

CSATVB



SCATBV

## NEWSLETTER

**August 2004**

### **Abstracts of the CSATVB Symposia Canadian Cardiovascular Congress Calgary, Alberta October 23-27, 2004**

#### **President's Report**

##### **In honour of Robert More:**

Emeritus Professor Robert More, McGill University, passed away recently in his early 90's. I had the very good fortune of being a resident in anatomic pathology at McGill University when Bob was Chair of Pathology and I remained his friend and colleague until the time of his death. Allow me to reminisce about a dear friend and mentor.

Robert More was indeed a true leader in Canadian Pathology and Atherosclerosis Research. His activities over the years, first as Chair of Pathology at Queen's University and then as Chair at McGill University, had a major influence on academic anatomic pathology and on vascular research in Canada. He did much to shape academic pathology over the past forty years both through his own actions and the activities of those whom he trained.

In today's jargon, what outcomes and benchmarks reflect Bob's impact? What was his impact number? To measure this, we have to list the number of academic pathologists in Canada who passed through his hands and then assess the quality of their scholarly activity. I don't pretend to present a complete list, and for those whom I

omitted, it was because I did not know the connection with Bob. These folks were trainees, junior staff, or even senior staff under Bob's chairmanships. He provided the guidance, maintained the infrastructure in which they taught and carried out scholarly activity, and provided them with opportunities for specialized training and for career development. Many, in fact, left his departments and became leaders in pathology in their own right elsewhere in Canada and the US. These include Jim Hogg, Whitey Thurlbeck, Henry Movat, Daria Haust, Ken Pritzker, Shao-nan Huang, Tom Seemayer, David Kahn, Serge Jothy, David Murray, Alex Forenzy, Rene Michel, George Rona, and Istavan Heutner.

Bob had a true understanding of what it takes to become an academic pathologist. He understood the need to expose trainees to high quality clinical and subspecialty clinical training. He worked hard to develop a workshop program at the annual Canadian Association of Pathologists meeting, borrowing the idea from his activities at the USCAP, then known as the IAP. He held weekly research seminars at which he expected all staff and residents to attend and participate in. He put much effort into providing high quality teaching, as he too had to deal with aggressive curriculum renewal efforts by the faculty of medicine. He encouraged residents to carry out research projects. He took a genuine interest in his residents and listened carefully to trainees

and faculty suggestions to improve the training program and keep it at the state-of-the-art level. Thus we were trained not only for the present but in anticipation of the needs of the future as well.

My interest during medical school and in my first year of internal medicine residency was cardiovascular medicine. Within a few weeks of beginning a year of pathology I was interviewed by Bob and he assigned me to do a cardiovascular research project with Shaonan Huang. I liked what I saw and stayed. Bob encouraged me, followed my progress, sent me to the American Heart Association meeting, and finally gave me the opportunity to spend seven weeks prior to my chief residency year taking the Physiology Course, which was a research intensive course given by leaders in cell and molecular biology at the Marine Biology Laboratory, Wood Hole, Massachusetts. This was indeed a defining period for me as I worked shoulder to shoulder with PhD students, MD/PhD students, and postdoctoral fellows. The faculty were a who's who of cell and molecular biology. I did a project with Tucker Collins, a young MD/PhD student who is now Chair of the Department of Pathology at Boston Children's Hospital. Bob was also available to provide suggestions, funds to go to interviews, and letters of support that helped me to be accepted into Jon Singer's laboratory at the University for California, San Diego, with an MRC Fellowship. I am sure many other trainees and young faculty have similar stories.

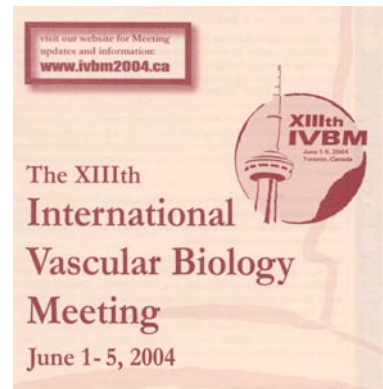
Even in retirement Bob continued his lifelong interest in atherosclerosis research. He had worked with Daria Haust and Henry Movat at Queen's and had a longstanding fruitful collaboration with Bernie Weigensberg at McGill. In retirement he turned his attention to help Daria Haust and Jean Davignon found our society, the Canadian Society for Atherosclerosis, Thrombosis and Vascular Biology.

The members of CSATVB are delighted to present the Robert H More Memorial Symposium at the Canadian Cardiovascular Congress, in the Society's program on October 26, 2004. We are pleased that Daria Haust will pay a tribute to her long-time colleague, Robert More.

**Avrum I. Gotlieb, MD, CM, FRCPC**  
**Professor and Chair**  
**Department of Laboratory Medicine and Pathobiology**  
**University of Toronto**

## XIIIth IVBM Hosted in Toronto

We welcomed about 1000 attendees from a truly international community of vascular biologists to Toronto for the XIIIth International Vascular Biology Meeting, June 1st to June 5th, 2004 at the Westin Harbour Castle Hotel. The conference was held entirely within this hotel and in the spacious conference centre conveniently attached to it. This maximized scientific interaction amongst the participants.



The International Vascular Biology Meetings have become a leading venue for the presentation and discussion of new findings and the development of collaborations among vascular biologists and clinicians. We continued this tradition in Toronto. Leading investigators from the international vascular biology community with diverse interests in the development, regulation and dysfunction of the vascular system lead presentations and discussions on emerging approaches to the study of the origin, function and therapeutic manipulation of vascular cells and tissues through a program of plenary sessions, workshops, poster sessions and a keynote address. Sixty-eight trainees were awarded travel awards to help them attend the meeting. These awards were supported by the American Society for Investigative Pathology (ASIP), Australian Vascular Biology Society (AVBS), Canadian Society of Atherosclerosis, Thrombosis and Vascular Biology (CSATVB), European Vascular Biology Association (EVBA), Heart and Stroke/Richard Lewar Centre of Excellence, University of Toronto (HSRLCE), Japan Vascular Biology & Medicine Organization

(JVBMO), National Heart, Lung and Blood Institute, National Institutes of Health (NHLBI, NIH), and North America Vascular Biology Organization (NAVBO).

***Trainee Travel Awardees supported by CSATVB included:***

**Jonathan Choy**, University of British Columbia  
**Katey Donaldson**, University of Ottawa  
**Martine Duval**, University of Montreal  
**Caroline Lemieux**, University of Montreal  
**Alison Maley**, University of Western Ontario  
**Ricardo Maliba**, Montreal Heart Institute  
**Imran Mungrue**, University of Toronto  
**Sebastian Taurin**, CHUM - Hotel Dieu  
**Maziar Rahmani**, University of British Columbia  
**Hubert Walinski**, University of British Columbia

There were 640 abstracts presented as oral and poster presentations. The program included 12 plenary sessions, 21 workshops, keynote and introductory talks and the Benditt Award Lecture sponsored by the North America Vascular Biology Organization (NAVBO). There were 96 invited lectures and chairs. The attendees were from 27 countries. The comments we received from our colleagues were extremely gratifying. We did indeed achieve what we set out to do - a high quality meeting with state-of-the-art well prepared lectures, lively discussion, opportunities for trainees and young scientists to present their work, and opportunities to network with colleagues and set up collaborations.

The next meeting will take place in 2006 in the Netherlands. For North American vascular biologists, it is not too early to begin to think about future venues for 2010 when IVBM is likely to return to North America. NAVBO has indicated that it will support the 2010 IVBM in North America.

Sincerely,  
Avrum I. Gotlieb, MD, CM, FRCPC  
Chair, Scientific Organizing Committee XIIIth IVBM 2004, Toronto, Canada

## CSATVB 2004 Meeting

Our primary scientific meeting continues to be in conjunction with the **Canadian Cardiovascular Congress** which will be held in **Calgary, Alberta**.



This year, some changes have been introduced into the program. In addition to replacing the Workshop with a third Symposium (the Robert H. More Memorial Symposium), we also added two oral sessions that incorporate abstracts and presentations to the CCC on atherosclerosis. Two of our Symposia (Symposia I and II) are supported by Pfizer Canada. We have also shortened our meeting by one day to allow earlier return home. The Program is now as follows:

### **Sunday, October 24, 2004**

9:00-1:00 Meeting of the Executive & Council  
2:00-4:30 Poster Presentations

### **Monday, October 25, 2004**

8:30-10:00	Oral Session I
10:30-12:00	Oral Session II
13:30-15:00	Symposium I
16:00-18:00	Symposium II
19:00-23:00	Calgary Night

### **Tuesday, October 26, 2004**

8:30-10:00	Oral Session I
10:30-12:00	Oral Session II
13:30-15:00	Symposium III
15:30-16:00	Annual General Meeting
16:00-17:00	Reception and Awards

In addition to supporting our two Symposia, Pfizer Canada have also supported the 2004 New Investigator Grant-in-Aid. The Society received six applications for this grant. Pfizer is also supporting the Young Investigators who are presenting their work at the Meeting. The CSATVB is grateful for this generous support.

*To include material in the CSATVB NEWSLETTER, please contact:*  
Bassam A. Nassar, PhD MBCh FRCPC FCACB  
Tel: 902 473 2225; Fax: 902 473 2123  
email: [bassam.nassar@cdha.nshealth.ca](mailto:bassam.nassar@cdha.nshealth.ca)



Canadian Society of Atherosclerosis, Thrombosis and Vascular Biology (CSATVB)/ Société canadienne d'athérosclérose, de thrombose et de la biologie vasculaire (SCATVB)

## Sunday, October 24, 2004

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## Monday, October 25, 2004

8:30-10:00 Oral Session I  
10:30-12:00 Oral Session II  
13:30-15:00 Symposium I:

**Recent Advances in Atherothrombosis: Roles of Hyperhomocysteinemia and Nitric Oxide**

**Chair:** Richard Austin

**Speakers:**

Donald Jacobsen: *Molecular Basis for the Vascular Pathology of Hyperhomocysteinemia*

Steven Lentz: *Vascular Effects of Hyperhomocysteinemia: Insights from Murine Models*

Jane Leopold: *The Role of Antioxidant Enzymes in Homocysteine-induced Endothelial Dysfunction*

**Supported by Pfizer Canada**

16:00-18:00 Symposium II  
**Atherosclerosis: Lipoproteins, Lipoprotein receptors, and Other Risk Factors**

**Chair:** Zemin Yao

**Speakers:**

Joachim Herz: *Mechanisms of signaling by lipoprotein receptors*

Gordon Francis: *Correction of impaired ABCA1 regulation and HDL formation in Niemann-Pick Type C disease*

**Winner of the 2004 Royal College of Physicians and Surgeons of Canada Gold Medal in Medicine**

Robert Ryan: *Apolipoprotein mediated regulation of plasma lipid*

MacRae Linton: *Macrophage functions in atherosclerosis*

**Supported by Pfizer Canada**

19:00-23:00 Calgary Night

## Tuesday, October 26, 2004

8:30-10:00 Oral Session III  
10:30-12:00 Oral Session IV  
13:30-15:00 Symposium III

**The Robert H. More Memorial Symposium**

**Advances in Understanding Arterial Dysfunction in Atherosclerosis**

**Chair:** Avrum I. Gotlieb

**Speakers:**

Aly Karsan: *The Role of Notch in Remodeling and Maintaining the Vasculature*

Michelle Bendeck: *Collagen Signaling through Discoidin Receptors in Atherosclerosis*

Avrum Gotlieb and Kristopher Cunningham:

*Shear Stress, Inflammation and Endothelial Dysfunction*

Daria Haust: *A Tribute to Robert H. More*

15:30-16:00

**Annual General Meeting**

16:00-17:00

**Reception and Awards**

**Adjournment**



Canadian Society of Atherosclerosis, Thrombosis and Vascular Biology (CSATVB)/  
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**Symposium I**  
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**Recent Advances in Atherothrombosis: Roles of Hyperhomocysteinemia and Nitric Oxide**

**Chair:** Richard Austin

*Supported by Pfizer Canada*



**Molecular Basis for the Vascular Pathology of Hyperhomocysteinemia**

Donald Jacobsen

Departments of Cell Biology and Cardiovascular Medicine, Lerner Research Institute, Cleveland Clinic Foundation, Ohio 44195, USA.

An elevated concentration of homocysteine (Hcy) in the blood (hyperhomocysteinemia) is associated with endothelial dysfunction and increased risk of cardiovascular disease. Free oxidized and reduced forms of Hcy are found in plasma but greater than 80% of plasma total Hcy is disulfide-bonded to protein cysteine (Cys) residues. We have identified specific proteins targeted by Hcy in plasma and have studied the mechanism of their formation. Thiol-disulfide exchange chemistry predominates in the formation of albumin-Cys<sup>34</sup>-S-S-Hcy rather than sulfhydryl group autooxidation. Albumin carries up to 70% of circulating Hcy but the fate of this Hcy form and its atherogenicity are unknown. The amyloid protein transthyretin binds Hcy to its Cys<sup>10</sup> residue. Concentrations of transthyretin-Cys<sup>10</sup>-S-S-Hcy *in vivo* are proportional to levels of plasma total Hcy. *In vitro* studies with fibronectin show that it is targeted by Hcy, and this impairs its ability to interact with fibrin. We propose that molecular targeting by Hcy may be fundamental to understanding the pathophysiology associated with hyperhomocysteinemia.



**Vascular Effects of Hyperhomocysteinemia: Insights from Murine Models**

Steven Lentz

Veterans Affairs Medical Center and Department of Internal Medicine, University of Iowa, Iowa City, IA, USA.

Hyperhomocysteinemia is associated with an increased risk of cardiovascular disease and stroke, but the mechanisms underlying this association are incompletely understood. We have used dietary and genetic approaches to produce hyperhomocysteinemia in mice. Our findings demonstrate that hyperhomocysteinemic mice develop endothelial vasomotor dysfunction in the aorta and cerebral arterioles and exhibit accelerated thrombosis after photochemical injury of the

carotid artery. Hyperhomocysteinemia also produces hypertrophy of cerebral arterioles and accelerated atherosclerosis in apolipoprotein E-deficient mice. Emerging data suggest that these vascular effects of hyperhomocysteinemia are multifactorial, and may involve oxidative inactivation of endothelium-derived nitric oxide, inhibition of nitric oxide synthase by its endogenous inhibitor, asymmetric dimethylarginine, and endoplasmic reticulum (ER) stress.



**The Role of Antioxidant Enzymes in Homocysteine-induced Endothelial Dysfunction**

Jane A. Leopold

Whitaker Cardiovascular Institute and Evans Department of Medicine,  
Boston University School of Medicine, Boston, MA 02118, USA.

Elevated levels of homocysteine have been shown to adversely affect vascular endothelial cell function resulting in an impaired vasodilator response to endothelium-dependent agonists. While the mechanisms underlying these effects remain incompletely characterized, it has been suggested that increased reactive oxygen species generation and decreased levels of bioavailable nitric oxide play a significant role in homocysteine-mediated endothelial dysfunction. Recent observations suggest that an additional mechanism by which homocysteine may modulate reactive oxygen species generation, and, thereby, levels of bioavailable nitric oxide, is to influence the expression and/or activity of key cellular antioxidant enzymes, notably glutathione peroxidase and glucose-6-phosphate dehydrogenase. These antioxidant enzymes regulate the vascular redox milieu and nitric oxide levels, and therefore, offer a protective benefit to vascular endothelial cells exposed to elevated levels of homocysteine.



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**Symposium II**  
**Monday, October 25, 2004**  
**16:00-18:00**

**Atherosclerosis: Lipoproteins, Lipoprotein receptors, and Other Risk Factors**

**Chair: Zemin Yao**

*Supported by Pfizer Canada*



**The Molecular Basis of Lipoprotein Receptor Signaling**

Joachim Herz

Department of Molecular Genetics, University of Texas Southwestern,  
Dallas, TX 75390-9046, USA

Most of the members of the low-density lipoprotein (LDL) receptor gene family are multifunctional cell surface receptors. Because of the well-known function of the LDL receptor in cholesterol transport, the family is most commonly associated with cellular transport processes, particularly of cholesterol and lipoproteins. However, over the last few years entirely different and fundamental functions of LDL receptor related proteins as cellular signal transducers have emerged. Several members of the family are involved in the regulation of a surprising variety of several established cellular signaling pathways in various cell types and tissues, both during the developmental period as well as in the adult. Here I will discuss the common underlying molecular mechanisms by which this ancient and highly conserved gene family on one hand regulates the development of the embryonic brain synaptic plasticity in the adult nervous system and on the other protects the vessel wall from atherosclerosis.



**Correction of Impaired ABCA1 Regulation and HDL Formation in Niemann-Pick Type C Disease**

Gordon A. Francis

Departments of Medicine and Biochemistry, University of Alberta, Edmonton,  
Alberta T6G 2S2, Canada

Niemann-Pick Type CI disease is characterized by impaired cellular cholesterol trafficking and neurodegeneration leading to premature death. We recently demonstrated that regulation and function of the rate-limiting protein for high density lipoprotein (HDL) particle formation, the ATP-binding cassette transporter AI (ABCA1), is impaired in human NPC disease fibroblasts, likely responsible for the presence of low HDL in the majority of NPC disease patients (Choi HY *et al.*, *J. Biol. Chem.* 2003;278:32569-32577). Previous studies suggested exogenous oxysterols, ligands of the liver X receptor (LXR), can alter cholesterol distribution and activate an ABCA1-promoter luciferase reporter construct in human NPC disease fibroblasts. To determine whether an exogenous LXR agonist can upregulate ABCA1 and enhance lipid mobilization to apolipoprotein A-I from NPC1<sup>-/-</sup> cells, NPC1<sup>+/+</sup> and NPC1<sup>-/-</sup> human fibroblasts were incubated in the presence of non-lipoprotein cholesterol or the LXR agonist T0901317. Cholesterol loading upregulated ABCA1 mRNA and protein levels in NPC1<sup>+/+</sup> but not NPC1<sup>-/-</sup> cells, while the LXR agonist increased ABCA1 expression in both cell lines. LXR agonist treatment increased mobilization of

radiolabeled LDL-derived cholesterol and phosphatidylcholine, as well as cholesterol mass, to apoA-I-containing medium of NPC1<sup>-/-</sup> cells, to the same levels seen in non-LXR agonist-stimulated NPC1<sup>+/+</sup> fibroblasts. LXR agonist/apoA-I co-incubations markedly diminished the accumulation of excess cholesterol in NPC1<sup>-/-</sup> cells as determined by fluorescent staining with filipin. These results suggest that the NPC1 protein mutation can be bypassed by LXR agonists to normalize ABCA1 expression and HDL particle formation in NPC1<sup>-/-</sup> cells.



### **Apolipoprotein Mediated Regulation of Plasma Lipid Levels**

Robert O. Ryan

Lipid Biology in Health and Disease Research Group, Children's Hospital  
Oakland Research Institute, Oakland, CA 94609, USA

Studies of naturally occurring mutations, and transgenic and gene disrupted mice, vividly illustrate the fundamental role played by exchangeable apolipoproteins (apo) in maintenance of plasma lipid levels. ApoE serves as a ligand for the low-density lipoprotein receptor (LDLR) family members, initiating a cellular process of receptor-mediated endocytosis. To characterize the molecular basis of apoE binding to the LDLR a soluble receptor fragment encompassing the extra-cellular portion of this 839 amino acid protein was expressed in stably transfected HEK293 cells. The isolated receptor was employed in binding studies with apoE containing lipid particles. Recombinant tryptophan-null apoE N-terminal domain was labeled with an extrinsic fluorescent probe that can serve as an energy acceptor from excited tryptophan residues and used in fluorescence assays of receptor binding. Results obtained reveal a correlation between apoE conformation and receptor binding as well as apoE-LDLR ligand binding cooperativity as a function of substrate lipid particle receptor-active apoE content. Studies of pH induced ligand release provide support for a model wherein the LDLR  $\beta$ -propeller motif functions as a cryptic, alternate ligand that displaces lipoprotein substrates, thereby facilitating delivery of their lipid cargo to lysosomes. The fluorescence-based soluble receptor-binding assay described has potentially broad application toward understanding the structural basis of LDLR ligand binding interactions.



### **Macrophage Functions in Atherosclerosis**

MacRae F. Linton

Atherosclerosis Research Unit, Vanderbilt University School of Medicine,  
Nashville, Tennessee 37235, USA

Atherosclerosis is an inflammatory disease process. The monocyte/macrophage plays key roles both in the initiation and progression of atherosclerosis. Recruitment of monocytes into the artery wall is one of the earliest events in atherosclerosis. In the intima, monocytes develop into macrophages, which are important mediators of inflammation, participating in both the innate (antigen-independent) and the acquired immune response in atherosclerosis. Macrophages contribute to the local inflammatory responses through production of cytokines, free oxygen radicals, proteases, and complement factors. The uptake of modified lipoproteins by macrophages leads to the accumulation of cholesterol esters and formation of macrophage-derived foam cells, the hallmark of the fatty streak. Macrophages also contribute to lesion remodeling and to plaque rupture by secreting matrix metalloproteinases. Recent studies indicate that LXR mediates a reciprocal regulation of macrophage genes involved in inflammation (e.g. COX-2 and iNOS) and in cholesterol homeostasis (e.g. ApoE, ACAT-1, and ABCA1). The adipocyte fatty acid-binding protein (FABP) aP2 is expressed by adipocytes and macrophages and modulates insulin resistance, glucose and lipid metabolism, and atherosclerosis. Macrophage aP2 promotes atherosclerosis through effects on both inflammatory pathways and lipid homeostasis. Thus, macrophages express a number of genes/proteins that contribute to atherogenesis, providing a variety of potential therapeutic targets for the prevention of atherosclerosis.



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**The Role of Notch in Remodeling and Maintaining the Vasculature**

Aly Karsan

Department of Pathology and Laboratory Medicine, University of British Columbia and British Columbia Cancer Agency, Vancouver, BC, Canada

The Notch proteins encompass a family of transmembrane receptors that have been highly conserved through evolution as mediators of cell fate, and are comprised of four members in mammals (Notch1 to 4). Following intracellular processing of the full-length protein, Notch is expressed at the cell surface as a heterodimeric receptor. Engagement by ligand results in a two-step cleavage of the Notch heterodimer, releasing the intracellular domain of Notch and allowing translocation to the nucleus. The intracellular domain of Notch interacts with the DNA-binding factor, CSL, resulting in transactivation at various promoters. In particular, various basic helix-loop-helix factors of the HES (Hairy and Enhancer of Split) and HRT families (Hairy-Related Transcription factor) are transcriptionally upregulated in response to Notch activation. Notch plays a critical and non-redundant role in vascular development and maintenance through the regulation of endothelial survival, proliferation and mesenchymal transformation. Our data demonstrate a novel mechanism of endothelial cell cycle arrest by Notch and demonstrate the ability of Notch activation to promote endothelial-to-mesenchymal transformation. Our findings suggest that modulating Notch signaling may have an impact in vascular remodeling and ischemic disease.



**Collagen Signaling Through Discoidin Receptors in Atherosclerosis**

Michelle Bendeck

Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada

Collagens in the extracellular matrix play important roles modulating the vascular response to injury during the progression of atherosclerosis and restenosis. Recent research has uncovered important functions regulating smooth muscle cell (SMC) proliferation, and SMC and macrophage migration and proteinase production. The discoidin domain receptors, DDR1 and DDR2, are novel transmembrane collagen receptors with tyrosine kinase activity, and signal to upregulate matrix metalloproteinase (MMP) expression. Research in our laboratory has been focused on the expression and functions of the DDRs in the cardiovascular system. DDR1 expression is increased following vascular injury. Using DDR1  $-/-$  mice, we have isolated SMCs

for study in tissue culture, and shown that DDR1<sup>-/-</sup> SMCs have a reduced capacity to proliferate and migrate, and have reduced MMP expression compared to DDR1<sup>+/+</sup> cells. We injured the carotid arteries of DDR1<sup>-/-</sup> mice, and found a dramatic reduction in neointimal thickening. We are currently studying the signaling pathways triggered by the DDR1, utilizing mutant receptor constructs, and measuring transcriptional activity for several genes (MMPs and collagen). In addition, we are investigating the role of the DDR1 in a mouse model of atherosclerosis, the LDL-R deficient mouse. These studies will allow us to elucidate the roles of collagen and the DDRs in atherosclerosis and restenosis.



### **Shear Stress, Inflammation and Endothelial Dysfunction**

Avrum I. Gotlieb and Kristopher S. Cunningham

Department of Laboratory Medicine and Pathobiology, University of Toronto,  
Toronto, Ontario, Canada

Laminar shear stress is necessary for normal endothelial function and arterial homeostasis. Mechanical shear stress is transduced into biochemical responses in endothelial cells and may involve elements from the extracellular matrix, cell membrane, multiple signaling pathways and cytoskeleton. Microarray technology has identified shear stress induced genes, many of which have shear stress responsive promoter elements. Endothelial cells may have different responses to various forms of blood flow such as laminar, turbulent and oscillatory flows. Different calibre arteries may also have varied gene expression profiles in response to disturbed flow. Many local and systemic factors proposed to be involved in atherogenesis such as inflammation, leukocyte adhesion, production of reactive oxygen species and enhanced endothelial permeability to serum constituents are directly or indirectly influenced by shear stress. Non-laminar flow can elicit a pro-apoptotic, pro-migratory and proliferative phenotype, which promotes development of atherosclerotic lesions in part through subendothelial insudation of lipoproteins. Multiple *in vitro* and *in vivo* models evaluating vascular shear stress and atherogenesis reveal that hemodynamic shear stress, in association with local and systemic factors, promotes atherosclerotic lesion formation and growth into clinically serious complicated plaques. In addition, appreciation for how disturbed flow can affect atherosclerotic plaque composition and arterial remodeling, in conjunction with developing imaging modalities, may help to identify vulnerable plaques where intervention could potentially prevent an acute coronary syndrome.



### **A Tribute to Robert H More**

Daria Haust

University of Western Ontario