



MEMORANDUM

Date: August 29, 2012

From: Ellen Feigal, MD
CIRM Senior Vice President, Research and Development

To: Independent Citizen's Oversight Committee

Subject: Extraordinary Petition for Application RB4-05764

Enclosed is a petition letter from Dr. Deborah Lieu of University of California Davis, an applicant for funding under RFA 11-03, CIRM Basic Biology IV Research Awards. This letter was received at CIRM on August 28, 2012 and we are forwarding it pursuant to the ICOC Policy Governing Extraordinary Petitions for ICOC Consideration of Applications for Funding.



Deborah K. Lieu, Ph.D.

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August 27, 2012

Re: CIRM Basic Biology Award IV application RB4-05764: Induction of pluripotent stem cell-derived pacemaking cells

Dear ICOC members:

We are submitting an extraordinary petition to respectfully request a reconsideration of our Basic Biology IV grant application which received a score of 68. During the programmatic discussion, a motion was initially made to move our application into Tier 1, Recommended for Funding, because it was viewed that the study addresses a very important area. Indeed, our work has the potential to not only improve the lives of patients with electronic pacemakers, which increase at a rate of 350,000 recipients a year, but more so for the 20,000 infants and premature babies suffering from congenital heart rhythm dysfunction who are not suitable recipients of such a device.

The motion to move our grant application to Tier 1 did not carry due to the concern that the principal investigator, although considered to be promising, is relatively inexperienced. I would like to respectfully appeal to the Committee that I do have a total of 24 publications with over 6 years of experience in the differentiation of cardiac muscle cells from human pluripotent stem cells, 12 publications (3 co-corresponding author) on human pluripotent stem cells and their cardiac derivatives, and 3 publications on the engineering of pacemaker cells. I have advised many CIRM funded laboratories, including Dr. Kit Lam (UC Davis), Dr. Min Zhao (UC Davis), Dr. Kara McCloskey (UC Merced), and Dr. Michelle Khine (UC Irvine), on the maintenance and differentiation of human pluripotent stem cells. Our proposal is further strengthened by a team of collaborators, Dr. Nipavan Chiamvimonvat (25% effort), Dr. Jan Nolte (5% effort) and Dr. Donald Bers (consultant), who are experienced and established scientists in their respective fields. Dr. Chiamvimonvat was the first to discover the existence of the SK channels in cardiac myocytes. This is the exact ion channel that we have proposed to manipulate to alter the Ca²⁺ signaling mechanisms during human induced pluripotent stem cell differentiation into pacemaking cells. Dr. Nolte is the director of the Stem Cell Program at UC Davis and has more than 20 years of experience in stem cell biology. Dr. Bers is the world renowned scientist on Ca²⁺ signaling in cardiac myocytes. Indeed, our team has been considered by the Reviewers to have the necessary expertise to execute the proposed study.

We would also like to address the Reviewers' concern regarding the dual institution appointment held by the PI at Mount Sinai School of Medicine. Since the submission of the proposal, I have resigned from my Assistant Professor position at Mount Sinai to focus my research entirely at UC Davis. I am 100% committed to this research project. Attached please find a letter from Associate Executive Dean Meyers, UC Davis School of Medicine, attesting to my leadership skills, my independence as an investigator, as well as the strong institutional support for the project. Thank you for your kind consideration of our petition.

Sincerely,

A handwritten signature in black ink that reads 'Deborah K. Lieu'. The signature is fluid and cursive, with the first name being the most prominent.

Deborah K. Lieu, Ph.D.



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August 27, 2012

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RE: CIRM Basic Biology IV Award RB4-05764

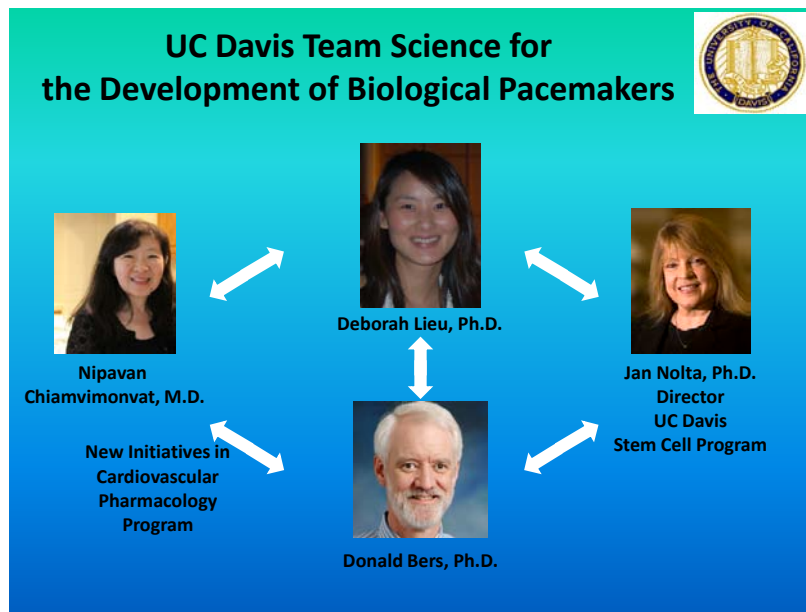
Dear Dr. Lieu,

I am delighted to provide my strongest support for your proposal entitled: "Induction of pluripotent stem cell-derived pacemaking cells," for the CIRM Basic Biology IV Award. I am fully committed to having regular meetings with you and to provide institutional support and guidance to ensure your successful career development. Your proposed strategy for generating pacemaking cells from human-induced pluripotent stem cells is novel and exciting. Your basic research will also fit well into our NIH-funded Clinical and Translational Science Center (CTSC) at UC Davis as it may help patients with electronic pacemaker who have to undergo necessary surgeries every 5-10 years for a battery change and those young patients who are unable to receive these implants.

I am pleased that you have resigned your Assistant Professor position at Mount Sinai School of Medicine after our discussion in April of this year to focus on developing the research program here at UC Davis. I fully support the almost completed process that will promote you into a full-time faculty research position. I will continue to be your strong advocate as you continue to launch your independent career. Indeed, the UC Davis School of Medicine strategic plan is explicit about the recruitment of junior, innovative, independent scientists like you who will also be a member of our stem cell research neighborhood. Your innovation and collaborative nature really shine at UC Davis. Other faculties have described to me how you have provided your expertise to their laboratories on the UC Davis campus on human pluripotent stem cell culture and differentiation. In addition to directing your own laboratory, with your unique background as a biomedical engineer, you are able to successfully contribute towards a multi-disciplinary team, such as your recent effort with an optical physicist, Dr. James Chan, to develop a novel label-free sorting method for human pluripotent stem cell-derived cardiac myocytes at the NSF Center for Biophotonics, Science and Technology. The project has a great translational potential and has already received great interest from GE Healthcare.

I am very impressed that as a junior investigator, you already have a total of **24 publications** in many respected journals including *Circulation*, *American Journal of Physiology: Cell Physiology*, *Tissue Engineering*, and *Heart Rhythms*. Importantly, you are co-corresponding author for three of these publications. Your 2008 publication in *Heart Rhythms* entitled "Over-expression of HCN-encoded pacemaker current silences bioartificial pacemakers: An optimal level is required for inducing atrial automaticity" has received a special commentary in the journal. Twelve of your publications and two provisional patents involving human pluripotent stem cells and/or stem-cell derived cardiac myocytes in the last four years strongly attest to your experience and knowledge in this fast paced and emerging stem cell field.

I have no doubt that your ongoing project on the generation of pacemaking cells from human-induced pluripotent stem cells for engineering biological pacemaker will be a fruitful one. Indeed, I believe that the results from your proposed study will provide new insights leading to the conduct of clinical and translational research in the near future. You have directed this project independently to date. Moreover, you have been able to assemble a very impressive team of more senior faculty to be part of your research program. Your team of experienced co-investigators, including Drs. Nipavan Chiamvimonvat, Jan Nolta, and Donald Bers, will be able to provide you with the necessary advice and support to ensure that your project is successful (please see attached Figure). UC Davis has a strong commitment to the development



of faculty as leaders in the stem cell/regenerative medicine fields. As a stem cell investigator with expertise in biomedical engineering, you will be able to provide the much needed interphase between the Stem Cell Program headed by Dr. Nolta and the new UC Davis initiatives in Cardiovascular Pharmacology Program spearheaded by Drs. Chiamvimonvat and Bers. Your interdisciplinary training as a biomedical engineer enables you to approach the field of human pluripotent stem cells from a unique perspective and to serve as the nexus between our Stem Cell Program, the new Cardiovascular

Pharmacology Program, the Department of Biomedical Engineering, and the NSF Center for Biophotonics, Science and Technology. Your catalytic role has facilitated research interactions and projects among various groups of investigators at our institution. We specifically support your effort towards this type of team science.

In conclusion, UC Davis is highly committed to supporting you through a high level of teamwork. The current Basic Biology grant application exemplifies our values by promoting the highest levels of teamwork and cooperation from investigators with different backgrounds and areas of expertise. Your research program will have our strongest level of commitment to guarantee a very robust, highly collaborative investigative environment with outstanding scientific resources, tools and facilities. I will make every effort to ensure the successful outcome of your research program.

Sincerely,

Frederick J. Meyers, MD, MACP
Executive Associate Dean
Professor of Medicine and Pathology
University of California, Davis, School of Medicine