HOTCHKISS BRAIN INSTITUTE

REPORT TO THE COMMUNITY 2016-2017

UNIVERSITY OF CALGARY

OUR MISSION

The Hotchkiss Brain Institute inspires discovery and applies knowledge towards innovative solutions for neurological and mental health disorders.

Feature story: An HBI-led Canadian clinical trial has shown that minocycline, a common acne medication, can slow the progress of relapsing-remitting multiple sclerosis (MS) in people who have experienced first symptoms. Learn how this discovery will help MS patients worldwide on page 10.

REPORT TO THE COMMUNITY
TABLE OF CONTENTS

MESSAGE FROM THE DIRECTOR

It is my pleasure to present to you our annual *Report to the Community*. I am particularly excited to have the opportunity to share this selection of incredible stories, which highlight the recent achievements of some of our best and brightest researchers and trainees.

At the HBI, we shoot for the stars. We are bold, we take risks, and as a result, our discoveries and successes have real impact that can be felt around the world.

But we don't do it alone. The HBI is an institute that was created in partnership with the community, and we continue to grow and thrive because of that ongoing partnership. We have been able to invest support from our community to attract and train the very best scientists, clinician-scientists and trainees, test the best ideas and ultimately change clinical practice and improve lives.

In our feature story, you will read about two of our most celebrated multiple sclerosis (MS) researchers: V. Wee Yong, PhD, and Dr. Luanne Metz. Their landmark discovery – an inexpensive acne medication that is effective in treating early-stage MS – will change the face of MS treatment worldwide by making it easier and more affordable. This work, which was 18 years in the making, was published in the *New England Journal of Medicine (NEJM)* – the top medical research journal in the world. This is the second HBI paper in just two years to be published in the *NEJM* – an impressive achievement and a true testament to the quality of work being done by our investigators.

I would like to acknowledge the Westman, Joseph and Swartout families, who have been dedicated supporters of MS research at the HBI for many years, as well as the numerous other generous donors and the Multiple Sclerosis Society of Canada, who further contributed to this remarkable breakthrough. Without this commitment from our community, life-changing discoveries like this one would not be possible.

Although we are proud of our success in receiving competitive funding and government grants, it is the support we receive from our community that keeps us ahead of the curve. Because of philanthropy, our researchers can test new therapies before grants are even in place – we can reach further, go faster and be outrageous in our endeavours. We have an edge that is allowing us to make a real change in the brain and mental health landscape.

In this issue, you will also read about some of our outstanding young investigators. I am proud of the exceptional cadre of young people that we have here at the HBI, they are the future of brain and mental health research and their achievements are already demonstrating real impact.

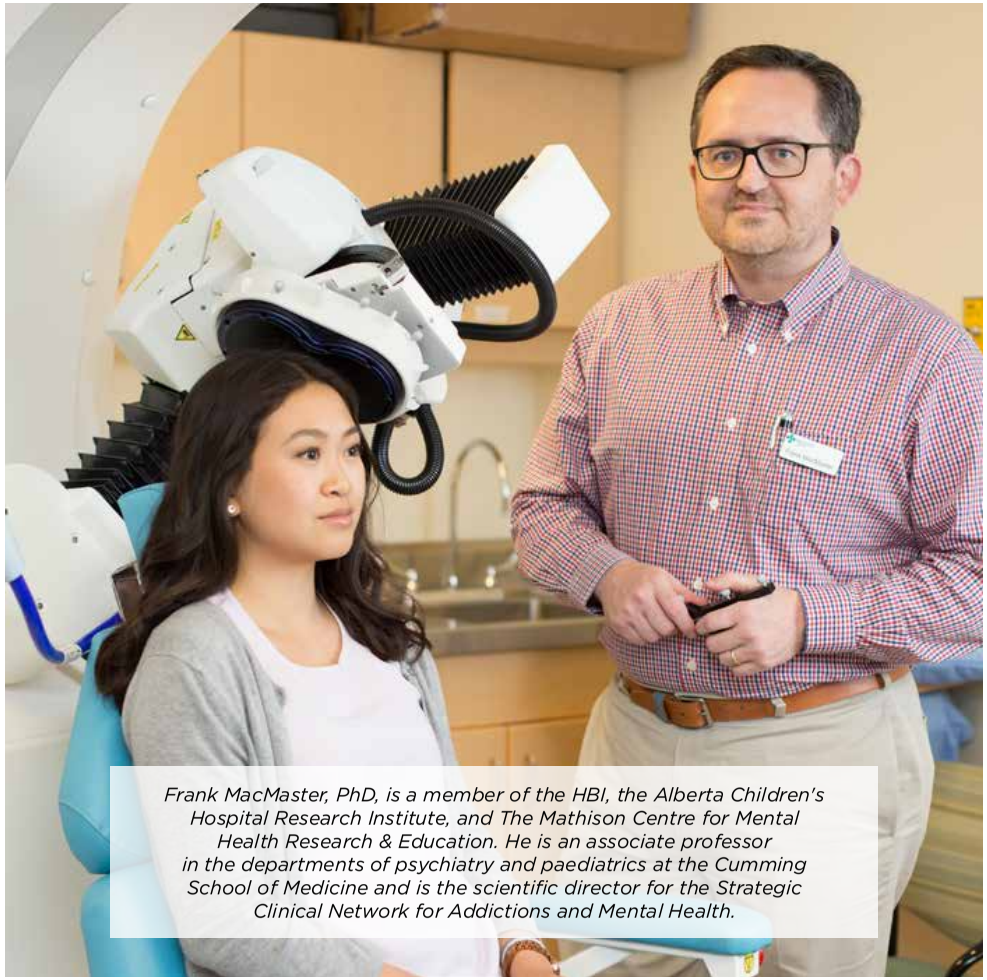
One example is Tuan Trang, PhD, and PhD candidate Nicole Burma, who have recently made a groundbreaking discovery in the field of pain research. Their work – which was published in the prestigious journal *Nature Medicine* – has discovered that an existing drug is effective in treating opioid withdrawal symptoms in rodents. Opioid use and abuse is a significant social, health and economic issue in Canada, and this research is currently being translated into a clinical trial with the Calgary Pain Clinic. Community support for these two young researchers through donor-funded start-ups and scholarships is an investment that is already yielding great returns and is sure to have an impact on one of the great challenges facing society today.

These are just two examples of how our community is enabling researchers and trainees at the HBI to test their ideas in a way that breaks down barriers and catalyzes discovery. World-class recruitments, bold pilot studies, and investments in innovative people and projects, create a rich environment that ultimately leads to major change in brain and mental health care.

It has been my pleasure to serve as the inaugural director of the HBI for the past 12 years. As you may have already heard, I will be moving on from the HBI to take on a new role as the scientific director of the Canadian Institutes of Health Research (CIHR), Institute of Neurosciences, Mental Health and Addiction (INMHA). It's a big role, with great responsibility, and I am feeling both humbled and energized by this new career direction and national brain research mandate.

When Harley and I came together to create the HBI in October 2004, we did so with a vision for a centre that would bring together Calgary's scientific and medical minds, to discover fundamental underpinnings, create new knowledge and better inform health care delivery for diseases and injury of the brain, spinal cord and peripheral nerves. I think we are doing just that. I look at what the institute is today and I know that Harley would be proud – as am I – of what we have all been able to accomplish together.

I thank you as always for your ongoing commitment and hard work towards our vision of healthy brains for better lives.



Frank MacMaster, PhD, is a member of the HBI, the Alberta Children's Hospital Research Institute, and The Mathison Centre for Mental Health Research & Education. He is an associate professor in the departments of psychiatry and paediatrics at the Cumming School of Medicine and is the scientific director for the Strategic Clinical Network for Addictions and Mental Health.

NON-INVASIVE BRAIN STIMULATION SHOWS PROMISE IN TREATING ADOLESCENT DEPRESSION

WORLD-CLASS TECHNOLOGY IN CALGARY IS STIMULATING NEW RESEARCH ACROSS NORTH AMERICA

Most kids spend elementary school dreaming of becoming an astronaut, an acrobat, or perhaps a taste-tester at a chocolate factory. Frank MacMaster, PhD, spent his formative years thinking about people's brains.

"I had a close friend in elementary school who had a brain tumour on his frontal lobe," he says. "When he came back after they'd taken the tumour out, he was a completely different kid. He went from being a regular kind of guy to being brash and impulsive."

Something struck MacMaster at that early age. He saw how a change in the brain can affect the course of someone's entire life. That curiosity and compassion helped guide him to where he is today, trying to crack the codes between the brain and behaviour. Specifically, he studies depression in youth.

"Depression is actually quite common," he says. "It's as common in teenagers as it is in adults. This is not the typical teenage blues; it really is clinical depression. It's just as harsh and as difficult as it is for adults."

That pain is starting to lift for some patients, thanks to a study MacMaster and fellow HBI member Dr. Adam Kirton have been conducting over the past four years using a treatment called Transcranial Magnetic Stimulation (TMS). TMS is a non-invasive way of stimulating small regions of the brain using magnetic fields. It's been used to effectively treat depression in adults, and MacMaster wanted to see if it could help teenagers as well. In particular, he's looking at patients whose depression isn't well controlled by medication. Although not yet published, the results so far have been better than expected.

"Clinically, our results are suggesting an effectiveness that may actually be better than adults," he says. "Our initial results show a batting average of about 65 to 70 per cent for treatment responders, meaning they had their symptoms cut in half. For a lot of kids who come through the study, they'll go from the severe depression range and down towards at least mild range and some into even the normal range."

MacMaster tells the example of one patient who finished treatment right before the Christmas holidays. She was doing so well, she went out to get a part-time job so she could buy presents for her family.

"This is someone who hadn't left the house much in the past two years," he says. "It doesn't work for every single person but for those it does work for, it's pretty profound."

The next challenge, he says, is to identify those potential success stories before the treatment even starts. The world-class brain imaging platforms available here in Calgary have given MacMaster a leg up on that search.

"We're actually hot on the trail of what we think might be a nice set of biomarkers that help predict response," he says. "This is important, because for mental health, there are no clinically useful biomarkers yet."

Based on results gleaned from their study, an American company is launching a large, randomized, controlled trial on the safety and effectiveness of TMS in adolescents in the hopes of making it available to more patients.

"We threw a little rock into a pond here in Calgary," says MacMaster, "and it's having ripple effects all over North America."

EXISTING DRUG EFFECTIVELY RELIEVES OPIOID WITHDRAWAL

CREATIVE APPROACH REVEALS THERAPEUTIC TARGET IN RODENTS AND LEADS TO HUMAN CLINICAL TRIAL

For Tuan Trang, PhD, it was more than just a love of science that inspired him to pursue a career in research.

As the child of Chinese immigrant parents who came to Canada in the 1980s, he was encouraged to pursue higher education as a path to success. Once in university, he found himself particularly drawn to the creative element of scientific research.

“Science isn’t all about precise measurements,” Trang explains. “It’s how you think about things, taking what might sound like a crazy idea and using that to creatively approach a question.”

Trang researches pain, and currently his work is looking at opioids – a potent class of drugs including morphine and fentanyl – that are used to treat pain. Stopping opioid use can result in severe withdrawal symptoms, which is a key contributor to continued use.

“Creative approaches can help us understand how things work and how different pieces fit together."

“Opioid withdrawal is aversive, debilitating and can compel individuals to continue using the drug in order to prevent these symptoms,” explains Trang. “Having the ability to alleviate withdrawal symptoms could have important implications for patients that may wish to decrease or stop their use of these medications.”

Trang and his team, including PhD candidate Nicole Burma, recently explored the underlying causes of opioid withdrawal and discovered an important target in the spinal cord that is responsible for producing withdrawal symptoms in rats and mice. They were then able to identify an existing Health Canada approved drug that acts on that target to prevent withdrawal symptoms from occurring. They published their research in the prestigious journal, *Nature Medicine*.

Prior to this work, the cellular mechanism of opioid withdrawal was not well understood, hampering the search for therapeutic treatments. Trang explains, “the focus has historically been on neurons themselves, so in our study we looked instead at key immune cells in the nervous system, which is something that hasn’t been explored before.”

Tuan Trang, PhD, is a member of the HBI and an assistant professor in the Faculty of Veterinary Medicine and at the Cumming School of Medicine, University of Calgary.

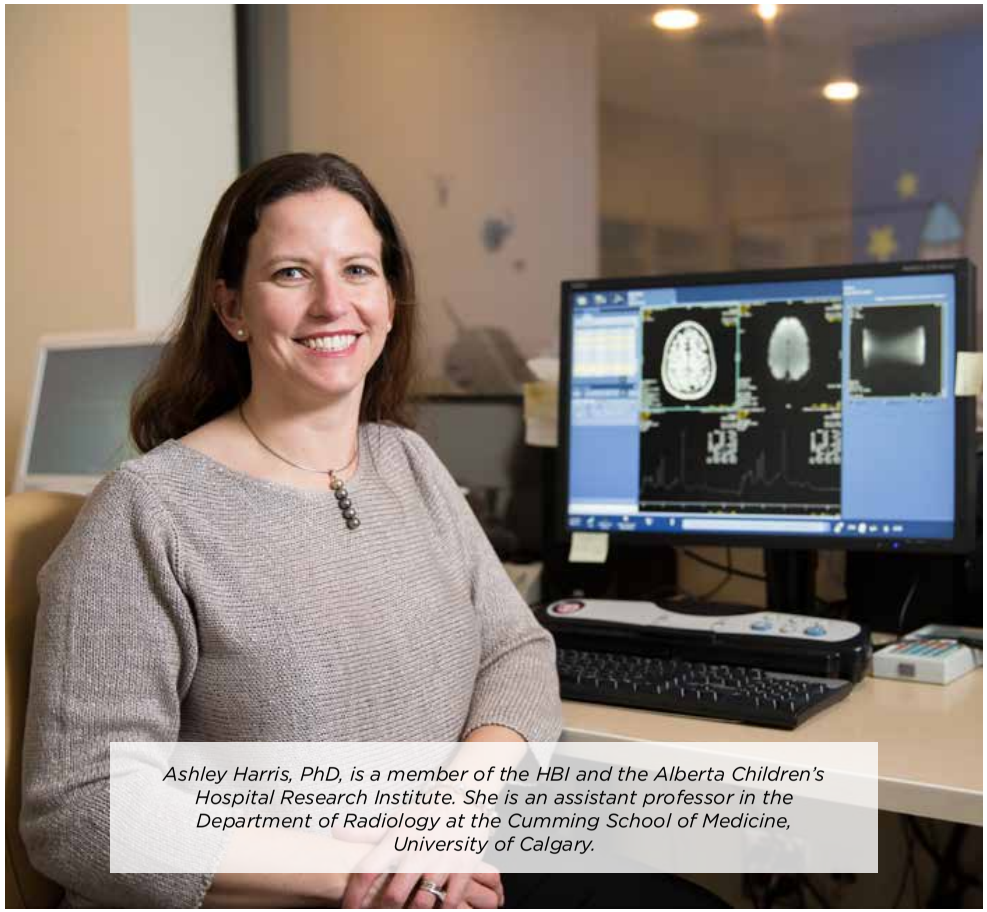
Nicole Burma is a PhD candidate at the HBI in the Cumming School of Medicine, University of Calgary..

The discovery represents a shift in understanding how withdrawal occurs. Given the strong reliance on opioids to control pain, as well as the current opioid crisis in Canada, this work could have tremendous therapeutic potential.

With such encouraging preclinical results, the researchers started looking at how to translate this discovery to humans. They are quickly moving forward with the Calgary Pain Clinic to design a clinical trial.

For Trang, this work further solidifies the value he places on thinking outside the box.

“Science isn’t all logical and linear,” he says. “Creative approaches can help us understand how things work and how different pieces fit together. That fundamental knowledge is an essential component to being able to translate our findings and the potential impact of that can be immense.”



Ashley Harris, PhD, is a member of the HBI and the Alberta Children's Hospital Research Institute. She is an assistant professor in the Department of Radiology at the Cumming School of Medicine, University of Calgary.

MAGNETIC RESONANCE SPECTROSCOPY TAKES A DEEPER LOOK INSIDE THE BRAIN

ADVANCED IMAGING TECHNIQUE COULD HOLD ANSWERS TO HEALTHY BRAIN DEVELOPMENT, AS WELL AS BRAIN INJURY AND DISEASE

For a self-described prairie girl, Ashley Harris, PhD, has travelled a long way to come back home. She returned to Calgary last year after a professional journey that took her to Halifax, Cardiff, Wales, and most recently, Baltimore.

"It's interesting what you miss from home when you're away," she says. "I love the mountains, but I also love the big open skies of the Prairies. And it might be cold in Calgary, but it's sunny!"

When Harris was recruited back to the University of Calgary, she brought with her an expertise in a developing form of neurotechnology that aims to provide more detailed answers about injury and disease in the brain. Magnetic Resonance Spectroscopy (MRS) takes imaging to the deepest level, allowing researchers to look at and compare metabolites – small molecules formed when proteins break down – in the brain.

"By looking at those and comparing different groups you can start to tease out some of the underlying differences in the mechanisms of injury," Harris explains. "The hope is to get right to the targets for treatment, or at least to understanding what's going wrong in the brain."

The method may provide more details, but getting the results can often be a challenge. Part of Harris's role is to make MRS more accessible to other researchers, by developing ways for them to detect and interpret the subtle differences this technology can expose.

"What I'm really motivated by is developing these rigorous methods to actually be useful in understanding healthy development and disease conditions," she says.

Harris is currently using MRS to pinpoint chemical differences in the brains of patients with developmental disorders such as autism, Tourette Syndrome and ADHD, and how those differences may explain changes in behaviour. By detecting what's happening to the brain at a tissue level, Harris hopes to better understand why some treatments work and others don't. This broader knowledge is also being applied to traumatic brain injury and concussion.

"People who have long-term symptoms compared to people who recover well, their images look the same on a regular MRI scan," she explains. "I'm hoping, by looking at the tissues, that the differences in the underlying neurochemistry will indicate when patients will spiral into these poor outcomes. It's really taking MRI to the next level."

As if all that wasn't enough to keep her busy, Harris also dedicates some of her time to studying chronic pain and understanding where that lives in the brain.

"Acute pain has a very important purpose," she says. "Chronic pain is a pain response that's no longer useful. Patients remain in pain despite the fact that the reason for the pain is gone."

Harris is hoping to use MRS to find out how the transition from acute to chronic pain occurs, and why the pain response moves from the sensory to the emotional regions of the brain. Understanding the emotional connection to chronic pain and its underlying neurochemistry may help researchers find ways to improve treatment and therefore the quality of life for these patients.

Despite her love for the city, Harris says it was the collaborative environment at the HBI and ability to interact with patients at the Alberta Children's Hospital that enticed her back home.

"Having that direct motivation for my work is really important to me," she says. "I feel that I can really make a contribution here and there is so much that we have yet to discover, it's really a very exciting time to be doing imaging science research."

FEATURE STORY

UNEXPECTED DISCOVERY WILL ALLOW GLOBAL ACCESS TO NEW MS TREATMENT

RESEARCHERS DISCOVER AN INEXPENSIVE ACNE MEDICATION IS EFFECTIVE IN TREATING EARLY-STAGE MS

Spend any time with V. Wee Yong, PhD, and you will quickly realize the key to his success: common sense, collaboration, and most of all, compassion for those he's trying to help. These are the very reasons Yong started down the path of multiple sclerosis (MS) research in the first place.

"It was just a natural step in terms of asking where I could apply my skills and knowledge," he says, looking back to his early days of postdoctoral work at the University of British Columbia in Vancouver.

Decades of dedication since then are now culminating in a discovery that will make medication more affordable for patients with early-stage MS. In collaboration with Dr. Luanne Metz, Yong helped discover a new way to delay the progression of the disease using a medication that already exists. The researchers capitalized on a growing indication that drugs created to treat one disease can often be repurposed to treat other conditions.

"All the medications we have – even though they are targeted to a particular disease process – will always have some other secondary properties," says Yong. "This was an example of that."

The painstaking process started close to 20 years ago, as Yong started searching through medical literature for a drug that could stop a specific enzyme from weakening the blood-brain barrier, a distinguishing feature of MS.

"Today's treatments offer MS patients a far better quality of life, and for these vital improvements, we have tireless research teams like the one at the HBI to thank."

Diana Joseph, who together with her brother, Jay Westman, began supporting MS research more than 20 years ago. In 2015, they launched the Westman Charitable Foundation with a $1 million gift to the University of Calgary in support of MS research.

Dr. Luanne Metz is a member of the HBI, co-leader of the HBI's Multiple Sclerosis NeuroTeam and professor in the Department of Clinical Neurosciences at the Cumming School of Medicine, University of Calgary. She is an Alberta Health Services neurologist and head of the Division of Neurology.

"I came across an old report that tetracycline – which is a family of antibiotics – had properties on that enzyme in certain conditions," he says. "So, we decided to test this and found that minocycline, an acne medication, was very active against that enzyme."

Cell culture studies led to further lab tests, which eventually resulted in three clinical trials over the course of 10 years, led by Dr. Metz. Most recently, she led a Phase III trial conducted across 12 centres in Canada.

Soft spoken and matter-of-fact, you would never guess Yong is explaining a discovery that could change the course of MS for patients around the world. The current cost of medication makes it difficult and sometimes impossible for patients to afford treatment, even though early intervention can help stall the disease. In Canada, the cost of current therapies is between $20,000 to $40,000 per year; elsewhere in the world, prices are even higher. Thanks to Yong and Metz, those bills could drop to a mere $600 a year.

"This cheap, generic drug is going to help a lot of MS patients around the world who otherwise would not be able to afford medication."

"The impact is going to be substantial," he says. "This cheap, generic drug is going to help a lot of MS patients around the world who otherwise would not be able to afford medication."

Dr. Metz sees additional benefits as well. "Patients will now have yet another option," she explains. "This treatment does not require injections, monitoring lab work, or special authorization by their insurance company. These processes can delay treatment initiation for three to four months whereas minocycline can be started immediately."

Yong admits he hasn't taken much time to enjoy this success. His journey through MS research seems similar to climbing a mountain. Each step is an achievement in itself, but it isn't the end goal.

V. Wee Yong, PhD, is a member of the HBI and leader of the HBI's Multiple Sclerosis NeuroTeam. He is a professor in the Department of Clinical Neurosciences at the Cumming School of Medicine, University of Calgary.

While this discovery will be life-changing for some patients by delaying MS, Yong recognizes that there is much work left to do. He is focusing now on identifying drugs that can repair brain and spinal cord damage in patients that are currently suffering from the debilitating disease – including those with progressive MS – which currently has few available treatment options.

"We haven't discovered the cure-all for MS," he says. "While it would be nice to sit back and smell the roses, we certainly are not there yet."

That point was brought home for him recently during a research update he gave to a group of patients. After his presentation, Yong opened the floor to questions. From the back of the room, a voice called out with a query, adding, "You can't see me because I can't stand up."

"That was a very sobering experience," says Yong, "a reminder that we still have a lot of work to do, many unanswered questions, and many challenges still to resolve."

MINOCYCLINE FACTS

Minocycline belongs to a class of second generation tetracycline oral antibiotics. It was introduced in 1971 as an acne medication.

In addition to its antibiotic effects, minocycline appears to lessen harmful immune responses and protect neurons from injury in models of disease. The combined anti-inflammatory and neuroprotective effects prompted researchers to investigate this drug as a potential treatment for early-stage MS.

MS FACTS

MS is currently classified as an autoimmune disease of the central nervous system (brain, spinal cord).

The disease attacks myelin, the protective covering of the nerves, causing inflammation and often damaging the myelin. Myelin is necessary for the transmission of nerve impulses through nerve fibres.

Canada has the highest rate of MS in the world, with an estimated 1 in 340 Canadians living with the disease.

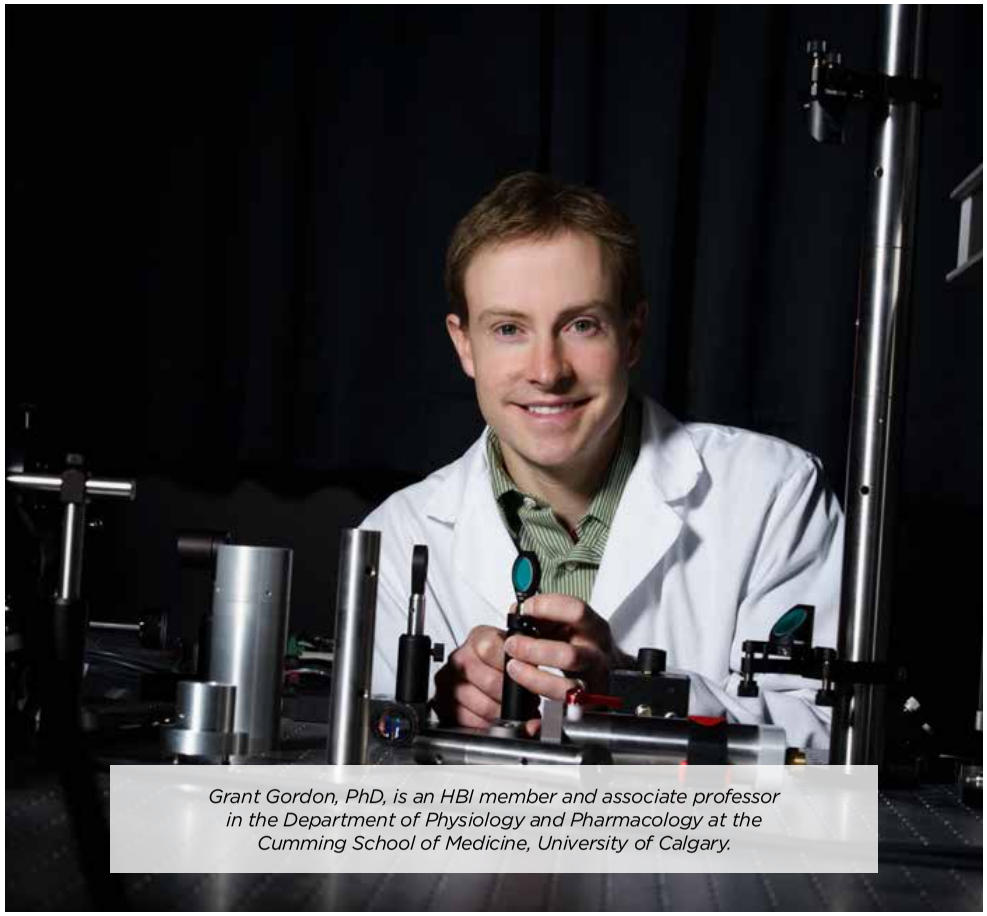
There are about 12,000 Albertans living with MS.

Twice as many women as men have MS.

While it is most often diagnosed in young adults aged 15 to 40, younger children and older adults are also diagnosed with the disease.

MS is unpredictable and can cause symptoms such as extreme fatigue, lack of coordination, weakness, tingling, impaired sensation, vision problems, bladder problems, cognitive impairment and mood changes.

For more information visit cumming.ucalgary.ca/ms



Grant Gordon, PhD, is an HBI member and associate professor in the Department of Physiology and Pharmacology at the Cumming School of Medicine, University of Calgary.

DEVELOPING NEW TECHNOLOGIES TO UNDERSTAND BRAIN BLOOD FLOW

CUSTOMIZED MICROSCOPE, DESIGNED AND BUILT IN CALGARY, ALLOWS RESEARCHERS TO OBSERVE HOW NEURONS COMMUNICATE WITH BLOOD VESSELS IN THE BRAIN

Grant Gordon, PhD, knew from a young age that he had an interest in science.

"I had a microscope when I was very young," he says, "and I loved my microscope."

Even with this youthful curiosity, it wasn't until graduate school that the award-winning neuroscientist fully latched onto science, diving into the unknown to explore novel questions and conduct his own experiments. In fact, his career path almost took an entirely different turn.

"I had to make a hard decision at the end of high school as to whether I was going to go to art college or do something more science related," he says, explaining his eventual choice of science. "Ultimately, it's worked out very well."

Gordon still draws on his artistic talents, adding hand-drawn illustrations to grant proposals and review articles, but his love for the microscope is what truly comes through in his day-to-day work.

A large part of Gordon's research focuses on how brain cells communicate with blood vessels to control blood supply in the brain. His work offers insights into a spectrum of neurological problems linked to abnormalities in brain blood flow, including dementia, migraine and stroke.

It's a challenging process to observe using traditional equipment, which is why Gordon and his team developed a custom microscope tailored to meet their experimental needs. What's more, they drew up plans so labs around the world can either recreate the one they use here or follow guidelines to customize one of their own.

The open source plans for his microscope have already been downloaded close to 1,200 times

"It's almost like Lego," says Gordon. "It's very adaptable and modular, using compatible hardware parts and lenses. You can build a high performance two-photon microscope for a fraction of the cost of a commercial system."

The open source plans for his microscope have already been downloaded close to 1,200 times and at least five labs in the United States, Canada and Taiwan have used them to build their own machines.

Gordon and his team are using this new technology to broaden their understanding of basal, or resting, blood flow in the brain. In particular, they're interested in how star-shaped cells called astrocytes control the diameter of blood vessels in the brain.

"We think we've discovered a new form of blood flow control in the brain," he explains, "that seems to be independent of neural activity."

Instead of having the neurons control how much blood is coming constantly into the brain, Gordon's research suggests the astrocytes could be running the ship, setting an optimal diameter of the blood vessels in order to provide adequate base levels of oxygen and glucose to brain cells.

"We think this may have implications for a variety of conditions," says Gordon, "anything from aging to Alzheimer's disease to vascular dementia. All of those are associated with a decline in overall brain blood flow."

While he remains focused on exploring this area of research for the time being, he is always on the lookout for new ideas. "I'm a curiosity-driven scientist," he says. "We're interested in blood flow control currently, but I don't know what we will be exploring in five years' time. We're really chasing observations. You don't want to miss something more exciting happening because you're so fixated on a certain idea."

GETTING PERSONAL IMPROVES HEALTH CARE DELIVERY FOR OLDER ADULTS

EDUCATION MODEL BRINGS STUDENTS INTO LONG-TERM CARE CENTRES TO DEVELOP INNOVATIVE MODELS OF CARE

The excitement of working with emerging technologies often captures the imaginations of students entering health care professions. From surgical robots to 3D printers, the breadth of possibilities is almost too great to grasp. It makes the job of Lorraine Venturato, PhD, all the more challenging. She's trying to attract students to an area of care that forces them to connect in a different way, one patient at a time.

As Chair in Gerontological Nursing and co-leader of the HBI's Dementia & Cognitive Disorders NeuroTeam, Venturato focuses her research on finding ways to improve care for older adults. It's a diverse demographic that has complex health needs – including a large proportion of individuals with brain and mental health concerns such as dementia, cognitive disorders or depression. Regardless of their physical needs, she says what's most important for these patients is genuine personal connections.

"Technology is a big part of our world," she says, speaking to the allure of faster-paced specialties. "Working with older adults in community and long-term care settings is more about relationships and people skills than technology skills."

As part of her research, which aims to improve health care delivery for older people, Venturato initiated a placement program for second-year nursing students. In the summer of 2016, the first group of 16 students took part in a pilot project at Calgary's St. Marguerite Manor, a supportive living community operated by Covenant Care. Students were paired with a resident in the home, all in what Venturato calls an attempt to challenge stereotypes of what it's like to work with older adults in long-term care.

"The residents we have working with us at St. Marguerite are really quite engaged," she says. "Some of them are retired registered nurses themselves. So the students get the benefit of working with older adults and the residents get the benefit of passing on their skills, knowledge and wisdom."

Students work closely with their resident partner, fostering a relationship that goes beyond caring for physical needs. The hope is, through developing these personal relationships, future nurses will think more favourably about working with older adults across a variety of settings.

"If we can alter attitudes through positive experiences then we know the students can come out with more positive attitudes towards older adults," Venturato says. Even so, she says it's still a struggle to change how students feel about working outside acute care centres. With the continued need for community care nurses, Venturato says this area of nursing education is becoming even more important.

Lorraine Venturato, PhD, is an HBI member and associate professor and Chair in Gerontological Nursing at the Faculty of Nursing, University of Calgary.

Venturato's research into models of care for older adults is contributing directly to the University of Calgary's Brain and Mental Health research strategy. Her connection with the Calgary Association of Lifelong Learners (CALL), including research panels with many former university staff and professors, is helping to inform her research direction and strategies, including the placement project at St. Marguerite. Through her conversations with its members, Venturato is getting a better idea of what's important and where care can improve for older adults in Calgary and around the world.

"The key for me is that all of my research is built around partnerships," she explains. "I want to make sure older adults are active partners in what we're doing and that they're truly engaged."

Left to right: HBI award-winning trainees Erin Stephenson, Haley Vecchiarelli and Agnieszka Zurek.

LEADING THE WAY: MEET THREE HBI TRAINEES RECOGNIZED WITH CANADA'S MOST PRESTIGIOUS RESEARCH AWARDS

For graduate students and postdoctoral scholars in Canada, the Banting Fellowship and Vanier Scholarship represent the highest achievements in academic excellence. In 2016, three HBI trainees, working across disciplines in post-traumatic stress, multiple sclerosis (MS) and anxiety, were recognized with these prestigious awards.

AGNIESZKA ZUREK
BANTING POSTDOCTORAL FELLOWSHIP

Agnieszka Zurek (pictured right) is one of four UCalgary postdoctoral scholars to receive a 2016 Banting Fellowship. As part of the lab of Jaideep Bains, PhD, Zurek's research focuses on how a major stressful event can cause sustained changes in the brain.

In normal brains, inhibitory neurotransmission "puts the brakes on" a response to stress. However, recent research has shown that after a major stressor, the brakes may fail and the system can become hyper-responsive to subsequent events. This results in an exaggerated stress response and anxiety, common in post-traumatic stress disorder.

"My research examines how changes to the brain's inhibitory system effectively form a 'memory' of a stressful event," explains Zurek, who is also the recipient of an Alberta Innovates fellowship. "My goal is to determine whether it is possible to interfere with these changes to the brain's inhibitory system, and prevent hyper-responsiveness to subsequent stressors."

As a member of Bains' team, she has access to the HBI's cutting-edge labs, collaborative learning environment and rich mentorship opportunities. "Being able to test these ideas in the laboratory and discuss the results with my colleagues is extremely rewarding," says Zurek.

ERIN STEPHENSON
VANIER CANADA GRADUATE SCHOLARSHIP

Working with V. Wee Yong, PhD, Erin Stephenson (pictured left) is an MD-PhD candidate investigating MS, and how inflammation in MS alters the brain matrix.

"The brain matrix is an interconnected network of proteins and sugars that exists for functional support, as well as to influence cellular behaviours, for better or – in cases of dysregulation – for worse," says Stephenson. "My research has found that neuroinflammation dysregulates the brain matrix, and this dysregulation also enhances inflammation."

Stephenson was part of a recent collaboration in the Yong lab, which identified a mechanism by which myelin, the protective covering surrounding nerve cells, repairs itself in MS lesions and reduces neuroinflammation. The discovery represents an important step forward in a new approach to MS research, and has potential for other neurological conditions such as traumatic brain injury, spinal cord injury and even stroke.

Beyond her research, Stephenson is active in Special Olympics Calgary, coaching adults with intellectual disabilities.

HALEY VECCHIARELLI
VANIER CANADA GRADUATE SCHOLARSHIP

Haley Vecchiarelli (pictured centre) is a PhD candidate working with Matthew Hill, PhD, at the HBI and The Mathison Centre for Mental Health Research & Education. Her research involves understanding changes to the brain that occur during chronic inflammation, and how these changes might lead to anxiety.

"In the Hill laboratory, we study the endocannabinoid system – the part of the brain that reacts to cannabinoids like marijuana, and also creates its own cannabis-like chemicals," says Vecchiarelli, who also won the HBI PhD Researcher of the Year Award in 2015. "We find that this system is altered in the brain during colitis, or gut inflammation, and we also see an increase in anxiety in these subjects. We have found that we can reverse colitis-induced anxiety by boosting the endocannabinoid system."

Vecchiarelli's research may provide insight into mechanisms underlying psychiatric comorbidities during chronic inflammation and illustrate the utility of cannabinoids as a dual-pronged approach to treat chronic inflammation and the ensuing changes in mental health.

When she is not in the laboratory, Vecchiarelli is passionate about giving back to the HBI and university communities. She has served on search and selection committees, and is an active member of the HBI Trainee Organization and the Graduate Students' Association.

MESSAGE FROM BRENDA MACKIE

Rebecca Hotchkiss (seated) and members of the Hotchkiss family serving on HBI committees. Standing, from left: Brenda Mackie, Jeff Hotchkiss and Richard Hotchkiss.

My father would be gratified to watch the continued progress of the institute which bears his name. The Hotchkiss Brain Institute has launched into its second decade as an internationally recognized centre of excellence for brain and mental health research and education. Nationally, the HBI has become one of the top four neuroscience research institutes.

This level of recognition has been earned by the efforts of everyone at the institute. The HBI has been led by Sam Weiss since its inception, and his visionary commitment to its core values has created a team of over 750 researchers, trainees and staff. Since 2007, the HBI has recruited over 50 top-calibre scientists whose groundbreaking work is leading to new discoveries that are already making an impact in our community and around the world.

The investigation by Drs. Metz and Yong into an affordable treatment for early-stage multiple sclerosis (MS), has led to a powerful discovery which will have a significant impact globally. Community support was critical in realizing this outcome. Your dollars matter – the HBI cannot achieve these successful translational results without your help.

One of the HBI's core values is collaboration. The institute's partnership with the Sheldon Kennedy Child Advocacy Centre, through The Mathison Centre for Mental Health Research & Education, will see a pilot study launched that will focus on the effects of child abuse on development. This partnership illustrates the power of collaboration, and, again with support from the community, will improve the lives of child abuse victims and their families.

These two examples demonstrate the impact of donor dollars on advancing critical areas of brain and mental health research. Looking forward, we are launching two major fundraising initiatives in 2017: one in support of the Research and Education Excellence Fund (REEF), and the other in support of The Mathison Centre.

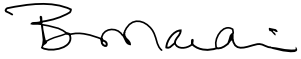
REEF has a goal of raising $10 million over the next five years to enhance existing programs and create new opportunities for discovery in several priority areas. Funding will support specialized training, facilities and cutting-edge technologies for investigators and trainees.

The Mathison Centre, made possible through a generous donation by Ron Mathison in 2012, uses a multidisciplinary approach to early identification, treatment and prevention of mental disorders; including depression, psychosis and anxiety. Community support is critical in enabling Director Dr. Paul Arnold and his team to continue their efforts to inform local and provincial mental health strategies.

Sam Weiss, as mentioned, has been the HBI director for nearly 13 years. We are sad to see his role here come to an end, as he has accepted a position at the Canadian Institutes of Health Research, effective July 1, 2017. The HBI took roots in the shared vision of Sam and my dad Harley, and flourished because of their passion, focus, and hard work. They had a respect for each other that never wavered. We as a family are forever indebted to Sam for all he has accomplished at the HBI, and we wish him every success in his forthcoming journey. We know our friendship will continue.

Dr. Keith Sharkey, who has been the HBI's deputy director for several years, will step in as institute director while we undertake an international search for a replacement for Sam, and we are very much looking forward to working with him.

My mom, Rebecca, my brothers and I remain firmly committed to the vision of the HBI, and we thank all of the supporters who continue to invest in this vision of a healthier world.



HBI BY THE NUMBERS

More than 130 members university-wide

More than 750 members, trainees, research and professional staff

More than 300 postgraduate scholars, graduate and undergraduate students

Research Revenue
$41.7M total research revenue in 2015 - 2016

Education
$362,000 spent on educational support for trainee scholarships and fellowships in 2016

Collaborations/Global Impact

Research collaborations on publications with researchers from 100 organizations in 14 countries in 2015

Strategic international research partnerships with eight global leaders in brain research

More than 27,500 citations of research in 2015

More than 470 scholarly articles published in 2015

32 HBI scholars with 5000+ citations on career publications

Scholarly Research

35 HBI scholars with 30+ h-index on career publications

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DIRECTORS

Samuel Weiss, PhD	Director (to June 30, 2017)
Keith Sharkey, PhD	Interim Director (effective July 1, 2017)
Richard Frayne, PhD	Deputy Director
Sarah McFarlane, PhD	Education Director

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