Stem cell scientists explore treatments for blood disorders and lung diseases

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UTHealth stem cell researchers Brian Davis, Ph.D., left, and Paul Simmons, Ph.D., received simulus award. Credit: The University of Texas Health Science Center at Houston (UTHealth)

Stem cell scientists at The University of Texas Health Science Center at Houston (UTHealth) were awarded stimulus grants totaling almost $2 million to research experimental treatments for blood disorders and inherited lung diseases affecting children.

The scientists received two of only seven National Institutes of Health Challenge (RC1) Grants for human embryonic stem-cell-related research awarded across the nation by the National Heart, Lung and Blood Institute. The two-year Challenge grants are funded through the American Recovery and Reinvestment Act of 2009 and are designed to

support research that should have a high impact in biomedical or behavioral science and/or public health.

Researchers are on the faculty of the UTHealth Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases (IMM), a research institute that seeks to investigate the cause of human diseases at the cellular and molecular levels using DNA and protein technologies to elucidate disease mechanisms.

The first research project is led by Paul Simmons, Ph.D., professor and director of the UTHealth Centre for Stem Cell Research, and is designed to address the shortage of a specific type of blood-forming stem cell used in the treatment of cancers of the blood and some inherited blood disorders.

These cells are called hematopoietic stem cells (HSC) and are killed as a consequence of chemotherapy or radiation. While they can be replaced with cells harvested from tissue-matched bone marrow, peripheral blood or umbilical cord blood, a very significant impediment continues to be the availability of appropriate tissue-matched HSC from these three sources, said Simmons, who is a past president of the International Society for Stem Cell Research.

Simmons' proposed solution to this problem is to use human embryonic stem cells to create a new source of HSCs. Much more versatile than adult stem cells, human embryonic stem cells can be coaxed to develop into hundreds of different cell types. A new strategy to generate transplantable HSCs will be tested under laboratory conditions.

Human embryonic stem cells are not the only cells capable of developing into a wide variety of cell types, which scientists describe as pluripotency. Skin cells can be converted into "induced pluripotent stem cells" or iPS cells, which are believed to have many of the same

capabilities as human embryonic stem cells.

If successful, Simmons' strategy could possibly be used to coax iPS cells into becoming HSCs, too. Researchers at UTHealth use human embryonic stem cells approved by the National Institutes of Health.

"This proposal seeks to develop markedly improved strategies to derive HSC from pluripotent stem cells and to further the development of novel cellular therapies for treating blood diseases," Simmons said.

The second research project is led by one of Simmons' colleagues at the UTHealth Centre for Stem Cell Research, associate professor Brian Davis, Ph.D., who along with UTHealth molecular medicine professor Rick Wetsel, Ph.D., is looking into a new way to treat two pediatric lung diseases linked to single gene defects - Surfactant Protein B Deficiency and Cystic Fibrosis.

Surfactant is a protein that helps keep lungs inflated and a shortage can lead to severe respiratory disease. Surfactant deficient infants are extremely ill and without neonatal intensive care intervention, including ventilation, they will die shortly after birth. Even with intensive care intervention, these infants may only survive for a short time (weeks to months) if they do not receive a lung transplant.

Cystic fibrosis is an inherited chronic disease that affects the lungs and digestive system of about 30,000 children and adults in the United States (70,000 worldwide), according to the Cystic Fibrosis Foundation. A defective gene and its protein product cause the body to produce unusually thick, sticky mucus that clogs the lungs and leads to life-threatening lung infections.

Davis said the researchers are exploring the use of an experimental treatment involving gene-corrected iPS derived cells generated using

zinc finger nuclease (ZFN) technology developed by Sangamo BioSciences, Inc. to address these two conditions.

"We're going to start with the skin cells of a patient with a lung disease, then take those cells and convert them into iPS cells and correct the genetic defect. Then finally, the disease free iPS cells will be used to generate lung cells that can be used for cell-based therapies," he said.

One of the benefits of this technique, according to Wetsel, is that because researchers are using the patient's own cells, it is far less likely that the patient's immune system will reject the gene-corrected cells. Wetsel is the William S. Kilroy Sr. Chair in Pulmonary Disease at the IMM and he is also the director of the Hans J. Mueller-Eberhard & Irma Gigli Research Center for Immunology and Autoimmune Diseases at the IMM.

The research funded by the second NIH award will support research in animal models. If these studies are successful, they may lay the foundation for the next generation of preclinical studies designed to explore the effectiveness of these approaches for eventually treating pulmonary diseases in patients.

C. Thomas Caskey, M.D., director and CEO of the IMM, said, "These awards recognize significant developments in two areas. The first award addresses issues critical to blood stem cell derivation from pluripotent stem cells with the potential to greatly benefit transplantation for various diseases of the blood forming system. The second award involves the conversion of skin cells to pluripotent stem cells from an individual with lung disease, and in common with the first award, enables personalized therapeutic initiatives. Both programs were enabled by Houston philanthropy prior to available federal funding. These are well-deserved awards. My congratulations to the donors and scientists for their perseverance and success."