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Landmark Study Links 13 New Genes to Heart Disease

Majority work independently of known risk factors

World's largest heart genetics study involves more than 100 research groups

OTTAWA – March 6, 2011 – Insight into the complex biological mechanisms that cause heart disease has taken a major step forward with the discovery of 13 new genes that increase the risk of coronary artery disease (CAD). The influence of the majority of the new genes is independent of other established risk factors, suggesting new, unsuspected causes of CAD. The discovery more than doubles the number of genes known to affect the progression of heart disease.

The research also verified the association of 10 previously identified genes to the population at large, meaning their influence is not confined to a specific population. Of the 23 genes discovered or confirmed, only 6 could be linked to known risk factors such as cholesterol and high blood pressure, underscoring the direct and indirect role that genes play in influencing the course and evolution of heart disease.

"This is a landmark result because we have identified so many genes and most operate using completely unknown mechanisms to us right now," said Dr. Robert Roberts, President and CEO, University of Ottawa Heart Institute. "It has opened up significant new avenues for new therapies and underlines the complexities of heart disease."

These discoveries were published online today in *Nature Genetics* by one of the world's largest consortiums examining the genetic basis of heart disease. More than 100 research organizations took part in the study, including such internationally-acclaimed centres as the University of Lubeck (Germany), Stanford University, Harvard Medical School, University of Iceland, Johns Hopkins University, University of Leeds (UK), Wellcome Trust Sanger Institute, the University of Ottawa Heart Institute and others.

The study is also one of the world's largest. Called CARDIoGRAM (Coronary Artery Disease Genome-wide Replication and Meta-Analysis), researchers evaluated the genetic samples of more than 140,000 people of European descent, of which one third exhibited heart disease and the remainder (the control group) did not. Data from genetic research centres in Europe, the United Kingdom, the United States and the Heart Institute were combined to provide the massive sample size, which is essential to ferret out subtle genetic indicators.

"The consortium examined more than 10 times the number of samples than the largest study ever published, so we magnified the power to detect small genetic variations," said Dr. Roberts. "Now our job is to understand how these genes work, develop a new group of drugs to target them and identify people who will benefit most to reduce their risk of heart attack and other cardiac events."

"Our main aim of this extremely large study is to locate and examine new disease mechanisms and improve our means of preventing cardiovascular disease," said Dr. Thomas Quertermous, Professor of Cardiovascular Medicine, Stanford University, which participated in the research.

The Heart Institute's contributions to the consortium were led by the Institute's Ruddy Canadian Cardiovascular Genetics Centre. The Ruddy Centre is the only one of its type in Canada and only one of a handful of cardiovascular genetics research centres worldwide. The Ruddy Centre's scientific team included the director and principal investigator, Dr. Roberts, laboratory director Alexandre Stewart, PhD, biostatistician George A. Wells, and Dr. Ruth McPherson, an endocrinologist and molecular biologist.

The CARDIoGRAM study is the latest significant progress to emerge from the Heart Institute. The Institute previously identified gene 9p21 which was the first genetic risk factor recognized for heart disease and the first major new cardiovascular risk factor since the discovery of cholesterol. The Institute has also located a variety of other genes influencing diseases such as atrial fibrillation and biological processes such as obesity.

Research has shown that up to 40% of heart disease can be prevented by modifying cholesterol, high blood pressure, smoking and other lifestyle causes. At the same time, it is known that about 50% of the risk of heart disease is due to genetic factors. Comprehensive prevention programs are needed that not only deal with lifestyle issues but also address the genetic aspects of heart disease. When this occurs, it is believed that heart disease will be dramatically reduced or possibly eliminated within 50 years.

About UOHI

The University of Ottawa Heart Institute is Canada's largest and foremost cardiovascular health centre dedicated to understanding, treating and preventing heart disease. We deliver high-tech care with a personal touch, shape the way cardiovascular medicine is practiced, and revolutionize cardiac treatment and understanding. We build knowledge through research and translate discoveries into advanced care. We serve the local, national and international community, and are pioneering a new era in heart health. For more information, visit www.ottawaheart.ca

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Editor: For more information on CARDIoGRAM, please visit

http://www.nature.com/genetics/index.html

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