Researchers generate iPSCs to further treatments for lung disease

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(Boston) A team of researchers from Boston University's Center for Regenerative Medicine and the Pulmonary Center have generated 100 new lines of human induced pluripotent stem cells (iPSC) from individuals with lung diseases, including cystic fibrosis and emphysema. The new stem cell lines could possibly lead to new treatments for these debilitating diseases. The findings, which appear in the current issue of *Stem Cells*, demonstrate the first time lung disease-specific iPSC have been created in a lab.

iPSCs are derived by reprogramming adult cells into a primitive stem cell state. This process results in the creation of cells that are similar to embryonic stem cells in terms of their capability to differentiate into different types of cells, including endoderm cells that can give rise to liver and lung tissue.

"iPSCs solve many major hurdles currently impacting embryonic stem cell research," said Darrell Kotton, the study's lead author and associate professor of medicine and pathology and laboratory medicine at Boston University's School of Medicine (BUSM). iPSCs do not require embryos, and the process used to cultivate iPSCs is easier than the techniques used to obtain embryonic stem cells. iPSCs are genetically identical to the patient's cells and potentially can be transplanted back without rejection.

"In a laboratory dish, these cells have the ability to multiply indefinitely so that researchers have more time to investigate the diseased cell and

correct its genes," said Kotton.

The study involved patients with different forms of lung disease – cystic fibrosis, alpha-1 antitrypsin deficiency-related emphysema, scleroderma (SSc) and sickle cell disease. The patients underwent skin biopsies and donated tissue samples, which the research team used to cultivate adult stem cells. Using a Boston University-patented vector in the form of a virus, named the Stem Cell Cassette (STEMCCA), the researchers were able to reprogram the skin cells into the primitive pluripotent stem cells known as iPSCs.

"The STEMCCA vector is proving invaluable for reprogramming cells from a variety of species, and this is the first report of the 'humanized' version of our vector for use in reprogramming human cells," said Gustavo Mostoslavsky, a co-author of the study and assistant professor of medicine at BUSM. Together Kotton and Mostoslavsky co-direct the new Boston University Center for Regenerative Medicine (CReM).

To test the differentiation power of the iPSCs, the team showed that the stem cells multiplied and could be differentiated into endoderm tissue, the natural precursor cells of the lung, the primary organ destroyed by the diseases cystic fibrosis and emphysema.

"We hope to build a bank of stem cells that could be used to help treat the two most common forms of inherited lung disease, cystic fibrosis and alpha-1 antitrypsin deficiency," said Kotton.

The next step, he said, is to correct the genetic mutations responsible for causing cystic fibrosis, emphysema and other lung diseases.

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