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EPIDEMIOLOGY

Genetic T2DM risk factor found

Identifying genetic risk factors that underlie common complex diseases such as type 2 diabetes mellitus (T2DM) may shed light on disease mechanisms and help predict future disease risk. A genome-wide association study has identified a new risk factor in Mexicans and Mexican Americans: common variants in the gene *SLC16A11* that predispose to T2DM in this population.

T2DM is more frequent in Latino populations than in populations of European ancestry; Mexico has one of the highest rates of T2DM worldwide. Researchers of the SIGMA Type 2 Diabetes Consortium analysed 9.2 million single nucleotide polymorphisms in 8,214 Mexicans and Mexican Americans (3,848 with T2DM and 4,366 nondiabetic control individuals). After adjusting for factors such as ancestry, age, BMI and study site, the investigators observed a number of statistically highly significant associations of common genetic variants with a risk of T2DM. Most genes had been implicated previously in studies of other populations.

One of the strongest associations with T2DM involved variants in the gene *SLC16A11* and was found in approximately half of all study participants. The risk of T2DM increased by approximately 20% per haplotype copy carried by an individual. "When we examined the frequency of the variants in other populations we discovered that the variants are rare or absent in populations from Africa and Europe," recounts corresponding author David Altshuler (Harvard Medical School). This finding may explain why the gene had gone undiscovered.

The *SLC16A11* gene is a member of a family of genes that encode solute carrier proteins, which transport metabolites in cells. The investigators found that *SLC16A11* is expressed in the liver. When *SLC16A11* was 'turned on' in cells not normally expressing this gene, the cells produced increased amounts of triglycerides, a known risk factor for T2DM. "Based on these observations, we hypothesize that *SLC16A11* contributes to T2DM development by transporting a metabolite involved in fat metabolism into the liver," says Altshuler.

Going forward, Altshuler and colleagues hope to elucidate the biology of *SLC16A11*, and how sequence variants alter its function to contribute to the development of T2DM. In addition, the Consortium will be studying patients who carry the *SLC16A11* variants to better understand their physiology and risk of disease. "The long-term goal is to understand how *SLC16A11* contributes to T2DM and to then develop strategies to reverse it," comments Altshuler. "New approaches to prevention and treatment require knowledge of the underlying causes of the disease. Studies of *SLC16A11* may shed light on the biology of T2DM and could contribute to the development of more effective treatment strategies."

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