

Noninsulin-producing alpha cells in the pancreas can be converted to insulin-producing beta cells

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In findings that add to the prospects of regenerating insulin-producing cells in people with type 1 diabetes, researchers in Europe -- co-funded by the Juvenile Diabetes Research Foundation -- have shown that insulin-producing beta cells can be derived from non-insulin-producing cells in the pancreas.

In results of a study published today in the journal *Cell*, the researchers, led by Patrick Collombat of the Max-Planck Institute for Biophysical Chemistry in Germany and Ahmed Mansouri of the University of Göttingen in Germany, in collaboration with researchers at the JDRF Center for Beta Cell Therapy in Diabetes in Brussels, discovered in mice that new insulin-producing [beta cells](#) can be generated from alpha cells in the islets of the pancreas by modifying the expression of a specific gene (Pax4) in alpha cells. (Alpha cells generate the hormone glucagon in response to low [blood sugar](#) to restore normal blood sugar levels.) They also discovered that the alpha cells that give rise to new beta cells originate from progenitor cells in the pancreas. The newly formed beta cells result in better glucose control and prolonged survival of younger mice with diabetes.

In [type 1 diabetes](#), the immune system attacks beta cells, stopping a person's pancreas from producing insulin, the hormone that enables people to get energy from glucose. One pathway towards a cure for type 1 diabetes may be to restore [insulin production](#) through regeneration of

insulin-producing beta cells within a person's body, an alternative to transplanting functional beta cells from a donor.

"This study suggests that regenerating beta cells may be a viable pathway towards restoring beta cell function in type 1 diabetes," said Richard Insel, M.D., Executive Vice President of Research of JDRF. "It reinforces the concept that there are progenitor cells in the mouse pancreas that can generate new beta cells under special circumstances. And it points to some potential cellular targets for beta cell regenerative therapeutics - both the pancreatic progenitor cells and the alpha cells. Further, the research identifies a critical protein and pathways that can be used to screen for small molecule drugs for developing beta cell regenerative therapeutics that target these cells."

By forcing expression in the pancreatic alpha cells of the protein Pax4 - a so-called transcription factor capable of modifying expression of multiple genes to regulate patterns of development or other key cellular functions - the researchers drove the conversion of alpha cells into insulin-producing beta cells in mice. The resulting reduction of alpha cells triggered the activation and differentiation of progenitor cells to replace the [alpha cells](#) that had switched to beta cells.

New Pathway for Research

The findings are important in advancing the prospects for beta cell regeneration-related therapeutics for type 1 diabetes. In addition to funding the research described in the Cell paper, JDRF has focused resources on other research involving the regeneration of beta cells and the reprogramming of other cells within the body to function as beta cells. Dr. Patricia Kilian, JDRF's Regeneration Therapeutic Director, noted that beta cell regeneration research represented one of the two largest areas for new research funding for JDRF in the just-ended fiscal year (June 30, 2009).

"From minimal funding just a few years ago, beta cell regeneration and reprogramming have become one of the top new research areas for JDRF," she said. "The research is very exciting but early stage; more work will need to be done to demonstrate the potential of these findings for human beta cell function and diabetes."

To accelerate development of this important research area, JDRF is funding multiple research projects in reprogramming and regeneration at several institutions, including the Broad Institute of MIT and Harvard, the Genomics Institute of the Novartis Research Foundation (GNF), and the Burnham Institute. Those projects are screening for small molecules that promote beta cell regeneration, including compounds that can substitute for transcription factors involved in determining cell fate. In addition, the foundation is supporting a wide range of projects, with leading scientific investigators at top academic institutions, targeting ways to replicate beta cells, regenerate them, or reprogram other cells to become beta cells.

Underscoring the importance of this rapidly evolving field, JDRF recently announced that it has entered into a novel collaborative research agreement with the Genomics Institute of the Novartis Research Foundation (GNF) to create a diabetes drug discovery and development platform. The four-year program, among the largest and most comprehensive collaborations in the 40 year history of JDRF, would establish a basic and translational research program in type 1 diabetes. Filling a gap in translating basic research to drug discovery and development, the partnership will look to build a diabetes product pipeline initially focused on beta cell regeneration, aimed at delivering a succession of novel drugs to the clinic for evaluation in type 1 diabetes.

About Type 1 Diabetes

In type 1 diabetes, the immune system stops a person's pancreas from

producing insulin, the hormone that enables people to get energy from food. To survive, people with type 1 diabetes must test their blood sugar levels multiple times per day by pricking their fingers to draw blood, and then administering insulin through multiple daily injections, or the use of a continuous infusion insulin pump.

While trying to balance insulin with the amount of food eaten (which raises blood sugar) and exercise (which lowers blood sugar), people with type 1 diabetes must constantly be prepared for potential life-threatening low or high blood sugar levels. Just as devastating, the long-term complications of diabetes include blindness, heart attack, kidney failure, stroke, nerve damage and amputations. While usually diagnosed in childhood, type 1 diabetes can also be diagnosed in adults. As many as 3 million people in the U.S. alone have type 1 diabetes.

Source: Juvenile [Diabetes](#) Research Foundation International ([news](#) : [web](#))

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