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Researchers validate important roles of iPSCs in regenerative medicine

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Researchers from Boston University's Center for Regenerative Medicine (CReM) have demonstrated that induced pluripotent stem cells (iPSCs) can differentiate into definitive endoderm cells, in vitro, with similar functional potential when compared to embryonic stem cells (ESCs), despite minor molecular differences between the two cell types.

These findings are particularly important given growing controversy in the scientific literature about whether subtle differences between iPSCs and ESCs should dampen enthusiasm for iPSCs to serve as an alternative source of differentiated precursor cells for various tissues, such as the liver, lung or blood. The new work provides compelling evidence that iPSCs have potential in regenerative medicine as an investigational tool for the development of treatments against diseases that affect endodermal-derived organs, such as cirrhosis, diabetes, cystic fibrosis and emphysema.

Darrell Kotton, MD, an associate professor of medicine and pathology at Boston University School of Medicine (BUSM), served as principal investigator and senior author for this study, which is published online in the Journal of Clinical Investigation (JCI). Constantina Christodoulou, BS, from BUSM's program in genetics and genomics, was the lead author of the study.

iPSCs, discovered in 2006, are derived by reprogramming adult cells into a primitive stem cell state. They are similar to ESCs in terms of their ability to differentiate into different types of cells in vivo, including

endoderm cells that give rise to liver and lung tissue. iPSCs do not require embryos and they are genetically identical to the patient's cells, suggesting their future potential to be transplanted back into the same patient without risk of rejection. Additionally, iPSCs could reduce the reliance on ESCs, which remain highly controversial and have limited availability due to federal regulation.

Recently, however, there has been debate regarding whether the molecular differences found in iPSCs make them as functional for research as ESCs when used in regenerative medicine research.

Kotton and his colleagues set out to understand the limits and potential of iPSCs and whether they should be utilized in research as a basis for the development of potential therapies. They focused their research on the capacity of iPSCs to undergo differentiation in vitro into endodermal tissue.

Working together with the laboratory of Gustavo Mostoslavsky, MD, PhD, assistant professor of medicine at BUSM, the teams of CReM investigators generated their own iPSC lines by reprogramming skin fibroblasts using a special stem cell cassette vector (STEMCC). They interrogated the global gene expression profiles of each cell line during endodermal differentiation and also compared the resulting cells to authentic endoderm from early developing mouse embryos.

"We found that although there are subtle molecular differences between iPSCs and ESCs, their functional potential to differentiate was virtually indistinguishable in vitro," said Kotton, who is a co-director of CReM. "It is important to understand that iPSCs offer many possibilities in regenerative medicine and developmental biology research and may hold the key to future medical treatments for many human diseases."

The next step, said Kotton, is to further differentiate iPSCs into more

specific cell types using both mouse and human stem cell lines. CReM currently has 100 stem cell lines from donors with lung-specific diseases that will be used in the research to develop potential treatments against diseases that affect the lungs.

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