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Mapping the Pancreatic Islets

Multi-million dollar grant will fund human atlas aimed at identifying changes leading to type 1 diabetes

The mechanism leading to development of type 1 diabetes remains a mystery, hampering the ability to find new ways to prevent, treat or even cure this condition. With a new $3.3 million grant, University of California San Diego School of Medicine researchers hope to create a high resolution reference map of pancreatic cells that will identify molecular changes that arise during type 1 diabetes.

"A human cell atlas of type 1 diabetes would help us understand what is happening in the pancreas, allowing us to reconstruct cell signaling networks so that we can see what leads to destruction of insulin-producing cells," said Maike Sander, MD, professor in the Departments of Pediatrics and Cellular and Molecular Medicine at UC San Diego School of Medicine, director of the Pediatric Diabetes Research Center and co-principal investigator on the grant. "We have a good idea of how type 1 diabetes develops in mouse models. Mice have been cured many times, but there are substantial differences with human disease so we have to analyze human tissue."

In the United States, 1.25 million people live with type 1 diabetes, an autoimmune disease that destroys pancreatic beta cells. These cells, found in groups called islets of Langerhans, help maintain normal blood glucose levels by producing the hormone insulin — the master regulator of energy (glucose). Impairment and the loss of beta cells interrupts insulin production, leading to type 1 and 2 diabetes.

The multi-year grant from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), part of the National Institutes of Health (NIH), teams Sander, an expert in islet biology and diabetes, with Kyle Gaulton, PhD, assistant professor in the Department of Pediatrics and the Pediatrics Diabetes Research Center, who brings expertise in genetics and genomics of diabetes, as well as David Gorkin, PhD, and Sebastian Preissl, PhD, associate directors of the UC San Diego Center for Epigenomics, directed by Bing Ren, PhD, professor of cellular and

molecular medicine. The Center for Epigenomics will provide the state-of-the-art technology needed to analyze biobank tissue from people with type 1 diabetes needed to create the cell atlas.

"The goal is to fully understand which immune cells and other cell types populate the pancreas when beta cells are destroyed," said Ren. "By generating a comprehensive map of pancreatic cells using cutting-edge epigenomic technologies, we may reveal critical interactions leading to the onset of type 1 diabetes."

Using samples from JDRF's Network for Pancreatic Organ Donors with Diabetes (nPOD), the team is employing epigenomic technology to analyze tissue at the single cell level. The information is a critical piece needed by a consortium of diabetes experts, the NIDDK Human Islet Research Network, of which Sander is a contributing investigator, to find innovative strategies to protect or replace functional beta cell mass in people living with diabetes.

"By generating an atlas of pancreatic cells from non-diabetic and type 1 diabetic individuals, we may identify novel biomarkers of disease that can inform strategies for early intervention or treatment," said Gaulton. "Together our findings may provide key insights into the pathogenic processes of cells in the pancreatic micro-environment that lead to beta cell loss in type 1 diabetes."

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