



HSF researcher Dr. Chris Ahern



HEART & STROKE FOUNDATION OF CANADA

Finding answers. For life.

Insight

A HEART AND STROKE FOUNDATION RESEARCH NEWSLETTER

FALL 2008

WHAT IF?

A new HSF fund gives Canada's most brilliant researchers the opportunity to test imaginative new ideas for defeating diseases.

Frederick Banting proved that sometimes you just have to follow your instincts. He had an idea about isolating part of the pancreas and, toiling in a Toronto lab in the long hot summer of 1921 with his assistant Charles Best, discovered insulin. Within a year of his breakthrough, diabetes ceased to be a death sentence for millions of people.

The Heart and Stroke Foundation has always supported the kind of imaginative and innovative work that Banting and Best personified. That support has been formalized with the creation of the HSF Novel and Exploratory Research Fund (NERF) to help some of our most accomplished medical minds follow well-informed hunches.

"We know these researchers are brilliant because our review committees have rated them as leaders in their fields," says Linda Piazza, Heart and Stroke Foundation of Canada director of research. "The idea is to give them a chance to develop an idea that – if it works – could change the world."

The one-year award will allow innovators to test out bold new ideas. Three awards were granted this year.



HSF researcher Dr. Khosrow Adeli

Dr. Khosrow Adeli, a professor of clinical biochemistry at the University of Toronto and a division head at The Hospital for Sick Children, has an idea about how to prevent the body from absorbing fructose – the fruit-based sweetener widely used in prepared foods and drinks.

Doctors believe that consuming too much

fructose can lead to insulin resistance and trigger type 2 diabetes. Dr. Adeli theorizes that blocking the intestinal absorption of fructose could thwart insulin resistance and prevent obesity, higher levels of triglycerides (a type of fat found in the blood), higher levels of "bad" cholesterol, and increased risk of coronary heart disease. He wants to test his theory by using a fructose analog – a similar, but not identical substance – to trick the intestine into ignoring the real stuff.



HSF researcher Dr. Sophie Lerouge

has an idea for saving lives in the treatment of abdominal aortic aneurysms, a condition that affects eight per cent of men over the age of 65.

Abdominal aortic aneurysms occur when an aortic blood vessel in the abdomen bulges, posing a deadly threat of rupture. Conventional treatment calls for surgery, which comes with considerable risk and means a long recovery in hospital. A simple, new procedure avoids that by inserting a stent-graft or tube through an artery to the site of the aneurysm.

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HEART AND STROKE FOUNDATION RESEARCH AT A GLANCE

The Heart and Stroke Foundation currently funds more than 900 researchers and research teams in medical institutes, universities, and hospitals across Canada. Their goal: to eliminate heart disease and stroke and improve the quality of life for thousands of Canadians affected by these conditions.

Every seven minutes in Canada someone dies from heart disease or stroke. Hundreds of thousands of Canadians are living with their effects. Foundation researchers put their hearts and minds into improving these odds.

The Heart and Stroke Foundation:

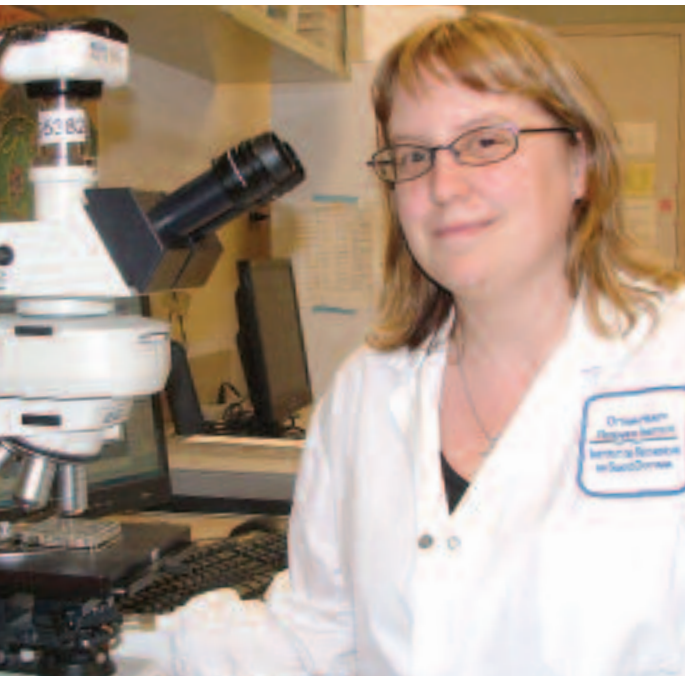
- invested close to **\$59 million** into peer-reviewed heart disease and stroke research in Canada in 2007
- invested over **\$1 billion** in research support since it was established in 1956
- works with partners to **act on research** by strategically linking it to health policy
- funds researchers **throughout their careers**, from high-school students working in research settings through to established senior scientists
- created the HSF Federation Research Fund to **advance knowledge** in the Foundation's mission priority areas using an innovative knowledge-to-action approach called the Managed Research Cycle
- delivers **leading-edge information** about heart disease and stroke to Canadians and their healthcare professionals
- advocates for changes to public policy to build healthy communities and ultimately a **healthier country**

WHAT IF?

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While the new process can save lives and shorten hospital stays, complications from blood leaking back to the aneurysm have limited its use.

Dr. Lerouge wants to optimize and test an injectable gel derived from the shells of shrimps and other crustaceans to act as a bioadhesive occlusive agent to prevent the leaks. If it works, this idea could have a huge impact on the treatment of aneurysms – saving lives and allowing more people to be treated with a minimally invasive procedure instead of major surgery.



HSF researcher Dr. Tamara M. Paravicini

Dr. Tamara M. Paravicini of the Ottawa Health Research Institute wants to know more about a newly identified molecule that grows inside cells when people eat too much salty food.

While it's well known that a high-salt diet can lead to high blood pressure, it also sparks an inappropriate growth of heart muscle cells and stiffens blood vessels, raising the risk of heart attack.

By looking closely at what the molecule is doing, Dr. Paravicini hopes to gather knowledge about how cardiovascular damage occurs from eating a high salt diet.

HSF research results changing lives

The Heart and Stroke Foundation's most important funded research advances and resulting public education initiatives include:

- research behind the development and use of the implantable pacemaker
- creating a scale that measures the severity of strokes
- the use of acetylsalicylic acid (ASA) in preventing heart attack and stroke
- clot-busting drugs that reduce mental and physical damage caused by 80 per cent of strokes
- public awareness of stroke signs and heart attack warning signals
- developing and updating guidelines for resuscitation (CPR)
- promoting public recommendations for the management of high blood pressure



HSFC Barnett Scholar Dr. Roger Thompson

THE MYSTERY CHANNEL

This year's HSFC Barnett Scholar believes a neuron channel holds the key to understanding what goes on in the brain during stroke

Scientists have long understood what causes the most common type of stroke: the blood flow to the brain is blocked by a clot. They also know what happens next: a massive number of brain cells quickly collapse after being deprived of oxygen and glucose, leading to death or disability.

What scientists haven't been able to figure out is exactly how it happens.

Dr. Roger Thompson, the 2008/09 HSFC Barnett Scholar, hopes to change that. And he may have the inside track on stroke-triggered cell death: a little-understood neural cell channel called pannexin-1.

The Barnett Scholarship will enable Dr. Thompson, an assistant professor at the University of Calgary's Hotchkiss Brain Institute, to build on findings he published in *Science* two years ago that opened up a new chapter in interpreting the intricacies of stroke.

His work has added another critical piece to understanding that necrosis – the rapid death of brain cells – is not just the blood-starved brain going haywire, but a programmed pattern of events.

"The ultimate goal is to identify new targets for drugs that stop cell death. I think developing a drug is quite feasible."

"Traditionally, it's been thought that the cell membrane breaks down and the cell dies – and that you

can't control it," says Dr. Thompson. "But there is more and more evidence, from my work and other researchers around the world, to indicate that there is a sequence of steps occurring. By understanding that sequence we might be able to develop some novel interventions."

When the brain is functioning well, the neurons carry the electrical charges that transmit messages or signals back and forth like a well-oiled machine. Cation (pronounced cat eye on) channels on the cell membranes open and close to allow positively charged molecules like sodium and calcium to enter and potassium to exit.

When the brain is deprived of blood, however, this machine-like organization begins to shut down. The cells overload themselves with calcium, causing death. Dr. Thompson identified pannexin-1, a veritable giant among cation channels, as crucial to the cell-death process. It opens just before cell death.

"I think pannexin-1 is going to turn out to be a critical player in rapid cell death," says Dr. Thompson. "If we can understand how it is reacting to oxygen deprivation, then we can understand how the brain cells are dying during stroke."

Dr. Thompson's long-term goal is to establish pannexin-1 as a target for new drugs to stop cell death when stroke hits.

"The ideal situation might be to develop a drug for people who are at risk for stroke – people who have already had small strokes or ischemic (restricted blood flow) events. These people could take a drug that stays in their system until a stroke occurs. Then it would block the pannexin-1 channel from opening."

The HSFC Henry J.M. Barnett Scholarship is presented annually to a highly rated New Investigator working in the area of stroke research.



OUR MISSION IS FOR LIFE

The Heart and Stroke Foundation, a volunteer-based health charity, leads in eliminating heart disease and stroke and reducing their impact through the

advancement of research and its application, the promotion of healthy living, and advocacy.

SHARING THE HEART TRUTH



Two leading cardiologists – an American and a Canadian – talk about the campaign to raise women’s awareness about heart disease and stroke

Heart disease and stroke kill one in three Canadian women. Yet only one in eight know it is their most serious health concern. In February 2008, the Heart and Stroke Foundation launched *The Heart Truth*, a cross-Canada effort to raise awareness that heart disease and stroke are the leading cause of women’s death. It’s modeled on the successful U.S. campaign that began in 2002.

Dr. Susan K. Bennett, clinical director of the women’s heart program at George Washington University Hospital in Washington D.C., is the 2008 HSFC Lecturer.

Dr. Beth Abramson, associate professor of medicine at the University of Toronto, is a spokesperson for *The Heart Truth*.



Dr. Susan K. Bennett

Q. Why was this campaign launched in the United States?

A. The main reason was that too many women were dying of heart disease that could be prevented. That was the spark.

Q. How successful has it been?

A. The bottom line is it has saved lives. Surveys have shown that awareness levels have gone up tremendously, from 34 per cent to 57 per cent, representing a significant opportunity to prevent heart attacks and strokes.

Q. Has the emphasis shifted over the years?

A. Recently we recognized that the final line of the public education campaign is to get women to talk to their doctors, because the medical care community has not absorbed the message of *The Heart Truth* the way the public has.

Q. Is this a case of the public getting ahead of the medical establishment?

A. Oh yes. In 2005, the American Heart Association published a survey of 500 physicians’ attitudes and awareness about women and cardiovascular disease. One of the things they asked was, ‘Is it true that more American women have died of cardiovascular disease than American men?’ Only eight per cent of primary care physicians knew that was a true statement. Among obstetricians/gynecologists it was 13 per cent. Among cardiologists, it was 17 per cent.

Q. Given that, what should women do?

A. Well, just like a woman wouldn’t go home from a store with a new dress without first checking the size and the label, she shouldn’t leave her doctor’s office without knowing her blood pressure and cholesterol levels.

Dr. Beth Abramson

Q. Why is a campaign like *The Heart Truth* necessary in Canada?

A. This is a life and death issue and women’s awareness is still low. National polling in 2007 revealed that only 13 per cent of women recognize that heart disease and stroke are their most important health issues. As women, we need to take charge of our



The Heart Truth spokesperson
Dr. Beth Abramson

heart health and understand what our leading health threat is.

Q. What statistic jumps out for you?

A. In Canada, the number of deaths from heart disease between women and men is now virtually the same – about 37,000 a year.

Q. Is there a gender gap when it comes to heart disease and stroke?

A. There is a gap in awareness. And there is data to suggest that women do not receive the same care that men do. We need to explore the reasons why and close that gap.

Q. Women often say they are too busy to take care of their heart health – that they have careers and families to look after. How do you react to that?

A. I often say that women are Type E personalities. They are everything to everyone, except themselves. Women need to slow down and take care of their own health so they can be around to take care of others. As part of an annual exam, women should talk to their doctors about their risks for heart disease and stroke.

Awareness is the key to reversing this trend. Find out how you can share the truth at thehearttruth.ca/health_professionals.



HSFC McDonald Scholar Dr. Chris Ahern

Going further

By looking at things from the cell out, a talented young scientist hopes to find a better way to treat a stroke-triggering heart condition

“What is at the root of heart arrhythmia? Why do the drugs we have now work in some cases, but not in others? Finding out will help in designing the next generation of heart drugs.”

Dr. Chris Ahern likes to take things further.

The 2008/09 HSFC McDonald Scholar has already devoted a decade to furthering the understanding of the inner workings of ion channels that, among other things, regulate the body’s electrical circuitry. The McDonald Scholarship will allow him to dedicate the next five years to use that work to attempt to solve a molecular mystery.

“I am committed to making the research happen,” says the transplanted American. “This award means it will happen much sooner.”

Dr. Ahern is interested in the root causes of cardiac arrhythmia. A growing health concern in a rapidly aging population, arrhythmia occurs when the electrical impulses in the heart go off kilter because the proteins (called ‘ion channels’) that move salt in and out of the cells misfire. It can cause blood clots that trigger stroke.

Drugs used for arrhythmia prevent the heart cells from misfiring but scientists don’t know the details of why or how.

And the drugs used to treat cardiac arrhythmia can affect similar ion channels in the brain or elsewhere in the body where, surprisingly, they can be used for epilepsy and chronic pain. While having multiple

treatment options for any disease is generally thought to be a good thing, Dr. Ahern believes that we can do better and hopes that his research leads to cardiac-specific drugs.

Dr. Ahern is working from the cell out to discover how these drugs interact with the proteins. Understanding what’s going on at the cellular level, he says, will help tailor treatments for cardiac arrhythmia.

“It’s an exciting field and a fascinating topic,” says Dr. Ahern. “There is so much work that has been done that sets the standards high. I’m intimidated but also excited to contribute to the field, to have the opportunity to take things further.”

The HSFC McDonald Scholarship is awarded to the Foundation’s highest-rated New Investigator.



HSF researcher Dr. Kim Raine

“In public health research it’s not like you’re working away at a lab bench and then submitting a paper for a journal so that other people working in that area will read it and build on it. In public health you don’t have a controlled environment. It’s the real world out there.”

MANAGING CHANGE

Inactivity and overeating crept into our culture, creating an obesity epidemic – but a leading Alberta researcher is confident Canadians can change

Dr. Kim Raine doesn’t need to look far to see how much life has changed in a short time. Just as far as the mouse that sits beside her computer.

“In my job, I read and research a lot of papers and articles,” says the University of Alberta professor who has been named one of Canada’s 14 applied public health chairs. “As recently as five years ago I would walk to the university library, retrieve the journals from the stacks, make my notes or go to a photocopier and then walk back to my office. Now I don’t have to do anything more than click my mouse to get the same result.”

It is exactly these kinds of day-to-day changes – conveniences that have crept in over time – that have led to Canadians living more sedentary lives, says Dr. Raine. Combined with over-eating, they have fanned an obesity epidemic that, in turn, is sparking a boom in diabetes, cancer, heart disease, and stroke. “Over the past 20 years, we have doubled to tripled our rates of obesity.”

Dr. Raine’s appointment as applied public health chair marks an important step in the battle against obesity. The research chair is supported by the Heart and Stroke Foundation of Canada, the CIHR Institute of Population and Public Health, and the Public Health Agency of Canada.

“My understanding is that the chairs will take high-quality research – particularly intervention research – and help to integrate it into communities and Canadian society,” says Dr. Raine. “It means facilitating change in the real world.”

Dr. Raine’s research attempts to understand and counter the changes in our society that have contributed to creating this culture of inactivity and over-eating.

“For example, it’s one thing to understand that we’ve created a culture in our schools where, in order to get a new scoreboard, they have to enter into a contract with a soft drink company,” says Dr. Raine. “But then, how do you deal with that? My focus will be to take all the research we’re doing to see what interventions work best. Beyond that, how do we translate it to decision-makers who can then apply it on a larger scale?”

An intervention can be something as simple as making sure those high school vending machines also have fruit juices and water available.

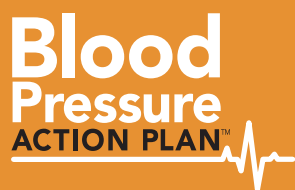
“We need interventions in the social environment to make it more acceptable to be active and eat a healthy diet,” says Dr. Raine.

While the task of overcoming obesity seems daunting, Dr. Raine is optimistic it can – and will – be done.

“I look at the tobacco reduction success of the past 30 to 40 years and think ‘Wow, who would have ever thought it would have been illegal to light up a cigarette in a public place?’ We can learn from the successes of tobacco. I just hope it won’t take us as long.”

FIND OUT MORE

- HSF patient resources include our website heartandstroke.ca, which includes the latest information on heart disease, stroke, resuscitation, and healthy living; heart-healthy recipes; and online self-management tools such the free Heart & Stroke Blood Pressure Action Plan™ (heartandstroke.ca/bp)
- Canadians can ask questions about heart disease and stroke prevention, risk factors, and healthy lifestyles; order HSF resources and brochures; and find out about HSF programs available in communities across Canada by calling the **Heart&Stroke InfoLine** (1-888-HSF-INFO)
- Visit hsf.ca/research regularly for updates on research competitions, previous competition results, and research program information
- Sign up for our monthly **research e-newsletter** at research@hsf.ca to get regular updates from the Heart and Stroke Foundation
- For more **HSF researcher profiles**, visit our website at heartandstroke.ca/putyourheartintoit



CANADA'S TOP 40 UNDER 40™ HONOURS FOUNDATION RESEARCHER

Dr. Jason Dyck, an investigator funded by the Heart and Stroke Foundation since 1990, has been named one of Canada's Top 40 Under 40™. The award celebrates the success of young Canadians who are already leaders in their field. Honourees are selected for their vision and leadership qualities, innovation and achievements, impact in their chosen field, community contribution, and growth and development strategies.

Dr. Dyck, from the University of Alberta, hopes to provide fundamental insights into how a protein called AMPK (AMP-activated protein kinase) functions in patients who have Wolff-Parkinson-White syndrome. This syndrome is characterized by abnormal fast heart rhythms and affects one to three people per 1,000.

In addition to gaining insights into how AMPK is involved in the development of this disease, this research will also provide fundamental insights into how AMPK works.



HSF researcher Dr. Jason Dyck