

Krembil

2017 ANNUAL REPORT

The Home of
**Future
Cures**



Krembil Research Institute ("Krembil") is the research arm of the Toronto Western Hospital (TWH). It is embedded within the University Health Network (UHN) and is one of five UHN research institutes.

Krembil's singular focus is to find innovative treatments and cures for chronic debilitating disorders, including diseases of the brain, spine, bones, joints and eyes.

Krembil's laboratories are located at the Krembil Discovery Tower and at TWH's Main, McLaughlin and Fell Pavilions; previous to November 13, 2015, Krembil was known as the Toronto Western Research Institute.

Krembil: The Home of Future Cures

Welcome Message	2
Krembil by the Numbers	4
Featured Research	
Thank You for Sharing Reimagining how transplanted cells promote vision recovery	6
Self Versus Self Preventing the immune system from attacking healthy tissue	8
A Sign of Change Researchers unearth markers that signal spine degeneration	10
A Gut Reaction The unlikely link between gut immune cells and joint disease	12
Making a Mental Map Computer models help predict how we navigate surroundings	14
Brain Storms Predicting where age-related brain damage will strike	16
Technology Transfer	
Better Diagnosis Unique protein profile warns of kidney inflammation	20
Helping Hands Assessing hand function in spinal cord injury survivors	21
Research Events	22
Research Distinctions	24
Krembil Researchers	28
External Sponsors	30
Financials	32
Krembil Research Council	34

Welcome



Dementia...arthritis...vision loss...these are just a few of the problems faced by Canada's aging population every day. Finding solutions for these conditions is a critical and daunting task; but let me assure you, we here at Krembil are up to this challenge.

The Krembil Research Institute ("Krembil") was created in November 2015, built upon the foundation of research excellence and commitment of its predecessor, the Toronto Western Research Institute. Our unifying ambition is nothing less than to be one of the world's leading biomedical research institutes, with a focus on chronic debilitating disorders of the nervous system, musculoskeletal system and vision. To achieve this, we will continue to support and grow our excellence in scientific scholarship, research and knowledge translation. More importantly, we want to make impact beyond traditional scholarly metrics ("numbers"); we want to realize discovery and innovations that make a difference in the lives of people within Canada and throughout the world. We want to enable a society for aging individuals with health and quality of life at home—rather than at nursing homes or chronic care facilities.

Our efforts in achieving this mission are already well underway. We have augmented our research capabilities with the recently built Krembil Discovery Tower, a \$174 million state-of-the-art research facility, which now houses Canada's largest concentration of scientists and clinicians focused on research in our three priority areas: brain and spinal cord; arthritis; and vision.

We have also made huge strides towards promoting collaboration between our researchers and clinicians by initiating the development of integrated programs, including the creation of the Donald K. Johnson Eye Institute—the first of three multidisciplinary program integrations planned. And in the near future we will further grow our base of world-leading expertise through recruiting young and talented researchers specializing in our research priority areas.

At Krembil, we are relentless in our pursuit of cures

Of course we cannot achieve this alone; getting to this point and realizing this mission will be dependent on renewing and building the essential partnerships and support of our donors, foundations, the University of Toronto, TAHSN partners, funding agencies and government.

I encourage you to look through this inaugural annual report—get a glimpse into who we are, how we are battling the chronic diseases faced by Canadians, and why Krembil is the *home of future cures*.

Donald Weaver, PhD, MD, FRCPC, FCAHS

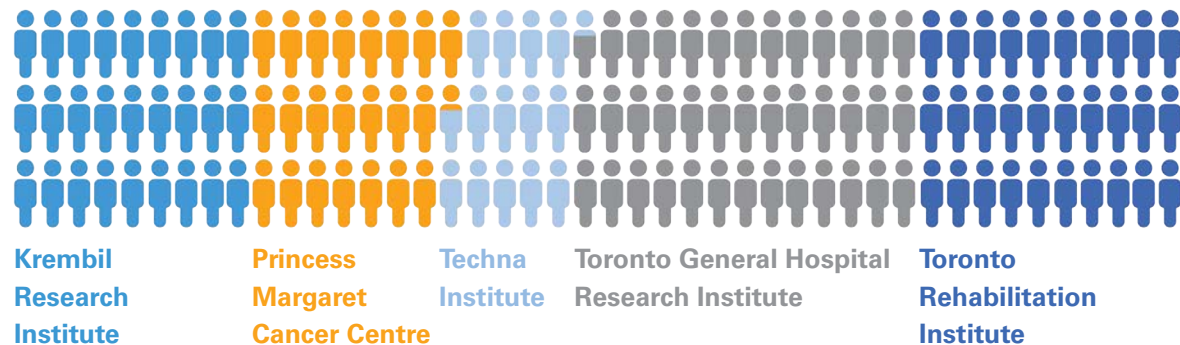
*Director, Krembil Research Institute
University Health Network*



Krembil by the Numbers

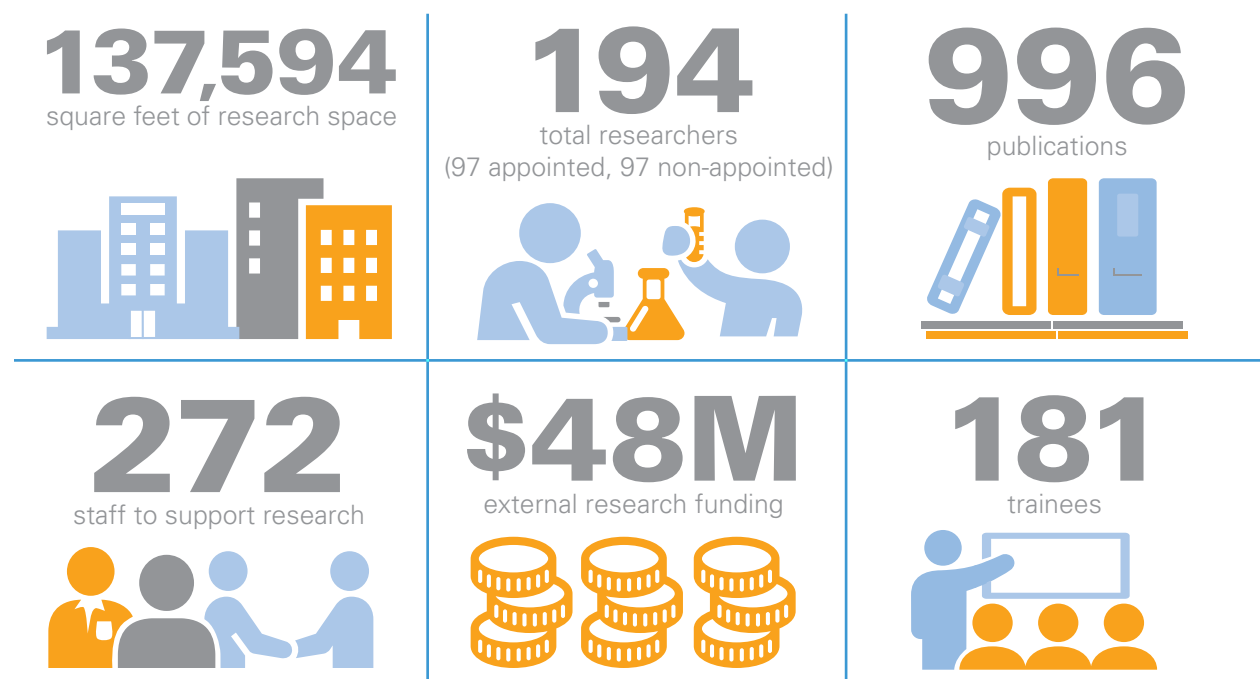
At University Health Network

Krembil is one of five research institutes at the University Health Network, which is Canada's largest research hospital. The graphic below approximates the proportion of the total appointed researchers within each institute. In total, UHN has 458 appointed researchers (2015-2016 data).



Krembil Research Snapshot 2017

Krembil's three **priority areas** are: brain and spine; vision; and arthritis, with a focus on chronic disorders. The current 2015-2020 strategic research plan maintains this focus, while laying the foundation for continued research growth. See the below snapshot for key research readouts^a.



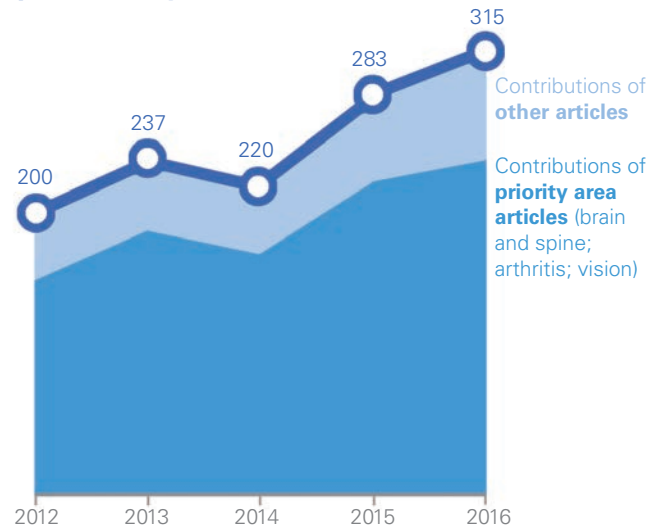
Impact

One way to measure scientific impact is to examine the volume and quality of scientific articles published.

In biomedical research, publishing articles requires extensive review by peers (known as the peer-review process). Once published, these articles become part of the global scientific literature and contribute to our basic understanding of health and disease.

The value of these papers within the scientific community can be represented by how often they are referenced (ie, cited) by peers. The graph (right) shows the annual trend for Krembil articles within the top 10% of cited papers, when corrected for research field and year published^a.

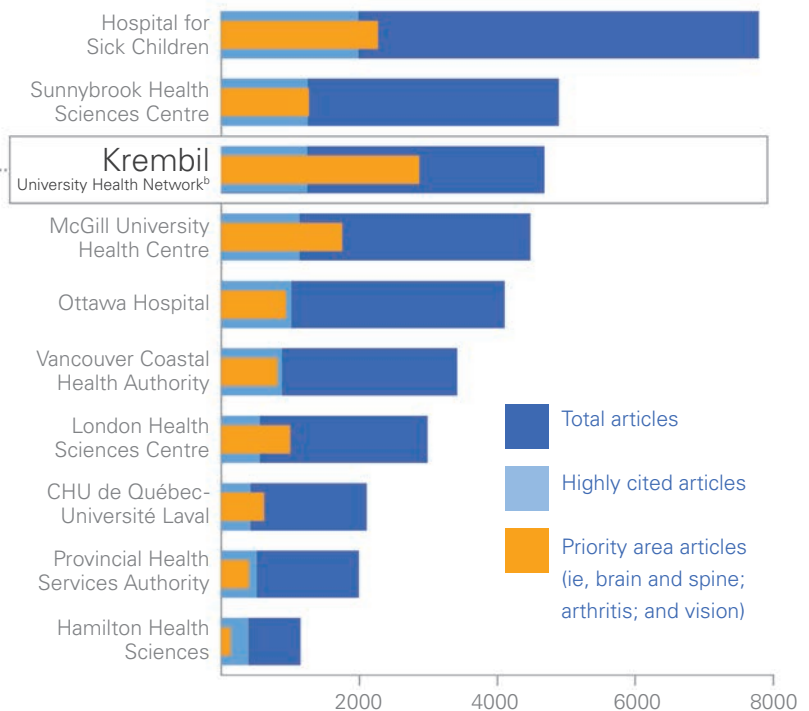
Number of highly cited scientific articles published by Krembil researchers



Benchmarking

When compared to Canada's top 10 research hospitals^a, Krembil was among the top ranked based on the number of scientific articles published between 2012 and 2016.

Scientific articles published by Canada's top research hospitals between 2012 and 2016



^aTo see how this data was prepared, see the disclaimer on page 34.

^bData is presented for Krembil researchers only and does not include data for other researchers at University Health Network.

Thank You for Sharing

Reimagining how transplanted cells promote vision recovery

Gone are the days of knowledge hoarding, when information alone was power. The willingness of researchers to collaborate and share knowledge is positively linked with productivity, cooperation and innovation.

While companies and organizations are beginning to clue in, recent research from Krembil Senior Scientist Dr. **Valerie Wallace** suggests that cells within the body already know about the power of sharing. Using advanced imaging techniques, she showed that when cells were injected into the retina (the layer of tissue at the back of the eye), rather than becoming fully functional cells themselves, they shared vision-saving cell contents with existing cells.

The findings are particularly important for the over one million Canadians with vision loss caused by incurable diseases. These diseases include retinitis pigmentosa and age-related macular degeneration, and involve damage to light-sensitive cells (photoreceptors) in the retina.

One strategy to restore vision loss that is being investigated involves injecting donor photoreceptors into damaged retinas—an approach that has produced promising results. However, exactly how the new cells contribute to vision rescue remains unknown.

Over the past decade, researchers have used a fluorescent marker, known as Green Fluorescent Protein (GFP), to illuminate and track injected photoreceptors. It was believed that the transplanted cells integrated into the recipient's retina, taking over the functions that were lost when existing photoreceptors became damaged.

"It was assumed that the GFP signal and associated vision rescue was a sign that the transplanted photoreceptors had successfully integrated into the recipient retinas," said Dr. Wallace, who is also Co-Director of Krembil's Donald K. Johnson Eye Institute. "However, recent findings from my lab suggest that this interpretation may not be accurate."

These results question long-held theories about how vision recovery works

Using new approaches that she developed to track transplanted photoreceptors, Dr. Wallace's team found that the transplanted cells, rather than 'integrating' into the retina, moved close by, but did not enter it. "Rather than functioning as normal photoreceptors, these cells may be sharing vital proteins with existing photoreceptors, restoring their function," said Dr. Wallace. "It may be that this transfer of materials, rather than cell replacement, is what leads to restored vision."

These results improve our understanding of how retinal cell transplantations work, which may help advance treatment strategies that restore vision.

Stem Cells. 2017 Apr;35(4):932-939. Supported by the Vision Sciences Research Program, the McEwen Centre for Regenerative Medicine, Brain Canada, the Foundation Fighting Blindness, the Ontario Institute for Regenerative Medicine, the Krembil Foundation and the Toronto General & Western Hospital Foundation (TGWHF). VA Wallace holds the TGWHF Donald K. Johnson Chair in Vision Research.



Image: The members of the Wallace lab are shown discussing results, including (L-R) Dr. Arturo Ortin-Martinez, Dr. Valerie Wallace, Lacrimioara Comanita, Dr. Philip Nickerson and Sam Tsai.

Self Versus Self

Preventing the immune system from attacking healthy tissue

Good health is achieved through a delicate balancing act—one that can depend on a finely tuned immune response. Too little of a response can leave you susceptible to infection, while too much can lead to chronic inflammation that damages healthy tissue.

Recent work from Krembil Scientist Dr. **Jeremy Sivak** revealed a new strategy that appears to prevent the overactive inflammatory response in the central nervous system (nerves of the brain, spine and eye)—a process known as reactive gliosis.

This process is particularly important because the damage that it causes can be irreversible: nerve cells within the central nervous system are unable to heal themselves after damage. Consequently, reactive gliosis has been linked to an array of incurable neurodegenerative diseases such as Alzheimer's and Parkinson's disease, and autoimmune conditions such as multiple sclerosis. In the eye, reactive gliosis can have dire consequences on vision. It is initiated after damage to the retina, and the process has been linked to vision loss resulting from glaucoma, retinal ischemia and diabetic retinopathy.

Dr. Sivak's team used neurons within the retina as a model system to study reactive gliosis. Key to the harmful process is a star-shaped cell known as an astrocyte, which normally helps nerve cells transmit signals. As known culprits of reactive gliosis, these cells become 'activated' after stress or injury, grow in size and start producing structural proteins, known as type III intermediate filaments, which are thought to provide added structural support to nerve cells.

Dr. Sivak's team explored whether type III intermediate filaments could be targeted as a way to stop reactive gliosis. They did this by injecting an inhibitor of the filaments, known as withaferin, into injured eyes that were actively undergoing reactive gliosis. The results showed that injection of withaferin prevented reactive gliosis and protected nerve cells.

Reactive gliosis, although important for repair, can have dire consequences on vision

"To our knowledge, this is the first study to demonstrate that injecting small molecule drugs, such as withaferin, into a living system can inhibit intermediate filament dynamics and protect neurons from the negative effects of reactive gliosis," says Dr. Sivak.

These findings greatly advance the field by revealing a new therapeutic strategy to prevent the harmful inflammation involved in a variety of related neurological diseases.

Cell Death Dis. 2016 Sep 29;7(9):e2386. Supported by the Canadian Institutes of Health Research, the Glaucoma Research Society of Canada, the Natural Sciences and Engineering Research Council of Canada, and the Toronto General & Western Hospital Foundation (TGWHF). JM Sivak holds the TGWHF Chair in Glaucoma Research.

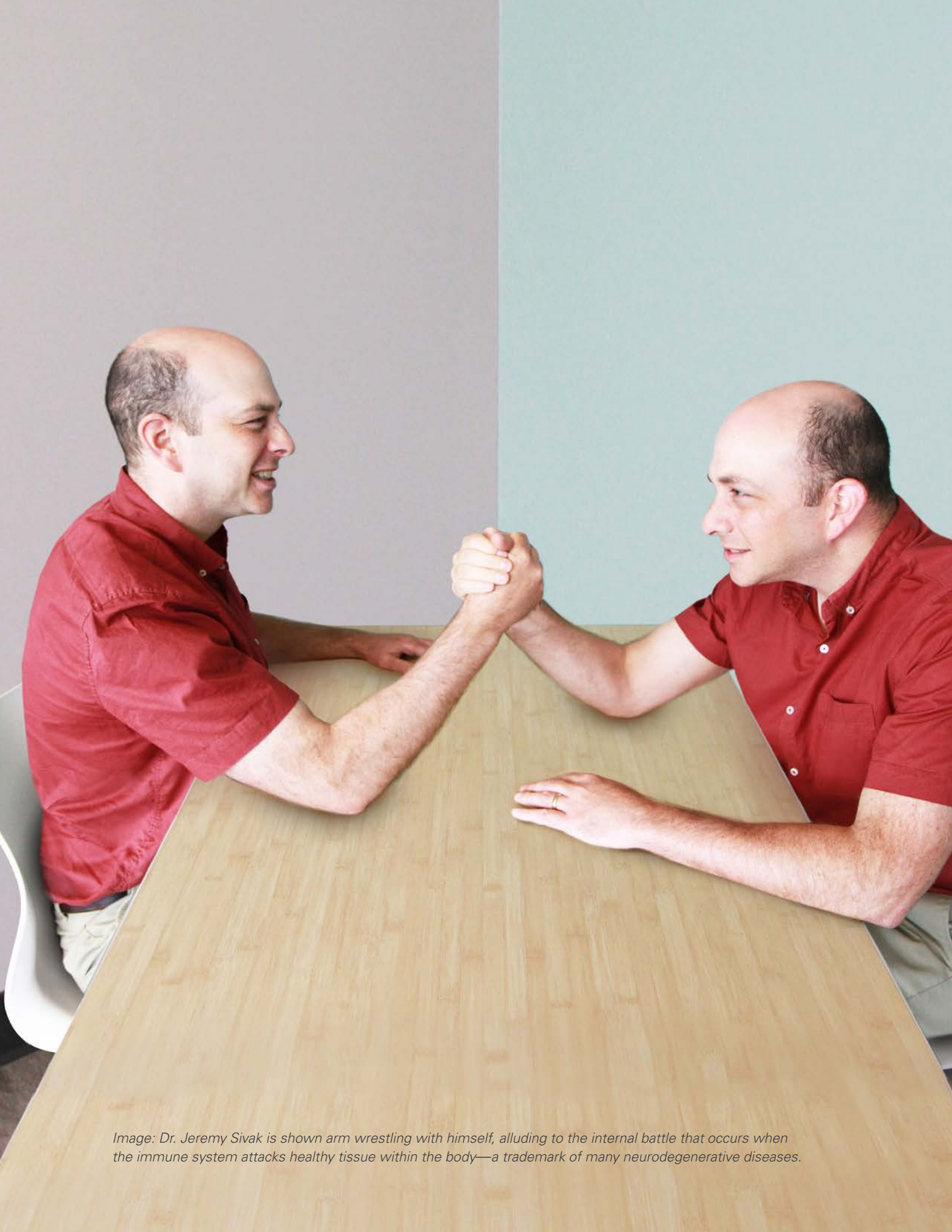


Image: Dr. Jeremy Sivak is shown arm wrestling with himself, alluding to the internal battle that occurs when the immune system attacks healthy tissue within the body—a trademark of many neurodegenerative diseases.



A Sign of Change

Researchers unearth markers that signal spine degeneration

Walking through a forest can awaken the senses—the sound of the leaves crunching under your feet forces you to take notice of your surroundings, giving you a new view of the world. That is, in a way, what Krembil Senior Scientist Dr. **Mohit Kapoor** did to find markers of osteoarthritis—he looked intently.

Dr. Kapoor's goal was to find a type of molecular fingerprint, known as a biomarker, that could be used to predict early stages of the disease so that preventative therapies can be deployed earlier—and to gain insight into why some people get the disease, while others do not.

This is particularly important for osteoarthritis (OA), a painful and debilitating degenerative condition that leads to the breakdown of protective cartilage in joints. OA affects about three million Canadians. Because there are no biomarkers for spine OA, the only way to identify the disease is through radiographs, which use x-rays to reveal damaged joints.

However, radiographs can only identify advanced stages of the disease, after the damage has already been done.

To solve this problem, Dr. Kapoor's team, which included postdoctoral fellow Dr. Akihiro Nakamura and Krembil Clinician Investigator Dr. Y. Raja Rampersaud, analyzed tissue biopsies from 55 patients with spine OA. Their search involved analyzing 2,100 biological molecules. This approach revealed two promising molecules, called microRNA-181a-5p and microRNA-4454, which may be able to help clinicians determine the severity of spine OA.

"The most critical aspect of this discovery is that we have found that these two molecules are actively involved in increasing inflammation and destroying cartilage. Thus, blocking the activities of these molecules may represent a new 'targeted' therapeutic strategy—one that has the potential to prevent damage," says Dr. Kapoor.

Next, the team will investigate whether these new biomarkers can be detected in the blood and whether they can be used to design an early detection test for OA. If they are present in the blood when early or mild symptoms arise, then clinicians will know to prescribe treatments that can help prevent significant damage before it begins. The researchers will also test if blocking these biomarkers can halt spine degeneration.

JCI Insight. 2016 Aug 4;1(12):e86820. Supported by the UHN Arthritis Program, the Krembil Foundation and the Toronto General & Western Hospital Foundation. I Jurisica (co-author on the study) holds a Tier 1 Canada Research Chair in Integrative Cancer Informatics.

Dr. Mohit
Kapoor



A Gut Reaction

The unlikely link between gut immune cells and joint disease

What do baby formulas, memory foam and smartphone cameras have in common? They all resulted from solutions originally developed by NASA for space travel. Just as technological innovations sometimes rely on seemingly unconnected factors, so do health and disease.

That is what Krembil Senior Scientist Dr. **Robert Inman** (pictured) found when searching for a link between gut inflammation and a joint disease known as ankylosing spondylitis.

There is currently no cure for ankylosing spondylitis, which causes painful swelling and stiffness in the neck and spine. Although it is known to result from inflammation mediated by the body's own immune system, the underlying cause of the disease remains a mystery.

To address this problem, Dr. Inman and Eric Gracey, a University of Toronto immunology graduate student, focused on one possible explanation: that a specific type of immune cell that originates in the gut, known as a mucosal-associated invariant T (MAIT) cell, is involved in the disease. The researchers chose to focus on MAIT cells because most people with ankylosing spondylitis also have inflammation of the gut. Furthermore, MAIT cells have been implicated in other chronic diseases such as inflammatory bowel disease.

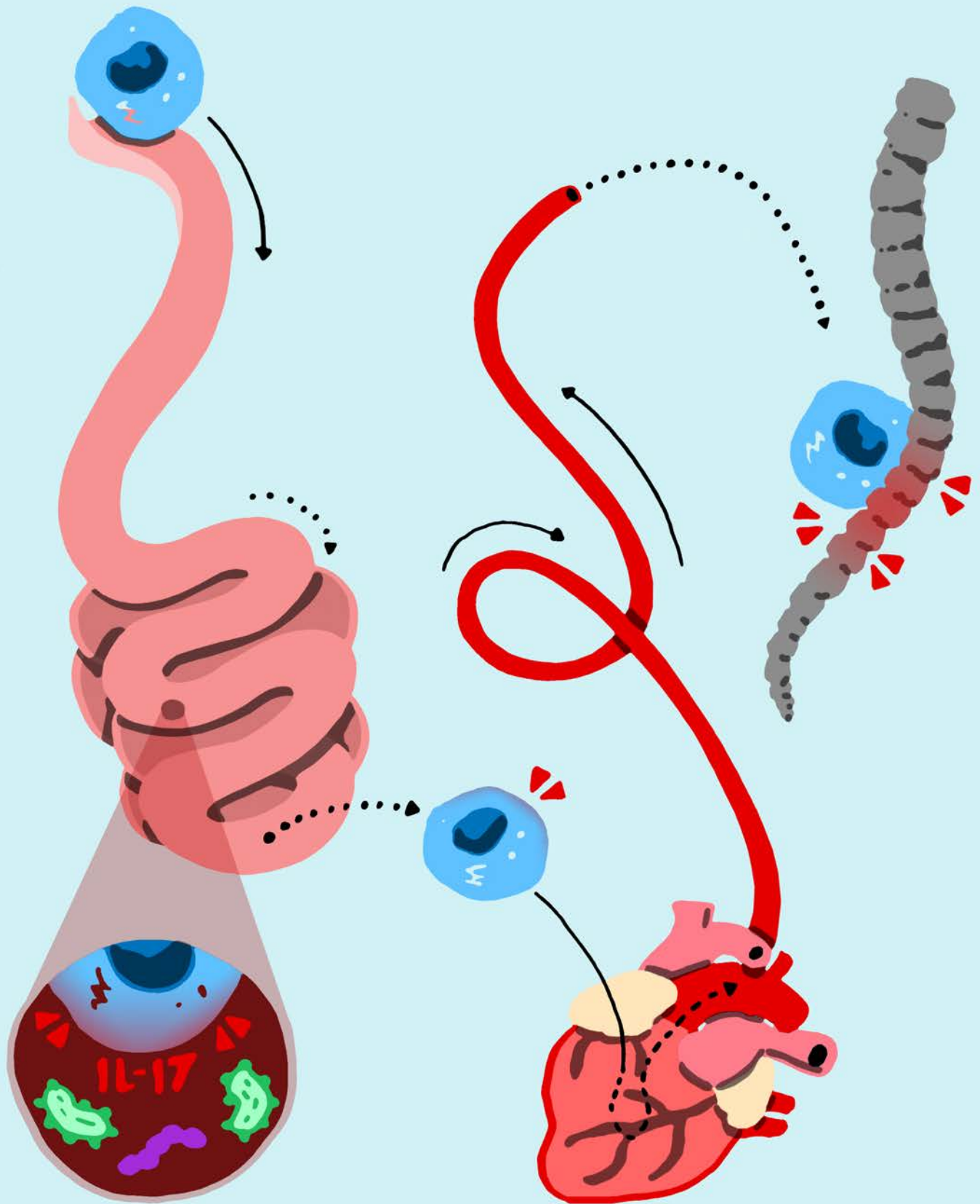
The results showed that people with the disease had fewer MAIT cells in their circulating blood than healthy individuals. This might seem counterintuitive; however, the researchers also found that MAIT cell levels were much higher within the fluid of diseased joints. This suggests that MAIT cells are recruited to inflamed joints in people with ankylosing spondylitis, leading to

fewer MAIT cells in their circulating blood. Furthermore, detailed analyses from joints revealed that many MAIT cells were 'activated' (ie, in a state that could promote harmful inflammation). Dr. Inman explains, "These cells displayed proteins on their surface that are known to promote inflammation—and one of these, known as interleukin-17, has been implicated in ankylosing spondylitis."

These results suggest that immune cells originating in the gut play a role in ankylosing spondylitis. This unlikely connection has revealed a new target that could be used for the development of novel treatments for this debilitating disease.



Ann Rheum Dis. 2016 Dec;75(12):2124-2132. Supported by the Canadian Institutes of Health Research, the Buchan Family Arthritis Research Centre and the Toronto General & Western Hospital Foundation.



The figure above illustrates a possible link between the gut and diseased joints: immune cells, known as MAIT cells (blue), become activated in the gut and travel to the affected joints, where they may promote harmful inflammation.

Making a Mental Map

Computer models help predict how we navigate surroundings

When navigating through familiar places, we rely on what is known as our spatial memory. A brain region called the hippocampus plays an integral role in spatial memory: recording information about one's environment and spatial orientation.

The same brain region also processes emotion—not surprising given that memories can often be emotionally charged. For this reason, damage to the hippocampus can cause a form of amnesia—known as anterograde amnesia—in which new memories can no longer be formed, while older memories may be left intact.

The challenge for researchers is figuring out exactly what went wrong. The brain is like a huge electrical network: specialized cells known as neurons communicate with each other by transmitting electrical signals. Proteins on the surface of neurons, known as ion channels, enable this transfer of information by controlling the flow of charged particles (ions) in and out of the cell.

One way to tackle this challenge is to develop and use computer models to simulate brain function. These models can be programmed to mimic the activity of individual cells or networks of cells within the brain.

Krembil Senior Scientist Dr. **Frances Skinner** and her PhD student, Vladislav Sekulić, recently used this approach to determine how ion channels in the hippocampus affect brain function.

Their models focused on the distribution of ion channels on particular types of neurons called O-LM cells, which are important for controlling the flow of information into the hippocampus.

At slower firing rates (4-7 times per second), they are believed to contribute to processing emotions, while at faster firing rates (7-12 times per second), they are believed to be involved in forming a mental map of your surroundings.

By artificially adjusting the distribution of ion channels in their models, the researchers found that specific combinations and distributions of ion channels on O-LM cells predispose or 'tune' them to fire at either slower or faster firing rates. Thus, their models suggest that O-LM cells predispose the hippocampus to process emotional or spatial information by virtue of having different and particular ion channel distributions.

"It is exciting to consider that our modeling approach has enabled us to make predictions about how specific cell properties influence memory processing," says Dr. Skinner. "As O-LM cell activity can be measured using implanted electrodes, the next step will be to test our models' predictions in experimental models. By working together, computer modellers and experimentalists can develop a more comprehensive understanding of how memory systems work and, by extension, help to discover new treatments for memory disorders."

Elife. 2017 Mar 20. pii: e22962. Supported by the Natural Sciences and Engineering Research Council of Canada; and the SciNet HPC Consortium.

Image: Dr. Frances Skinner is shown navigating through Toronto's Kensington market area.



Brain Storms

Predicting where age-related brain damage will strike

Much like a flash of lightning can alert us of an impending storm, 'bright spots' that light up in magnetic resonance imaging (MRI) brain scans, called leukoaraiosis or white matter hyperintensities (WMHs), can serve as a warning sign of impending age-related brain damage and intellectual decline.

WMHs occur in the brain's white matter—a type of tissue that facilitates electrical communication between brain regions. They were initially thought to represent structural brain changes that occur as part of normal aging because they are more commonly observed in the elderly, but they have since been linked to a number of neurological disorders, such as dementia and age-related intellectual decline.

It has recently been proposed that WMHs represent localized 'mini-strokes'—small brain regions that are damaged as a result of limited blood flow. Despite this hypothesis, much remains unknown about what causes WMHs and how to prevent them.

Recent findings from Krembil Senior Scientist Dr. **David Mikulis** (pictured on this page), published in the prestigious *Annals of Neurology*, have now revealed a way to predict where these bright spots could strike.

In the study, Dr. Mikulis and his team used MRI to obtain detailed brain images from 45 patients (aged between 50 and 91 years old) at the start of the study and one year into the study.

Using the MRI data, he measured what is known as the cerebrovascular reserve, which describes the capacity of specific brain regions to increase blood volume. He did this using a carefully

controlled approach, which involved stimulating the blood vessels in the brain to widen.

The results showed that white matter regions with lower cerebrovascular reserve had a higher probability of developing WMHs.

Dr. Mikulis comments, "We found that areas of the brain with decreased blood flow reserve were at greater risk for future brain injury. The specific type of injury that can be predicted, known as ischemic demyelination, has been implicated in age-related brain damage. Thus, this new marker could be used for early detection of damage and to monitor the effects of new preventative therapies to stop brain damage before it occurs."

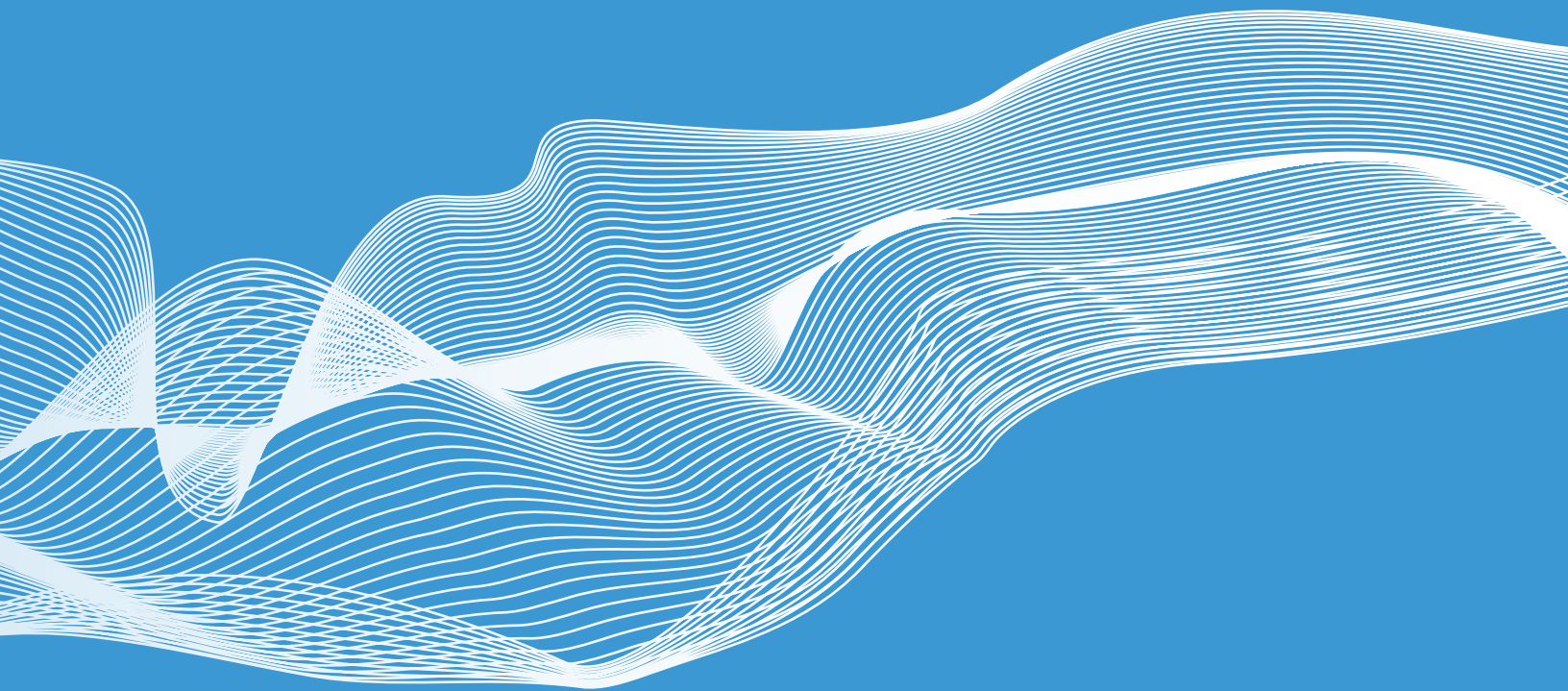


Ann Neurol. 2016 Aug;80(2):277-85. Supported by the Canadian Stroke Network; the Ontario Ministry of Research, Innovation and Science; and the Academic Health Science Centre Alternative Funding Plan.



Technology Transfer

From molecule to mankind: research at Krembil is translated to tangible products that can improve patients' lives



Better Diagnosis

Unique protein profile warns of kidney inflammation



Krembil Senior Scientist Dr. **Joan Wither** (pictured above) and colleagues identified a panel of protein biomarkers found in urine that can be used to identify people with the autoimmune disease systemic lupus erythematosus (SLE) who have active kidney inflammation.

Seventy percent of SLE patients will develop kidney inflammation, called nephritis, which can ultimately lead to kidney failure. As a result, approximately 15% of those with nephritis require dialysis or a kidney transplant to stay alive. Being able to accurately diagnose the type and severity of nephritis in people with SLE will revolutionize how the disease is treated and go a long way towards improving patients' quality of life and reducing health care costs.

Because the biomarkers that Dr. Wither identified return to normal levels when kidney inflammation is resolved, they may have clinical utility as a non-invasive method to monitor response to therapy. Improving disease tracking will greatly reduce the number of patients who take powerful drugs that suppress the immune system and carry serious side effects.

And because the panel of proteins can be read from urine samples, it could help reduce the burdens on certain patients that currently require invasive kidney biopsies for a definitive diagnosis of nephritis.

Dr. Wither and her team also found that a subset of these biomarkers can be used to predict which patients are most likely to respond to standard therapy. Thus, the panel can be used to glean information about what treatment course will work best for individual patients.

In April 2016, Dr. Wither was awarded a *Proof of Principle Program* grant from the Canadian Institutes of Health Research to determine the most accurate combination of urinary biomarkers for flagging SLE patients with nephritis. She also submitted a US patent application in 2016 for her biomarker panel.

Supported by the Canadian Institutes of Health Research, the Lupus Research Alliance, the Arthritis and Autoimmunity Research Centre of the University Health Network, The Arthritis Society, the Arthritis Centre of Excellence and the University of Toronto.

Helping Hands

Assessing hand function in spinal cord injury survivors



A team of UHN researchers and international collaborators have developed a clinical tool that can assess hand function in patients with partial or total paralysis following traumatic cervical spinal cord injury (SCI). The tool, known as the Graded and Redefined Assessment of Strength, Sensibility and Prehension (GRASSP), comprises clinical measurements that can assess three readouts of hand function: strength, sensation and prehension (the act of grasping).

Currently, it is difficult for clinicians to assess whether an intervention is effective in promoting recovery from SCI. GRASSP addresses this problem by enabling care providers to reliably measure minute changes in hand function over time; using GRASSP they can test the effectiveness of rehabilitation programs (eg, for partial spinal cord injuries) and experimental therapies at enhancing functional recovery, facilitating the development of novel therapies.

GRASSP is already making a difference. It is currently being used to measure treatment success in investigator- and pharmaceutical-led studies, which will use it to assess experimental treatments in patients with SCI.

It is also being used by a large US health care organization to assess the effectiveness of rehabilitation programs for tetraplegic patients.

Two new versions of GRASSP were released in 2016: an optimized 'version 2.0' that was created by incorporating user feedback; and 'GRASSP-Myelopathy', which can be used to assess upper limb impairment in people with non-traumatic cervical SCI, such as those with amyotrophic lateral sclerosis and multiple sclerosis.

The creation of GRASSP was led by a group of UHN researchers and collaborators, including former Krembil Clinician Investigator and TRI Affiliate Scientist Dr. **Sukhvinder Kalsi-Ryan** (pictured above), Krembil Senior Scientist Dr. **Michael Fehlings**, along with TRI Affiliate Scientist Dr. Molly Verrier and Dr. Armin Curt from the University of Zurich.

This work was supported by the Dana and Christopher Reeve Foundation, the Rick Hansen Institute, the Ontario Neurotrauma Foundation, the Physiotherapy Foundation of Canada, the Canadian Institutes of Health Research and the Craig Neilsen Foundation. M Fehlings holds the Gerry and Tootsie Halbert Chair in Neural Repair and Regeneration.

Research Events



Krembil Research Day 2016

The 16th Annual Krembil Research Day was held on May 18, 2016. It was commenced by UHN's former Executive Vice President, Science and Research, Dr. Christopher Paige; as well as the Director of the Krembil Research Institute, Dr. Donald Weaver.

The first presentation of the day was given by Dr. Eugenia Kumacheva, University Professor at the University of Toronto's Department of Chemistry. She described her research into microfluidic platforms for use in cell biology and medicine, which incorporates innovative and advanced single-cell culture approaches.

The keynote speaker was Dr. Betty Diamond, from The Feinstein Institute for Medical Research. She is a leading expert in the molecular and immunologic factors that influence the severity of systemic lupus erythematosus, also known as lupus. Her talk was titled *Antibodies and the Brain* and described her research on the role of anti-DNA antibodies in lupus and the potential mechanisms that lead to neurological symptoms of the disease.

The Annual Research Day also provided a venue for trainees to present their findings via oral and poster presentations. Awards for the top three graduate and postdoctoral presentations were selected by Krembil Researchers.



A New Vision, a New Institute

Creation of the Donald K. Johnson Eye Institute was announced on September 20, 2016.

The Institute merges UHN's Ophthalmology Department (previously the Donald K. Johnson Eye Centre) and the Division of Vision Sciences.

This transformation will facilitate collaborations between clinicians, researchers and educators, with the ultimate goal of improving patient care and finding cures to restore vision. "The greatest research advances often stem from simple conversations between clinicians and researchers, which spark new ideas. The organizational structure of the Institute will ensure that these conversations happen," says Dr. Wallace, who is co-leading the Institute with Dr. Robert Devenyi.

Dr. Valerie Wallace will serve as research lead and is Head of Vision Sciences, a Krembil Senior Scientist and the Donald K. Johnson Chair in Vision Research. Dr. Robert Devenyi will serve as clinical lead and is the Director of Retinal Services, a Krembil Clinician Investigator and the Karen and William Barnett Chair in Ophthalmology.

Creation of the Institute was made possible by the continued generosity of philanthropists Donald K. Johnson and his wife, Anna McCowan-Johnson (pictured addressing the crowd at the event). The name of the Institute reflects their long-standing support for clinical efforts and basic research.



A Catalyst for Discovery

The first ever Discovery Ball—a fundraising initiative led by the Toronto General & Western Hospital Foundation—took place on October 15, 2016. The goal of the event was to promote the Krembil's research successes and raise capital to support research.

The Discovery Ball planning committee was co-chaired by Mrs. Stacey Krembil, who was the brainchild of the event, and Dr. Michael Baker, who hosted the event. The night was well attended, with nearly 400 distinguished guests, including philanthropists, UHN leadership and Krembil-affiliated researchers.

The event included a raffle for prizes such as a diamond rivière necklet, as well as a candid conversation between Krembil Director Dr. Donald Weaver and science communicator Jay Ingram (pictured). A live auction, hosted by broadcaster, award-winning writer and producer Husein Madhavji, capped the event. The highest bidders won the opportunity to tour the labs of Dr. Weaver and Krembil Senior Scientist Dr. Mohit Kapoor.

The event raised nearly \$1 million to support research at the Krembil. Because of its success, the Discovery Ball will continue as a staple of the Toronto General & Western Hospital Foundation's fundraising efforts, with the next event scheduled for October 2018.



Researchers Seize the Day

The Anne & Max Tanenbaum Symposium on the Frontiers of Science took place on November 2, 2016. The event was hosted by the Anne & Max Tanenbaum Chair in Cognitive Neuroscience and Krembil Senior Scientist Dr. Peter Carlen.

The symposium, which was titled *Listening and responding to the brain: neuroengineering and epilepsy*, bridged the latest technological advances in seizure therapeutics with recent fundamental research findings. It featured a series of intriguing presentations given by leading experts in epilepsy research, including Dr. Carlen, who spoke about the brainstem's role in seizures and seizure-related death, and keynote speakers Dr. Dominique Durand from Case Western Reserve University and Dr. Gregory Worrell from the Mayo Clinic. Dr. Durand spoke about harnessing the power of single brain cells to prevent seizures, while Dr. Worrell's talk focused on methods to forecast future epileptic seizures.

Other speakers were Krembil Scientist Dr. Taufik Valiante, and Drs. Roman Genov and Berj Bardakjian from the University of Toronto. "By bringing together neuroengineers and epilepsy biologists, the Anne & Max Tanenbaum Symposium has helped to foster interdisciplinary collaboration, which will no doubt spark future scientific progress," says Dr. Carlen.

Research Distinctions

Selected honours bestowed upon Krembil researchers

Dr. Vinod Chandran

2017 Young Investigator Award, Canadian Rheumatology Association

Dr. Karen Davis

2017 Outstanding Pain Mentorship Award, Canadian Pain Society

Dr. Michael Fehlings

David Lostchuck Memorial Research Award, Canadian Spinal Research Organization

Dr. Brenda Gallie

Member, Order of Canada

Dr. Dafna Gladman

2016 Evelyn V. Hess Award, Lupus Foundation of America

Dr. Nigil Haroon

2016 Young Investigator Award, Canadian Rheumatology Association

Dr. Sidney Kennedy

Fellow, Canadian Academy of Health Sciences

Dr. Anthony Lang

MDS Pan-American Section Leadership Award, International Parkinson and Movement Disorder Society

Dr. Andres Lozano

Officer, Order of Canada

2017 Khwarizmi International Award, Iranian Research Organization for Science and Technology

Dr. Antonio Strafella

Tier 2 Canada Research Chair in Movement Disorders and Neuroimaging (renewal)

Dr. Charles Tator

Officer, Order of Canada

Dr. Michael Tymianski

Member, Order of Canada

Dr. Murray Urowitz

Lifetime Achievement Award, Lupus Ontario

Dr. Donald Weaver

Tier 1 Canada Research Chair in Drug Design for Protein Misfolding Disorders



Krembil Researchers

Krembil research is organized into six divisions that are directed towards the development of diagnostics, treatments and management strategies for the following priority research areas:



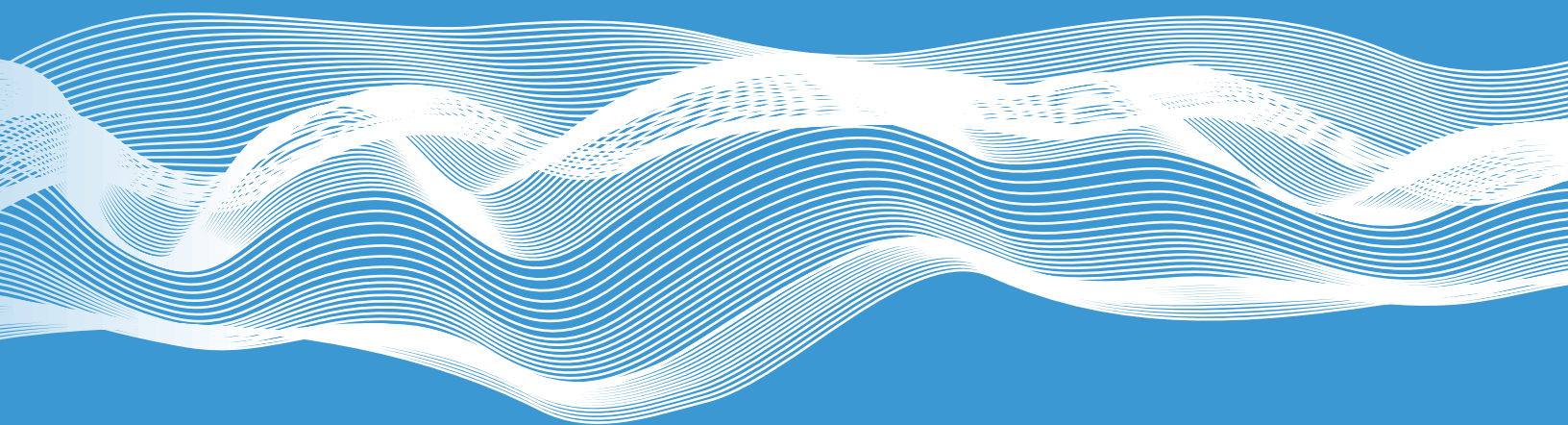
Brain and spine disorders



Bone and joint disorders



Vision disorders



Appointed Researchers by Division

Brain, Imaging & Behaviour – Systems Neuroscience

Division Head

Karen Davis

Senior Scientists

Jonathan Brochie
Robert Chen
Karen Davis
William Hutchison
Sidney Kennedy
Andres Lozano
Mary Pat McAndrews
David Mikulis
Antonio Strafella

Scientists

Jonathan Downar
Mojgan Hodaie

Affiliate Scientists

Mark Guttman
Clement Hamani
Walter Kucharczyk

Fundamental Neurobiology

Division Head

Peter Carlen

Senior Scientists

Peter Carlen
Frances Skinner
Shuzo Sugita
Michael Tymianski
Donald Weaver

Scientists

Jérémie Lefebvre
Ivan Radovanovic
Taufik Valiante

Affiliate Scientists

Magdy Hassouna
Liang Zhang
Georg Zoidl

Genetics & Development

Division Head

James Eubanks

Emeritus Scientist

Charles Tator

Senior Scientists

Cathy Barr
James Eubanks
Michael Fehlings
Robert Inman
Mohit Kapoor
Lyanne Schlichter
Elise Stanley
Florence Tsui
Joan Wither

Scientists

Mark Erwin
Nigil Haroon
Suneil Kalia
Lorraine Kalia
Armand Keating

Affiliate Scientists

Arjun Sahgal
Sowmya Viswanathan

Healthcare & Outcomes Research

Division Heads

Elizabeth Badley
(until April 2017)
Aileen Davis
(effective April 2017)

Emeritus Scientist

Murray Urowitz

Senior Scientists

Elizabeth Badley
Aileen Davis
Dafna Gladman
Nizar Mahomed

Scientist

Anthony Perruccio

Affiliate Scientists

Vinod Chandran
Cheryl Cott
Paul Fortin
Monique Gignac
Rosemary Martino

Patient-Based Clinical Research

Senior Scientist

Anthony Lang

Donald K. Johnson Eye Institute

Co-Directors

Valerie Wallace
Robert Devenyi

Senior Scientists

Christopher Hudson
Philippe Monnier
Martin Steinbach
Graham Trope
Valerie Wallace
Agnes Wong

Scientist

Jeremy Sivak

Affiliate Scientists

Moshe Eizenman
John Flanagan
Brenda Gallie

Clinician Investigators

Dimitri Anastakis
Heather Baltzer
Mark Bernstein
Anuj Bhatia
Michael Brent

Daniel Buchman
 Frances Chung
 Melanie Cohn
 Robert Devenyi
 Dean Elterman
 Alfonso Fasano
 Susan Fox
 Kenneth Fung
 Rajiv Gandhi
 Timothy Jackson
 Efreem Mandelcorn
 Daniel Mandell
 Shane McInerney
 Roger McIntyre
 Renato Munhoz
 Laura Passalent
 Fayez Queresby
 Raja Rampersaud
 David Rootman
 Cheryl Rosen
 Allan Slomovic
 David Tang-Wai
 Maria Carmela Tartaglia
 Zahi Tuma
 Christian Veillette
 Elizabeth Wilcox
 Mateusz Zurowski

Non-Appointed Researchers

Ronit Agid
 Jamil Ahmad
 Danielle Molinari Andrade
 Yaron Avitzur
 Paul Binhammer
 Arthur Bookman
 Vera Bril
 Richard Brull
 Yvonne Buys
 Simon Carette
 Leanne Casaubon

Rodrigo Cavalcanti
 Jas Chahal
 Clara Chan
 Vincent Chan
 Kenneth Chapman
 Angela C Cheung
 Angela M Cheung
 Ki Jinn Chin
 Michael Cusimano
 J Roderick Davey
 Jose Martin del Campo
 Michael Easterbrook
 Sherif El-Defrawy
 Richard Farb
 David Frost
 Fred Gentili
 Alberto Goffi
 Allan Gordon
 Brent Graham
 Sindhu Johnson
 Moira Kapral
 Hans Katzberg
 Ron Keren
 Ed Keystone
 Kyle Kirkham
 Paul Kongkham
 Stephen Kraft
 Timo Krings
 Richelle Kruisselbrink
 Jeffrey Kwong
 Robert Lam
 Johnny Lau
 Stephen Lewis
 Joel Lexchin
 Mark Mandelcorn
 Pirjo Manninen
 Samuel Markowitz
 Connie Marras
 Theodore Marras
 Wayne Marshall
 Eric Massicotte
 Steven McCabe
 Ali Naraghi

Ahtsham Niazi
 Ivy Oandasan
 Darrell Ogilvie-Harris
 Allan Okrainec
 Karen Okrainec
 Dimitrios Oreopoulos
 Christian Pagnoux
 Philip W Peng
 Vitor Pereira
 Aleksandra Pikula
 Atul Prabhu
 Arun Prasad
 Sidney Radomski
 Sapna Rawal
 Shail Rawal
 Aylin Reid
 Lisa Richardson
 Jorge Sanchez-Guerrero
 Paul Sandor
 Hemant Shah
 Frank Silver
 Martin Simons
 Jeff Singh
 Mandeep Singh
 Sumeet Sodhi
 Peter St George-Hyslop
 Matthew Stanbrook
 Peter Tai
 Susan Tarlo
 Karel terBrugge
 Karen Tu
 Lashmi Venkatraghavan
 Herbert von Schroeder
 Adam Weizman
 Richard Wennberg
 David H Wong
 David T Wong
 Jean Wong

External Sponsors

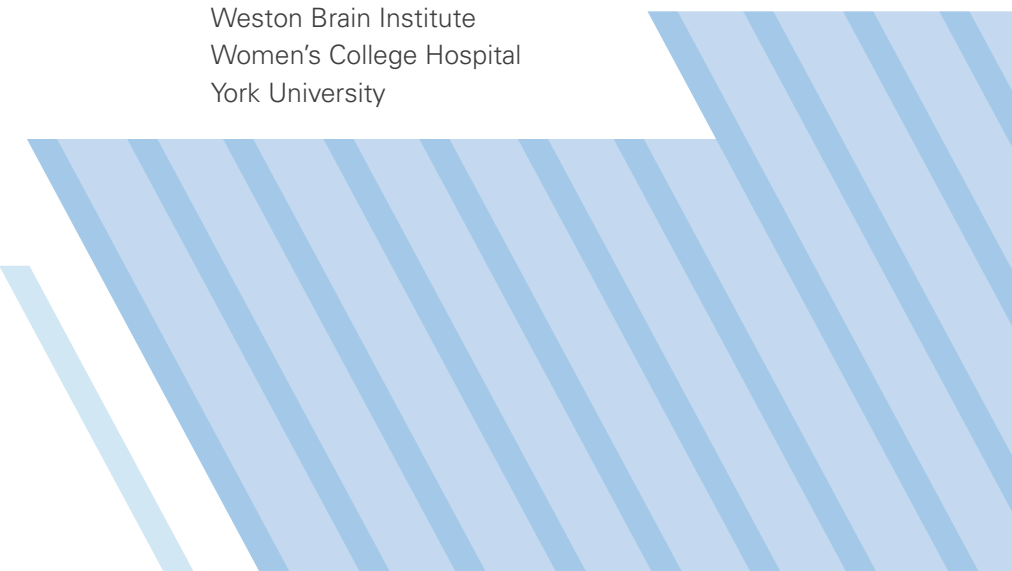
Thank you to our partners, who provide key support for our research and efforts to conquer debilitating diseases

Abbott Laboratories
AbbVie
Acorda Therapeutics
ActiveO
Adamas Pharmaceuticals
Alfred Health
Alion Pharmaceuticals
Alzheimer Society of Canada
AOSpine
Arthritis Research Foundation
Assessment of SpondyloArthritis international Society
Association of University Radiologists
Astellas Pharma
Bayer
BioCanRX
Biogen
Boehringer Ingelheim
Boston Scientific
Brain & Behavior Research Foundation
Brain Canada
Bristol-Myers Squibb
Buchan Family Foundation
Canada Foundation for Innovation
Canada Research Chairs Program
Canadian Association of Psoriasis Patients
Canadian Institutes of Health Research
Celgene
Centre hospitalier de l'Université de Montréal
Cervical Spine Research Society
Covidien
Cynapsus Therapeutics
Dystonia Medical Research Foundation
Eli Lilly Canada
Emory University

Foundation Fighting Blindness
Friends of FACES (Finding A Cure for Epilepsy and Seizures)
GE Canada
Genentech
Gilead Sciences
Glaucoma Research Society of Canada
GlaxoSmithKline
Heart and Stroke Foundation of Canada
InSightec
Insmed
Intercept Pharmaceuticals
International Rett Syndrome Foundation
InVivo Therapeutics
J.P. Bickell Foundation
Jaeb Center for Health Research
Janssen
Krembil Foundation
Kyowa Hakko Kirin
Lawson Health Research Institute
London Health Sciences Centre
Lumena Pharmaceuticals
Lundbeck Canada
Lupus Foundation of America
Lupus Research Alliance
Medical Decision Modeling
Medtronic
Merck
Merz Pharma
Ministry of Education
Ministry of Research, Innovation and Science
Mitacs
Morton Cure Paralysis Fund
Mount Sinai Hospital
Multiple Sclerosis Society of Canada



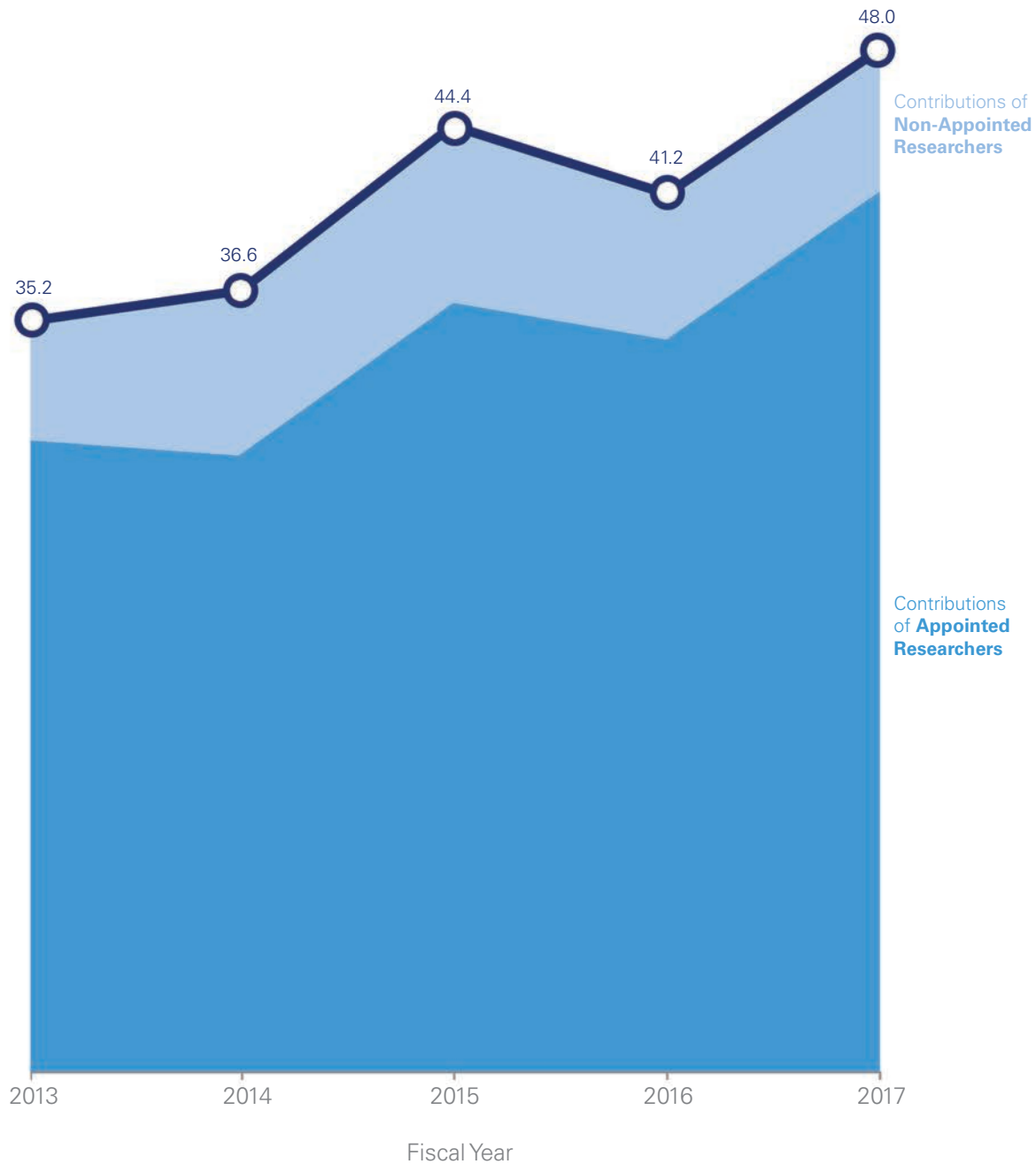
National Institutes of Health
NeuroDevNet
New Era Pharma
Northwestern University
Novartis
Onkocellular
Ontario Best Practices Research Initiative
Ontario Brain Institute
Ontario Institute for Regenerative Medicine
Ontario Neurotrauma Foundation
Ontario Rett Syndrome Association
Ophthotech
Paralyzed Veterans of America Education
Foundation
Parexel
Parkinson Canada
Parkinson's Disease Foundation
Pfizer
PharmaNet
Physicians' Services Incorporated Foundation
Protagen
PuraPharm
Recro Pharma
Research Institute of the McGill University Health
Centre
Rick Hansen Foundation
Roche
Sanofi
Savoy Foundation
SickKids
Skoll Foundation
St. Michael's Hospital
Stanley Medical Research Institute
Stem Cell Network
StemCells



Sunnybrook Health Sciences Centre
TauRx Therapeutics
Temerty Family Foundation
The Arthritis Society
The Foundation of the American Society of
Neuroradiology
The Michael J. Fox Foundation for Parkinson's
Research
The Princess Margaret Cancer Foundation
The Toronto General & Western Hospital
Foundation
The W. Garfield Weston Foundation
Tocagen
Tourette Association of America
University Hospital Tübingen
University of British Columbia
University of California, San Francisco
University of Medicine and Dentistry of New
Jersey
University of Michigan
University of Pennsylvania
University of Toronto
University of Washington
Vertex Pharmaceuticals
Virginia Commonwealth University
Weston Brain Institute
Women's College Hospital
York University

Financials

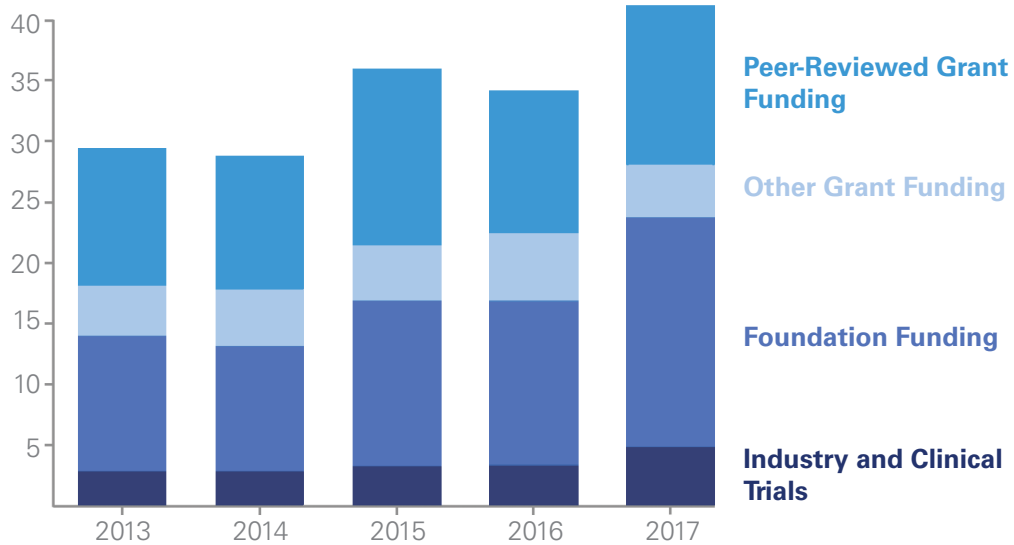
Research Funding Trends (\$, Millions)^a



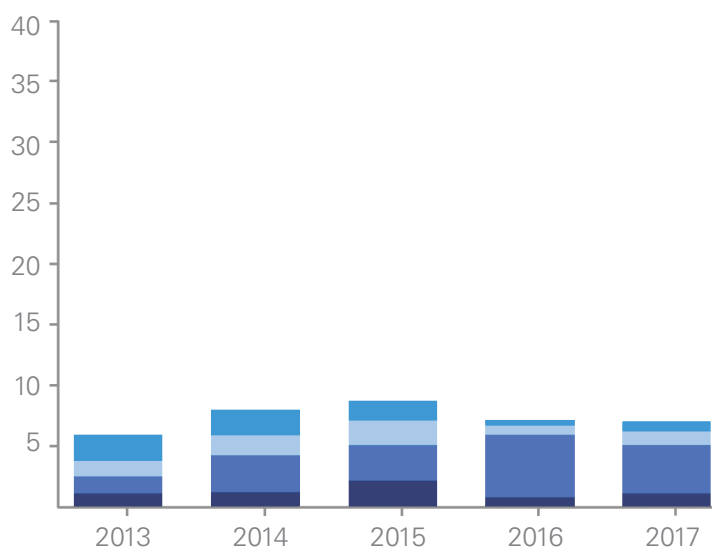
^aThe Research Funding amounts listed above include all Krembil research funds (\$CAD) that have come into UHN accounts from external sources, including UHN Foundations, within the indicated fiscal years. Krembil has 97 appointed researchers (including: 34 Senior Scientists, 12 Scientists, 16 Affiliate Scientists, 2 Emeritus and 33 Clinician Investigators) and 97 non-appointed 'Clinical Researchers'. For a detailed disclaimer, see page 34.

Research Funding by Type (\$, Millions)

Appointed Researchers



Non-Appointed Researchers



Krembil Research Council

Director and Chair, Krembil Research Institute
Donald Weaver

Co-Director, Donald K. Johnson Eye Institute
Valerie Wallace

Division Head, Healthcare & Outcomes Research
Aileen Davis*

Division Head, Fundamental Neurobiology
Peter Carlen

Division Head, Brain, Imaging & Behaviour – Systems Neuroscience
Karen Davis

Division Head, Genetics & Development
James Eubanks

Medical Director, Orthopaedics; Director, Arthritis Program
Nizar Mahomed

Clinical Representative, Arthritis Program
Robert Inman

Chair, Trainee Affairs Committee
Frances Skinner

Executive Director, Research Operations
Lisa Alcia

Senior Vice President, UHN and Executive Lead, TWH
Janet Newton

Executive Vice President, Science and Research
Bradly Wouters**

**role held by Elizabeth Badley until April, 2017*

***role held by Christopher Paige until October, 2016*

Disclaimers

Financials: Figures provided by UHN Research Financial Services. All data represent the fiscal years ending in March 31.

Personnel: Appointed and non-appointed researchers, trainee and staff numbers provided by Krembil Directorate Office. Researcher listing is accurate as of March 31, 2017.

Publications: Publication data provided by UHN's Research Program Planning & Analysis team. Citation data are accurate as of July 1, 2017. Publications jointly authored by multiple Krembil investigators are counted only once in the Krembil publication total. In cases where publications overlap more than one major research theme (ie, neuroscience, arthritis and/or vision) they are counted more than once in theme subanalyses but only once in the Krembil publication total. The bibliometrics presented include data based on all Krembil researchers, which includes appointed researchers and non-appointed researchers (ie, researchers that are not subject to Krembil's scientific and performance reviews). Non-appointed researchers are defined as principal investigators who are based at Toronto Western Hospital and who are listed as first or senior author on at least one publication in the 2016 calendar year and/or held research funding over the 2017 fiscal year.

Benchmarking: 5-year publication data comprised articles, reviews and proceeding papers published in Web of Science (WoS)-indexed journals and was derived using an author name-based search of Krembil researchers. Appointment and departure dates were strictly applied. Publications for comparator hospitals were identified using the organizational name, affiliated institutions and variations thereof, and retrieved within the same week to ensure contemporaneous data. Comparator research hospitals were selected using *ReSearch Infosource's* list of "Canada's Top 40 Research Hospitals 2016", which ranks institutions by total research spending in the previous fiscal year. Journals were categorized into Krembil priority areas (ie, 'Brain & spine', 'Arthritis' and 'Vision') by assigning one or more of these priority areas to WoS themes (ie, every journal in WoS is assigned one/multiple themes; for example, the journal *PAIN* has the themes 'Anesthesiology', 'Clinical Neurology' and 'Neurosciences'). A WoS theme was assigned to a priority area when >20% of the articles within the theme were judged relevant to one or more priority areas; this was determined by considering the research focus of the Krembil author and the title of the article. The same theme assignments were used for comparator research hospitals. New themes that were not already categorized using Krembil publications were assigned to the 'other' category (a decision that was made after a random sampling of 300 papers from 50 new themes revealed that only ~5% were relevant to a Krembil priority area). While articles assigned two/three priority areas were counted twice/three times when assigning WoS themes, these publications were only counted once during publication and citation analyses.

Space: Data provided by UHN Research Facilities Planning & Safety. Space data are accurate as of March 31, 2017.

Production Credits: This report is published by the Directorate Office, Krembil Research Institute. Graphic design, writing, editing and production of this report was completed by UHN's Strategic Research Initiatives Development (StRiDe) Team.

Contact

Directorate Office, Krembil Research Institute
60 Leonard Street, Krembil Discovery Tower, Toronto Western Hospital, 4KD478; Toronto, Ontario, M5T 2S8, Canada
krembil@uhnresearch.ca
discoverkrembil.ca

If you are interested in donating to support Krembil research, please contact the Toronto General & Western Hospital Foundation:
E: foundation@uhn.ca; T: 416-603-5300; F: 416-603-6224; Toll free donation hotline: 1-877-846-4483 (UHN-GIVE); website: www.tgwhf.ca

This report was printed on environmentally friendly paper, which achieved the following savings:



6 trees



*875 kg CO₂
5,854 km driven*



*21,727 L of water
62 days of water consumption*



*5 GJ
24,146 60W light bulbs for one hour*



*266 kg of waste
5 waste containers*



*1 lb NO_x
emissions of one truck over 3 days*

Source: calculateur.rollandinc.com



FSC® is not responsible for any calculations on saving resources by choosing this paper



Krembil

Relentless.

Scientists at the Krembil Research Institute are relentlessly pursuing cures for diseases of the brain, spine, bones, joints and eyes.

discoverkrembil.ca

Brain and Spine

Clusters of a potassium-transporting ion channel with microglia in an injured spinal cord

Dr. Lyanne C. Schlichter
Senior Scientist, Krembil Research Institute

Bone and Joint

Fluorescence image of human cartilage stained to show live and dead cartilage cells

Dr. Mohit Kapoor
Senior Scientist, Krembil Research Institute

Eyes

Slice of an adult retina stained with blue to show all the nuclei of neurons

Dr. Valerie Wallace
Senior Scientist, Krembil Research Institute



UNIVERSITY OF
TORONTO

Krembil Research Institute 2017 Annual Report | Directorate Office, Krembil Research Institute
60 Leonard Street, Krembil Discovery Tower, Toronto Western Hospital, 4KD478, Toronto, Ontario, M5T 2S8