

DNA variants explain over 10 percent of inherited genetic risk for heart disease

November 8 2012

About 10.6% of the inherited genetic risk for developing coronary artery disease (CAD) can be explained by specific DNA variations, according to research reported today at the American Society of Human Genetics 2012 meeting.

The research, conducted by scientists in the CARDIoGRAMplusC4D consortium, pinpointed 20 previously unidentified mutations during a two-stage meta-analysis of 63,746 patients with CAD, which causes more deaths worldwide than any other disease.

These genetic variants generally were infrequently found in the DNA of the 130,681 individuals without heart disease who were in the control group.

The new mutations have boosted to 47 the total number of DNA variants that have thus far been linked to an increased risk for developing CAD, said Panos Deloukas, Ph.D., who co-led the study and heads the Genetics of Complex Traits in Humans research group at the Wellcome Trust Sanger Institute, Cambridge, UK.

Scientists had previously estimated that 30 to 60% of the variation in CAD might be attributable to [genetic risk factors](#), according to a study published in 2005*. The research reported at ASHG 2012 expands the number of specific genes that are likely involved.

"We no longer assume that [coronary heart disease](#) is triggered by just a

handful of genes, each with a strong effect on a person's risk for the disease," said Dr. Deloukas. "Our research supports the current assumption that [heart disease risk](#) is determined by a large group of genes, each with a modest effect on risk."

Identifying the [genetic mutations](#) that set the stage for CAD enables researchers to investigate the underlying mechanisms of the disease, which may lead to therapeutic targeting through drugs, he said.

Many of the newly identified variations are in genes that operate in biological pathways involved in the body's metabolism of lipids or fats as well as in inflammation.

The build-up of fatty cholesterol-rich plaque in blood vessels, a classic feature of CAD, not only can impair blood circulation but also can unleash the clots that obstruct blood flow to the heart and thereby cause heart attacks.

"Exactly how inflammation plays a role in heart attack remains a topic of ongoing research," said Dr. Deloukas, adding that the consortium's findings underscore the roles of high cholesterol levels and inflammation in CAD.

More information: The researchers' presentation is titled, "Coronary artery disease loci identified in over 190,000 individuals implicate lipid metabolism and inflammation as key causal pathways; evidence for independent signals in many of the risk loci."

*"Distinct Heritable Patterns of Angiographic Coronary Artery Disease in Families With Myocardial Infarction," *Circulation*. 2005;111:855-862.

Provided by American Society of Human Genetics

Citation: DNA variants explain over 10 percent of inherited genetic risk for heart disease (2012, November 8) retrieved 18 April 2024 from <https://medicalxpress.com/news/2012-11-dna-variants-percent-inherited-genetic.html>

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