**From:** "Wagers, Amy J" <amy_wagers@harvard.edu>
**Date:** Monday, May 13, 2024 at 4:48 PM
**To:** Scott Tocher <stocher@cirm.ca.gov>, Claudette Mandac <cmandac@cirm.ca.gov>
**Cc:** "irv@stanford.edu" <irv@stanford.edu>, "tal6933@stanford.edu" <tal6933@stanford.edu>
**Subject:** [EXT] Letter of support - TRAN4-16091 (Weissman)

Dear Drs. Tocher and Mandac,

I write to express my enthusiastic endorsement for Dr. Irving Weissman's recently reviewed application, TRAN4-16091 "Purification of human hematopoietic stem cells (HSCs) for clinical stem cell transplantation". I understand from Dr. Weissman that reviewer scores of this resubmitted proposal place it at the borderline for funding approval. I therefore felt it important to reach out to the council, as a colleague in the stem cell field who has followed Dr. Weissman's work for almost three decades, to emphasize the novelty, significance and translational importance of the work he will pursue under this project.

As noted in my previous letter of support, submitted after the prior review of his proposal, I have had the opportunity to witness first-hand the compelling data that motivates Dr. Weissman's proposal, and I am convinced by the clear evidence that his work provides of the need to develop appropriate reagents and protocols to support clinical-grade purification and transplantation of autologous HSCs for the treatment of metastatic breast cancer. Treatment outcomes for these patients are dismal, and novel approaches are urgently needed. While autologous hematopoietic cell transplants have been considered previously for these cancers, Dr. Weissman's approach of using ***purified*** stem cell grafts (as opposed to "bulk" or "enriched" CD34+ cells) is utterly unique and of singular importance. This is because bulk CD34+ cells, even if magnetically enriched for CD34, are always contaminated with other cell types, including most importantly metastatic cells that can reintroduce the cancer into transplant recipients. While this crucial distinction between Dr. Weissman's approach of using purified cells and prior efforts using bulk cells may seem at first blush to be one of detail or degree, this is in fact a ***critical*** distinction demonstrated in an early pilot scale trial to make all the difference in treatment outcome and survival for the handful of patients that were able to access it.

With this in mind, I urge you emphatically to recommend Dr. Weissman's proposal for funding in this round so that he can continue his novel and exciting work without delay. I am certain that the advances he will achieve through these efforts will translate to safer, more effective therapies for metastatic breast cancer, and potentially other malignancies. This is exactly the type of transformative work CIRM was created to enable, and essential to reshape the futures of hundreds of thousands of current and future patients.

With kind regards,

Amy Wagers

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