Hotchkiss Brain Institute

REPORT TO THE COMMUNITY

2014-2015: HEALTHY BRAINS FOR BETTER LIVES

UNIVERSITY OF CALGARY

OUR MISSION

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

Healthy Brain Aging feature story: 'Time is brain' when it comes to stroke. Read more about the ESCAPE Stroke Trial and the new treatment that is changing the standard of stroke care around the world on page 18.

REPORT TO THE COMMUNITY

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On the cover: *HBI researchers, from left: Dr. Chantel Debert, Dr. Zahinoor Ismail, Stephanie Borgland, PhD, Dr. Gerald Pfeffer, Ashley Harris, PhD and Jaideep Bains, PhD.*
On the back cover: *HBI trainees, from left: Erin Mazerolle, PhD, Rami Halabi and Haley Vecchiarelli.*

MESSAGE FROM THE DIRECTOR

In October 2014, the HBI celebrated 10 years of excellence in brain and mental health research and education. More than 400 community supporters of the HBI celebrated this milestone with us at the Opening Minds gala, presented by the friends and family of Harley Hotchkiss and with the support of the Calgary Health Trust.

While our tenth anniversary offered an opportunity to reflect on a decade of successes at the HBI, it was also an opportunity to look toward the future. Guided by a new vision — *healthy brains for better lives* — we launched a new strategic plan in February 2015.

The HBI's 2015 Strategic Plan is built upon our strengths in Research, Education and Community & Partnerships.

Inspiring discovery in brain and mental health

A collaborative and innovative NeuroDiscovery Framework positions new interdisciplinary teams of researchers, or NeuroTeams, to advance brain and mental health research across the life course. Research is addressing three areas that present increasingly important challenges to our community: Brain & Behaviour; Neural Injury & Repair; and Healthy Brain Aging (learn more on page 4).

The plan also includes two exciting new initiatives. The first is the NeuroTechnologies platforms, which aims to provide researchers with the most advanced equipment available to help keep us on the cutting technology edge. These technologies will create an environment that acts as a springboard for creativity and excellence in research (learn more on page 6).

The second is the NeuroResearch Clinics initiative, a collaborative effort that aims to involve more patients in research and clinical trials at our academic health centre clinics, via state-of-the-art, standardized registry platforms that will collect, store and manage patient data. Ultimately, this initiative will also provide Calgarians with authoritative knowledge and pathways to brain and mental health care backed by the latest research.

Based on the strength of our strategic plan, the University of Calgary announced the HBI as the leaders of the Brain and Mental Health research strategy, one of six research themes guiding the university toward its *Eyes High* goals. As such, the Institute is poised to play an even stronger leadership role in university-wide collaborative research.

A year of impact

As a result of the remarkable and tireless efforts of our faculty members, trainees and staff, it has been a tremendous year at our Institute.

Transformative research from the HBI is leading to outcomes that are improving health care in our community and beyond.

Results from the ESCAPE Stroke Trial, led by Drs. Michael Hill, Andrew Demchuk and Mayank Goyal, made international headlines earlier this year and contributed to

changes in stroke care guidelines in Canada and throughout the world (learn more on page 18).

In Education, with the support of our community, we successfully launched two new REALISE career development training programs: the Community Mentorship program, pairing our award-winning graduate students and postdoctoral scholars with local professionals; and the Career Encounters program, providing diverse work experience placements for our trainees (learn more on page 22).

Our community outreach partnerships continue to be strengthened as we collaborate with local partners including our incredible friends at Shaw Communications, the Calgary Public Library and Jay Ingram, among others.

On the international front, the HBI, in partnership with Campus Alberta Neuroscience, presented the Israel–Alberta Neuroscience Symposium in June 2015. Local researchers from the universities of Alberta, Calgary and Lethbridge engaged with neuroscientists from The Hebrew University of Jerusalem and the Technion – Israel Institute of Technology, exchanging knowledge and ideas to foster international collaborations.

We continue to attract to Calgary the best researchers in brain and mental health — with promise for dramatic impact on the city's health outcomes.

A shining example is the new Director of The Mathison Centre for Mental Health Research & Education, Dr. Paul Arnold, who came to Calgary from the Hospital for Sick Children in Toronto and will establish the first neurogenetics laboratory in Alberta to study genetics of childhood mental health.

A leading pediatric psychiatrist, Dr. Arnold will also treat youth with obsessive-compulsive disorder at the Alberta Children's Hospital and serve as the Alberta Innovates – Health Solutions Translational Health Chair in Child and Youth Mental Health.

Dr. Arnold's leadership will drive transformative research into the early identification, treatment and prevention of mental illnesses to better inform health care strategies — offering new hope to families in our community.

Community support is a cornerstone of the HBI's success

The HBI's success is a result of the enormous community support we have received over the years.

Our supporters provide us with philanthropic gifts that add huge value to our efforts and accelerate our abilities to put knowledge into practice and improve health outcomes. Equally important is the personal time many of our community supporters provide us, by serving on our committees for governance, education, outreach and engagement.

It is this community generosity and commitment that has allowed us to build an outstanding Institute with state-of-the-art infrastructure; recruit internationally-recognized researchers; attract the brightest students and trainees; and conduct transformative research for the benefit of our community.

Last, but not least, a major thank you to my great friends in the Hotchkiss family — whose ongoing commitment to the HBI plays an integral role in our success. I have no doubt Harley would be proud of all that the HBI has accomplished in the last 10 years, and be proud of our way forward.

On behalf of the more than 750 faculty members, trainees and staff of the HBI, we are truly grateful for the continued support of our community. As the stories in the pages of this report illustrate, *together*, we are well on our way of achieving our vision of *healthy brains for better lives*.

Samuel Weiss, PhD, FRSC, FCAHS
Professor and Director
Hotchkiss Brain Institute

RESEARCH THAT MATTERS

The HBI aims to achieve internationally recognized key discoveries and transformative clinical research in brain and mental health.

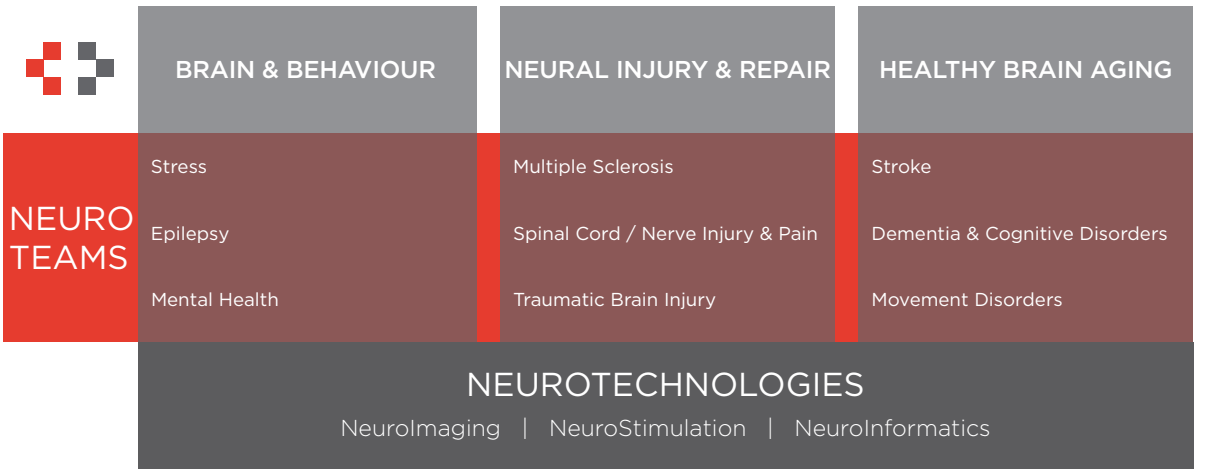
With one in three Canadians affected by a serious brain or mental health condition during their lifetime, this research has never been more critical.

The “NeuroDiscovery Framework” aligns research within three themes of Brain & Behaviour; Neural Injury & Repair; and Healthy Brain Aging.

Each theme is composed of interdisciplinary “NeuroTeams." By integrating the research of foundational scientists, clinicians who work with patients, technical experts and population health researchers, the HBI is going beyond scientific discoveries to improving lives.

A springboard environment of “NeuroTechnologies,” along with core facilities and support programs allow these teams of investigators to pursue their research goals.

NeuroDiscovery Framework



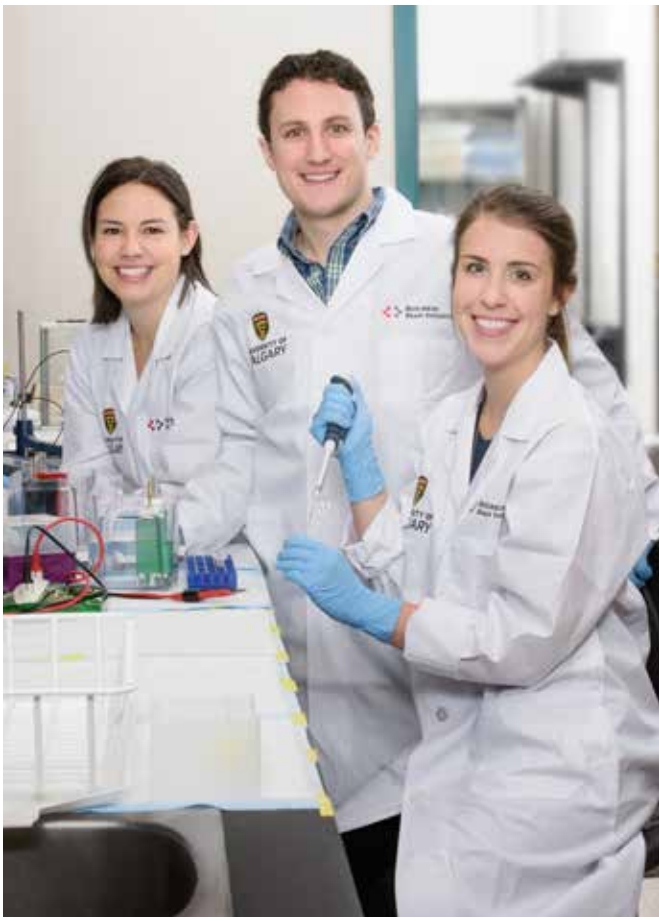
Leading a new era of brain and mental health research and education in our community

EDUCATION FOR A BRIGHT FUTURE

The HBI is working towards becoming the premiere place to train in the neurosciences and mental health in Canada.

The HBI attracts the best and brightest trainees, who help to advance brain and mental health research. Undergraduate and graduate students, and postdoctoral and clinical fellows make up the HBI's over 300 trainees.

The Institute's education programs not only train the next generation of leading neuroscientists and mental health experts, but also propel them to success in the subsequent stages of their careers.



ENGAGED WITH OUR COMMUNITY

The HBI engages with the community and our partners as a locally relevant and internationally recognized centre of excellence for brain and mental health.

The Calgary community is integral to the HBI's continued success. The HBI has a responsibility to be relevant to our community, as leaders in brain and mental health. We take a proactive role in fostering research and educational partnerships that contribute to our mission on the provincial, national and international stages.

NEUROTECHNOLOGIES

Cross-cutting "NeuroTechnologies" at the HBI span the Institute's entire research framework and provide researchers across all areas of brain and mental health with the most advanced equipment available.

Three NeuroTechnology Platforms are currently under development:

- NeuroImaging — imaging and recording technology to improve our ability to observe and record fundamental brain structure, physiology and function.
- NeuroStimulation — revolutionary tools that can establish causal links between neural circuits and behaviour and may lead to new, non-invasive treatments for brain and mental health diseases.
- NeuroInformatics — computational approaches to analyze the enormous amount of data we record.

OPTOGENETICS: SHEDDING LIGHT ON BRAIN AND BEHAVIOUR

More than a century ago, scientists began looking at the structure of the brain to explain human behaviour. Today, thanks to advances in foundational neuroscience and rapidly evolving technologies, we are moving closer to unlocking the many mysteries of the body's most complex organ.

Pioneering techniques now enable us to look at individual nerve cells, or neurons, to determine how their interactions form our most complex behaviours.

Neurons communicate with each other in circuits. Research at the HBI is focused on understanding exactly how our billions of neurons communicate and work together to execute complex behaviours and functions of the body.

"We can observe that a circuit turns on when a particular behaviour happens," says Jaideep Bains, PhD. "However, we still can't say that the circuit is actually causing that behaviour." It's the cause and effect that Bains is most interested in discovering and he's using cutting-edge techniques to do just that.

Bains is among a group of researchers at the HBI utilising a new and powerful technique that uses light to control and observe networks of neurons in an effort to learn more about brain and behaviour.

The process, called optogenetics, is a combination of biology, genetics and state-of-the-art optical technologies. Animal models are genetically engineered with light-sensitive proteins from algae and certain types of bacteria inserted into specific neurons in the brain, making them responsive to different colours of light.

"Normally neurons respond to chemical and electrical impulses. We've modified the cells slightly so that they respond to different wavelengths of light, effectively creating an on/off switch," explains Bains.

"Blue light will turn a circuit on, for example, and yellow light will turn it off. We put these tools into neurons that normally respond to stress and then asked: What will happen if we when we turn these neurons on or off?"

The results paint a clear picture of cause and effect.

Currently, this technique is primarily used in mice, but the information revealed about neural circuits is remarkably robust and translatable.

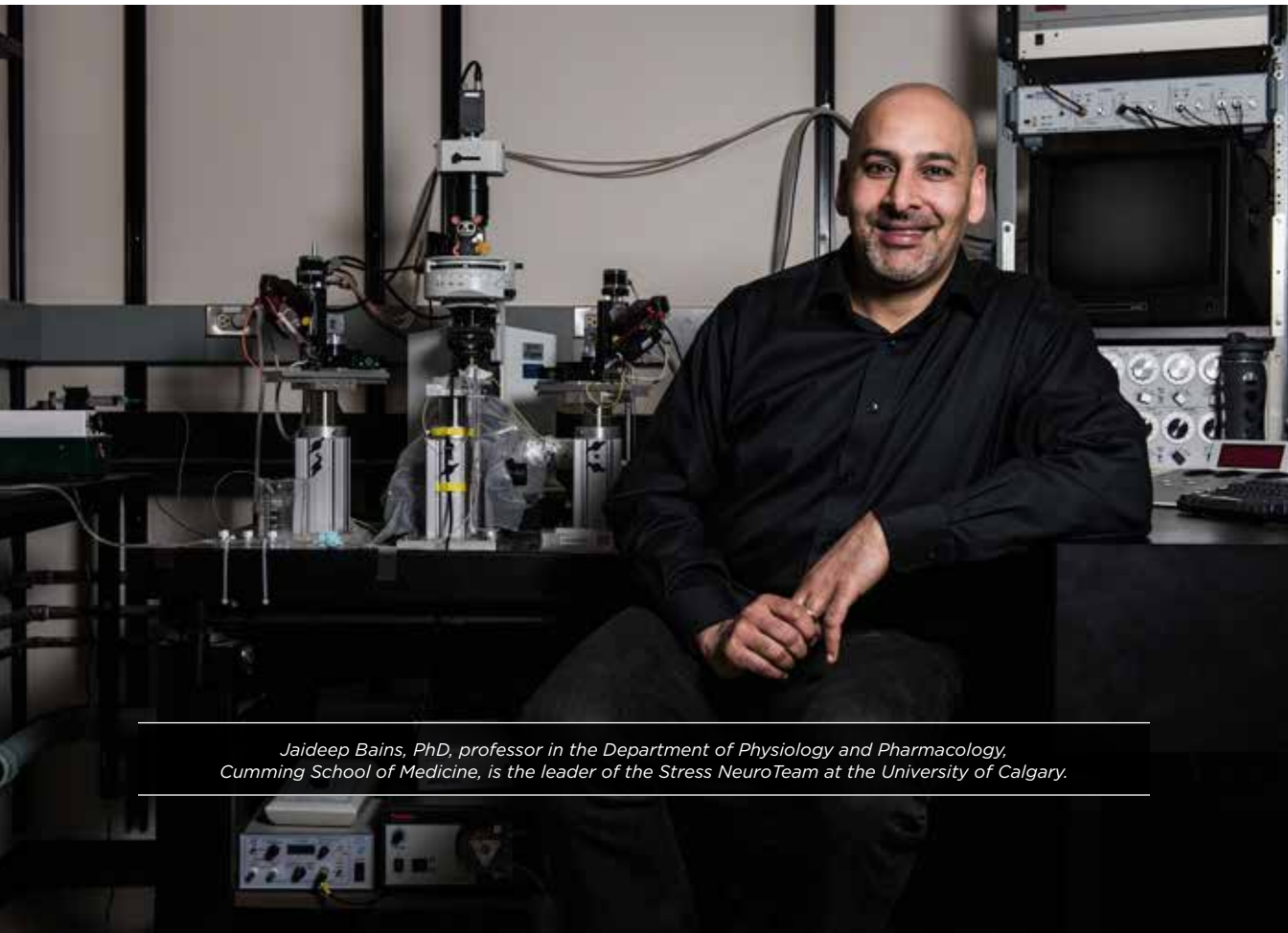
In experiments using an animal model, Bains has utilized optogenetics to demonstrate the circuit within the mouse brain that is directly responsible for a stress-induced compulsive behaviour. This discovery could be used as a model for stress-related mental health conditions in humans, such as obsessive-compulsive disorder.

"Optogenetics causally links neuron function to behaviour. Once we know how the circuit works, we can begin to design strategies aimed at manipulating, or even reversing, a given circuit when things go wrong," says Bains.

Already, researchers at the HBI are using optogenetics to learn more about the mechanisms involved in compulsive behaviours like eating and drug addiction, as well as stress, pain and even cerebral blood flow.

"The translational potential for this research is far-reaching," says Bains. "The knowledge and technology is advancing at such an incredible pace, it's astonishing to think about what might be possible in the very near future."

"We can use the knowledge gained from our experiments to develop therapies that could, one day, target the same cellular networks in people." – Jaideep Bains, PhD



Jaideep Bains, PhD, professor in the Department of Physiology and Pharmacology, Cumming School of Medicine, is the leader of the Stress NeuroTeam at the University of Calgary.

BRAIN & BEHAVIOUR

How behaviours are controlled or modified, how thoughts are turned into actions and how memories are gained or lost will be understood by studying the synaptic circuitry of the brain. Brain and mental health conditions that range from epilepsy to the mental health disorders of depression and anxiety also have their basis in structural and/or functional alterations in the circuitry of the brain. A key trigger for many brain disorders is stress, and the functional circuitry of stress remains to be fully understood.

Understanding the basis of brain and mental health conditions that frequently affect adolescents and young adults is the focus of the Brain & Behaviour research theme at the HBI.

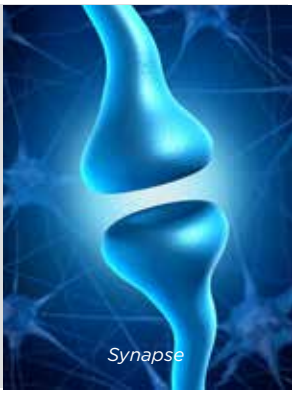
Dr. Paul Arnold (left) is an expert on the genetic origins of neuropsychiatric disorders and the new director of The Mathison Centre for Mental Health Research & Education. Launched in 2012, the centre was made possible by a $10-million investment from Ronald P. Mathison (right).

STRESS

Stress is an important trigger for mental health disorders and strongly correlated with the development of many physical conditions. Understanding the neural basis of stress is the focus of this NeuroTeam.

The endocannabinoid system — comprised of cell membrane receptors in the brain and nervous system — helps regulate stress and emotional behaviour.

Matthew Hill, PhD, a 2015 Canadian Institutes of Health Research Foundation Grant award winner, is examining how genetic variances in the endocannabinoid system impact anxiety traits, and if states of chronic inflammation (such as colitis) compromise endocannabinoid function to increase stress and anxiety. Translating clinical findings of stress-related illnesses into animal models helps to understand the neurobiological mechanisms of psychiatric conditions and could lead to development of potential neurochemical therapeutic targets for people affected by chronic stress and anxiety.



Synapse

EPILEPSY

Building on their strengths in epilepsy and seizure disorders, this NeuroTeam has strong links to the Alberta Children's Hospital Research Institute (ACHRI) to develop a translational continuum from childhood through to adulthood; from bench to bedside to population health studies.

The ketogenic diet is a high-fat, low-carbohydrate diet that helps to control seizures in some people with epilepsy. Ketone bodies are molecules that fuel the brain, produced by the metabolism of fatty acids during the diet.

Epilepsy NeuroTeam and ACHRI member Dr. Jong Rho led a multi-institutional study in Canada and the U.S. published in July 2015 — the first study to demonstrate an underlying molecular mechanism, called mitochondrial permeability transition, directly linking ketone bodies to seizure control. The discovery in an animal model of epilepsy identifies a potential target for the development of novel metabolic therapies to treat the neurological disorder.

Mitochondrion

MENTAL HEALTH

This NeuroTeam is centred in The Mathison Centre for Mental Health Research & Education. Mental health research includes an interdisciplinary approach to the early identification, treatment and prevention of mental disorders including depression, psychosis, schizophrenia and other conditions.

An HBI–Oxford research partnership has been awarded donor-directed HBI funding for an innovative study of mood disorders.

University students and youth at genetic risk of bipolar disorder will use mobile phone and web-based technology to record self-reported health measures including psychological processes, anxiety, mood and sleep data on a weekly basis. Co-led by Dr. Anne Duffy, in collaboration with researchers and trainees from the Mathison Centre and the University of Oxford, the study aims to identify warning indicators that will inform strategies for early detection of mood disorders in at-risk youth.

IMPROVING QUALITY OF CARE FOR EPILEPSY PATIENTS

Health services research is informing the treatment of neurological disorders.

Julius Caesar, Joan of Arc, Sir Isaac Newton and Agatha Christie all had it.

Today, 65 million individuals worldwide and 190,000 Canadians are affected by epilepsy, a seizure disorder associated with abnormal electrical activity in the brain that leads to debilitating seizures of varying frequency, intensity and effects.

"Epilepsy is a serious condition that can be associated with a number of poor outcomes such as unemployment, memory difficulties, injuries and even premature mortality," explains Dr. Nathalie Jetté, leader of the Epilepsy NeuroTeam and Canada Research Chair in Neurological Health Services Research at the University of Calgary.

A member of the HBI and O'Brien Institute for Public Health, Jetté's comprehensive research program aims to produce transformative research in neurological health care services with a focus on epilepsy.

While 70 per cent of epilepsy patients can live seizure-free by taking daily medication, the 30 per cent of patients who don't respond to the medication are candidates for more elaborate strategies including epilepsy surgery.

"For patients who do not respond to medications, the battle against their illness can last a lifetime and they can suffer from significant discrimination," says Jetté, who is also president of the Canadian League Against Epilepsy and chair of the International League's Task Force on Stigma in Epilepsy.

"In spite of the extensive body of evidence proving the effectiveness of epilepsy surgery, we've found that neurologists are often reluctant to consider epilepsy surgery, due in part to misconceptions about the risks of brain surgery."

Neurosurgical procedures to resect, disconnect or stimulate the area of the brain involved in seizures can significantly reduce or eliminate seizures from occurring. However, the average time between onset of seizures and surgery is 20 years for adults, and 10 years for children.

To facilitate earlier surgical treatment, Jetté is spearheading an international team of experts collaborating on a novel tool for epilepsy surgery evaluation. She is the principal investigator of the Appropriateness Study of Epilepsy Surgery that developed toolsforepilepsy.com.

Fellow HBI members and Epilepsy NeuroTeam colleagues from the Cumming School of Medicine also contributed to the development of the tool, with co-investigators on the study including Dr. Jayna Holroyd-Leduc and Dr. Samuel Wiebe, the school's associate dean of clinical research.

The online resource allows physicians to determine in less than two minutes if their patient should be referred for an epilepsy surgery evaluation, improving quality of care for epilepsy patients around the world through efficient assessment of surgical candidates.

Funding provided by the HBI, the Canadian Institutes of Health Research, Alberta Innovates – Health Solutions, American Epilepsy Society, Milken Family Foundation and Alberta Health Services has supported the deployment of the tool and ensured

its broad reach. "We're currently applying for additional funding to translate the tool in various languages and implement an offline mobile app version," adds Jetté.

And the health services researcher sees even greater potential for how online tools could be used in the future — beyond epilepsy care.

"Dr. Holroyd-Leduc and I are now collaborating with the World Health Organization in Geneva, Stanford University and the Alzheimer Society of Alberta and Northwest Territories to test and implement an online tool for caregivers of persons with dementia."

Jetté, Holroyd-Leduc and Wiebe are also joining forces with HBI members Dr. Scott Patten and Andrew Bulloch, PhD, from The Mathison Centre for Mental Health Research & Education. Their 2014 HBI/Pfizer Canada Psychiatry Research Award-funded program aims to see if an eHub of self-help resources can help people with neurological conditions manage depression more effectively.

In her quest to make health care more effective, equitable and efficient for neurological patients, Jetté takes inspiration from a quote by Johann Wolfgang von Goethe. "'Knowing is not enough; we must apply. Willing is not enough; we must do.' That is my motto," she shares. "We must take our research one step forward and ensure it changes lives."

Dr. Nathalie Jetté, professor in the Departments of Clinical Neurosciences and Community Health Sciences, Cumming School of Medicine, and leader of the Epilepsy NeuroTeam.

NEURAL INJURY & REPAIR

Injuries to the brain or peripheral nervous system have lifelong consequences for otherwise healthy people. Injuries can be initiated by immune mechanisms inside the body, as is the case for multiple sclerosis (MS); changes in blood flow to the brain, as occurs after a stroke; or through trauma or accidents, as is the case for concussion and spinal cord injuries.

A fundamental understanding of the mechanisms of neural injury — developing approaches to speed recovery and rehabilitate those who have neural injuries — is the focus of the HBI's Neural Injury & Repair research theme.

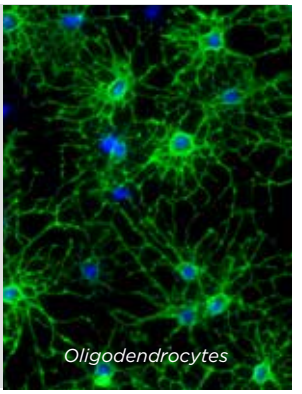
Shalina Ousman, PhD, (right) investigates protective molecules and mechanisms in multiple sclerosis and peripheral nerve regeneration, pictured in her lab with PhD student Vahid Hoghooghi.

MULTIPLE SCLEROSIS

MS research is a long-standing focus area at the HBI, where basic and clinical researchers support a cyclical process of discovery and translation, contributing to new treatments for patients. The high prevalence of MS in Alberta reinforces the continued importance of this NeuroTeam.

HBI scientists continue to investigate new medicines for repairing damage and reducing disability in patients with MS.

Researchers at the HBI have identified a number of drugs that may impact disease progression in secondary progressive MS — a common type of MS that is currently untreatable. Dr. Marcus Koch is leading a team in a new approach to testing these drugs in clinical trials. Drugs that show promise in a short futility trial will go on to be tested in randomized controlled trials, but the futility model will allow more rapid selection of the most promising therapies to fight the disease.



Oligodendrocytes

SPINAL CORD / NERVE INJURY & PAIN

The mechanisms of injury and rehabilitation of the spinal cord and peripheral nervous system is the focus of this NeuroTeam. The triggers and neural pathways of pain are also a growing area within this team.

The retina is the neural tissue at the back of the eye containing light-sensing neurons that allow us to see.

Carol Schuurmans, PhD, was the recipient of a 2015 Canadian Institutes of Health Research Operating Grant for her study of the molecular mechanisms guiding the formation of a functional retinal architecture. Research to further our understanding of the fundamental molecular and cellular pathways that control retinal development is essential for development of regenerative strategies to replace retinal neurons in patients who have lost their sight.

Retina

TRAUMATIC BRAIN INJURY

This team works closely with the Alberta Children's Hospital Research Institute, the Faculty of Kinesiology and the Department of Psychology as the leaders of an integrated, university-wide program to address sports-related concussion and other forms of traumatic brain injury.

A novel research approach is underway using body fluids to study diagnostic markers in sport concussion.

Dr. Chantel Debert and co-investigators from Winsport Canada and the University of Lethbridge are analyzing urine samples collected from 50 concussed athletes to determine if the end product of a cellular process leaves a unique metabolic fingerprint in these patients. The study is supported by the HBI/Department of Clinical Neurosciences Pilot Research Fund Program. Early-phase data is expected to provide a foundation to expand this research program that aims to identify biological indicators that may help diagnose and predict recovery in acute sport concussion.

HEAD-TO-HEAD BATTLE AGAINST CONCUSSION

Researchers across campus tackle prevention, diagnosis and rehabilitation of traumatic brain injuries.

Each year approximately 300,000 Canadians suffer a concussion and nearly half of those cases involve children under the age of 19, according to renowned pediatric neuropsychologist Keith Yeates, PhD.

"We want to prevent these injuries whenever possible, although we're never going to stop all concussions from happening," says Yeates. "But through high impact, transformative research, we can find ways to improve the lives of those affected by the injury."

Yeates is the leader of the interdisciplinary Traumatic Brain Injury (TBI) NeuroTeam and also lead for the integrated concussion research program at the University of Calgary.

A concussion is a traumatic injury to the brain resulting from a forceful bump, blow or jolt. Short-term symptoms of mild brain injuries can include temporary impairments of an individual's thinking, equilibrium, and consciousness. Longer-term symptoms can include headaches, dizziness, sleep disorders and even depression.

Children typically suffer concussions while playing sports or engaging in recreational activities. While approximately 75 to 85 per cent of young patients recover well from their injuries within 12 weeks, the remaining 15 to 25 per cent have a prolonged recovery.

"Insults to the brain manifest themselves in unique ways in children that makes it even more challenging to diagnose, treat and rehabilitate," explains Yeates.

"In children, especially very young patients, we're faced with additional hurdles associated with their limited communication abilities, rapid physiological development, and even their family environment."

Yeates is the former chief of the section of pediatric psychology and neuropsychology at Nationwide Children's Hospital in Columbus, Ohio and professor of pediatrics, psychology and psychiatry at Ohio State University College of Medicine. He was recruited to the University of Calgary's Faculty of Arts in 2014. He holds the Ronald and Irene Ward Chair in Pediatric Brain Injury.

Yeates was recently awarded a prestigious Canadian Institutes of Health Research Foundation Grant to support his research on the assessment and management of concussion in children and adolescents.

His work will focus on determining how neurobiological and psychosocial factors interact to determine the outcomes of concussion, and identifying modifiable risk factors that can be targeted for treatment.

As a member of the HBI and the Alberta Children's Hospital Research Institute, Yeates provides leadership to the cross-cutting research efforts on brain injury and concussion.

Colleagues from across faculties contributing to research in the TBI NeuroTeam include Dr. Willem Meeuwisse and Carolyn Emery, PhD (Faculty of Kinesiology); Dr. Karen Barlow, Brian Brooks, PhD, Dr. Chantel Debert, Dr. Sean Dukelow, Dr. Michael Esser, Bradley Goodyear, PhD, and Catherine Lebel, PhD (Cumming School of Medicine); and Richelle Mychasiuk, PhD (Faculty of Arts).

"Having an insightful and experienced group of researchers from a wide range of disciplines jointly tackle these problems is critical to fast-tracking and growing our understanding of brain injuries," says Yeates.

He is confident that advances in brain injury and concussion research will ultimately translate to improvements in clinical care and treatment for patients.

"Among many positive outcomes, this collaborative research will lead to the development of optimized and new rehabilitation protocols that will more effectively meet individual patient needs."

Keith Yeates, PhD, professor in the Department of Psychology, Faculty of Arts, and leader of the Traumatic Brain Injury NeuroTeam.

HEALTHY BRAIN AGING

In an aging population, the average Canadian now faces an increased risk of dysfunction associated with degenerating nervous and vascular systems. Statistics Canada has reported that, for the first time in Canada's history, there are more people aged 65 and older than children under the age of 15. Dementia has already become the most expensive medical condition in the Canadian health care system. Other brain conditions such as stroke and Parkinson's disease, to name only two, are also a concern for our communities.

The HBI's research theme of Healthy Brain Aging is focused on understanding the fundamental causes of, and developing new and improved treatments for, conditions affecting the aging brain.

Richard Frayne, PhD, is focused on the development and application of new imaging techniques for the study, detection and treatment of vascular disease.

STROKE

The Calgary Stroke Program provides a strong clinical foundation for this integrated NeuroTeam, which also works closely with the Libin Cardiovascular Institute of Alberta. The Stroke NeuroTeam is developing an international expertise in acute stroke treatment.

A transient ischemic attack (TIA) occurs when a blood clot causes a temporary blockage that stops blood flow to the brain for a short time. Stroke-like symptoms occur briefly but do not cause permanent damage. However, diagnosing a TIA is critical as the temporary dysfunction can be a warning sign of a major stroke.

Clinician-scientist Dr. Shelagh Coutts is leading a study to develop a more effective method to detect TIA in patients by measuring protein markers in the blood. This has the potential to change clinical practice for diagnosing TIA and reduce the rate of major strokes occurring.

DEMENTIA & COGNITIVE DISORDERS

This NeuroTeam conducts research into the varied causes of dementia and other cognitive impairments, including vascular dementia and Alzheimer's disease. Early identification and intervention are a focus of this NeuroTeam's work. The Dementia & Cognitive Disorders NeuroTeam is also a key collaborator in the Canadian Consortium on Neurodegeneration in Aging.

Aging and physical inactivity are associated with declines in cognitive abilities and brain blood flow, as well as an increased risk of vascular disease in the blood vessels of the brain.

The Brain in Motion study, led by Marc Poulin, PhD, is the first in the world to examine the effects of aerobic exercise on both brain blood flow and cognition in an older population. This study harnesses translational physiology to further our understanding of the biological mechanisms that explain how exercise promotes healthy brain aging and could demonstrate the potential of exercise to prevent age-associated cognitive decline.

MOVEMENT DISORDERS

The Movement Disorders NeuroTeam takes an interdisciplinary approach to studying the mechanisms and origins of the cognitive deficits observed in Parkinson's disease and other movement-related disorders of the aging population.

Patients with Parkinson's disease experience increased difficulty in walking. Dr. Bin Hu is leading an international initiative spanning five countries to test *Ambulosono*, a new technological platform for Parkinson's rehabilitation.

Ambulosono utilizes wearable movement sensors and motivational music rewards to stimulate key brain networks that control walking. This innovative training method has the potential to improve Parkinson's symptoms and slow the progression of the disease as new brain connections emerge after training. The invention of *Ambulosono* has been supported by the Canadian Institutes of Health Research, Alberta Innovates – Health Solutions, the HBI and local philanthropists.

Co-principal investigators of the ESCAPE Stroke Trial and professors in the Cumming School of Medicine, from left: Drs. Andrew Demchuk, Mayank Goyal and Michael Hill.

‘TIME IS BRAIN’ WHEN IT COMES TO STROKE

Novel clinical research transforms standard of care for stroke treatment.

The summer of 2014, Blaine Toone experienced a loss of sensation in his left arm while at work. Mindful of the symptoms associated with a stroke and suspicious of his condition, the 62-year-old immediately phoned his wife.

“We didn’t want to take any risks so we called 911 and the ambulance took him to the Foothills hospital right away,” his wife Peg recalls.

Two hours later Toone suffered an ischemic stroke — caused by a blood clot that blocks an artery to the brain, depriving the brain of critical nutrients. Toone was rushed into surgery to undergo a revolutionary clot retrieval procedure that may have saved his life.

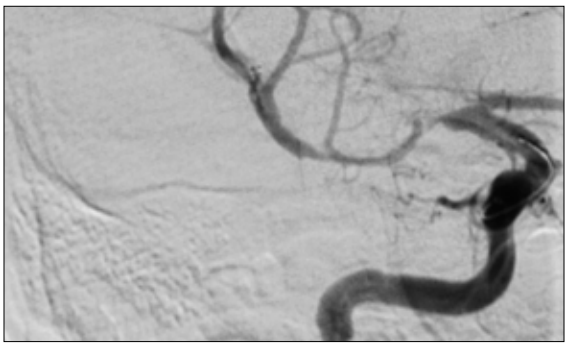
The procedure, called endovascular treatment (ET), was proven effective by an HBI-led clinical trial and is now transforming ischemic stroke care guidelines around the world.

“In these highly critical cases, every second counts to ensure the successful recovery of patients,” says Dr. Andrew Demchuk, leader of the university-wide Stroke NeuroTeam.

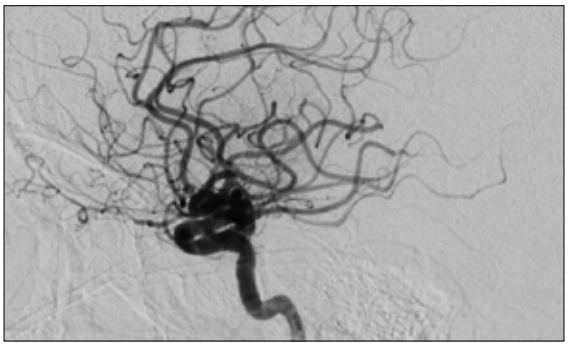
“Prior to our research, the standard of care for dealing with this extremely time sensitive condition was to administer a drug called tPA when appropriate,” explains Demchuk, a stroke neurologist and clinician-researcher. Known as a ‘clot buster,’ the drug dissolves the clot and blood flow to the brain can be restored within hours of being administered. But in many patients with large strokes the clot-dissolving drug is not effective, and it also comes with associated risks, such as excessive bleeding into the brain.

Demchuk, along with HBI colleagues Drs. Michael Hill and Mayank Goyal, are co-principal investigators on the ESCAPE (Endovascular treatment for Small Core and Anterior circulation Proximal occlusion with Emphasis on minimizing CT to recanalization times) Stroke Trial. The study demonstrates the benefits of ET compared to conventional treatment for patients with acute ischemic stroke.

ET is performed by inserting a thin tube into an artery in the groin, passing it through the body and into the brain vessels to the clot, under image-guided care using an X-ray. The clot is then removed by a retrievable stent, restoring blood flow to the brain.



Cerebral angiography: injection of contrast dye shows where the vessel is blocked, stopping blood flow.



After the blood clot is retrieved, the vessel is now open and blood flow to the brain is restored.

Globally, 316 patients in 22 medical care sites across Canada, the U.S., the U.K., Ireland and South Korea participated in the ESCAPE Stroke Trial. Candidates who met the criteria for ET were randomized to standard medical care or standard medical care plus ET.

Overall, positive outcomes for patients increased from 30 per cent to 55 per cent. In many cases, instead of suffering major neurological disability, patients went home to resume their lives. The overall mortality rate was reduced from two in 10 patients for standard treatment of care to one in 10 patients — a 50 per cent reduction with ET.

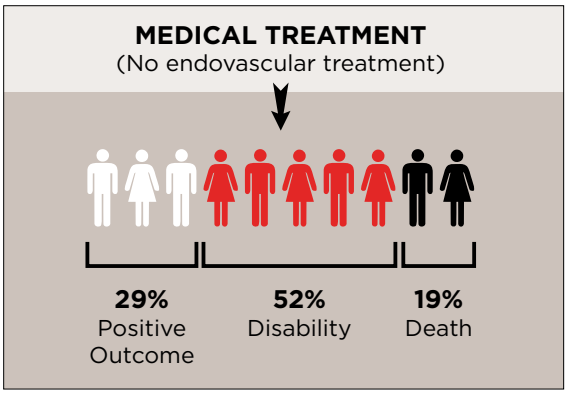
"Our study is only the second one in history to demonstrate the efficacy of ET and the first to prove the treatment's efficacy in reducing mortality rates," says Hill, senior author of the study.

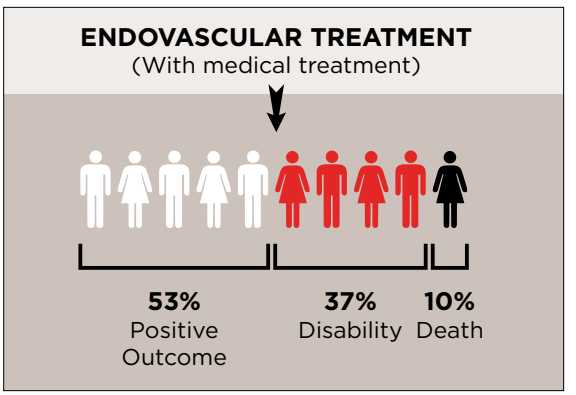
The results of the ESCAPE study, published in February 2015 by the *New England Journal of Medicine*, have subsequently contributed to a change in protocol for stroke care around the world. Guidelines in Canada, the U.S., Australia and Europe now include recommendations for the use of ET as the standard of care for patients with acute ischemic stroke.

Although endovascular treatments were first developed in the 1990s, ET has only recently been technically possible thanks to advances in imaging and device technology.

In the ESCAPE trial, ET was performed in less than 90 minutes — from computed tomography (commonly known as CT) scans to assess whether the patient was a candidate for the procedure, to blood flow being restored to the brain. This represented a two-hour improvement over previously reported ET trials.

"This is the most significant and fundamental change in acute ischemic stroke treatment in the last 20 years. These results will impact stroke care around the world." – Dr. Michael Hill





Three key reasons are credited for the success of the ESCAPE trial.

"Firstly, selecting appropriate patients using novel imaging technology; secondly, better organization and workflow to expedite treatment; and thirdly, use of modern technology to open the blood vessels," says Goyal, lead interventional neuroradiologist and first author on ESCAPE.

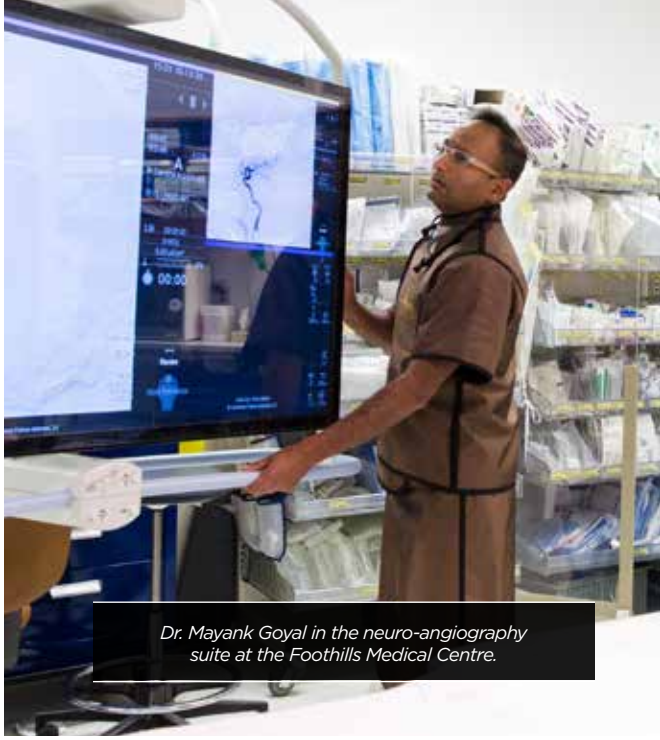
The ESCAPE study was funded by The Heart & Stroke Foundation of Canada, Alberta Innovates – Health Solutions and Medtronic along with generous donations to the HBI stroke team and the Calgary Stroke Program.

Recognized as a leading program in North America for stroke treatment and research at the Foothills Medical Centre, the Calgary Stroke Program is a joint venture between the University of Calgary and Alberta Health Services. Demchuk is director

of the program, where Hill is director of the Stroke Unit and Goyal is director of Imaging and Intervention.

Extensive collaboration between members of the HBI and Calgary Stroke Program on the ESCAPE trial showcases how groundbreaking clinical research can lead to better health care for the community.

The ultimate outcome is for stroke patients to be able to go on and lead normal lives, but many stroke treatments only work if administered in a set period of time, concludes Demchuk. “Many patients don’t get to the hospital in time. With stroke, every minute matters.”



Dr. Mayank Goyal in the neuro-angiography suite at the Foothills Medical Centre.

Members of the Calgary ESCAPE Stroke Trial team at the Foothills Medical Centre.

STROKE WARNING SIGNS (FAST)

- **F**acial droop
- **A**rm weakness
- **S**peech slurred or garbled
- **T**ime to call 9-1-1

Stroke Facts

- About 19 million brain cells die for each minute the brain is not receiving blood.
- 6,000 Albertans suffer ischemic strokes each year. Of those, about 1,500 are severe cases and candidates for endovascular treatment.
- Stroke is a leading cause of death in Canada and a leading cause of serious long-term disability in adults.
- Stroke can happen at any age.

HBI INTERNS TAKE ON THE WORLD OF BUSINESS

Making the jump from a neuroscience research laboratory to the business world isn't easy. But for postdoctoral scholars and graduate students at the HBI, a new professional development initiative is helping trainees who are interested in careers outside of academia to bridge the gap between the laboratory and the corporate sector.

The REALISE Career Encounters program explores how skills developed through graduate training translate into the private sector, government and non-profit organizations.

Project-based work experience provides brain and mental health trainees with an opportunity to discover the world outside of the laboratory, demonstrating the immense value that analytical minds can offer organizations in meaningful, yet sometimes unexpected ways.

Launched in 2014, the Career Encounters program was championed by HBI community supporter William G. Sembo, who recognized the potential for specialized postgraduate education in business applications. Sembo serves on the board of directors at CEDA, an oil and gas services company.

Forward-thinking executives at CEDA initially created two six-month internship positions for HBI trainees at their Calgary head office.

"We came up with two opportunities that were research based: one in workforce management and the other in tailings technologies," says Roberta Roesler, chief information officer and executive vice president of Corporate Services at CEDA.

"We wanted someone who would come and look at these issues and opportunities in a completely different way."

Impressed by the calibre of the REALISE interns, CEDA later created a third internship to further benefit from the innovative thinking of HBI trainees.

Chris Bladen, PhD, originally hired as a tailings analyst intern, demonstrated initiative and made a quick transition into the business environment.

"What Chris didn't know, he found answers to," says Paul Massel, vice president of Corporate Development and Bladen's internship supervisor. "Chris has been challenging me in lots of ways, which has been fantastic," Massel adds of their collaborative working relationship.

Bladen's leap from ion channels to tailings ponds wasn't as great as one might think. His undergraduate degree is in ecology and, at the time of hiring, he was halfway through completing a certification in environmental management alongside his PhD. Coupled with astute problem-solving skills augmented as a researcher at the HBI, Bladen was well-suited to analyze recent tailings pond legislation.

This role quickly expanded as Bladen's supervisors saw his skills in action. He became more integrated into business development, identifying opportunities to capitalize on the changing landscape of tailings management.

When a new job posting as an environmental specialist came up with CEDA, Bladen's combined education, experience and skillset made him an ideal candidate, earning him the offer of a permanent position.

Shadna Rana, left (postdoctoral scholar from the laboratory of Quentin Pittman, PhD), Brett Simms, second from left, and Chris Bladen, right (PhD students from the laboratory of Gerald Zamponi, PhD) are pictured with Roberta Roesler, chief information officer and executive vice president, Corporate Services at CEDA.

"This internship was invaluable in opening a door. Once you are through that door, it becomes apparent that researchers have highly transferable skills." – Chris Bladen, PhD

Fellow intern, Brett Simms, PhD, was initially hired on CEDA's workforce management team to find the reasons behind — and possible solutions to — high employee turnover. CEDA were able to implement cost-reducing changes in this area as a result of Simm's work.

"Graduate school and the HBI train you to think analytically," Simms says. "The research conducted inside the HBI is similar to research in the business world. We all ask ourselves: what's the real problem, where can I find the answer — and once you have the potential solutions — how could they be implemented?"

Originally a business improvement intern with CEDA, Shadna Rana, PhD, worked on project aimed at improving information and knowledge sharing across the company. She is confident the skills gained as a researcher helped her face the steep learning curve in this new role.

"Our training as researchers hones our communication skills," says Rana. "We have experience writing proposals, manuscripts and theses which are valuable skills in business."

Simms and Rana were both transitioned into business analyst roles at CEDA. Simms credits the HBI and its REALISE program for helping show both trainees and potential employers that scientists don't just belong in the lab.

Director of the REALISE program, Sarah McFarlane, PhD, believes it's important for students and faculty to understand the value that academic and research skills can contribute to organizations. "We're not only showing our people how to apply the skills they learn in the lab to the outside world. We're also letting the outside world know that there are smart, hard-working people here who could be a benefit to their organization," says McFarlane, who is a professor in the Department of Cell Biology and Anatomy.

With a demonstrated return on investment, Roesler is encouraging other companies to take on HBI interns. "I would absolutely recommend it," she says, adding the key to their success was to pair interns with company experts to ensure the newcomers have access to institutional knowledge. Beyond that, she says, it's all about having an open mind.

COMMUNITY PHILANTHROPISTS ADVANCE HEALTHY BRAIN AGING RESEARCH

The HBI's unified effort for the improved health of aging brains has been amplified, thanks to the generosity of supporters from the Calgary community. A new centre dedicated to Healthy Brain Aging research officially opened at the HBI in June 2015. This unique collaborative space is the result of a remarkable $6-million gift from the Ronald and Irene Ward Foundation.

The aging brain is susceptible to conditions such as dementia, stroke and Parkinson's disease. Many of the university's leading researchers, working together to better understand the intricacies of the aging brain, are now integrated in the Ron and Rene Ward Centre for Healthy Brain Aging Research.

Located at the Cumming School of Medicine, the Centre brings together scientists, clinical researchers, imaging specialists and trainees with diverse perspectives to study how the brain ages, what goes wrong to cause aging brain disorders and how best to treat and prevent them from happening. This interdisciplinary and collaborative research will lead to innovative health care solutions in our community.

HBI members, who also draw support from committed philanthropic and government partners, are among the experts that now have the opportunity to work more closely together in the Centre. This includes Oury Monchi, PhD, Tourmaline Oil Chair in Parkinson's Disease; Bruce Pike, PhD, Campus Alberta Innovation Program Chair in Healthy Brain Aging; and Dr. Eric Smith, Kathy Taylor Chair in Vascular Dementia.

The Centre is named after Ron and Rene Ward. Ron lived an energetic, health-driven life. Even at 70 years old, he was an avid skier and golfer who ran three to four miles a day. Near the end of his life, Ron was diagnosed with Lewy body dementia — a condition associated with Parkinson's disease that causes rigid muscles, tremors and slows movement. It's the second most common type of progressive dementia after Alzheimer's disease, and it resulted in Ron's passing in 2007.

"It's difficult to watch someone deteriorate so quickly," says Paul Wanklyn, nephew of Ron and Rene, and trustee of the Foundation. "Seeing how excited the researchers are and how hard they're all working to produce fantastic results for better health in our community is important to our family."

For the Ward family, the experience created a desire to help further research in the area of dementia. The breadth and variety of expertise in the Centre will open new avenues of looking at dementia diseases.

"When you bring people with the diversities of experiences, perspective and methodological knowledge together in this kind of milieu, you get collaborative outcomes that are much greater than the sum of their parts," says Smith. "Such collaborations will allow me to answer questions that I would never be able to answer on my own."

Magnifying the HBI's existing network of expertise in the area of Healthy Brain Aging, the Centre is enhancing the Institute's ability to recruit

Paul Wanklyn (left), his mother Val Wankling, family of Ronald and Irene Ward, and Dr. Eric Smith at the launch of the Ron and Rene Ward Centre for Healthy Brain Aging Research.

"The community's involvement is essential if we're going to make progress in studying aging and dementias. There is no substitute to community participation." – Bruce Pike, PhD

research leaders as well as attract the future generation of leaders.

"With such cross-pollination, trainees are exposed to a broader range of views," says Pike. "The Centre will be an incredibly rich environment for them."

The Centre is a technological hub for clinical imaging and data analysis at the HBI. Research focused on brain imaging techniques are important in understanding the changes in a normal functioning brain, compared to how disease or age changes the brain. Studying those differences will lead to new methods of treatment, which HBI researchers will be able to test rapidly through seamless collaboration between the laboratory and clinic.

Pike is one of the world's leading experts on applying quantitative methods to brain imaging. "We will use newer, more sensitive and quantitative methods to understand and track the disease at the earliest stage," he says. "Earlier detection means we have a better chance of effectively intervening."

Monchi employs neuroimaging and neurostimulation techniques to study the cognitive deficits in Parkinson's disease, with the goal of early prediction of cognitive decline in the disease.

In an example of a clinical trial at the Centre, Monchi is conducting a therapeutic study of transcranial magnetic stimulation in Parkinson's disease that involves applying a non-invasive, magnetic stimulation to the outer surface of the patient's brain. His preliminary results indicate the potential of this approach to improve memory and decision-making in patients with Parkinson's.

With its many components, the Ron and Rene Ward Centre for Healthy Brain Aging Research will help investigators to accelerate research on debilitating brain conditions in the aging population.

Translating discoveries into treatment and prevention strategies will ultimately improve health outcomes in the community.

Members of the Hotchkiss family serving on HBI Committees. Seated: Rebecca Hotchkiss. Standing, from left: Richard Hotchkiss, Brenda Mackie, Jeff and Sheryl Hotchkiss.

MESSAGE FROM THE HOTCHKISS FAMILY

Beyond the oilfield and the ice rink, my father had a passion for serving his community. His love of learning, and his belief that medical research would lead to a healthier population, was exemplified through his commitment to support the Hotchkiss Brain Institute at the University of Calgary.

The HBI's core values — *excellence, collaboration, integrity, impact, creativity and relevance* — are values that dad wholeheartedly believed in and lived by, which my family strives to uphold. These values have contributed to the success of the HBI's first decade. And with the launch of the HBI's new strategic plan, these values will continue to guide the Institute to greater levels of impact in brain and mental health research and education.

Through my family's involvement with the HBI, I have been fortunate to be a part of the impact the HBI has made in our community. I have seen levels of understanding emerge about how the brain works, and about why research and education in this area are so crucial. And I have witnessed how this knowledge kindles new hope for those affected by diseases of the brain and mental illness.

We celebrated these accomplishments at the HBI's tenth anniversary in October 2014, when, together as a community, we toasted a decade of discovery and a future of unlimited possibilities at the HBI. Already, we are seeing these 'unlimited possibilities' become a reality.

In 2015, the HBI's ESCAPE Stroke Trial showcased how research can lead to new, life-saving treatments and better delivery of health care, not only in our community but around the world. My family and I are proud of the far-reaching impact of this research, led by HBI members, and look forward to sharing in the successes of more globally-relevant discoveries to come out of the HBI.

We also take great pride in seeing my father's vision being fulfilled, as Alberta becomes a thriving hub of medical research and practice.

The Rebecca Hotchkiss International Scholars Exchange program — named in honour of my mother and established in 2011 thanks to support from the community — enables trainee exchanges, research visits and initiatives that strengthen ties between the HBI and other world-renowned neuroscience institutions. Through these international collaborations, the HBI is taking a leading role in brain and mental health research and education, attracting the world's best and brightest neuroscientists to Calgary.

I would like to thank HBI director Sam Weiss for his visionary leadership that drives the Institute forward, and the HBI's growing network of researchers, trainees and staff for their dedication and energy. By working together, and with the community, the HBI has shown how it can make a real difference.

This impact is made possible because of the time and generous contributions invested by so many people — donors, champions and supporters — all of whom recognize that the transformative research accomplished at the HBI is leading to healthier and better lives. Thanks to this continued community support, building a stronger platform to inspire discovery, the HBI is poised to achieve even greater breakthroughs for innovative solutions in brain and mental health.

On behalf of my mother and brothers, thank you all for your support, commitment and investment in the HBI for the betterment of our community.

Brenda Mackie

HBI BY THE NUMBERS

About **750** members, trainees, research and professional staff working together at the HBI.

More than **130** full members spanning **9** faculties and **16** departments university-wide.

12 new faculty recruited by the HBI to the University of Calgary since the start of 2014.

More than **300** postgraduate scholars, graduate and undergraduate students training with HBI members, contributing to brain and mental health research at the University of Calgary.

8900 m² of occupied space in our HBI footprint.

Over **360** scholarly articles and **1150** citations of research published in 2014.

$32.8M in research revenue in 2014.

$461K spent on educational support for trainee scholarships and fellowships in 2014.

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