

**Discovery of key role played by new gene  
in high blood cholesterol**

Montreal, May 30, 2003—Researchers working in Dr. Nabil Seidah's team at the IRCM have identified a new genetic mutation that contributes to hypercholesterolemia. The results of their work will be published in the June 2003 issue of the very prestigious journal *Nature Genetics*.

High blood cholesterol is one of the principal risk factors associated with heart disease. This condition, hypercholesterolemia, is characterized by an increase in LDL cholesterol (bad cholesterol), which may be caused by certain genetic mutations.

To date, scientists have identified two of these mutations: one affecting LDL receptors and the other affecting the APOB gene. Dr. Seidah demonstrated the importance of a family of protease enzymes, known as proprotein convertases, which play a major role in the activation of hormone precursors, enzymes, growth and transcription factors, receptors and proteins linked to pathogenic agents. One of these convertases, NARC-1, was identified in a chromosome present in the sector of the genome associated with the regulation of cholesterol. The researchers developed the hypothesis that NARC-1 might play a key role in the metabolism of cholesterol.

In order to verify this hypothesis, IRCM researchers collaborated with the team of the French physician Dr. Cathérine Boileau, who is treating numerous cases of hypercholesterolemia that did not exhibit the mutations that usually result in high blood cholesterol. Dr. Seidah then suggested that they check the status of the NARC-1 gene in these patients. This research identified two mutations in three families and demonstrated that unregulated NARC-1 could result in abnormally high and potentially deadly cholesterol levels.

This discovery opens a third pathway in the diagnosis and treatment of high blood cholesterol, one of the most widespread and deadly diseases in the Western world.

*The Institut de Recherches Cliniques de Montréal is recognized as one of the best research centres in the country. It has a mission to develop a link between medical research and the patient as well as to promote the prevention of disease. The IRCM has 30 research units preparing future researchers by training almost 250 students each year. More than 450 people work at the IRCM.*

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