

Multiple Studies Identify Genetic Risks of Developing Type 2 Diabetes

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There was a dual message in a talk at UCSF by Michael Boehnke, biostatistics professor at University of Michigan: large studies that may involve 10,000 or more patients could potentially suggest an inherited increased susceptibility. But the rapid rise in development of type 2 diabetes still needs to be addressed through diet and exercise.

Boehnke was principal investigator of a cooperative research study between Finnish and U.S. investigators looking for genetic alterations that might predispose people to type 2 diabetes (FUSION). He is the Richard G. Cornell Collegiate Professor of Biostatistics and Director of the University of Michigan Center for Statistical Genetics and Genome Science Training Program.

His talk, hosted by the UCSF Institute for Human Genetics, was arranged by the Diabetes Center's Wen-Chi Hsueh, M.P.H., Ph.D., an assistant professor of medicine who focuses on analysis of complex genetic traits in metabolic diseases associated with aging, including type 2 diabetes.

"We have an epidemic of diabetes going on right now and it's not because our genome is changing so rapidly," Boehnke commented. "Still critically important is lifestyle."

What's really exciting about these genetic studies is that they have identified new genes and pathways to work on that weren't predictable," said Mark Anderson, M.D., Ph.D. He is renowned for developing a mouse model at UCSF's Diabetes Center to elucidate autoimmune disease issues. This means that we now have more work to do on unraveling type 2 diabetes, however, there is little doubt that this work will lead to improving our understanding of this disease. This is an understanding that goes hand-in-hand with preventive measures patients can take, like dieting and exercise. Joint statistical analyses of large studies, he said, can suggest regions of the chromosome to investigate for mutations that cause metabolic errors.

For instance, Boehnke decreed that one spot, called SLC30A8, suggests beta cell function breakdown as a juncture that may be common in genetic variants contributing to type 2

diabetes. This gene for the beta cell zinc transporter, he explained, may affect zinc accumulation in insulin granules, which impacts their proper behavior.

Overall, the study published in the April 26, 2007 issue of *Science Express* [1] set forth 10 gene variants that associated with increased risk for type 2 diabetes. Put in the context of prevalence of type 2 diabetes in the general population, Boehnke said, the presence of a genetic variant could lead to up to a four-fold risk of developing the disease.

Boehnke pointed out that his late colleague, pioneering human geneticist Jim Neel, called analysis of hereditary factors in type 2 diabetes "a geneticist's nightmare," but he added that it is now a very exciting time for disease genetics.

"I've been slogging in the wilderness for 13 years trying to identify things that we could believe are important in something as complex as type 2 diabetes. It's still challenging, but progress is being made." Boehnke and his UCSF colleagues greatest hope is that identifying which genes and what mistakes lead to type 2 diabetes could ultimately provide the information we need to prevent the disease entirely. .

The FUSION study was supported by the National Institutes of Health, the National Human Genome Research Institute, the American Diabetes Association, a Wenner-Gren Fellowship, and a Calvin Research Fellowship.

Its results appeared in the online edition of *Science* with two related reports of genome-wide association studies in type 2 diabetes; one from the Diabetes Genetics Initiative [2] of the Broad Institute of Harvard and MIT, Lund University and Novartis Institutes; and the other from the Wellcome Trust Case Control Consortium.

Source URL: <http://www.diabetes.ucsf.edu/news/multiple-studies-identify-genetic-risks-developing-type-2-diabetes>

Links:

[1] <http://www.sciencemag.org/cgi/content/abstract/1142382v1>

[2] http://www.eurekalert.org/pub_releases/2007-04/biom-gsu042507.php