New miniature organ to understand human pancreas development

Dresden and Copenhagen researchers establish human pancreas culture system.

The pancreas is a little organ behind the stomach and has two main functions – digestion and blood sugar regulation. How the human pancreas develops has been relatively unexplored for ethical and practical reasons. Researchers from the Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG) in Dresden, Germany, the Novo Nordisk Foundation Center for Stem Cell Biology (DanStem) in Copenhagen, Denmark, and several other international collaborators, including CIC bioGUNE in Bilbao, Spain, were now able to establish a human pancreas miniature organ in cell culture. Another result of the study is also an atlas of single cells in the human fetal pancreas, which allows researchers to see which genes are expressed in the different cell types during development. This miniature organ and the atlas could offer insights into human syndromes impairing pancreas development and can help in generating replacement beta cells for diabetes therapy.

Even though the pancreas is a little organ, sitting behind the stomach, it is an essential organ producing digestive enzymes and hormones, notably insulin and glucagon. To study the development of this vital organ, Anne Grapin-Botton, a director of the MPI-CBG and former professor at the DanStem, developed in past studies culture methods that allow mouse pancreas cells to grow in three-dimensional conditions, forming tree-like structures that resemble a miniature mouse pancreas. Those miniature organs are also referred to as organoids. The development of the human pancreas in embryos has been challenging to research and there was little information available on how its cells develop in 3D.

Carla Gonçalves, a doctoral student in the research lab of Anne Grapin-Botton, worked together with colleagues in both DanStem and MPI-CBG to develop a similar culture system for human pancreas cells in order to study the developing human pancreas. The researchers then compared these newly generated human pancreas organoids and human pancreas cells in traditional flat cell culture to a reference single cell transcriptome of the human fetal pancreas. This single cell transcriptome atlas shows all the genes expressed in each cell during development, as only a subset of the genetic code is converted into RNA molecules and then proteins. “When comparing the two cell culture systems, we found that the pancreatic progenitor cells in the three-dimensional cell culture system are more similar to the cells in the human fetal pancreas. The method to generate the miniature human pancreas is very robust, so it will allow us to explore many questions related to human pancreas biology in the future,” explains Carla Gonçalves. “Indeed, organoids can be observed with microscopes as they develop and easily subjected to experiments, which we are doing at the MPI-CBG,” adds Anne Grapin-Botton. The labs of Antonio del Sol at CIC bioGUNE and the LCSB – Luxembourg Centre for Systems Biomedicine used the data generated from the human fetal pancreas in a cell-cell communication network model to study how cells communicate by tracing which cells produce which signal and which ones receive it.

“Our cell culture system enables us to study human pancreas development in three-dimensions. Diseases like diabetes can have their origin already during the development of a fetus. With this new three-dimensional miniature organ, we can get more insight into the human pancreas development,” says Anne Grapin-Botton. “We now have a benchmark how a normal human pancreas should develop and study how diabetes may occur when development goes wrong. We
can also study how the beta cells that make insulin are formed to produce them more efficiently for future cell therapies of diabetes.”

About the MPI-CBG
The Max Planck Institute of Molecular Cell Biology and Genetics (MPI-CBG), located in Dresden, is one of more than 80 institutes of the Max Planck Society, an independent, non-profit organization in Germany. 550 curiosity-driven scientists from over 50 countries ask: How do cells form tissues? The basic research programs of the MPI-CBG span multiple scales of magnitude, from molecular assemblies to organelles, cells, tissues, organs, and organisms. The MPI-CBG invests extensively in Services and Facilities to allow research scientists shared access to sophisticated and expensive technologies.
www.mpi-cbg.de

About the Novo Nordisk Foundation Center for Stem Cell Biology (DanStem)
The Novo Nordisk Foundation Center for Stem Cell Biology (DanStem) was instituted in 2011 as an international research center for basic stem cell and developmental biology with a grant from the Novo Nordisk Foundation. DanStem is solving complex problems in stem cell and developmental biology, spanning early embryonic development and organogenesis through advanced disease development and cell or drug-based therapies. The center is part the Faculty of Health and Medical Sciences of the University of Copenhagen.
www.danstem.ku.dk

About CIC bioGUNE
The Centre for Cooperative Research in Biosciences (CIC bioGUNE), located in the Bizkaia Technology Park, is a biomedical research organisation conducting cutting-edge research at the interface between structural, molecular and cell biology, with a particular focus on generating knowledge on the molecular bases of disease, for use in the development of new diagnostic methods and advanced therapies. CIC bioGUNE has been accredited as a “Severo Ochoa Centre of Excellence”, the highest level of recognition for centres of excellence in Spain.
www.cicbiogune.es

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