Researchers uncover gene's role in type 1 diabetes

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Researchers at the University of Virginia Health System have identified an enzyme thought to be an important instigator of the inner-body conflict that causes Type 1 diabetes. A chronic condition that affects nearly three million American children and adults, Type 1 diabetes is more severe than Type 2. Type 1 diabetes, also called autoimmune diabetes, arises when the body's infection-fighting white blood cells start destroying the beta-cells that produce insulin in the pancreas.

To shed light on how this conflict begins, UVa researchers focused on a single gene, 12/15-lipoxygenase (12/15-LO). This gene leads to the production of the enzyme, which appears to have an important role in the activation of white blood cells in the pancreas.

Researchers developed non-obese diabetic female mice to serve as a model of Type 1 diabetes. After turning off the 12/15-LO gene in study mice, they discovered that these mice without the enzyme were 97 percent less likely to develop diabetes than mice that had normal levels of it, according to the study, published online in the journal *Diabetes* (to be published in print in February 2008).

"This research is exciting because it advances our knowledge of a new gene that is involved in causing Type 1 diabetes and could pave the way for new treatments to prevent or reverse this increasingly prevalent disease," said Dr. Jerry L. Nadler, who is chief of the UVa Division of Endocrinology and Metabolism.

UVa researchers also discovered that study mice that did not have the 12/15-LO gene and remained non-diabetic demonstrated better glucose tolerance than non-diabetic NOD mice that were matched for age. (Worse glucose tolerance is an indication of having a pre-diabetes condition). The same group of study mice also had improved beta cell mass and less severe insulitis than their non-diabetic NOD counterparts.

Insulitis is a change in the islet cells that includes a high-fluid volume and too many white blood cells. While white blood cells normally help to fight off infections, they can cause damage over time when they infiltrate the islet cells of the pancreas.

“Our findings have two practical implications,” said co-author Marcia McDuffie, professor of Microbiology at UVa. “First, they help us to understand the complicated process that produces self-destructive white blood cells. This knowledge may be useful in predicting which children may be at risk for developing Type 1 diabetes before significant damage has occurred in the islets. Second, we may be able to design drugs targeting this enzyme that may help to prevent Type 1 diabetes in people at risk for the disease and also to prevent recurrence of disease in transplanted islets.”

Type 1 diabetes requires insulin injections, because the body cannot produce insulin on its own.

Source: University of Virginia Health System