Largest coronary artery disease study shows evidence of link between inflammation and heart disease

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The University of Ottawa Heart Institute (UOHI) participated in the largest genetic study of Coronary Artery Disease (CAD) to date. Researchers from the CARDIoGRAMplusC4D Consortium report the identification of 15 genetic regions newly associated with the disease, bringing to 46 the number of regions associated with CAD risk.

The Ruddy Canadian Cardiovascular Genetics Centre, at the Heart Institute, was the main genetic centre in Canada contributing most patient cases involved in this study and analyzing patient cases from across North America.

In this unparalleled study, published today in the prestigious scientific magazine *Nature*, the team identified a further 104 independent genetic variants that are very likely to be associated with the disease, enhancing our knowledge of the genetic component that causes CAD.

Researchers, including Dr. George Wells and Dr. Alexandre Stewart from the Heart Institute, used their discoveries to identify biological pathways that underlie the disease and showed that lipid metabolism and inflammation play a significant role in CAD.

CAD and its main complication, myocardial infarction (heart attack), are some of the most common causes of death in the world and approximately one in five men and one in seven women die from the

disease in the UK. CAD has a strong inherited basis.

"These findings show, for the first time, clear evidence that several of the genetic risk factors for CAD function through known inflammatory pathways," said Dr. Robert Roberts, President and CEO of the Heart Institute and Director of the Ruddy Canadian Cardiovascular Genetics Centre. "This identifies a novel pathway for the prevention of heart disease and establishes molecules that can now be targeted for developing new therapies."

The Consortium spanning over 180 researchers from countries across Europe (UK, Germany, Iceland, Sweden, Finland, France, Italy, Greece), Lebanon, Pakistan, Korea, USA and Canada analyzed DNA from over 60,000 CAD cases and 130,000 apparently unaffected people. The researchers integrated the genetic findings into a network analysis and, unsurprisingly, found the metabolism of fats being the most prominent pathway linked to CAD. The second most prominent pathway, however, was inflammation which provides evidence at the molecular level for the link between inflammation and heart disease.

The importance of the work is that while some of the genetic variants that were identified work through known risk factors for CAD such as high blood pressure and cholesterol, many of the variants appear to work through unknown mechanisms. Understanding how these genetic variants affect CAD risk is the next goal and this could pave a way to developing new treatments for this important disease.

This study provides a useful framework for future projects to elucidate the biological processes underlying CAD and to investigate how genes work together to cause this disease.

Provided by University of Ottawa