

**UNIVERSITY OF TORONTO**

**HEART AND STROKE/RICHARD LEWAR CENTRE  
OF EXCELLENCE IN CARDIOVASCULAR RESEARCH**



**BIENNIAL REPORT  
JULY 1, 1999 TO JUNE 30, 2001**



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## MESSAGE FROM THE DIRECTOR

The year 2001 will be remembered as an extraordinary one on the clock of world history. It was also an extraordinary year for the Heart and Stroke/Richard Lewar Centre of Excellence. Cardiovascular research at the University of Toronto has been permanently transformed. Coincidental with the dawning of the new century, a new era of collaboration and focus on excellence has arrived.

The year started with a superbly productive strategic planning retreat attended by members of the Centre. The members clearly identified three priority platforms for scientific collaboration and implementation: (I) Transgenic Physiology for Models of Disease, (II) Gene and Cell Based Therapy, and (III) Gene Discovery through Genotype-Phenotype Data Matrix. These platforms continue to champion the guiding principles of the Centre's activities: innovation, excellence and collaboration. To make an impact, our first priority is novel discoveries that can change the paradigm of understanding of disease processes or have the potential to benefit patients broadly. All scientific endeavors must be based on internationally accepted standards of excellence. Further, to build our strengths, all projects or infrastructure supported through the Centre must be collaborative in nature.



Implementation of Platform I on transgenic physiology has proceeded admirably. The Transgenic Physiology Laboratory is now fully operational and is the first unit of its kind in the world. This new 6,500 square foot state-of-the-art laboratory is dedicated to the investigation of miniaturized models of human cardiovascular disease, created through genetic or environmental manipulations. Its completion was made possible through the extraordinary efforts of the Basic Science Committee (BSC) and the BSC Chairs, Drs. Lee Adamson and Peter Backx, utilizing the Centre's resources and matching funds of \$1.7 million from the Canada Foundation for Innovation and the Ontario Challenge Fund. We are proud to introduce Dr. Peter Backx as the new Director of the facility, who together with an excellent team, will fast track cardiovascular research at the University in the post-genomic era.

Platform II will support collaborative gene-based investigation and therapy programs at the University. A core laboratory to generate genetic tools and vectors has been set up to support this important effort directly impacting on patients at the bedside. The University of Toronto is already a leading player in cardiovascular gene therapy on the world stage, and this effort, led by Dr. Duncan Stewart, has just received matched funding from the Canada Foundation for Innovation (\$3.2 million) and the Canadian Institutes for Health Research (CIHR) University-Industry program (\$2.3 million) to accelerate the pace of these investigations. A second strategic planning retreat on stem cell based cardiovascular therapy will take place in Spring 2002.

Platform III supports gene discovery through large-scale genotype-phenotype correlations. The cardiovascular group is at the leading edge of research in terms of large-scale gene screening using "gene-chips" containing 12,000 to 19,000 gene arrays. This effort will be matched by the establishment of large clinical databases, e.g., heart failure, atherosclerosis intervention and congenital heart disease. This platform is currently supported through an External Group grant from the CIHR, and will be expanded through additional grant applications and industry funding partners. This platform will be crucial in creating a bench to bedside continuum in the post-genomic era.

A strong Centre can only be built on the strengths of its individual members, who have also realized extraordinary accomplishments this past year. In addition to ongoing large group grants and new research chairs and awards, members of the Centre were also successful in obtaining three New Frontiers Program grants from the CIHR. Drs. Duncan Stewart (Gene and Cell Based Therapies) and Lowell Langille (Vascular Biology) will host national meetings in Toronto to determine the national agenda for research in these areas.

Dr. Jack Tu at the Institute for Clinical Evaluative Sciences (ICES) has also obtained joint CIHR-Heart and Stroke Foundation of Canada (HSFC) funding for his CCORT project (Canadian Cardiovascular Outcomes Research Team), mapping out the cardiovascular outcomes and identifying means of improvement for Canada. Dr. Josef Penninger continues with his amazing pace of discovery with regular publications in Nature and Cell.

The Centre was delighted to host the new Director of the Institute of Circulatory and Respiratory Health (ICRH) of the CIHR, Dr. Bruce McManus. He is most pleased with the Centre's ability to bring cardiovascular research together in a transdisciplinary manner, fitting the vision of the CIHR for health-based research in the new century. The goals of the Centre also coincide with much of the goals of the ICRH, including: (1) training of clinician-scientists; (2) multi-disciplinary collaborative research; (3) improving the health of vulnerable populations (e.g., congenital heart disease in children and heart failure in elderly), and (4) strengthening research in genomics.

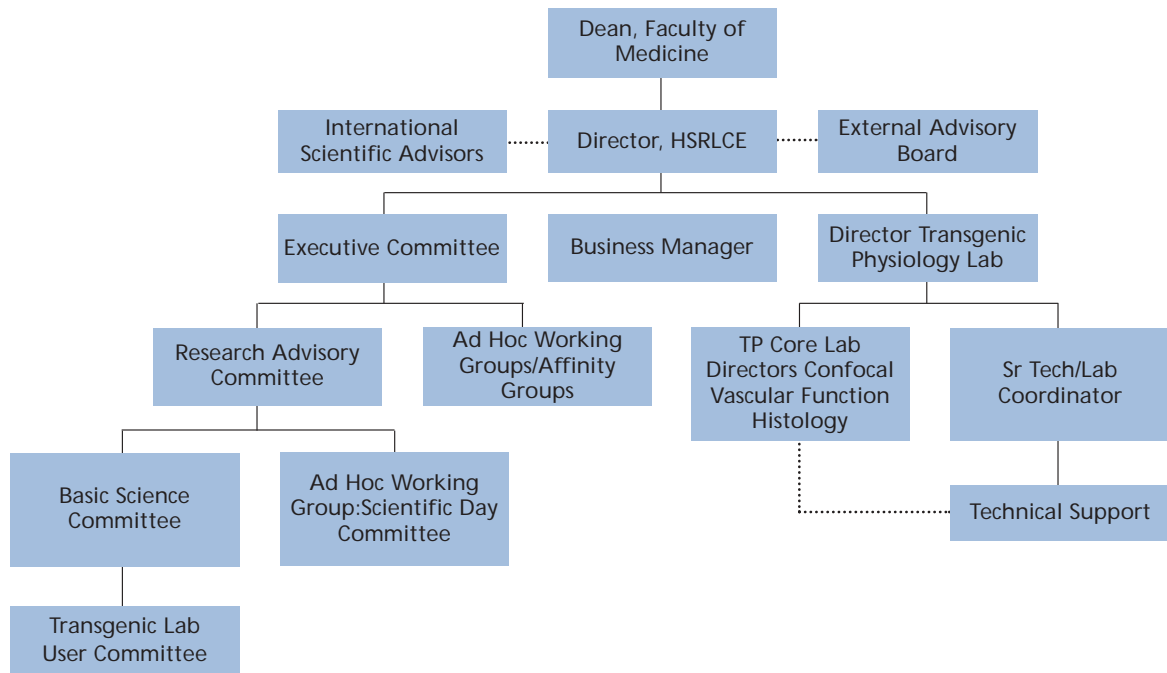
I would like to take this opportunity to express my gratitude to members of the Centre for their extraordinary support and for advice that they have provided me throughout the year. Particular thanks are due for members of the Executive, Research Advisory, External Advisory and Basic Science Committees, who tirelessly volunteered their time to make the Centre what it is today. I would also like to thank our talented Business Manager, Ms. Wendy Kubasik, for her tireless dedication. Thanks also to Dr. Carin Wittnich and her team for assistance with educational programs, and to Dr. Michael Sole, who founded and directed the Centre for Cardiovascular Research and led its evolution into the Heart and Stroke/Richard Lewar Centre of Excellence.

Over the next year, we aim to build further on Platforms II and III, and to hold a strategic planning session on "Stem cell based therapy" in cardiovascular disease. We will also critically examine the issue of training in the new context and strengthen our community through strategic recruitment. I am confident that through innovation, excellence and collaboration, we will look back and realize how extraordinary the year 2001 was. The events in 2001 brought everyone closer, and we realized more than ever how precious life is. We at the Centre will continue to work to better the lives of our patients, and in the process, understand ourselves better.



Peter Liu, MD

## ORGANIZATIONAL CHART OF THE CENTRE OF EXCELLENCE



**Dean, Faculty of Medicine**  
Dr. C. David Naylor

### Administration

**Director:**  
Dr. Peter Liu

**Associate Director:**  
Dr. Duncan Stewart

**Deputy Director:**  
Dr. Marlene Rabinovitch (to November 2001)

**Business Manager:**  
Ms. Wendy Kubasik

**Director, Transgenic Physiology Lab:**  
Dr. Peter Backx

**Head, Education Program:**  
Dr. Carin Wittnich

**Senior Technician/Lab Coordinator:**  
Mrs. Van Nguyen

**International Scientific Advisors**  
Dr. Victor Dzau  
Dr. Robert Roberts

### External Advisory Board

Mr. Robert W. Luba (Chairperson)  
Mr. Thomas H. Brent  
Mr. Richard Gallop  
Ms. Wendy Kubasik (Secretary)  
Mr. Wilfrid G. Lewitt  
Dr. Peter Liu  
Dr. C. David Naylor  
Mr. Gil Newman  
Ms. Maureen Quigley  
Dr. Michael J. Sole  
Ms. Laura Syron  
Mr. David A. Ward

### Executive Committee

Dr. Peter Liu (Chairperson)  
Dr. Avrum Gotlieb (01-)  
Ms. Wendy Kubasik  
Dr. Marlene Rabinovitch (99-01)  
Dr. Michael J. Sole  
Dr. Duncan Stewart

### Research Advisory Committee

Dr. Peter Liu (Chairperson)  
Dr. Lee Adamson  
Dr. Patricia Brubaker (99-01)  
Dr. John Floras  
Dr. Avrum I. Gotlieb  
Ms. Wendy Kubasik (Secretary)  
Dr. John MacDonald (01-)  
Dr. Marlene Rabinovitch  
Dr. Martin Myers  
Dr. Harry Rakowski  
Dr. Michael J. Sole  
Dr. Duncan Stewart  
Dr. Richard D. Weisel  
Dr. Carin Wittnich  
Dr. Terry Yau  
Dr. Cecil Yip

### Basic Science Committee

Dr. Lee Adamson (Co-Chairperson)  
Dr. Peter Backx (Co-Chairperson)  
Dr. John Challis  
Dr. Myron Cybulsky  
Dr. Dan Dumont  
Dr. Mansoor Husain  
Dr. Peter Liu  
Dr. Phil Marsden  
Dr. Marlene Rabinovitch  
Dr. Duncan Stewart  
Dr. Michael Ward

### Scientific Day Program Committee (2001)

Dr. Carin Wittnich (Chairperson)  
Dr. Lee Adamson  
Dr. John Floras  
Dr. Stephen Femes  
Dr. Anatoly Langer  
Dr. Peter Liu  
Dr. Marlene Rabinovitch  
Dr. Duncan Stewart  
Dr. Jack Tu

### Scientific Day Planning Committee (2001)

Dr. Peter Liu (Chairperson)  
Ms. Wendy Kubasik  
Ms. Victoria Simpson  
Dr. Carin Wittnich

### Mission

The purpose of the Heart and Stroke/Richard Lewar Centre of Excellence (HSRLCE) is to bring the best of cardiovascular sciences at the University of Toronto together, including basic sciences, clinical investigations and community health. Research at the Centre is focused on the prevention and cure of atherosclerosis, heart failure and congenital heart disease. From this research will evolve diagnostic, prognostic, and therapeutic innovations that can impact on the health of all Canadians.

### Vision

The Centre of Excellence aims to become an internationally pre-eminent institution in cardiovascular research, through innovations in science, collaboration of minds, and training and recruitment of the best and brightest leaders in research.

### Overall Theme, Goals and Objectives

The activities of the Heart and Stroke/Richard Lewar Centre of Excellence are founded on the following broad themes and principles:

- To provide an environment and infrastructure for research in post-genomic cardiovascular medicine at the University of Toronto;
- To encourage solutions to specifically target priority areas of research in terms of infrastructure, recruitment, start-up funding, and support of young scientists. The criteria by which all the programs will be judged for support will be innovation, excellence, and collaboration.

The Centre aims to foster excellence in cardiovascular research through:

- Formation of affinity groups (a critical mass of investigators interested in a common area) with identified leader(s) and infrastructure;
- Development of group research programs to answer key questions;
- Development of collaborative infrastructure to facilitate knowledge and technique sharing;
- Recruitment of top level scientists within focused priority programs;
- Training the next generation of research leaders; and,
- Improvement of communication within the cardiovascular community.

### Structure and Administration

The Centre is built around the following core groups:

- Research and administrative staff;
- Members – University of Toronto faculty;
- Affinity groups (may include research associates, graduate students and post-doctoral fellows).

Faculty from the University of Toronto comprise a diverse network of Centre of Excellence "members". A complete listing of our membership is included in the "Personelle" section of the report.

### Principles of Funding

As the Centre has only limited funds for a large group of investigators, it abides by the following principles:

- To leverage available funds to maximize the benefit for groups (e.g., despite cash outlay of only \$550,000 in its first year budget, the Centre's investigators, through collaboration and creativity, have already levered more than \$5.4 million dollars of peer reviewed funding for the priority programs, a leverage factor of 10:1 (mainly through group grants and CFI funding);
- All funding will be done with the general principle of leverage, with partnerships expressly stated or implied;
- Funding will be provided for projects and individuals based on the common criteria of excellence, innovation and collaboration. Funding will be primarily earmarked for areas of research priority, but any excellent proposal that fits within the mission and vision of the Centre will also be entertained;
- All major funding allocation will be done on a competitive basis with peer review (i.e., recommendation of the Research Advisory Committee).

On January 18, 2001, the Centre completed the first stage of its strategic planning process. Strategies for development of the Centre consist of both research programs as well as an intersecting administrative infrastructure to facilitate these programs.

The research programs of the Centre will be divided into three priority platforms for scientific collaboration and implementation, as follows:

### **Priority Platform I: Transgenic Physiology**

### **Priority Platform II: City Wide Gene and Cell Therapy Program for Angiogenesis and Regeneration**

### **Priority Platform III: Clinical Genomics and Proteomics**

#### **Priority Platform I: Transgenic Physiology**

The Heart and Stroke/Richard Lewar Centre of Excellence Transgenic Physiology Laboratory began operation during the fall of 2001 with the completion of renovations to the FitzGerald Building on the University of Toronto campus. Dr. Peter Backx was appointed Director of this research facility, which is dedicated to providing state-of-the-art analyses of cardiovascular structure (pathology) and function (physiology). The facility will assist members of the University of Toronto research community with research involving primarily, but not limited to, transgenic mice. It will bring together researchers from across the University in a collaborative, group-oriented environment.

The laboratory provides equipment and resources for cardiovascular assessment of transgenic mice. Equipment available includes:

- Ultrasound machine;
- Confocal microscope;
- Gas chromatograph;
- Telemetry monitoring system;
- Millar catheters.

The Centre also provides general surgical services for the generation of coronary artery ligation, aortic banding and vessel damage as well as in vivo hemodynamics, ultrasound imaging, tail cuff recordings, Langendorff heart preparations (both isometric and working heart), electrocardiograms and telemetry. At the present time, all measurements are done on-site in the FitzGerald Building, with the exception of the ultrasound recordings.

The Transgenic Physiology Laboratory also houses a cellular/multicellular function core to perform studies to assess contractile mechanics, excitation-contraction coupling and cellular electrophysiology of cardiac or smooth muscle cells and tissues. The cellular function has the capability to isolate cardiac myocytes, smooth muscle myocytes, cardiac trabeculae and individual vessels. The cellular assessment facility also contains an inverted Olympus confocal microscope and there are plans for a histology core as well.

The animal housing area, intended to hold mice on a short-term basis, will be equipped with cages in the near future. The facility will begin receiving mice during spring 2002. In the meantime, small numbers of animals have been transferred to the facility for acute studies.

The Transgenic Physiology Laboratory has recruited Ms. Van Nguyen as the Laboratory Coordinator/Senior Technician. Ms. Nguyen is able to assist members with their research, performing in vivo measurements on mice, and is responsible for the administration of the facility. The Centre will hire additional technicians to focus on cellular measurements.



### **Priority II: City Wide Gene Therapy Program for Angiogenesis and Regeneration**

The Heart and Stroke/Richard Lewar Centre of Excellence was established to provide cardiovascular researchers at the University of Toronto with a unique resource to support innovative research programs addressing questions related to the diagnosis, treatment and prevention of heart and vascular diseases. The goal of Platform II is to translate fundamental research advances into novel clinical diagnostic and therapeutic strategies. In the past year, there has been significant progress towards the initiation of a multicentre clinical trial to assess the efficacy and safety of a gene therapy for coronary angiogenesis, which will be led by the Centre and the University of Toronto, under the direction of Dr. Stewart and co-workers at St. Michael's Hospital (SMH). This trial builds on phase I/II safety studies which have been completed over the last year at SMH, and will utilize an innovative navigational and mapping catheter system for intramyocardial gene injection, which was acquired with support provided by the Canadian Foundation for Innovation Cardiovascular Gene Therapy Initiative, co-sponsored by the Centre. Six centres will participate (University Health Network/Mount Sinai Hospital, St. Michael's Hospital, Sunnybrook & Women's College Health Sciences Centre, Victoria, Montreal Heart Institute and Quebec City) in a randomized double blind trial. With the support of the Centre, VEGF165 cDNA has been cloned into the "humanized" pVAX-1 plasmid vector and manufactured according to GMP-like standards for use in the human trial. Almost \$500,000 in funding has been secured from the Heart and Stroke Foundation of Ontario (HSFO) and Canadian Institutes for Health Research (CIHR) for operational aspects of this trial, and Biosense Canada (Johnson & Johnson) is providing over \$1 million in in-kind contributions in the form of mapping and injection catheter sets. The Clinical Trials Application (CTA) has been submitted to the Biologicals Division of Health Canada, and approval is anticipated for April 2002.

Under the auspices of the Centre, an application for a New Frontiers Program in Cell and Gene Therapy of Cardio-Respiratory Diseases was submitted and funded by the CIHR and HSFC. A meeting was held on January 12, 2002 involving researchers from across Canada and representing all pillars of the CIHR. The purpose was to identify emerging research questions and advise the CIHR and HSFC concerning funding opportunities. This meeting was highly successful and overall blueprint for innovative translational research in Canada in this area was outlined in a Final Report. This report may form the basis of an application for a Centre of Excellence, in which the HSRLCE will be taking a leadership role, with a letter of intent (LOI) due July 2002.

### **Priority Platform III: Clinical Genomics and Proteomics**

The completion of the Human Genome Project (HGP) has placed a finite boundary on the quest for novel genes in the human organism, but opened an entirely novel challenge of understanding gene function in health and disease. To rapidly identify the function of genes, modules and pathways in the proper context of health and disease, systematic high throughput strategies to evaluate families of gene behavior under stress can provide unique clues to their domains of influence. To support this effort, the Centre has developed an in-house high throughput gene and protein comparison algorithms and associated bioinformatics infrastructure. This is the most advanced microarray infrastructure currently in Canada designated primarily for cardiovascular research. This effort is complemented by collaborative microarray manufacturing robotics, collaborative proteomic expertise (with Queen's University) and large-scale polymorphism screens. This platform interfaces intimately with Platforms I and II in an iterative fashion, and is using this infrastructure to discover novel diagnostic and therapeutic targets in heart failure and atherosclerosis.

The cardiovascular group is at the leading edge of research in terms of large-scale gene screening using "gene-chips" containing 12,000 to 19,000 gene arrays. This effort will be matched by the establishment of large clinical databases, such as that in heart failure, atherosclerosis intervention and congenital heart disease. This platform is currently supported through an External Group grant from the CIHR, and has just received additional funding through the CIHR Institute of Cardiovascular and Respiratory Health Gene-Environment Interaction initiative. The latter funding will be matched by the Heart & Stroke Foundation of Canada and industrial partners. This will be an important platform in creating the bench to bedside continuum in the post-genomic era in the coming years.

Priority platform III is currently led by the group program investigators. We are continuing to look for expansion in this program to facilitate bioinformatics, proteomics, clinical databases and training to create a unique gene-environment interaction program in Canada.

### Affinity/Research Groups

#### Heart Failure

Heart failure is a disease of inappropriate response of host to external cardiac injury and stress. The group (now formally recognized through CIHR/MRC peer review mechanism) will use microarray technology, transgenic mutational models, transgenic physiology and the micromanipulation techniques to identify patterns of genes responsible for heart failure progression. The targets identified will be fed back as targets for either genetic or pharmacological testing at the bench. Thus, the goals of this affinity group are:

- To define novel mechanisms of heart failure progression;
- To define the molecular basis of heart failure through basic models and clinical diseases;
- To employ microarray technology to identify novel targets for heart failure therapy;
- To identify novel genes at the bedside and population level (in coordination with single gene and complex genetic trait analysis program).

#### Vascular Biology/Atherosclerosis

The goal of this research group is to develop novel insights into the molecular and cellular pathogenesis of atherosclerosis, including the endothelium, smooth muscle and extracellular matrix formation. From this will derive potential therapeutic strategies for future targeting in the clinical population. Through various cell and animal models of vascular disease, and through sophisticated imaging techniques, the initiation and progression of vascular disease will be studied. These will be accompanied by transgenic manipulation and potential screening of novel targets to develop gene-structure-function relationships.

#### Development Biology and Congenital Heart Disease

The goals of this affinity group include:

- Identification of the fundamental genes responsible for cardiac development;
- Identification of how these processes can go wrong to produce congenital heart disease;
- Derivation of a novel means of diagnosis or therapy for CV developmental abnormalities;
- Translation of this knowledge into acquired disease settings, e.g. re-expression of fetal genes in disease.

In addition to the affinity groups outlined above, work is underway to bring together researchers interested in the pursuing the following areas:

- Clinical genomics – single gene disorders;
- Complex cardiovascular disease and genetic epidemiology;
- Bioinformatics;
- Genome based biotechnology;
- Translational research;
- Clinical trials/outcomes/pharmacogenomics;
- Gene/cell therapy for heart disease – new targets;
- Genes that determine the birth and death of the heart;
- Infection and inflammation and heart disease.

### **The Canadian Cardiovascular Outcomes Research Team (CCORT)**

**Submitted by: Jack V. Tu**

The Canadian Cardiovascular Outcomes Research Team (CCORT) was established in January 2001 by a five-year \$4.7 million grant in the Canadian Institutes for Health Research (CIHR) Interdisciplinary Health Research Team (IHRT) competition. There are 25 investigators on the CCORT, representing the provinces of Nova Scotia, Quebec, Ontario, Alberta and British Columbia. The national coordinating Centre is located at the Institute for Clinical Evaluative Sciences (ICES) in Toronto.

The overall goal of the CCORT initiative is to measure and improve the quality of cardiovascular care in Canada. The research team will conduct a series of multi-disciplinary studies that will focus on improving the quality of care of patients with acute myocardial infarction (AMI) and congestive heart failure (CHF), and the outcomes of patients undergoing cardiac catheterization, percutaneous coronary intervention, and coronary artery bypass grafting surgery in Canada.

The CCORT investigators will conduct a number of projects over the next five years including a randomized trial comparing the effectiveness of report cards based on clinical vs. administrative data for improving AMI and CHF care in Ontario. A set of quality indicators for measuring the quality of AMI and CHF care provided in Canadian hospitals will be developed as part of this project. Regional and inter-provincial variations in the treatment of cardiac patients in Canada will be studied and a Canadian Cardiovascular Atlas produced. The investigators are also developing a student-training program for training the next generation of cardiovascular outcomes researchers in Canada.

The CCORT investigators believe that their research will have a positive impact on the delivery of cardiac care in Canada and look forward to working with cardiovascular practitioners across Canada in their research studies. For those wishing to learn more about CCORT, please visit the CCORT website at [www.ccort.ca](http://www.ccort.ca).

### **The Canadian Heart Research Centre (CHRC)**

**Submitted by: Anatoly Langer**

The Canadian Heart Research Centre (CHRC) is a federally incorporated academic clinical research organization dedicated to the conduct of clinical research and education in the treatment and prevention of cardiovascular disease in Canada. The CHRC is a multi-faceted organization that has an intimate understanding of the needs of physicians and industry. Growing rapidly, with an emphasis on information technology and operations infrastructure, CHRC is now on the leading edge of cardiovascular research and education.

The mission of CHRC is to be a leader in the conduct and management of clinical trials and to provide an innovative approach to physician and patient education in the area of cardiovascular medicine. Within the Canadian Heart Research Centre are several specialized units each with dedicated technologies developed to their specific research and teaching activities. These include:

- Clinical Trials Unit Coordination and Study Monitoring;
- Site Management and Finance Administration;
- Data Management and Information Technology;
- Holter/ECG Central Data Laboratory;
- Quantitative Coronary Angiography Central Laboratory;
- Central Clinical Laboratory Management;
- Sponsor and Site Administration;
- Professional Development and Continuing Medical Education;
- Symposium and Education Event Coordination.

Information management is a principal element in all activities of the Canadian Heart Research Centre and core to the efforts of its academic mission. Accordingly, the CHRC has available three independent local area networks (LANs). Data entry stations are available with thematic activities of the Canadian Heart Research Centre, which permits programmatic statistical review to occur regularly from designated administrative office locations. Additional Internet capabilities are available through email and web site development. Bridging new developments in the understanding of genetic mechanisms, the Canadian Heart Research Centre will unfold an array of clinical registries, which through education of patients and physicians, will not only improve delivery of care, but also bring about new insight into pathophysiology and management of cardiovascular disease in Canada.

If you would like to learn more about the CHRC, please call (416) 977-8010.



HSRLCE Transgenic Physiology Laboratory

## PERSONNEL

For the purpose of distinguishing between personnel on the basis of affiliation, the Heart and Stroke/Richard Lewar Centre of Excellence has devised the following categories:

- Research and administrative staff;
- Members – University of Toronto faculty;
- Affinity groups (may include research associates, graduate students and post-doctoral fellows).

The daily operations of the Centre are conducted by the Director, Business Manager and Director of the Transgenic Physiology Laboratory. Policy direction for the Centre is provided by the Executive Committee with crucial input from the External Advisory Board, Research Advisory Committee, and International Scientific Advisors. Ad hoc working groups are struck to complete specific tasks (e.g., Basic Science Committee, Recruitment, etc.). Additionally, the Centre has worked to develop and formalize relationships with the University cardiovascular community in order to facilitate the mission and vision of the Centre, and enhance research and communications activities. This has resulted in the addition of the category "members".

### Centre of Excellence Members

The following is a list of Centre of Excellence members including their degrees, current positions, and a brief summary of current research interests.

**UWE ACKERMANN (BSc, MSc, PhD)**, Professor, Department of Physiology, Faculty of Medicine, Institute of Biomedical Engineering and Centre for Research in Education, University of Toronto, Associate Professor, Division of Biological Sciences, Canadian Memorial Chiropractic College. *Atrial natriuretic peptides and the nervous system.*

**S. LEE ADAMSON (PhD)**, Professor, Department of Obstetrics and Gynecology, University of Toronto, Director, Mouse Physiology Screening Laboratory and Senior Scientist, Samuel Lunenfeld Research Institute, Mount Sinai Hospital. *Developmental cardiovascular physiology (emphasis on the placenta and on the perinatal period).*

**KHOSROW ADELI (PhD, FCACB, DABCC)**, Professor, University of Toronto, and Head, Clinical Molecular Biochemistry Division, Hospital for Sick Children. *Cellular biology of lipoprotein metabolism in cardiovascular disease, insulin resistance syndrome, type 2 diabetes and obesity; molecular basis of genetic disorders of lipoprotein metabolism and dyslipidemias.*

**PETER BACKX (PhD)**, Associate Professor, Departments of Physiology and Medicine, Director, Heart and Stroke/ Richard Lewar Centre of Excellence Transgenic Physiology Laboratory, University of Toronto and Division of Cardiology, University Health Network. *Ion channels and heart disease.*

**MICHELLE P. BENDECK (PhD)**, Assistant Professor, Laboratory Medicine and Pathobiology, University of Toronto. *Atherosclerosis and restenosis, with an interest in determining the molecular and cellular mechanisms involved in smooth muscle cell (SMC) migration and accumulation in atherosclerotic plaques; has found that SMCs use a family of enzymes, the matrix metalloproteinases (MMPs) to facilitate clearance of the extracellular matrix during migration.*

**T. DOUGLAS BRADLEY (BA, MD, FRCPC)**, Professor, Department of Medicine, and Director, Centre of Sleep and Chronobiology, University of Toronto, Director, Cardio-pulmonary Sleep Disorders and Research Centre and Staff Physician, Division of Respiriology, University Health Network, Director, Sleep Research Laboratory, Toronto Rehabilitation Institute, and Senior Scientist, Canadian Institutes of Health Research. *Pathophysiological interactions of sleep apnea and the cardiovascular system, clinical trials on effects of sleep apnea with CPAP.*

**DINA BROOKS (PhD)**, Assistant Professor, Department of Physical Therapy, University of Toronto. *Rehabilitation of individuals with cardiac disease, especially after surgery, measures that predict long-term outcome, and the implementation of rehabilitation from the acute hospital to the community.*

**BENOIT BRUNEAU (PhD)**, Assistant Professor, Department of Molecular and Medical Genetic, University of Toronto, and Scientist, Cardiovascular Research, The Hospital for Sick Children. *Understanding the genes that are important for the formation of the heart during embryogenesis, and how disruption of these genes results in congenital heart disease; using genetic engineering in mice to address these issues.*

**JAGDISH BUTANY (MBBS, MD)**, Professor, Department of Laboratory Medicine and Pathobiology, University of Toronto and Pathologist and Director, Autopsy Service, University Health Network. *Cardiovascular pathology; coronary artery disease; and, native and prosthetic heart valves.*

**ANGELA CHEUNG (MD, PhD, FRCPC)**, Assistant Professor, Departments of Surgery, Medicine, Public Health Sciences and Health Administration, University of Toronto and Associate Director, Women's Health Program, University Health Network. *Postmenopausal women's health, especially as it relates to cardiovascular disease. Her expertise is in conducting randomized controlled trials and cohort studies, and performing health services and health policy research.*

**ERIC COHEN (MD, FRCPC)**, Associate Professor, Department of Medicine, University of Toronto and Director, Cardiac Catheterization Laboratory, Sunnybrook & Women's College Health Sciences Centre. *Interventional cardiology including adjunctive pharmacotherapy; evaluation of new interventional devices; outcomes and cost-effectiveness of percutaneous revascularization.*

**DAVID COURTMAN (PhD)**, Assistant Professor, Departments of Surgery and Laboratory Medicine and Pathobiology and the Institute for Biomaterials and Biomedical Engineering, University of Toronto and Staff Scientist, St. Michael's Hospital. *Research undertaken in Dr. Courtman's laboratory include: the roles of extrinsic coagulation and matrix degradation in blood vessel remodeling; the development of tissue engineered blood vessels and heart valves; and, the molecular epidemiology of abdominal aortic aneurysm.*

**MYRON I. CYBULSKY (MD)**, Associate Professor, Department of Laboratory Medicine and Pathobiology, University of Toronto, Pathologist, University Health Network and Senior Scientist, Toronto General Research Institute. *Functions of endothelial cell and leukocyte adhesion molecules in leukocyte emigration during inflammation and atherosclerosis; cellular molecular mechanisms of endothelial cell NF kappa B signal transduction in different regions of the arterial tree during the initiation of atherosclerotic lesions.*

**PAUL DORIAN (MD, MSc, FRCPC)**, Staff, Division of Cardiology, Department of Medicine, St. Michael's Hospital, Chief of Electrophysiology, St. Michael's Hospital. *Dr. Dorian's research interests include cardiac electrophysiology, antiarrhythmic drug pharmacology, and quality of life in patients with cardiac arrhythmias.*

**DAN DUMONT (PhD)**, Associate Professor and Research Scientist, Department of Medical Biophysics, University of Toronto. *Dr. Dumont's lab is interested in the control of angiogenic response. His lab uses both a biochemical and a mouse molecular genetic approach to study the importance of receptor tyrosine kinase signaling during angiogenesis.*

**C. ROSS ETHIER (BSc, SM, MA, PhD)**, Professor of Mechanical Engineering, Biomedical Engineering and Ophthalmology, University of Toronto. *Bioengineering studies of blood flow and mass transfer in large arteries, study of hemodynamic basis of arterial disease, blood flow.*

**GEORGE FANTUS (BSc, MDCM)**, Professor, Departments of Medicine and Physiology, University of Toronto and Director, Banting and Best Diabetes Centre Core Laboratory. *Dr. Fantus' lab is working to identify the insulin signaling defect in adipose and muscle cells in type 2 diabetes mellitus as well as mechanisms of high glucose induced alterations in gene expression in mesangial cells. The goal is to identify novel targets to develop drugs to prevent microvascular and macrovascular disease which complicates diabetes.*

**JOHN FLORAS (MD, Dphil, FRCPC, FACC, LMCC)**, Professor, Department of Medicine, University of Toronto, Clinical Director, Cardiology, Mount Sinai Hospital, Director of Cardiology Research, University Health Network. *Regulation of the heart and circulation in healthy men and women by the autonomic nervous system, endogenous peptides, purines and hormones, by the endothelium and by exercise. Current projects include studies of menopause (hormonal replacement therapy), heart failure, hypertension, renal insufficiency, and lupus.*

**STEPHEN E. FREMES (MD, MSc, FRCSC, FACP, FACC)**, Professor, Department of Surgery, University of Toronto, Head, Division of Cardiovascular Surgery and Cardiovascular Intensive Care Unit, Sunnybrook & Women's College Health Sciences Centre and Senior Adjunct Scientist, Institute for Clinical Evaluative Sciences. *Perioperative myocardial protection and the influence of arterial conduits on the short and long-term of patients following coronary bypass surgery.*

**JACK GOODMAN (PhD)**, Associate Professor, Faculty of Physical Education and Health, University of Toronto. *Left ventricular response to acute and chronic exercise stress in both health and disease, central and peripheral limitations to exercise performance, and the mechanisms of cardiovascular adaptation to cardiac rehabilitation.*

**AVRUM GOTLIEB (BSc, MD, CM, FRCPC)**, Professor and Chair, Department of Laboratory Medicine and Pathobiology, University of Toronto, Director, Vascular Research Laboratory, Dept. of Pathology and Banting and Best Diabetes Centre, University Health Network. *Cell biology of atherosclerosis and cell biology of the mitral valve as it relates to pathobiological processes which induce heart valve dysfunction and disease.*

**MANSOOR HUSAIN (MD)**, Assistant Professor, Department of Medicine, University of Toronto and Scientist, Toronto General Hospital Research Institute. *Molecular regulation of vascular smooth muscle cell proliferation and contractility and genetic models of atherosclerosis and hypertension in mice.*

**JANE IRVINE (D.Phil, C.Psych)**, Associate Professor, Departments of Psychiatry, Public Health Sciences, Surgery and Family and Community Medicine, University of Toronto, Associate Professor, Department of Psychology, York University, Research Scientist, Behavioral and Health Sciences Division, University Health Network. *The bio-behavioral mechanisms underlying the effects of negative emotions on the cardiovascular system with a specific focus on myocardial ischemia and cardiac arrhythmias, cognitive-behavior therapy for promoting health behavior change and adaptation to illness, enhancing adherence to health behavior change, and quality of life assessment.*

**FRED W. KEELEY (PhD)**, Professor, Department of Biochemistry and Department of Laboratory Medicine and Pathobiology, University of Toronto and Senior Scientist, Research Institute, The Hospital for Sick Children. *Mechanisms of regulation of aortic elastin synthesis and assembly into the extracellular elastic matrix with normal development and in pathological circumstances, sequence/structure/function and evolutionary relationships between elastin and elastin-like proteins in cartilage of lower vertebrates, the role of hydrophobic domains of elastin in extracellular assembly of the elastic matrix and self-alignment and polymeric assembly of recombinant human elastin and other elastin-like proteins with the potential for fabrication of biomaterials with unique and useful physical properties.*

**ANATOLY LANGER (MD, BSc, FRCPC, FACC)**, Director, Canadian Heart Research Centre and Associate Professor, Department of Medicine, University of Toronto. *Clinical trials, continuing professional development, and medical education.*

**LOWELL LANGILLE (PHD)**, Professor, Department of Laboratory Medicine and Pathobiology and Department of Obstetrics and Gynecology, University of Toronto, Director, Heart & Stroke Foundation of Ontario Program in Cell Biology of Atherosclerosis and Senior Scientist, Toronto General Research Institute. *Dr. Langille's research investigates the influences of physical forces in the biology of vascular cells and tissues. He is studying mechanotransduction pathways in vascular endothelium and smooth muscle cells, and how these pathways regulate cellular activities and tissue remodeling in cell culture and animal models. His goal is to understand how mechanical forces elicit adaptation in arteries and how this adaptation affects vascular development as well as vascular pathologies, especially atherosclerosis and restenosis.*

**GARY LEWIS (MD, FRCPC)**, Associate Professor, Department of Medicine, University of Toronto, Division of Endocrinology, University Health Network, Head, Division of Clinical Investigation and Human Physiology, Toronto General Hospital Research Institute, University Health Network. *Insulin regulation of lipoprotein production; mechanism of HDL lowering in hypertriglyceridemia; investigation of the effects of portal vs. peripheral insulin delivery on hepatic glucose and lipoprotein production in humans; and the effect of free fatty acids on pancreatic beta cell secretory function.*

**REN-KE LI (MD, PhD)**, Associate Professor, Department of Surgery, University of Toronto and Division of Cardiovascular Surgery, University Health Network. *Cell culture technology development, cell transplantation into myocardial scar tissue to repair the damaged heart or heart defect, and contribution of growth factors to regional myocardial hypertrophy in patients with idiopathic hypertrophic cardiomyopathy.*

**THOMAS LINDSAY (MDCM, MSc, FRCSC)**, Assistant Professor, Department of Surgery, University of Toronto, Research Supervisor, Institute of Medical Sciences, Staff Surgeon, Vascular Surgery, University of Toronto. *Organ injury and failure following rupture of an abdominal aortic aneurysm and the mediators of remote organ injury including the role of the neutrophil, cytokines and complement.*

**PETER LIU (MD, FRCPC)**, Professor, Department of Medicine, Heart & Stroke Polo Chair for Cardiovascular Research, Director, Heart and Stroke/Richard Lewar Centre of Excellence, University of Toronto and Staff Cardiologist, University Health Network. *Inflammatory and immune mechanisms of cardiovascular disease, role of host responses to cardiovascular injury in producing heart failure, investigated through the use of transgenic mouse models and translation of heart failure investigation from the bench to the bedside through clinical trials and health service research.*

**ALEXANDER LOGAN (MD, MSc, FRCPC)**, Professor, Departments of Medicine and Public Health Sciences, University of Toronto, Medical Staff, University Health Network and Mount Sinai Hospital. *Genetic epidemiology and gene identification in human hypertension; clinical trials in heart failure; clinical investigations assessing sleep apnea in refractory hypertension.*



**PHILIP MARSDEN (MD)**, Professor, Department of Medicine and Laboratory Medicine and Pathobiology, Keenan Chair in Medical Research Division of Nephrology, University of Toronto and St. Michael's Hospital. *Endothelial-derived vasomediator gene expression.*

**DON MICKLE (MSc, MD)**, Professor, Department of Laboratory Medicine and Pathobiology, University of Toronto and Director, Western Division Laboratories and Clinical Biochemistry, University Health Network. *Myocardial cell transplantation.*

**MARTIN MYERS (MD, FRCPC)**, Professor, Department of Medicine, University of Toronto and Attending Staff, Division of Cardiology, Sunnybrook & Women's College Health Sciences Centre. *Ambulatory blood pressure monitoring and other automated approaches to the measurement of BP, the IMAGINE study (compares quinapril with placebo post-coronary bypass surgery), the VALIANT study (examines the use of valsartan post-MI), the VALUE study (compares valsartan with amlodipine in hypertension) and, the ACTION study (examines nifedipine in high risk coronary patients).*

**MICHAEL OPAS (PhD)**, Professor, Departments of Anatomy and Cell Biology, Laboratory Medicine and Pathobiology, Medical Biophysics, and the Institute of Medical Science, University of Toronto. *The cytoskeleton, cell adhesion, and motility; as any of these depend on Ca homeostasis, Dr. Opas' interests extend to the cell biology of Ca-binding proteins.*

**DANIEL OSMOND (PhD)**, Emeritus Professor, Departments of Physiology and Medicine, University of Toronto. *New Pressor Protein (NPP) related to coagulation factor Beta-FXIIa (which profoundly elevates heart rate, stroke volume and cardiac output as well as systemic blood pressure).*

**JOHN PARKER, (MD, FRCPC)**, Associate Professor, Department of Medicine, University of Toronto, Service Chief, Cardiology, Director, Harrowstown Heart Failure Clinic and Director, Cardiovascular Clinical Research Laboratory, Mount Sinai Hospital. *Autonomic physiology; nitrate pharmacology; and kinetics.*

**JOSEF PENNINGER (MD)**, Associate Professor, Departments of Immunology and Medical Biophysics, University of Toronto, Associate Professor, Department of Experimental Pathology, University of Innsbruck, Austria and Staff Scientist, Amgen Institute, Ontario Cancer Institute/Princess Margaret Hospital. *Pathogenesis of heart and bone diseases and cancer using gene-targeting technology in mice.*

**MARLENE RABINOVITCH (BS, MD)**, Professor, Departments of Pediatrics and Laboratory Medicine and Pathobiology, University of Toronto, Director, Cardiovascular Research, The Hospital for Sick Children. *Pulmonary circulation in congenital heart disease; pulmonary hypertension; and molecular mechanisms regulating vascular endothelial and smooth muscle cell extracellular matrix interactions, specifically related to a novel endogenous vascular elastase and fibronectin.*

**HARRY RAKOWSKI (MD, FRCPC)**, Professor, Department of Medicine, University of Toronto, Staff Cardiologist and Director, Clinical Cardiology, University Health Network. *Hypertrophic cardiomyopathy; valvular heart disease; echocardiography.*

**JEAN ROULEAU (MD, FRCPC)**, Professor, Department of Medicine, University of Toronto and Head, Division of Cardiology, University Health Network. *Heart failure and myocardial infarction.*

**JAMES SCHOLEY (MD, FRCPC)**, Associate Professor, Department of Medicine, University of Toronto, Staff Physician and Chair of Fellowship Awards, University Health Network. *Growth factors; cell signaling; diabetes; mechanical strain.*

**MICHAEL SEFTON (BAsc, ScD)**, Professor, Department of Chemical Engineering and Applied Chemistry and Director, Institute of Biomaterials and Biomedical Engineering, University of Toronto. *Assessment of biomaterial associated thrombogenesis, angiogenesis and inflammation with a focus on platelet, leukocyte and complement activation, tissue engineering using cell encapsulation with an emphasis on control of immune/inflammatory response, the LIFE initiative (tissue engineering of hearts and cardiovascular components), and gene delivery in the vascular system using nanoparticles.*

**SAM SIU (MD, SM, FACC, FRCPC)**, Associate Professor, Department of Medicine, University of Toronto, Director of Research, University of Toronto Congenital Cardiac Centre for Adults, Director of Echocardiography, University Health Network and Mount Sinai Hospital. *Adult congenital heart disease, pregnancy and heart disease, and quantitative echocardiography.*

**MICHAEL SOLE (BSc, MD, FRCPC, FACC)**, Professor, Departments of Medicine and Physiology, University of Toronto, Staff Cardiologist, University Health Network and Mount Sinai Hospital. *Genetics of hypertrophic and dilated cardiomyopathy, conditioned nutritional requirements and pathogenesis of myocardial failure, and the role of the biological clock and circadian rhythms in myocyte renewal, myocardial growth and remodeling in the normal and diseased heart.*

**GEORGE STEINER (BA, MD, FRCPC)**, Professor, Departments of Medicine and Physiology, University of Toronto, Senior Staff Physician, University Health Network, Project Director, Diabetes Atherosclerosis Intervention Study and Head, WHO Collaborating Centre for the Study of Atherosclerosis in Diabetes. *Diabetes, lipoproteins and atherosclerosis.*

**DONNA STEWART (MD, FRCPC)**, Professor and Chair of Women's Health, University of Toronto and University Health Network. *Gender differences in cardiovascular disease and rehabilitation, women's health, psychosomatic medicine, information and decisional preferences, and health services.*

**DUNCAN J. STEWART (MD, FRCPC)**, Professor, Department of Medicine and Laboratory Medicine and Pathobiology, Director, Division of Cardiology, Associate Director, Heart and Stroke/Richard Lewar Centre of Excellence, University of Toronto and Head, Division of Cardiology, St. Michael's Hospital. *Vascular biology, in particular the cell biology of endothelium as it relates to atherosclerosis and other vascular diseases as well as translational research in the field of gene-based therapies, particularly therapeutic angiogenesis and pulmonary hypertension.*

**BRADLEY STRAUSS (MD, PhD)**, Professor, Departments of Medicine and Laboratory Medicine and Pathobiology, University of Toronto, Cardiology Staff and Director, Interventional Cardiology, St. Michael's Hospital. *Determining mechanisms of repair after arterial injury with a focus on the extracellular matrix proteins and proteolytic enzymes, discovery of new agents that can be used as stent coating to prevent restenosis after coronary stenting, identification of novel risk factors for restenosis and the development of new therapies for coronary interventions.*

**SCOTT G. THOMAS (PhD)**, Associate Professor, Department of Physical Therapy, University of Toronto Graduate Coordinator, Graduate Department of Rehabilitation Science. *Cardiovascular and musculoskeletal function and aging including factors governing the rate of physiological adaptation to regular physical exercise, interactions of exercise and other therapies on physiological function and physical capacity, and minimally invasive studies of whole body physiology with people.*

**ROBERT TSUSHIMA (PhD)**, Assistant Professor, Department of Medicine, University of Toronto. *In the heart, a number of nonselective cation (NSC) channels have been described that are activated by elevated intracellular calcium ( $[Ca^{2+}]_i$ ), increases in extracellular ATP, by stretch, or during exposure to reactive oxidative agents and lysophospholipids. Opening of NSC channels enhances  $Na^+$  and  $Ca^{2+}$  influx, depolarizes the resting membrane potential, and leads to the onset of arrhythmia and calcium overload. Understanding the properties and regulation of these channels is the primary focus of our research. Studying the properties of NSC channels will lead to a better understanding of the role these channels play in the initiation of arrhythmias, and the development and progression of heart disease.*

**JACK TU (MD, PhD, FRCPC)**, Associate Professor, Departments of Medicine, Public Health Sciences and Health Administration, Member, Institute of Medical Sciences and School of Graduate Studies, University of Toronto and Senior Scientist, Institute for Clinical and Evaluative Sciences (ICES). *The Canadian Cardiovascular Outcomes Research Team, acute myocardial infarction care, OECD study of cross-national differences in treatments, costs, and outcomes in ischemic heart disease, effectiveness of congestive heart failure guidelines in Ontario, late results of the warm heart trial, and carotid endarterectomy health services research.*

**MICHAEL WARD (PhD)**, Associate Professor, Department of Medicine and Laboratory Medicine and Pathobiology, University of Toronto and Department of Medicine, St. Michael's Hospital. *The role of oxygen tension in regulating vascular smooth muscle and endothelial cell phenotype and proliferative potential to discover the molecular basis for the alterations in structure and function of the systemic circulation in response to reductions in oxygen availability (results will advance the understanding of vascular remodeling during perinatal development and the pathophysiology of vascular dysfunction in cardiopulmonary diseases and shock and during high altitude exposure), nitric oxide, endothelin, vascular smooth muscle, contractile proteins, hypoxia, atherosclerosis and angiogenesis.*

**GARY D. WEBB (BSc, MDCM)**, Senior Staff Cardiologist, Toronto General Hospital, University Health Network, Director, University of Toronto Congenital Cardiac Centre for Adults, Toronto General Hospital. *Clinical and research aspects of adult congenital heart disease and Marfan syndrome and the teaching of clinical cardiology.*

**RICHARD WEISEL (MD)**, Chair, Division of Cardiac Surgery, University Health Network, Department of Medicine, University of Toronto. *Cell transplantation to prevent heart failure; alternative techniques of myocardial protection during heart surgery, diabetes and cardiac surgery, the role of diabetes on the cellular mechanisms of saphenous vein atherosclerosis, and the role of cell therapy for diabetic cardiomyopathy.*

**CARIN WITTNICH (CVMA, DVM, MSc, CVO)**, Professor, Department of Surgery, Director, Collaborative Program in Cardiovascular Sciences, Head, Education Program, Heart and Stroke/Richard Lewar Centre of Excellence, University of Toronto, Scientific Staff, Department of Surgery, Hospital for Sick Children. *The "high risk" heart patient population with particular emphasis on newborn children and women and development and maturation and the role of gender in the heart's ability to tolerate stress and how this influences heart disease patterns.*

**TERRENCE YAU (MD, MSc, FRCSC)**, Staff Surgeon, Division of Cardiovascular Surgery, University Health Network, Assistant Professor, Department of Surgery, University of Toronto. *Myocardial gene therapy; cell transplantation; ventricular dysfunction.*

This bibliography is intended to provide only an indication as to the breadth of research undertaken by members of the Heart and Stroke/Richard Lewar Centre of Excellence for the period of the report. Readers should bear in mind that titles are listed only once, although more than one member of the Centre may have been involved in the completed work.

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"Accuracy of computational hemodynamics in complex arterial geometrics reconstructed from MRI", Moore JA, Steinman DA, Holdsworth DW, **Ethier CR**. *Annals of Biomedical Engineering*, 27: 32-41, 1999

"Action potential and [Ca<sup>2+</sup>] changes are related to reduction in Kv4.2 and Kv4.3 currents following myocardial infarction in rat", Kaprielian R, Wickenden AD, Kassiri Z, Parker TG, **Liu P, Backx PH**. *Journal of Physiology*, 517:229-245, 1999

"Acute and chronic effects of airway obstruction on left ventricular performance", **Parker JD, Brooks D**, Kozar LF, Render-Teixeira CL, Horner RL, **Bradley TD**, Philipson EA. *American Journal of Respiratory and Critical Care Medicine*, 160: 1888-1896, 1999

"Adenosine myocardial protection: preliminary results of a phase II clinical trial", Mentzer RM, Birjiniuk V, Lowe JE, Rahko PS, **Weisel RD**, Wellons HA, Barker ML, Lasley RD. *Annals of Surgery*, 229: 643-649, 1999

"Adventitial fibroblasts: Defining a role in vessel wall remodeling", **Strauss BH, Rabinovitch M**. *American Journal Respir Cell Mol Biol*, 22:1-3, 2000

"Aerobic capacity in adults with various congenital heart diseases", Fredriksen PM, Veldtman G, Hechter S, Therrien J, Chen A, Warsi MA, Freeman M, **Liu P, Siu S**, Thaulow E, Webb G. *American Journal of Cardiology*, 87:310-4, 2001

"Agarose enhances the viability of intraperitoneally implanted microencapsulated L929 fibroblasts", Lahooti S and **Sefton MV**. *Cell Transplant*, 9: 785-796, 2000

"Alterations in action potential profile enhance excitation-contraction coupling in rat cardiac myocytes", Sah R, Ramirez RJ, Kaprielian R, Backx PH. *J Physiol*, 533: 201-214, 2001

"Altered fetal pituitary-adrenal function in the ovine fetus treated with RU486 and meloxicam, an inhibitor of prostaglandin synthase-II", McKeown KJ, Challis JRG, Small C, Adamson SL, Bocking AD, Fraser M, Rurak D, Riggs KW and Lye SJ. *Biology of Reproduction*, 63:1899-1904, 2000

"Ambulatory congenital cardiac clinics for adults: Increasing workload and evolving patterns of referral", Gatzoulis MA, Hechter S, **Siu SC, Webb GD**. *Heart*, 31: 57-61, 1999

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"Amiodarone to prevent recurrences of atrial fibrillation", Roy D, Talajic M, **Dorian P**, Connolly S, Eisenberg MJ, Green M, Kus T, Lambert J, Dubuc M, Gagné P, Nattel S, Thibault B. *New England Journal of Medicine*, 342(13): 913-920, 2000

"Angiotensin-converting enzyme inhibitors in adults after the Mustard procedure", Hechter SJ, Fredriksen PM, Liu P, Veldtman G, Merchant N, Freeman M, Therrien J, Benson L, **Siu S, Webb G**. *American Journal of Cardiology*, 87:660-3, A11, 2001

"ANP in regulation of arterial pressure and fluid-electrolyte balance: lessons from genetic mouse models", Melo LG, Steinhilber ME, Pang SC, Tse Y, **Ackermann U**. *American Journal of Physiology and Physiol Genomics*, 278: 45-48, 2000

"Aortic valve sparing operations: an update", David TE, Armstrong S, Ivanov J, **Webb GD**. *Annals of Thoracic Surgery*, 67(6): 1840:2, Discussion, 1853-6, June 1999

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"Are prostaglandin's involved in ANP mechanisms of cardiovascular control?", Bandali KS, **Ackermann U**. *Canadian Journal of Physiology and Pharmacology*, 77: 211-215, 1999

"Are we there yet? The representation of women as subjects in clinical research", **Stewart DE, Cheung AM**, Layne D, Evis M. *Annals of the Royal College of Physicians and Surgeons*, 33: 229-231, 2000

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- "Autologous porcine heart cell transplantation improved heart function after myocardial infarction", **Li R-K**, **Weisel RD**, **Mickle DAG**, Jia ZQ, Kim EJ, Sakai T, Tomita S, Schwartz L, Iwanochko M, Husain M, Cusimano R, Burns R, **Yau T**. *The Journal of Thoracic and Cardiovascular Surgery*, 119: 62-68, 2000
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- "Autologous transplantation of bone marrow cells improves damaged heart function", Tomita S, **Li R-K**, **Weisel RD**, **Mickle DAG**, Jia ZQ. *Circulation*, 100: 247-256, 1999
- "Baseline characteristics of the study population in the diabetes atherosclerosis intervention study (DAIS), Steiner J, **Sole MJ** and the DAIS Project Group. *American Journal of Cardiology*, 84: 1004-1010, 1999
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## ANNUAL FUNDING

### 1999-2000<sup>1</sup>

Competitive Funding:	
Grants Held by Individual Members	\$ 3,770,543
Group Grants held by Members	\$ 7,224,099
<i>Sub-total Competitive Funding:</i>	\$ 10,994,642
Industry Funding:	
Grants Held by Individual Members	\$ 260,000
Group Grants held by Members	\$ 45,600
<i>Sub-total Industry Funding:</i>	\$ 305,600
Centre Funds:	
Competitive Funding – Annual Grants	\$ 857,400
Draw on Trusts and Endowments	\$ 578,490
Industry Funding	\$ 25,000
<i>Sub-total Centre Funds:</i>	\$ 1,460,890
<b>GRAND TOTAL 1999-2000:</b>	<b>\$ 12,761,132</b>

### 2000-2001

Competitive Funding:	
Grants Held by Individual Members	\$ 6,875,668
Group Grants held by Members	\$21,129,596
<i>Sub-total Competitive Funding:</i>	\$ 28,005,264
Industry Funding:	
Grants Held by Individual Members	\$ 669,736
Group Grants held by Members	\$ 45,600
<i>Sub-total Industry Funding:</i>	\$ 715,336
Centre Funds:	
Competitive Funding <sup>2</sup> – Annual Grants	\$ 857,400
Draw on Trusts and Endowments	\$ 1,151,046
Industry Funding	\$ 67,000
<i>Sub-total Centre Funds:</i>	\$ 2,075,446
<b>GRAND TOTAL 2000-2001:</b>	<b>\$ 30,795,606</b>

<sup>1</sup> The amount indicated is per annum, NOT the sum total of the entire grant/award. The figures for the Centre Trusts/Endowments reflect the annual draw on funds, not the total of the grant.

<sup>2</sup> Note: In 2000-2001, Centre members were awarded several large one-time-only grants.



The education arm of the Heart and Stroke/Richard Lewar Centre of Excellence strives to further the Centre's mandate by providing ongoing continuing education activities, financial support for trainees, and other initiatives that will enrich the academic and research environment of the Centre's faculty and students.

### *Distinguished Visiting Professors Lecture Series*

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The Centre organized a Distinguished Visiting Professors Series with sponsorship acquired through Merck Frosst Canada and Co. Through this series, a forum is provided whereby external experts performing cutting edge research in priority areas will be invited to speak and interact with Centre's members and in turn, the activities of the Centre are profiled to the world's opinion leaders. Most seminars take place in room 103 FitzGerald Building on the University of Toronto campus, although the Centre does collaborate with University of Toronto departments and teaching hospital. Faculty, clinicians, students and visitors are encouraged to attend. Continuing Medical Education (CME) credits are available.

The following is a listing of seminars presented during the period of this report:

January 14, 2000

**"Vasopeptidase Inhibition - A New Target in Cardiovascular Disease"**

*Dr. John Burnett*, Professor of Medicine, Mayo Clinic

(Host: Cardiovascular Sciences Collaborative Program, University of Toronto)

February 25, 2000

**"Videoscopic and Robotic Mitral Valve Surgery at Dawn of the New Millennium"**

*Dr. Randy Chitwood*

(Host: Division of Cardiac Surgery, Dept. of Surgery, University of Toronto)

April 10, 2000

**"Diastolic Heart Failure - Cellular and Extracellular Mechanisms"**

*Dr. Michael Zile*, Professor of Medicine, Medical University of South Carolina Heart Center, Charleston, South Carolina

April 17, 2000

**"The Global Burden of Cardiovascular Disease"**

*Dr. Salim Yusuf*, Professor of Medicine, Head, Division of Cardiology, McMaster University

April 18, 2000

**"Importance of Treating Hypertension: Current and Future Treatment Options"**

*Dr. Björne Dahlöf*, Associate Professor of Medicine, Director, Clinical Trials Unit, Sahlgrenska University Hospital/Östra, Göteborg University, Sweden

May 1, 2000

**"Vascular Gene Transfer: New Biology and New Technology"**

*Dr. David A. Dichek*, Associate Investigator, Gladstone Institute of Cardiovascular Disease, Associate Professor of Medicine/Cardiology, UCSF Investigator, Cardiovascular Research Institute, UCSF (Host: Division of Cardiology, Toronto General Hospital, University Health Network)

September 18, 2000

**"Genetic Studies of Atherosclerosis in Canadian Sub-Populations"**

*Dr. Robert Hegele*, Professor of Medicine and Biochemistry, Blackburn Scientist, Robarts Research Institute, University of Western Ontario

October 16, 2000

**"Novel Approaches to the Management of Arrhythmias in Complex Congenital Heart Disease in the Adult"**

*Dr. Barbera J. Deal*, Professor of Pediatrics, Northwestern University Medical School, Director, Electrophysiology Service, Children's Memorial Hospital, Chicago, Illinois, University of Western Ontario

November 20, 2000

**"Apoptosis and its Relevance to Vascular Biology"**

*Dr. Pavel Hamet*, Professor, Departments of Medicine, Physiology and Nutrition, University of Montreal, Director of Research, Research Centre of the Centre Hospitalier de l'Université de Montréal (CHUM)

February 12, 2001

**"Genetic Engineering in the Heart by Transgenesis and DNA-virus Transfer"**

*Dr. Joseph Metzger*, PhD, Associate Professor of Physiology and Internal Medicine, The University of Michigan Medical School

March 26, 2001

**"Proteoglycans and Hyaluronan are Extracellular Matrix Molecules that Regulate Key Events in Atherosclerosis and Restenosis"**

*Dr. Thomas N. Wight*, Affiliate Professor of Pathology, University of Washington, and Chair, Vascular Biology, Hope Heart Institute, Seattle, Washington

April 23, 2001

**"Molecular Pathways Controlling Coronary Smooth Muscle Differentiation from Proepicardial Cells"**

*Dr. Mark W. Majesky*, Associate Professor, Department of Pathology, Center for Cardiovascular Development Baylor College of Medicine, Texas A&M University, Houston, Texas

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### **Annual Cardiovascular Scientific Day**

In order to bring together faculty from the Heart and Stroke/Richard Lewar Centre of Excellence and from across the University of Toronto, the Centre continued the tradition of the original Centre for Cardiovascular Research with an annual Cardiovascular Scientific Day. The goal of Scientific Day is to provide updates on the frontiers of cardiovascular sciences. Each symposium focuses on either clinical or basic science research; it is intended that discussion will promote cross-fertilization of ideas and research direction. A registration fee has not been charged, and CME credits are available.

During 1999-2001, two very successful conferences were conducted (May 18, 2000 and May 17, 2001) at the Inn on the Park Hotel. In 2000, the theme was "Genetic Inheritance: How to win when the Genes are against you!" The theme for 2001 was "Search for the Truth: Tools of New Science". Copies of these programs are available on the Centre's web site at [www.hsrice.on.ca](http://www.hsrice.on.ca).

## **Fellowship Program**

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Each year, the Heart and Stroke/Richard Lewar Centre of Excellence awards several research fellowships at the Masters and PhD levels. The purpose of these awards is to provide an infrastructure to attract top candidates into cardiovascular research at the University of Toronto; to lever funding to maximize training resources to priority research programs; and to compete with the best cardiovascular programs internationally for excellent trainees. In order to be eligible, applicants must:

- Be primarily supervised by members of the Centre;
- Intend to pursue a career in cardiovascular research;
- Complete work primarily in the area of cardiovascular sciences;
- Have first applied for other external sources of funding (e.g. OGS, HSFC, MRC, etc.).

In addition, the research traineeship competition is available for MSc/PhD trainees' only and applicants for the post-doctoral fellowship competition must have PhD degree or MD degree or equivalent, and must be primarily pursuing research training.

The first annual Fellowship application was held in 2000. A total of twenty-two applications were submitted, consisting of 18 graduate students and 4 post-doctoral applicants. A total of nine awards were distributed. In 2001, a total of forty applications were received, consisting of 28 graduate students and 12 post-doctoral applicants. The Centre funded nine OGSST graduate students (11 with full, 2 semester or 1 semester funds), three Heart and Stroke/Richard Lewar Centre of Excellence graduate students, and 3 Heart and Stroke/Richard Lewar Centre of Excellence post-doctoral applicants. In addition to this, two additional graduate students received external funding while five additional post-docs received external funds.

In the future, expanded fellowship programs will require endowment from both industry and private sector partners, as well as leverage through existing and ongoing group or program grant applications.

## **Graduate Student Supervision**

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In 2000-2001, members of the Centre supervised the dissertations or theses' of 46 Doctoral candidates and 41 Masters candidates. The topics covered a wide range of subjects, and were completed through various graduate departments including Laboratory Medicine and Pathobiology, Immunology, Kinesiology, Medical Biophysics, and Physiology, to mention a few.

## HONOURS AND AWARDS

During 1999-2001, members of the Heart and Stroke/Richard Lewar Centre of Excellence were very successful in receiving honours and awards. Several distinguished members of the Centre received important peer-reviewed recognition of their accomplishments. Drs. Marlene Rabinovitch and Peter Liu received Heart and Stroke Foundation of Ontario Chairs, Dr. Duncan Stewart was awarded a University of Toronto Chair, Dr. Philip Marsden and Dr. Donna Stewart received Hospital Chairs, and Drs. Gary Lewis, Josef Penninger and Jack Tu were awarded Canada Research Chairs. In addition, Dr. Rabinovitch was recognized with the Distinguished Scientist Award, and Dr. Douglas Bradley with the Senior Scientist Award from the Canadian Institutes of Health Research (CIHR). Dr. Lewis was also awarded the HSFO Career Investigator Award as well as the Heart & Stroke Foundation of Canada Colonel and Mrs. Sifton Distinguished Scientist Award.

Other notable accomplishments during 1999-2001 include Dr. Dina Brooks, who was awarded the Shining Star Award from the Department of Physical Therapy as well as a CIHR New Investigator Award. Dr. Benoit Bruneau received a Heart & Stroke Foundation of Canada/CIHR New Investigator Award. Dr. Mansoor Husain was awarded the CIHR Clinician Scientist Award for his work on "Molecular Regulation of Vascular Smooth Muscle Cell Proliferation". Dr. Gary Lewis received the William Goldie Research Award as well as the Canadian Diabetes Association, Great-West and London Life Young Scientist Award. Dr. Ren-Ke Li was awarded the Clemson Award for Applied Research by the Society for Biomaterials, and Dr. Thomas Lindsay received the Wightman-Berris Academy Award for individual teaching excellence. Dr. Lee Adamson won the Sir William Riley Lecture 2000, was named a Career Investigator with the Heart & Stroke Foundation of Ontario for 1995-2000, and along with Ms. Marion Snyder, received a Service Excellence Award from the Centre. The Centre also honored Dr. Daniel Osmond for his outstanding contributions to the cardiovascular sciences. Dr. Jack Tu received the Canadian Society of Internal Medicine Young Investigator Award and the Allan Bruce Robertson Young Investigator Award. Finally, Dr. Carin Wittnich was awarded the Lister Prize by the University's Department of Surgery.

Several Centre members received additional special awards. The Young Investigator award at American College of Cardiology was presented to Kyle Cowan (supervisor: Dr. Marlene Rabinovitch) and the Student Research Competition Award at the Canadian Cardiovascular Society was awarded to Anne Opavsky (supervisor: Dr. Peter Liu), Susanna Mak (supervisors: Drs. Newton and Liu) and Jeff Borger (supervisor: Dr. Richard Weisel). Further, the winner of the Research Achievement for 2000 at the Canadian Cardiovascular Society was Dr. Richard Weisel.

In 2001, Dr. Avrum Gottlieb assumed the Presidency of the American Society for Investigative Pathology (ASIP). Drs. Jagdish Butany and Avrum Gottlieb have also been appointed as co-editors-in-chief for Cardiovascular Pathology, the official journal of the Society for Cardiovascular Pathology, published by Elsevier.



*Heart & Stroke/Richard Lewar Centre of Excellence and  
Lorne Phenix Graduate Award Recipients  
2000-2001*

## OUTREACH AND COMMUNICATIONS

In order to facilitate and improve communications with the cardiovascular community, the Heart and Stroke/ Richard Lewar Centre of Excellence has launched several outreach initiatives, including a comprehensive web site at [www.hsrlice.on.ca](http://www.hsrlice.on.ca). The Centre also distributes regular e-mail updates, and published a semi-annual Newsletter. More information on all of these initiatives is available at our web site.

On the 21st of June 2001, the Centre held a Grand Opening Ceremony for the Transgenic Physiology Laboratory facility. Many friends of the Centre attended including Mr. and Mrs. Stephan Lewar and members of the Heart & Stroke Foundation of Ontario. The Centre was grateful to have an opportunity to thank Mr. and Mrs. Lewar as well as the HSFO for the support and advice provided.



Mr. Gary Kaye, HSFO, Dr. Peter Liu, Mrs. Sophie Lewar and Mr. Stephan Lewar at grand opening ceremony for the Transgenic Physiology Laboratory facility

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