Medical Xpress

Researchers pool data to search for genetic risks in heart disease

October 5 2010

In an unprecedented international project, researchers have found multiple genetic mutations that play a role in heart attack or coronary artery disease (CAD) risk.

The Coronary ARtery DIsease Genome-wide Replication And Meta-Analysis (CARDIoGRAM) — published in *Circulation: Cardiovascular Genetics*, an American Heart Association journal — consists of data from every published whole-genome study on genetic mutations in heart attack or CAD risk. Researchers are also pooling data from several unpublished genome-wide association studies to see if any new mutations can be uncovered.

The consortium will analyze the complete genetic profiles of more than 22,000 people of European descent with CAD or a heart attack history, and 60,000 healthy people — 10 times more than in the next largest whole-genome study to date.

Investigators have examined an average 2.2 million single nucleotide polymorphisms (SNPs) in each of the whole-genome studies included in the review. SNPs, or "snips," are genetic variants at specific locations on individual chromosomes. Sometimes these variants manifest themselves as a disease or susceptibility to a disease. Modern technology allows hundreds of thousands of SNPs to be scanned in a person.

"Only a small proportion of the inheritability of CAD has been explained," said Heribert Schunkert, M.D., a professor of medicine at

the University of Lübeck in Germany and a spokesman for CARDIoGRAM. "We have to accept that almost all persons of European ancestry carry multiple small genetic defects that mediate some coronary artery disease risk. The main aim of the consortium is to identify new disease mechanisms to improve risk prevention."

The task is challenging because of the complex nature of atherosclerosis, with multiple genetic factors contributing in small ways to the disease, he said.

Genome-wide association studies provide an unprecedented sensitivity to detect genetic variants affecting disease risk, and researchers rely on the studies' sample size. However, in a typical genome-wide association study with about 1,000 patients and controls, the power to detect a SNP with a significant effect is low.

"Collectively, our consortium increases the power of these findings 10-fold," Schunkert said. "By pooling all of the published and unpublished data, we hope to make discoveries that might have been overlooked. Given that up to 2.5 million comparisons are carried out, in parallel, for each whole-genome scan, distinguishing between true and false associations has been difficult."

The data will be maintained in a central database, and each SNP that appears related to heart disease will be subjected to replication studies to confirm its significance. Numerous SNPs and the proteins they express increase risk of CAD or heart attack. But it's unknown whether they're acting alone or with other genetic variables, Schunkert said.

"We hope that by combining all of the known whole-genome data, we will be able to provide some answers," he said.