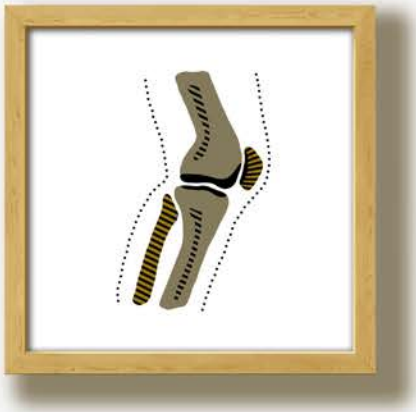




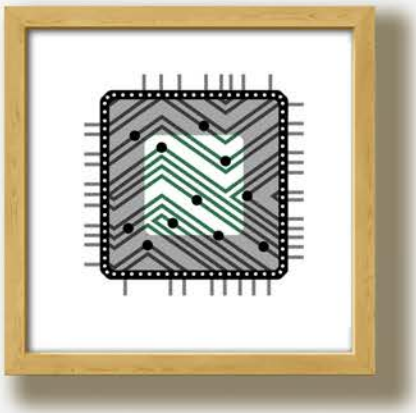


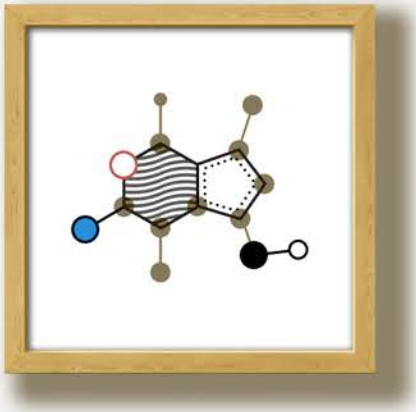

IN IT TOGETHER

Krembil

2018 Annual Report

The Krembil Research Institute ("Krembil") is the research arm of the Toronto Western Hospital (TWH), and it is one of the five research institutes at the University Health Network (UHN). Most of Krembil's research programs focus on the brain, the eye and arthritis. Its laboratories are located at the Krembil Discovery Tower and at TWH's Main, McLaughlin and Fell Pavilions. Prior to November 13, 2015, Krembil was known as the Toronto Western Research Institute.

About the cover: The framed icons represent Krembil's areas of expertise, including its three priority areas: arthritis (knee joint icon), eye and brain. Other areas of research expertise represented are medical imaging (X-ray icon), molecular and cellular biology (DNA double helix icon), computational biology (computer chip icon) and the spinal cord (vertebral column icon). Many Krembil researchers are practicing physicians at TWH, and their medical knowledge and experience (stethoscope icon) enhance its research programs. The institute's expertise in medicinal chemistry and drug development (molecule icon) is important for advancing research discoveries into new therapies and diagnostics.

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In It Together

to improve health and quality of life

It takes a community to make a scientific discovery and translate it into something real that will benefit society.

The Krembil Research Institute (Krembil) is such a community. It comprises dedicated groups of people working together to achieve the medical advances that are desperately needed to improve the lives of people suffering from a variety of severely disabling disorders.

We are principal investigators overseeing research programs, scientific staff and trainees performing experiments and analyzing data, and administrative staff providing ancillary services.

We are experts in multiple areas of biomedical research, many of which are represented by the icons on the cover page of this report. Although our research interests are broad, we focus our efforts in three priority areas: the brain, the eye and arthritis. Our expertise also encompasses a comprehensive range of methods and technologies—such as medical imaging, computational biology and experimental models of disease. We wield these tools to improve our understanding of human health and disease in each of our priority areas.

We work closely with a vast network of collaborators extending across Canada and throughout the world, realizing successes that depend on the generous support of our donors and external sponsors.

Many of our patients volunteer to participate in clinical studies, requiring them to receive experimental drugs or provide tissue samples or personal information. Without their selfless contribution, much of our work would be impossible.

Like the cogs in a wheel, all of these groups work together and form an efficient, smoothly functioning whole that is so much greater than their sum. This synergy enables us to move faster and closer towards our collective goal of improving the health and quality of life of the millions of people affected by chronic, debilitating diseases of the brain, eyes and joints.

This year's annual report contains many exciting stories of progress and success emerging from our laboratories and is a testament to the wonderful things that we are achieving together.

Thank you for sharing this journey with us.

Donald Weaver, MD, PhD, FRCPC, FCAHS
Director, Krembil Research Institute
University Health Network


Krembil
Relentless.

ARTHRITIS

One disease that encompasses many

At first glance, a Russian nesting doll appears to be only one doll; however, it includes many other dolls, hidden within itself. While we typically think of one disease when we hear the term arthritis, just like the nested dolls, it actually refers to a family of over 100 diseases, all of which cause inflammation and painful joints. Krembil researchers are making important advancements in the understanding and the treatment of several common and disabling forms of arthritis.

Providing Relief

Promising new drug eases symptoms of psoriatic arthritis

Several states exist between illness and health—this is especially true for patients living with psoriatic arthritis.

In the state of full-blown illness, patients have stiff and painful joints as well as psoriasis, a skin condition characterized by red skin patches that can be itchy and painful.

Although medications can be prescribed to alleviate these symptoms and help patients achieve a state of health and well-being, they are not always effective. Moreover, if the disease is left untreated, it can lead to severe joint damage and disability.

The most commonly prescribed medications for psoriatic arthritis are known as tumour necrosis factor (TNF) inhibitors. While effective for some, these medications fail to help approximately 40% of those affected by the disease: either their symptoms are not improved by the drug, or they cannot take it because of its adverse side effects.

Dr. **Dafna Gladman** published a report in the prestigious *New England Journal of Medicine* showing that the drug tofacitinib is an effective treatment for patients with psoriatic arthritis who do not respond to TNF inhibitors.

The researchers revealed the effectiveness of the drug through a large clinical trial that involved 350 patients from 14 countries. They found that approximately half of the patients taking tofacitinib experienced significant improvement in their joint symptoms and physical function, and that high doses of the drug could also improve skin symptoms.

"Our findings show that tofacitinib could help manage psoriasis and psoriatic arthritis in the 40% of patients who are not being treated. As such, this drug has the potential to provide relief to more patients affected by this disease," explains Dr. Gladman.

Gladman D, et al. N Engl J Med. 2017 Oct 19;377(16):1525-1536. Supported by Pfizer and the Toronto General & Western Hospital Foundation (TGWHF). Image: illustration above depicts, from left to right, the various states that exist between illness and health that can be experienced by people with psoriatic arthritis.

Balancing Act

New therapeutic target could help keep scar tissue in check

The body must produce just the right amount of scar tissue to stay healthy. Too little of it interferes with the healing of a tissue injury, whereas the accumulation of too much of it—through the process of fibrosis—can lead to loss of organ function and even organ failure.

For example, fibrosis stiffens the joints in osteoarthritis, can impair the lungs in rheumatoid athritis and can compromise the heart, lungs and kidneys in systemic scleroderma.

Presently, there are no adequate medications that can stop fibrosis or reverse the damage that it causes.

Dr. **Mohit Kapoor** led a team, including Dr. David Lagares and the late Dr. Andrew Martin Tagers at Harvard University, that discovered a new drug target for the treatment of fibrosis.

Using patient tissue samples and experimental models of lung fibrosis, the researchers demonstrated that a molecule known as soluble ephrin-B2 promotes lung fibrosis, whereas inhibiting the molecule's production reduces it.

Dr. Kapoor and other researchers are now beginning to understand that ephrin-B2 may promote fibrosis in other parts of the body, including the heart, kidneys and knee joints.

"Collectively, these results suggest that targeting the production of soluble ephrin-B2 could be an effective treatment for fibrosis in the lungs and other organs—and could represent a powerful new approach to treat a wide range of related diseases," says Dr. Kapoor.

Lagares D, et al. Nat Med. 2017 Dec;23(12):1405-1415.
Supported by TGWHF, the National Institutes of Health (NIH), the Université de Montréal, the American Thoracic Society Foundation, the Pulmonary Fibrosis Foundation, the Scleroderma Foundation and the Scleroderma Research Foundation.

A Missing Piece

Molecule may be elusive link between gut and arthritis

Dr. **Nigil Haroon** and his team identified a molecule—known as macrophage migration inhibitory factor (MIF)—that appears to link inflammation in the gut to ankylosing spondylitis, a form of spinal arthritis.

This discovery may help to resolve a longstanding mystery in the field. It is unclear why over half of ankylosing spondylitis patients have an inflamed bowel and up to 10% of patients are diagnosed with inflammatory bowel disease.

To help answer these questions, Dr. Haroon examined joint fluid and blood taken from 147 patients available through the UHN Spondylitis Program. The Program maintains a collection of biological samples taken from over 1,000 patients, which is the largest of its kind in the world.

"Our team found evidence that MIF is produced by cells in the intestine and travels through the blood stream to the spine. Once MIF reaches the spine, it promotes inflammation and the formation of new bone in spinal joints, which are hallmarks of ankylosing spondylitis," explains Dr. Haroon.

The researchers also showed that elevated MIF levels in the blood could predict progression of the disease.

Future studies will be focused on advancing the use of MIF in the clinic to predict the progression of ankylosing spondylitis, as well as the development of new therapeutics that target MIF to slow or stop the disease.

Ranganathan V, et al. Arthritis Rheumatol. 2017 Sep;69(9):1796-1806. Supported by TGWHF, the Canadian Institutes of Health Research (CIHR), the Arthritis Society and the Krembil Foundation.

BRAIN

Unearthing the roots of neurological disease

The architecture of the brain consists of a highly complex network of over a billion neurons. These interconnected neurons enable the brain to communicate with different parts of the body, which allows us to feel the warmth of the sun or hear the melody of a bird's song. Krembil researchers are revealing how disruptions to these connections underpin neurological diseases such as Parkinson disease and epilepsy.

The Root Cause

Mutation of KRAS gene increases risk of hemorrhagic stroke

Roots grow to sustain trees. They split from the main stem and become progressively smaller as they burrow deeper into the soil to seek nutrients and water. Likewise, the arteries in our body grow and branch out into smaller blood vessels that feed and nurture our cells.

In rare cases this process is disrupted and poorly formed blood vessels develop in the brain. These are referred to as brain arteriovenous malformations (BAVMs). These vessels are weaker and more likely to rupture and cause a stroke.

To get more insight into how BAVMs develop and why they are prone to rupturing or leaking, Dr. **Ivan Radovanovic** co-led a study, with Dr. Jason Fish from the Toronto General Hospital Research Institute, that examined the genetic content of BAVM tissue that was surgically removed from patients.

The researchers found that BAVMs from more than half of the patients contained a mutated version of the KRAS gene, which is best known for its role in promoting the growth and survival of cancer cells. The altered gene was only found in the cells lining the BAVMs where it weakened the blood vessels.

"Fortuitously, there are cancer drugs available that dampen KRAS' effects on cells. The next step will be to test whether these drugs can reverse the effects of mutated KRAS in experimental models of BAVMs," says Dr. Radovanovic.

Nikolaev SI, et al. 2018 Jan 18;378(3):250-261. Supported by CIHR, TGWHF, Novartis, the Canada Foundation for Innovation (CFI), the Natural Sciences and Engineering Research Council of Canada (NSERC), the Swiss Cancer League, the European Research Council, the American Heart Association, the Canada First Research Excellence Fund, the Government of Ontario, the Brain Aneurysm Foundation and UHN's Department of Surgery and Division of Neurosurgery. JE Fish holds a Tier 2 Canada Research Chair (CRC) in Vascular Cell and Molecular Biology. M Tymianski holds a Tier 1 CRC in Translational Stroke Research.

Parkinson State of Mind

Discovering alternate brain states that shed new light on Parkinson disease

Just as the appearance of trees can drastically change between two seasons—green and vibrant in spring to leafless and barren in winter—new evidence suggests that the human brain can also exist in two different states.

This intriguing discovery was made by Dr. **Antonio Strafella** and his team by using a highly sophisticated imaging technique called dynamic functional connectivity to visualize the brains of people with or without Parkinson disease.

The researchers discovered that the brain switches back and forth between two states: in the first state, the brain has sparse connections between cells that transmit information very efficiently; whereas in the second state, it has many connections that transmit information inefficiently.

By comparing the brain states of those with or without Parkinson disease, his team found that people with the disease were more likely to get stuck in the second state. Moreover, a shift in brain state from the first to the second was associated with more severe disease symptoms.

"We are the first to identify this second brain state," says Dr. Strafella. "Our results indicate that the brain of a patient with Parkinson disease is not very efficient at sending information. Our next step is to figure out what role this process plays in the evolution of the disease."

Kim J, et al. Brain. 2017 Nov 1;140(11):2955-2967. Supported by CIHR and TGWHF. A Strafella holds a Tier 2 CRC in Movement Disorders and Neuroimaging.

Changing Diagnosis

Genetic tests could improve diagnosis and treatment in patients with unexplained epilepsy

The brain is full of electrical activity. These electrical signals move from one cell to another, branching out to different parts of the brain and body where they control everything that we do.

In patients affected by epilepsy, these signals misfire and cause recurrent surges of abnormal electrical activity that lead to seizures. The cause of these surges is not well understood; however, researchers have shown that it can involve genetics, head trauma, developmental disorders, prenatal brain damage or infections.

Dr. **Danielle Andrade** recently examined the utility of a genetic test to help determine the cause of unexplained epilepsy in adults with an intellectual disability. The test detects a type of genetic alteration known as copy number variation (CNV), which has been linked to other diseases.

Dr. Andrade and her colleagues discovered that a high proportion of these patients carried rare CNVs that contributed to their epilepsy. Of the CNVs identified, eight were found to affect genes previously implicated in intellectual disability, autism and epilepsy.

"This study shows that genetic testing could provide clinicians with important information that may improve the diagnosis and treatment of epilepsy. Based on these findings, adults with epilepsy of unknown cause should be re-investigated with modern DNA technologies," says Dr. Andrade.

Borlot F, et al. JAMA Neurol. 2017 Nov 1;74(11):1301-1311. Supported by TGWHF, the Ontario Brain Institute (OBI) and the Government of Ontario. AS Bassett holds a Tier 1 CRC in Schizophrenia Genetics and Genomic Disorders.

EYE

Threading through the intricacies of vision

The eye is a complex organ that consists of many different parts that work in concert, and with the brain, to enable vision. Any damage or malfunction in its components or connections to the brain can lead to vision loss, blindness and other seemingly unrelated conditions—like photophobias. Krembil researchers are striving to understand how vision works in healthy and diseased eyes to prevent or cure these vision-related impairments.

Connectivity Issues

Exosomes could help to re-establish communication between the brain and eyes

When our computer loses its connection to the internet, we have a few easy fixes such as resetting the router or calling the internet provider.

Unlike re-connecting to the internet, it is much more difficult to re-establish disrupted connections between our organs and the brain.

Nerve fibres are the network cables that transmit and receive signals between the eyes and the brain. Once damaged, the resulting loss in connectivity is often irreversible, leading to blindness.

This year, Dr. **Philippe Monnier** discovered a new strategy to promote the repair of damaged nerve fibres that relay messages between the eyes and the brain.

This strategy relies on exosomes, which are tiny particles released by one cell and absorbed by another. Exosomes are one of several ways through which neighbouring cells communicate with each other. "An exosome is like a message in a bottle that one cell throws to another," explains Dr. Monnier.

The research team found that treating damaged eye nerves with exosomes from a specific type of cell—a fibroblast—enhanced the repair and regeneration of the nerve fibres. Fibroblast cells play an important role in wound healing.

"Our study is the first to show that fibroblast exosomes trigger the regeneration of nerve cells," explains Dr. Monnier. "These exosomes can be an effective tool for developing precise regenerative therapies to repair damaged nerves throughout the body."

Tassew NG, et al. Cell Rep. 2017 Jul 5;20(1):99-111. Supported by CIHR, TGWHF, the Krembil Foundation and the Heart and Stroke Foundation of Canada.

Shining Light on Photophobia

A bright idea to improve our understanding of debilitating light sensitivities

We have all experienced the visual discomfort caused by looking directly at a camera flash. However, even normal ambient light levels can be difficult to tolerate for those with certain health conditions—such as a migraine headache or cataracts.

Dr. **Agnes Wong** and her team have come up with an ingenious idea to improve our understanding of the mechanisms underpinning visual discomfort triggered by light—also known as photophobia.

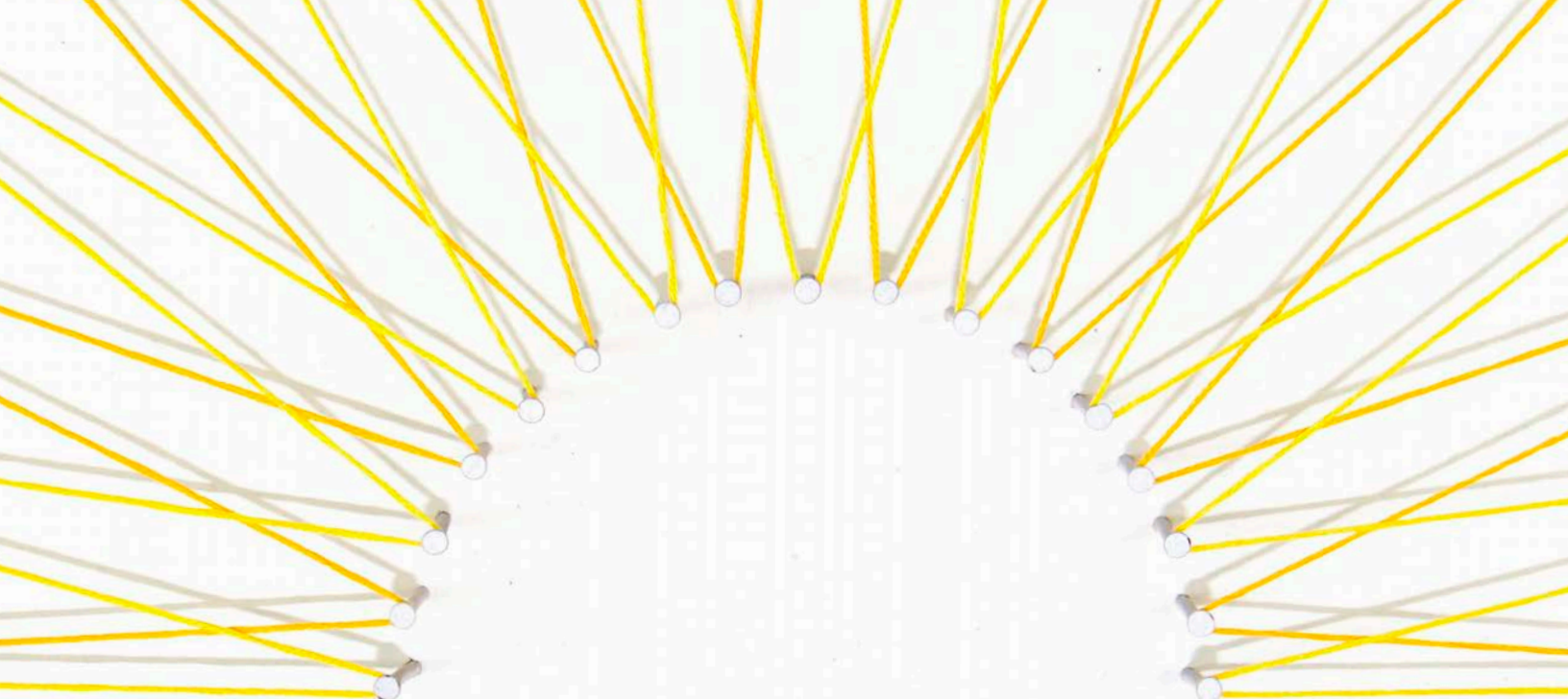
They developed a new test that enables researchers to measure a person's visual discomfort triggered by light in real time. The test uses a device that emits controlled flashes of light of varying colours and is linked to two push buttons, through which patients indicate when they experience visual discomfort.

When a small group of adults with no history of visual disorders tried the test, the research team found that blue light was more likely to induce discomfort than red light. This finding suggests that the intrinsically photosensitive retinal ganglion cell (ipRGC)—which is activated by blue light—is involved in the experience of visual discomfort.

"Although several lines of evidence have implicated ipRGCs in photophobia, there is limited clinical data to support this, until now," says Marija Zivcevska, the graduate student who led the study under Dr. Wong's supervision.

The test—the first of its kind—provides a more rigorous way to assess the light conditions that cause discomfort and will facilitate the development of new therapies for photophobia.

Zivcevska M, et al. Invest Ophthalmol Vis Sci. 2018 Mar 1;59(3):1467-1474. Supported by CFI, TGWHF, the John and Melinda Thompson Endowment Fund for Vision Neuroscience and the Department of Ophthalmology and Vision Sciences at The Hospital for Sick Children.



New Therapy on the Horizon

A molecule that protects nerve fibres could represent a new approach to treat glaucoma

Glaucoma is the most silent of all thieves: the cells in the optic nerve gradually irreversibly lose function until the eyes perceive only darkness. The theft of sight often goes unnoticed until it is too late. So far, researchers have not yet found a way to prevent vision loss in glaucoma.

Dr. **Jeremy Sivak** and his collaborators recently discovered a new molecule that has the potential to help people suffering from glaucoma.

The team found that a molecule called LXB4 protects the optic nerve against the harmful effects of glaucoma in experimental models of the disease. LXB4 is normally present in healthy eyes, where it acts as a neuroprotective agent. However, its levels are reduced in diseased eyes.

"By restoring LXB4 we can protect injured nerve cells against dysfunction and death," explains Dr. Sivak.

"A particularly exciting part of this discovery is that we don't think this effect is limited to glaucoma," he adds. "LXB4's neuroprotective properties may also help treat diseases caused by the loss of brain cells, such as Parkinson or Alzheimer disease."

The next step for the research team is to understand the underlying mechanisms responsible for LXB4's activity, with a view of designing a new therapy for protecting the vision of glaucoma patients.

Livne-Bar I et al. J Clin Invest. 2017 Dec 1;127(12):4403-4414.
Supported by CIHR, NSERC, NIH and TGWHF.

Building our Computational Strength

Krembil is upping its computational game. In the past three years, the institute has been building its capacity in computational biology to accelerate research discoveries in each of its three pillars.

Computational biologists use methods from mathematics, engineering, physics and computer science to improve our understanding of a biological system, such as a cell, organ or person.

Since 2015, Krembil has recruited the following international researchers to complement and extend its expertise in computational biology:

• Dr. Jérémie Lefebvre, who builds and analyzes brain models to understand how electrical stimulation affects the activity of brain cells and how it can restore healthy patterns of brain activity in neuropsychiatric disorders, such as depression;

• Dr. Igor Jurisica, who uses large data sets to identify biomarkers and therapeutic targets for diseases such as cancer and osteoarthritis;

• Dr. Michael Reber, who examines the development and organization of cell networks responsible for vision; and

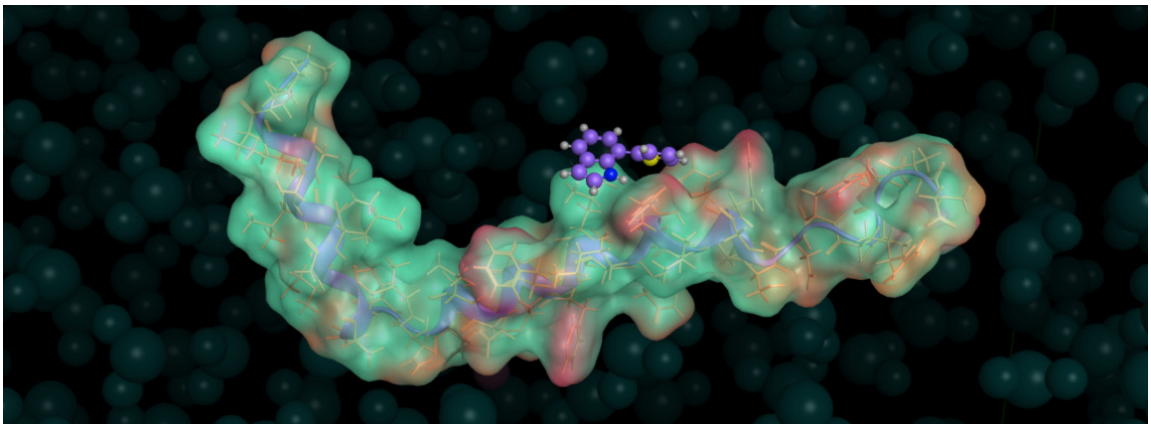
• Dr. Milad Lankarany whose research program aims to understand how information is processed by individual brain cells and networks of brain cells.

These new researchers joined Krembil's existing contingent of computational biologists, including Drs. Frances Skinner and Taufik Valiante.

In addition, Krembil is establishing a partnership with the newly created Krembil Centre for Neuroinformatics (KCNI) at the Centre for Addiction and Mental Health. KCNI's overall goal is to improve the diagnosis and treatment of mental illness by leveraging large collections of data related to the brain.

Photo: Rabiya Noori is a graduate student in computational biology supervised by Dr. Jérémie Lefebvre.

Partnership to Stop Alzheimer Disease



The French drug company Servier established a new partnership to develop much-needed treatments for Alzheimer disease with Treventis Corp., a biotech company founded by Dr. Donald Weaver and based in part at Krembil.

Alzheimer disease affects millions of people worldwide. Currently, there are no treatments to stop or slow its progression.

Several years ago, Dr. Weaver and Treventis developed a computer program that screens thousands of chemical compounds for activity against two proteins—beta-amyloid and tau—known to play an important role in Alzheimer disease. They identified several promising candidates that could form the basis of future drugs.

In 2013, Treventis was awarded $4.7 million by the Wellcome Trust, a global charitable foundation based in the United Kingdom, to further investigate the chemical compounds, with the goal of designing a drug that can treat people by targeting tau and beta-amyloid in their brains.

"This funding allowed us to get to the point where we have a molecule that works, but needs some fine-tuning," says Dr. Weaver. "Partnering with Servier is the next logical step."

As part of their agreement, Servier will fund all research costs, and researchers at Servier and Treventis will work together to optimize promising drug candidates and evaluate them in preclinical and clinical studies.

Other organizations that provided significant support for the project over the years include the Alzheimer Society of Canada, the Canadian Institutes of Health Research, the Toronto General & Western Hospital Foundation, the W. Garfield Weston Foundation, the BrightFocus Foundation and the Krembil Foundation.

Image: illustration of drug-like molecule (purple) binding to a beta-amyloid protein (green).

Great Ideas Attract New Research Funding

Every year, Krembil researchers submit applications to various governmental and charitable organizations to obtain funds to support their research programs. A selection of the past year's most notable funding success stories include the following:

- A team of researchers from Krembil, the Toronto Rehabilitation Institute and the University of Toronto raised $21 million to establish the CenteR for Advancing Neurotechnological Innovation to Application (CRANIA). CRANIA aims to develop implantable devices to treat a variety of neurological diseases or disorders such as epilepsy, depression and Parkinson disease. Funding for CRANIA was provided by the Canada Foundation for Innovation (CFI), the Ontario Research Fund (ORF) and philanthropic support.

- Dr. Rosemary Martino was awarded USD $8.5 million from the Patient-Centered Outcomes Research Institute to lead a multi-site study examining the benefits of proactively providing swallowing therapy to patients treated for head and neck cancer. These patients are at high risk of developing swallowing problems as a result of their cancer treatment.

- Drs. Philippe Monnier, Michael Tymianski and Valerie Wallace received $732,474 from CFI and ORF to acquire new equipment to support vision research.

- Dr. Donald Weaver was awarded over $1.4 million to develop new drugs to treat glioblastoma multiforme, a devastating form of brain cancer, by targeting the brain's immune system.

- In the 2018 fiscal year, Krembil researchers were awarded $11 million from the Canadian Institutes of Health Research (CIHR) Project and Foundation Grant competitions. CIHR is the primary federal agency for funding health and biomedical research in Canada.

When Trainees Shine

Krembil Research Day is a special event that happens once a year. It's a day when the Krembil research community gets together to celebrate the hard work and accomplishments of its trainees.

Research Day 2017 was held on May 10 and gave Krembil's 152 trainees the opportunity to share their latest findings through oral and poster presentations, as well as 'elevator pitches', which are three-minute oral presentations by trainees describing their research and its implications. Those who did the best job presenting their work were rewarded with an honorary certificate (some of the winners are pictured above).

The day also included a lecture given by guest speaker Dr. Eve Marder, a Professor of Biology at Brandeis University. Dr. Marder is a leading expert in neural networks, which are groups of interconnected cells within the brain that work together to fulfill the brain's diverse functions.

Enriching our Research

In April 2018, Krembil welcomed its newest member: Dr. Michael Reber, a neurobiologist with expertise in computational biology and mathematics.

Dr. Reber's research program examines the brain's visual network, which consists of interconnected 'webs' of cells that transmit and process visual information from the eyes. He uses a combination of experimental and mathematical models to reveal how the development and organization of the visual network is directed by particular molecules in the brain and eye.

Before joining Krembil, Dr. Reber was an Associate Professor at the Institute of Cellular & Integrative Neurosciences in Strasbourg, France. His recruitment was made possible by the generous support of Donald K. Johnson and Anna McCowan-Johnson through the Toronto General & Western Hospital Foundation.

Krembil Featured in Magazine Series

Krembil partnered with *The Globe and Mail*, one of Canada's largest newspapers, to produce a magazine series highlighting its research advancements. "The magazines contain many exciting stories of progress and success emerging from our laboratories; however, it's only a sampling of what we do and what we are capable of," says Dr. Donald Weaver. Print copies of each magazine in the series were distributed to 30,000 households across Canada.

Research Distinctions

Selected honours bestowed upon Krembil researchers

Dr. Elizabeth Badley

2017 Distinguished Scholar Award, Association of Rheumatology Health Professionals

Dr. Dafna Gladman

2018 Carol Nachman Prize for Rheumatology

Dr. Armand Keating

2017 Lifetime Achievement Award, Canadian Hematology Society

Dr. Andres Lozano

2017 Bachmann-Strauss Prize for Excellence in Dystonia Research, Michael J. Fox Foundation for Parkinson's Research

Doctor Honoris Causa, University of Seville

2017 Neurobionic Award, International Neurobionic Foundation

Dr. Mary Pat McAndrews

2017 Excellence in Research Award, Canadian League Against Epilepsy

Dr. Antonio Strafella

2017 Award for Young Investigators in Applied and Theoretical Sciences, Italian Scientists and Scholars of North America Foundation

Dr. Murray Urowitz

2017 Distinguished Scholar Award, American College of Rheumatology

Krembil Researchers

Emeritus Scientists
Charles Tator
Murray Urowitz

Senior Scientists
Elizabeth Badley
Cathy Barr
Jonathan Brotchie
Peter Carlen
Robert Chen
Aileen Davis
Karen Davis
James Eubanks
Michael Fehlings
Dafna Gladman
Christopher Hudson
William Hutchison
Robert Inman
Igor Jurisica
Mohit Kapoor
Sidney Kennedy
Anthony Lang
Andres Lozano
Nizar Mahomed
Mary Pat McAndrews
David Mikulis
Philippe Monnier
Michael Reber
Lyanne Schlichter
Jeremy Sivak
Frances Skinner
Elise Stanley
Martin Steinbach†
Antonio Strafella
Shuzo Sugita
Michael Tymianski
Valerie Wallace
Donald Weaver
Joan Wither
Agnes Wong

Scientists
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W Mark Erwin*
Nigil Haroon
Mojgan Hodaie
Lorraine Kalia
Suneil Kalia
Armand Keating
Jérémie Lefebvre
Anthony Perruccio
Ivan Radovanovic
Taufik Valiante
Liang Zhang

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Paul Fortin
Brenda Gallie
Monique Gignac
Esther González
Mark Guttman
Clement Hamani
Magdy Hassouna
Walter Kucharczyk
Rosemary Martino
Sowmya Viswanathan
Georg Zoidl

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Danielle Andrade
Heather Baltzer
Mark Bernstein
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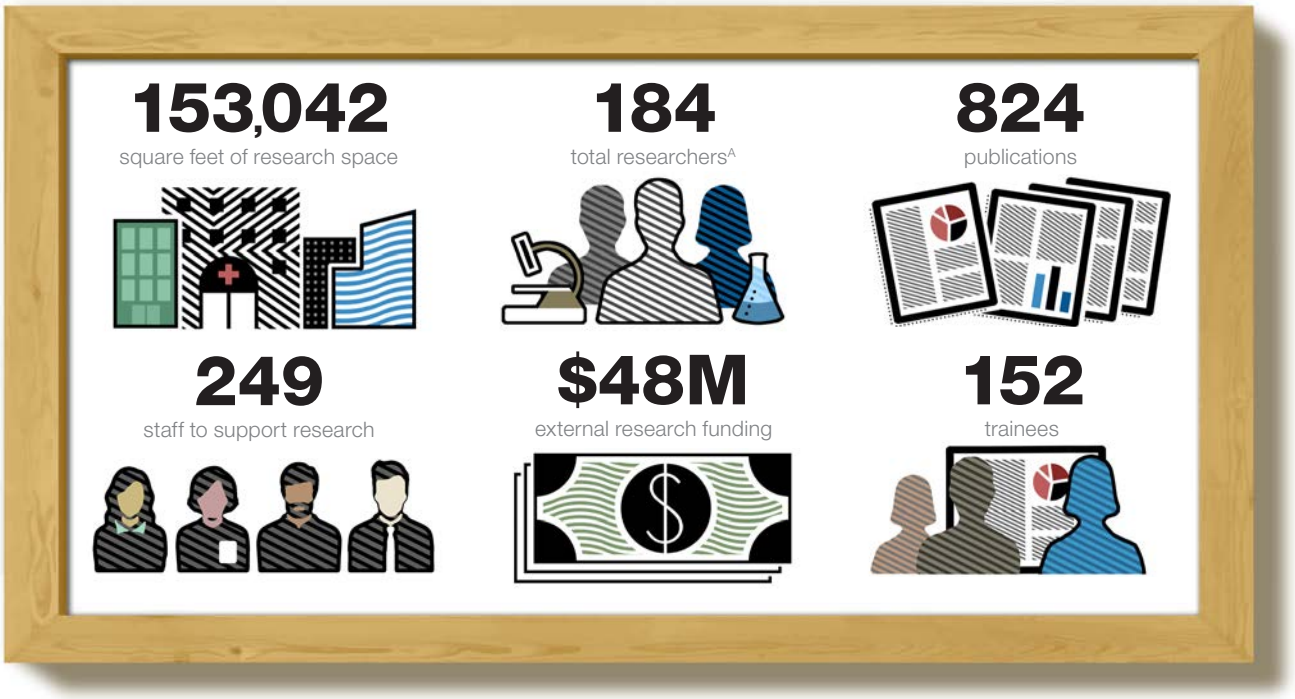
Daniel Buchman
Melanie Cohn
Frances Chung
Robert Devenyi
Dean Elterman
Alfonso Fasano
Susan Fox
Kenneth Fung
Rajiv Gandhi
Timothy Jackson
Efrem Mandelcorn
Daniel Mandell
Shane McInerney
Roger McIntyre
Renato Munhoz
Laura Passalent
Fayez Quereshy
Yoga Raja Rampersaud
Aylin Reid
David Rootman
Cheryl Rosen
Allan Slomovic
David Tang-Wai
Maria Carmela Tartaglia
Zahi Touma
Christian Veillette
M Elizabeth Wilcox
Mateusz Zurowski

Non-Appointed Researchers
Elia Abi-Jaoude
Ronit Agid
Jamil Ahmad
Lori Albert
Eduard Bercovici
Jeff Bloom
Arthur Bookman
Sarah Brode
Richard Brull
Yvonne Buys
Simon Carette
Leanne Casaubon
Rodrigo Cavalcanti
Jaskarndip Chahal
Vincent Chan
Clara Chan
Kenneth Chapman
Ki Jinn Chin
J Roderick Davey
Jose Martin del Campo
Marc Doucet
Richard Farb
David Frost
Fred Gentili
Peter Giacobbe
Michael Gofeld
Raed Hawa
Robert Iwanochko
Cheryl Jaigobin
Sindhu Johnson
Benjamin Kaasa
Patti Kastanias
Kyle Kirkham
Diana Kljenak
Timo Krings
Richelle Kruisselbrink
Dennis Kussin
Jeffrey Kwong
Johnny Lau
Timothy Leroux
Stephen Lewis
Louis Liu
Meeran Manji
Pirjo Manninen
Rodrigo Mansur
Patricia Marr
Connie Marras
Theodore Marras
Steven McCabe
Victoria McCredie
Rakesh Mohankumar
Ahtsham Niazi
Ivy Oandasan
Allan Okrainec
Daniel Panisko
Sagar Parikh
Kimberley-Anne Partridge
Philip Peng
Vitor Pereira
Anahi Perlas
Atul Prabhu
Rose Puopolo
Sidney Radomski
Sapna Rawal
Shail Rawal
Jorge Sanchez-Guerrero
Paul Sandor
Kathleen Sheehan
Frank Silver
Martin Simons
Jeffrey Singh
Mandeep Singh
James Skembaris
Elizabeth Slow
Roger Smith
Sumeet Sodhi
Peter Tai
Susan Tarlo
Maria Tassone
Graham Trope
Yvonne Tse
Karen Tu
Lashmi Venkatraghavan
Richard Wennberg
Robert Willinsky
David T Wong
Jean Wong

Image: Krembil researchers (opposite page, clockwise from the top-left corner) depicted are Drs. Aylin Reid, David Tang-Wai, Rosemary Martino, Mohit Kapoor, Valerie Wallace, Daniel Buchman, and Nigil Haroon (L) and Robert Inman (R). *†See page 30 for disclaimers.*

Krembil by the Numbers

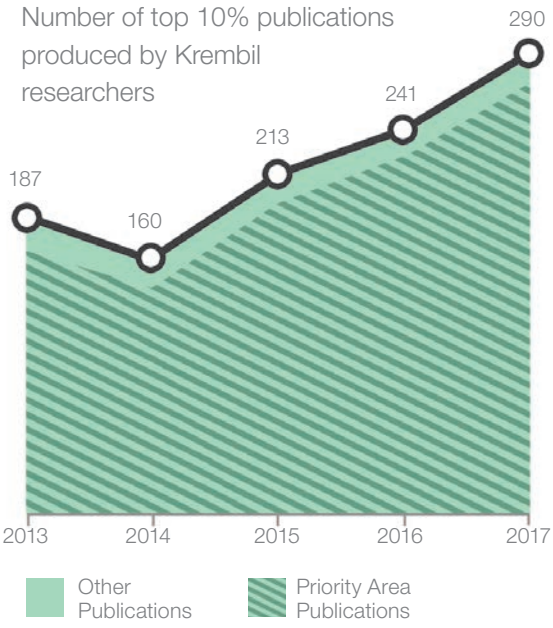


Impact

Krembil's research impact can be measured by the number of publications collectively produced by its researchers and the value of each publication in its field. A publication's value can be approximated by the number of times it is referenced by other researchers.

In 2017, Krembil produced a total of 824 publications. Of these, 290 are ranked among the top 10% of the most highly referenced publications within their respective fields that were published in the same year.

As shown in the graph on the right, Krembil's number of top 10% publications has been increasing since 2014. Also, the majority of these are related to its priority research areas (i.e., arthritis, brain and eye)[B].



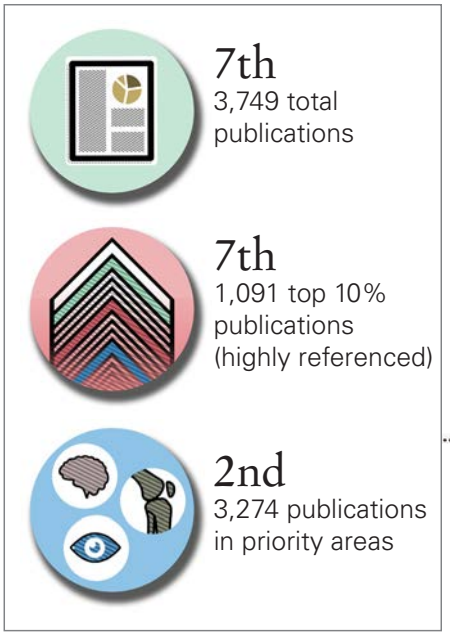
Benchmarking

Krembil's research impact compares favourably to that of top Canadian research hospitals with a focus in the same priority research areas.

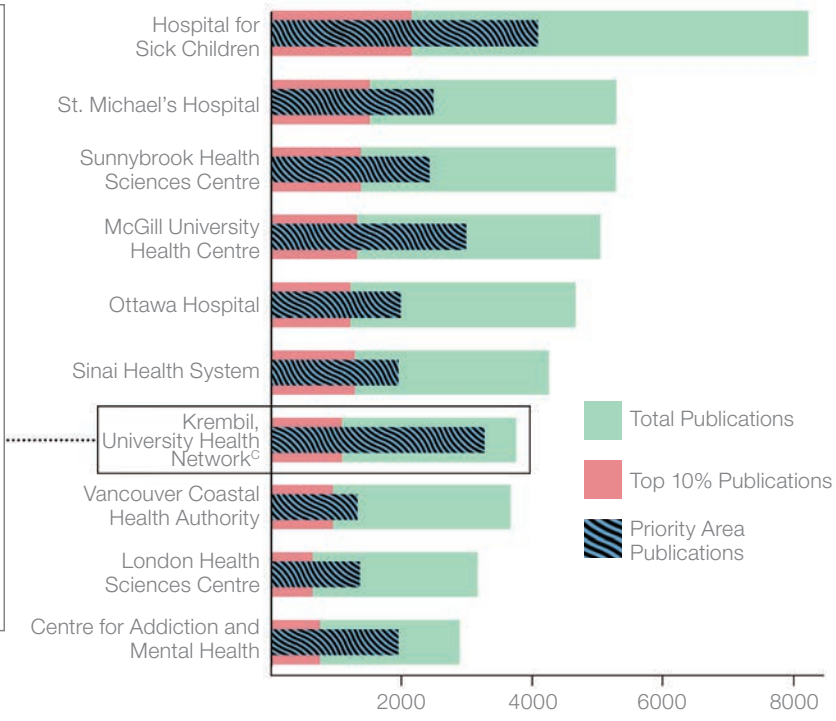
The graph below shows the total number of publications, top 10% publications and publications in Krembil's priority research areas produced by Krembil (one of UHN's five research institutes) and top Canadian research hospitals between 2013 and 2017[B].

Although Krembil ranks seventh for its total number of publications and number of top 10% publications, it ranks second for its number of priority area publications.

Current Krembil Ranking



Publications produced by Canada's top research hospitals between 2013 and 2017



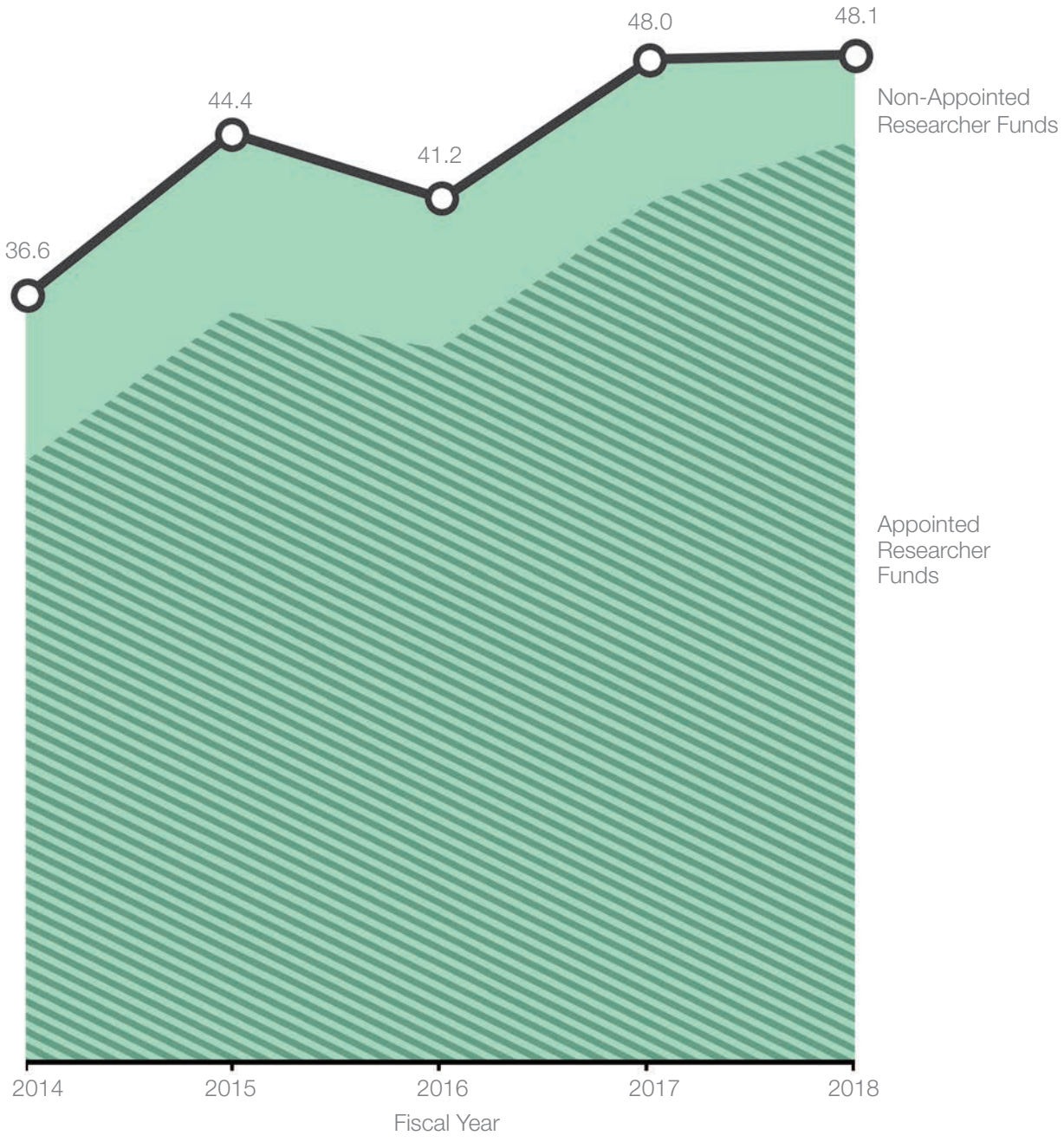
[A] Total comprises 97 appointed and 87 non-appointed researchers.

[B] Methods used to calculate these data are different than those used for last year's report. They were changed to produce data that are more accurate and informative, and are described in the disclaimer on page 30.

[C] Data are presented for Krembil researchers only and does not include data for other researchers at the University Health Network, including those who may perform research within the priority research areas.

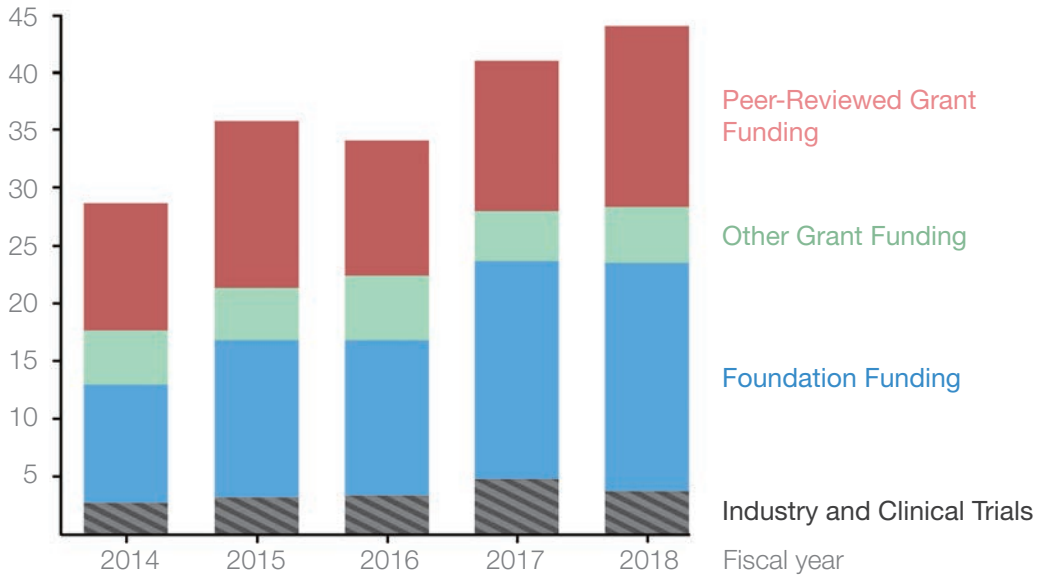
Financials

Research Funding Trends ($, Millions)[A]

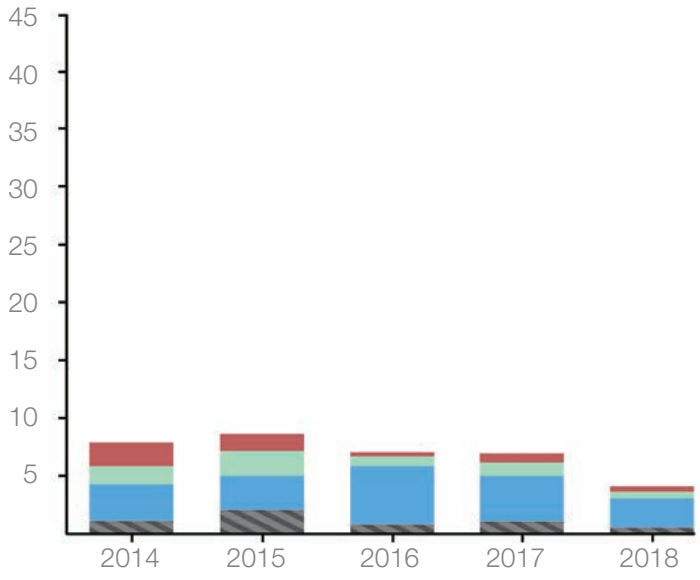


Research Funding by Type ($, Millions)[A]

Appointed Researchers



Non-Appointed Researchers



[A]*See disclaimer on page 30.*

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Disclaimers

Space. *Data provided by UHN Research Facilities and are accurate as of March 31, 2018.* **Financials.** *Data provided by UHN Research Financial Services. Research Funding represents the total research project funding spent by appointed and non-appointed researchers in each fiscal year.* **Researchers, Staff and Trainees.** *Number of appointed researchers, trainees and staff provided by Krembil Directorate Office. Only staff and trainees employed/engaged by either appointed researchers or Krembil Research Institute are included in the count. Data accurate as of March 31, 2018. Number of non-appointed researchers provided by UHN Research Program Planning & Analytics (RPPA) and UHN Strategic Research Initiatives Development (StRIDe). Non-appointed researchers are defined as UHN staff who are based at the TWH campus AND were either a first or last author on at least one publication in the 2017 calendar year OR owner of a UHN research account that spent money in the 2018 fiscal year. Non-appointed researchers can be affiliated with but cannot hold a research appointment at other UHN research institutes. In addition, they cannot be postdoctoral or clinical fellows or scientific staff employed by appointed researchers. Non-appointed researchers are not subject to Krembil's scientific and performance reviews. †Dr. Martin Steinbach passed away in June 2017. *Drs. John Flanagan and W. Mark Erwin left during the 2018 fiscal year. Their research funding and publications are included in the Krembil counts.* **Publication and Impact Data.** *Data provided by RPPA and are accurate as of July 30, 2018. Total number of Krembil publications includes all articles, reviews and proceedings papers with at least one appointed or non-appointed researcher listed as a co-author, published in the 2017 calendar year in Web of Science (WoS)–indexed journals. Publications jointly authored by multiple Krembil researchers are counted only once. InCites Essential Science Indicators (Clarivate Analytics) was used to identify publications that rank among the 10% most highly referenced publications relative to others from the same year and field of research.* **Benchmarking Data.** *Data provided by RPPA and are accurate as of July 30, 2018. Top Canadian research hospitals (as per RE$EARCH Infosource 2017) that produced the most 2012–2016 publications relevant to Krembil's priority research areas (i.e., arthritis, brain, eye) were selected as comparators. Publications from the most recent 5-year period (i.e., 2013–2017) include articles, reviews and proceedings papers published in WoS-indexed journals with at least one author affiliated with the institution of interest. WoS assigns publications to one or more subject categories based on journal. Using Krembil 5-year publications, 24 journal subject categories were identified to represent one or all priority areas. Comparators' 5-year publication lists were generated using an organization-based search in WoS. Krembil and comparator publications were then allocated to one or more of the priority areas based on journal subject category. A Medline search using priority-themed keywords was used to supplement Krembil and comparator publication lists with relevant priority-themed publications not identified using the 24 subject-specific journal categories. Krembil and comparator publications data were retrieved within the same week to ensure citation data was contemporaneous. Highly referenced publications were identified as described in the 'Publication and Impact Data' section.* **Production Credits.** *This report is published by Krembil's Directorate Office. Graphic design, writing, editing and production of this report was performed by StRIDe.*

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Brain
Clusters of potassium-transporting ion channels with microglia in an injured spinal cord

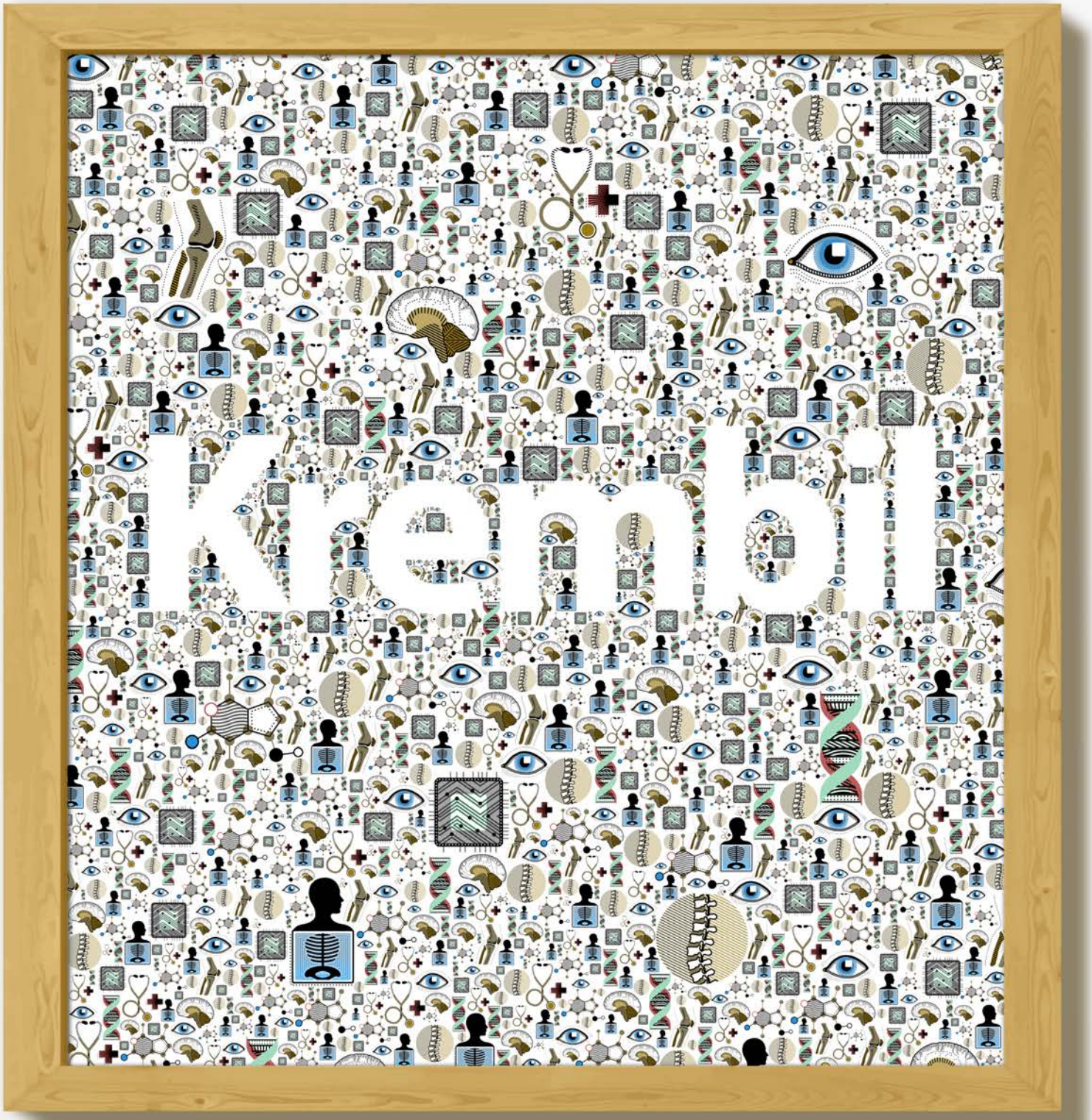
Dr. Lyanne C. Schlichter
Senior Scientist, Krembil Research Institute

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

Dr. Mohit Kapoor
Senior Scientist, Krembil Research Institute

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

Dr. Valerie Wallace
Senior Scientist, Krembil Research Institute



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