Application Number: TRAN4-15225

From: Ravindra Majeti <rmajeti@stanford.edu>
Sent: Monday, October 23, 2023 9:21:16 PM
To: Scott Tocher <stocher@cirm.ca.gov>
Subject: [EXT] RE: CIRM Trans Grant Application: TRAN4-15225

Dear CIRM Scientific Officer and Review Panel,

I am writing to provide my support and advocacy for the above referenced application from Dr. Irv Weissman. To introduce myself, I am the Virginia and D.K. Ludwig Professor, Professor of Medicine (Hematology), and Director of the Institute for Stem Cell Biology and Regenerative Medicine at Stanford University. I have extensive experience in human hematopoietic stem and progenitor cell biology and clinical applications of these cells – and thus feel qualified to provide these comments. Note, that I am not a collaborator on this project and have not had any direct involvement in the proposed research from Dr. Weissman.

As you know, this grant application aims to develop and implement methods for the purification of CD34+CD90+ human HSCs for use in clinical transplantation applications. While the field has long implemented CD34+ purification as a method for HSC enrichment – this population is actually comprised of few HSCs with more than 95% of the cells being non-stem progenitor cells. Thus, it is a misnomer for reviewers to label CD34+ cell products as HSCs, and suggests an incomplete consideration of hematopoietic stem cell biology on their part. Why does this matter? The clinical significance of this is most pronounced in the proposed use of the cells as a source of cancer-free stem cells for bone marrow reconstitution following high dose chemotherapy (particularly in metastatic breast cancer patients). Through the course of rigorous cell purification of CD34+CD90+ HSCs, this process results in depletion of any contaminating cancer cells in the bone marrow product, which is not achieved with just CD34+ cell enrichment. For autologous transplantation, this results in a potential novel therapy for patients, that is high dose chemotherapy followed by HSC transplantation to overcome potentially fatal bone marrow failure induced by the chemotherapy. This approach is supported by historical data as reported by Dr. Weissman showing potential for significant clinical benefit in patients, and thus is worthy of further investigation in new patients. It is on this key point of advancing a novel therapy that may potentially benefit patients that I provide my support and advocate for this application.

Thank you for your consideration,
Dr. Ravi Majeti

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