Discover Research

2009/2010

HEART & STROKE FOUNDATION OF BC & YUKON

Finding answers. For life.

Introduction

Welcome to the seventh edition of Discover Research, our annual publication highlighting the most recent cutting-edge research projects funded by the Heart and Stroke Foundation of BC & Yukon. Since the Foundation's beginnings in the late 1950s, we have contributed more than $100 million to research in British Columbia, helping to build the province into a leading cardiovascular research centre.

The new projects you will read about in the following pages have all been supported because they promise to advance our knowledge of how to prevent or treat heart disease and stroke in crucial ways. They cover a wide range of themes and topics, from the genetics of obesity and heart rhythm disorders to the influence of sleep and stress on the development of cardiovascular disease. This year's new projects also continue the Foundation's long history of supporting research into atherosclerosis and stroke rehabiliation.

Regular readers of Discover Research will notice that this year we are also featuring Strategic Research projects. Most of the research supported by the Foundation takes place through Grants-in-Aid, or operating grants, used to fund investigator-driven projects, but we also target research funding to specific areas of cardiovascular health. The two strategic grants profiled here focus on dealing with stroke from multiple perspectives and support the Heart and Stroke Foundation-led development of the BC Stroke Strategy.

All of this work is only made possible with the support of tens of thousands of people across British Columbia and the Yukon. Communities, individuals, families, employees, and businesses commit their time and energy, putting in countless hours to raise the money that supports all the Foundation's research projects. I want to thank you all for your dedication and support for our vision: generations free of heart disease and stroke.

Bobbe Wood, MA
President & CEO
Heart and Stroke Foundation of BC & Yukon

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Heart and Stroke Foundation of BC & Yukon Research Chairs

The Heart and Stroke Foundation of BC & Yukon is a major contributor to two endowed Research Chairs and a Professorship as well as a specialized cholesterol laboratory. These prestigious awards recognize and support outstanding scientists and leaders in cardiovascular disease research.

The Sauder Family and Heart and Stroke Foundation of BC & Yukon Professorship in Clinical Stroke Research

zoomphotographics

Dr. Philip Teal

Dr. Philip Teal was named in 2006 to the Sauder Family and Heart and Stroke Foundation of BC & Yukon Professorship in Clinical Stroke Research. Dr. Teal is an internationally recognized expert in stroke. He is the director of the Vancouver Hospital and Health Sciences Centre Stroke Program, chairman of the Canadian Stroke Consortium, and a board member of the Canadian Stroke Strategy. His clinical focus includes stroke prevention, acute stroke management, neuroprotection strategies, and the planning, organization, and management of clinical trials.

Pfizer/Heart and Stroke Foundation of BC & Yukon Chair in Cardiovascular Prevention Sciences at St. Paul's Hospital

Dr. Scott Lear is the new Pfizer/Heart and Stroke Foundation of BC & Yukon Chair of Cardiovascular Prevention Sciences at St. Paul's Hospital. The Chair was created in 2008 and Dr. Lear accepted the five-year appointment in 2009. In this position, his work will focus on identifying the social, community and physiological level determinants of heart disease for the development of prevention and treatment strategies, at the population and individual levels, incorporating innovative technologies for their delivery.

Rob Moses Photography

Dr. Scott Lear

The Heart and Stroke Foundation of BC & Yukon Chair in Stroke Research

Dr. Yu Tian Wang is the Heart and Stroke Foundation of BC & Yukon's Chair in Stroke Research. Dr. Wang accepted this appointment in 2002 and moved into the new Brain Research Centre at UBC, where he directs a laboratory of 20 research assistants, graduate students, post-doctoral students, and technicians. The current goal of Dr. Wang's research is to develop interventions that could minimize or prevent brain damage in the brief period immediately following a stroke.

zoomphotographics

Dr. Yu Tian Wang

Heart and Stroke Foundation of BC & Yukon Lipid Laboratory

zoomphotographics

Dr. Gordon Francis

Dr. Gordon Francis is director of the Heart and Stroke Foundation of BC & Yukon Lipid Laboratory that was established at St. Paul's Hospital in 2007. He is also director of the hospital's Healthy Heart Program Prevention Clinic. Dr. Francis is one of North America's most highly regarded lipid and cholesterol researchers. His work focuses on ways of promoting the production of HDL – good cholesterol – in the bloodstream as a means of cardiovascular disease prevention.

The Four Themes of Research

Cardiovascular research does not always involve laboratories and test tubes. For example, research studies can compare patients receiving alternative treatments for a disease, survey the availability of support services, or look at the impact of stress on the development of cardiovascular disease. The Heart and Stroke Foundation, along with other Canadian health research organizations, recognizes the spectrum of prevention, research, and discovery by classifying health research into four areas, called the 'Four Themes of Research.' A Grant-in-Aid application to the Heart and Stroke Foundation can propose research in any of the themes.

Basic Biomedical Research

Laboratory-based research exploring biological or biochemical processes at the molecular, cellular, organ system, and whole body levels.

Clinical Research

Patient focused research aimed at improving diagnosis and treatment of disease and injury by applying biomedical findings to new treatments, technologies, and more.

Health Services and Health Systems Research

Multidisciplinary research looking at how to improve the delivery of health care services through changes to practice and policy.

Social, Cultural, Environmental and Population Health Research

Research examining the way in which socioeconomic, cultural, and environmental factors impact health status.

Training Awards and Scholarships

The Heart and Stroke Foundation of BC & Yukon builds capacity in cardiovascular and stroke research by supporting the most promising young researchers and students. Through two national level awards and two provincial scholarships, and the High School Summer Research Program, we provide resources to train the next generation of leading researchers.

High School Summer Research Program

July 2009 marked the 15th anniversary of HSFBCY's High School Summer Research Program. Every summer, ten outstanding Grade 11 students from across the province are selected to take part in this unique opportunity. The program is designed to give talented science students the chance to explore research as a career option, thus increasing BC's capacity in cardiovascular and stroke research. Students work in the state-of-the-art labs of Foundation-funded researchers to gain valuable skills in the field. Aside from gaining incredible hands-on laboratory experience, students take part in a series of training and seminar sessions. These include viewing open-heart surgery, joining paramedics on an ambulance ride-along and touring the GF Strong rehabilitation facilities. Students are housed at UBC's Gage towers where they cook heart healthy meals together and get an early taste of campus life. The program is described by students as an "unforgettable" and "life-altering" experience. Participants are highly motivated to complete university degrees in medicine or science and long-term evaluations indicate that a large percentage of the students go on to be employed in research and related fields.

The 2009 Heart and Stroke Foundation of BC & Yukon's High School Summer Research Program Participants

Left to right: Andrew Guy, Shelly Chopra, Shoshanna Kervin, Lisa Choi, Ravina Binning, Marie Low, Steven Cheng, Lauren Cuthbertson, Bryson Siemens, and Fraser Parlane

Current Personnel Awardees

New Investigator Award

2009

Dr. Victoria Claydon
Dept. of Biomedical Physiology and Kinesiology, Simon Fraser University
Cerebrovascular control following spinal cord injury.

2008

Dr. Christopher Ahern
Dept. of Anesthesiology, Pharmacology, and Therapeutics, University of British Columbia
Investigating anti-arrythmic inhibition of voltage-gated sodium channels with unnatural amino acids and fluoresence spectroscopy.

Dr. Thomas Claydon
School of Biomedical Physiology and Kinesiology, Simon Fraser University
Structural dynamics of hERG potassium channel gating studied using voltage clamp fluorimetry.

2007

Dr. Angela Devlin
Dept. of Pediatrics, University of British Columbia/Child and Family Research Institute
Nutrition, epigenetics, and risk for cardiovascular disease.

2005

Dr. Gregory Miller
Dept. of Psychology, University of British Columbia
Depression, inflammation, and risk for coronary heart disease.

Research Fellowship Award

2009

Dr. Allen Chan
Brain Research Centre, University of British Columbia
Role of the NMDA receptors in recovery of dendritic structure after stroke.

Dr. Michael Hughes
Dept. of Medical Genetics, University of British Columbia
Molecular mechanisms regulating vascular development, repair, and function.

Dr. David Marchant
The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research
Matrixmetalloproteinases during coxsackievirus induced myocarditis.

Dr. Anuradha Natarajan
Biomedical Research Centre, University of British Columbia
Role of macrophages in regulating regeneration and repair.

Dr. Stephan Pless
Dept. of Anesthesiology, Pharmacology, and Therapeutics, University of British Columbia
Investigating anti-arrhythmic inhibition of voltage-gated sodium channels with unnatural amino acids and fluoresence spectroscopy.

Dr. Anamika Singh
Michael Smith Laboratories, University of British Columbia
Functional effects of omega-3 fatty acids on T-type calcium channel splice variants expressed under normal and cardiopathic conditions.

2008

Dr. Nicole Acerra†
Dept. of Physical Therapy,
University of British Columbia
Promoting stroke recovery via somatosensory cortex stimulation.

Dr. Vincent Chen
Dept. of Cellular and Physiological Sciences, University of British Columbia
Investigating neuroprotective roles of gap junctions by functional proteomics.

Dr. Hyun Beom Choi†
Dept. of Psychiatry, University of British Columbia/Brain Research Centre
A novel pathway in astrocytes providing a neuronal energy substrate during ischemic conditions.

Dr. Dawn Cooper
Dept. of Pathology and Laboratory Medicine, University of British Columbia/ The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research
Targeting granzyme B as a therapeutic approach to atherosclerosis.

Dr. Zhifang Dong
Brain Research Centre, University of British Columbia
Investigation into molecular mechanisms mediating excitotoxicity – developing novel strategies in stroke treatment.

Dr. Jingbo Huang
Dept. of Anesthesiology, Pharmacology, and Therapeutics, University of British Columbia
Further studies of KCNQ1 long-QT mutations present in a Canadian aboriginal population.

2007

Dr. Mitra Esfandiarei
Child and Family Research Institute
Dept. of Anesthesiology, Pharmacology, and Therapeutics, University of British Columbia
The role of integrin-linked kinase in modulation of vascular smooth muscle migration and atherosclerotic intimal thickening in type II diabetes.

Dr. Maziar Rahmani
Genome Sciences Centre, BC Cancer Research Centre
Genetics of healthy cardiovascular aging.

Dr. Debbie Rand†
Dept. of Physical Therapy, University of British Columbia
Quantification of upper-extremity movement in post-stroke participants: Transition from hospital to community.

Doctoral Research Award

2009

Kristin Bowden
Dept. of Medicine, University of British Columbia/The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research
Cholesterol ester storage disease as a model for understanding intracellular homeostasis and HDL biogenesis.

Katie Dragert
Rehabilitation Neuroscience Laboratory, University of Victoria
Efficacy of phased resistance training to stabilize ankle muscle strength after stroke.

Jordan Queridо†
Dept.of Human Kinetics, University of British Columbia
Can hyperoxia enhance the baroreflex in patients with obstructive sleep apnea?

2008

Dr. Minsuk Kim
Faculty of Pharmaceutical Sciences, University of British Columbia
Metabolic basis for diabetic heart diseases: role of cardiac lipoprotein lipase.

Matthew Fingas†
Dept. of Psychiatry,
University of British Columbia
Determining the timing and mechanism of stroke rehabilitation at the level of individual synapses in vivo.

Leanne Ramer
International Collaboration on Repair Discoveries (ICORD)
The role of peripheral plasticity in episodic hypertension following spinal cord injury.

2007

Ni Bai
Dept. of Anesthesiology, Pharmacology, and Therapeutics, University of British Columbia/The James Hogg iCAPTURE Centre for Cardiovascular and Pulmonary Research
Mechanisms underlying particulate matter in air pollution-induced atherosclerosis.

Dustin J. Hines
Dept. of Psychiatry,
University of British Columbia
Microglia cells limit the spread of neurotrauma in a model of stroke.

Marc Klimstra†
School of Exercise Science, Physical, and Health Education, University of Victoria
Neuromechanical basis for using arm movement to facilitate leg muscle activity during walking.

Chao Tai
Dept. of Psychiatry,
University of British Columbia
R-type VGCC's and TRP channels contribute to stroke-induced neuronal death.

Ning Zhou
Dept. of Psychiatry,
University of British Columbia
Signaling pathways underlying spreading depression and ischemic depolarization.

†*Focus on Stroke* Competition

Heart and Stroke Foundation of BC & Yukon
New Grant-in-Aid and Strategic Grant Awards

2009/2010

Grants-in-Aid (GIAs) and Strategic Grants fund the operating costs of research projects. Both types of grant are funded through open competitions. However, GIAs support research in any cardio- or cerebrovascular-related topic. Strategic grants focus on various aspects of the Foundation's key priorities: stroke, resuscitation, and obesity. All applications are reviewed and scored by a group of experts in the field. Only the top scoring applications are approved for funding.

As in past years, the new 2009-2010 projects span the full range of cardiovascular research. Some projects will harness powerful new techologies to focus on the ways some of the body's tiniest molecules interact to affect our health. Others look at the connections between physical health and the environment, mental health and physical health, and exercise and rehabilitation.

The rising number of young investigators receiving grants is also an exciting development. Attracting talented new researchers is essential to keep BC at the leading edge of cardio- and cerebrovascular research. Foundation grants play an important role in this process, insuring that funds are available to support the most interesting and innovative research.

Obesity

The terms "overweight" and "obese" refer to the over-accumulation of body fat resulting from an imbalance between calorie intake and energy use. If calories are not burned off during physical activity, they are converted into fat and stored in fat cells, also known as adipose tissue. As fat accumulates, the cells grow bigger and increase in number, adversely affecting the body's metabolic processes in a number of ways. Excess body fat contributes to type 2 diabetes, high blood pressure, and some cancers, and is a key risk factor for heart disease and stroke. This is a particular concern because one-third of Canadian adults are overweight and an additional 23% are obese. More than one quarter of Canadian children are also overweight or obese.

Is there a genetic basis to obesity?

Obesity is a major risk factor for heart disease and stroke that is increasing at an alarming rate among Canadians. In seeking to understand obesity, researchers have focused on the interaction of individual behaviour with the environment, especially issues involved with diet and physical activity. However, we are now starting to realize that our genetic make-up also has a powerful influence over the way our bodies process food and handle physical activity. Some people are more likely than others to become obese, even though they may eat the same types of food and have the same level of physical activity. Genes can even influence our appetite and affinity for exercising. Dr. Clee's lab has discovered a region of the genome that seems to be related to the regulation of body weight. In this project, her team will use advanced DNA sequencing technology to identify the exact genetic sequences involved in this process and how they work. By understanding the genetics of obesity, we will be able to develop new ways of helping people lose weight and reduce their cardiovascular risk.

Rob Moses Photography

Dr. Susanne Clee
Dept. of Cellular & Physiological Sciences
University of British Columbia

In today's climate of increasingly tight competition for limited funding, this grant from the Heart and Stroke Foundation has been essential for establishing this project in my laboratory, and it provides the support necessary to perform these studies. As a new investigator, this significant investment in my work allows me to spend more time in the lab working with my students on the project, and allows us to push forward with multiple experiments at once. This will allow us to more quickly find the specific genetic sequences affecting obesity with the aim of translating our findings into new therapeutic strategies much sooner.

How does the body create fat cells?

In recent years, scientists have come to a new understanding of body fat. New research shows us that fat cells produce key hormones that help regulate our metabolism, keeping our blood sugar and lipids in balance. But when fat cells expand, leading to excess fat, as happens in obesity, they are less able to play this vital role. This is one reason why obesity endangers our cardiovascular health. Yet, despite the importance of fat cells to our health, we know very little about how the body actually creates them. Dr. Rossi is one of Canada's leading stem cell researchers. In earlier work, his lab focused on developing new methods for isolating the adult stem cells that create fat cells. Building on this, his team will now apply these techniques, trying to identify those stem cells in order to understand how they work and their role in metabolic control. This knowledge will lead to new paths for the prevention and treatment of obesity-related cardiovascular disease.

Rob Moses Photography

Dr. Fabio Rossi
Dept. of Medical Genetics/
Biomedical Research Centre
University of British Columbia

Funding from HSFBCY has allowed me to expand in an area of research that is completely new, not only for me but also in general: the role of stem/progenitor cells in modulating metabolism. This new interest stems from key findings obtained studying tissue regeneration. As often happens, we serendipitously discovered new cell types that may well play a key role in determining the likelihood of an individual to develop insulin resistance and the associated cardiovascular problems. This funding will allow us to focus on this novel aspect of stem cell biology and explore the potential of these cells to reduce cardiovascular risk.

Heart Disease

Heart diseases such as heart attack or heart failure affect people of all ages. They can produce a range of effects, from lifelong conditions that compromise lifestyle and health, to sudden cardiac death. The heart has coordinated electrical and muscular systems that allow it to pump regularly and effectively. Heart diseases can alter these processes, causing changes in the rhythm or heartbeat. Changes in heart rhythm are a common cause of death in heart disease patients. Cardiovascular diseases such as cardiomyopathy, hypertrophy, leaky or narrowed heart valves, arrhythmias, atrial fibrillation and heart failure may be due to genetic causes, certain infections, or injuries from the environment such as restriction in the amount of oxygen reaching the heart muscle.

How can we improve the success of heart transplant surgery?

The rejection of a new heart is a major barrier to the success of heart transplant surgery. This happens when the immune system responds too aggressively to the transplanted heart because the new heart is detected as a foreign object. Dr. Choy has shown that the actions and effects of the human immune system on transplanted tissues are increased by a molecule called nitric oxide. At this point, though, it is not clear exactly how nitric oxide influences the human immune system. We do know that after transplant surgery nitric oxide is produced and that it increases the number of activated T cells, which is a specific immune cell type important for rejection of transplanted organs. In this project, Dr. Choy and his team will conduct a series of experiments that will improve our understanding of the role of nitric oxide in regulating the immune system by determining how nitric oxide prevents cell death of human T cells. This could potentially point the way toward new approaches and therapies that may improve the success rate for heart transplants.

Rob Moses Photography

Dr. Jonathan Choy
Dept. of Molecular Biology
and Biochemistry
Simon Fraser University

Financial support from the Heart and Stroke Foundation is important for my research program because it allows us to study questions relevant to understanding human heart disease. In addition to this financial support, the affiliation of my research program with the Heart and Stroke Foundation provides national recognition and exposure that facilitates interactions with other research programs across Canada with similar interests. These interactions are crucial for the maximization of research efforts towards understanding the causes of human disease. Finally, support from the Heart and Stroke Foundation is particularly helpful in maintaining a connection between basic biomedical research and clinically-relevant findings due to the clear mission of the Foundation to eliminate heart disease and stroke.

Can we identify genes that underlie heart problems in adults?

The advancement of genetic technology is making it possible for us to understand more about heart disease than ever before. We are now starting to learn how the early development of the heart in the womb can affect us as adults. In earlier work, Dr. Hoodless and her team identified a set of genes that is involved not only in the embryonic formation of heart valves, but also in the development of cartilage, tendons, and bones. This suggests that the formation of heart valves *in utero* may be linked to the hardening of the heart valves in adults, a process called valve calcification because the valve tissue becomes increasingly boney. When this happens, the valves can't work properly. In this project, Dr. Hoodless will explore the common genetic pathways that influence heart valve formation and valve calcification to see how these linkages occur. This work will lead to the development of interventions to prevent or treat gene-based valve defects.

Our work on heart development began as part of a large scale genomics project. Within this project we began examining the genes involved in the formation of the valves of the heart. This led to our new project exploring the linkages between valve formation and cartilage development in the limb. We are extremely grateful that HSFBCY has chosen to assist us on this venture. This funding is allowing us to continue our work that has evolved from a broad genomics analysis to address a specific problem of importance. Furthermore, it has allowed me to recruit new, talented trainees to BC to tackle this project. Without this funding, this project would not be pursued in BC.

Rob Moses Photography

Dr. Pamela Hoodless
BC Cancer Agency/
Dept. of Medical Genetics
University of British Columbia

How do sleep and stress affect our heart health?

Dr. Linden's research is concerned with the interaction of psychological and physiological factors in the genesis of cardiovascular disease. His earlier work has focused on the relationship between stress and health, showing how failure to recover from stress is bad for heart health. In this study, Dr. Linden will look at the relationship between stress and sleep to determine if problems with sleeping are caused by long-term stress and if they can lead to negative health outcomes. The results of this work will help us learn more about environmental and behavioural factors in cardiovascular health and lead us toward new interventions to prevent disease.

Rob Moses Photography

Dr. Wolfgang Linden
Dept. of Psychology
University of British Columbia

I have been fortunate to receive Heart and Stroke Foundation of BC & Yukon (HSFBCY) funding for many projects over the years and this support has been pivotal to the success of my work. There has been a complementary pattern in what HSFBCY and related agencies like CIHR favor in terms of fundable projects. It appears to me that HSFBCY's mission of having a broad desire to improve knowledge, but also a keen eye on improving care in this province, breathes additional life and excitement into the locally funded projects. I am very grateful for having had the chance to "knock" on different funding doors.

How do genes affect heart functioning?

Familial hypertrophic cardiomyopathy, or FHC, is an inherited disorder that is one of the leading causes of sudden cardiac death in young adults. FHC is caused by genetic mutations that induce structural changes in the heart during adolescence that can result in fatal arrhythmias. Although several genetic mutations have been associated with this disorder, we still don't know how these mutations cause the pathological growth of the heart and how this leads to arrhythmias that can be lethal. In this project, Dr. Tibbits will explore the pathways that lead from the genetic mutation to pathological conditions associated with FHC. In particular, he will look at how these genetic mutations influence the work of calcium, which is a key element in maintaining the heart's ability to contract normally. The results of this research will not only give us a new understanding of the mechanisms underlying FHC, they may also provide the basis for new therapies for heart failure.

The Heart and Stroke Foundation of BC & Yukon has played an instrumental role in developing this province as one of the strongest centres for cardiovascular and stroke research in Canada and beyond. This has had a profound impact on not only the ability to attract bright young scientists to the area but has also impacted the quality of cardiovascular clinical care in the province. Like most cardiovascular researchers in BC, HSFBCY was critical in giving me the opportunity to set up and maintain a state-of-the-art research lab and training environment that has allowed us to be very competitive in attracting federal research funding and highly talented trainees, many of whom have gone on to be strong basic scientists or cardiologists in their own right. We all owe a huge debt of gratitude to the hard working and enthusiastic administration, staff and volunteers of this tremendous organization.

zoomphotography.ca

Dr. Glen Tibbits
Child and Family Research Institute/
Dept. of Biomedical Physiology
and Kinesiology
Simon Fraser University

What can we learn about heart disease by imaging proteins that regulate heartbeats?

A regular heartbeat depends on the release of calcium in heart muscle cells. A special set of proteins called ryanodine receptors (RYRs) enables the calcium release. Sometimes an inherited defect in these proteins will impair the flow of calcium. Without a proper calcium supply, the heartbeat can become erratic, resulting in what cardiologists call an arrhythmia or irregular heartbeat. In turn, arrhythmias can lead to stroke, heart failure, heart attacks, or cardiac arrest. Scientists have studied RYRs for many years with only limited success. We haven't been able to characterize the defects and ways to address them because nobody knows what RYRs look like at high resolution. Dr. van Petegem proposes to change this situation with an exciting project that will use cutting edge imaging technology to generate high resolution images of RYRs. By enabling comparison between normal and defective proteins, these images will break new ground for the development of drugs to treat this kind of inherited disorder.

Rob Moses Photography

Dr. Filip van Petegem
Dept. of Biochemistry and
Molecular Biology
University of British Columbia

The contraction of our heart muscles relies on specialized proteins. Understanding how these function is impossible without knowing their three-dimensional structure, yet they are too small to be studied via standard microscopic techniques. In my laboratory, we employ a specialized technique called "protein X-ray crystallography," which allows us to deduce the position of nearly every atom in the proteins. This implies bombarding protein crystals with high intensity X-rays. The support from HSFBCY allows me to generate pure proteins, crystallize them, and perform X-ray diffraction experiments at various particle accelerators within North America. In addition, we are able to recruit and train new personnel to become experts in protein crystallography.

Stroke

A stroke is a sudden loss of brain function caused by an interruption in the flow of blood to the brain (ischemic stroke), or the rupture of a blood vessel in the brain (hemorrhagic stroke). Both ischemic and hemorrhagic strokes cause cells in the affected area to die. The consequences of a stroke depend on where the brain was injured as well as how much damage occurred, and can range from mild disability to immediate death. Abilities that may be lost as a result of stroke include the capacity to move, see, remember, speak, reason, read, or write. Stroke affects approximately 50,000 Canadians each year, and about 300,000 Canadians are living with the effects of stroke.

CLINICAL/HEALTH SERVICES STRATEGIC GRANT

Will aerobic exercise improve stroke rehabilitation outcomes?

Stroke or atherosclerosis can sometimes lead to Vascular Cognitive Impairment (VCI). This refers to the loss of brain function that results from a blocked or narrowed artery and is directly implicated in a range of problems with mobility and other forms of physical and social impairment. VCI is the second most common cause of dementia. Dr. Liu-Ambrose will lead a team of researchers in studying the effects of aerobic exercise on seniors who are at risk of dementia as a result of VCI. Patients will take part in a six month exercise program. Changes in their brain function will be closely monitored at the beginning and end of the program as well as six months later. In the context of an aging population, this project will give us important information about how to counter an increase in dementia caused by arterial disease.

Rob Moses Photography

Dr. Teresa Liu-Ambrose
Centre for Hip Health and Mobility, Vancouver Hospital and Health Sciences Centre/Dept. of Physical Therapy, University of British Columbia

Receiving this funding from the Heart and Stroke Foundation has provided me with an invaluable opportunity to examine the role of exercise in promoting cognitive and physical health among those at significant risk of dementia. Current evidence strongly supports the role of physical activity in promoting cognitive function across the lifespan. However, more research is needed to determine the role of targeted exercise interventions among those at risk of cognitive decline, such as those who have suffered a stroke or with VCI. Also, as a direct result of this funding, I have the privilege of working with a collaborative and transdisciplinary research team. Together, we aim to conduct research that will positively impact the health of those affected by VCI.

How can we improve stroke recovery therapy?

Stroke is the main cause of acquired adult disability in Canada. The majority of stroke survivors have problems moving their arms and/or hands. Many also have some problems with leg movement. Research has shown that the more exercise a stroke survivor gets in an affected area, the better their chances of recovering movement. However, with increasing pressure on health budgets, most patients don't get the level of therapy they need. Dr. Eng's pioneering investigation into stroke rehabilitation has provided an answer to this dilemma. She and her team have developed a practical and inexpensive system of exercises for stroke survivors that can be done at home to supplement in-hospital therapy. In this project, she will be looking at how to complement this with a new exercise system to help improve leg movement. This will result in a better quality of life for stroke survivors and their families and less pressure on the health care system.

I have been able to develop innovative and effective rehabilitation interventions to improve functional abilities in people with stroke with operating funds from the Heart and Stroke Foundation. In particular, the Foundation's commitment to research has allowed me to take calculated risks and chances in the hope of making significant health care advances. Their funding has permitted me to not only undertake rigorous randomized controlled trials in stroke rehabilitation, but also to develop partnerships to translate my research to improve the quality of life for Canadians and reduce the economic burden of stroke. My novel stroke rehabilitation interventions funded by the Heart and Stroke Foundation have been implemented in communities across the world, including BC, Canada, US, Hong Kong, Australia and Iceland.

zoomphotographics

Dr. Janice Eng
GF Strong Rehabilitation Centre/
Dept. of Physical Therapy
University of British Columbia

Is rapid intervention after a TIA the most effective way to reduce the burden of stroke?

A TIA, or transient ischemic attack, is a mini stroke that may be signalling an impending major stroke. Unfortunately, TIAs often go unmanaged, as symptoms are unrecognized or go away quickly, and there are many imposters ("mimics"). TIAs are now known to be much more dangerous than previously suspected, particularly in the first few days after they occur. However, rapid early intervention appears to be a highly effective way of preventing a subsequent stroke. Dr. Penn's team will be investigating the logistics of triaging large volumes of patients with symptoms suggestive of TIA to the Stroke Rapid Assessment Unit in Victoria and a north island satellite for rapid intervention. They will examine the outcome of patients after TIA and the shifting incidence of stroke on Vancouver Island in relation to this intervention. Lessons learned should provide guidance to other rapid assessment units being built around the province under the auspices of the British Columbia Stroke Strategy.

Rob Moses Photography

Dr. Andrew Penn
Stroke Rapid Assessment Unit, Vancouver Island Heath Authority

Funding from the Heart and Stroke Foundation has had a dramatic effect on my ability to care for patients with stroke, and to engage in research in stroke in British Columbia. The BC Stroke Strategy, directed by the Heart and Stroke Foundation of BC & Yukon in conjunction with the Ministry of Health, is working to allow us to offer cutting edge services throughout the province. Funding for this research grant on the rapid management of TIA patients, is allowing us to measure the impact of our new interventions so that we can fine tune our care, maximizing the impact of our limited health care resources.

Can stroke survivors use their arms to give their legs a "helping hand" during walking?

Stroke survivors often have problems recovering their ability to walk. The most effective therapy for mobility recovery requires a level of technology and skilled labour that makes it quite costly and sometimes inaccessible to many people. Dr. Zehr has already shown that arm and leg movements are connected through nerve centres in the spinal cord, rather than only in the brain. As a result, the arms can provide sensory feedback through the spinal cord that can be used to help recover leg movement. In this study, Dr. Zehr and his team will pinpoint the particular arm movements and the kind of sensations that can be used to send signals to the legs to improve their mobility. They will use this information to help assess a model of recovering leg mobility that can provide an alternative to the more expensive and less accessible technology.

Without exaggeration, the funding I have received from the Heart and Stroke Foundation has been instrumental in establishing the pioneering approach we have taken to understand how the arms interact with the legs during walking. Through this work, my lab has emerged at the leading edge of international research in this area. Our HSFBCY funded discoveries have allowed us to understand that during walking the arms do have a "connection" to our legs within the nervous system that is similar to what is seen in other four legged mammals like our pet cats or dogs. Importantly these connections may have a useful application in therapies aimed at improving walking after stroke and only through HSFBCY funding has this been possible.

University of Victoria Communications

Dr. Paul Zehr
School of Exercise Science, Physical, and Health Education
University of Victoria

Blood and Blood Vessels

Blood vessels play a significant role in cardiovascular health. Cardiovascular disease alters the structure of the blood vessels and increases the stiffness of the vessel wall, either by hypertension or atherosclerosis. Hypertension is marked by increased muscle thickness leading to a rise in arterial blood pressure. Atherosclerosis develops inside the blood vessels as a result of fatty deposits called plaques that cause the blood vessels to stiffen and narrow. The plaques restrict the flow of blood and can cause a blockage if one breaks away and becomes trapped in an artery. If a coronary (heart) artery is blocked, it will cause a heart attack. If the blockage is in the brain, it will cause a stroke. Atherosclerosis and hypertension have been identified as leading causes of death in the western world.

Can we intervene to prevent atherosclerosis before it starts?

Macrophages are a type of white blood cell that act as scavengers in our blood vessels and play an important role in the immune system. They clean up our blood by 'eating' dead or damaged cells, germs, and other debris that float through our circulatory system. However, they also play a key role in promoting atherosclerosis or hardening of the arteries, one of the leading causes of heart problems and stroke. Together with his collaborator, Dr. Urs Steinbrecher, Dr. Duronio focuses on understanding the interaction of macrophages with LDL cholesterol, known as 'bad cholesterol'. When cholesterol is exposed to oxygen molecules in the blood, macrophages try but are unable to completely ingest it. This forms the basis of the plaques on the inner lining of arteries that give rise to atherosclerosis. By looking for the proteins that control this process, the Duronio lab wants to develop ways to prevent and treat atherosclerosis before it starts.

My research investigates the chemical signals that control decisions of life and death within the cells of the blood. Knowledge of these processes can lead to new drugs that may be used to control abnormal behaviour. HSFBCY funding has allowed us to investigate the actions of cells called macrophages that are relevant for the very early stages of developing atherosclerosis (or hardening of the arteries). The benefit of having this funding has been to concentrate on one particular cell type that is so important in development of a specific disease. Ultimately, all researchers hope that their findings can help people be healthier, and that is what I hope will be gained from our HSFBCY-supported studies.

Rob Moses Photography

Dr. Vincent Duronio
Divison of Experimental Medicine/
Division of Respiratory Medicine
University of British Columbia

What molecules regulate the growth of plaques in blood vessels affected by "hardening of the arteries"?

Hardening of the arteries, or atherosclerosis, is a major cause of heart attack and stroke. A molecule called Versican plays an important role in the development of blood vessels and heart tissue. A growing body of research suggests that Versican also contributes to the development of atherosclerosis. However, scientists do not yet understand exactly how this happens.
Dr. McManus's laboratory has found that Versican may orchestrate the laying down of excess connective tissue by cells within injured blood vessel walls. In this phase of their studies, he and his team will follow up on their novel findings to uncover the means by which Versican fosters fibrous plaques in arteries. The results of this work will provide new avenues for prevention of and therapy for thick-walled, narrowed arteries.

zoomphotographics

Dr. Bruce McManus
Providence Heart + Lung Institute/
Pathology and Laboratory Medicine
University of British Columbia

The Heart and Stroke Foundation staff and its many volunteers are relentlessly devoted to creating new knowledge to change what we understand about heart and blood vessel risks, diseases and consequences. They are also devoted to moving knowledge into action through education and broad dissemination. Our research team has had the good fortune of Heart and Stroke Foundation grants and personnel awards support over many years. This funding has allowed us to decipher the basis of blood vessel disease in heart transplant patients, and to figure out ways to stop virus infections of heart muscle. We are deeply appreciative of the Foundation's generosity. We would simply not be on this journey of discovery without their enormous commitment to better preventive and therapeutic approaches for the heart.

Is it possible to prevent health-endangering blood clots?

Viruses are infections that are able to hijack the body's own molecules to reproduce inside it. In this study, Dr. Pryzdial is looking at two very common viruses that have been implicated in heart disease due to their ability to promote unnecessary blood clotting. Blood clots that are not needed to heal injuries inside the body are dangerous. These cause heart attacks and stroke. Dr. Pryzdial's lab has shown that two viruses with a life-long presence in the body, herpes simplex 1 (cold sores) and cytomegalovirus, exploit the body's natural clotting agents to reproduce themselves. They hijack these agents to bypass the body's natural anti-clotting defences. Based on this research, Dr. Pryzdial wants to identify the molecules by which these two viruses initiate blood clotting. By identifying the biochemical processes that link these viruses to blood clots, he will be able to point us in a new direction for treatment of disease caused by clotting, from hardening of the arteries to thrombosis to stroke.

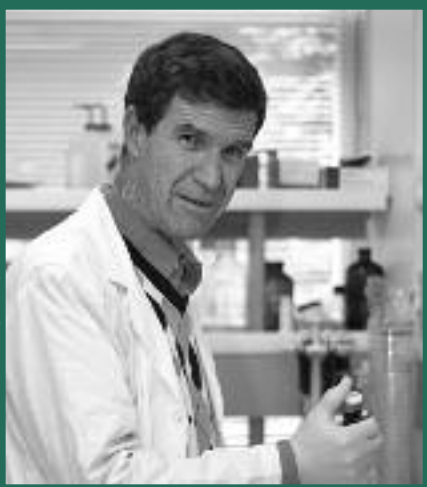
At least one in twenty Canadians has been diagnosed with vascular disease, which is the single largest burden to our national healthcare system. The Heart and Stroke Foundation of BC & Yukon is doing a terrific job of acquiring and providing the funding essential for targeting this huge medical problem. I am grateful for their tireless effort, without which our work and others' into understanding and treating heart disease and stroke could not progress.

zoomphotographics

Dr. Edward Pryzdial
Canadian Blood Services/
Centre for Blood Research/
Dept. of Pathology and
Laboratory Medicine,
University of British Columbia

Can we reverse or improve atherosclerosis caused by air pollution?

Air pollution, especially the ultra fine particles that are smaller than 10 one millionths of a metre (called PM_{10}), is now an accepted risk factor for cardiovascular disease. Dr. van Eeden's lab was the first to show that these particles can lead to cardiovascular disease by causing atherosclerosis, or hardening of the arteries. Scientists now commonly believe this happens because PM_{10} is absorbed deep into the lungs, triggering inflammation in the arteries. In this study, Dr. van Eeden will assess the effects of statins on atherosclerosis caused by exposure to PM_{10}. Statins are now widely used to combat cholesterol buildup in the blood. Because they also reduce blood vessel inflammation, statins may prove beneficial in preventing atherosclerosis caused by air pollution. The results of the study will both confirm whether PM_{10} is linked to heart disease via inflammation of the arteries and provide evidence for a remedy for atherosclerosis caused by air pollution.



Rob Moses Photography

Dr. Stephan van Eeden
Providence Heart + Lung Institute/
Division of Respiratory Medicine
University of British Columbia

In the early 1990s the first convincing epidemiological studies showed an association between exposure to fine particulate matter air pollution and morbidity and mortality from cardiovascular disease. With the support from the Heart and Stroke Foundation our group was the first to show that exposure to ambient air pollution particles causes progression and instability of atherosclerosis, the underlying vascular disease that results in heart attacks and stroke. This finding has since been confirmed by several other groups across the world in both animal models and in humans with the result that excessive exposure to air pollution is currently recognized as a risk factor for the development and triggering of heart and blood vessel disease. The support from the Heart and Stroke Foundation for my work at a stage when there was very little biological evidence for this concept showed their vision and willingness to support innovative ideas, as well as their broader support for research that addresses important public health issues regarding heart and blood vessel disease. The Heart and Stroke Foundation's continued support of my research on air pollution associated blood vessel disease has allowed our laboratory to be on the forefront of new knowledge regarding this important public health issue.

2009–2010 Continuing Grant-in-Aid Awards

Diabetes Research

Dr. Catherine Pang
Dept. of Anesthesiology, Pharmacology, and Therapeutics, University of British Columbia

Cardiovascular role of iNOS in diabetes.

Dr. Brian Rodrigues
Faculty of Pharmaceutical Sciences, University of British Columbia

High fat induced changes in cardiac metabolism and its consequences.

Heart Disease Research

Dr. Eric Accili
Dept. of Cellular & Physiological Sciences, University of British Columbia

Molecular regulation of pacemaker channel function.

Dr. Thomas Claydon
Dept. of Biomedical Physiology and Kinesiology, Simon Fraser University

Structural dynamics of hERG potassium channel gating studied using voltage clamp fluorimetry.

Dr. David Fedida
Dept. of Anesthesiology, Pharmacology, and Therapeutics, University of British Columbia

Activation and inactivation gating of cardiac voltage-gated potassium channels studied by electrophysiology and time-resolved fluorescence changes.

Contribution of the dynein motor system to surface expression and cellular localization of voltage-gated potassium channels.

Further studies of KCNQ1 long-QT mutations present in a Canadian First Nations population.

Dr. Karin Humphries
BC Cardiac Services/ Dept. of Medicine, University of British Columbia

Sex differences and the determinants of health status post acute myocardial infarction in younger adults.

Dr. Aly Karsan
BC Cancer Agency/ Dept. of Pathology and Laboratory Medicine, University of British Columbia

Dissecting gene regulatory networks in cardiac cushion development.

Dr. Scott Lear
Healthy Heart Program, St. Paul's Hospital/School of Kinesiology, Simon Fraser University

Randomized trial of a cardiac rehabilitation proram delivered remotely through the Internet.

Dr. Honglin Luo
Providence Heart + Lung Institute/ Dept. of Pathology and Laboratory Medicine, University of British Columbia

The ubiquitin/proteasome system in cardiac remodeling.

Mechanisms of impaired cardiac function in coxsackievirus-induced myocarditis.

Dr. Louise Pilote
Division of Clinical Epidemiology, McGill University Health Centre

Genesis Praxy: Gender and sex determinants of cardiovascular disease from bench to beyond in premature acute coronary syndrome.

Dr. Keith Walley
Providence Heart + Lung Institute/ Dept. of Medicine, University of British Columbia

Genetic determinants of neurocognitive dysfunction following cardiopulmonary bypass.

Dr. Decheng Yang
Providence Heart + Lung Institute/ Dept. of Pathology and Laboratory Medicine, University of British Columbia

Specific delivery of antiviral drugs to target cells using ligand-mediated pRNA nanoparticles.

Stroke Research

Dr. Lara Boyd
Brain Research Centre/
Dept. of Physical Therapy, University of British Columbia

Promotion of brain reorganization after stroke.

Dr. Nadia Khan
Centre for Health Evaluation and Outcomes Sciences/ Dept. of Medicine, University of British Columbia

Sex and ethnic differences in stroke prognosis and quality of care.

Dr. Timothy Murphy
Brain Research Centre/
Dept. of Psychiatry, University of British Columbia

Using in vivo imaging to resolve if, when, and where excitotoxicity and oxidative stress occur during stroke.

Dr. Christian Naus
Dept. of Cellular and Physiological Sciences, University of British Columbia

Gap junctions and neuroprotection in stroke.

Dr. Yu Tian Wang
Brain Research Centre/
Dept. of Medicine, University of British Columbia

Investigation into the molecular mechanisms mediating excitotoxicity - developing novel post-stroke therapies.

Dr. Cheryl Lea Wellington
Child and Family Research Institute/
Dept. of Pathology and Laboratory Medicine, University of British Columbia

Role of lecithin: Cholesterol acyltransferase (LCAT) in brain lipoprotein metabolism.

Blood and Blood Vessel Research

Dr. Leslie Burtnick
Centre for Blood Research/
Dept. of Chemistry, University of British Columbia

The structure of gelsolin-capped actin filaments.

Dr. Victoria Claydon
Dept. of Biomedical Physiology and Kinesiology, Simon Fraser University

Cerebrovascular control following spinal cord injury.

Dr. Angela Devlin
Child and Family Research Institute/
Dept. of Pediatrics, University of British Columbia

Hyperhomocysteinemia and epigenetic regulation of hepatic lipid metabolism.

Dr. David J. Granville
Providence Heart + Lung Institute/
University of British Columbia

Granzyme B in atherosclerosis and xanthomatosis.

Dr. Michael Hayden
Centre for Molecular Medicine and Therapeutics, University of British Columbia

The functional role of palmitoylation of ABCA1 and its effects on HDL metabolism and atherosclerosis.

Dr. Aly Karsan
BC Cancer Agency/
Dept. of Pathology and Laboratory Medicine, University of British Columbia

Molecular mechanisms of endothelial survival/apoptosis.

Dr. Kelly McNagny
Biomedical Research Centre/
Dept. of Medical Genetics, University of British Columbia

Role of endoglycan in hematopoesis, vascular biology, and cancer.

Dr. Edward Pryzdial
Canadian Blood Services/Centre for Blood Research/
Dept. of Pathology and Laboratory Medicine, University of British Columbia

Effects of plasmin on prothrombinase.

Bettina Hamelin, Director Research and Development, Western Canada (top of stairs) and members of the Western Medical Team (from top to bottom) Valencia Remple, Darren Cowan-Bittner, Nana Rezai, Alexander Dubyk, Tara Moroz, Joan Saskatch and Lamia Kalfane.

About Pfizer Canada

- Pfizer Canada is a leader in Canadian healthcare research, investing more than $137 million in research and development activities, contributions and partnerships in 2007.
- The company has invested more than $1 billion in R&D since 2000.
- Pfizer Canada's cardiovascular research targets the disease and its risk factors including diabetes and smoking cessation.

Pfizer Canada Inc. Working Together From the Heart

Cardiovascular disease remains a significant health burden in Canada. Through the efforts of the Heart and Stroke Foundation of BC & Yukon, and committed researchers and scientists across the country, we are making progress in evolving our understanding of this deadly disease.

While we understand that it takes more than medication to be healthy, at Pfizer Canada, we are dedicated to bringing life saving medicines to Canadians through innovative research in partnership with the Canadian scientific and healthcare community. Since 2006, we have significantly strengthened our capacity to continuously develop and maintain a vast research network, and partner with key academic institutions, universities, biotechnology companies and hospitals in Western Canada. Through the work of our Western medical team we have created, in partnership with Simon Fraser University, the Heart and Stroke Foundation of BC & Yukon and the St. Paul's Hospital Foundation, the *Pfizer/Heart and Stroke Foundation Chair in Cardiovascular Prevention Research at St. Paul's Hospital*, with a contribution of $1.25M. We have invested over $1.1M in cardiovascular research initiated by BC researchers and $0.8M in the Healthy Heart Society that works with the BC Ministry of Health on ways to improve access to and quality of primary health care delivery in the province. Pfizer Canada has also become a key supporter of initiatives that aim at bridging the commercialization gap of discoveries from BC investigators and has contributed $1M respectively to the *Centre for Drug Research and Development* lead by Ms. Natalie Dakers as well as to the PRevention Of epidemic Organ Failure (PROOF): *Solutions for Hearts, Lungs and Kidneys* initiative lead by Drs. McManus, Keown and McMaster from UBC. Finally, we are excited to collaborate with Drs. Harrigan and Montaner at the *BC Centre for Excellence in HIV/AIDs* ($3M) and Drs. Hayden and Carleton at the *Centre of Molecular Medicines and Therapeutics* ($1.5M) in initiatives that will increase our ability to administer the right dose of the right drug appropriately to the right patient. With these efforts we seek to realize our number one goal: bringing new and innovative medicines to our patients and ensuring that the many existing treatments are accessible and appropriately used.

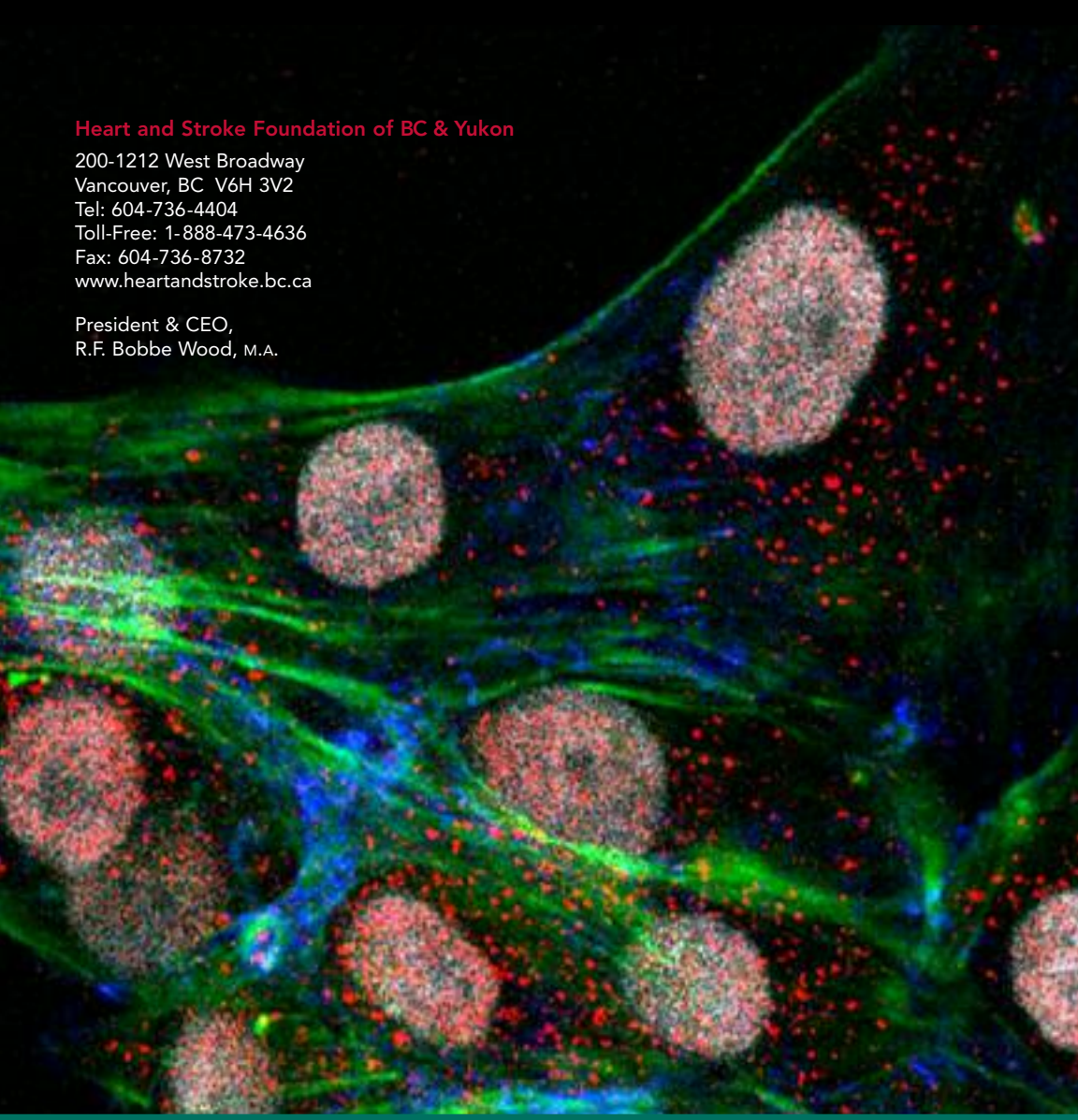
Pfizer is proud to partner once again with the Heart and Stroke Foundation of BC & Yukon in support of this publication. It is a vivid example of how the Foundation extends the power of innovative research through health promotion. Through this leadership, we learn as individuals to take action to prevent cardiovascular disease and avoid its often disabling complications.

Together, we want to make a difference. Pfizer Canada's commitment to helping Canadians live happier, healthier and longer lives extends beyond medication.

Pfizer

Working for a healthier world™

www.pfizer.ca



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This support does not imply an endorsement by the Foundation of the products or services of Pfizer Canada.

Front photo courtesy of David Lane (UBC James Hogg Research Centre, Providence Heart + Lung Institute). Smooth muscle actin stress fibre formation in lung fibroblasts, in response to treatment with TGF-beta (blue = nucleus, green = smooth muscle actin). Taken with Nikon Eclipse TE300 Florescent Microscope.

Back photo courtesy of Brian Wong (UBC James Hogg Research Centre, Providence Heart + Lung Institute). Untreated Aortic Smooth Muscle cells (blue = beta-catenin, red = versican, green = f-actin, white = nucleus). Taken with Leica Inverted Fluorescence microscope with Confocal Scanner.