Skysong Innovations
Advancing the Arizona State University Knowledge Enterprise

1475 N. Scottsdale Road, Suite 200
Scottsdale, AZ 85287-3538
Phone: 480 884 1996 Fax: 480 884 1984

Case ID:M17-159L^
Published: 12/10/2021

Inventors

Mo Reza Ebrahimkhani
Samira Kiani
Jeremy Velazquez
Ryan LeGraw

Contact

Jovan Heusser
jovan.heusser@skysonginnovations.com

Genetically Engineered Human Fetal Liver Niche

Despite significant advances in our understanding of hematopoietic stem cells (HSCs), their widespread use is hindered by the scarcity of human leukocyte antigen-matched donors. Although HSCs can be harvested from umbilical cord blood, adult bone marrow, and peripheral blood, the number of recovered HSCs in these sources is so low that either large volumes of donor tissues are needed or the HSCs need to be significantly enriched to be of use. Many techniques for ex vivo expansion of HSCs and progenitor cells require manually and sequentially adding multiple growth factors and other compounds, complicating reproducibility and making the therapeutic strategy cost prohibitive. Better ex vivo expansion strategies are desperately needed to permit the use of samples with low HSC numbers.

Researchers at Arizona State University have developed a platform to expand hematopoietic stem cells ex vivo in genetically engineered human fetal liver niche (FLiN) tissue. This platform has the capacity to act as a niche to support the biomanufacture, expansion and differentiation of HSCs ex vivo. Progenitor cells were genetically engineered to co-differentiate and self-organize sequentially into vascularized fetal liver tissue in vitro without supplementation of any growth factors forming the complex FLiN tissue. HSCs are then seeded onto the FLiN tissue and cultured in highly defined but xeno-free conditions to promote and enhance proliferation for a period of days after which they are recovered for use.

Using synthetic biology and genetic engineering technologies, this platform provides customizable FLiN tissue for enhanced HSC expansion and differentiation ex vivo.

Potential Applications

- Production of HSCs for use in:

o Treating hematologic diseases – e.g. sickle cell disease, beta-thalassemia, anemia, etc.

o Treating immune system disorders – e.g. HIV, histiocytic diseases, Wiskott-Aldrich Syndrome, etc.

o Cancer treatments – e.g. leukemia, lymphoma, myeloma, etc.

Benefits and Advantages

- The FLiN tissue is self-organizing and continues evolving without having to add exogenous growth factors
- Reduces the cost of HSC production by about 700 times
- Ease of engineering - the progenitor cells can be cryopreserved multiple times with minimal handling requirements
- Scalable – robust cultures that are permissive to scalability
- Enables a 2-10-fold expansion of HSCs
- The FLiN tissue mimics key features of the fetal liver including several subsets of stromal cells, endothelial cells and cell signaling cues

For more information about this opportunity, please see

Velazquez et al - bioRxiv - 2020

For more information about the inventor(s) and their research, please see

Dr. Santello's departmental webpage

Dr. Santello’s laboratory webpage