



Left to right: Drs. Garnette Sutherland, Jos Eggermont, Zelma Kiss, V. Wee Yong, Jan Braun, John Remmers Photos: Trudie Lee Photography

From the Director



Dr. Samuel Weiss, Director

Photo: Trudie Lee Photography

Welcome to the Hotchkiss Brain Institute's first Report to the Community. This is an opportunity for us to share with you some examples of the important work being done by our institute's members. These stories highlight how we are striving to improve the health and wellness of our community through neurological and mental health research and education.

The strength of our institute is its members. We have over 100 member researchers who work in laboratories, patient clinics, and the community, looking for the next research breakthrough. Our members work together within nine research and education programs. These programs provide areas of focus for our members, allowing them to collaborate and quickly move new discoveries into real world application.

Connections with our community are vitally important to our institute and the work we do. Our institute's Community and Partners Advisory Committee provides us with a key link to the communities that we serve. Many of our activities and events are enhanced by the generous support of community members. Our education efforts reach beyond our institute and we invite the public to learn more about our activities through a number of awareness events that we hold throughout the year.

I appreciate your interest in the Hotchkiss Brain Institute. I hope that you enjoy the stories that follow. You may also want to visit our website, www.hbi.ucalgary.ca, to learn more about our programs, our members and the progress that we are making.

Advancements in Stroke Research

Attacking Stroke program leaders and associate professors with the Department of Clinical Neurosciences, Drs. Michael Hill and Andrew Demchuk and their team are playing a significant role in two new international research projects. Two multi-centre clinical trials, led by the stroke program team and funded by the National Institutes of Health (NIH) in the United States, will investigate new stroke treatment approaches.

The first clinical trial is studying the effects of high-dose albumin therapy - a plasma protein - as a new treatment for acute stroke. A second trial is comparing the use of the clot-busting drug t-PA delivered intravenously (the current standard of care) or

delivered via the patient's artery directly into the brain. The team is aiming to further decrease time-to-treatment and improve recovery for people with stroke with these two research projects.

Advancements in stroke research discovered by program researchers and physicians have already made a difference in the lives of stroke patients, including that of stroke survivor, Reid Hutchinson. By combining advanced imaging with the latest combination of treatments, Dr. Phil Barber, Department of Clinical Neurosciences, and the stroke team were able to stop a debilitating stroke event in its tracks last summer. This allowed Mr. Hutchinson to return to an active lifestyle just months after his visit to the hospital.



Mr. Reid Hutchinson (right), thanks Dr. Phil Barber (left) for his second chance at life after benefiting from the advancements made in stroke research.

Research Helps Migraine and Pain Sufferers



Dr. Gerald Zamponi's research is providing insights into possible new treatments for migraine and pain sufferers.

Effective pain relief is critically important for a number of health conditions. Many of the pain treatments that we rely on as mainstays were discovered decades or even centuries ago, yet many unknowns remain about

how they work. By better understanding how pain medication alters the transmission of pain signals, we can use existing drugs more effectively and develop new, targeted pain therapies that are even better.

Recent advancements in understanding how pain signals and our sensitivity to morphine can be altered within the nervous system were made by Dr. Gerald Zamponi, co-leader of the NeuroConnections program and professor, Department of Physiology and Biophysics, and his research team. Pain begins with sensory nerve cells or neurons called nociceptors. A pain message is transmitted along these neurons to the spinal cord and then on to the brain where it is perceived as pain. Morphine and other pain relieving drugs bind to receptors to block the message before it reaches the brain and is perceived as pain. Dr. Zamponi's team published their discoveries in the prestigious journal *Nature Neuroscience*, describing

the interplay between two components of a pain signaling complex that is found on nerve cells. One of the components is a channel that allows calcium to enter into the sensory neuron which in turn allows this neuron to relay its pain message to the brain. The second component is a receptor that acts like a lock, which can only be 'unlocked' or activated by a specific molecule that has been shown to have pain relief properties. The team found that when this molecular 'key' activated the receptors it led to the channels relocating to the inside of the nerve cells, where they could no longer allow pain signals to be transmitted.

Dr. Zamponi's research team is currently examining whether morphine suppresses pain signals through a similar mechanism. This could lead to both the more effective use of morphine and the discovery of new drugs to target and treat pain.

New Key to Treating Depression



Dr. Jaideep Bains' research discovery may uncover new therapies for depression.

Only 20% of the cells in the brain are nerve cells or neurons. The remaining 80% are glial cells, which were long thought to act as the 'glue' of the brain, simply supporting the neurons and playing no direct role in

transmitting signals through the brain. Researchers like Dr. Jaideep Bains, associate professor, Department of Physiology and Biophysics, have been challenging the dogma that glial cells are not active participants in the communication processes within the brain. This is leading to exciting results, including Dr. Bains' recent discovery that could help us better understand how new treatments for depression and other mental health conditions work.

When Dr. Bains and his team set out to study how norepinephrine, a chemical released in the brain when a person is stressed, acts on neurons, they realized that it doesn't work directly on the neurons. Instead, it acts first on glial cells, causing them to release a second chemical messenger (ATP), which then

strengthens the communication connections between nearby neurons. Some anti-depressant therapies target norepinephrine uptake, allowing this chemical messenger to have a longer lasting effect in the brain.

Uncovering how norepinephrine acts on glial cells, which in turn release a chemical that strengthens connections between neurons, provides an important clue about how some anti-depressant therapies may produce their effects. Dr. Bains' findings have led to new experiments designed to test a broader role for glial cells in brain function, including learning and memory. The hope is that these discoveries may uncover new therapeutic targets and lead to the development of new strategies for those living with mental health conditions.

Analyzing MS Treatments to Provide Better Care



Dr. Luanne Metz, director of the Calgary MS clinic is developing a research database to understand individual needs of MS patients and make better decisions, thus providing better patient care.

Alberta has one of the highest rates of multiple sclerosis (MS) in the world, for reasons that are not well understood.

The large number of MS patients from throughout southern Alberta who are treated at the Calgary MS clinic serve as a rich source of information on the way the disease affects patients and the effectiveness of the various treatments that are used to manage the disease. Arresting MS program co-leader and professor with the Department of Clinical Neurosciences, Dr. Luanne Metz, is developing an extensive clinical and research database to capture this information from the thousands of patients who are treated through the Calgary MS clinic. Analyzing this large pool of information will enable Dr. Metz and her colleagues to assess the effectiveness of various

approaches to managing MS, allowing them to quickly deliver improved care to each individual patient based on what they learn from the collection of patients who visit the clinic. Previously unseen factors that underlie MS and the way that it progresses will be identified through the analysis of this large pool of information. The ability to evaluate new treatments in the patient clinic will be enhanced through the capabilities of this database system.

This ambitious research project was made possible through a \$1million gift from Teva Neuroscience to the Hotchkiss Brain Institute's Arresting MS program.

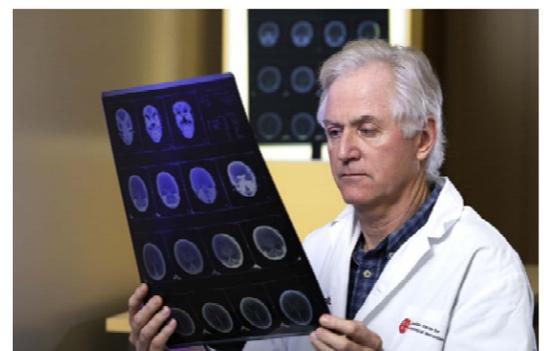
Stimulating Stroke Recovery

The interruption of the normal flow of blood to the brain during a stroke can cause extensive damage to critical brain areas. People who have suffered from a stroke often need to build new networks in their brain as they relearn both skills and movements that have been affected by the stroke. Dr. Bryan Kolb, a member of the Attacking Stroke program working at the University of Lethbridge, has been investigating ways to enhance the process of building new networks in the brain. The goal is to allow stroke survivors to recover more quickly and regain the skills and movements that they have lost because of the stroke.

Dr. Kolb believes that stimulation can help the brain build new networks, speeding up the rehabilitation

process and helping stroke survivors recover more quickly from a stroke. He has found that nicotine stimulates the formation of new brain connections and it has its effects on a large area of the brain, including the motor area that is critical for stroke recovery.

Dr. Kolb continues to investigate the effects of other types of stimulation on the enhancement of brain network formation, including environmental stimulation. The unique laboratory facilities at the Canadian Centre for Behavioural Neuroscience allow Dr. Kolb to test the effects of various stimulants on both the formation of new brain connections and the recovery of skills and movement following stroke. This will allow promising findings from this study to be transferred into human



Dr. Bryan Kolb, University of Lethbridge, has found a promising key to stroke recovery in nicotine.

patient studies so that new tools for stroke recovery can be made available to stroke doctors and their patients.

Exercise Benefits Parkinson's Patients



Dr. Oksana Suchowersky's study demonstrates the benefits of a home exercise program for Parkinson's patients.

Exercise has long been recognized as essential for managing symptoms and maintaining quality of life for Parkinson's disease patients.

Previous studies established that people with Parkinson's disease who continue to perform routine daily activities and follow a physiotherapist-supervised

exercise program have less difficulty initiating movements and maintaining balance and they enjoy improved dexterity. As their disease can make it more challenging to get around, many patients find it difficult to regularly attend and maintain interest in a supervised exercise program outside of the home.

Because regular, effective exercise therapy is as vital as the right medication for Parkinson's disease patients, Dr. Oksana Suchowersky, co-leader of the Movement Disorders and Therapeutic Brain Stimulation program and Head, Department of Medical Genetics, sought to investigate alternatives to supervised exercise programs for her patients. Dr. Suchowersky, in collaboration with Dr. Victor Lun in the

Faculty of Kinesiology, compared a supervised exercise program with an exercise program done by patients at home on their own. Whether in a supervised program or at home, they found that patients who regularly participated in either program showed improvements in gait, tremor, grip strength and motor coordination on tasks requiring fine control.

Our Movement Disorders and Therapeutic Brain Stimulation program members are continuing to explore the benefits of exercise and movement for Parkinson's disease patients. They have just launched a major, cross-country study that will look at the ways that dancing and music can help Parkinson's disease patients overcome their mobility problems.

Nausea is Controlled by the Brain



Dr. Keith Sharkey's discovery of a second cannabinoid receptor in the brain has garnered international attention and may help reduce the side-effects of cancer treatments.

Although they are unpleasant to experience, nausea and vomiting serve an important purpose as protection from dangerous foods and other toxins. These important reactions are controlled by the brain. Treatments for some diseases, such as cancer, can

cause severe nausea as a side effect. In order to ensure that patients can continue to receive life-saving treatment, it is equally important to make sure that the associated nausea is kept at bay.

Manipulating the body's own systems to reduce the nausea and vomiting caused by these treatments may be possible following a breakthrough finding by Hotchkiss Brain Institute member and professor, Department of Physiology and Biophysics and Medicine, Dr. Keith Sharkey. His team recently discovered a second cannabinoid receptor, CB2, in the brain and described in their findings in the prestigious journal *Science*.

Cannabinoids, such as marijuana, have received considerable attention over the past few years because of the potential they or their derivatives have as novel therapies, for example to treat nausea, chronic pain, epileptic seizures, stroke and multiple sclerosis.

Mimicking the body's own chemical messengers, cannabinoids have been shown to bind to a cannabinoid receptor, CB1, in the brain. CB1 receptors are located throughout the brain in areas that control body movement, memory and vomiting. Activating the CB1 receptors in these areas of the brain produces both the therapeutic and the mind-altering effects of cannabinoids.

Previously, CB2 receptors had been found on cells in the immune system, where they have an anti-inflammatory role. The discovery of the CB2 receptor in the brain by Dr. Sharkey and his group may allow us to use the body's own chemical messengers, endocannabinoids, to control the action of these receptors in the brain. This could allow us to reduce the side-effects of treatments for cancer and to develop new treatments for chronic pain, epilepsy and other brain diseases while avoiding the mind-altering effects associated with cannabinoids and the CB1 receptors.

Testing New Treatments for Spinal Cord Injury

After a fall, car accident or other injury that damages the spinal cord, tissue damage to the spinal cord continues to develop for days and weeks after the initial accident. This compounds the injury and makes rehabilitation more difficult or impossible. Spinal cord injury is a leading cause of disability for young adults and there are approximately 1200 spinal cord injury cases per year in Canada.

A key spinal cord regeneration project in our institute involves research that began three years ago in the laboratory of Dr. Wee Yong, co-leader of the Arresting Multiple Sclerosis program. A new therapy discovered by Dr. Yong, that has benefited patients with multiple sclerosis, is now being tested as a treatment for spinal cord injuries.

In a clinical trial overseen by neurosurgeons in the Department of Clinical Neurosciences, Dr. John Hurlbert and Dr. Steve Casha of the Spinal Cord and

Nerve Regeneration program, the antibiotic minocycline is being evaluated for its ability to reduce damage to the spinal cord after a traumatic injury. Dr. Yong's earlier research demonstrated that minocycline acts as a neuroprotective agent, preventing nerve cells from dying after spinal cord injury and reducing the extent of progressive tissue damage. Much of the nervous system damage and paralysis that follows spinal cord injury is caused by substances from the patient's own immune system that enter the spinal cord after the trauma takes place. When minocycline is administered shortly after injury, it appears to partially prevent this from taking place, diminishing the scope of the injury.

The interactions that regularly take place in our institute between researchers in the laboratory and the clinic are leading to ground-breaking advances for people suffering from spinal cord injuries.



Dr. John Hurlbert, right, is studying whether minocycline reduces the damage caused by spinal cord injury.

Cooling the Brain to Prevent Further Injury



Dr. David Zygun and STARS air ambulance crews are working together to protect the brain using hypothermia for head traumas.

Lowering the body temperature by about one degree within a few hours of a stroke or heart attack has been used to reduce brain damage and the risk of death. In the operating room, hypothermia has been used to give doctors more time to perform longer and more complex operations on the blood vessels supplying the brain. Cooling the body is now being tested for individuals suffering from traumatic brain injury to protect the brain from further damage. Hotchkiss Brain

Institute member Dr. David Zygun, Department of Critical Care Medicine, is placing Calgary at the forefront of this experimental therapy for head trauma. Every year in Canada, over 11,000 people die as a result of a brain injury. It is the leading cause of death and disability among children.

Leading one of two teams in the world studying the treatment of head traumas with hypothermia therapy, Dr. Zygun is working with the STARS air ambulance crew to find out if quickly cooling down brain injury patients improves their chances for survival.

Hypothermia therapy involves cooling the body a few degrees to help control brain swelling and ease pressure on the brain, which can also lead to a secondary injury if left unchecked. After a head trauma, the brain produces certain chemicals that are harmful to the injured tissues and it is believed that moderate hypothermia may slow or prevent the production of these chemicals. Hypothermia also decreases the amount of oxygen needed by the brain, which may

provide some protection during this critical period, allowing the brain and other vital organs to heal. However, the clock starts ticking as soon as the injury occurs. The longer individuals are left at their normal body temperature following a head trauma, the less likely the therapy will work.

This is why the STARS air ambulance crew is playing a key role in the study. The crew will begin the hypothermia treatment prior to the patient's arrival to the emergency room. Brain injury victims will have their body temperature reduced as they travel to the hospital. Once at the hospital, patients will continue with the cooling therapy to reduce the swelling in damaged tissues and give the brain an opportunity to repair itself.

By treating the patient immediately after the injury, Dr. Zygun and his team are hoping to give individuals with brain injuries a higher chance of survival and a life without a severe disability.

Improving the Safety of Shift Workers



Dr. Michael Antle studies the body's internal clock to improve the health and safety of shift workers.

Nowhere are the effects that lifestyle has on sleep more evident than in shift work. Nearly 20% of the workforce in industrialized countries are employed in shift work, which often requires them to drastically change their sleep habits.

When a person works shift or night work, their body gets out of sync. This disorientation can lead to feelings of fatigue and disorientation. Human functions tend to follow a daily cycle of circadian rhythms that are controlled by the body's internal clock. Sleeping, waking, digestion, body temperature, blood pressure and pulse are all regulated by this internal timepiece which is set for high activity during the day and low activity at night.

A person can usually adjust to working a new shift, if the change is permanent. Operating on a 24-hour cycle, circadian rhythms will remain constant once the body adapts. Adjusting to a schedule change may take a while, but it is possible. Because most shift workers frequently change shifts, their circadian rhythms are disrupted. This can lead to fatigue, errors, accidents and injuries. The issue becomes more alarming when you consider that shift workers are often employed in

the most dangerous jobs, such as firefighting, law enforcement and security.

Imagine being able to easily adjust to a changing work schedule. Dr. Michael Antle, a Hotchkiss Brain Institute member with the U of C's Department of Psychology, has brought us closer to doing just that. His recent discovery illustrated that the 20,000 time-keeping cells located in the human circadian clock are organized in a complex network of groups that perform different functions. By understanding how this internal timepiece works, Dr. Antle is hoping to find a way to reset the circadian clock when a shift in schedule occurs, so that workers can remain alert and work effectively. Experimenting with a technique that involves resetting this timepiece by altering neurotransmitters, he aims to be able to easily move people ahead eight hours, improving the health and safety of shift workers and those around them.

Pregnancy Experiences and the Newborn Brain

The ongoing development of our brain and our behaviours can be influenced by events that occur before birth. Experiences that occur during pregnancy play a key role in future brain development and brain injury recovery. Dr. Robbin Gibb at the University of Lethbridge is studying how exercise and stimulation for the mother during pregnancy can affect babies' intelligence and the ability to recover from early-brain injury. Her research has demonstrated that exercise along with an interactive and social environment for the mother during pregnancy can lead to babies that have an enhanced ability to solve problems. And for babies that receive early brain injury, their prenatal experience can make a difference in how they recover.

A newly launched Hotchkiss Brain Institute research initiative on perinatal determinants of brain and mental health will allow Dr. Gibb and a team of researchers from across Alberta to advance our understanding of how brain development is affected by experiences before birth. Funded by the Alberta Heritage Foundation for Medical Research, this initiative will bring together researchers at the Universities of Alberta, Calgary, and Lethbridge. They will be studying how experiences before birth can affect development through childhood and how we can reverse the effects of negative experiences that occur before birth, to ensure the healthy development of our children.

Dr. Robbin Gibb is studying how exercise and stimulation for the mother during pregnancy is helping babies recover from early brain injuries.



Reaching Out to the Community

The Hotchkiss Brain Institute provides the public with updates on our research advances through a variety of activities and events that take place throughout the year. To ensure that our research and education efforts are serving the community, the institute receives input from a group of business and volunteer leaders from Calgary and area. This group, the institute's Community and Partners Advisory Committee (CPAC), helps to guide our activities and communicate the Hotchkiss Brain Institute's progress and impact to the general public.

Over the past year, the institute has worked with our founding partners and a number of community service organizations to reach out to the public. This has taken place through a number of events and activities including a play, lectures, newsletters, a redesigned website and features in the local media.

Our programs are having a real impact on patient care. At a number of our events we've heard from patients who have benefited from the research advances being made by our members. We've shared with the general public the progress we are making in the areas of spinal cord injury, stroke, multiple sclerosis and Alzheimer disease.

Rick Hansen and Premier Ralph Klein helped launch the Spinal Cord and Nerve Regeneration program with news of a \$1.5 million award from the Neuroscience

Canada Foundation. Community leader and multiple sclerosis patient Diana Joseph of Wen-Di Interiors spoke at the Arresting Multiple Sclerosis program launch about how research is improving multiple sclerosis patient care in southern Alberta. The program received over \$3 million in new funding for research projects. At a third launch event, the impact of the Attacking Stroke program's research excellence was exemplified by stroke survivor Reid Hutchinson's tale of rapid recovery and the announcement of two \$20 million international clinical trials funded by the National Institutes of Health in the United States.

The second annual Margarete Wuensche lecture featured Dr. Oliver Sacks, a world-renowned neurologist and author. Speaking to over 700 guests, Dr. Sacks talked about his patients' transformation and survival in the face of severe neurological challenges in a lecture called "Neurology and the Soul".

The Hotchkiss Brain Institute celebrated International Brain Awareness Week with a series of events for the local community and Calgary high school students. With the aid of CPAC members, an evening designed for caregivers and families living with Alzheimer Disease was organized and attended by over 200 people. This evening featured a moving one act play about the impact of Alzheimer disease on a man and his family, followed by a series of short research presentations.



A scene from "Closer and Closer Apart", written by playwright Eugene Stickland and featuring Grant Reddick as Joe and Maureen Jones as Melody.

The Hotchkiss Brain Institute members also hosted 15 students from Calgary area high schools for the 1st Annual Brain Science Day. Visiting a number of research labs and the Seaman Family MR Research Centre, the students got hands on lab experience and discovered what it's like to be a neuroscientist.

As it is critical to our success, the institute is grateful for the support provided by our founding partners, the Calgary Health Region and University of Calgary; our members and their academic departments; our donors; and the community service organizations that we work with.