one staff person are currently dedicated to the SRL and two additional hires (100% time) will bring the number to a total of six. • The Program Directors have proven stem cell expertise, education experience and the management. However, an experienced iPSC biologist would be required for daily

	operations for the stem cell based modeling component in the SRL. This is not addressed in the revision. ● My concern is this SRL might operate as an expansion of the imaging core. The users could reach out for imaging instruments but not for conducting stem cell based modeling research. ● The criteria focusing on SRL lab set up, charge system, hiring and workshop is fully commissioned. In the revision, the training plan is more clear. The outcome criteria for the increased stem cell services is unclear.
GWG Votes	**Does the project effectively uphold the principles of diversity, equity and inclusion?**
Yes: 12 **No:** 0	● This institution is well positioned to to train historically marginalized and underrepresented students. The student body reflects the ethnic diversity of its community (55% Hispanic, 20% Asian/Pacific Islander, 4.5% African American/Black, <1% Native American, 10% White, 3% Multiracial). ● It is expected that the SRL will play an important role in the region making stem cell training and education accessible to underserved communities (e.g., Hispanic, Native American, African-American, Asian-American, Pacific Islander). ● This is an underserved area with a majority minority population. This team will be an asset to this endeavor. ● The SRL aims to provide access to shared research facilities and equipment to support stem cell biology and regenerative medicine research in the California Central Valley. ● Fills a need in the local research community and can offer services to other stem cell investigators in this part of the state. ● Newly established iPSC lines will reflect population diversity and inclusion. ● The SRL team is scientifically diverse and will also proactively seek individuals with diverse backgrounds, cultures, and experiences, cultivating a range of viewpoints.
GWG Votes	**<u>IF PROPOSED, is the Stem Cell Techniques Course well designed?</u>**
Yes: 11 **No:** 0	● As recommended by the reviewers, the applicant has separated the courses. The first course is an online introductory course on stem cells. The second course is a two-week in-person course with hands-on labs on iPSC generation, culture, and characterization. The third course is a one-week in-person course with hands-on labs on stem cell transplantation and imaging techniques. ● The team has improved the courses based on previous suggestions and it will serve the population well. ● Yes, the proposed are well designed supporting stem cell researchers with different needs, especially the training for Stem Cell Transplantation Techniques, which currently very few stem cell cores provide.

Application #	INFR6.1-15478 #2
Title (as written by the applicant)	The Live Cell Biotechnology Discovery Lab
Project Objective (as written by the applicant)	We aim to bring stem cell-derived neuronal models to underserved classrooms by taking advantage of cloud-enabled microscopes, electrophysiology and fluidics devices. These cloud technologies will allow students anywhere in the state to access, monitor and manipulate experiments in real time.
Summary (as written by the applicant)	We will build and establish a Shared Resources Laboratory (SRL) that will use novel cloud-enabled technologies to facilitate project-based educational curricula for stem cell and neuroscience training in schools without access to stem cell facilities. Throughout the state of California, there is a great disparity in access to stem cell facilities for education and research. Compared to coastal CA educational centers, regions with Latinx-majority populations, such as the Central Valley and the Salinas Valley, have few programs to effectively introduce students to stem cell modeling and techniques. This reality translates into an underrepresentation of racial minorities in the stem cell workforce. Building new resources for stem cell education faces at least 3 important barriers: 1) High infrastructural and equipment costs, 2) Specialized training for teachers and mentors, and 3) Potential exposure to hazardous materials, including viruses, human cell lines and other biosafety level 2 materials. It is therefore difficult to build stem cell teaching capacity at every location. Cloud technologies have the potential to eliminate these disparities by enabling real-time stem cell-based experiments through remote monitoring and manipulation of a centrally located core of stem cell incubators. Moreover, the use of cloud technologies is economically scalable as hundreds, or even thousands of users could access the experiments simultaneously. We will take advantage of cloud-connected in-incubator technologies, such as microscopes, electrophysiology and fluidics devices in order to enable remotely-controlled live experiments of pluripotent stem cell-derived 2D and 3D neuronal models. We will work with faculty and students at community colleges, small 4-year universities and high schools to generate community-driven projects that will be used to transmit complex concepts in stem cell topics, such as neuronal differentiation, characterization of complex phenotypes, and drug screenings. In addition, we will create a publicly available repository of education materials, including raw and processed data, educational slides and worksheets, that can be used by additional educators, students or self learners. Our SRL will host frequent training sessions for instructors and students, as well as community sessions that bring together members of academia, patient advocates and the general public in order to generate new educational modules. Altogether, our SRL will enable underserved communities to receive state of the art training and education in stem cell biology, while integrating the voices, concerns and aspirations of the California community.
Statement of Benefit to California (as written by the applicant)	Currently there is a large disparity in access to stem cell technology throughout the state. The establishment of this shared laboratory core will enable live experiments for education and training in stem cell and neuroscience to undergraduate students in schools who otherwise would not have access to this technology. This in return will generate a more diverse workforce of highly trained individuals dedicated to stem cell research and treatments.
Funds Requested	$5,399,996
GWG Recommendation	**Tier 3: sufficiently flawed, cannot be resubmitted**

Process Vote	All GWG members unanimously affirmed that "The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the GWG." Patient advocate members unanimously affirmed that "The review was carried out in a fair manner and was free from undue bias."

SCORING DATA

Final Score: 3

Up to 15 scientific members of the GWG score each application. The final score for an application is the majority score of all of the individual member scores. Additional parameters related to the score are shown below.

Highest	3
Lowest	3
Count	13
Votes for Tier 1	0
Votes for Tier 2	0
Votes for Tier 3	13

- A score of "1" means that the application has exceptional merit and warrants funding.
- A score of "2" means that the application needs improvement and does not warrant funding but, at the applicant's option, may be resubmitted to address areas for improvement if the Application Review Subcommittee has not approved an application for funding following the Grants and Facilities Working Group's review.
- A score of "3" means that the application is sufficiently flawed that it does not warrant funding.

KEY QUESTIONS AND COMMENTS

Proposals were evaluated and scored based on the key questions shown below, which are also described in the PA/RFA. Following the panel's discussion and scoring of the application, the members of the GWG were asked to indicate whether the application addressed the key question and provide brief comments assessing the application in the context of each key question. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

GWG Votes	Does the proposed SRL offer a significant value proposition?
Yes: 3 **No:** 10	• This application proposes to create a virtual shared resource lab that can be used by students in underserved communities across California. The lab will allow students across the state to control lab instruments through the cloud to perform real experiments using real stem cells. • The idea of enabling remote stem cell research is exciting, with the potential to engage students anywhere in the world in basic research. • While an online stem cell resource of this nature could add great value, it is not clear if this should be the one. • The largest weakness of this proposal is that the plan for integrating community college students with applicant institution students is not feasible. • Twenty college/high school locations are noted as a target but ~13 are listed. • It is difficult to determine the value proposition as a major criterion seems to be having students transfer to the applicant institution. • As noted previously, the website has some major flaws, and seems like it went live without anyone checking the content/links. It has not been updated since these flaws were noted in the previous submission.
GWG Votes	**Is the project well planned and designed?**
Yes: 0 **No:** 13	• The idea behind the project is laudable - the ability to allow remote students to perform real lab experiments is a great idea and really makes science hands-on to students in areas that just don't have access to these kinds of model systems. • It remains unclear how the students working in person at the bench and students working remotely will do a joint project.

	• It is somewhat unclear why the applicant institution is proposing to service places in San Francisco. As noted by the program director, "the majority of stem cell research and training capabilities in California are located near large urban hubs," which is true. Why then should the applicant be servicing places in San Francisco? • There are several weaknesses including the listing of a website that is clearly out of date and was not updated with the revision of the application. The lack of plans to truly integrate community college students with the applicant institution students is another issue. • The proposal does not include the required expertise for a successful science education project. It needs to involve discipline-based stem education researchers and experts in assessment of learning.
GWG Votes	**Is the project feasible?**
Yes: 3 **No:** 10	• Assuming the renovations are completed on time, the core should be functional within the proposed timeline. • The applicant institution has demonstrated strong support for this project including funds for building and renovation, access to shared equipment, and computing resources. • The team has an excellent track record and a long list of support letters from educators who are interested in using the remote lab. • Establishing the SRL is likely to be successful. However, the proposal suggests activities that are highly unlikely to be successful. Of particular concern is the "partnership" with community colleges. Community college faculty are not substantively engaged in planning the research course such that it meets the local needs for student learning, inclusion, or success. • The assessment plan is insufficient to measure student learning and other important outcomes such as persistence in science and research. Even if students benefit from the experience, we won't know whether they learned anything.
GWG Votes	**Does the project effectively uphold the principles of diversity, equity and inclusion?**
Yes: 8 **No:** 5	• The ability to provide stem cell problem-based learning to remote California populations is a strength of this proposal. • A strength of this proposal is the ability to reach underserved communities in ways that are relevant to those communities specifically. Through community outreach, the course and project-based learning can be focused on issues that affect the communities being served. • Will serve diverse areas of CA. • The proposal describes an ambitious plan to involve diverse students, particularly by including community college students in the stem cell research course. However, it does not effectively involve these communities in planning the activities. Such approaches undermine inclusion. • A strength of the proposal is its intention to involve local communities in determining research questions to be explored. However, the proposal does not make one confident that community involvement will be successful. Instead, the inclusion efforts focus more on outreach than on serving the communities.
GWG Votes	**IF PROPOSED, is the Stem Cell Techniques Course well designed?**
Yes: 5 **No:** 7	• The investigators significantly revised the course plan based on the comments of the reviewers on the last submission. • There is a plan to educate faculty at other institutions on how to use the resource. • The syllabus and instructors are appropriate for a successful course. • The investigators have also proposed post-class resources such as a transfer admission guarantee program, fee waivers for low-income students, and mentoring to help the community college students transition to a 4-year program. However, there is still a concern that these students will not be able to integrate well with the applicant institution students taking the course. • The purpose of this course appears to get students in community colleges to transfer to the applicant institution. What if students do not want to transfer or would like to go somewhere else? • The course would benefit from a more robust assessment plan that goes beyond student grades and course evaluations. There is an opportunity for education research that is completely missed.

Application #	INFR6.1-15517 #2
Title (as written by the applicant)	Shared Resource Laboratory for Human Stem Cell-Based Modeling (SRL-hSC)
Project Objective (as written by the applicant)	Our Shared Resource Laboratory for Human Stem Cell-Based Modeling (SRL-hSC) will provide modeling resources and educational offerings to researchers, educators, and students in our rural and remote geographic area.
Summary (as written by the applicant)	Our Shared Resource Laboratory for Human Stem Cell-Based Modeling (SRL-hSC) will provide modeling resources and educational offerings to researchers, educators, and students in our rural and remote geographic area. Specifically, our Shared Resource Laboratory will provide: ●Facilities and high-cost and highly specialized technologies needed for human stem cell-based modeling for regional researchers to conduct stem cell-based modeling experiments. ●Educational workshops for college, high school, and middle school students designed to catalyze their entry into human stem cell biology, regenerative medicine and related career opportunities. ●Educational outreach to the diverse communities of our rural, medically underserved region. ●Well characterized, unmodified hiPS cell line cultures derived from the diverse populations of our geographic area. ●Offering professional development opportunities for local clinical professionals to increase regional access to cellular and genetic therapies. Through these activities we will 1.) accelerate discoveries in regenerative medicine; 2.) grow the cohort of stem cell researchers in the state; 3.) increase the ethnic diversity of the iPS cell lines available through CIRM iPSC Repository; 4.) increase community understanding of the ability of cellular and genetic therapies to meet unmet medical needs; and 5.) support reproducibility of stem cell-based modeling experiments within and across laboratories. As part of the statewide CIRM network, it will also contribute to the advancement of standards and reproducibility of stem cell-based models.
Statement of Benefit to California (as written by the applicant)	The proposed Shared Resource Laboratory will provide the facilities and equipment for regional researchers to conduct human stem cell-based modelling, educational workshops for college, high school, and middle-school students, educational outreach to the diverse communities of our rural region, well characterized diverse hiPSC lines, and professional development opportunities for local clinical professionals in our medically underserved rural region.
Funds Requested	$4,399,888
GWG Recommendation	**Tier 1: warrants funding**
Process Vote	All GWG members unanimously affirmed that “The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the GWG.” Patient advocate members unanimously affirmed that “The review was carried out in a fair manner and was free from undue bias.”

SCORING DATA

Final Score: 1

Up to 15 scientific members of the GWG score each application. The final score for an application is the majority score of all of the individual member scores. Additional parameters related to the score are shown below.

Highest	1
Lowest	1
Count	13
Votes for Tier 1	13
Votes for Tier 2	0
Votes for Tier 3	0

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- A score of "3" means that the application is sufficiently flawed that it does not warrant funding.

KEY QUESTIONS AND COMMENTS

Proposals were evaluated and scored based on the key questions shown below, which are also described in the PA/RFA. Following the panel's discussion and scoring of the application, the members of the GWG were asked to indicate whether the application addressed the key question and provide brief comments assessing the application in the context of each key question. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

GWG Votes	Does the proposed SRL offer a significant value proposition?
Yes: 13 **No:** 0	• The applicant institution serves a unique population with limited access to stem cell research activities. The institution is 300 miles from the nearest R1 stem cell research centers. There is a great need to improve access in this mostly rural setting. • The offerings have been clarified and have a strong focus on education. The Shared Resource Laboratory (SRL) is proposed to grow and diversify the hiPS cell lines in the CIRM iPSC Repository and contribute to diversifying the researcher pool in the state. • The applicant makes a compelling case that their SRL will add significant value in the region. Eight users have already been identified and an additional four have expressed interest. • As noted previously, the strength of the proposal is the location of the campus and the population of students it will serve. • The proposed SRL will increase stem cell research potential in an underserved area of California. • The proposal will increase the availability of stem cell lines from Native Americans, through a well-designed, culturally sensitive approach that engages the communities. • The assessment plan is robust and will provide information about what works in stem cell education and why.
GWG Votes	**Is the project well planned and designed?**
Yes: 13 **No:** 0	• The proposal shines in the area of education and outreach, especially in providing stem cell experiences for rural/tribal populations. • The offering of stem cell products has been defined and is much more focused. The core will now focus on adding to the CIRM iPSC Repository to create iPSC cell lines that reflect the gender, race, and ethnic demographics of their region and make them available to researchers. This is a reasonable goal that should be feasible. • The educational offerings are excellent. The curriculum is well thought out and is a mixture of lectures and hands-on experience. The summer course will be co-taught by the PI and another Key Person on this grant. Guest lecturers will be identified and CIRM Bridges Alumni will contribute (letters are provided). • A stem cell biology class is already established and the offering will be expanded. The planned course on lipid analysis and Biosensors, Biomaterials and Bionanotechnology is interesting. • The plan is well aligned with local needs. It's clear that a lot of thought went into the proposal, beginning with specific, measurable goals.
GWG Votes	**Is the project feasible?**

Yes: 13 **No:** 0	• The previous issue in the prior application was the potential difficulty in hiring in a remote region of CA. The current application notes that many of the 100+ alumni of the Bridges program would like to come back and work at the institution. • The educational goals are highly feasible. The resource goals are a bit risky as there is currently no staff in place to generate the lines but a plan has been identified to recruit appropriate staff. • The leadership team for this project is very experienced and has demonstrated success with previous CIRM-funded projects. • In their revised proposal, the applicant has provided strong responses to questions raised during the initial review. As a result, prior concerns have been eliminated. • The applicant institution has been running a CIRM Bridges Program for over 15 years, with outstanding outcomes.
GWG Votes	**Does the project effectively uphold the principles of diversity, equity and inclusion?**
Yes: 13 **No:** 0	• Overall this is an outstanding proposal, especially in terms of outreach and education. • The team will offer online workshops about regenerative medicine to rural middle and high school students, including those from tribal partners, and summer laboratory workshops to high school students. • By building on existing, long-term partnerships with diverse access organizations, the project will engage diverse students from middle school through college in stem cell education and research. • The goal to increase stem cell diversity is also appropriate and a detailed discussion of how diversity will be increased is provided. • A major strength of the proposal is the evidence-based approach to increase diversity, equity and inclusion, including the plan to derive stem cell lines from Native Americans. • The application is much improved with greater clarity of the required resources and the modifications of the plans for adoption. The overall program will support diverse goals and perspectives. In particular there are unique considerations given the location and the ability to draw on diverse populations.
GWG Votes	**IF PROPOSED, is the Stem Cell Techniques Course well designed?**
Yes: 10 **No:** 0	• The courses are part of the main offerings. • n/a • n/a

Application #	INFR6.2-15440 #2
Title (as written by the applicant)	Shared Resource Laboratory for Stem Cell-Based Modeling: Resources for Exploring the Biological Underpinnings of Aging and Age-Associated Pathologies
Project Objective (as written by the applicant)	We seek to engage more Californians in stem cell research by providing access to cell models (including those for modeling the aging brain) derived from a uniquely characterized human cohort, thereby progressing toward better treatment options for age-associated neurological disorders.
Summary (as written by the applicant)	Cell Resources. We have created a bank of human fibroblasts and associated induced pluripotent stem cells (iPSCs) derived from an extensively phenotyped cohort that spans the full range of adult human chronological age. We have also banked fibroblasts and iPSCs from a well-studied cohort of individuals with Alzheimer's disease (AD), suspected AD, and age-matched healthy controls. We seek to enable the California stem cell community to take advantage of these resources through the expansion, diversification, extensive quality control, characterization, and distribution of these cell lines, as well as by helping researchers assemble optimal cohorts for addressing specific biological questions. Finally, we will provide additional cell resources relevant to the aging brain. Focus on the Aging Brain. We have expertise in generating brain cell types from human iPSCs or directly from donor fibroblasts. iPSC-derived cell types exhibit a rejuvenated phenotype, as hallmarks of aging are reset to embryonic benchmarks, whereas directly reprogrammed cells retain aging signatures of donor cells and thus are ideally suited for studying the aging brain. To facilitate the use of direct reprogramming to better understand age-associated brain pathologies, we will create and distribute extensively characterized fibroblast cell lines that contain molecular cassettes for their direct reprogramming into neurons and other brain cell types. We will establish protocols and reagent packages to promote consistency in both direct conversion and iPSC maturation efforts. We will provide iPSC-derived and directly induced brain cell types upon request and perform extensive quality control analyses to ensure between-experiment consistency. We will offer sophisticated phenotyping services to characterize induced cell types. We plan to expand the existing cohort to include those with additional neurodegenerative conditions and diseases of the brain. We will also collect longitudinal biological samples from subjects enrolled as healthy controls but later transitioned to AD. Experimental Reproducibility and Training. To promote rigor and reproducibility of stem cell-based efforts across California, we will perform rigorous quality control analyses of all fibroblasts, iPSCs, and induced cell types generated and distributed by our SRL. We will establish, optimize, and distribute standardized protocols for generating brain cell types from donor fibroblasts and iPSCs. We will provide hands-on training in general stem cell techniques and in more specialized techniques for genome editing and for the direct conversion of somatic cells into brain cell types. Outreach and Access. With the goal of maximizing uptake of these resources and training opportunities by the California research community, we will work closely with the CIRM SRL Network, CIRM Bridges Programs, and other stem cell organizations (e.g., the Inland Empire Stem Cell Consortium) to advertise our resources and services.
Statement of Benefit to California (as written by the applicant)	The distribution of quality-controlled stem cell resources will provide numerous avenues for California researchers to make important strides toward understanding aging and neurodegeneration, potentially leading to breakthroughs in diagnostics and therapeutics. Emphasis on training and the standardization of cell resources and protocols will foster reproducible research, bring new Californians into the stem cell field, and ensure that the state remains at the forefront of stem cell biology.
Funds Requested	$3,641,064
GWG Recommendation	**Tier 1: warrants funding**
Process Vote	All GWG members unanimously affirmed that “The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the GWG.”

	Patient advocate members unanimously affirmed that "The review was carried out in a fair manner and was free from undue bias."

SCORING DATA

Final Score: 1

Up to 15 scientific members of the GWG score each application. The final score for an application is the majority score of all of the individual member scores. Additional parameters related to the score are shown below.

Highest	1
Lowest	2
Count	13
Votes for Tier 1	12
Votes for Tier 2	1
Votes for Tier 3	0

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- A score of "3" means that the application is sufficiently flawed that it does not warrant funding, and the same project should not be resubmitted for review for at least six months after the date of the GWG's recommendation.

KEY QUESTIONS AND COMMENTS

Proposals were evaluated and scored based on the key questions shown below, which are also described in the PA/RFA. Following the panel's discussion and scoring of the application, the members of the GWG were asked to indicate whether the application addressed the key question and provide brief comments assessing the application in the context of each key question. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

GWG Votes	Does the proposed SRL offer a significant value proposition?
Yes: 13 **No:** 0	• The core's goal is to help overcome California stem cell researchers technical hurdles in using stem cells for aging research. Offerings will include extensive quality control, molecular characterization, and distribution of specifically Alzheimer's disease (AD) banked fibroblasts and iPSCs from a well-studied cohort of individuals with AD, suspected AD, and age-matched healthy controls. • There is a great interest in understanding the biological aging process. It's critical to have improved human cell models that enable research directly relevant to human aging. The proposed SRL will provide cell resources, services, and education for investigators across California so that they can perform studies for the aging process. • The creation and distribution of well-characterized fibroblast and iPSC lines, specifically targeting neurodegenerative conditions such as Alzheimer's disease, support the significant demand within the research community. • They will establish detailed protocols and reagent packages to promote consistency in both direct conversion and iPSC maturation efforts; creation and distribution of extensively age-characterized fibroblast cell lines, the derived iPSC line, and the induced neurons and other brain cell types; They will have high-end equipment in place to enable the rigorous analyses of generated brain cell types that are traditionally hard to access for the study of aging and cellular processes. • The team will also create and distribute extensively characterized fibroblast cell lines that contain molecular cassettes for their direct reprogramming into neurons and other brain cell types that should increase demand. • My original major concern was the anticipated users of the SRL. The users identified were mostly collaborators specializing in aging and neuron research. It was unclear how to reach a more diverse audience and potential users. In the revision, the team has surveyed a much broader swath of the California research community and found great

	enthusiasm for the proposed SRL, including from investigators that are not yet collaborators in this field. They have now collected broader letters of support from potential users, including from biologists who study aging who have not used stem cells, stem cell biologists new to the field of aging, and researchers new to both stem cell and aging biology. ● Outreach efforts and new potential users have been identified.
GWG Votes	**Is the project well planned and designed?**
Yes: 13 **No:** 0	● The project is appropriately designed. Starting with existing cohorts, they will perform intensive fibroblasts characterizations for aging, QC controls, provide cell line distributions, iPSCs and induced neuron services, aging phenotype analysis, as well as detailed protocols and reagent packages. Trainings are related to iPSCs, induced neurons, and gene editing. They also plan to expand the existing cohort to include additional neurodegenerative diseases. ● The project plan is well described and tasks of individuals are clearly defined. ● The access plan to offerings has been revised and is reasonable and previous hurdles have been eliminated. The goal to provide training for users who do not have sufficient experience with the tools is a strength. ● The proposed SRL will offer quality control and characterization services for the banked fibroblasts, iPSCs, and neurons derived from iPSCs or fibroblasts sourced from both aging and disease cohorts. These services will provide researchers with a valuable and versatile cell line resource for cell aging modeling. ● Extensive quality control measures, including RNA-seq and methyl-seq analyses ensure high fidelity and reproducibility of the cell lines. ● They will have high-end equipment in place to enable the rigorous analyses of generated brain cell types (e.g., imaging, mitochondrial, and electrophysiological analyses). This will offer comprehensive end-to-end services for brain cell types which will expand the capabilities of investigators across California to conduct a broad analysis for cell aging processes. ● In the revision, the team added that the resources will be made available on a first-come-first-served basis, and will work with each investigator to select the appropriate cohort and to design the most robust experiments possible, which is appropriate.
GWG Votes	**Is the project feasible?**
Yes: 13 **No:** 0	● Overall feasibility is demonstrated and the offerings are exceptional. The team is highly qualified. ● Well-defined organizational structure, with dedicated full-time staff who have extensive experience in stem cell research and core facility management. ● The proposed plan is feasible. Lab space is available, major equipment for cell culture and analysis exists. Requesting equipment for rigorous analyses of generated brain cell, such as imaging, mitochondrial, and electrophysiological analyses. Leadership and management of the proposed SRL are well-versed in experiments, operation and proposed services. ● There was concern whether the SRL would be fully self-sustaining beyond the project period of the proposal. In the revision, the team estimated that as the developing biorepository of well-characterized cell lines expands, potential new users will be informed via the network. Recharge rates will be developed using existing direct-cost analysis methodology and implemented with modest increases each year as CIRM funding tapers. Future costs will be recovered through a combination of recharge revenue and subsidizing grant support, as well as institutional support.
GWG Votes	**Does the project effectively uphold the principles of diversity, equity and inclusion?**
Yes: 13 **No:** 0	● The applicant institution has made great progress in institutionalizing diversity, equity, and inclusion (DEI) to create a culture that supports all members of its community. The SRL can provide service and collaboration for the projects with diverse goals, such as neuron diseases using donor cell models, stem cell models, brain cell models, gene editing and aging phenotype analysis. ● The current aging and AD cohorts are well diversified in terms of sex, and therefore users will be able to obtain a sex-balanced cohort of stem cell resources, and research outcomes will be applicable to both males and females. ● The current aging and AD cohorts are diverse in terms of sex, but not diverse in terms of ancestry, and this is recognized as an issue in proposed SRL to be addressed. They will

	put efforts to reaching Latino communities to diversify the aging cohort and the AD cohort from other connections and collaborations. • One of the SRL team members leads efforts to recruit individuals into the aging cohort. They perform physiological assessments of hallmarks of biological age and sends biopsies to the Stem Cell Core where fibroblast and iPSC lines are derived and banked. They are committed to reaching Latino communities to diversify the aging cohort. • For the AD cohort, the Program Director is co-Director of an iPSC bank at a center focused on Alzheimer's Disease. The AD cohort is currently not diverse; leadership have begun addressing this issue. They have formed a Latino Core with the objective of integrating the growing, yet underserved Latino populations into research activities of this center. • They recognize that significant barriers must be overcome to engage Latino participation in AD research and are working toward this goal. Thus, although the current cohort is not diverse, efforts are underway to begin remedying this situation. Moving forward, the SRL will prioritize the import of diverse cell samples from the AD center. • The proposal includes specific outreach efforts to diversify the aging and AD cohorts by recruiting participants from the Hispanic/Latino population in the region. • Personal statements from the team show the commitment to mentorship and retention for the field. • The project includes collaboration with institution's Office of Diversity, Equity, and Inclusion (DEI) to build and track success metrics related to diversity. • Personal statements from each of the team are on point and speak to the effort around DEI culture. • Letters of commitment from a number of institutions suggest a broad interest in the course offerings. A plan for tracking success metrics has now been added. • The new commitment of covering all costs for 15 trainees for the proposed 2-week course during the first two years of CIRM support will allow access of students from all backgrounds. This is a major improvement and will provide excellent training. • A thoughtful plan of funding beyond the first two years is provided.
GWG Votes	**IF PROPOSED, is the Stem Cell Techniques Course well designed?**
Yes: 13 **No:** 0	• Courses are excellent and well defined. Exceptional mentors and teachers have been identified. • The curriculum covers essential topics in stem cell biology, from basic techniques to advanced genome editing and transdifferentiation. • The three courses proposed are well designed targeting researchers with different skill levels. Starting with the basic stem cell techniques course, to the trans-differentiation course, and the advanced gene editing course. The courses will be open to applicants ranging from high school to college and graduate programs, as well as PIs, technicians, and everyone in between. • The named instructors for each of the proposed courses are appropriately qualified and experienced. • Prioritizing CIRM Bridges/COMPASS students and those from diversity training programs for course enrollment. • It's unclear why the stem cell course is not offered through the local consortium, which was created as a collaborative effort involving the various institutions in the local area.

Application #	INFR6.2-15416 #2
Title (as written by the applicant)	Expanding and enhancing molecular, cell biological and bioengineering resources for stem cell-based models
Project Objective (as written by the applicant)	The primary objective is to expand accessibility to stem cell-based models and to cutting-edge technologies essential for their comprehensive characterization and phenotyping as well as to train future stem cell scientists through the technique's course.
Summary (as written by the applicant)	The core mission of the proposed Shared Resource Lab (SRL) is to establish a powerful technology platform for the targeted manipulation of stem cell fate, thereby establishing a world-renowned laboratory outfitted with the latest technologies to conduct in-depth analyses of human pluripotent stem cells (hPSCs) and their differentiated derivatives. In addition to the commitment to scientific excellence, the SRL is dedicated to sharing knowledge and technical expertise with the broader stem cell research community through training and techniques courses that will be available to researchers across the state of California. To that end, we are committed to fostering a research environment that champions diversity, equity, and inclusion (DEI) as essential cornerstones of our scientific mission and have established an outreach program to facilitate public education in underserved communities. The SRL staff and affiliated faculty at this and collaborating institutes will establish and disseminate a robust technology pipeline that leverages a lipid nanoparticle (LNP) delivery system for the targeted differentiation, trans-differentiation, and genome editing of hPSCs. This LNP platform can be readily adapted to deliver a variety of payloads, such as nucleic acids (including mRNAs), proteins (such as CRISPR/Cas9 editing tools), peptides, and small molecules to instruct stem cell fate. Users of the SRL will be able to obtain pre-formulated or custom LNPs to apply to their stem cell-based models. To support these endeavors, the SRL will also acquire and then provide cutting-edge instrumentation, including a state-of-the art cell sorter, flow cytometer, and confocal microscope, for the characterization, isolation, and purification of LNP-targeted cell populations. The vision extends beyond just advancing research and aspires to create thriving scientific environments that serve as hubs for innovative technologies in the stem cell and regenerative medicine arena and for comprehensive training and techniques courses. Collaboration and knowledge exchange will accelerate fundamental discoveries in stem cell research, propelling the field toward the ultimate goal of clinical development.
Statement of Benefit to California (as written by the applicant)	Support for this project will enable our shared resource facility to expand our capabilities to better provide stem cell-based models to scientists within our community and within the state of California. Additionally, we will be in a better position to work with California academic groups and biotechnology companies to translate their discoveries into potential therapies that will benefit patients with unmet medical needs.
Funds Requested	$4,000,000
GWG Recommendation	**Tier 2: needs improvement, could be resubmitted**
Process Vote	All GWG members unanimously affirmed that “The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the GWG.” Patient advocate members unanimously affirmed that “The review was carried out in a fair manner and was free from undue bias.”

SCORING DATA

Final Score: 2

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Highest	1
Lowest	3
Count	13
Votes for Tier 1	1
Votes for Tier 2	11
Votes for Tier 3	1

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KEY QUESTIONS AND COMMENTS

Proposals were evaluated and scored based on the key questions shown below, which are also described in the PA/RFA. Following the panel's discussion and scoring of the application, the members of the GWG were asked to indicate whether the application addressed the key question and provide brief comments assessing the application in the context of each key question. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

GWG Votes	Does the proposed SRL offer a significant value proposition?

Yes: 8
 	
No: 5
	• This is a strong application that will enhance and partially join two existing cores to increase access to novel stem cell-based models across California. The project will also provide a comprehensive resource for use of lipid nanoparticles (LNPs) to manipulate stem cells.
	• The proposed LNP delivery pipeline for differentiation and gene editing is supported by a detailed plan for equipment purchase, with justification.
	• The Program Director has an excellent track record of successfully running one of the current cores for nearly 20 years. During this time the core has consistently provided new offerings.
	• Yes and no. The training course and syllabus are much improved. The addition of faculty and staff from an additional institution increases the feasibility and reach of the project. However, a large portion of the proposed budget (>$1M) remains focused on the purchase of cell sorters, which are not required for stem cell modeling. Also, there are several other sorters currently available in the existing core.
	  ◦ The rationale for the Novaocyte Quanteon cell sorter ($210K) is more convenience than scientific need.
	  ◦ There is no stem cell-specific rationale for the S8 Sorter ($830K). This is a very new image-based sorter, and the specific applications listed (i.e., removal of dead cells, sample cleanup, morphology sorting, deeper characterization) do not justify purchase of this instrument for stem cell research.
	• The services and technologies are not of sufficient significance and can probably be covered by other core facilities at the institution.
	• Cell sorting is a widely used technology and various LNPs are also commercially available. Hence, the value proposition is unclear.
	• In addition, multiple institutions in the area need not have a separate services and training offerings - these could be combined into a joint effort.
	• Reviewers had many questions about the maturity of the LNP technology.

GWG Votes	**Is the project well planned and designed?**
Yes: 7 **No:** 6	• This SRL is well designed. A strength is the cohesive nature of the services it plans to provide: 1. The manufacture and 2. purification of the mRNA particle payloads through the 3. LNP assembly and 4. hPSC bank available to the 5. differentiation and editing SOPs through the 6. analysis of the outcomes. All of the above are critical to the success of generating new stem cell-based models and using these models to gain knowledge of potential therapies. • While the training portion is much improved, this proposal is largely based on flow cytometry rather than stem cell biology.

GWG Votes	Is the project feasible?
Yes: 8 **No:** 5	• The track record of the investigators is strong - the Program Director has been running this core in a sustainable way for nearly 20 years. • *[Named institution]* has committed $300K to cover salaries and the *[second named institution]* has committed another $350K to cover equipment support. • The proposal includes great facilities, support, and leadership.
GWG Votes	**Does the project effectively uphold the principles of diversity, equity and inclusion?**
Yes: 12 **No:** 1	• The DEI section is non-specific (i.e., access to hiPSCs of different genetic backgrounds), but does uphold the principles of DEI. • Overall, this proposal is still weak with regard to DEI. There are diverse collections of hPSC that the applicant could leverage. The applicant could also incorporate more outreach to underserved communities into the project. • The applicant hopes to generate more lines from a wide range of participants. Given that neighboring institutions have collections that are stated to be more diverse, why aren't they obtaining some of those lines?
GWG Votes	**IF PROPOSED, is the Stem Cell Techniques Course well designed?**
Yes: 10 **No:** 1	• The course offerings consist of three courses - a basic, hands-on 2-week class on culturing, reprogramming, characterization, differentiation, and gene editing; a 5-day mini-course on LNP technology; and a 10-week lecture course that covers basic and applied research with stem cells and ethics. • The training courses merit funding. The proposal for the courses is much improved and appears to be a merger of proposals from two institutions, which strengthens the proposal greatly. • This resubmission contains a much better description of the courses. • The LNP course is the most unique part of the technique course.

Application #	INFR6.2-15475 #2
Title (as written by the applicant)	Shared Resource Laboratory for Advanced Stem Cell-Based Modeling
Project Objective (as written by the applicant)	This proposal will create a laboratory that will provide training in advanced stem cell modeling technology, particularly organ chip technology. This laboratory aims to train stem cell researchers in using these 2D and 3D stem cell systems and make the expertise available across California.
Summary (as written by the applicant)	The Shared Resource Laboratory for advanced stem cell modeling will lean into our strength in human iPSC production and differentiation and expand our organ chip core collaborations to enable researchers throughout California access to this exciting and powerful new technology. Several of our faculty are highly experienced in this area of research and have history of training CIRM students through CIRM educational programs. We will provide outstanding training in the growth and differentiation of iPSCs from patients with many different diseases available from our world-renowned human iPSC core, using 2 Dimensional (2D) and 3D organoid models. However, the unique aspect of this SRL is the training of stem cell researchers in organ chip technology. These microfluidic devices enhance tissue interactions and support both flow of various biological fluids (e.g., blood, cerebrospinal fluid) and mechanistic forces (stretch) to optimize the disease model and provide a more physiologically-relevant system. Highlights of the SRL include: •Cutting-edge iPSC core facility with the latest equipment and highly trained faculty and staff •Generated over 1000 patient iPSC lines that are ready for use in disease models •Deep knowledge of iPSC differentiation into many different human tissues •Long history of developing novel 2D and 3D organoid/organ chip iPSC-based model systems •Commitment from a leading organ chip company to provide training and support •Several leading CA institutions have already expressed interest in using the proposed SRL •Provided to trainees from diverse backgrounds and under-represented groups in CA who may not normally have access to these systems
Statement of Benefit to California (as written by the applicant)	The proposed project will benefit the State of California and its citizens by granting educational and didactic training in stem cell biology to academic trainees, industry partners, and underserved communities not traditionally represented in stem cell research. We will address the needs of underserved communities by providing education and training opportunities and collaborating with community-based organizations to ensure that our resources and services are reaching those who need them most.
Funds Requested	$3,991,879
GWG Recommendation	**Tier 1: warrants funding**
Process Vote	All GWG members unanimously affirmed that “The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the GWG.” Patient advocate members unanimously affirmed that “The review was carried out in a fair manner and was free from undue bias.”

SCORING DATA

Final Score: 1

Up to 15 scientific members of the GWG score each application. The final score for an application is the majority score of all of the individual member scores. Additional parameters related to the score are shown below.

Highest	1
Lowest	1

Count	12
Votes for Tier 1	12
Votes for Tier 2	0
Votes for Tier 3	0

- A score of "1" means that the application has exceptional merit and warrants funding.
- A score of "2" means that the application needs improvement and does not warrant funding but, at the applicant's option, may be resubmitted to address areas for improvement if the Application Review Subcommittee has not approved an application for funding following the Grants and Facilities Working Group's review.
- A score of "3" means that the application is sufficiently flawed that it does not warrant funding, and the same project should not be resubmitted for review for at least six months after the date of the GWG's recommendation.

KEY QUESTIONS AND COMMENTS

Proposals were evaluated and scored based on the key questions shown below, which are also described in the PA/RFA. Following the panel's discussion and scoring of the application, the members of the GWG were asked to indicate whether the application addressed the key question and provide brief comments assessing the application in the context of each key question. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

GWG Votes	**Does the proposed SRL offer a significant value proposition?**

Yes: 12
 	
No: 0
	• This is a much improved proposal from a strong institution; this consolidation of services will provide large benefits to the stem cell community.
	• The applicants have:
	  ◦ Extensive experience with stem cell technology and over 1,000 human iPSC lines.
	  ◦ Differentiation protocols and characterization for numerous cell types.
	  ◦ Experience with organ-on-a-chip system for different organ system models and sufficient numbers of units for training and research.
	• The expected outcomes are reasonable with self-sufficiency of the program being most critical.

GWG Votes	**Is the project well planned and designed?**
Yes: 12 **No:** 0	• Yes, the responses have clarified remaining issues and this should be a successful core. • In the revision, the applicants detailed the number of organ-on-a-chip systems at the institution and the user base for training and research purposes. This information clarified a major weakness of the original application.
GWG Votes	**Is the project feasible?**
Yes: 12 **No:** 0	• Previous concerns about the core director's limited experience managing multi-investigator projects or core facilities were well addressed by highlighting the directors experience and training and leveraging additional senior leadership. • Space for this project has been committed. The Vice Dean for Research commits to providing the space and ensures institutional support for the proposal. • The Program Directors have been involved with other CIRM and institutional training and core facilities. • A plan is described for the long-term operation of the core as long as demand persists.
GWG Votes	**Does the project effectively uphold the principles of diversity, equity and inclusion?**
Yes: 12 **No:** 0	• Overall, they address the educational outreach and commitment to hiring/training a diverse workforce. Educational program outreach seems right - reaching out to the different local colleges where a more diverse population enrolls and attends school. • The institution has a good track record of providing educational opportunities to underrepresented minorities. Targeting 50% underserved communities by doing outreach to local institutions. • This was a strong aspect previously and remains so.

	• In the revision, the applicants detail their efforts to increase the number of iPSC lines from diverse groups. • The institution has clarified the recruitment of people in to the program with more experience in this area. • The applicant institution has multiple outreach programs to recruit a more diverse student population for the labs and these courses. Information on the demographics of labs associated with this program would provide a basis for judging the success of these activities.
GWG Votes	**IF PROPOSED, is the Stem Cell Techniques Course well designed?**
Yes: 12 **No:** 0	• It is a comprehensive program that will provide an excellent resource and skills to train the next generation of researchers and they have staff and facilities to do it. • The course meets the need of introducing participants to the field and experience with the latest technologies in the field. The course is well suited for the faculty and students since they already have a core group using organoids and the organ-on-a-chip system. • In the revision, the applicants have clarified the number of students per module for the Stem Cell Models course; the number (8) appears adequate. They also provide more information on the staffing and access to core resources for training and research projects.

Application #	INFR6.2-15403 #2
Title (as written by the applicant)	Enhancing/Expanding Stem Cell-Based Modeling at a Shared Research and Training Facility
Project Objective (as written by the applicant)	The primary objectives are to prepare a diverse California workforce for careers in regenerative medicine while maintaining fiscal stability and contributing to the CIRM SRL Network that will ensure the highest quality research and training standards across California.
Summary (as written by the applicant)	This application proposes to expand and enhance an existing self-sustaining shared stem cell research service and training facility that supports dedicated laboratory space for the culture of human pluripotent stem cells, and training for all career stages in CIRM supported and other training programs. The resources and infrastructure currently in place meet the intended mission by providing access to key services and equipment; teaching and training users in the high-quality standards required for culture and analysis of human stem and progenitor cells; and standardized methods and protocols such as those to ensure sterility, assessments of pluripotency and lineage commitment, and well-characterized model systems. Progress in the regenerative medicine field is dependent on resources where high standards are maintained and rigor and reproducibility in research and training is emphasized. The current infrastructure proposes to build on these strengths and capabilities by enhancing and expanding specialized and advanced services and training that include both hands-on and distanced learning in gene transfer, somatic cell genome editing, stem cell labeling for imaging, and 3D model systems. Faculty and staff have extensive expertise in techniques, tools, and technologies that will be offered as service, educational, and training opportunities, and include applications for pluripotent and lineage committed or adult stem cells in two-dimensional or three-dimensional cultures. Enhancing trainee skillsets and core competencies, as well as emphasis on the importance of data management and sharing within the California regenerative medicine research community, is a high priority. Preparing a diverse workforce for careers in regenerative medicine is strongly supported in the facility and through CIRM training programs and California partners. Key goals are to increase users across California, and ensure the facility remains self-sustainable and at the cutting edge of regenerative medicine and gene therapy research services and training now and in the future. The program will integrate with the CIRM SRL Network and Steering Committee and contribute substantially to establishing common standard operating procedures and methods to ensure rigor and reproducibility, and an effective data management and sharing plan.
Statement of Benefit to California (as written by the applicant)	The proposed enhancements will provide benefits to California and its citizens by contributing to scientific advancements by providing users with high quality services and training within an established infrastructure that supports human stem cell research, and tools and technologies for gene transfer and editing. The educational opportunities will ensure core competencies and contribute to the diversity of California's workforce that will benefit patients and communities.
Funds Requested	$3,760,466
GWG Recommendation	**Tier 2: needs improvement, could be resubmitted**
Process Vote	All GWG members unanimously affirmed that “The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the GWG.” Patient advocate members unanimously affirmed that “The review was carried out in a fair manner and was free from undue bias.”

SCORING DATA

Final Score: 2

Up to 15 scientific members of the GWG score each application. The final score for an application is the majority score of all of the individual member scores. Additional parameters related to the score are shown below.

Highest	1
Lowest	2
Count	12
Votes for Tier 1	2
Votes for Tier 2	10
Votes for Tier 3	0

- A score of "1" means that the application has exceptional merit and warrants funding.
- A score of "2" means that the application needs improvement and does not warrant funding but, at the applicant's option, may be resubmitted to address areas for improvement if the Application Review Subcommittee has not approved an application for funding following the Grants and Facilities Working Group's review.
- A score of "3" means that the application is sufficiently flawed that it does not warrant funding, and the same project should not be resubmitted for review for at least six months after the date of the GWG's recommendation.

KEY QUESTIONS AND COMMENTS

Proposals were evaluated and scored based on the key questions shown below, which are also described in the PA/RFA. Following the panel's discussion and scoring of the application, the members of the GWG were asked to indicate whether the application addressed the key question and provide brief comments assessing the application in the context of each key question. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

GWG Votes	Does the proposed SRL offer a significant value proposition?
Yes: 11 **No:** 1	• The expansion of the core will add new services which are cutting edge technologies not previously offered. These new services, in particular gene editing and generation of reporter iPSC lines, will definitely attract new users. Providing 3D stem cell models is another new services that is very attractive and should expand the user base. It's regrettable that the core will not be offering iPSC generation as a service. • The genome editing service is still very unclear. What services will actually be provided? Can end users ask for any modification in any iPSC line (KO, point mutation, het-KO, tag, etc)? Prime editing is mentioned, but not really explained how it fits into the services. How many projects can they do a year with the proposed staffing? • Organ-on-a-chip and the advanced imaging techniques seem niche. We need a better idea of interest in these services to evaluate whether this proposal warrants funding. Funds will partly go to expensive instrumentation that isn't necessarily stem cell focused.
GWG Votes	**Is the project well planned and designed?**
Yes: 6 **No:** 6	• The revised proposal makes a good attempt at detailing the new services that will be offered by the core. However, the description of these services are still vague and ill defined. For example, for gene editing, is the core making custom edited lines based on user requests or just offering pre-existing edited lines? What reporter lines will be available and how will they be generated? • The proposal has a vague description of services and pricing. Overlap of core offerings is still not well addressed. • Overlap of offerings with the existing stem cell core is still a concern and not well explained. • The proposal needs additional details about the new services proposed. Services are now clarified, but specifics are lacking. • There are few details to help reviewers understand the impact of the proposal and the amount of interest or use from potential users.
GWG Votes	**Is the project feasible?**
Yes:	• Yes. The institutional commitment, Program Director, and facilities are excellent.

12 **No:** 0	• The plan proposed is feasible and likely to be on schedule. The facilities and resources are excellent. The Program Director and the institution have a good track record of establishing cores and there is appropriate institutional support. Proposed staff for the expansion is well thought out and details are provided in the proposal.
GWG Votes	**Does the project effectively uphold the principles of diversity, equity and inclusion?**
Yes: 12 **No:** 0	• The SRL offerings will enable both a broad set of experimentation and access to a variety of groups based on the demonstrated track record of the applicant institution related to multiple past and on-going CIRM grants. • Yes. The team has access to diverse background iPSCs through institutional health cord blood collection programs. • Yes, the project effectively upholds the principles of diversity, equity and inclusion.
GWG Votes	**IF PROPOSED, is the Stem Cell Techniques Course well designed?**
Yes: 12 **No:** 0	• This is the best section of the proposal. It proposes both basic techniques and advanced techniques. • No additional comments on the course. It is well designed.

Application #	INFR6.2-15457 #2
Title (as written by the applicant)	Shared Resources Laboratory for Stem Cell-Based Modeling in Stem Cell Biology and Engineering
Project Objective (as written by the applicant)	We propose to expand and enhance our stem cell core, a key resource for the local area.This project will accelerate new therapies and train stem cell scientists.
Summary (as written by the applicant)	We propose to expand and enhance The Laboratory for Stem Cell Biology and Engineering, an essential stem cell core facility on campus. This successful facility, established in the early 2000s, serves as a key resource for the local area. Its clients include not only campus investigators, but also researchers and students from nearby colleges, universities, research institutes, and biotechnology companies. The major goals of our program are: • Enhancement of the Core Laboratory via the addition of new, modern equipment to support stem cell culture and analysis • Expansion of access for diverse investigators and students to state-of-the-art technology for research in stem cell biology and engineering • Sharing of unique stem cell-based models related to neural development and disease. • Novel patient-derived hiPSC and CRISPR-engineered hPSC lines for modeling neural disease • Integrated embryo models for modeling early neural development • Brain and retinal organoid models for modeling the development of neural connectivity, neural disease, and ocular maladies • Access to advanced imaging, single cell RNAseq, omics and multi-electrode array analysis of cells and cell assemblies • Access to the BioFoundry for culture optimization, genetic and pharmacological screening • Access to the Materials Research Lab for investigation of novel materials for encapsulation and scaffolding to support cell therapies • Establishment of two hands-on laboratory training courses: Advanced Stem Cell Techniques and Quantitative Stem Cell-Based Modeling.
Statement of Benefit to California (as written by the applicant)	We propose to expand and enhance our stem cell core, a key resource for the local area. Its clients include campus investigators, students from local colleges, universities, and biotechnology companies. We will establish two new courses. This project will accelerate new therapies and train a diverse future generation of stem cell scientists and wlll be of great benefit to the state of California as we develop new therapies and train stem cell scientists.
Funds Requested	$3,999,995
GWG Recommendation	**Tier 1: warrants funding**
Process Vote	All GWG members unanimously affirmed that “The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the GWG.” Patient advocate members unanimously affirmed that “The review was carried out in a fair manner and was free from undue bias.”

SCORING DATA

Final Score: 1

Up to 15 scientific members of the GWG score each application. The final score for an application is the majority score of all of the individual member scores. Additional parameters related to the score are shown below.

Highest	1
Lowest	1
Count	13
Votes for Tier 1	13
Votes for Tier 2	0
Votes for Tier 3	0

- A score of "1" means that the application has exceptional merit and warrants funding.
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- A score of "3" means that the application is sufficiently flawed that it does not warrant funding, and the same project should not be resubmitted for review for at least six months after the date of the GWG's recommendation.

KEY QUESTIONS AND COMMENTS

Proposals were evaluated and scored based on the key questions shown below, which are also described in the PA/RFA. Following the panel's discussion and scoring of the application, the members of the GWG were asked to indicate whether the application addressed the key question and provide brief comments assessing the application in the context of each key question. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

GWG Votes	Does the proposed SRL offer a significant value proposition?
Yes: 13 **No:** 0	• This application focuses on the addition of new equipment to an existing core, the addition of new iPSC lines, and the sharing of new stem cell-based models of neural differentiation. • The applicant points out that their campus location is an area of the CA central coast that does not have many laboratory resources. The lack of other resources in this area allows the applicant to attract local researchers who are interested in this work but haven't had opportunity. • The overall objective to expand and enhance the Laboratory for Stem Cell Biology and Engineering at the applicant institution and is valid and well-justified. • Reviewers' previous questions regarding impact have been addressed in this revised application. The applicant provides a list of potential users that will be recruited via a new partnership. • The revised proposal clarifies an expanded user base for the brain organoid, retinal organoid, and early embryo models. It also details new interest from local bioengineering faculty and biotechs, and how these local investigators will use the BioFoundry facility/equipment. Together, these revisions provide a clearer view of the models, cell lines and services that will be offered by the core and were the primary driver of my score.
GWG Votes	**Is the project well planned and designed?**
Yes: 13 **No:** 0	• The proposed SRL is focused on neurodevelopment and disease. The applicant team has gathered a number of iPSC suitable for this purpose. • The applicant also proposes integrated embryo models for modeling early neurodevelopment. Using these 3D models may provide insights that can't be gained in other ways. This is a newer technology that is not widely available. • This application also plans to offer brain and retinal organoid models as well as tools to analyze individual cells and cell assemblies. • The offerings are impressive and encompass many existing and novel patient-derived hiPSC and CRISPR-engineered hPSC lines cell lines for a multitude of diseases. The inclusion of over 50 hIPS cell lines harboring fluorescent protein fusion constructs that light up over 40 individual organelles/structures is exciting. • Access to sophisticated imaging tools and the institution's Materials Research Lab for investigating encapsulation and scaffolding approaches is an additional strength. • Success criteria for each activity have been listed, with the addition of the new criterion "successful integration of new users". • A pay structure has been outlined, which is a strength.

	• The establishment of a partnership with the BioFoundry Project is exciting although it remains unclear how the partnership will work what, if any, financial support is involved. • The emphasis remains heavily on the neural models, retinal, and embryo models, as well as support for the BioFoundry and materials lab expansion activities. These also fit nicely with the course and workshop plans and are in line with the strengths of the team.
GWG Votes	**Is the project feasible?**
Yes: 13 **No:** 0	• The applicants have done an excellent job identifying additional faculty experts to help them successfully offer the planned new technologies. • A significant portion of the budget is for replacing outdated equipment and bringing in the new equipment needed to support the new technologies. • Investigators with relevant expertise will contribute to the offering. The timeline to reach full operational status is reasonable. • There is ample institutional support and commitment for this core, which has existed since the early 2000s. • Yes. Feasibility is bolstered by the applicant's finance plan via tuition. • In addition to the original team, they have added an additional researcher to the Materials Research Lab team and have additional interest from engineering faculty. • The applicant has continued to raise additional private and public funding to help support the current lab, suggesting long-term sustainability. • The plan to phase in recharges to labs and industry seems reasonable in this context. • Absolutely.
GWG Votes	**Does the project effectively uphold the principles of diversity, equity and inclusion?**
Yes: 13 **No:** 0	• The offerings planned in this application would be suitable to a wide range of researchers. The institution has a demographic reach that includes many traditionally underserved populations. • Program leaders and current users have been active in reaching underserved groups on campus. • The core is open to a wide variety of investigators and all banked cell lines are characterized and offered free of charge during Phase A and B. This provides users with limited resources equal access to valuable material. • Courses and workshops are free of charge during the first 3 years of the program, allowing access of a variety of students with limited resources. • While the applicant did not comment on diversity of stem cells, they have added an adequate section that highlights the already existing diversity of their lines and the commitment to increase diversity. • They have made progress in substantially building DEI values into their culture. In the revision they were careful to describe the demographics of their area and describe how they intended to draw on the diversity of the Central Coast to recruit students. • The applicant has made DEI a core concern. They have budgeted resources for scholarships for trainees from groups not well represented in biomedical research. They describe the recruitment and training efforts they will make to include not only university-trained students but also students from numerous community colleges in the region. • The applicant is planning to institute robust hands-on training courses to a diverse group of students. The applicant institution has demonstrated a commitment to diversity over a long period. This was not very well highlighted in the previous proposal. The team as described in the revised proposal is extremely impressive in their DEI committment. • In this revision they are much clearer about the need to improve the diversity of cell lines that are typically available and how this affects different groups with different disease profiles. They report that their global sources contain a degree of ethnic variability. • The DEI statement has been greatly improved to address a missed opportunity in the original application. The applicant now highlights the institution's strengths with regard to DEI and activities that have been conducted by the applicant team to expand participation across diverse backgrounds. • A discussion of the diversity of cell lines to be used in the core is expanded with particular examples of where diversity in ancestry is considered (e.g., a familial AD cohort relevant to Hispanic populations that will be offered). These revisions highlight how the choice of lines enhances applicability of findings. These revisions were the second factor driving my score.
GWG Votes	**IF PROPOSED, is the Stem Cell Techniques Course well designed?**

Yes: 13 **No:** 0	• The proposed courses include an advanced stem cell techniques course, a quantitative stem cell modeling course, and four specialized differentiation workshops. • The course is well designed and the course accessibility has been clarified. In addition, specific learning objects have been added to both courses and these are appropriate. • The workshops are an additional strength. • Recruitment strategies have been added and detailed. • The revision has added learning objectives and outcomes for the two courses as well as new recruitment plans. Letters of Support from partner institutions that are sources of students are provided. • It is now much clearer that the courses fit the user base and match the expertise and services to be offered by the core.

Application #	INFR6.2-15513 #2
Title (as written by the applicant)	A Comprehensive Biorepository of Human Induced Pluripotent Stem Cells and Their Cardiovascular Derivatives
Project Objective (as written by the applicant)	Harness the potential of iPSCs to revolutionize cardiovascular research, enabling precise disease modeling, novel therapeutic insights, and improved patient outcomes. Simultaneously, empower researchers and students through comprehensive training, driving advancements in regenerative medicine.
Summary (as written by the applicant)	This project addresses the global challenge of cardiovascular diseases (CVDs), which contribute significantly to morbidity and mortality. CVDs manifest with diverse disease profiles and varying drug responses among patients, particularly evident in conditions such as peripartum cardiomyopathy (PPCM) and congenital heart disease (CHD). To address these challenges, induced pluripotent stem cells (iPSCs) have emerged as a transformative tool in cardiovascular research and medicine. iPSCs possess the unique ability to self-renew indefinitely and differentiate into various human cell types, thereby opening new avenues for advancing cardiovascular disease modeling and developmental disorder research. Despite notable progress in iPSC research, significant obstacles remain that hinder their full potential for cardiovascular studies. The existing biobank has made commendable strides in overcoming challenges by amassing a diverse iPSC collection and enabling external distribution. However, certain gaps persist, especially in enlisting both genetic and non-genetic disease cohorts and addressing early developmental diseases. To bridge these gaps, our innovative Shared Resource Laboratory (SRL) Core has set forth ambitious objectives: (i) To expand the iPSC collection by recruiting diverse genetic and non-genetic cohorts, with a special focus on PPCM and CHD donors; (ii) To provide iPSC-derived cardiac cells to facilitate precise cardiac tissue modeling, disease investigation, and drug evaluation; and (iii) To foster extensive collaboration with researchers by offering training and support in iPSC reprogramming, 2D and 3D cardiac cell culture techniques. This collaborative approach empowers the scientific community to fully harness the potential of iPSCs and iPSC-derived cardiac cells for comprehensive cardiovascular studies. The SRL core is led by a distinguished team of experts, with combined expertise ensuring the seamless execution of the project's objectives, heralding a new era in cardiovascular research and shaping the trajectory of personalized medicine in the field. In unity with the shared mission, the SRL Core is poised to offer pioneering techniques, abundant resources, and strategic collaborations that hold the promise of catalyzing advancements in cardiovascular research.
Statement of Benefit to California (as written by the applicant)	The SRL Core's pioneering cardiovascular research using iPSCs will position California as a leader in scientific innovation. Collaboration among experts and institutions will drive knowledge sharing, while training initiatives will cultivate a skilled workforce for future breakthroughs. Enhanced cardiovascular health and personalized medicine outcomes will establish California as a frontrunner in biomedical research.
Funds Requested	$3,994,062
GWG Recommendation	**Tier 2: needs improvement, could be resubmitted**

Process Vote	All GWG members unanimously affirmed that "The review was scientifically rigorous, there was sufficient time for all viewpoints to be heard, and the scores reflect the recommendation of the GWG." Patient advocate members unanimously affirmed that "The review was carried out in a fair manner and was free from undue bias."

SCORING DATA

Final Score: 2

Up to 15 scientific members of the GWG score each application. The final score for an application is the majority score of all of the individual member scores. Additional parameters related to the score are shown below.

Highest	1
Lowest	3
Count	13
Votes for Tier 1	2
Votes for Tier 2	10
Votes for Tier 3	1

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- A score of "2" means that the application needs improvement and does not warrant funding but, at the applicant's option, may be resubmitted to address areas for improvement if the Application Review Subcommittee has not approved an application for funding following the Grants and Facilities Working Group's review.
- A score of "3" means that the application is sufficiently flawed that it does not warrant funding, and the same project should not be resubmitted for review for at least six months after the date of the GWG's recommendation.

KEY QUESTIONS AND COMMENTS

Proposals were evaluated and scored based on the key questions shown below, which are also described in the PA/RFA. Following the panel's discussion and scoring of the application, the members of the GWG were asked to indicate whether the application addressed the key question and provide brief comments assessing the application in the context of each key question. The responses were provided by multiple reviewers and compiled and edited by CIRM for clarity.

GWG Votes	Does the proposed SRL offer a significant value proposition?
Yes: 10 **No:** 3	• This application proposes a SRL in which 400 iPSC from diverse cardiac disease patients and healthy cohorts are created, differentiated and distributed to researchers across the state. This large number of iPSC from subjects with specific cardiovascular diseases will be useful in advancing clinical strategies. • The response to previous concerns was strong; providing significant evidence-based data of current use and additional interested researchers. • The revised proposal includes letters of support from over 50 additional anticipated new California users. The combined total anticipated California user base makes the proposal a significant improvement over the original submission. • They have done an excellent job of gathering letters of support from CA based researchers that are interested in using these resources, so this would appear to increase the size of the field, but may not be transformative in terms of impacting new users in underserved areas.
GWG Votes	**Is the project well planned and designed?**
Yes: 12 **No:** 1	• The iPSC to be generated as well as the cardiac differentiation models are well described, this time including much more information on the derivation and characterization of the lines.

	• The reduction in the number of new iPSC lines and iPSC-derived cardiac lineages proposed and the more targeted approach of generating 3D organoid models on-demand make this proposal more feasible. • It would have been preferable for the proposal to have kept naive iPSCs generation as an on-demand service because naive cells are very useful for modeling developmental disorders. • Reducing the number of cell lines would make this an achievable proposal. • The revised plan for core personnel is appropriate for the studies and the revised timeline is more feasible. • There was reviewer significant concern about the budget - i.e., $1.4 million requested in a way that CIRM may not be able to fund.
GWG Votes	**Is the project feasible?**
Yes: 5 **No:** 8	• Yes, proposed plan is realistic and feasible within the timeframe of the project. The additional 15-classroom space secured for the training course, plus the 2,000 square feet of lab/tissue culture space are sufficient to execute the project plan. • The Program Director and institution have strong track record and sufficient commitment to support the proposed core. • The leadership is very qualified. There is clear experience in stem cell biology, cardiac differentiation, and biobanking. • Although this resubmission reduced the number of iPSC lines to be generated, there are still a very large number proposed. • It remains questionable if 400 new high-quality iPSC lines with the necessary basic characterization can be generated and distributed in an academic setting. • The plan for a large number of lines to be generated is likely not feasible within the overall budget. Also, there are budget errors in the application. • Budget concerns seriously detract from the feasibility of the project. • Since the applicant will need to remove nearly $1.4M from the budget (for personnel to maintain equipment), they may not be able to accomplish the proposal.
GWG Votes	**Does the project effectively uphold the principles of diversity, equity and inclusion?**
Yes: 12 **No:** 1	• The applicant institution has an extremely strong track record related to diverse training, patient enrollment, and access to clinical trials. It has therefore scored highly on the DEI criterion on multiple CIRM grants. • This resubmission includes additional info about a panel of team members who have a track record in DEI. • The project effectively upholds the principles of diversity, equity and inclusion. • This proposal is still lacking in this area. There is no clear plan given for identifying diverse subjects from which to generate the iPSC and no plan to reach out to underserved groups to use the facility or be trained. • The investigators plan to reprogram samples from any minority subjects they recruit but, again, do not describe how they will get minority groups into the clinic for sampling. Often, lack of diversity in cell lines is not due to the scientist's lack of interest, but due to the difficulty of attracting these subjects. • Overall this segment is still lacking definitive plans to include underserved groups. It reads more like a list of facilitating groups that the applicant will reach out to, but needs more details. When and how often will outreach occur? How can they get these groups seriously involved?
GWG Votes	**IF PROPOSED, is the Stem Cell Techniques Course well designed?**
Yes: 12 **No:** 0	• This application proposes a quarterly course covering all aspects of hPSC biology from culturing protocols to advanced techniques for working with cardiomyocytes. • The instructors of the course have a wide range of experience in all topics being taught. • This is a well thought out, excellent, and comprehensive stem cell course. • The application states that the course is open to all students - high school, college, graduate students and researchers, but gives no details on how they will entice underrepresented groups. However, the course is fully supported by the institution and will be free of charge, which benefits individuals that could not normally afford to take the course.