MedicalXpress

Scientists identify 95 genetic variants associated with cholesterol, triglycerides

August 4 2010

A global team of researchers co-led by the University of Michigan School of Public Health has discovered or confirmed 95 regions of the human genome where genetic variants are associated with blood cholesterol and triglyceride levels, which are major indicators of heart disease risk.

Of the total, 59 variants were associated with cholesterol and triglyceride lipid levels for the first time, said Tanya Teslovich, a postdoctoral research fellow at the U-M School of Public Health and first author on the study. Teslovich said identifying the 59 new variants on the genome is "probably the most exciting part of the study," which is scheduled to appear Aug. 5 in the journal *Nature*.

Researchers look at four lipid traits: total cholesterol, LDL-cholesterol, (the so-called bad cholesterol), HDL-cholesterol (good cholesterol), and triglycerides. A combination of genetics and environment plays a role in determining those levels in our blood.

Teslovich combined results from 46 different studies resulting in data representative of more than 100,000 people, said Michael Boehnke, SPH professor of biostatistics and co-senior study author.

Two of the regions identified in the study contain known drug targets, in addition to many loci not previously associated with lipid metabolism, he said. Many of the common variants discovered by the study also are in or near genes known to have mutations associated with more extreme

shifts, in cholesterol or triglycerides levels. Further, many of the variants identified in these European-origin populations were shown to influence lipid traits across East Asian, South Asian, and African American populations as well.

"What's interesting to me is that for these common variants in the genome, there seems to be a lot of similarity between different racial or ethnic groups in terms of their impact on lipid values and more generally on risk of disease," said Boehnke, whose team is seeing similar multiethnic consistency of results for common variants in his current work on type 2 diabetes.

"The similar findings across different ancestry groups and the discovery of common variants in and near known lipid genes argues strongly against recent suggestions that these associations are due to the effects of rare variants much further away in the genome."

"The majority of the variants that we identified associated with LDL-cholesterol are also associated with cardiovascular disease," Teslovich said. "So these are now variants that are interesting in the context of LDL. We all want our LDLs to be in a healthy range, but these are now also potentially predictive for cardiovascular events and potentially (therapeutic) targets for cardiovascular disease."

The paper is entitled "Biological, Clinical, and Population Relevance of 95 Loci Mapped for Serum Lipid Concentrations."

A companion paper published in the same journal by Daniel Rader, Sekar Katherisan and colleagues describes in detail how one of the identified variants influences the gene SORT1, and shows how manipulating liver SORT1 levels alters blood levels of LDL-cholesterol. Teasing apart the steps in complicated pathways such as this should identify new potential targets for drug development.

Provided by University of Michigan