UNIVERSITY OF CALIFORNIA, SAN DIEGO UCSD

BERKELEY • DAVIS • IRVINE • LOS ANGELES • MERCED • RIVERSIDE • SAN DIEGO • SAN FRANCISCO SANTA BARBARA • SANTA CRUZ

OFFICE: (858) 534-8857
FAX: (858) 534-5220
EMAIL: mtuszynski@ucsd.edu

9500 GILMAN DRIVE
LA JOLLA, CALIFORNIA 92093-0626

Mark H. Tuszynski, M.D., Ph.D.
Professor of Neurosciences
Director, Translational Neuroscience Institute

December 7, 2017

ICOC Board
1999 Harrison Street, Suite 1650,
Oakland, California 94612

Re: CIRM Grant DISC2-10665, ***Neural Stem Cell Relays for Severe Spinal Cord Injury***

Dear Independent Citizen Oversight Committee Members:

I would greatly appreciate your consideration of our DISC2 application, "***Neural Stem Cell Relays for Severe Spinal Cord Injury***." We received a score of 80 on a project that aims to advance a new approach for stem cell treatment to human clinical trials.

CIRM has historically funded approximately 20 grants related to the problem of spinal cord injury (SCI), but it currently only funds 5. Our program is in late stage development and, following work that we propose in the DISC2 application, can proceed to final IND-enabling studies that would initiate a clinical trial. Thus, the stage of our research is highly aligned with CIRM goals to bring therapies to people.

Our approach to using stem cells to treat SCI is fundamentally different from other programs, and uniquely offers the possibility of benefiting ***severely*** injured patients. The other late stage program that CIRM is funding aims to enhance the function of ***spared*** connections in less severely injured patients, and their program is rational and promising; however, they do not aim to **build new neural connections**. Our program aims to ***replace*** connections that are lost after SCI by implanting neural stem cells in the injury site that relay electrical impulses from ***above*** the injury to ***below*** the injury: we basically splice the injured circuit.

Using our methods, neural stem cells can grow new connections through the injured spinal cord in astonishing numbers over very long distances: in our non-human primate studies, human neural stem cells extend hundreds of thousands of new axons to formnew connections for distances up to 50 mm below an injury site. Prior to using stem cells, we achieved growth of only 100 axons for a distance of 1mm; thus, the effects of neural stem cells exceed previous efforts by 50,000-fold. This is an unleashing of huge growth potential that has a realistic chance to benefit human injury.

And our approach has the potential to benefit humans with ***severe*** SCI, which constitutes the majority of injured patients.

The basis of our request to CIRM to consider our proposal, which was close to the funding threshold, is the following:

1. There is a great unmet medical need among thousands of Californians to recover function after SCI. At present, CIRM is only funding one other translational program for SCI, an imbalance relative to previous funding priorities. Patients are anxious for new therapies for SCI, and we are poised to bring one to the clinic.

2. Our approach aims to ***build new neural connections*** after SCI, with the potential to benefit ***severe*** injury. Stem cell treatments currently funded by CIRM are unlikely to impact the most severe patients with the greatest need. In several different animal models from mice to monkeys, we have significantly improved function after severe injury, and repeatedly demonstrated 50% recovery of hand function after cervical (neck) level injury.

3. As the present round of CIRM funding winds down, this may be our last opportunity to develop this work to benefit the citizens of the State of California. CIRM is currently aiming to fund translational studies, and that is exactly the developmental space that we occupy. With funding, we will characterize the final cell lines that will move to human trials.

4. Our team is strong and highly collaborative, involving clinicians and scientists at UCSD, UC Irvine, UCLA, UCSF and UC Davis. We have brought the most experienced spinal cord injury researchers to this program, providing internal checks and balances regarding the quality of the work and the feasibility of human translation. Ours is the only program to successfully test neural stem cell therapies for SCI in non-human primates. In the last 5 years we have published the results of this work in top biomedical journals, including *Cell* (2012)*, Neuron* (2014)*, Nature Medicine* (2017)*, Journal of Clinical Investigation* (2017)*, Nature Communications* (2017) and *Science Translation Medicine* (2017)*.*

We believe that the science, data, results and team backing this proposal are strong, and that this may represent the last opportunity to bring this to patients through CIRM.

Thank you for taking the time to consider this request.

Sincerely yours,

Mark H. Tuszynski, M.D., Ph.D.