UC San Diego Health

Diabetes in a Dish

With NIH grant, UC San Diego researchers hope to build bits of miniature pancreas

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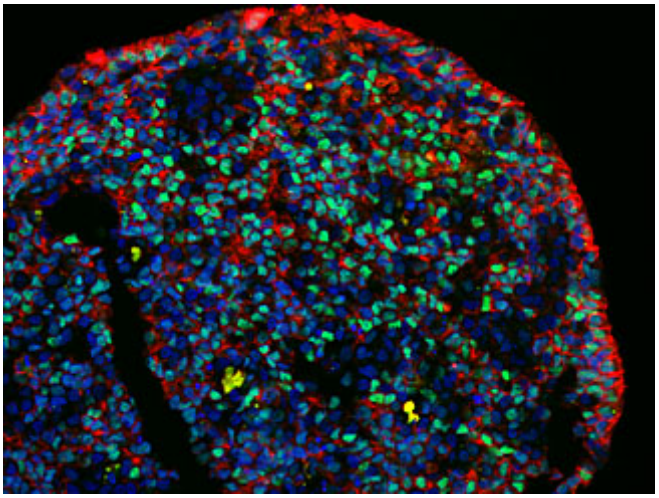
Although type 1 diabetes can be controlled with insulin injections and lifestyle modifications, major advances in treating the disease have not been made in more than two decades and there remain fundamental gaps in what is understood about its causes and how to halt its progression.

With a 5-year, $4-million grant from the National Institutes of Health, researchers at University of California, San Diego School of Medicine and bioengineers at UC San Diego Jacobs School of Engineering, with colleagues at UC Irvine and Washington University in St. Louis hope to change this.

The team's goal is to bioengineer a miniature pancreas in a dish, not the whole pancreas but the organ's irregularly shaped patches – called Islets of Langerhans – that regulate the body's blood sugar levels.

"The bottleneck to new cures for type 1 diabetes is that we don't have a way to study human beta cells outside of the human body," said Maike Sander, MD, professor in the departments of Pediatrics and Cellular and Molecular Medicine and director of the Pediatric Diabetes Research Center at UC San Diego and Rady Children's Hospital-San Diego. "If we are successful, we will for the first time be able to study the events that trigger beta cell destruction."



Beta cells in islets secrete the hormone insulin. In patients with type 1 diabetes, the beta cells are destroyed and the body loses its ability to regulate blood sugar levels. Researchers, however, are unsure of the mechanism by which beta cells are lost. Some researchers believe that the disease may be triggered by beta cell apoptosis (self-destruction); others believe that the body's immune system initiates attacks on these cells.

Stem cells differentiating into pancreatic cells. Cells are made visible by blue dye and red marker. Transcription factor shows in green.

To actually bioengineer the pancreas' endocrine system, researchers plan to induce human stem cells to develop into beta cells and alpha cells, as well as other cells in the islet that produce hormones important for controlling blood sugar levels. These cells will then be co-mingled with cells that make blood vessels and the cellular mass will be placed within a collagen matrix mimicking the pancreas. The matrix was developed by Karen Christman, PhD, associate professor of bioengineering at the Jacobs School of Engineering.

"Our previous work with heart disease has shown that organ-specific matrices help to create more mature heart cells in a dish," Christman said. "I am really excited to apply the technology to diabetes research."

If the pancreatic islets can be successfully bioengineered, researchers could conduct mechanistic studies of beta cell maturation, replication, reprogramming, failure and survival. They say new drug therapies could be tested in the 3D culture. It would also be possible to compare beta cells from people with and without the disease to better understand the disease's genetic component. Such work might eventually lead to treatments for protecting or replacing beta cells in patients.

The project is being funded through the National Institutes of Health Consortium on Human Islet Biomimetics.

Other grant co-recipients include Christopher Hughes, PhD, chair, Molecular Biology and Biochemistry School of Biological Sciences, UC Irvine and Steven George, MD, PhD, chair of the Department of Biomedical Engineering at Washington University in St. Louis.

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