UNIVERSITY OF OTTAWA
HEART INSTITUTE
INSTITUT DE CARDIOLOGIE
DE L'UNIVERSITÉ D'OTTAWA

FOR IMMEDIATE RELEASE | POUR PUBLICATION IMMÉDIATE

New Research Uncovers Fresh Evidence Linking Genes to Heart Disease

OTTAWA – May 3, 2007– Researchers at the University of Ottawa Heart Institute (UOHI) have identified a piece of the DNA sequence that boosts a person's susceptibility to heart disease by up to 40 per cent regardless of other established risks such as cholesterol, blood pressure and diabetes. The discovery could help identify people at high future risk for heart disease, enabling early preventive therapies, including lifestyle changes and medication to reduce their risk. This finding may also lead to a better understanding of the biological pathways that lead to heart attacks.

A study led by Dr. Ruth McPherson, Director of UOHI's Lipid Clinic and Lipid Research Laboratory in collaboration with Dr. Jonathan Cohen at the University of Texas Southwestern Medical School, examined the DNA of heart patients and healthy 'controls' from Ottawa. The participants were part of the Ottawa Heart Study in which the DNA of 1,300 patients and 1,500 healthy 'controls' were scanned for genetic variants. Heart Institute researchers then collaborated with scientists directing several other large-scale heart disease studies in the United States and Denmark to verify their findings.

The results, published May 3 in *Science Express (Vol.316, Issue 5825, May 4, 2007)*, showed that a region on chromosome 9 was strongly linked to premature heart disease. Individuals carrying the genetic variant (about 25% of the population) had a 30 to 40% higher risk of heart disease than those individuals who do not carry this genetic variant. This increased risk was not related to effects on known heart disease risk factors such as cholesterol, blood pressure, diabetes or smoking.

The study results were based on samples from more than 23,000 people in Canada, the U.S. and Denmark. These included 2,765 in Ottawa, 10,578 Danish men and women who form the Copenhagen City Heart study, 11,478 men and women enrolled in the U.S.-based Atherosclerosis Risk in Communities (ARIC) project and the Dallas Heart Study. In all three 'validation' studies, this genetic variant was significantly associated with coronary heart disease.

"This is an important finding for several reasons," said Dr. McPherson. "This is a common genetic variant which has a very strong effect on heart disease risk that isn't related to other factors that we already know about," said Dr. McPherson. "To put this into perspective - of the groups studied in Ottawa, about 33 per cent of people with early onset heart disease had this genetic variant versus 24 per cent of healthy elderly people."

"Heart disease is a major cause of death in western countries and the lifetime risk of developing heart disease is about one in two for men and one in three for women. If we can identify genetic factors which influence heart disease risk over and above known risk factors, we can do a better job of identifying those people who will benefit most from early intervention to reduce their risk."

The Heart Institute scientific team included Dr. McPherson, an endocrinologist and molecular biologist, Dr. Robert Roberts, UOHI President and CEO, who is both a cardiologist and a geneticist, and Alexandre Stewart, PhD, Principal Investigator, Ruddy Canadian Cardiovascular Genetics Centre.

"Our research is uncovering the genetic predisposition to heart disease so that we might soon be able to develop individually tailored treatments," said Dr. Roberts. "Science has excellent insight as to how to cope with environmental factors such as obesity, but genetic influence on heart disease is less clear. The Heart Institute is targeting these questions."

The Heart Institute employs a state-of-the-art Affymetrix GeneChip®, which processes massive amounts of miniature arrays, identifies genes and allows researchers to determine patterns of genetic activity. The Ottawa Heart Study is considered to be the first genome-wide scan to search for CHD genes using an even larger number (500,000) of genetic markers and is likely to reveal still more about the genetic causes of heart disease.

In the Ottawa study, men older than 65 years and women older than 70 years who had no symptoms or history of coronary heart disease (CHD) were recruited. The patients selected for the study had severe premature CHD. People with diabetes and very high cholesterol were excluded.

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.

- 30 -

For further information please contact:

Marlene Orton
Senior Manager, Public Affairs
University of Ottawa Heart Institute
(613) 761-4427
morton@ottawaheart.ca

Genetic Research and the University of Ottawa Heart Institute

The Human Genome Project yielded the first complete sequence of the 3.2 billion base pairs that comprise the genetic makeup of a person. Roughly 99.9% of that DNA is identical among people. Variations exist on about 3 million of these base pairs.

A **genome** is the complete set of genetic information of an organism, including chromosomes, DNA (deoxyribonucleic acid) and RNA (ribonucleic acid).

Researchers at UOHI identified two SNPs (pronounced snips)**: rs10757274 and rs2383206** SNP stands for single nucleotide polymorphism, a common DNA sequence variation. These variants do not generally cause people to be predisposed to a disease. Scientists believe common SNPs are useful markers to identify gene variants that make people susceptible to a particular disease or influence their response to a particular drug.

The Ruddy Canadian Cardiovascular Genetics Centre is the only one of its kind in Canada dedicated to coronary heart disease. Alexandre Stewart, PhD (organismal biology and anatomy, University of Chicago), is principal investigator. Stewart works with genes and the encrypted information that passes between parts of the cell machinery - from DNA to the functional proteins. His interest lies specifically in transcription regulation.

The Ruddy Centre is equipped with more than $2 million in advanced gene sequencing, DNA analysis and other equipment. The Centre employs the most advanced DNA microarray technology, in which robotic machines arrange thousands of gene sequences - the long strings of encoded DNA information - onto two microchips. UOHI employs the Affymetrix GeneChip®, to process massive amounts of miniature arrays and identify genes. This allows researchers to spot genetic differences that may account for disease. Each microarray has 250,000 probes and the pair of microchips together enables the identification of 500,000 genetic markers. This allows more precision in screening for heart disease and allows scientists to catch genes they may have missed previously. (Affymetrix and GeneChip are registered trademarks of Affymetrix Inc.)

Other Heart Institute genetic research has discovered that atrial fibrillation is caused by a genetic mutation that occurs during development in the womb. The research was led by Dr. Michael Gollob, a clinical arrhythmia specialist and geneticist. Dr. McPherson is also sorting through genes of obese and thin people, hunting for genes that might be the root cause of obesity among people who gain weight regardless of diet and exercise.

In the ARIC study, heart patients and healthy ‘controls’ in four U.S communities have been followed and tested over a 15-year period. The Copenhagen study began in 1976 with a randomly selected population group that has been examined at several intervals in the following years. In 1991, blood samples were obtained to isolate DNA. The Dallas study is a multi-ethnic population sample of Dallas County residents who have been interviewed and studied in clinics.