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Researchers continue to find genes for type 1 diabetes

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Genetics researchers have identified two novel gene locations that raise the risk of type 1 diabetes. As they continue to reveal pieces of the complicated genetic puzzle for this disease, the researchers expect to improve predictive tests and devise preventive strategies.

"As we add to our knowledge of the biology of type 1 diabetes and better understand details of the disease's genetic risk, we will be able to develop better diagnostic tests that meaningfully predict who will develop diabetes," said study leader Hakon Hakonarson, M.D., Ph.D., director of the Center for Applied Genomics at The Children's Hospital of Philadelphia.

The study appeared online Oct. 7 in *Diabetes,* the journal of the American Diabetes Association. Hakonarson's co-leader in the study was Constantin Polychronakos, M.D., director of Pediatric Endocrinology at McGill University in Montreal.

Type 1 diabetes, formerly called juvenile diabetes, usually begins in childhood, when the body's immune system malfunctions and destroys insulin-producing beta cells in the pancreas. Without insulin, blood sugar levels run out of control and can impair blood flow and damage the eyes, nerves and kidneys. It is second only to asthma as the most common chronic disease in American children. Patients are dependent for life on insulin injections or insulin medications.

Type 1 diabetes is a complex disease, in which a variety of genes interact

with each other to cause the biological events in the immune system that remove the body's control of blood sugar levels. Over the past two years, large research collaborations, including groups led by Hakonarson and Polychronakos, have used highly automated, sophisticated gene-scanning tools to pinpoint genes implicated in the disease.

Based on initial data from previous researchers, scientists in the current study refined their search in DNA samples of thousands of patients, family members and control subjects from Philadelphia, other parts of North America, Canada, Europe and Australia. The genotyping work identified two new gene locations associated with type 1 diabetes.

The genes at those locations, UBASH2A, on chromosome 21, and BACH2, on chromosome 6, are active in immune cells that play key roles in autoimmune disorders such as type 1 diabetes. "Much work remains to be done to discover exactly how these genes may function in molecular pathways involved in diabetes, but the genes are apparently biologically relevant to the disease," said Hakonarson.

Hakonarson expects that increasingly advanced genotyping technology will reveal the remaining undiscovered genes that contribute to type 1 diabetes. "We believe we have captured the vast majority of common gene variants in the disease," he added. "We are now focusing on rare gene variants. As we increase the number of known genes, we will be able to develop better diagnostic tests. Furthermore, as we better understand the gene pathways that give rise to type 1 diabetes, this knowledge may suggest ways to intervene early in life with therapies that target those pathways and prevent the disease from developing."

Source: Children's Hospital of Philadelphia