Short Communication

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Journal of
Stem cell biology and transplantation

2021
Vol. No. S(7)

Modeling Pancreatic Adenocarcinoma, Cystic Fibrosis and pancreatitis Using Pluripotent Stem Cell-Derived Human Pancreatic Ductal Epithelial Cells

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Abstract

The pancreatic duct system contains a number of epithelial cell types. These are the minor cells of total pancreas comprising 10% of all other pancreatic cells. On the other hands, they are exclusively involved in a number of very serious pathological diseases including lethal pancreatic adenocarcinoma, cystic fibrosis and pancreatitis. We established an efficient strategy to direct human pluripotent stem cells, including human embryonic stem cells (hESCs) and an induced pluripotent stem cell (iPSC) line derived from patients with cystic fibrosis, to differentiate into pancreatic ductal epithelial cells (PDECs). After purification, more than 98% of hESC-derived PDECs expressed functional cystic fibrosis transmembrane conductance regulator (CFTR) protein. In addition, iPSC lines were derived from a patient with CF carrying compound frameshift and mRNA splicing mutations and were differentiated to PDECs. PDECs derived from Weill Cornell cystic fibrosis (WCCF)-iPSCs showed defective expression of mature CFTR protein and impaired chloride ion channel activity, recapitulating functional defects of patients with CF at the cellular level. These studies provide a new methodology to derive pure PDECs expressing CFTR and establish a "disease in a dish" platform to identify drug candidates to rescue the pancreatic defects of patients with CF. This is the landmark achievement towards the cutting edge modeling of pancreatic epithelial cell originated lethal diseases with more accuracy and faster validation.

Biography

Semen Simsek is from Department of Biological Sciences and Bioengineering. Weill Cornell Medical College, New York.Current Institution is Sabanci University. Semen Simsek has done more than 2 Publications. More interested in Pluripotent stem cell technology.

Publication of speakers

1. Senem Simsek et al; Modeling cystic fibrosis using pluripotent stem cell-derived human pancreatic ductal epithelial cells,2016
2. Senem Simsek et al; P57. Self-renewal of hESCs is maintained in hypoxia through cooperation of Notch and Shh pathways,2010

Citation : Senem Simsek; Modeling Pancreatic Adenocarcinoma, Cystic Fibrosis and pancreatitis Using Pluripotent Stem Cell-Derived Human Pancreatic Ductal Epithelial Cells; Stem Cell 2021; February 10; Dubai ,UAE.