University of Ottawa Heart Institute
Institut de cardiologie de l'Université d'Ottawa

Landmark Genetic Discovery Unlocks Cause of a Common Form of Heart Disease

Heart Institute Research Expected to Fuel New Therapies for Atrial Fibrillation

OTTAWA – June 22, 2006 – Research at the University of Ottawa Heart Institute has revealed that one of the most common forms of heart disease – atrial fibrillation (AF) – is caused by a genetic mutation that occurs during in-utero development. The landmark discovery provides a fresh view of how common diseases may develop and is expected to fuel targeted therapies that help eliminate or prevent AF, which affects millions of North Americans and is responsible for more than a third of all strokes.

Details of the discovery are being reported in today's issue of The New England Journal of Medicine (vol. 354, No. 25, pp. 2637-2744, www.nejm.org). The work has been led by the Heart Institute's Dr. Michael Gollob, a clinical arrhythmia specialist and geneticist who heads the Arrhythmia Research Lab affiliated with the Institute's Canadian Cardiovascular Genetics Centre™.

Atrial Fibrillation is the most common form of cardiac arrhythmia (irregular beat). AF is a rapid, irregular fluttering of the heart's beat caused by random electrical discharges. Instead of pumping effectively, the condition can allow blood to pool and clot in the heart, and sometimes can trigger a stroke. In the U.S., more than 3.0 million people and in Canada some 250,000 people are estimated to have persistent AF. AF increases the risk of stroke significantly and is responsible for more than 75,000 strokes in the U.S. at a cost of more than US$1 billion.

It is known that defective genes can be inherited and can lead to familial disease. However, it has not been well established that mutations during in-utero development (somatic mutation) can also trigger disease. Noting that cases of familial AF are rare, the researchers hypothesized that cases of AF for which there is no obvious cause (idiopathic) might be due to a somatic mutation confined to the heart tissue.

Dr. Gollob and colleagues focused on a gene (GJA5) which makes a protein known as Connexin 40. The protein is specific to the atrial tissue of the heart and plays a crucial role in how electrical impulses are conducted. They discovered genetic mutations in the Connexin 40 gene in AF patients. Researchers proved the disease was tissue-specific and not present in all body cells by detecting the mutation only in the heart tissue and not in the blood cells of affected patients.

Currently, AF is treated with medications that do not specifically target the Connexin 40 protein. A mechanical procedure called catheter ablation is also employed but it is invasive and significant complications can arise, including stroke and death. By unlocking the mechanism responsible for AF, it is expected that novel drug treatments that target Connexin 40 will be developed to modify or control the disease.

"First, this study confirms that Connexin 40 plays a critical role in the electrical conduction in the atrium of the heart," said Dr. Gollob. "Second, current medications have a moderate effect at best. These findings suggest that drugs targeting Connexin 40 may lead to more effective treatment for AF. Third, it also shows that common idiopathic diseases may have a genetic basis with the genetic defect confined to the diseased tissue."

“This is a significant development in understanding the causes of heart disease,” said Dr. Robert Roberts, President & CEO. “We salute the impressive accomplishment of Dr. Gollob and his team and note the important contribution of the Canadian Cardiovascular Genetics Centre.”

About UOHI

The University of Ottawa Heart Institute is one of the largest heart centres in North America dedicated to the prevention, diagnosis, treatment, rehabilitation, research and education of cardiovascular disease. Annually, UOHI serves over 76,000 outpatients, more than 6,000 inpatients, and an alumnus of some 10,000 patients. UOHI is also home to the Canadian Cardiovascular Genetics Centre™, an emerging international leader and the first in Canada dedicated to mapping, identifying and determining the function of genes responsible for heart disease. For more information, visit www.ottawaheart.ca.

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