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January 22, 2014

Dr. Jonathan Thomas, Chair
Independent Citizens Oversight Committee
California Institute for Regenerative Medicine (CIRM)
210 King Street, San Francisco, CA 94107

Dear Dr. Thomas and Board Members:

I am writing to seek your consideration of our proposal [RB5-07398, "*Engineered matrices for control of lineage commitment in human pancreatic stem cells*"], which was submitted in response to RFA-13-02, Basic Biology Award V. It received a score of 67 and is in Tier 2 of the GWG recommendations. We have contacted Dr. Gilberto Sambrano at CIRM, and believe we have resolved all the concerns raised by the reviewers in a satisfactory manner. We believe that the research we propose is unique in combining synthetic extracellular matrix (ECM) and human progenitor cells, could have great translational impact, and would expand CIRM's diabetes portfolio in a significant way.

The ultimate goal of our research is to generate large numbers of functional, human, beta-like cells suitable for transplantation to treat patients with end-stage type 1 diabetes. The goal of this grant application is to identify defined, artificial ECM proteins that drive the differentiation of human pancreatic progenitor cells into beta-like cells in culture. Importantly, we use human progenitors cells harvested from cadaveric material – the same source of islet cells approved for use in transplantation.

CIRM has been key in building stem cell research programs in California that address a variety of diseases for which there are no current cures or treatments. Although we understand that the programs at CIRM are not designed to be "disease oriented," diabetes has been relatively under-represented in the portfolio of grants supported by CIRM. For example, CIRM currently supports a total of six (6) grants related to the treatment and cell replacement therapy of diabetes. Of the 6, 2 were awarded to UC San Diego and the 4 to Viacyte, Inc.

In summary, I urge you to consider funding our proposal for the following reasons:

1. FDA Approval: While the other funded grants use hESCs as the starting point or source of cells, our proposal uses progenitor cells harvested from human pancreas. This cell

source has already been approved for transplantation, lowering the bar for FDA approval in the future.

2. Translational Path: Although this is a Basic Biology application, it has a very direct path toward translation. The defined ECM proteins are excellent candidates for future clinical use.

3. Complements Other Studies: Our use of human adult progenitors is complementary to existing studies that depend on human pluripotent stem cells. While there is no overlap with the projects currently funded by CIRM, we may discover new pathways that can enhance and instruct studies that use hESCs.

4. Innovation: The reviewers clearly indicated that our proposal is highly innovative and our approach is unique. Thus, we provide an alternative approach to stem cell therapy for diabetes. Adding our proposal to CIRM's diabetes portfolio expands the possibility that one of these funded approaches will, in the long run, be the best option for patients with diabetes.

Thank you for considering our views and our proposal.

Sincerely,

David A. Tirrell
Ross McCollum – William H. Corcoran Professor
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