Stanford MEDICINE | Laboratory for Cell & Gene Medicine

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Irving Weissman
Virginia & D.K. Ludwig Professor of Clinical Investigation in Cancer Research
Professor of Pathology and Developmental Biology
Stanford University School of Medicine
Stanford, CA

Dear Irv:

I am writing to express my highest level of enthusiasm for your CIRM TRAN4 grant application entitled, "Purification of Human Hematopoietic Stem Cells (HSCs) for Clinical Stem-Cell Transplantation." The primary goal of your project is to enhance the effectiveness of hematopoietic cell transplants (HCT) by introducing cancer and T cell-free hematopoietic stem cells (HSC) transplants. We have successfully collaborated with your group on assay design and development of protocols for HSC purification at the Stanford Laboratory for Cell and Gene Medicine (LCGM). The proposed project reflects our shared goal of broad distribution of HSC purification tools and assay parameters, which will enable increased accessibility for this important technology.

The Stanford LCGM is an innovative, cutting-edge facility staffed by world class professionals extensively trained in development of cGMP compliant manufacturing processes and manufacturing of innovative cell and gene therapies. LCGM is a translational laboratory and cGMP manufacturing facility that is FACT accredited and compliant with US FDA current Good Manufacturing Practices (cGMP - 21 CFR Parts 210, 211), Human Cells, Tissues, and Cellular and Tissue-Based Products (21 CFR Part 1271). The 23,000 square foot LCGM facility was designed as a multi-product facility and has sufficient space, equipment, and qualified staff to develop cGMP compliant manufacturing and analytics and manufacture, release and store cell and viral vector products intended for phase I/II clinical investigations. The facility contains separate spaces to produce cell and viral vector final products with mechanical systems and operating procedures designed to prevent the adulteration of raw materials or products.

As you know, we have successfully demonstrated proof of concept for the proposed HSC purification method at the LCGM. Two full scale runs were performed with MCF7-spiked MPB from healthy donors, with CD34+ selection on the CliniMACS Prodigy®, followed by CD34+CD90+ sorting using the original Systemix antibodies. Our data demonstrates the purification potential of the SONY CGX10 cell isolation system, with each sort achieving a highly viable target fraction with >96% purity and >20% recovery of the CD34+CD90+ population (see

Table 3 in the Scientific Rationale section), as we are purifying only the $CD34^{high}CD90^{high}$ cell population. We will continue to optimize the HSC purification sorting process using re-engineered GMP monoclonal antibodies (see Scientific Rationale, Aim 1) and after completing a process feasibility run, quickly move into engineering runs and GMP document preparation to support manufacturing at Stanford and technology transfer to other clinical sites.

Upon completion of this project, we aim to have a scalable, validated HSC purification protocol and reagents ready for manufacturing and subsequent clinical trials. This will enable a distributed manufacturing model, with technology transfer from LCGM to collaborating medical centers. This is an established model, as LCGM has successfully performed technology transfers to multiple contract manufacturing organizations, academic collaborators, and industry partners. Ultimately, we aim to enable rapid implementation of innovative and refined HSC purification techniques across a network of medical practices, which will address significant barriers in the advancement of HSC-based therapies for a wide range of conditions.

We look forward to continuing our productive collaboration.

Sincerely,

Steven A. Feldman, Ph.D.

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