

Dr. Bouchard holds the position of associate professor of genetics and epigenetics at the Department of Biochemistry, Faculty of Medicine and Health Sciences, Université de Sherbrooke and is head of the Department of Molecular Biology and Genetics at the university-affiliated Chicoutimi Hospital. After his Ph.D. studies in genetic epidemiology at Université Laval under the mentorship of Dr. Louis Pérusse, he completed postdoctoral fellowships in transcriptomics (Dr. Marie-Claude Volh, CHU de Québec) and epigenomics (Dr. Arturas Petronis, University of Toronto). From 2008 to 2010, he was assistant professor, Department of Medicine, Université de Montréal.



Since 2009, he has been leading a research group dedicated to understanding how epigenetic mechanisms are involved in the development of obesity, diabetes and cardiovascular disease, and identifying causal epigenetically-modified genes. His group is at the forefront of this growing field of research. With its analyses of specific obesity, diabetes and lipid candidate genes and the use of state-of-the-art analytical methods to survey a large fraction of the epigenome, this group was the first to report that maternal hyperglycemia and familial hypercholesterolemia are associated with DNA methylation changes (a central epigenetic mechanism) in several genes with many of them being involved in metabolic and cardiovascular disease pathways. He now has the goal to demonstrate that these epigenetic changes could explain why some children have an increased risk of developing obesity and diabetes, as per the Developmental Origin of Health and Disease (DOHaD) hypothesis, and to identify new markers for cardiovascular disease.

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## Abstract

### **Increasing evidence supporting epigenetic programming and regulation of HDL-cholesterol metabolism.**

Atherosclerosis, the primary cause of cardiovascular disease (CVD), affects endothelial and smooth muscle cells of large arteries and is characterized by chronic low-grade inflammation. Its development is a long process sometimes beginning in early childhood with possible fetal origins. High-density lipoprotein-cholesterol (HDL-C) is known to have an athero-protective role according to its role in reverse cholesterol transport and its antioxidant, anti-inflammatory and antithrombotic properties. These all contribute to HDL's ability to prevent coronary artery disease. However, recent clinical trials aiming to improve the CVD risk profile by increasing HDL-C levels have been unsuccessful, clearly underlying the need to better understand HDL-C metabolism and properties.

Indeed, HDL-C levels in blood have a clear genetic component that remains difficult to explain with traditional genetic approaches. This has led to suggest that epigenetics could be involved in programming and regulating HDL-C metabolism. Epigenetics refers to the regulation of DNA transcription that is independent of the DNA sequence. DNA methylation occurring at position 5' of the cytosine pyrimidine ring is the more stable and best understood epigenetic phenomenon. DNA methylation is partially inherited but is also dynamic. More recently, new aspects of the structural complexity of HDL have been revealed with the discovery that HDL carries microRNAs with functional capabilities. MicroRNAs are small RNA molecules that bind specific messenger RNA (mRNA) to regulate gene expression and protein synthesis. They are implicated in the regulation of central metabolic pathways and considered by many as an epigenetic mechanism. Both DNA methylation and miRNAs variations have profound phenotypic effects.

This conference will present examples of the most recent evidence supporting epigenetic programming and regulation of HDL-cholesterol metabolism and perspectives on the high potential of microRNAs.