# Recovering 'bodyguard' cells in pancreas may restore insulin production in diabetics

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The key to restoring production of insulin in type I diabetic patients, previously known as juvenile diabetes, may be in recovering the population of protective cells known T regulatory cells in the lymph nodes at the "gates" of the pancreas, a new preclinical study published online October 8 in *Cellular & Molecular Immunology* by researchers in the Department of Bioscience Technologies at Thomas Jefferson University suggests.

Tatiana D. Zorina, M.D., Ph.D., an Assistant Professor in the Department of Bioscience Technologies, Jefferson School of Health Professions, and colleagues addressed a question of whether type I diabetic patients' own beta cells, which produce insulin, could recover/regenerate if protected from autoimmune cells. If successful, such an approach would promote the patient's own insulin production without need for its supplementation by insulin injections or beta cell transplantation from the cadaver organ donors.

Type 1 diabetes is usually diagnosed in children and young adults. As many as 3 million Americans have type 1 diabetes, and each year, more than 15,000 children and 15,000 adults are diagnosed in the United States. Type 1 diabetes is a disease that occurs as a result of destruction of beta cells producing insulin by autoimmune cells. The resulting lack of insulin, which is needed to metabolize/process the sugar, leads to increased levels of sugar in the blood and all clinical symptoms of type 1 diabetes. The only currently available therapies for type 1 diabetes patients are based on insulin provision (by different means).

In healthy people, the autoimmune cells are also present, but insulin-producing beta cells (residing in the pancreas) are normally protected from their attack by the T regulatory cells, or Treg cells. Treg cells confront and disable the autoimmune cells in the pancreatic lymph nodes (which play a role of the gates of the pancreas) and thus protect beta cells in the pancreas from being destroyed.

It was shown in this study conducted by Dr. Zorina's group that in the mouse model of type 1 diabetes the Treg cells that normally play a role of the beta cells' "bodyguards" fail to accumulate in the pancreatic lymph nodes, and hence to protect beta cells from being destroyed by the autoimmune cells. The researchers found a therapeutic regiment that normalized the observed deficiency of the Treg cells in the pancreatic lymph nodes in diabetic mice.

As a result of this treatment, the animals were cured from diabetes: their beta cells re-grew (being protected from the autoimmune cells by the Treg cells) and they had normal blood sugar levels for the rest of their lives.

However, the therapy that was utilized to treat these mice was based on bone marrow transplantation, and this treatment cannot be used for diabetic people because of its serious complications. The objective of the next step of this study was to explore the mechanisms that were responsible for results observed in the mouse model for their future adaptation into a clinically safe therapeutic protocol.

The article by Dr. Zorina and colleagues, entitled "Treg Cells in Pancreatic Lymph Nodes: the Possible Role in Diabetogenesis and β Cell Regeneration in T1D Model" reports data suggesting a new approach for normalization of Treg cells' protective function in type 1 diabetes. The function of the CXCR4/SDF-1 chemokine axis that is responsible for the Treg cells' trafficking and homing was shown in this study to be

significantly decreased in pancreatic lymph nodes in type 1 diabetes. This means that the Treg cells' decreased accumulation and compromised protective effect in the pancreatic lymph nodes could be improved by rectification of the function of this axis.

"Our study represents a new and very specific approach to confront the local autoimmune reactions in type 1 diabetes," said Dr. Zorina. "What we've shown here is that normalizing the Treg cell population in the pancreatic lymph nodes of diabetic mice is associated with the regeneration of their own insulin-producing beta cells and the resulting normalization of their blood sugar levels."

"The ultimate goal of our research is to establish an immunomodulatory protocol that would increase accumulation of the Treg cells in the vicinity of the insulin-producing beta cells in humans by rectification of function of molecules responsible for their homing in this area. This approach to confront insulin deficiency in type 1 diabetes by allowing the patients' own beta cells to recover through the control of Treg cell accumulation in the pancreatic lymph nodes might become a new therapy for type 1 diabetes," said Dr. Zorina."

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