



Left to right: Dr. Keith Sharkey, Trudi Stickland, Dr. Manuel Hulliger, Karl Iremonger, Dr. Colleen Maxwell Photos: portraits by Trudie Lee Photography; lab photos by Dan Doll

From the Director



Dr. Samuel Weiss, Director
Hotchkiss Brain Institute

"Thanks to the support of the Institute's friends and partners we are making significant research advances in the lab, clinic and community."

Welcome to our second annual Report to the Community. Although the Hotchkiss Brain Institute is still young, our programs and initiatives are producing great results and translating research discoveries into practice. In this report we will share some of the Institute's success stories from the past twelve months.

The Hotchkiss Brain Institute has eight research programs that bring our members together to work on common problems, such as stroke, movement disorders, mental health, and epilepsy. We also have an education program that is developing new ways of attracting, supporting, and training the best graduate students and post-graduate fellows.

In addition to our core programs, we are looking towards the future by supporting four exciting new research initiatives. These new initiatives are innovative in their approach, as they cut across multiple disciplines. They allow our members to creatively address complex issues by bringing together experts from our Institute, other institutes in Calgary, and universities in other cities. Our new initiatives are addressing issues of great importance to the community:

1. Obesity: Dr. Keith Sharkey is leading a group that is investigating the role that the brain plays in obesity and developing new ways of tackling this condition.

2. Brain cancer: Dr. Gregory Cairncross is leading a team of cancer and diagnostic imaging researchers to more effectively identify and attack brain tumours.
3. Early life determinants: Dr. Bryan Kolb and a team from three Alberta universities are looking at the long term impact on health caused by events occurring around birth.
4. Clinical Research Unit: Dr. Samuel Wiebe is leading a group of clinical trial experts who provide support and guidance for the initial testing of new Institute discoveries and tools with patients.

This past year also saw the first site visit from our Expert Advisory Committee (EAC). This committee is made up of an international group of preeminent scientists and educators. The EAC strongly validated our efforts and progress to date and they offered us a number of excellent suggestions that will help guide our strategic planning and future growth.

The stories that follow in this report will provide you with a few examples of the remarkable activities taking place within our Institute. In just two years, our members, working together in programs and new initiatives, have made important advances on a number of fronts. I invite you to visit our website, www.hbi.ucalgary.ca, for updates on our research progress, news and events throughout the year.

The Role of the Workplace in Preventing Depression



Dr. JianLi Wang is partnering with local companies to help prevent depression in the workplace.

Nearly three million Canadians will experience depression at some time in their life. Depression cuts across society, affecting people of all ages and walks of life. It can lead to reduced productivity, lost work days, and increased employee turnover. Because depression most often strikes during productive working years, between the ages of 24 and 44, the impact on the workplace is significant.

Dr. JianLi Wang, an assistant professor in the

Departments of Psychiatry and Community Health Sciences, realized that the workplace also provides us with an opportunity to address and reduce some of the risk factors that can lead to depression. Maintaining a balance between various aspects of life, at both work and home, can increase one's overall wellness. Dr. Wang has initiated a new research project to develop and study the effectiveness of new workplace initiatives that enhance work-life balance with the specific goal of preventing depression.

Dr. Wang's project takes research into a 'living laboratory' – that is to the high rise buildings of downtown Calgary. To begin with, he sits down with employees and managers to evaluate their work environment and to find out what the employees need to create a more balanced and supportive workplace. Information that is gathered at this point serves as a point of comparison later on, to allow for the effectiveness of the project to be evaluated. Next, Dr. Wang's team provides education and awareness sessions to employees and managers, to equip everyone with mental health 'first aid' tools that are designed to improve work and home life balance. The

idea is to improve the work environment and to reduce the stigma associated with depression.

The project is starting with a pilot phase, which is being launched with two local companies. One of the pilot study participants is the Royal Bank of Canada's Alberta Region and 200 of their Calgary-based employees. An evaluation of the effectiveness of the education, awareness, and training provided through this program will take place at the end of the pilot study. Success will be measured by a reduction in lost productivity, sick days, and employee turnover due to depression. If the results of the pilot study are positive, the tools and techniques that have been developed and tested will be made widely available to other companies as a program for all of their employees.

This is one example of how our research creates benefits in our local community. The companies participating in this study will be helping their employees enhance their work-life balance. We believe that this will lead to a measurable reduction in sick days and an increase in productivity.

Improving Movement for Parkinson's Patients



Dr. Gerlinde Metz is finding ways to overcome the effects of Parkinson's disease on precise muscle movements.

Parkinson's is a progressive disease that can lead to a loss of movement and muscle control. Drug therapies and surgical treatments can help to reduce unwanted

movements and to regain lost mobility. In addition to drugs and surgery, activity and exercise programs have been shown to help Parkinson's disease patients maintain their ability to move.

While maintaining mobility is important for Parkinson's patients, being able to independently carry out daily activities, such as eating, writing, and grooming, is just as important to maintaining a high quality of life. The movement and muscle control required for these activities is different—it involves a number of small muscles in the hand and requires a high degree of accuracy in how the muscles are used.

Our Movement Disorders and Therapeutic Brain Stimulation Program is investigating new ways to improve movement and muscle control for Parkinson's disease patients. Program member Dr. Gerlinde Metz, an associate professor at the University of Lethbridge, carries out research in the facilities of the Canadian Centre for Behavioural Neuroscience (CCBN), located

at the University of Lethbridge. The CCBN facilities allow Dr. Metz to use different types of animal housing, ranging from single cages to multi-level 'condos', that provide varying degrees of physical activity and social interaction. She tests the role that living in an 'enriched environment', where different types of physical activity and social interactions with other animals are encouraged, has on the maintenance of movement control in an animal model of Parkinson's disease.

Dr. Metz found that the 'Parkinson' animals housed in an enriched environment scored significantly better at skilled movements such as walking and reaching for objects. Additionally, the 'Parkinson' animals in the enriched environment were able to grab small objects with greater accuracy.

For Parkinson's disease patients, these findings underscore the importance of remaining active, both physically and socially, to maintain the ability to carry out daily activities that require accurate muscle control.

Regenerating Nerves with Electronic Chips

Damage to nerves that run outside the spine and brain, for example down the arms and legs, is common and debilitating. These peripheral nerves are slow to regenerate and they can become the source of neuropathic pain. Peripheral nerve damage can have many different causes, including diabetes, infections, injury, and inflammation. Two Hotchkiss Brain Institute researchers are leading a revolutionary new approach to regrowing damaged peripheral nerves.

This initiative, the Electronic Axon Interface project, combines computer engineering with biology to help repair the 'wiring' of the nervous system. Previous work at our Institute has shown that individual brain cells can be combined with electronic chips, allowing communication to take place between the cells and the circuits of the chip. Other research has demonstrated that electrically stimulating damaged nerves, both those used for muscle control and those that convey

sensory information, can accelerate the regrowth process. If the precision control and small size of electronic chips could be utilized to directly deliver electrical stimulation to damaged nerves, even greater regeneration of damaged nerves might be possible.

Led by Dr. Douglas Zochodne, professor, Department of Clinical Neurosciences and Dr. Naweed Syed, professor and head, Department of Cell Biology and Anatomy, the Electronic Axon Interface project is working to develop new, flexible electronic devices that can be directly interfaced with damaged nerves. The intelligent electrical control of these devices can then be used to enhance the regeneration of damaged nerves.

The size and complexity of this project has resulted in a number of collaborations being established across western Canada. Experts ranging from electrical



Dr. Douglas Zochodne (left) and Dr. Naweed Syed (right) are studying the use of electronic chips for nerve regeneration.

engineers to neurosurgeons are working together on the Electronic Axon Interface. The team is prepared to quickly move their research discoveries into real world application to help patients suffering from peripheral nerve damage.

A Pregnancy Hormone to Treat MS



Dianne Rogers' MS symptoms improved during pregnancy. She is hopeful that prolactin will help all MS patients.

Photo credit: Calgary Herald

Multiple sclerosis (MS) impacts Albertans: the rate of people suffering from MS in our province is well above the national and international average. Interestingly, women are three times more likely to develop MS than men.

Women with MS who become pregnant often find that their MS symptoms improve during their pregnancy. A Hotchkiss Brain Institute graduate student, Chris Gregg, wondered what was causing this. He hoped that the

answer might point towards a new way of treating MS. By uncovering the specific cause of this temporary improvement, a treatment could be developed that would be helpful for all MS patients—whether they were pregnant or not.

To seek out these answers, a collaborative project was launched within the Institute, bringing together the hormone and stem cell expertise of Dr. Samuel Weiss' lab with the MS expertise of Dr. Wee Yong's group. The team's work focused on prolactin, a hormone that naturally increases during pregnancy.

Signals are carried through our nervous system at great speed, in part because of an insulating covering, known as myelin, that is formed on the nerves running through the body. MS attacks the myelin, which then leads to a slowing down or loss of signal transmission through the nervous system. This collaborative research team wondered if the natural increase in prolactin that occurs during pregnancy might somehow be repairing the damage to the myelin that is caused

by MS.

The results were even better than the team had hoped for. They were able to show, in an animal model of MS, that an increase in prolactin caused regrowth and repair of the myelin. This was particularly significant as it was the first time that regrowth of the myelin had been achieved. Prolactin activated the growth of stem cells that were already part of the nervous system and were waiting for a signal to jump into action. These stem cells were then able to mature into the specific type of cell that produces myelin and applies it to nerves. By increasing the number of myelin producing cells that are at work in the nervous system, prolactin repairs the myelin covering that has been attacked by MS.

A local MS patient, Dianne Rogers, whose symptoms improved while she was pregnant, sees hope in these research findings. "If this hormone could not only stop or delay the damage but actually alleviate that damage and repair that damage - how fabulous is that?"

Studying the Role of Stem Cells in Brain Tumours



Dr. John Kelly is studying the role stem cells may play in brain tumour development. Photo credit: AHFMR

Brain cancer is a devastating disease that strikes both young and old and it is most commonly seen in children aged 3 to 12 and adults 40 to 70 years of age. Coming up with better ways of detecting and treating brain cancer requires a multi-pronged research effort,

combining an understanding of the biology of cancer with an understanding of the brain. A recent partnership between the Hotchkiss Brain Institute and the Southern Alberta Cancer Research Institute, led by Dr. Gregory Cairncross, professor and head, Department of Clinical Neurosciences, is designed to do just that - to bring together cancer and neuroscience experts to uncover new clues in the fight against brain cancer.

This partnership, as part of the Integrative Brain Tumour Research Centre, is advancing research and patient care on a number of fronts. One project is building on a previous discovery by Dr. Cairncross that the genetic makeup of the cancer cells in a brain tumour can have a dramatic impact on how vulnerable the tumour is to chemotherapy. The centre is now developing sophisticated genetic analysis systems to allow for the rapid and precise evaluation of tumour chemotherapy and radiotherapy sensitivity. Additionally, in collaboration with Dr. Ross Mitchell of the Advanced

Imaging program, new methods of evaluating the treatment sensitivity of tumours based on magnetic resonance images are being developed.

At the same time, this research team is probing the very origins of brain tumours. An intriguing notion is that stem cells may play a role in the earliest stages of brain tumour development. Dr. John Kelly, a neurosurgery resident and Ph.D. student at the Hotchkiss Brain Institute, is studying the role that stem cells may play in the formation of brain tumours. He has been able to isolate cells from brain tumours that share many of the characteristics of stem cells, with one key difference: normal stem cells only divide when necessary and require specific stimulation to replicate. In contrast, the cells isolated from the brain tumours will divide without any stimulation. It could be that the ability of these cells to divide uncontrollably provides the 'seed' for the formation of tumours. Dr. Kelly's research is leading us closer to finding the 'initiator cell' in brain cancer - which will lead us to more targeted therapies for brain cancer patients.

Investigating the Brain's Control of Fever

Our body's response to infections involves communication between the brain and the immune system. As immune cells send signals back to the nervous system, the brain activates the body's defenses. To fight infections, one of the first responses by the brain is to initiate a fever, to make it harder for foreign bacteria and viruses to survive.

Dr. Quentin Pittman, a professor in the Department of Physiology and Biophysics, studies the interplay between the brain and the immune system. Of particular interest to Dr. Pittman are the effects that immune system challenges occurring very early in life can have later on, through to adulthood. Recent work by Dr. Pittman's research group investigated what happens in the adult years when the immune system is activated to fight infections at a very young age.

Dr. Pittman's group simulated the effects of both a bacterial and a viral infection in rats, across an age range equivalent to pre-term through newborn babies. They found that the immune response directed by the brain is programmed in dramatically different ways, depending on the nature of the original infection. On one hand, they found that there were narrow windows of time during early development when having an infection would have a long lasting effect. Activation of a newborn animal's immune system resulted in a reduced ability of the brain to respond to subsequent infections with a fever. This effect lasted into adulthood. On the other hand, Dr. Pittman's group found that this programming is specific to the type of the original infection. If the childhood infection was bacterial, the adult response to a bacterial, but not a viral infection was reduced. Similarly, if the early infection was viral, the adult response to a viral infection was reduced but the response to a bacterial infection was normal.



Dr. Quentin Pittman is investigating how infection and fever in newborns affect us as adults.

Understanding how our brain and body are programmed by early events, such as infection and fever, will allow us to come up with new ways to minimize or even reverse the negative effects of early life events.

Using fMRI to Help Epilepsy Patients



Dr. Paolo Federico (right) with graduate student, Cameron Cunningham (left) are looking at new ways of using advanced imaging tools to precisely locate the source of seizures.

Over 15,000 people in Canada learn that they have epilepsy each year. Their first line of treatment is usually one of the many drug treatments that are available to help control seizures. Some patients find that their seizures don't respond to prescription drugs and surgery is often the next treatment option. The goal with epilepsy surgery is to maximize seizure

control while minimizing any potential disruption of normal brain activity. So before surgery is considered, the area of the brain that serves as the start zone for the seizures needs to be located and precisely mapped out.

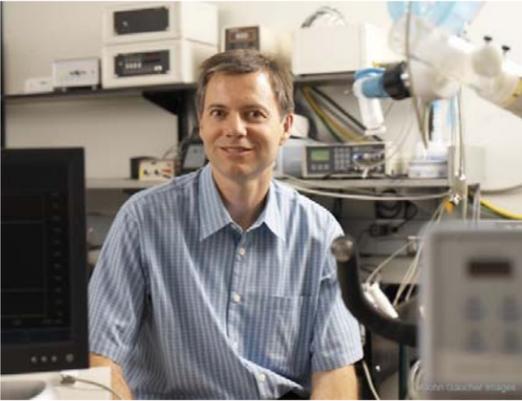
Epilepsy and Brain Circuits program member Dr. Paolo Federico, a neurologist and assistant professor in the Department of Clinical Neurosciences, carried out studies using functional magnetic resonance imaging (fMRI) to study seizure activity. The fMRI system in the Seaman Family MR Research Centre allows Dr. Federico to see and record, in real time, the areas of the brain that are being activated. Studying epileptic patients, who had seizures while being monitored in the MR scanner, Dr. Federico saw unusual brain activity patterns well in advance of the seizures starting. In some cases, this pre-seizure activity moved around to different areas of the brain, indicating that for some patients the start zone for their seizures may not be localized to one well defined part of the brain. This is an important finding for people being considered for

epilepsy surgery, as some patients may not have a well defined start zone that can be targeted with surgery.

Based on these findings, Dr. Federico realized that the tools available to map out the seizure sites in the brain could be improved. In collaboration with our Advanced Imaging program, Dr. Federico is developing new ways of measuring brain activity, by combining electrode-based electroencephalography (EEG) and fMRI. Both of these tools, on their own, map activity in the brain. By combining these two approaches, Dr. Federico's group is hoping to create a more powerful and precise way of locating the source of the seizures.

Because fMRI is carried out inside a giant magnet, the first step was to demonstrate the safety of having a patient with implanted metal electrodes inside the MR scanner. Dr. Federico's team has found that the electrodes are safe and they are proceeding with a clinical trial of this new technique, combining EEG and fMRI, to improve the results for epilepsy patients undergoing surgery.

Linking Stroke Risk and Sleep Apnea



Dr. Marc Poulin's efforts will be used to improve the outcomes for patients with sleep apnea. Photo credit: John Gaucher

Obstructive sleep apnea is a chronic condition that affects up to 4% of the Canadian population and causes brief interruptions in breathing during sleep.

These disruptions in breathing lead to reduced oxygen levels in the blood.

There is a strong link between sleep apnea and stroke. It is estimated that three quarters of the people who have had a stroke also have obstructive sleep apnea. This is significant because people suffering from sleep apnea who then have a stroke typically have a worse outcome than do stroke patients without sleep apnea.

Dr. Marc Poulin, associate professor, Departments of Physiology and Biophysics and Clinical Neurosciences, investigated the brain's ability to respond to oxygen levels in the blood by increasing the flow of blood to the brain. Dr. Poulin tested both sleep apnea patients and normal subjects to see if he could find a difference between these two groups.

Dr. Poulin and his team used advanced Doppler ultrasound equipment to monitor the regulation of brain blood flow in response to reduced oxygen levels. The team found that sleep apnea patients were not able to respond as effectively to reduced blood oxygen levels by increasing the flow of blood to their brain. When a stroke occurs, the oxygen levels in the brain are sharply reduced—so the ability of the body to respond and deliver more oxygen is critical.

Dr. Poulin's team also tested the sleep apnea patients after their condition had been treated. He found that after treatment, their brain blood flow response returned to normal. This underscores the importance for sleep apnea patients to get their condition treated. Not only will they improve their sleep and quality of life, they may be much better off should they have a stroke.

Clinical Research Unit: Discoveries into the Clinic

Moving research discoveries from the bench to the bedside is one of the fundamental goals of the Hotchkiss Brain Institute. Translating research findings into new ways of preventing, detecting, and treating health conditions often requires clinical testing to demonstrate safety and effectiveness. Small clinical evaluations are often the first step in this process.

One of the Institute's new initiatives, the Clinical Research Unit, was created to help our members move their research findings through an initial clinical evaluation with patients. This initiative, led by Clinical Research Director Dr. Samuel Wiebe, a professor and Head of the Division of Neurology in the Department of Clinical Neurosciences, provides a central resource for our researchers. Two critical elements of support are provided through this initiative; the expertise and

mentorship of Institute clinical trial specialists and small amounts of money to kick start these pilot studies. This support allows our members to establish the safety and effectiveness of their new discoveries, enabling them to eventually seek additional support from other agencies for larger clinical studies.

The Clinical Research Unit is currently supporting three projects: the early evaluation of therapeutic brain stimulation for 'untreatable' depression, led by Drs. Kiss and Ramasubbu; cognitive behavioural therapy for depression in early psychosis, led by Dr. Donald Addington; and the development of a rating tool to better identify candidates for epilepsy surgery, led by Dr. Nathalie Jette. The Clinical Research Unit is bridging a critical gap by enabling the early evaluation of new discoveries and ideas with patients.



Dr. Samuel Wiebe is helping our members to put research discoveries into clinical testing.

Reaching Out to the Community

The Hotchkiss Brain Institute regularly connects with the community. Over the past year, we held a number of successful events for the public. Some of these events were focused on specific neurological conditions, while others showcased the full spectrum of our programs and the work being done in our Institute.

In April 2006, we launched our Movement Disorders and Therapeutic Brain Stimulation program with the help of a number of distinguished guests: Health Minister Tony Clement, U of C President Harvey Weingarten, Calgary Health Region President and CEO Jack Davis, Canadian Institutes of Health Research President Alan Bernstein and country music singer Paul Brandt. Dr. Bernstein was on hand to announce a \$1.5 million grant to support a research project studying movement in Parkinson's disease patients. This project, a cross-country collaboration, is looking at how music and dance can help some Parkinson's patients overcome 'gait freezing' and regain lost mobility.

In June 2006 we hosted the third annual Margarete Wuensche lecture featuring Massachusetts Institute of Technology (MIT) President Dr. Susan Hockfield. She is the first woman and the first life scientist to lead MIT. Speaking to over 250 guests, Dr. Hockfield spoke on "*The Art of Translation: Science,*

Engineering, Health, and the Marketplace". Her presentation focused on the importance of collaboration as a way to move ideas and discoveries into real world application.

In March 2007, the Institute celebrated International Brain Awareness Week with two events. Our second annual Brain Science Day brought a group of students from Calgary and surrounding area high schools to the Institute. During their full day with us, the students visited a number of laboratories, three clinical research units, and the Seaman Family MR Research Centre. The students experienced 'hands-on' research activities and left with a better understanding of education and career opportunities in the neurosciences.

Our second event of the week, the Brain Awareness Open House, brought over 350 people of all ages to the Institute to learn more about the work being done by Institute members and a number of neurological and mental health community organizations in southern Alberta. In addition to the booths set up by the participating organizations and various children's activities, there were three interesting and engaging presentations: on multiple sclerosis, Parkinson's disease and early life brain development.



Dr. Susan Hockfield, President of Massachusetts Institute of Technology, with Dr. Greg Cairncross (left) and Dr. Samuel Weiss (right) gave the third annual Margarete Wuensche Lecture.

Our Institute connects with the community throughout the year with regular meetings of our Community and Partners Advisory Committee and its thirty dedicated members. This group provides us with feedback on the needs of the community, they help to guide our activities, and they communicate the Institute's progress back to the community at large.

This past year, our Institute achieved remarkable success through our research and education programs and our communication activities. We would like to thank our founding partners, the Calgary Health Region and the University of Calgary; our members; our donors; and the organizations that we work with. Their support has been critical to our success.