The new cells prevented the onset of diabetes in an animal model of the disease

SAN FRANCISCO, CA?January 6, 2016?Scientists from the Diabetes Center at UCSF and the Gladstone Institutes have successfully converted human skin cells into fully functional pancreatic cells. The new cells produced insulin in response to changes in glucose levels, and, when transplanted into mice, the cells protected the animals from developing diabetes in a mouse model of the disease.

The new study, published in Nature Communications, also presents significant advancements in cellular reprogramming technology, which will allow scientists to efficiently scale up pancreatic cell production and manufacture trillions of the target cells in a step-wise, controlled manner. This accomplishment opens the door for disease modeling and drug screening and brings personalized cell therapy a step closer for patients with diabetes.

?Our results demonstrate for the first time that human adult skin cells can be used to efficiently and rapidly generate functional pancreatic cells that behave similar to human beta cells,? says Matthias Hebrok, PhD, director of the Diabetes Center at UCSF and a co-senior author on the study. ?This finding opens up the opportunity for the analysis of patient-specific pancreatic beta cell properties and the optimization of cell therapy approaches.?

In the study, the scientists first used pharmaceutical and genetic molecules to reprogram skin cells into endoderm progenitor cells?early developmental cells that have already been designated to mature into one of a number of different types of organs. With this method, the cells don?t have to be taken all the way back to a pluripotent stem cell state, meaning the scientists can turn them into pancreatic cells faster. The researchers have used a similar
procedure previously to create heart, brain, and liver cells.

After another four molecules were added, the endoderm cells divided rapidly, allowing more than a trillion-fold expansion. Critically, the cells did not display any evidence of tumor formation, and they maintained their identity as early organ-specific cells.

The scientists then progressed these endoderm cells two more steps, first into pancreatic precursor cells, and then into fully functional pancreatic beta cells. Most importantly, these cells protected mice from developing diabetes in a model of disease, having the critical ability to produce insulin in response to changes in glucose levels.

?This study represents the first successful creation of human insulin-producing pancreatic beta cells using a direct cellular reprogramming method,? says Sheng Ding, PhD [4], a senior investigator in the Roddenberry Stem Cell Center at Gladstone and co-senior author on the study. ?The new cellular reprogramming and expansion paradigm is more sustainable and scalable than previous methods. Using this approach, cell production can be massively increased while maintaining quality control at multiple steps. Now we can generate virtually unlimited numbers of patient-matched insulin-producing pancreatic cells.?

The Diabetes Center?s Holger Russ, PhD, and Gladstone?s Saiyong Zhu, PhD, were co-first authors on the paper. Funding was provided by the Roddenberry Foundation, National Institutes of Health, National Heart, Lung, and Blood Institute, National Eye Institute, National Institute of Child Health and Human Development, National Institute of Mental Health, California Institute of Regenerative Medicine, Prostate Cancer Foundation, and the Leona M. & Harry B. Helmsley Charitable Trust.

Caption: Functioning human pancreatic cells after they've been transplanted into a mouse. (Photo: Saiyong Zhu)

For more information, visit http://diabetes.ucsf.edu [5].

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