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Found: A gene that may play a role in type 1 diabetes

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Scientists at Stanford University have identified a gene that may play a role in the development of type 1 diabetes, an autoimmune disease in which the immune system attacks the body's insulin-producing cells. Insulin, a hormone produced by cells of the pancreas, helps the body to absorb sugars found in food and to maintain blood sugar at appropriate levels.

The study team, led by C. Garrison Fathman, M.D., examined genes from mice that develop a type 1 diabetes-like disease. Dr. Fathman is a grantee of the National Institute of Allergy and Infectious Diseases and the National Institute of Diabetes and Digestive and Kidney Diseases, both components of the National Institutes of Health. Additional funding for the study was provided by the Special Statutory Funding Program for Type 1 Diabetes Research, a special appropriation for research on the prevention and cure for type 1 diabetes.

The investigators found that cells in the pancreatic lymph nodes of mice make two forms of the same gene called deformed epidermal autoregulatory factor 1 (Deaf1). One form is full-length and functional and the other is a shorter, nonfunctional variant form. The full-length, functional form of Deaf1 controls the production of molecules needed to eliminate immune cells that can destroy insulin-producing cells. The presence of the Deaf1 variant was found to prevent the full-length Deaf1 protein from functioning normally. Further experiments showed that the variant form blocked the genes needed to produce certain molecules involved in immune regulation.

When the researchers measured the levels of these two forms in people with type 1 diabetes and in healthy individuals, levels of the variant form were found to be higher in people with type 1 diabetes compared with those in healthy controls. In addition, the variant form, as in mice, inhibited the full-length form from functioning normally.

The researchers propose that the development of type 1 diabetes may in part be due to increased levels of the Deaf1 variant protein in pancreatic lymph nodes of people with this disease. Increased levels of Deaf1 variant may, in turn, lead to reduced production of molecules that are required to educate the immune system not to attack the body's own cells, including the insulin-producing cells of the pancreas. These results show that Deaf1 variant form is a risk factor for type 1 diabetes and provide a target for drug development to combat the disease.

More information: L Yip et al. Deaf1 isoforms control changes in PTA gene expression in the PLN during T1D pathogenesis. *Nature Immunology*. DOI: 10.1038/ni.1773 (2009).

Source: NIH/National Institute of Allergy and Infectious Diseases