



Left to Right: Dr. Cam Teskey; Natalia Liapounova; and Dr. Keith Sharkey; Photos by: Charles Hope

Director's Message



Dr. Samuel Weiss, Director of the Hotchkiss Brain Institute.

Welcome to our annual Report to the Community. As we approach our four year anniversary as an Institute, we are taking a look back on our

accomplishments with an eye towards our future opportunities to make a difference in our community. This report highlights the activities of just a few of the more than one hundred members who make up our Institute.

The support we receive from members of the community and community-based organizations is central to our success and our ability to pursue new opportunities. All of our Hotchkiss Brain Institute (HBI) programs have received substantial support through philanthropy and non-profit organization funding. We are seeing the results of this support – from new, specialized research space that brings together scientists and physician-scientists working on new treatments to the recruitment of internationally recognized research leaders.

We listen to the needs of our community and develop programs and initiatives in those areas where our research strengths can be effectively applied towards finding new solutions. For example, we know that mental health issues are having a large and ever growing impact on our families, workplaces, and the community generally. As a result, we have been drawing on the mental health research expertise within the HBI and across the

university to develop a comprehensive research and education agenda.

Our research focus brings together a diverse group of mental health experts that are investigating new ways of identifying and preventing depression, psychosis, and addictions. Recent additions to the HBI, such as Dr. Glenda MacQueen, the new Head of Psychiatry who specializes in studying mood disorders, and Dr. Jean Addington, the new Novartis Chair in Schizophrenia Research, are adding additional strength to our research and education capabilities in this area. Recently, with help from our partner organizations, the HBI was able to solidify the creation of a new Mental Health Centre for Research and Education. This centre will house our clinical and community focused mental health experts and give them the support they need to make a difference in mental health outcomes.

This report features stories from our research programs and also highlights our community-based activities over the past year. For updates on our achievements we invite you to visit our website at www.hbi.ucalgary.ca throughout the year. Thank-you for your continued support of our Institute and I hope you enjoy our Report to the Community.

Guiding Nerves through Tubes

JONATHAN DAVIES



Dr. Rajiv Midha's goal is to improve the efficacy of guidance tubes.

Peripheral nerves are nerves that exist outside of the brain and spinal cord, such as nerves in your limbs. Imagine reversing paralysis in peripheral nerves by inducing them to grow through a tube - it's called a nerve guidance conduit and HBI member Dr. Rajiv Midha is helping to make it the preferred treatment for peripheral nerve injury.

Dr. Rajiv Midha was interested in peripheral nerve research even before he started medical school. Now

he's a neurosurgeon and a member of the HBI's Spinal Cord and Nerve Regeneration program where he's specializing in peripheral nerve repair in both laboratory and clinical settings. Specifically, he's researching nerve guidance conduits, and how to make them better.

Each year, 36,000 Canadians suffer peripheral nerve injury, a breakage in nerves that connect the spinal cord to muscles and sensory receptors. Traditionally, peripheral nerve damage was treated by nerve transplant, however, poor functional recovery and donor tissue problems have limited this approach. More recently, nerve guidance tubes have emerged as a viable alternative to nerve grafting. Tubes are essentially a scaffold that spans between the two sections of injured nerve, providing a clear path for nerve growth and reconnection. Presently, full functional recoveries are limited.

"Tubes are only now rivalling nerve grafts in terms of functional recoveries" says Midha. "Another problem" he says, "is that they're currently only useful for bridging gaps up to three centimetres, which is shorter than the average nerve injury".

It is clear that better solutions are needed. Midha's research takes two approaches. Firstly, his team is focusing on the application of two growth factors, NGF and FGF. They've found that the

optimal concentration of these two growth factors produces greatly enhanced nerve outgrowth. They're now extending the study to investigate whether introducing different cocktails of these and other growth stimulators over time can enhance this regeneration further. The second approach focuses on replacing the glial (Schwann) cells that retract after nerve injury. Midha uses skin-derived precursor cells - a type of 'limited' stem cell - that can be induced to grow into Schwann cells.

Once inside the tube, it is hoped that these progenitor cells will migrate to the wall of the tube surrounding the regenerating nerve, form Schwann cells, and begin producing and releasing the required growth factors.

Together, these approaches should provide an improved environment for the regenerating nerve, leading to better functional outcomes in peripheral nerve repair. Also, it will hopefully make nerve regeneration possible in injuries wider than three centimetres, where current treatments fail.

Nerve conduits aren't new technology but Dr. Midha is redefining their application. With the support of the Hotchkiss Brain Institute and funding provided by the Canadian Institutes of Health Research, his findings may not be too far from the clinic.

Boone Pickens Centre - Up and Running

LISA FLEECE



Mr. Boone Pickens (left) surprised his longtime friend Mr. Harley Hotchkiss (right) by announcing a bequest for the Institute.

After years of planning and much anticipation, HBI members, University officials and a few of our generous donors gathered together in June for the official opening of the HBI's new research space and offices.

Our new space, which is located on the first floor

of the Health Research and Innovation Centre, is in one of two new buildings at the Faculty of Medicine. The floor is named the *Boone Pickens Centre for Neurological Science and Advanced Technologies*, in recognition of a \$2.25 million donation from Texas businessman and philanthropist Mr. Boone Pickens.

For the official opening of the Centre, Reach! (the joint fundraising initiative between the University of Calgary and Alberta Health Services - Calgary Health Region) organized a luncheon for a small group of donors and local dignitaries. Mr. Pickens attended the event, held at the Faculty of Medicine, as the guest of honour. Mr. Pickens astounded the audience when he announced a bequest of an additional \$25 million to the HBI.

The *Boone Pickens Centre for Neurological Science and Advanced Technologies* consists of 2,800 m² of new laboratory space for HBI members and their

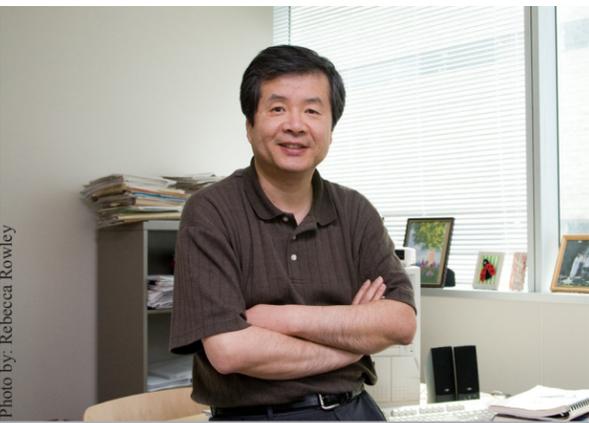
trainees. In fact, with the build-up of excitement, it didn't take long for researchers to move their high-tech equipment and settle into their new space. Research labs in the Boone Pickens Centre are combining technology and biomedical engineering to investigate various aspects of epilepsy, movement disorders, and spinal cord injuries.

Dr. Tom Feasby, Dean of Medicine, notes that generous gifts from donors, in this case Mr. Boone Pickens, along with support from funding partners, allows the Institute, as well as, the Faculty of Medicine to continue to achieve new levels of expertise. "The bottom line is - it promotes healthcare discoveries that will benefit Canadians."

When asked about the space, one trainee said, "Moving into a newer, modern facility, really allows us to live up to the world renowned research institute that the HBI is."

New Laboratories Strengthen Collaborative Research

LISA FLEECE



Dr. Bin Hu, co-leader of our Movement Disorders and Therapeutic Brain Stimulation program, is excited about the possibilities of the new laboratory space.

With the opening of the *Boone Pickens Centre for Neurological Science and Advanced Technologies* our Movement Disorders and Therapeutic Brain Stimulation (MDTBS) program was able to move into new, larger lab space which has provided numerous opportunities for research advancement.

Program co-leader Dr. Bin Hu explains that previously research in the MDTBS program was taking place between several buildings, making it difficult for scientists to collaborate. "But now," he continues with a smile on his face, "we are all together".

In its new configuration, basic science research labs are directly across the hall from clinical labs where human observations and trials take place. Such close proximity has literally broken down the "wall" that often separates basic and clinical research.

"Research between animals and humans is closely linked and our new space, which houses both types of research, promotes knowledge exchange." According to Dr. Hu, the nervous system's use of the senses to help control movement is investigated throughout the program at different levels using different techniques. In Dr. Hu's lab for example, they use animal models to search for brain circuits that help convert sound cues into motor commands.

Across from Dr. Hu's lab are two human laboratories where advanced technological and neurophysiological studies are being conducted with healthy people and movement disorder patients. For example, program members Ed Block, Geoffrey Melvill Jones, William Fletcher, and Bin Hu have developed a Pocket Mobility Analyzer which is being used by Dr. Oksana Suchowersky, a neurologist and program co-leader, to study how and why music and exercise can improve walking in Parkinson's patients.

The larger lab space also allows Dr. Zelma Kiss, a

neurosurgeon, to study Brain Pacemaker implants in Parkinson's patients and examine how the brain responds to music during natural walking. Previously, our MDTBS clinical researchers had to try and observe patient movements and gait in a small, crowded office using cumbersome technology.

"We can take the discoveries and technologies made in the lab, walk across the hall and share the information with clinical researchers. In turn, they can take results from their research with patients and share it with us. The cycle of research and research translation is fundamental for application in the real world.", says Dr. Hu.

He also comments that the new space will provide an enhanced learning environment for students and trainees. "They will have more opportunities to exchange ideas and research, thereby expanding their education experience."

Dr. Hu adds that the new labs continue to provide positive outcomes for the MDTBS program and have also resulted in cross-talk within the HBI. "Researchers in other HBI programs have found new opportunities to collaborate on projects by taking only a few strides to the Boone Pickens Centre. The possibilities are truly exciting."

Analyzing Seizures on a Computer Chip

LISA FLEECE

HBI member Dr. Michael Colicos and research colleague Dr. Evgeny Pavlov have created a new technology to examine brain cells or neurons during a seizure.

Although the concept seems like something from a science fiction novel, in actual fact the technology combines silicon computer chips with cells from the hippocampus; a region of the brain believed to be important in seizure initiation.

By growing the neurons on silicon chips and then applying photoconductive or light stimulation, they are able to induce seizure-like activities in the neurons. The seizure-like activities are then video recorded so researchers can observe the cells in minute detail.

Results of the stimulation also prompts the chip to communicate information back to a computer,

enabling the researchers to better comprehend what happens to neurons during seizures. Understanding how cells communicate before and after seizures will help them target their research. Dr. Colicos and his team can also observe why some cells die during seizures which is particularly important as it can hinder normal brain function or even impair the nervous system.

As a scientist and a father, Colicos's research efforts have taken on new meaning since his 2 year old daughter, Alexandra, was diagnosed with a seizure disorder. Thankfully, this cutting-edge technology will be useful for exploring new therapeutic solutions.

Dr. Colicos and his team hope to test new anti-epileptic therapies and see the effects they have on the cells.



Dr. Michael Colicos is using bio-computer technology to study the cause of neurological disorders like epilepsy.

Dr. Colicos is an Alberta Heritage Foundation for Medical Research Scholar.

Preventing Stroke Progression with MRI

NATALIE ST-DENIS



Dr. Shelagh Coutts believes that advanced imaging techniques will improve outcomes for stroke patients.

A new study challenges the common belief that patients suffering from a transient ischemic attack (TIA) or a minor stroke will likely go on to have a recurrent stroke in a new area of the brain. Instead, a high number of patients were found to suffer from a progression of damage that started from the original site of the TIA or minor stroke.

“Rather than experiencing a new stroke, this study

showed that 90 percent of TIAs and minor strokes continue to progress from their initial event for days following the onset of symptoms,” says Dr. Shelagh Coutts, HBI member and Assistant Professor of Clinical Neurosciences at the University of Calgary.

The study, which included 180 patients experiencing a TIA or a minor stroke, captured brain images using an MRI scanner within 24 hours of the attack. Patients were seen again 30 days later for a follow-up MRI, which clearly identified that most of the new lesions had progressed from the original injured site. For many of these patients, the progression of damage was ‘silent’, or without visible symptoms and could only be detected using MRI. Patients were seen again after three months for a final clinical session. The results from this study, *Recurrent Events in Transient Ischemic Attack and Minor Stroke*, were published in the journal *Stroke* in September.

“Brain imaging is an important tool to assess the amount of brain damage following a TIA or a minor stroke,” says Dr. Coutts. In fact, in the

future, neurologists may increasingly rely on brain imaging technologies, rather than the expression of symptoms, to dictate the best approach to treatment. “It may be that different medications are required to prevent progression of the symptoms rather than to prevent a recurrent stroke or event,” explains Dr. Coutts.

But before stroke neurologists can completely rely on brain images to predict further events and determine appropriate treatments, more clinical trials are needed. “The use of MRIs in stroke care isn’t mainstream yet,” says Dr. Coutts, “but right now it’s ideal for clinical trials as this technology can capture the location and rate at which brain damage is occurring.”

“Ideally we want to reduce or completely stop the progression of a stroke to avoid further brain damage,” says Dr. Coutts. “We certainly believe that advanced brain imaging techniques will facilitate diagnosis and eventually improve treatment and outcome of stroke patients.”

Commitment to Clinical Research Excellence

JONATHAN DAVIES

Clinical research is a multi-step process that is critical to medical discovery. It allows basic findings to be applied to patients in a clinical setting and then further translated into health care delivery and improved population health. However, the progression of new findings from bench to bedside and on to populations is not easy. It takes time, financial support, and substantial guidance and mentorship.

The HBI is committed to helping its members succeed with clinical research, which is why in 2006, under the supervision of Head of Neurology, Dr. Samuel Wiebe, the Clinical Research Unit (CRU) was born. Now in its third year, the CRU is expanding, and providing valuable resources for HBI members.

The CRU offers a number of services to HBI members. These include an internal peer review of grant applications to external funding agencies and monthly CRU methods rounds, where HBI members meet to discuss clinical research methodology related to their projects.

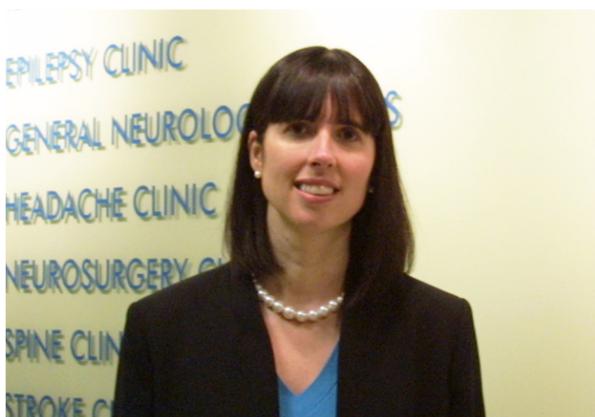
Last year, the CRU began a pilot funding program in which a number of HBI members were awarded a \$10,000 start up grant to pilot clinical studies before undertaking larger, externally funded projects. In the first round, three HBI members were awarded funding and have achieved success in their pilot projects. All three members attribute the initial funding from the CRU as a critical factor in the success of their projects.

Based on last year’s success, the CRU offered an expanded competition in 2008, in which four HBI members secured CRU pilot funding. These project leaders are; Dr. Brad Goodyear, an MRI specialist who is piloting a tool to assess Parkinson’s patients; Dr. Walter Hader, a pediatric neurosurgeon who is developing an epilepsy surgery registry; Dr. Sophie Macrodimitris, who is applying cognitive behavioral group therapy for epilepsy patients and Dr. Jianli Wang whose research focuses on individuals with depressive and anxiety disorders. The CRU anticipates a further expansion in 2009.

Currently, the CRU is involved in fourteen studies at different stages of development. HBI initiatives such as the CRU give our members the support they need to succeed in clinical research.

Migraines Associated with Mental Health Disorders

NATALIE ST-DENIS



Dr. Nathalie Jette is a Clinician Researcher in the Department of Clinical Neurosciences at the Foothills Hospital.

Nearly three million Canadians suffer from migraine headaches. Migraines are a common neurological ailment believed to be triggered by bloodflow changes in the brain. In order to provide better pain management for migraine sufferers, researchers are diligently trying to find out more information about the causes and symptoms of migraines.

HBI members, Dr. Nathalie Jette and Dr. Scott Patten recently completed a population health study to determine the prevalence of psychiatric conditions in people who experience migraines. Astonishingly, their study found that migraine

sufferers are twice as likely to experience mental health disorders during their lifetime.

The study, published in *Headache*, is the first ever national survey on migraines and mental health. Nearly 37,000 Canadians, coast to coast, were interviewed using a well-validated psychiatric diagnostic tool.

“Our study demonstrates that migraines and psychiatric conditions such as; major depression, bipolar and panic disorders, and social phobias are strongly associated,” says Dr. Jetté. “In fact psychiatric conditions occur more than twice as often in those that suffer from migraines.”

Drs. Jetté and Patten also found that individuals with both migraines and a psychiatric disorder experienced much poorer health-related outcomes and reported lower life-satisfaction compared to individuals suffering from only one of the conditions. Researchers also found that the association between migraines and psychiatric conditions are not related to socio-demographic variables such as age, gender or education levels. The results did, however, support the fact that women are more likely to have migraines than men.

“These results are important,” says Jetté, “because not recognizing psychiatric comorbidities (co-existing conditions) such as major depressive disorder in migraine sufferers could result in an increased burden to patients, their families, and society.”

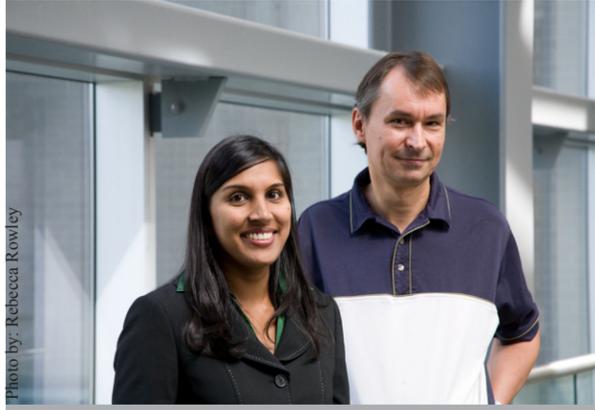
What the study doesn’t reveal, however, is why the association between migraines and psychiatric disorders exist. “Because the study relies on cross-sectional data we only sample the population at one place at one time, so we can’t tell which disorder came first and how exactly they are related,” says Dr. Scott Patten, who is also a psychiatrist with Alberta Health Services.

Further neurological studies investigating the underlying causes for migraines and psychiatric conditions are needed. Once these causes are determined and understood, researchers can fully explore the biological factors that both conditions share.

“Medications alone are often not sufficient to address these comorbid conditions,” says Jette. “We strongly believe that patients who suffer from both migraines and a psychiatric condition are best treated as part of a multidisciplinary program.”

New Members Help to Arrest MS

JONATHAN DAVIES



Dr. Shalina Ousman and Dr. Peter Stys are two of HBI's new recruits in 2008.

Multiple sclerosis (MS) is a key research focus at the HBI. Our Arresting MS program brings together a multidisciplinary team of more than 50 basic and clinical researchers and trainees who investigate the many different aspects of the disease.

This year the HBI welcomed two new additions to the Arresting MS program, Drs. Shalina Ousman and Peter Stys. Their unique research experience strengthens our program and is helping our team put the mechanisms of MS under the microscope.

For the past eight years, Dr. Shalina Ousman has been distinguishing herself in the neuroimmunology field, with research experience at McGill, the Scripps Institute, and Stanford. Ousman brings with her an impressive resume of skills in genetics, molecular biology, biochemistry, and immunology that enhance the Arresting MS program.

Dr. Ousman studies the brain's natural protective mechanisms and harnesses them in the fight against

MS. One such mechanism is a signaling molecule called alphaB-crystallin, a protein, that is normally found in the eye but increases in the brain in MS. Ousman found that this molecule has anti-inflammatory and neuroprotective properties.

"When we injected alphaB-crystallin into the brain, we found less immune cells being activated, and less immune cells migrating to the brain" she said.

Ousman, who is working alongside program leaders Drs. Wee Yong and Luanne Metz, recognized that joining the HBI was a great opportunity.

"I was impressed by the great research atmosphere," she said. "Everyone here is so motivated to find solutions."

Another major factor in her decision was the program's multifaceted approach to finding a cure for MS. This multifaceted approach includes a large contingent of potential collaborators within the Institute, including physicians who can help translate her discoveries into clinical realities.

The other new addition to the HBI is renowned clinical scientist, imaging expert, and newly appointed Dr. Frank LeBlanc Chair in Spinal Cord Research, Dr. Peter Stys. Although he started out researching neuronal death in stroke at Yale, Stys realized that there were many similarities between the way cells die in stroke and MS.

Stys now studies mechanisms of white matter injury, which is highly relevant to MS. One of his major discoveries is a signaling pathway between neurons and their coating, myelin, through myelin-bound

NMDA receptors. He showed that over-activation of these receptors, as may happen in MS, stresses and eventually destroys myelin. This discovery provides insight into not only MS, but other disorders such as stroke and spinal cord injury.

As his research progressed, Stys discovered technical limitations to existing experimental methods, so he set out to develop new techniques to investigate MS. One of those is an advanced laser imaging system that allows him to closely investigate interactions between living neurons and glia.

"Imaging is now a very powerful and rapidly evolving field," said Stys. "With these new live tissue imaging techniques, we can track the progression of white-matter injury in real-time".

Dr. Stys was attracted by a generous startup package that allowed him to set up a shared use imaging facility for the University of Calgary. This funding also gives him the freedom to pursue some of the "left field" projects that he is known for. However, this wasn't the primary motive behind his decision.

"I was genuinely impressed by the enthusiasm of the researchers here," he said.

No doubt, the recruitment of Drs. Stys and Ousman adds to the already high caliber roster of researchers here at the HBI. We are honored to welcome these two outstanding scientists to the Institute. The recruitment of these and other successful researchers, reflects the success and growth of the HBI.

Community Outreach - Year in Review

LISA FLEECE



High School students are tested in neuroscience at Calgary's first Brain Bee this past March.

The past year presented the HBI with opportunities to host a community event nearly every month. The following is a chronological look at some of this year's highlights.

In February, the HBI teamed up with UofC's External Relations to host a Science Café. Science Cafés are intimate and interactive science discussions that take place at an informal location. In this case, HBI members Dr. Michael Hill and Dr. Naweed Syed and about 100 people (with a thirst for beer and knowledge) gathered at the Unicorn Pub to discuss future treatments for brain injuries.

The second week in March is internationally

recognized as Brain Awareness Week. The purpose of this week is to advocate neuroscience research and the HBI hosts several events locally. Our annual High School Science Day offers a select group of grade 11 students the opportunity to spend a day at the Institute. Activities include tours of basic science labs and working clinics.

In addition to High School Science Day, the HBI partnered with the Alberta Heritage Foundation for Medical Research (AHFMR) to offer Calgary's first Brain Bee competition. Similar in format to a spelling bee, this live competition tests the neuroscience knowledge of high school students. The event offered cash prizes and an all-expense paid trip to the national event for the winner.

In May, the HBI hosted its 2nd Annual Mental Health Symposium. This year, the Mental Health Commission of Canada (MHCC) joined the HBI in presenting this event which focused on 'stigma' as the key theme. To view a video summary of the symposium check out the MHCC website at <http://www.mentalhealthstigma.ca>.

Our flagship lecture series, the Margarete Wuensche Lecture, commemorated its fifth successful year this past June. We marked the occasion by hosting

the distinguished Professor Sir John Bell, Regius Professor of Medicine, from Oxford University. By all accounts, the lecture was enlightening and the reception that followed was enjoyable.

Each summer, the HBI participates in the Heritage Youth Researcher Summer (HYRS) program. This program, offered by AHFMR, provides high school students summer work in a research environment. This past summer HBI's financial support enabled three students to work in HBI laboratories. Not only does this program provide much needed assistance for our HBI researchers, it also enlightens students about careers in neuroscience.

Finally, in November, we co-hosted another Science Café. The topic of this event was seizures and epilepsy and featured basic science researcher Dr. Cam Teskey and clinician-researcher Dr. Paolo Federico. Together, these doctors spoke to a large audience about current research taking place at the Institute; research that aims to improve the lives of those suffering from seizures disorders.

With events such as Science Cafés, it is our aim to continue to educate the public about the importance of neuroscience research.

 **HOTCHKISS
BRAIN INSTITUTE**

Hotchkiss Brain Institute
3330 Hospital Dr. N.W.
Calgary, Alberta
T2N 4N1



FACULTY OF MEDICINE | UNIVERSITY OF
CALGARY

Phone: (403) 220.3558
Fax: (403) 210.9382
Email: hbi@ucalgary.ca
Website: www.hbi.ucalgary.ca