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Tracy C. Grikscheit, MD
4650 Sunset Boulevard Mailstop #100
Los Angeles, CA 90027
DISC2-10979 Universal Pluripotent Liver Failure Therapy (UPLiFT)

Dear Tracy,

This letter signals our ongoing intention to support your DISC-2 Quest Award Application to perform steps toward translating a defined differentiation strategy to generate liver precursors from induced pluripotent stem cells (iPSCs). In brief terms, successful funding of this grant would allow us together to take the preclinical steps toward an off-the-shelf stem cell therapy for children with metabolic disorders of the liver, without the requirement for a lifelong course of drugs to suppress the immune system. There is no current therapy like this that is available.

We were delighted to learn that you had the fourth highest score from the grant working group that reviewed these applications, with a median score of 90 out of 100. These planned induced pluripotent stem cell differentiations and subsequent in vivo applications to forestall or repair liver failure are designed to create therapeutic solutions for patients, a goal that we share. We also share your interest in proceeding to clinical trials with dispatch, and generating the data from the studies described in the grant application is the important next step for this cell therapy. As the CSO and co-founder of Universal Cells (now a subsidiary of Astellas), we have had productive discussions around the potential applications of universal donor iPSCs that we are generating for these kinds of translational strategies. We intend to support your Universal Pluripotent Liver Failure Therapy (UPLiFT) project by providing you at no cost with a research grade version of the GMP Lonza iPSC line that has been gene-edited as a Universal donor line. This line is derived from the GMP grade of the same cell line that you have used to generate your pilot data, LiPSC-GR1.1(1, 2). And you have also generated pilot data with our research grade universal lines derived from the Elf-1 ESC line, that were similarly engineered.

We are hopeful that work on the UPLiFT project will result in a transplantable cell population of hepatic progenitor cells that will not require immunosuppression because of the gene editing that has resulted in expression of the non-polymorphic HLA-E protein as the sole HLA Class I molecule. We wish you luck with the application and look forward to continuing our discussions.

Sincerely,

David Russell, MD, PhD
CSO, Universal Cells, Inc.
Seattle, WA 98105

1. **Baghbaderani BA, Syama A, Sivapatham R, Pei Y, Mukherjee O, Fellner T, Zeng X, and Rao MS**. Detailed Characterization of Human Induced Pluripotent Stem Cells Manufactured for Therapeutic Applications. *Stem Cell Rev* 12: 394-420, 2016.
2. **Baghbaderani BA, Tian X, Neo BH, Burkall A, Dimezzo T, Sierra G, Zeng X, Warren K, Kovarcik DP, Fellner T, and Rao MS**. cGMP-Manufactured Human Induced Pluripotent Stem Cells Are Available for Pre-clinical and Clinical Applications. *Stem Cell Reports* 5: 647-659, 2015.