

Application Number: TRAN4-15225

From: David Miklos <dmiklos@stanford.edu>

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To: Scott Tocher <stocher@circm.ca.gov>; Irving L. Weissman M.D. <irv@stanford.edu>; mporteus <mporteus@stanford.edu>; Steven A Feldman PhD <feldmans@stanford.edu>

Subject: [EXT] Purified Human HSC remains high priority need

Dear CIRM colleagues,

I am writing in support of Dr Irv Weissman's TRAN grant to re-introduce high speed cell sorting technology to Stanford Laboratory Of Cell and Gene Medicine (LCGM) in support of subsequent human translational research treating women with triple negative metastatic breast cancer. As Executive Director of LCGM (along with Dr Mathew Porteus) and Chief of Stanford BMT and Cell Therapy Program since 2020, I am providing my strongest letter of support for Dr Weissman's effort to establish high speed cell sorting for HSC isolation at Stanford LCGM. In collaboration with Dr. Weissman's team, LCGM Director, Dr. Steve Feldman, has tested both the Sony machines and the new Miltenyi Tyto demonstrating their isolation of ultrapure HSC from PBMC spiked with large numbers of human breast cancer cells, and the HSC were in sufficient numbers and viability to engraft humans just treated with myeloablative high dose combination chemotherapy.

As always, Dr Weissman is leading our Stanford HSC isolation technologies that will not only benefit woman with triple negative breast cancer but the reintroduction of high-speed sorters will also benefit our allogeneic HSC transplantation using engineered grafts. Dr. Rob Negrin introduced Influx sorters to Stanford in 2005 to isolate human HSC and T regulatory cells pursuing human translational research where addition of purified Tregs prevented GVHD. These influx machines are no longer supported due to extreme technical needs and specialized operator costs. The new Sony and Miltenyi Tyto sorters will overcome these limitations and benefit many Stanford Investigators in addition to the important clinical trial work Dr Weissman has pursued for over two decades.

In summary, as the leading BMT clinician at Stanford, I assure the CIRM committee that HSC isolation using high speed cell sorters remains our high priority research at Stanford University. Dr Weissman has proposed and organized the necessary MoAb and cell sorter technologies that will benefit

women with metastatic triple negative breast cancer and allogeneic HSC patients at Stanford. Please support his TRAN research proposal.

David

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