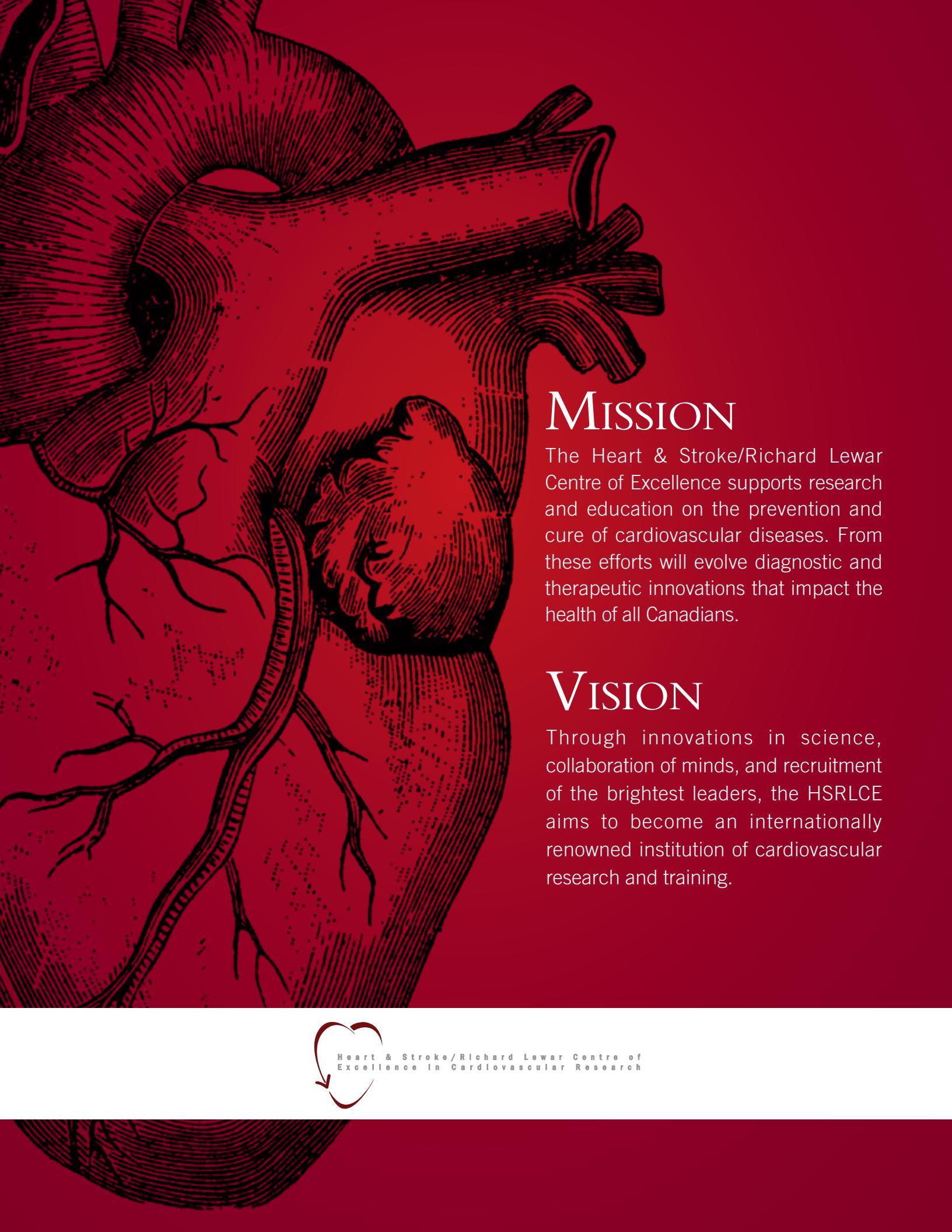




THE HEART & STROKE/RICHARD LEWAR CENTRE OF EXCELLENCE IN CARDIOVASCULAR RESEARCH

10  
YEARS  
OF EXCELLENCE  
2000-2010

A detailed black and white anatomical illustration of a human heart and its associated blood vessels. The heart is shown from a slightly elevated angle, revealing its internal chambers and the network of veins and arteries branching out from it. The style is reminiscent of a woodcut or engraved print.

## MISSION

The Heart & Stroke/Richard Lewar Centre of Excellence supports research and education on the prevention and cure of cardiovascular diseases. From these efforts will evolve diagnostic and therapeutic innovations that impact the health of all Canadians.

## VISION

Through innovations in science, collaboration of minds, and recruitment of the brightest leaders, the HSRLCE aims to become an internationally renowned institution of cardiovascular research and training.



Heart & Stroke/Richard Lewar Centre of  
Excellence in Cardiovascular Research

# Dean's Report

on the HSRLCE

**C**ardiovascular research at the University of Toronto dates back many decades within our clinical departments and our basic science departments. Our Faculty of Medicine in partnership with our affiliated hospitals and their research institutes has focused continually on discovery of the workings of the cardiovascular system and the underlying causes of disease. We have also contributed significantly to improved treatments and care of individuals with cardiovascular illness. More recently, our scientists have turned their attention to understanding the molecular basis of myocardial and vascular cell dysfunction. Progress in regenerative medicine and the use of stem cell therapy to improve cardiac function heralds a new era of miraculous intervention. We are just beginning to understand how epigenetics modifies cellular and organ function leading to hypertension, diabetes and a host of influences on the cardiovascular system. In this context, the Mission and Vision of the Heart & Stroke/Richard Lewar Centre of Excellence are even more relevant than a decade ago at its launch.

Built on the success of the Centre for Cardiovascular Research founded by Dr. Michael Sole in 1988 at the Toronto General and Mt. Sinai Hospitals, the generous funding of the Heart & Stroke Foundation of Ontario and the Richard Lewar family enabled the establishment of one of Canada's premier research centres focused on research and education in cardiovascular sciences. The founding Director Dr. Peter Liu and current Director Dr. Mansoor Husain have guided this Centre along a path of

innovation and excellence attracting top talent and facilitating collaboration among hundreds of faculty members, students, trainees and postdoctoral fellows across the Toronto Academic Health Science Network. Importantly, the initial expendable investment has attracted significant external funding and has established unique infrastructure for research, such as the Transgenic Physiology Laboratory led by a world authority on electrical remodeling in heart disease, Dr. Peter Backx.

Under Dr. Peter Liu's leadership, the initial years of the HSRLCE led to success in applying for several large-scale peer-reviewed grants from the Canadian Institutes of Health Research, including an inter-disciplinary Health Research Team Grant and administered a Strategic Training CIHR Program grant ("TACTICS"). These, and many more collaborative awards, set in motion 10 years of outstanding productivity and increased cohesion among our affiliated hospital research sites.

The HSRLCE has also contributed to recruitment of outstanding new faculty members, including Steffen-Sebastian Bolz (Physiology), Anthony Gramolini (Physiology); Scott Heximer (Physiology); Jason Fish (Laboratory Medicine & Pathobiology); and Michael Farkouh (Director of Clinical Investigations in Cardiology; Department of Medicine).

Recruitment and retention of excellent faculty is the life-blood of our academic enterprise. The Centre's investment in partnership with our university departments has been determinant in ensuring cardiovascular research at the University of Toronto remains at the leading edge.

The education mission of the HSRLCE has been closely aligned with the award-winning Collaborative Graduate Program in Cardiovascular Sciences directed by Professor Carin Wittnich. This is one of the largest and most successful inter-disciplinary graduate programs at the University. The doctoral students from this program represent a generation of leading scientists and clinical investigators now engaged in cardiovascular research locally, nationally and globally.

The HSRLCE has led the way in our Faculty demonstrating *integration* (among disciplines and institutions), *innovation* and *impact*. Congratulations to all who have contributed to the leadership and success of this Centre emerging after a decade of remarkable accomplishment as a major force in cardiovascular research.

**Catharine Whiteside, MD, PhD**  
**Dean of Medicine**





# the Founding History of the HSRLCE

A DECADE OF EXCELLENCE

**T**he University of Toronto and its teaching hospitals have a legacy of achievement in the cardiovascular sciences dating back over 60 years. Murray, Bigelow, Mustard in Cardiovascular Surgery, Keith and Wigle in Cardiology, Best and later MacLennan in Physiology were names known around the world. Although Cardiovascular Surgery and Cardiology at the Hospital for Sick Children and the Toronto General Hospital and Physiology at the University of Toronto were well recognized internationally, there was remarkably little communication between these units and the general University community of biological scientists. The rapid development of cardiovascular biology, particularly molecular cardiology and new research funding opportunities in the 1970s and '80s made such communication and reorganization imperative.

In 1985, I convened a group of clinical and basic cardiovascular investigators; leaders in Cardiology, Cardiovascular Surgery, Physiology, Pathology and the Institute of Medical Sciences. We developed an organized vision of a University-wide centre of excellence. In 1989, I made a formal presentation to the University of Toronto Research Committee; with their unanimous support and that of the Toronto General Hospital and Mount Sinai Hospital, the Centre for Cardiovascular Research (CCR), a joint venture between the then Toronto Hospital, Mount Sinai Hospital and the Faculty of Medicine was established. I became the Founding Director.

The research activities of the CCR were encouraged to be interdisciplinary and covered the spectrum from fundamental molecular studies of atherosclerosis and heart muscle growth and the electrophysiology of sudden death to the development of new surgical technologies and the evaluation of new therapies by clinical trials. Fifty-six senior scientists formed the core of the CCR and were represented through a Scientific Committee. The base CCR endowment was established through the Generation Campaign of

The Toronto Hospital, the donation of a Cardiovascular Clinical Research Catheterization Laboratory at Mount Sinai Hospital. In 1989 the CCR along with Dr. Carin Witnich and the Collaborative Program in Cardiovascular Sciences initiated the Annual University of Toronto Cardiovascular Research Scientific Day. The CCR, through its Scientific Committee, established the Distinguished Visiting Speakers Program, Annual CCR Fellowships and Studentships, a Major Equipment Fund, a Pilot Project Fund and a Fund to assist the competitive recruiting of brilliant cardiovascular research faculty. Some of these new research faculty included: Dr. Peter Backx from Johns Hopkins (molecular biology of ion channels), Dr. Mansoor Husain from MIT (vascular molecular biology), Dr. John Parker from Harvard University (to direct a human physiology Research Catheterization Laboratory), Dr. Thomas Parker from Baylor University (cardiac molecular biology), Dr. Heather Ross from Stanford University (heart transplantation), Dr. Mark Iwanochko from University of Toronto (nuclear imaging), Dr. Sam Siu from Harvard University (echocardiography, cardiovascular disease and pregnancy) and Dr. Rob Tsushima from University of Toronto (molecular physiology).

In 1999, while I served as Chief of Cardiology and Director of the CCR, Dr. Harry Rakowski, University Health Network Director of Clinical Cardiology, presented me the possibility of a donation of \$6 million from the parents of the late Richard Lewar. I proposed that we try for a match and that the money be used to establish a national cardiovascular research Centre of Excellence at the University of Toronto and its Hospitals – the culmination of that original vision in 1985. Heart & Stroke Foundation of Ontario (HSFO) would not fund a Hospital Institute but had long sought to expand the success of the CCR at a University-wide level. This new proposal was unanimously supported by the Research Committee (of which I was a member), HSFO President, Richard Gallop and the Board. The

HSFO donated \$5 million to the new Centre plus a \$2 million endowed chair for the Director. With the enthusiastic support of the Dean of Medicine, Arnie Aberman, and the University President, Rob Pritchard, the fund of \$13 million established the Heart & Stroke/Richard Lewar Centre of Excellence (HSRLCE) at the University of Toronto.

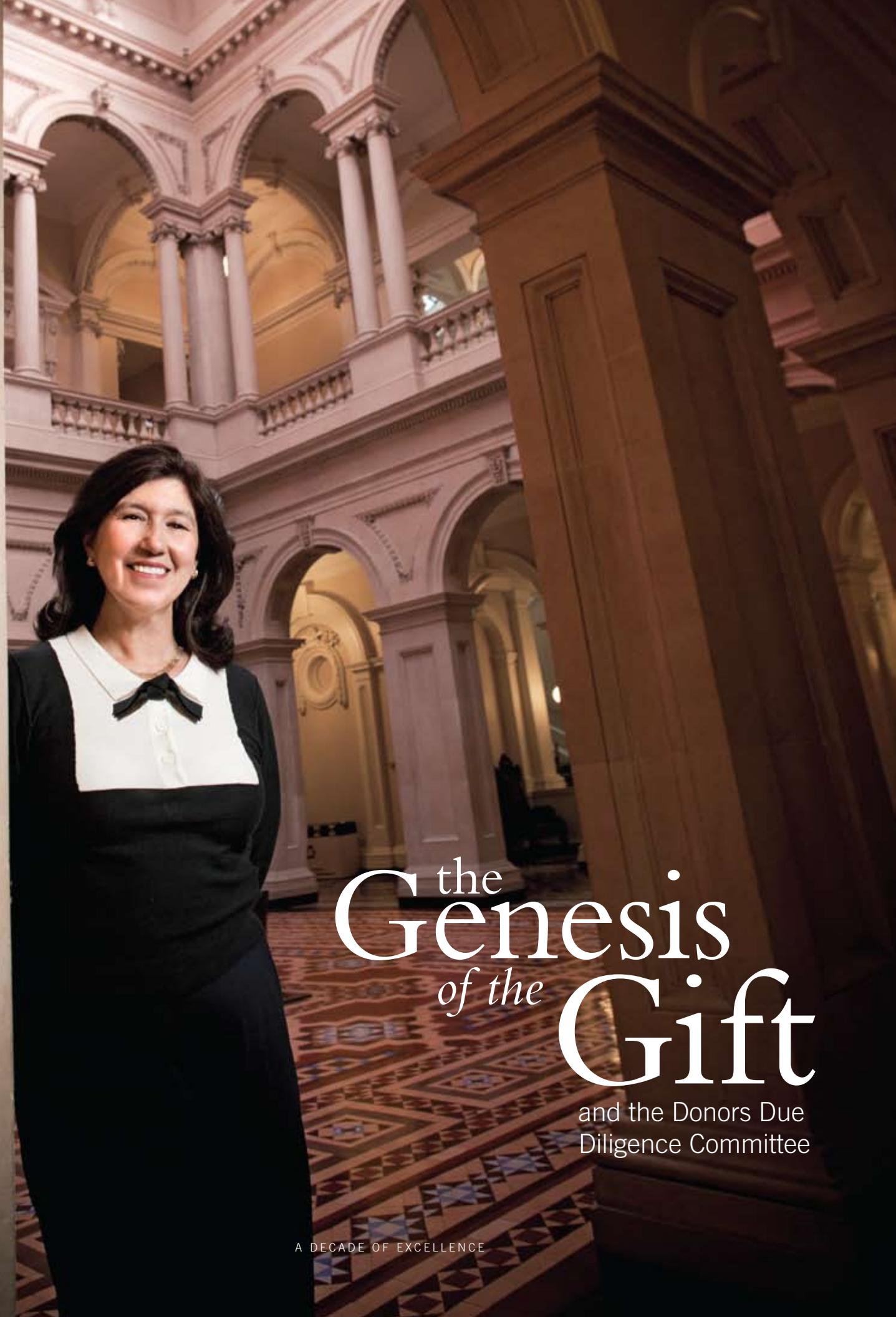
The HSRLCE had a mandate to become an internationally renowned centre for cardiovascular research and a national resource for cardiovascular discovery. Its Founding Document states: "As an organized interdisciplinary Cardiovascular Centre of Excellence in research and training, it will provide a much-needed focus for cardiovascular research in Toronto, attracting visiting scientists, fellows, graduate and post-doctoral students with ability, energy and imagination from around the world. The Centre's common core of support facilities will rationalize resources and provide economies of scale. The Centre will attract and retain some of the brightest investigators in the cardiovascular sciences by creating an exciting, collaborative, supportive environment with new cardiovascular research opportunities."

I was Founding and served as Acting Director of this new Centre until a new Director was chosen (my obvious conflicts of interest made any other appointment impossible).

Dr. Peter Liu became the first Director of the HSRLCE. Under his guidance, space in the Fitzgerald Building at the University was renovated and three specific platforms for research were formed: (1) a Transgenic Physiology Laboratory (under Dr. Peter Backx); (2) a University-wide gene therapy and vector generation facility (under Dr. Duncan Stewart) and (3) a micro-array (gene-chip) facility (under Dr. Peter Liu) to evaluate global patterns of gene expression in heart disease.

A solid interdisciplinary foundation for cardiovascular research at the University and its teaching hospitals was in place at last.

**Michael Sole, MD**



# the Genesis *of the* Gift

and the Donors Due  
Diligence Committee

**W**hen Stephan and Sophie Lewar's son, Richard, passed away in 1998, they decided to donate their son's inheritance to charitable causes. Mr. Lewar turned for advice to my father, Gilbert Newman. Mr. Lewar had been his client when Mr. Newman, by then retired, was in private practice as a chartered accountant.

Mr. Lewar's wish was to make significant donations to medical research. My father first suggested consulting Dr. Harry Rakowski, his highly respected cardiologist at the Toronto General Hospital (UHN), who is now the E.D. Wigle Chair in Hypertrophic Cardiomyopathy Research. Dr. Rakowski recommended involving Dr. Michael Sole, who was already directing research in conjunction with the

new research facility named for both donors, the Lewar family and the Heart & Stroke Foundation.

The agreement creating the Centre provided for an Advisory Committee — now called the Donors Due Diligence Committee — whose role is to meet periodically to review the operations of the Centre in order to ensure that the objects and goals of the original donors continue to be implemented.

The original agreement provides:

The Advisory Committee shall meet on a regular basis with the Director and receive reports on the progress of the Centre. The Advisory Committee will have the right to inform the President of the University if, in its view, the Centre is not operating as expected and request that an external review be conducted.

## He stipulated that his donation was to be used for research that would produce tangible benefits for people suffering from disease

Heart & Stroke Foundation.

Mr. Lewar did not want his money going into "bricks and mortar." He stipulated that his donation was to be used for research that would produce tangible benefits for people suffering from disease, in this case, heart disease. While he gave generously to other very worthwhile causes, his largest gift of \$6 million went to establish the Heart & Stroke/Richard Lewar Centre of Excellence in Cardiovascular Research.

Such an endeavour required legal as well as financial advice, and so my father brought in his long-time colleague, David Ward, founding partner of the law firm of Davies Ward and Beck (now Davies Ward Phillips & Vineberg LLP). Together they negotiated an agreement among the Lewars, the Heart & Stroke Foundation, which provided matching funds, and the University of Toronto Faculty of Medicine, to create the

Both Gilbert Newman and David Ward were made original members of the Donors Due Diligence Committee to represent the interests of the Lewar family.

My father continued to attend the meetings of the Committee until his death in September 2004. He also assisted Mr. Lewar in the process of making several other significant donations for medical research to a number of physicians and hospitals in Toronto. In 2000, my parents attended with Stephan and Sophie Lewar when Stephan received the Order of Ontario for his "unparalleled philanthropy."

After my father died, David Ward suggested that I be invited to continue in his place on the Donors Due Diligence Committee representing the interests of the Lewar family, and I was delighted to do so.

When I joined the Committee in

2004, Dr. Peter Liu was the Director of the Centre. Dr. Liu is a brilliant and talented scientist, and a dynamic leader, who seemed irreplaceable in 2006 when he accepted a prestigious appointment as Scientific Director of the CIHR Institute of Circulatory and Respiratory Health, and had to resign as Director of the Centre.

I was privileged to be a member of the search committee for a new Director in 2007. A number of well-qualified candidates presented their visions for the Centre. Among them was Dr. Mansoor Husain, an exceptional physician and inspired scientist, who had already demonstrated his organizational and leadership skills as the acting Director of the Centre from September 2006. He persuasively outlined his vision for the Centre as a collaborative research partnership involving the University of Toronto and UHN, as well as potentially other Toronto teaching hospitals, with a new focus on translational research, which aims to use the results of scientific research to directly improve patient care.

Having been appointed as the new Director in 2007, Dr. Husain has worked to make his vision a reality with a new collaborative structure, involving both the University and the Toronto teaching hospitals, which will invigorate the Centre and its mission going forward.

After David Ward passed away in 2009, Ms. Laura Syron, Vice-President, Research of the Heart & Stroke Foundation, and I are the continuing outside members of the oversight committee representing the original donors. It has been an honour to serve with her and to watch the Centre thrive and grow. I am confident that the Centre will continue to make a substantial and important contribution to our society by performing the kind of innovative medical research that was imagined and hoped for by the original donors and their advisers.

**Justice Kathryn Feldman  
Court of Appeal for Ontario**



# a new Scientific Partnership

for a common mission

When the Heart & Stroke Foundation of Ontario partnered with the Lewar family and the University of Toronto in 1998 to create a world-class research centre focused on heart disease, it marked a milestone in the way science was undertaken in this province.

For decades, Ontario had singled itself out as a place where many of the world's

top cardiovascular researchers could be found in areas as diverse as heart surgery, congenital heart disease and atherosclerosis. But often, these researchers worked alone or with their individual institutional colleagues and teams.

**...it marked a milestone in the way science was undertaken in this province.**

More than 10 years have passed since the Centre was first established and its focus and direction are more critical than ever. The gains that have been made in reducing deaths from heart disease over the past 50 years are now at risk. The “perfect storm” of heart disease is looming – baby boomers are turning 65 and entering their “at risk” years, many

of Ontario’s culturally diverse communities suffer from heart disease earlier and more intensely than their Caucasian counterparts, and childhood obesity is at epidemic proportions resulting in diagnosis of heart disease risk factors for these children in their teen years. As this storm moves towards us, the Centre will play a crucial role in identifying, exploring and bringing to practice new methods of treating cardiovascular risk factors and the disease itself. Many of the Centre’s scientists are also front-line physicians, providing care to those who are at risk of and who suffer from heart disease.

The Heart & Stroke Foundation of Ontario congratulates the HSRLCE as it celebrates this important milestone. The Foundation is proud to have played a seminal role in its establishment and looks forward to its continued scientific success.

**Laura Syron**  
**Vice-President Research,**  
**Advocacy & Health Promotion**  
**Heart & Stroke Foundation of Ontario**

# Reflections over the last decade

of the HSRLCE

A decade has gone by so quickly, that it seemed just like yesterday that we were planning for the inception of the Heart & Stroke/Richard Lewar Centre of Excellence (HSRLCE). The HSRLCE was born at the critical juncture at the end of the 20<sup>th</sup> century. At that time, the first draft of the human genome map was just about to be completed, the transformation of the Medical Research Council into the Canadian Institutes of Health Research (CIHR) had begun, cardiovascular research at the University of Toronto was undergoing a renaissance but was fragmented, and the Heart & Stroke Foundation of Ontario (HSFO) and Mr. Stefan Lewar came together to make the HSRLCE possible. We were indebted to Dr. Michael Sole, Dr. Harry Rakowski, Mr. Rick Gallop (HSFO), and Dean Aberman for creating the conditions for the creation of the Centre.

As the inaugural Director of the Centre, I had the privilege of taking the Centre's vision into reality. Working together with the tireless friends and colleagues at our University and various institutions, the Centre took

shape, increased its membership and fostered collaborations that underscored the fundamental strengths of our cardiovascular community. We created a state-of-the-art Transgenic Physiology Laboratory, created translational linkages and hubs, fostered research clusters, set up the research fellowship and studentship programs, and hosted distinguished speakers from different parts of the world.

With the ingenuity and dedication of our members, the Centre attracted new talents from North America and Europe, who continue to flourish as stars in our community. The existing talents also leveraged the Centre's resources to garner major national and international research grants and awards, to a tune of over \$22 million in the first 5 years. The collaborative publications increased steadily, with many in the highest impact journals in the field of science. The young talents who will be future leaders in the cardiovascular community came to Toronto, and benefited from our TACTICS CIHR Strategic Training Programs, and the excellent research environment the Centre provides.

Over the last five years, the Centre has continued on its trajectory and momentum under Mansoor Husain's leadership. I had the privilege of observing this nationally and appreciated the strength and depth of the talents at the HSRLCE from the point of view of a Scientific Director at CIHR. Toronto will continue to grow based on the rich opportunities with translation tools to achieve clinical impact.

Now, with the perspective of the World Heart Federation, where I am serving to achieve its goals to quell cardiovascular and stroke suffering worldwide, I come to appreciate further the excellence of the work and global impact achieved by our Toronto research teams in broad domains across cardiovascular research. We are truly reaching the original goal of excellence that we have envisioned and strived for in the original creation of the Centre. I look back with pride at what we have accomplished, and I look forward to the exciting developments in the next decade.

**Peter Liu, MD**





Innovations in cardiovascular  
**Research &  
Education**  
at the University of Toronto and beyond

**I**n this special commemorative issue of our biennial reports, the Centre's administrative staff and I thought that some reflections on the recent academic trajectory of cardiovascular sciences at the University of Toronto would be of interest. To this end, I am grateful to several key members of our community for taking the time to share their thoughts on this topic as the Centre enters its second decade of service to our founding Mission and Vision.

My thanks go out to Justice Kathryn Feldman and Ms. Laura Syron, who have most ably represented the Lewar family and the Heart & Stroke Foundation of Ontario respectively on our Donors Committee. I also appreciate the reflections of Drs. Michael Sole and Peter Liu. Dr. Sole founded the Centre for Cardiovascular Research in 1988 and, along with Dr. Harry Rakowski, paved the way for the HSRLCE's conception in 1999. As the HSRLCE's first Director (1999–2006), Dr. Liu established the standards of scientific excellence and collaborative research we continue to follow today. Finally, I am indebted to Dean Catharine Whiteside for her continued support of cardiovascular research and education at the University of Toronto and its affiliated hospital research institutes in the Toronto Academic Health Sciences Network (TAHSN). I hope you will enjoy the perspectives that each of these leaders has shared with us in this report.

For me, the 5 years that I have been privileged to serve as Director of the HSRLCE have been full of promise and pride. Building on the achievements of Dr. Peter Liu, I have worked closely with an expanded and highly dedicated Steering Committee that now represents every constituency of the cardiovascular sciences community at TAHSN, to broaden the impact of the Centre, and to continue to facilitate the research priorities we developed at a strategic planning retreat in 2007.

Notable examples of our investments

include the Centre's support of a Large Animal Clinic at the Sunnybrook Health Sciences Centre, and a Microvascular Research Centre at St. Michael's Hospital. I am grateful to the leadership shown by Dr. Bradley Strauss at Sunnybrook, and Dr. Steffen-Sebastian Bolz in Physiology for creating the collaborative environments in which these two strategic priorities could be realized.

I am particularly excited by our plans at the Toronto General Hospital, where, in collaboration with Pathology and the Peter Munk Cardiac Centre, the HSRLCE will support the creation of a Cardiovascular Biobank and a Molecular Diagnostics Laboratory. Building on previous investments in genomics and proteomics, and the aforementioned resources for large animal and small vessel work, I believe the success of these initiatives will transform our capacity for translational research in cardiac and vascular diseases in Ontario. Similarly, under the leadership of Dr. Chris Calderone at the Hospital for Sick Children, the HSRLCE plans to support a University-wide Clinical Database in Cardiovascular Surgery that will be sure to enhance our internationally-recognized achievements in this discipline.

As we celebrate the accomplishments of our trainees and faculty on our Annual Cardiovascular Science Day, I wish to draw particular attention to the role played by our Centre in providing trainee stipends, hosting continuing education events and enabling recruitment of our outstanding faculty.

With generous donations from sanofi aventis Canada and the Dr. Albert and Doris Fields Memorial Fund, we have now secured graduate student funding for many years to come. With the ongoing support of industry partners, most notably Merck Canada (since our inception) and more recently Servier Canada, the Centre has continued to host several Distinguished Visiting Professors annually from leading

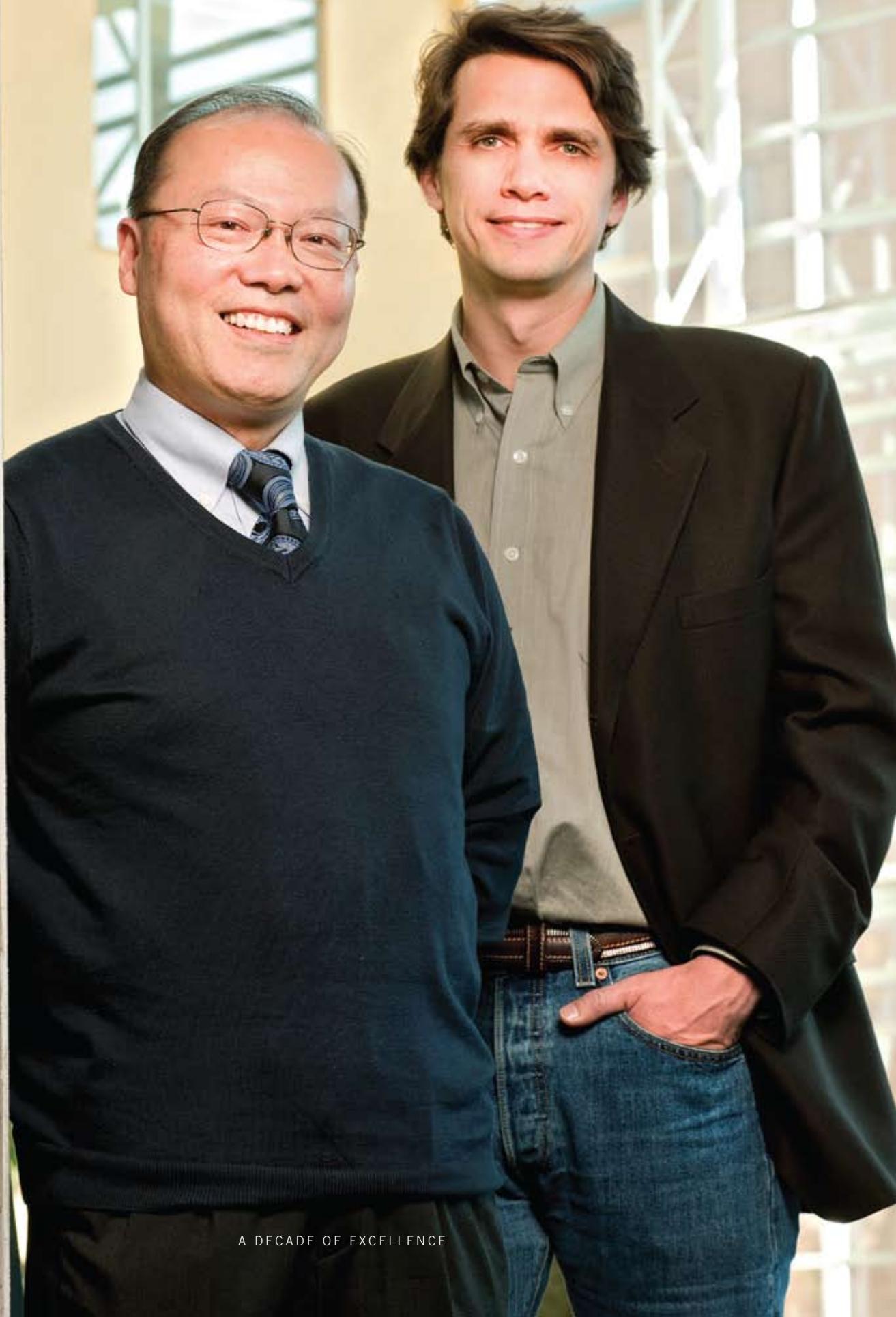
research Universities around the world. Through a generous donation of Dr. Marvin and Mrs. Roma Auerback, the Centre was delighted to establish a Professorship in Developmental Biology and Congenital Heart Research in 2005, whose inaugural recipient was Dr. Seema Mital of the Hospital for Sick Children.

Finally, the success of any extra-departmental unit such as the HSRLCE depends on the enthusiasm with which the faculty from participating Departments reach out and work together in multidisciplinary approaches to cardiovascular research and education. To this end, I want to acknowledge Professors Stephen Matthews, Richard Hegele and Wendy Levinson for their inspired leadership of the Departments of Physiology, Laboratory Medicine & Pathobiology, and Medicine, respectively, with whom the Centre has partnered to recruit 5 new faculty to our cardiovascular science community.

In closing, the Centre could not begin to keep its many faculty members informed and aware of its activities, or support the many more trainees that benefit from our awards and educational events, without the tremendous dedication of its administrative staff. I am privileged to work with Ms. Tracey Richards (Business Manager) and Ms. Sandra Monkewich (Education & Research Officer), to whom I owe considerable thanks for their unwavering support of the Centre's activities.

As I look back on the history of the HSRLCE, I cannot help but feel that our best days lie ahead. I believe that we are poised on the verge of transformative revolutions in genomic and regenerative medicine that will undoubtedly impact cardiovascular medicine. As the Centre sets out on its next decade of activities, I encourage you all to strive for the unimaginable.

**Mansoor Husain, MD  
Director, Heart & Stroke/Richard Lewar Centre of Excellence**



(left to right)  
Peter Liu and  
Anthony Gramolini



# Canadian Heart Failure Network

## an integrated Canadian strategy in heart failure

The number of new cases of heart failure continues to increase every year. Once diagnosed this disease is usually progressive and often fatal with patients placing an increasing burden on our health care system.

To fulfill an urgent need for early detection of heart failure and the need for novel treatments to improve the lives of those with heart failure, the Canadian Heart Failure Network, coordinated by the HSRLCE, was formed. With \$2.5 million in funding from the Canadian Institutes of Health Research (CIHR) and the Heart & Stroke Foundation of Canada (HSFC), this interdisciplinary group

sought new and better ways of predicting, preventing and treating heart failure and thus formed a research network on gene-environment interactions in heart failure: molecules to populations; peptides to patients.

Bringing together scientists from universities across the country (University of British Columbia, University of Alberta, University of Manitoba, University of Western Ontario, McMaster University, University of Toronto, Queen's University and the University of Montreal) the CHFNET team made several breakthroughs in our understanding of basic mechanisms and potential novel therapies for heart failure.

## A Genome Canada Project

### protein expression profiling platform for heart disease biomarker discovery

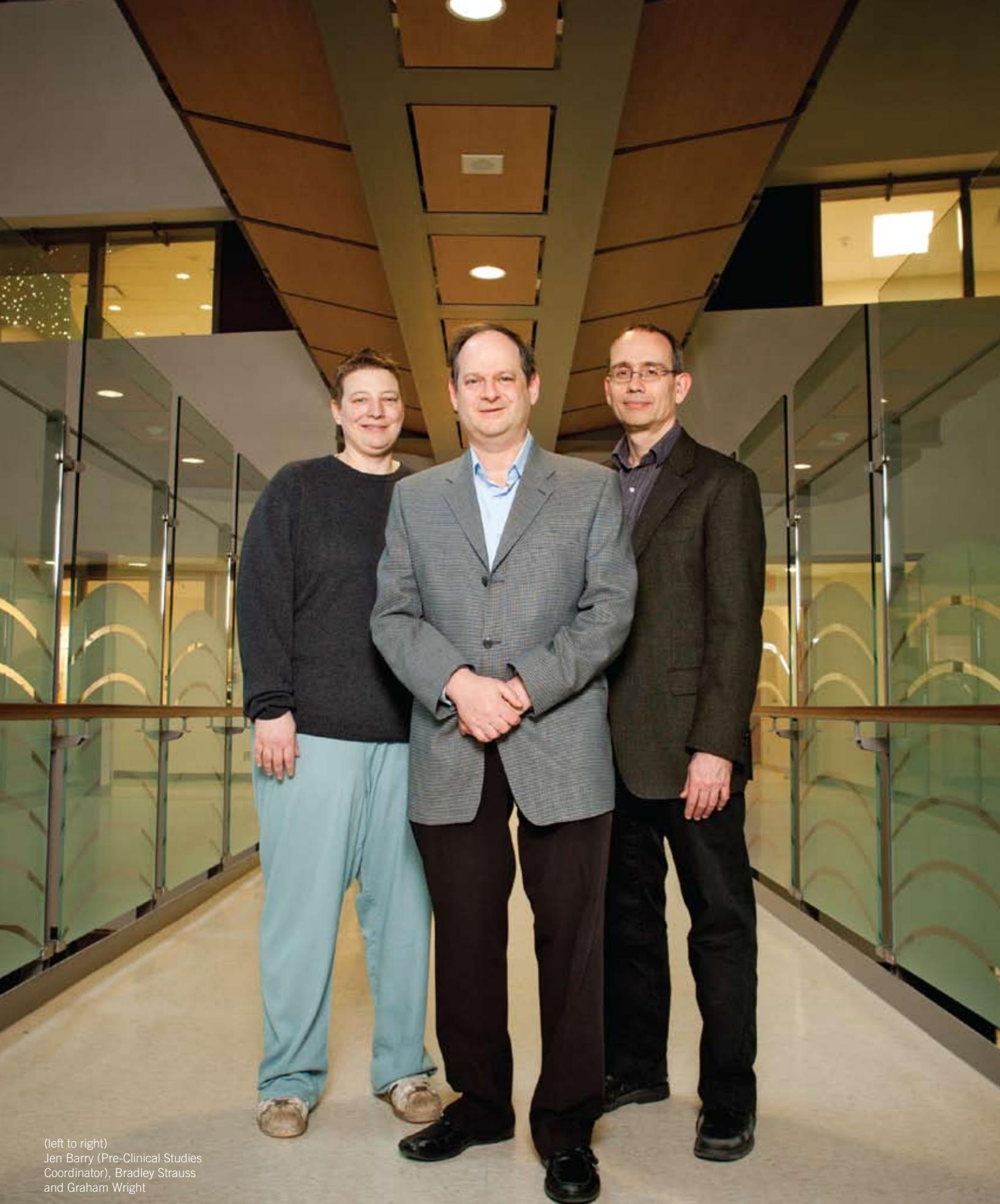
In 2003, a team from our Centre made up of Drs. Peter Liu, Andrew Emili, Anthony Gramolini and David MacLennan submitted an application for the Genome Canada “Applied Genomics and Proteomics Research in Human Health” Competition. As announced in April 2004, this proposal was funded at the level of \$6.1 million over a period of three years. The partner in this innovative and exciting project, Roche Diagnostics GmbH, is the world’s leader in developing new diagnostic assays for biomarkers. The project involved investigating the effects of heart failure disease progression on the cardiac tissue proteome using two complementary techniques to identify novel biomarkers of heart failure.

Heart failure patients are typically diagnosed with end stage disease when few effective avenues for restorative intervention remain and clinical outcomes are poor. Therefore, innovative preventive and therapeutic measures are needed for more effective early detection and treatment of at-risk patients. Heart cell proteins, biomarkers, are incredibly useful for making early diagnoses. Using proteomics and microarray data the project aimed to identify candidate biomarkers and then define a subset of proteins that are detectable at elevated levels in early stage disease and whose levels reflect the extent of disease progression. The availability of human cardiac tissue and a mouse model of heart failure made it possible for the team to identify the presence of 40 mouse ventricular proteins in a proteomics screen

of the analogous corresponding human disease. Furthermore, the collaboration led to the development of broadly applicable algorithms for prioritizing lists of proteomics datasets, and a comprehensive description of the heart proteome.

In 2010, Drs. Peter Liu, Andrew Emili and Anthony Gramolini submitted a follow-up grant application entitled “Cardiovascular Biomarker Discovery in Disease and Development through Predictive Precision Proteomics” to the Ontario Research Global Leadership Round In Genomics And Life Sciences Competition, along with other Centre members Drs. Gordon Keller, Thomas Kislinger, Seema Mital, John Coles, Peter Zandstra and Milica Radisic, to utilize human stem cells as an additional source of biomarkers for cardiac disease. This proposal was funded at the level of \$6.6 million over a period of five years.

Since the levels of heart failure in North America have increased steadily over the last two decades, approaching an epidemic level, the discovery of these new biomarkers will have a huge impact on this usually fatal condition. Ultimately, these biomarkers could lead to the development of clinical assays suitable for routine diagnosis of early stage disease and long-term prognostic monitoring. With this type of information, patients would be able to select healthy treatments or lifestyle modifications long before any symptoms have developed, and potentially prevent a disease.



(left to right)  
Jen Barry (Pre-Clinical Studies  
Coordinator), Bradley Strauss  
and Graham Wright

# Sunnybrook

## large animal clinic

**E**stablished in 2009, a major focus of the cardiovascular research efforts at Sunnybrook Health Sciences Centre is the integration of large animal models of cardiovascular disease with novel imaging modalities such as x-ray, MRI, ultrasound, optical coherence tomography and CT scanning (including micro-CT). The research at the clinic includes various forms of vascular disease (chronic total occlusions (CTOs) and atherosclerosis) and myocardial damage. Vascular disease models available include: bilateral peripheral and coronary CTO and aortic atherosclerotic plaques. Currently, the CTO models display intraluminal fibrosis and the development of microchannels. Efforts are under way to extend the model to include calcifications. For studies on myocardial damage, there is a model for re-perfused cardiac infarct.

To further this unique resource, the HSRLCE supports a Pre-Clinical Studies Coordinator. The Coordinator and the rest of the team at the clinic are very involved in knowledge translation and collaborative opportunities with cardiovascular groups at other sites in Toronto. To facilitate this, the team functions in several capacities: 1. they are available to present lectures at other centres giving an overview of the models currently being used. Furthermore, they also provide hands-on surgical assistance and expertise in order to help establish models at other sites; 2. to provide guidance for groups wishing to collaborate with Sunnybrook researchers working with established models to evaluate therapies and/or create new ones at Sunnybrook; and 3. to provide training workshops to demonstrate the various techniques and modalities that we have established. In addition, they will host planning workshops to consider the establishment of new models such as a porcine model of heart failure.



# Microvascular research centre

The Toronto Microvascular Research Centre (TMVRC) is a joint venture between the University of Toronto's Departments of Physiology and Anesthesia and St. Michael's Hospital in conjunction with the HSRLCE. The TMVRC initiative aims to advance our knowledge of microvascular function by translating existing concepts and techniques from animal models directly to human tissues and then to clinical treatment.

Hypertension is a major risk factor for many cardiovascular diseases such as heart disease and stroke. The emerging consensus identifies resistance arteries as the primary contributors to hypertension. Changes to the structure and function of these small blood vessels are important pathogenic factors that promote and sustain cardiovascular diseases. Current methods used to understand the molecular signalling that underlies these changes are technically difficult and time consuming. Dr. Steffen-Sebastian Bolz has developed a new organ-based device employing polymer chip-based technology that innovates holding and fixing an artery and eliminates traditional technical challenges. The ability to precisely manipulate an artery's spatiotemporal environment on the microfluidic platform will allow us to address fundamentally new biological questions. The goal is to correlate changes in microvascular function with a specific disease process in patients promoting patient-oriented diagnostics and therapeutics. The implementation of this novel method will promote rapid expansion of the scope of the TMVRC and increase its experimental efficiency.

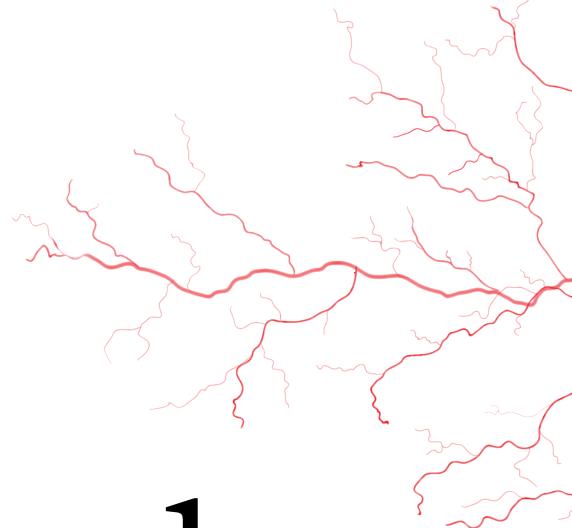
Ultimately, the inherent translational and therapeutic promise of this initiative is to add a novel and innovative diagnostic and therapeutic perspective to the management of cardiovascular diseases that will complement the existing approaches focusing on heart and large artery diseases. Together, Dr. Bolz's technology and development of the TMVRC will enable us to routinely study human microvessels as a first step towards an integrated personalized medicine approach in cardiovascular medicine.



(left to right)  
Steffen-Sebastian Bolz,  
David Mazer, Greg Hare,  
and Julia Voitlander Bolz



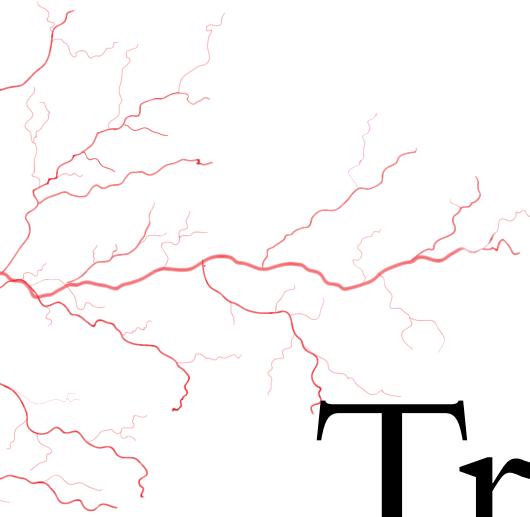
(left to right)  
Avrum Gotlieb, Myron Cybulsky,  
Jagdish Butany and Jason Fish,  
Cardiovascular Pathology,  
Toronto General Hospital



# Cardiovascular biobank

Plans are underway for a HSRLCE-supported cardiovascular biobank at the Toronto General Hospital (TGH). Identified as a strategic priority in 2007, the HSRLCE has worked with key members of the Department of Pathology at TGH to envision and implement the long-term storage of samples of human blood, heart muscle, heart valve, arteries and veins for research purposes. By linking these invaluable blood and tissue specimens to carefully standardized clinical data, we will create a clinicopathological repository or biobank of a variety of human cardiovascular diseases. For example, we hope to store specimens from patients with arrhythmias, coronary artery disease, aortic aneurysms, congenital heart diseases, hypertrophic cardiomyopathy, heart failure, and others. Our goal is to harness and expand on biobanking infrastructures, protocols, and procedures already in place at TGH with the goal of facilitating our member's access to both normal and diseased human cardiovascular tissues through approved project-specific research protocols.

A coordinator will be dedicated to the cardiovascular biobank to facilitate all operations, including specimen handling, review of requests, preparation and submission of specific applications to the research ethics board, and to oversee retrieval of specimens for member access. The cardiovascular biobank will be governed and operate under principles and ethics protocols already in place at TGH.



# Transgenic physiology laboratory

**A**t the inception of the HSRLCE, Director Dr. Peter Liu, with Dr. Janet Rossant, submitted an application to the Canada Foundation for Innovation for infrastructure funds to renovate and equip the space that would later become the Centre's Transgenic Physiology Laboratory. It began operations during the fall of 2001, led by Director Dr. Peter Backx. The mandate of the Transgenic Physiology Laboratory is to enhance basic research in the cardiovascular sciences within the University of Toronto community by providing the environment, expertise and resources for evaluation of cardiovascular function in experimental models, with an emphasis on models of altered cardiovascular function: LAD ligation, carotid injury, and aortic banding. The Transgenic Physiology Laboratory continues to bring together researchers from across the University in a collaborative, group-oriented environment and has facilitated the development of major programs in regenerative medicine, heart failure and disease biomarker identification.

The HSRLCE supports a Research Associate position in the Laboratory to provide the generation of animal models of heart and vascular disease using mice and other small mammals (surgical procedures include coronary artery ligation, pulmonary artery banding, aortic banding and vascular injury); and cardiovascular assessments using tail-cuff recordings, pressure and pressure-volume Millar catheters, echocardiography, programmed electrical stimulation, telemetry and electrocardiograms (ECGs). The lab's imaging stations include a confocal microscope, a high accuracy VEVO- 770TM imaging system (Visual Sonic), and the capacity to measure single-cell contractility on isolated myocytes.

The Backx laboratory also focuses on electrical remodeling in heart disease – especially the relationship between changes in potassium currents with changes in mechanical function and arrhythmias in heart failure, the relationship of the molecular structure and the physiological role of cardiac ion channels to heart function in normal and diseased myocardium. The ultimate goal of these studies is to develop therapeutic agents to treat cardiovascular disease by targeting ion channels.

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(left to right)  
Sanja Beca  
(Research Associate)  
and Peter Backx



(left to right)  
Sandra Monkewich  
(Research Officer)  
and Kim Connely  
(TACTICS Alumni)

# Research & Education

**S**ince its inception, the Heart & Stroke/Richard Lewar Centre has aimed to improve communication and collaboration within the local cardiovascular community to maximize our research capacity and impact.

The HSRLCE hosts a number of educational events to facilitate collaborative research across institutions and disciplines to bring together faculty from the HSRLCE and across the University of Toronto, including an annual Cardiovascular Scientific Day held each year in April. The goal is to provide updates on the frontiers of cardiovascular sciences. Symposium topics are drawn from all research themes, from basic biomedical to clinical to outcomes; it is hoped that discussion will promote cross-fertilization of ideas and research direction.

In addition, the Centre runs a Speaker Series of Distinguished Visiting Professors to provide a forum whereby external experts performing cutting edge research in priority areas are invited to speak and interact with the Centre's members and trainees. In turn, the activities of the Centre are profiled to the world's opinion leaders. The Centre works with various University of Toronto Departments and teaching hospitals in selecting speakers for the series. Since our establishment, the Centre has hosted 64 renowned researchers of whom 47 have been international invitees.

The Centre prioritizes the importance of training the next generation of research leaders. The Tailored Advanced Collaborative Training in Cardiovascular Science (TACTICS) Strategic Training Initiative in Health Research (STIHR) was launched in 2002 and administered through the HSRLCE. Funded through a partnership between the Canadian Institutes of Health Research (CIHR) and the Heart & Stroke Foundation of Ontario, this elite training program was designed to prepare trainees for running their own laboratories. The goal of the program was to foster tomorrow's leaders of cardiovascular research in Canada and globally, and to ensure their successful transition to independent investigators. We focused our efforts on post-doctoral training in two streams: Clinician-Scientists and PhD Scientists, to create a formalized training program of excellence during this critical stage of training. The program provided the breadth and depth of knowledge in cardiovascular research, while providing a creative flexible environment within a structured framework. From 2003 to 2009, we recruited, trained and mentored an outstanding collection of young cardiovascular investigators in both basic and clinical sciences. The recruitment and application process that we developed has identified a total of 40 outstanding TACTICS fellows (in seven cohorts). Approximately 80 per cent of these were also able to compete successfully for an external fellowship award from major granting agencies, or were subsequently awarded one. Their efforts regularly appeared in the highest impact journals and their graduation from our program was marked by numerous Assistant Professor appointments in leading universities.

Each year, the Centre also supports research and education on the prevention and cure of cardiovascular diseases with its own fellowship funding program to support trainees in cardiovascular science. These fellowships aim to enrich the productive research enterprise in Toronto. In the past 10 years, it has funded 37 fellows and sees an increasing enrolment each year. Graduate studies also play a key role in helping to ensure future research capacity. In recognition of this, the Centre has established the HSRLCE studentship program. To date, 46 recipients have received our stipend support and we expect these trainees to become the scientific leaders of tomorrow.

# Educational Activities

## from the last 10 years

### Annual Cardiovascular Scientific Day

- 2010 Bringing the Best Cardiac Care to all Canadians: Research & Practice  
2009 Aging of the Cardiovascular System; Turning Back the Clock  
2008 Complex Genetics: Breaking the Code to Future Care  
2007 Regenerative Medicine  
2006 Molecular Phenotyping: Clinical Medicine's New Frontier
- 2005 Translational Medicine  
2004 New Technologies, Innovation and Outcomes  
2003 Multidisciplinary Health Research  
2002 Cardiovascular Research the Bench to Bedside Approach  
2001 Search For Truth: Tools of New Science  
2000 Genetic Inheritance: How to Win when the Genes are Against You

### Distinguished Visiting Professors

#### 2001

Dr. Carlos M. Ferrario, Wake Forest University  
School of Medicine  
Dr. Simon Pimstone, Xenon Genetics Inc.  
Dr. Jennifer E. Van Eyk, Queen's University  
Dr. Mark W. Majesky, Texas A&M University  
Dr. Thomas N. Wight, University of Washington  
Dr. Joseph Metzger, University of Michigan  
Medical School

Dr. E. Dale Abel, University of Utah

Dr. Stephen L. Archer, University of Alberta

Dr. David Beech, University of Leeds

Dr. Mordecai Blaustein, Maryland Center  
for Heart, Hypertension and Kidney Disease

#### 2005

Dr. Rick Moss Chair, University of Wisconsin  
Dr. Jean-Claude Tardif,  
Montreal Heart Institute Research Centre  
Dr. Jagut Narula, University of California, Irvine  
Dr. Ralph A. Kelly, Genzyme Corporation  
Dr. Gordon F. Tomaselli, Johns Hopkins University  
Dr. Evangelos Michelakis,  
University of Alberta, Edmonton  
Dr. Steven R. Houser, Temple University  
School of Medicine

Dr. Gary Lopaschuk, Mazankowski

Alberta Heart Institute

Dr. Richard Schulz, University of Alberta

Dr. David Guterman,  
Medical College of Wisconsin

Dr. Paul Kubes, University of Calgary  
Health Sciences Centre

Dr. Donald Bers, Loyola University Chicago

#### 2002

Dr. Josef Penninger, University of Innsbruck  
Dr. Joshua M. Hare, Johns Hopkins University  
School of Medicine  
Dr. Marlene Rabinovitch,  
The Hospital for Sick Children  
Dr. Janet Rossant, Samuel Lunenfeld  
Research Institute, Mount Sinai Hospital  
Dr. Mark L. Entman, Baylor College of Medicine

#### 2006

Dr. Charles Murry, University of Washington  
Dr. Ed Yeh, University of Texas  
Health Science Center  
Dr. Ron Victor,  
Southwestern Medical Center at Dallas  
Dr. Joseph Loscalzo,  
Brigham and Women's Hospital  
Dr. Lorrie A. Kirshenbaum, St. Boniface  
General Hospital Research Centre  
Dr. Kenneth Walsh, Institute Boston  
University School of Medicine

Dr. Heinrich Taegtmeyer, University of Texas

Health Sciences Center at Houston

Dr. Don Maurice, Queen's University

Dr. Stanley Nattel, University of Montreal,  
Montreal Heart Institute

Dr. Todd Anderson, University of Calgary

Dr. Ira Goldberg, Columbia University

Dr. Peng-Sheng Chen, Indiana University  
School of Medicine

#### 2003

Dr. Karl T. Weber, University of Tennessee  
Health Sciences Center  
Dr. Richard Theodore Lee,  
Harvard Medical School  
Dr. Michael Schneider,  
Baylor College of Medicine  
Dr. Peter Paré, University of British Columbia  
Dr. Kenneth Chien,  
University of California at San Diego  
Dr. Scott Heximer, University of Toronto

#### 2007

Dr. Michael Gollob, University of Ottawa  
Heart Institute  
Dr. William Sessa,  
Yale University School of Medicine  
Dr. Daniel P. Kelly, Washington University  
School of Medicine  
Dr. Avril V. Somlyo, University of Virginia  
School of Medicine  
Dr. Bruce McManus,  
University of British Columbia

#### 2010

Dr. Aly Karsan, BC Cancer Research Centre  
Dr. Jason Dyck, University of Alberta  
Dr. Derek Yellon, University College London  
Hospital & Medical School  
Dr. Geoff Pickering,  
University of Western Ontario  
Dr. Martin Bennett, Addenbrooke's Centre  
for Clinical Investigation,  
Dr. Stefan Offermanns, University of Heidelberg  
Dr. Hartmut Weiler, Medical College of Wisconsin  
Dr. Edward O'Brien,  
University of Ottawa Heart Institute  
Dr. Michael Rosen, Columbia University

#### 2004

Dr. Murray W. Huff, University of Western Ontario  
Dr. Alvin H. Schmaier, University of Michigan  
Dr. Eric Peterson, Duke University Medical Center  
Dr. Robert Califff, Duke Clinical Research Institute  
Dr. Jeffery D. Molkentin,  
Children's Hospital Medical Center

# The Centre's Dedicated Faculty

(2010)

## Members

Adamson, Lee	Goodman, Jack	Newton, Gary
Adeli, Khosrow	Gotlieb, Avrum	Ni, Heyu
Backx, Peter	Grace, Sherry	Opas, Michal
Belik, Jaques	Gramolini, Anthony	Parker, Thomas
Belsham, Denise	Gross, Gil	Parker, John
Bendeck, Michelle	Heximer, Scott	Pawson, Anthony
Bolz, Steffen-Sebastian	Hinek, Aleksander	Radisic, Milica
Butany, Jagdish	Husain, Mansoor	Rakowski, Harry
Chan, Christopher	Jankov, Robert	Rao, Vivek
Chauhan, Vijay	Kantor, Paul	Robinson, Lisa
Cheung, Angela	Keeley, Fred	Ross, Heather
Cohen, Eric	Khokha, Rama	Rubin, Barry
Connelly, Kim	Kislenger, Thomas	Scott, Ian
Connelly, Philip	Ko, Dennis	Sefton, Michael
Courtman, David	Langer, Anatoly	Simmons, Craig
Cybulsky, Myron	Lee, Douglas	Sole, Michael
Delgado, Diego	Leong-Poi, Howard	Stanford, William
Dorian, Paul	Letarte, Michelle	Strauss, Bradley
Drucker, Dan	Lewis, Gary	Tsushima, Robert
Dumont, Dan	Li, Ren-Ke	Tu, Jack
Dzavik, Vlad	Lindsay, Thomas	Verma, Subodh
Emili, Andrew	Liu, Peter	von Harsdorf, Rudiger
Fantus, George	Logan, Alexander	Weisel, Richard
Feng, Zhong-Ping	MacLennan, David	Wittnich, Carin
Fish, Jason	Marsden, Philip	Wright, Graham
Floras, John	Mital, Seema	Yang, Burton
Fremes, Stephen	Moody, Alan	Zandstra, Peter
Giacca, Adria	Nanthakumar, Kumar	

## Current HSRLCE Steering Committee

Dr. Mansoor Husain, Director, Heart & Stroke/Richard Lewar Centre of Excellence	Dr. John Floras, Division of Cardiology, Mount Sinai Hospital/University Health Network
Dr. Paul Dorian, St. Michael's Hospital, Division of Cardiology	Dr. Andrew Redington, Hospital for Sick Children
Dr. Peter Backx, Director, Transgenic Physiology Lab	Dr. Janet Rossant, Hospital for Sick Children
Dr. Richard Weisel, Toronto General Research Institute	Dr. Michael Farkouh, Clinical Trials, Division of Cardiology MSH/UHN
Dr. Bradley Strauss, Sunnybrook Health Sciences Centre	Dr. Richard Hegele, Department of Laboratory Medicine and Pathobiology, U of T
Dr. Graham Wright, Sunnybrook Health Sciences Centre	Dr. Stephen Matthews, Department of Physiology, U of T
Dr. Avrum Gotlieb, University of Toronto	



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