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Study identifies new genetic risk factors for type 2 diabetes

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Ten genetic variants associated with type 2 diabetes, a disease which impacts more than 170 million people worldwide, have been identified or confirmed by a U.S.-Finnish team led by scientists at the University of Michigan School of Public Health.

The discoveries could lead to the development of new drugs for diabetes, permit more effective targeting of drug and behavioral therapies, and help scientists and physicians better predict who will develop diabetes, said Michael Boehnke, the Richard G. Cornell Collegiate Professor of Biostatistics at the U-M School of Public Health.

Boehnke is the lead scientist on the Finland-United States Investigation of Non-Insulin-Dependent Diabetes Mellitus Genetics (FUSION) study group, which collaborated with two other groups of scientists to conduct the most comprehensive study to date of genetic risk factors for type 2 diabetes.

"Until recently we knew very little about the genetic architecture of type 2 diabetes," said Boehnke, adding that diabetes has been called 'the geneticist's nightmare' because there are so many behavioral and environmental factors---in addition to genes---that are risk factors for the disease. "This is certainly not the complete genetic architecture for diabetes, but we have come a long way in better understanding the genetic basis for this disease."

The groups identified at least four new genetic factors associated with

increased risk of diabetes and confirmed the existence of another six. The findings of the three groups, published simultaneously today in the online edition of the journal Science, boost to at least 10 the number of genes confidently associated with increased susceptibility to type 2 diabetes.

"One of the nicest aspects of this study has been the collaboration between the three groups," Scott said. "Most of these variants would have taken substantially longer to identify if each group had proceeded independently."

Type 2 diabetes is characterized by high levels of blood sugar, caused by the body's inability to utilize insulin to move blood sugar into the cells for energy. Type 2 diabetes affects nearly 21 million in the United States and the incidence of the disease has skyrocketed in the last 30 years. Diabetes is a major cause of heart disease and stroke, as well as the most common cause of blindness, kidney failure and amputations in U.S. adults.

"By identifying these genes, we are identifying potential loci for drug action and suggesting classes of compounds that might be useful to help develop drugs to treat diabetes," Boehnke said.

In the study, researchers used a relatively new strategy known as a genome-wide association study, Boehnke said. Researchers began by scanning the genomes of more than 2,300 Finnish by typing more than 300,000 strategically selected markers of genetic variation. About half of the participants had type 2 diabetes and the other half had normal blood glucose levels.

To validate their findings, the researchers compared their initial findings with results from genome-wide studies of 3,000 Swedish and Finnish participants carried out by the Diabetes Genetics Initiative and 5,000

British participants done by the Wellcome Trust Case Control Consortium and UK Type 2 Diabetes Consortium. After identifying promising leads through this approach, the three research teams jointly replicated their findings by testing more focused sets of genetic markers in additional groups totaling more than 22,000 people from Finland, Sweden, Poland, the United States and the United Kingdom. All told, more than 32,000 people were tested for the study, making it one of the largest genome-wide association and follow-up efforts conducted to date.

"This achievement represents a major milestone in our battle against diabetes. It will accelerate efforts to understand the genetic risk factors for this disease, as well as explore how these genetic factors interact with each other and with lifestyle factors," said Elias A. Zerhouni, director of the National Institutes of Health. "Such research is opening the door to the era of personalized medicine. Our current one-size-fits-all approach will soon give way to more individualized strategies based on each person's unique genetic make-up."

The newly identified diabetes-associated variations lie in or near:

The diabetes-associated genetic variants that were confidently confirmed by the new research are: TCF7L2, SLC30A8, HHEX, PPARG, KCNJ11 and FTO.

Source: University of Michigan