We Are Krembil

Improving lives through research and care

2022 Annual Report

The Krembil Research Institute (Krembil) is the research arm of the Toronto Western Hospital (TWH) and a research institute at the University Health Network (UHN). Krembil's research programs focus on the brain and spine, 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.

We acknowledge that the land on which we work is the traditional territory of many nations, including the Mississaugas of the Credit, the Anishnabeg, the Chippewa, the Haudenosaunee and the Wendat peoples, and is now home to many diverse First Nations, Inuit and Métis. We also acknowledge that Toronto is covered by Treaty 13 with the Mississaugas of the Credit. We remember and honour the legacy of the peoples who have been here before us and all who strive to make the promise and the challenge of Truth and Reconciliation real. We are grateful to have the opportunity to live and work on this land.

We are committed to championing inclusion, diversity, equality, equity and accessibility in the learning, work and service environments. We believe that our differences enrich our ability to develop creative and innovative approaches to delivering exemplary patient care, research and education.

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About the cover
Design: Twayne Pereira; Photography: Twayne Pereira and Tim Fraser
Cell images provided by Drs. Donald Weaver, Mohit Kapoor, Lyanne Schlichter, Jeremy Sivak and Valerie Wallace

Inside

We Are Krembil

When I started out as a neurologist and began seeing patients with Alzheimer disease back in the 1980s, I did so with the knowledge and sorrow that I had very little to offer them.

In the past five to ten years alone, we have made tremendous progress.

We now recognize that Alzheimer disease is not a single disease, but likely many. We can better treat its symptoms, such as depression and anxiety, and we are making progress towards developing therapies that may stop or even reverse the disease.

This is the power of science—and it is only one example of one disease that we study.

Six million Canadians live with arthritis, 5.5 million have an eye disease that can cause vision loss and 3.6 million are affected by a neurological condition, such as Parkinson disease, epilepsy or stroke.

These chronic illnesses far too often take away our independence, negatively impact our relationships and shorten our careers—disrupting what would otherwise be the best years of our lives.

At Krembil, our goal is to help our patients thrive by improving their quality of life and giving them hope.

When I began my tenure as Krembil's Director almost a decade ago, my goal was to foster a synergistic approach to research and patient care that would accelerate the translation of discoveries from bench to bedside. Today, I am incredibly pleased with what we have achieved.

In this report, you will read about a new treatment target for a severe form of arthritis, a new tool for testing and optimizing drugs for eye diseases such as glaucoma, and an experimental model for screening potential drugs for Parkinson disease.

You will also read about some of our public outreach events and initiatives, including a new podcast geared towards making science accessible and engaging to everyone.

Each of our achievements is a direct result of teamwork—of many people with unique ideas, perspectives and skills coming together with a shared goal of creating a better world.

Every time a researcher begins a new experiment, a wave of possibility washes over them. Whenever a clinician or health care worker takes on a challenging case or develops an innovation in care, there is a rush of adrenaline and excitement.

To be a part of it all is thrilling.

This will be my last Welcome Letter, as I head back to the lab and immerse myself in science full time.

I step down as Institute Director knowing that what we have accomplished in the last nine years is nothing short of inspirational.

Building on our successes, there is no limit to what we can—and will—achieve together, with your support.

Thank you,

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

Dedicated & Relentless

Emily Paige Mills
Postdoctoral fellow supervised by Dr. Karen Davis, Krembil Brain Institute

I use brain imaging to study the neural mechanisms of chronic pain. My research explores whether brain structure and function can predict how patients with neuropathic pain will respond to treatments. Developing more objective tools to predict treatment outcomes will significantly advance personalized care for patients with chronic pain.

Working at Krembil means being part of a diverse and collaborative community of highly motivated researchers and trainees. As a postdoctoral fellow at Krembil, I have incredible opportunities to work with world-renowned researchers and clinicians and interact closely with patients.

Krembil is a unique training environment in that it supports trainees who wish to simultaneously pursue professional interests outside the lab. I have recently been able to apply the knowledge that I have gained in the lab to develop a podcast sponsored by the UHN Office of Research Trainees called *Seeds of Science*. The goal of this podcast is to enable graduate students and postdoctoral fellows across UHN's research institutes to share their experiences in research and provide insights to junior trainees.

Nadeem Murtaza
PhD student supervised by Dr. Karun Singh, Donald K. Johnson Eye Institute

My research focuses on clarifying the causes of autism spectrum disorder (ASD), one of the most common neurodevelopmental disorders. A major hurdle in understanding what causes ASD is a limited understanding of the relationships between the hundreds of genes that we know to be disrupted in individuals who have the condition.

The aim of my research is to understand how these genes work together. We are particularly interested in determining whether these genes all contribute to the same pathology or if there are distinct groups of genes with similar roles in ASD. If the latter is true, particular groups of genes could define subcategories of ASD.

Krembil is an environment that pushes the advancement of science. Working at Krembil has given me the opportunity to learn from exceptional scientists and clinicians who are incredibly passionate about what they do.

My career goal is to lead a lab of my own and continue studying neurodevelopmental and neurological disorders. I have always been very interested in understanding how the brain works and translating discoveries into tools that can help patients.

Zoha Faheem
PhD student supervised by Dr. Joan Wither, Schroeder Arthritis Institute

I study the immune system changes that cause flare-ups in lupus, a chronic autoimmune disorder that can affect many different tissues. In Dr. Wither's lab, we use a technique called high-dimensional mass cytometry to study interferon, an immune protein that is believed to play an important role in the development of lupus.

I chose this research field because I have always been interested in how autoimmunity arises in the body and what we can do to restore the immune system to a healthy state.

At Krembil, I am surrounded by people who are devoted to advancing science and excelling in their pursuits through hard work and dedication. I am inspired by the positive and forward-looking culture at the Institute and I am proud to be part of the Krembil team.

In the future, I would like to work in the field of science communication and help to bridge the gap between researchers and the public by making science more accessible. Outside the lab, I enjoy travelling, playing board games and reading. I also enjoy mentoring students who are interested in pursuing training and careers in biomedical research.

Qais Sa'di
Neurologist and clinical fellow supervised by Dr. Alfonso Fasano, Krembil Brain Institute

I am completing my clinical fellowship in the Movement Disorders surgical program at the Krembil Brain Institute, where we treat movement disorders such as Parkinson disease using a neurosurgical procedure called deep brain stimulation (DBS).

With Dr. Fasano, I am studying adaptive DBS. This new therapeutic technique involves using machine learning to enable DBS systems to detect changes in a patient's motor function and adapt the stimulation as needed.

This fellowship has enhanced my expertise in DBS and the field of movement disorders in general. This branch of neurology is one of the most needed subspecialties in my home country, the Hashemite Kingdom of Jordan. I am looking forward to applying what I have learned during my training at Krembil to help my patients there in the future.

It has been amazing to be a part of the Krembil community. The Institute has given me the opportunity to improve my knowledge and research skills while treating patients with a variety of conditions. When I am not working, I enjoy meeting new people and exploring the many beautiful places in Toronto.

Hartej Mehta

Technical Analyst, UHN Digital

I am a proud member of UHN Digital - Research, providing software and hardware support for devices on UHN's research network. I joined UHN in 2012 and have worked at Krembil since 2018.

In my role, I install and update applications, replace device parts, manage networks and shared drives, and encrypt internal and portable devices. I also work with vendors, manage device warranties and software licenses, and troubleshoot issues. This job requires a willingness to continually adapt to changing technologies and user needs, to problem solve and to help others.

To support UHN's recent transition to EPIC—a new electronic patient record system—our group worked closely with various teams and clinical programs across the Institution with a shared goal of providing the best service possible to clinicians, health care personnel, patients and researchers.

I am especially appreciative of Krembil's researchers, trainees and staff who are extremely talented in their respective fields, and who are always patient and accommodating when we are at capacity. I am passionate about providing high-quality solutions for all IT-related issues and am always ready to help the Krembil team.

Lacrimioara Comanita

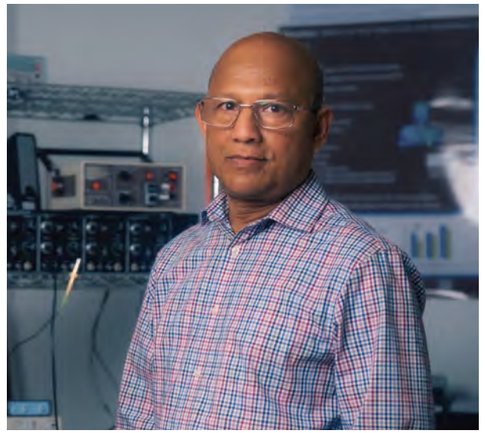
Senior Research Technician, Donald K. Johnson Eye Institute

I am a Senior Research Technician in Dr. Valerie Wallace's lab at the Donald K. Johnson Eye Institute. Our lab has developed a platform to study the transplantation of specialized cells to repair the damaged retina. We are using this platform to explore how transplanted cells communicate with one another and with cells in the host retina—an approach that is key to developing strategies to treat vision loss.

I am a member of our lab's transplantation team, where I work with postdoctoral fellows and graduate students to perform cell transplantation and analyze how the retina changes after this procedure.

Although I had research experience before joining the Wallace Lab, the work that we do here is unique and requires specific expertise. Since joining this group, I have developed numerous skills related to cell transplantation. The research that we conduct has also allowed me to gain experience with a vast array of techniques, such as ophthalmic surgeries, retina cell recordings, and confocal and electron microscopy.

I feel very privileged to work with my colleagues in the Wallace Lab and to be a part of the Krembil research community. I believe that the research that we conduct today will lead to the clinical breakthroughs of tomorrow.



Utpal Kumar Saha

Research Associate, Krembil Brain Institute

As a research associate in Dr. Robert Chen's lab, I help to train new lab members, design experimental protocols, conduct experiments, and collect and analyze data—all the tasks that are necessary for the successful operation of our lab.

At the Krembil Brain Institute, some patients are treated with deep brain stimulation (DBS)—a therapy in which electrodes are implanted in the brain to modify abnormal brain activity.

The Chen Lab uses sophisticated equipment to detect and modify brain activity in these patients. This equipment includes devices for electroencephalography, focused ultrasound and different forms of brain stimulation. One of my responsibilities is to ensure that these devices are maintained in excellent condition and are ready to use.

Working at Krembil means a lot to me; it is my home away from home. There is always something new to learn and the breadth of innovative research that is taking place at the Institute is inspiring.

I enjoy the time that I spend here and I love working with Krembil's many nationally and internationally recognized scientists and clinicians and our excellent students.

Marcia Correale

Provincial Practice Lead, Schroeder Arthritis Institute

The Rapid Access Clinic – Lower Back Pain (RAC-LBP) program offers an innovative model of care in which patients receive rapid assessments for lower back pain along with education and evidence-based plans for self-management. This shared-care model was designed to reduce the prevalence of chronic lower back pain, unnecessary diagnostic imaging and specialist referrals.

In my role, I provide leadership to enable standardized patient assessments and comprehensive management of complex spine conditions to a network of over 170 clinicians across Ontario.

As an advanced physiotherapy practitioner at the Schroeder Arthritis Institute, I correlate patients' imaging findings with their clinical presentations and teach patients about their condition. I also facilitate referrals to specialists for surgical interventions and other therapies. The knowledge and skills that I have gained enable me to help manage various complex spinal conditions.

I love being a member of TeamUHN because I get to work with a multidisciplinary team to provide the best evidence-based care for patients. Krembil fosters critical thinking, creativity and a commitment to excellence in research, education and patient care.

A Worm's Eye View of Drug Discovery

Lorraine Kalia (left), Senior Scientist; Suneil Kalia (right), Senior Scientist; Krembil Brain Institute

Researchers develop a model of early-stage Parkinson disease, leading the way to new therapies.

As Parkinson disease progresses, neurons are killed. Because neurons cannot regenerate, researchers are searching for ways to detect and treat the disease at its earliest stages, before significant damage has occurred.

Most experimental models of Parkinson disease are limited because they lack measurable markers of neuron degeneration in the early stages of the disease.

A team led by Drs. Lorraine Kalia and Suneil Kalia developed an experimental model of early-stage Parkinson disease using the small roundworm *Caenorhabditis elegans (C. elegans)*. Using the model, in tandem with artificial intelligence and cell culture systems, the team screened more than 600 drugs to identify potential treatments.

The neuron degeneration that occurs in Parkinson disease is associated with the accumulation of the protein alpha-synuclein, and causes motor dysfunction. "Our *C. elegans* model has a defect related to the production of alpha-synuclein," says Dr. Lorraine Kalia. "Worms with the defect coil up much more frequently than worms without it, and we can measure the amount of coiling behaviour to determine the effectiveness of potential treatments for humans."

The researchers used artificial intelligence to rank a library of drugs that are approved for use in humans based on their ability to reduce the accumulation of alpha-synuclein and tested the top 40 drugs in cells. They then tested the six most promising drugs using their *C. elegans* model and found that five of them reduced the worms' coiling behaviour.

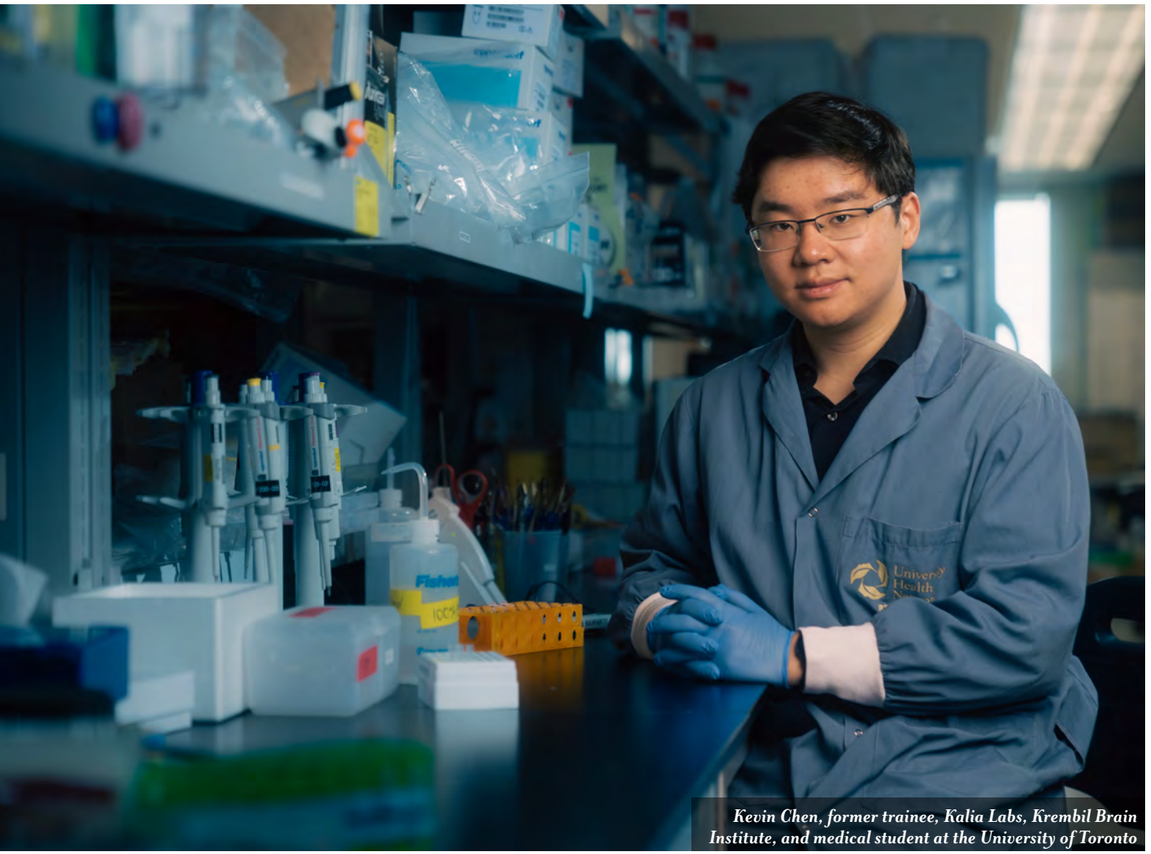
Next, the researchers tested these drugs in more advanced models of the disease to determine which ones could prevent alpha-synuclein from killing brain cells. Using this approach, they identified the antibiotic rifabutin as a potential treatment.

"Coupled with artificial intelligence technologies, our *C. elegans* model has the potential to be scaled up to identify drugs that might treat the disease in humans," explains Dr. Suneil Kalia.

"Parkinson disease is a complex and multifaceted condition, and no single experimental model is likely to capture all of its underlying mechanisms and symptoms," adds Kevin Chen, a former Master's student in the Kalia labs and the first author of the study. "By incorporating multiple models in a multistep drug screening process, we can more effectively identify potential drugs and translate our discoveries to clinical trials."

This work was supported by the Natural Sciences and Engineering Research Council of Canada, the Canadian Institutes of Health Research, the Ontario Brain Institute, Parkinson's UK and the UHN Foundation. Dr. L. Kalia is an Associate Professor of Medicine (Neurology) at the University of Toronto. Dr. S. Kalia is an Associate Professor of Surgery (Neurosurgery) at the University of Toronto.

Chen KS et al. Mol Neurodegener. 2021 Nov. 10.1186/s13024-021-00497-6



Kevin Chen, former trainee, Kalia Labs, Krembil Brain Institute, and medical student at the University of Toronto

Stimulating the Brain

Luka Milosevic, Scientist; Krembil Brain Institute

Researchers model the effects of deep brain stimulation on different brain regions.

Researchers led by Dr. Luka Milosevic have characterized how cells in different brain regions respond to deep brain stimulation (DBS)—a therapy commonly used to treat severe movement disorders.

During DBS, microelectrodes implanted in the brain emit pulses of electricity to change the activity of nearby neurons. Surgeons can adjust the frequency, intensity and duration of these pulses to reduce disease symptoms.

"Despite the observed benefits of DBS, there are still many unknowns regarding how the treatment changes brain activity," explains Dr. Milosevic. "We wanted to understand how stimulation changes the activity of neurons in different brain areas, to clarify the mechanisms underlying symptom improvement."

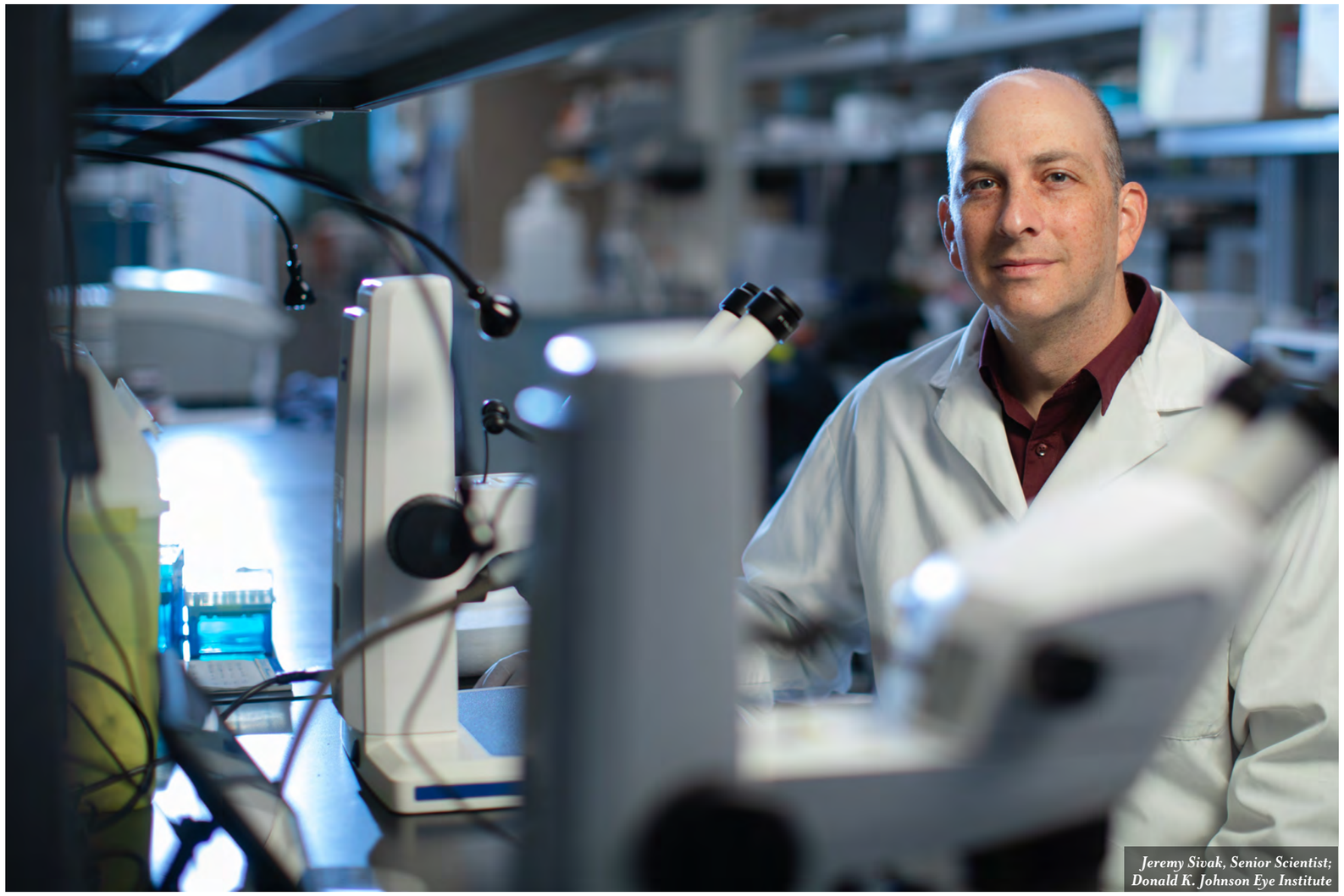
The researchers studied neuron activity in four brain regions involved in movement control in patients with either Parkinson disease or essential tremor—a disorder that causes involuntary shaking. They programmed the electrodes to deliver stimulation at various frequencies and monitored changes in neuron activity. They also developed a mathematical model to predict how neurons in each region would respond to the stimulation.

The team discovered that the effects of electrical stimulation varied by brain region, depending on the local concentration of chemicals that stimulate or suppress neuron activity. The team also discovered that prolonged high-frequency stimulation suppressed activity across regions, likely because neuron communication could not keep up with the stimulation.

This study has improved our understanding of how DBS benefits patients and will help researchers fine-tune DBS for Parkinson disease and other conditions.

Full Story / *Scientific Article*

Modelling the Human Eye



Jeremy Sivak, Senior Scientist; Donald K. Johnson Eye Institute

Researchers validate a new method for studying drug distribution in the eye.

A research team led by Dr. Jeremy Sivak have developed an experimental model to study the behaviour of drugs that are delivered to the eye through intravitreal (ITV) injection.

ITV injection enables clinicians to deliver medication to a space at the back of the eye. The injected therapeutics eventually make their way to the retina—the neural tissue that senses light and sends visual signals to the brain. This approach is widely pursued for treating eye diseases that cause progressive vision loss due to retinal degeneration.

Although ITV drug delivery is a promising approach for treating eye diseases, drug particles can move from the back portion of the eye to the front. This forward drug movement can raise the pressure inside the eye and increase a person's risk of developing other conditions, such as glaucoma.

"It is challenging to predict how drugs will behave in the human eye, because what we observe in experimental models does not always match what happens in humans," explains Darren Chan, a research technician working in Dr. Sivak's lab and the first author of the study. "The lack of suitable models to study the behaviours of new drugs creates a major bottleneck for bringing new therapies to the clinic."

To address this issue, the team adapted a model that mimics how fluid flows between different compartments of the eye. They optimized features of the model, such as temperature and fluid flow, to more closely mimic the conditions present in the eye. They also used tiny synthetic beads to mimic injected drugs,

which enabled them to track how particles move within the eye following ITV injection.

"To test how well the model can replicate a real clinical scenario, we then validated the optimized model using the drug GNE-947—a potential treatment for macular degeneration," says Dr. Sivak. The team performed the study in collaboration with Dr. Vladimir Bantseev, a Senior Scientist and Ophthalmology Therapeutic Area Lead at Genentech, a biotechnology company that has been developing the drug.

GNE-947 had been observed, unexpectedly, to migrate to the front portion of the eye in preclinical studies, increasing the risk of serious side effects. The team found that the drug behaved within the model the same way that it did in the preclinical studies, suggesting that the model accurately predicts drug behaviour in the human eye.

"This study demonstrates that a simple experimental model of the eye can replicate the complex movement of drug particles following ITV injection," says Dr. Sivak. "This model can now serve as a platform for researchers to explore how new drugs will behave in the human eye and could ultimately help to expedite the preclinical development of therapeutics."

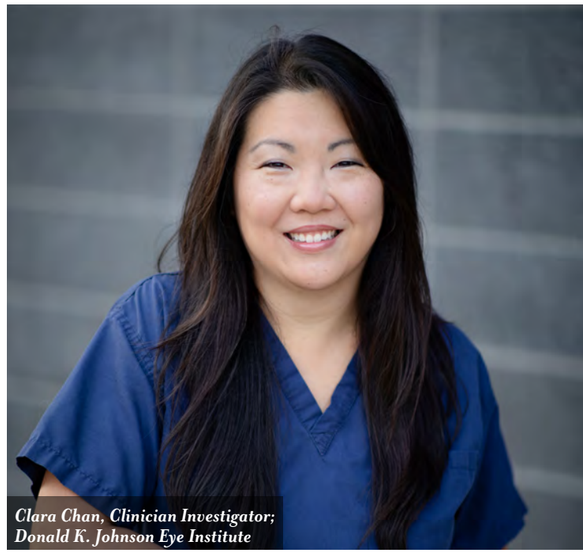
This work was supported by the Canadian Institutes of Health Research, Genentech Inc. and the UHN Foundation. Dr. J. Sivak is an Associate Professor of Ophthalmology & Vision Sciences at the University of Toronto.

Chan D et al. J R Soc Interface. 2022 Jan. 10.1098/rsif.2021.0734

Darren Chan, Research Technician, Sivak Lab; Donald K. Johnson Eye Institute

A New Tool to Restore Sight

Allan Slomovic, Clinician Investigator; Donald K. Johnson Eye Institute



Clara Chan, Clinician Investigator; Donald K. Johnson Eye Institute

Customized prosthetic device improves vision in individuals with corneal conditions.

A team of scientists and clinicians led by Drs. Allan Slomovic and Clara Chan have shed light on patient experiences surrounding the use of a device to treat complex corneal conditions.

Corneal conditions, such as irregularly shaped corneas and corneal degeneration, are associated with pain and discomfort and are a leading cause of vision loss. These conditions are typically treated with artificial tears, medications and specialized contact lenses.

Patients who do not respond to these standard treatments have recently benefitted from a therapy called PROSE—Prosthetic Replacement of the Ocular Surface Ecosystem. PROSE involves daily use of a custom, saline-filled lens that rests on the white of the eye.

PROSE is a relatively new treatment in Canada and there is still much to be learned about patient experiences with it. The team analyzed medical records from 78 adults who underwent lens fitting to determine the reasons for treatment and whether it improved vision.

The resarchers discovered that doctors recommended PROSE for a variety of corneal conditions that cause light sensitivity, blurry vision and other symptoms. PROSE improved vision and could be worn comfortably for long periods, indicating that it is an effective treatment for individuals who do not benefit from traditional therapies.

The Kensington Vision and Research Centre was the first centre in Canada to make the PROSE lens available to patients and is the only Canadian centre where the cost of the lens is covered by the provincial government.

Full Story / Scientific Article

Homing in on a Target

Nigil Haroon, Senior Scientist; Schroeder Arthritis Institute

Researchers clarify disease mechanisms and drug targets in axial spondyloarthritis.

An international research team led by Dr. Nigil Haroon has identified a potential treatment target for axial spondyloarthritis, a chronic inflammatory disease that affects the joints and other tissues.

Individuals with axial spondyloarthritis have elevated levels of a protein called macrophage migration inhibitory factor (MIF) in their blood and tissues. MIF plays an important role in inflammation, and its levels in a patient's blood are linked to disease severity.

"Axial spondyloarthritis is a devastating disease with very few therapeutic options for most patients," explains Dr. Haroon. "Because MIF activates inflammatory pathways, we examined whether it contributes to the clinical features of the disease and whether we can target it for future treatments."

Using experimental models of the disease, the researchers observed that MIF is produced in large quantities by a type of white blood cell. They also found that increasing the levels of MIF or the number of these white blood cells increased disease symptoms. In contrast, inhibiting the production or activity of MIF reduced disease severity.

The researchers also determined how MIF triggers inflammation. "We found that MIF increases the production of a subtype of T cells—immune cells that cause inflammation," says Dr. Akihiro Nakamura, a postdoctoral fellow in Dr. Haroon's laboratory and the first author of the study. "This is in line with what we see in the clinic, where blood and joint fluids from patients with the disease contain high levels of these T cells."

This study indicates that MIF plays an important role in axial spondyloarthritis and is a potential treatment target for the disease, as well as other inflammatory conditions. If a drug can reduce the levels of MIF in a patient's blood, it may slow or stop disease progression.

"Moving forward, we need to further characterize how MIF causes T cells to change and induce inflammation," says Dr. Haroon. "Although more research is needed, our study lays a strong foundation for clinical trials to test the safety and efficacy of new therapies that target this protein."

This work was supported by the Canadian Institutes of Health Research, Arthritis Society Canada, the American College of Rheumatology, the National Institutes of Health, the Natural Sciences and Engineering Research Council of Canada, the Canada Foundation for Innovation, the Ontario Research Fund, IBM, the Ian Lawson van Toch Cancer Informatics Fund and the UHN Foundation. Dr. N. Haroon is an Associate Professor of Medicine (Rheumatology) at the University of Toronto.

Nakamura A et al. Sci Transl Med. 2021 Oct. 10.1126/scitranslmed.abg1210

Akihiro Nakamura, Postdoctoral Fellow and Rheumatologist; Schroeder Arthritis Institute

New Model for Osteoarthritis

Researchers devise a method to rapidly test potential therapies for osteoarthritis.

A team led by Dr. Sowmya Viswanathan has developed an experimental model of late-stage osteoarthritis that enables scientists to rapidly test potential therapies.

Osteoarthritis occurs when joint tissues wear away, causing pain and reduced flexibility. Disease progression is caused by many factors, including inflammation in the synovium—a tissue that lubricates and protects the joint.

Experimental models of osteoarthritis do not always mimic how the disease affects joint tissues in the body. To address this, the team created a model using cartilage and synovial tissues that were donated by individuals who underwent knee-replacement surgery for late-stage osteoarthritis.

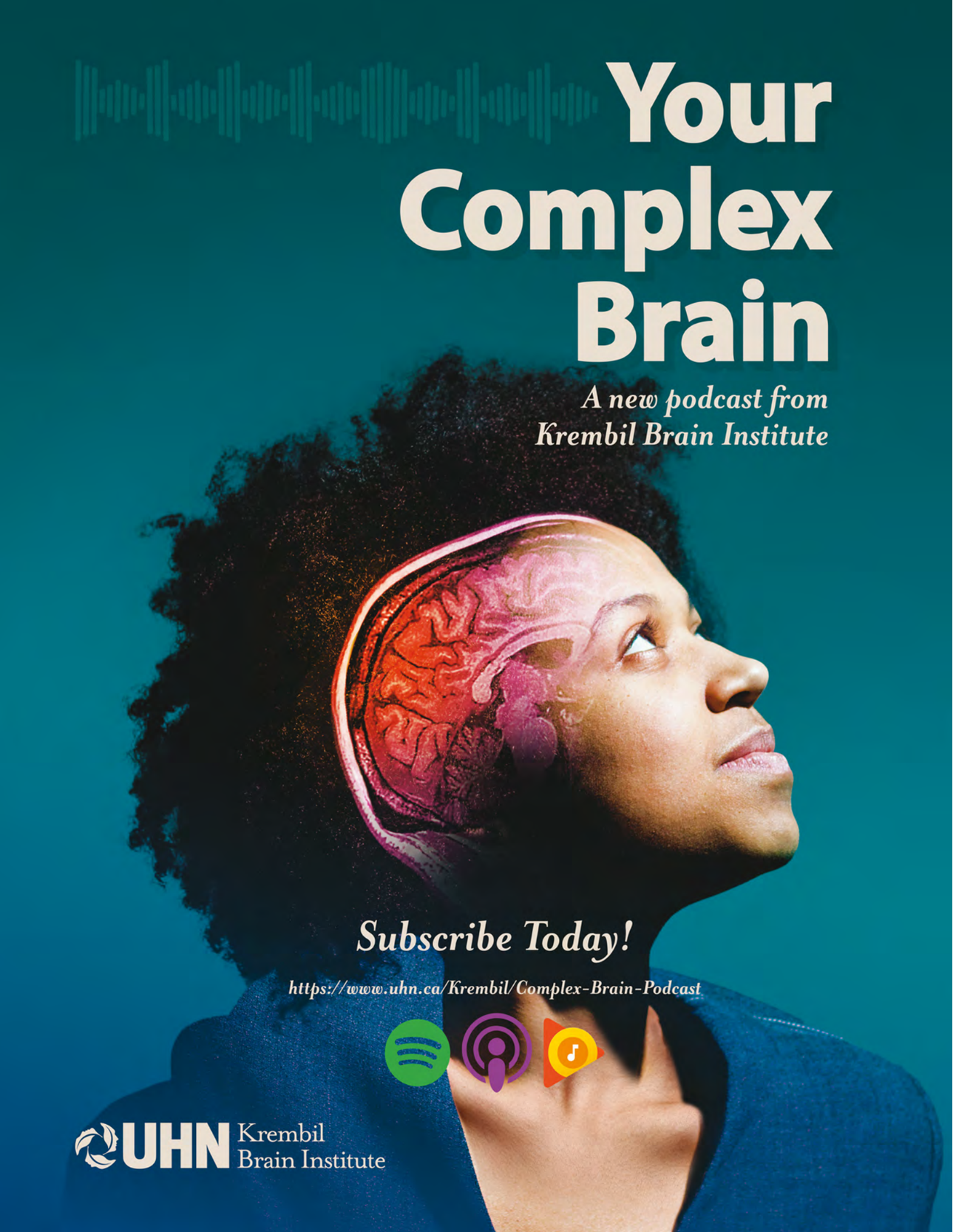
The researchers developed a strategy to preserve the tissues for up to a week. During this time, they conducted molecular analyses to monitor how the tissues evolved.

By examining changes in immune cells, genes, proteins and chemicals in the tissues, the researchers created a detailed picture of how joints are affected by osteoarthritis. They also tested how the tissues are affected by a steroid that is commonly used to treat the condition. This drug reduced the expression of genes associated with inflammation, which is consistent with the relief provided to patients.

These findings indicate that the group's new model is an effective tool for screening therapies and may accelerate the development of effective treatments.

Full Story / Scientific Article

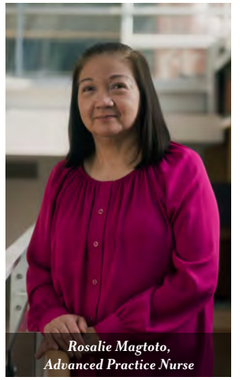
Sowmya Viswanathan, Scientist; Schroeder Arthritis Institute




Asma Naheed, MRI Technician


Joshua Johnston, Patient Partner


Analynne Salas, Patient Partner


Rosalie Magtoto, Advanced Practice Nurse

On March 22, 2022, the Krembil Brain Institute launched its podcast, *Your Complex Brain*. This educational podcast explores mysteries, myths and cutting-edge science about the brain and brain diseases, such as Alzheimer and Parkinson disease, stroke, epilepsy, brain cancer, brain injury, chronic pain and mental health disorders.

Your Complex Brain features interviews with leading neuroscientists, clinicians and health care staff from the Krembil Brain Institute, and heartfelt and inspirational personal accounts of brain disease, injury and recovery from patients and their families.

This podcast is meant to inform, engage and inspire people who are directly affected by brain disease, as well as those who are interested in learning more about the brain and how to protect their brain health.

The podcast is hosted by Krembil's Manager of Communications, Heather Sherman and is produced by Krembil team members Carley McPherson, Dr. Amy Ma, Twayne Pereira, Suzanne Wice and Krembil Public Affairs intern Sara Yuan.

Topics covered in season one include:
» What it will take to cure Alzheimer's
» The rise of stroke in young adults
» The effects of music on seizures in epilepsy
» Long-term effects of concussion
» A blood test for diagnosing brain cancer
» Advances in treating spinal cord injury
» Psychedelics and mental health conditions
» COVID-19 and the brain

A particularly touching episode features Rick Arkell, speaking about his late wife Ally's brain cancer diagnosis. "I don't want Ally's memory to be forgotten," he says. "We have to support brain cancer research, so we can find a cure."

This podcast is the latest initiative by the Krembil Brain Institute, which is commited to breaking down barriers between science and the public through outreach initiatives.

As of September 2022, just six months after the podcast launched, the episodes have been downloaded more than 11,000 times across streaming platforms. "The secret to this podcast's success is that we are making brain science interesting and accessible to everyone," says Dr. Donald Weaver, Co-Director of the Krembil Brain Institute.

"Our goal is to inform and engage people to be proactive in their brain health"

-Dr. Donald Weaver

Your Complex Brain is available on all major podcast platforms, including Apple Podcasts, Spotify and Google Podcasts. For more information about the podcast, visit www.uhn.ca/Krembil.


Fred Gentili, Neurosurgeon; Toronto Western Hospital

Remembering Fred Gentili

UHN remembers neurosurgeon Dr. Fred Gentili. Dr. Gentili died on January 15, 2022 of glioblastoma—an aggressive brain cancer for which he treated many of his patients.

Dr. Gentili specialized in skull base surgery, pituitary surgery and radiosurgery. He completed neurosurgical training at the University of Toronto in 1980 and joined the neurosurgical staff at the Toronto General Hospital in 1982. At the time of his death, he was a Professor of Surgery at the University of Toronto and a Clinician Investigator at the Princess Margaret Cancer Centre.

Dr. Gentili touched the lives of innumerable colleagues and patients, and his legacy of surgical innovation, research excellence and patient care lives on through the generations of neurosurgeons and scientists whom he trained.

"Fred advanced traditional neurosurgery and he was able to skillfully adapt to changes in the field," says Dr. Alan Hudson, former President and CEO of UHN, and a long-time friend and colleague of Dr. Gentili. "He will always be remembered as the guy who never hesitated to take on the toughest clinical cases."

In a touching video about his experience becoming a patient, Dr. Gentili and his colleagues discussed their deepened appreciation of the difficulties that patients face and the importance of patient advocacy.

"If we are able to gather as many perspectives as possible, to be guided by those who live through the disease to improve the care that we deliver, then we have it right," remarks Dr. Gelareh Zadeh, Co-Director of the Krembil Brain Institute and a friend and colleague of Dr. Gentili.

To honour Dr. Gentili, UHN is establishing the Dr. Fred Gentili Skull Base Clinic.

Historic Gift for Vision

In celebration of his belated 86th birthday, legendary Bay Street investment banker and philanthropist Donald K. Johnson announced a historic $50 million donation to support and expand his namesake, the Donald K. Johnson Eye Institute.

As the largest donation to a vision program in Canada, this investment will advance vision research and patient care for the more than five million Canadians who are living with eye disease. With this donation, Mr. Johnson will have committed over $65 million to support the exceptional vision scientists and clinicians at UHN.

Mr. Johnson's generous gift will provide long-term financial resources to expand clinical research, retain and recruit top talent in vision science and clinical care, and accelerate technological innovation. In addition, this gift will create three endowed clinical fellowships.

"We are humbled by and so grateful for Don's continued generosity and commitment to investing in the best talent, tools and training, to ensure that our hospital leads the world in vision care," comments Tennys Hanson, CEO of the UHN Foundation.


Donald K. Johnson, Member of the Order of Canada

Women in Science

Women account for less than 30% of scientific researchers worldwide. To increase participation of women and girls in the fields of science, technology, engineering and mathematics (STEM), the United Nations declared February 11 as the International Day of Women and Girls in Science.

To celebrate the day, Krembil hosted a free livestream for middle and high school students, to spark their interest in science.

The event was moderated by Dr. Eugenia Addy, founder & CEO of Visions of Science Network for Learning, a Toronto not-for-profit organization that promotes STEM engagement among youth from low-income and marginalized communities. "Science needs everyone," says Dr. Addy.

Postdoctoral fellow Dr. Tahani Baakdhah and researchers Drs. Sindhu Johnson and Mary Pat McAndrews gave talks about their lives and careers, and what inspired them to enter the fields of vision, arthritis and brain research.

Guest speakers were actress Amy Poehler and aspiring scientist and TIME magazine's first ever Kid of the Year, Gitanjali Rao.


Left to right: Tahani Baakdhah, Sindhu Johnson, Mary Pat McAndrews and Eugenia Addy

Martin Ingelsson, Senior Scientist; Krembil Brain Institute

Chasing a Cure for Alzheimer's

Joining the Krembil Brain Institute as a Senior Scientist this year was Dr. Martin Ingelsson, a geriatrician and neuroscientist with expertise in neurodegenerative diseases.

His research is focused on characterizing the molecular mechanisms that underlie neurodegenerative diseases, such as Alzheimer disease, and developing strategies to diagnose and treat these conditions.

Prior to joining Krembil, Dr. Ingelsson published a detailed characterization of the Uppsala mutation—a mutation in the amyloid precursor protein gene that leads to an early-onset form of Alzheimer disease. His studies of this mutation have yielded important insights into the formation of amyloid-beta, a peptide that accumulates in the brains of patients with the disease.

"There is currently no effective treatment for Alzheimer disease, likely because of our limited understanding of its underlying mechanisms," explains Dr. Ingelsson. "It is thrilling to characterize disease-causing processes and develop strategies to counteract them."

At Krembil, Dr. Ingelsson is exploring the causes of Alzheimer disease and other dementias. He also explores biomarkers of neurodegeneration and works to develop improved treatments for dementia, with a focus on gene therapies.

Regarding his recruitment to Krembil, Dr. Ingelsson comments that he looks forward to "collaborating with the exceptional researchers at the Institute to advance our understanding of devastating brain diseases and how to diagnose and treat them."

Christopher Kim, Scientist; Schroeder Arthritis Institute

New Osteoarthritis Therapies

Krembil is pleased to welcome its newest Scientist, Dr. Christopher Kim. Dr. Kim is an Orthopaedic Surgeon in the Sprott Department of Surgery at UHN, and an Assistant Professor in the Department of Surgery at the University of Toronto.

Prior to joining Krembil, Dr. Kim studied stem cells, gene editing and cell therapeutics in the Institute of Medical Science at the University of Toronto, under the supervision of Dr. Andras Nagy. His research involved the use of genetically engineered cells to deliver compounds that reduce joint inflammation and the loss of cartilage in experimental models of osteoarthritis.

"Current therapies for osteoarthritis include anti-inflammatory drugs, physical therapy and injections. These therapies can be very effective at reducing symptoms such as pain and inflammation, but they are not cures," explains Dr. Kim. "Designer cell therapies that reduce inflammation and repair joint tissues are a new type of therapy with enormous potential for stopping disease progression and helping patients reduce joint pain and inflammation and regain function."

At Krembil, Dr. Kim will continue this line of research, focusing on gene and cell therapies to treat and prevent osteoarthritis.

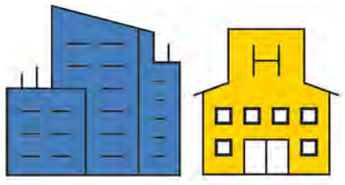
"I admire the supportive, academically rigorous and patient-centred environment here at Krembil," says Dr. Kim. "I am excited to work closely with other scientists and clinicians at the Institute to explore the mechanisms of osteoarthritis and develop therapies to advance patient care."

Krembil by the Numbers

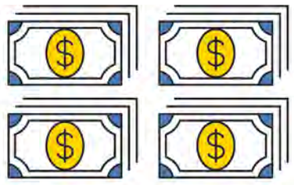
201
Principal Investigators

262
Trainees

137.8K
sq. ft. of Research Space



$49.6M*
External Funding



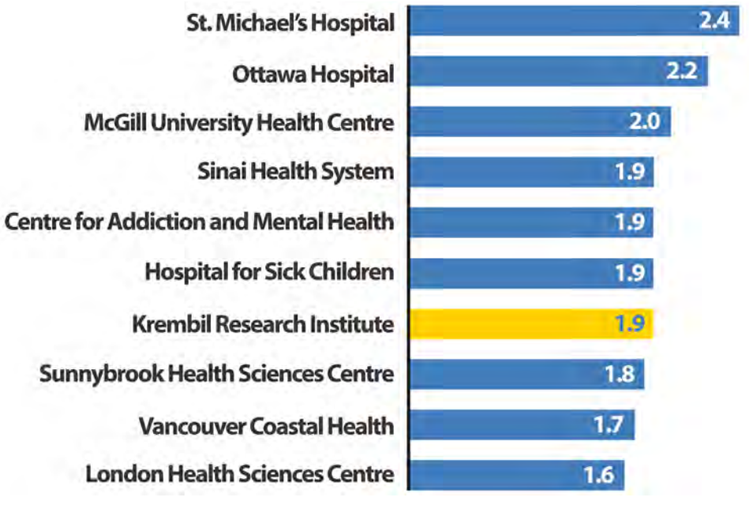
1218
Publications

298
Staff Members

**This value represents the total research project funding expended by Krembil researchers in each fiscal year. Note that this value differs from the external funding amount in the 2022 UHN Research Report, which includes project and organizational expenses.*

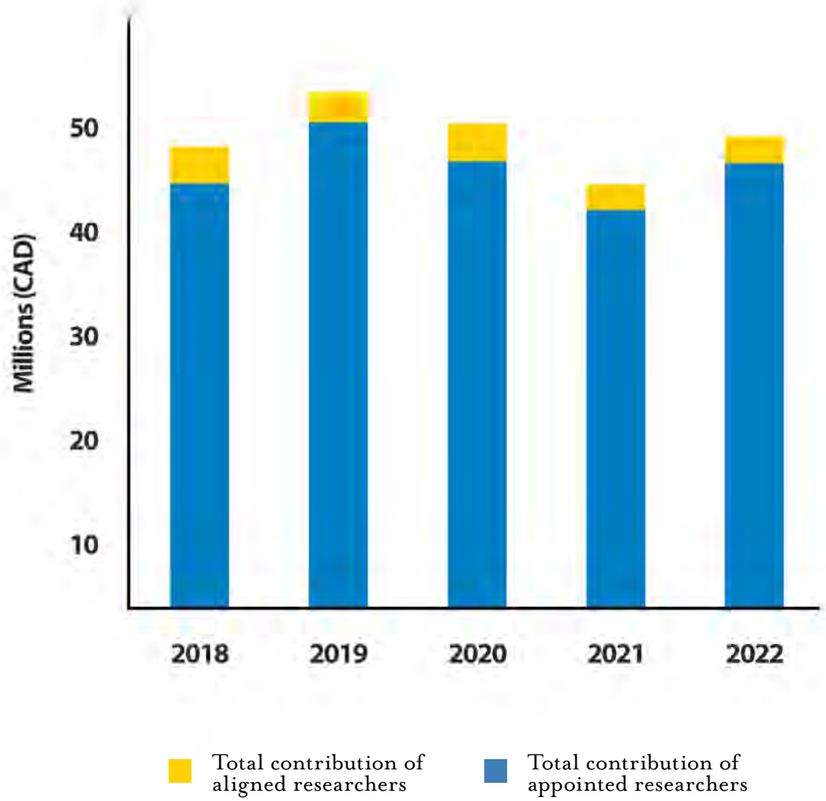
All Publications

Citation Impact



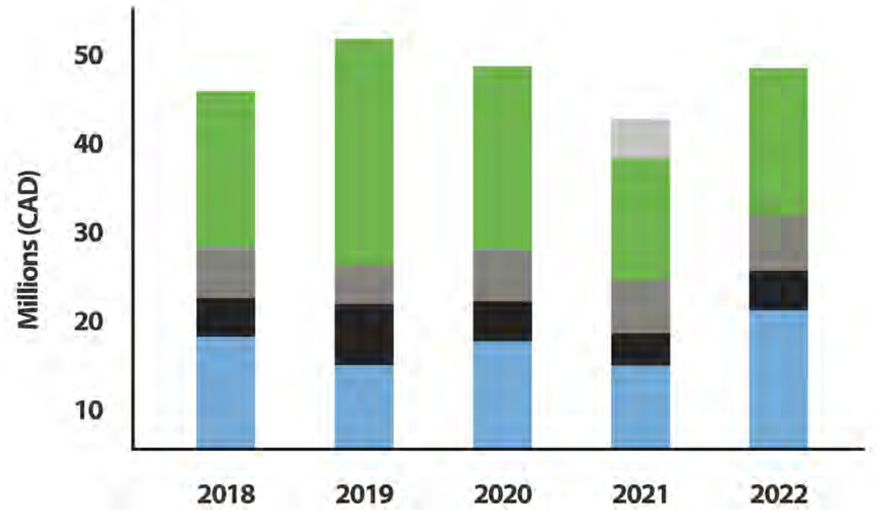
Citation impact values are based on Clarivate's Category Normalized Citation Impact and were obtained from Clarivate's InCites database.

Research Funding

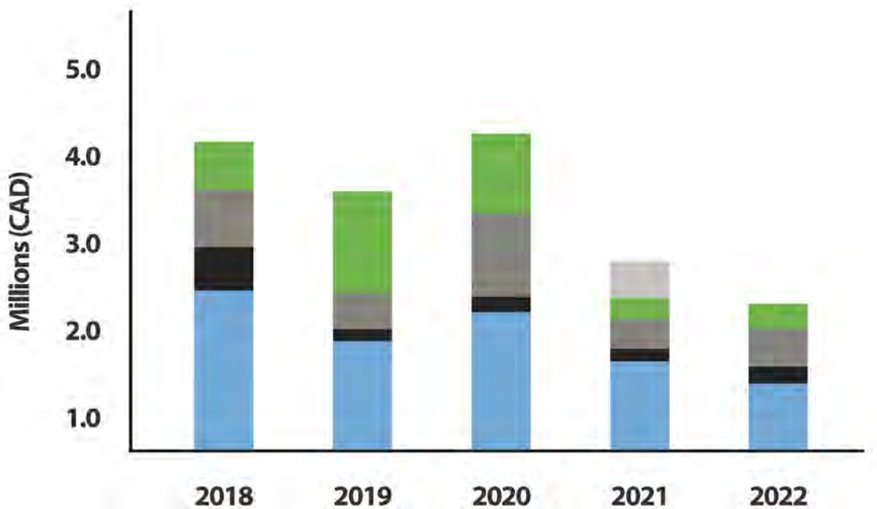


Krembil researchers include those appointed by the Institute and those aligned with the Institute. Only Krembil-appointed researchers are subject to the Institute's scientific and performance reviews.

Appointed Researcher Funding



Aligned Researcher Funding



Awards and Distinctions

Esther Bui
Canadian Leader in Neurology, Cambridge University Press

Yvonne Buys
Mel Mitzel Research Excellence Award, Glaucoma Research Society of Canada
International Scholar Award, American Glaucoma Society

Ki Jinn Chin
Presidential Scholar Award, American Society of Regional Anesthesia and Pain Medicine

Michael Fehlings
Apple Award, American Spinal Injury Association

Dafna Gladman
Women Who Lead Award, National Psoriasis Foundation

Nigil Haroon
President, Canadian Rheumatology Association

Anthony Lang
Jay Van Andel Award for Outstanding Achievement in Parkinson's Disease Research, Van Andel Institute
Margolese National Brain Disorders Prize, University of British Columbia

Andres Lozano
Dandy Medal, Walter E. Dandy Neurosurgical Society
International Gold Medal, Saudi Association for Neurological Surgery

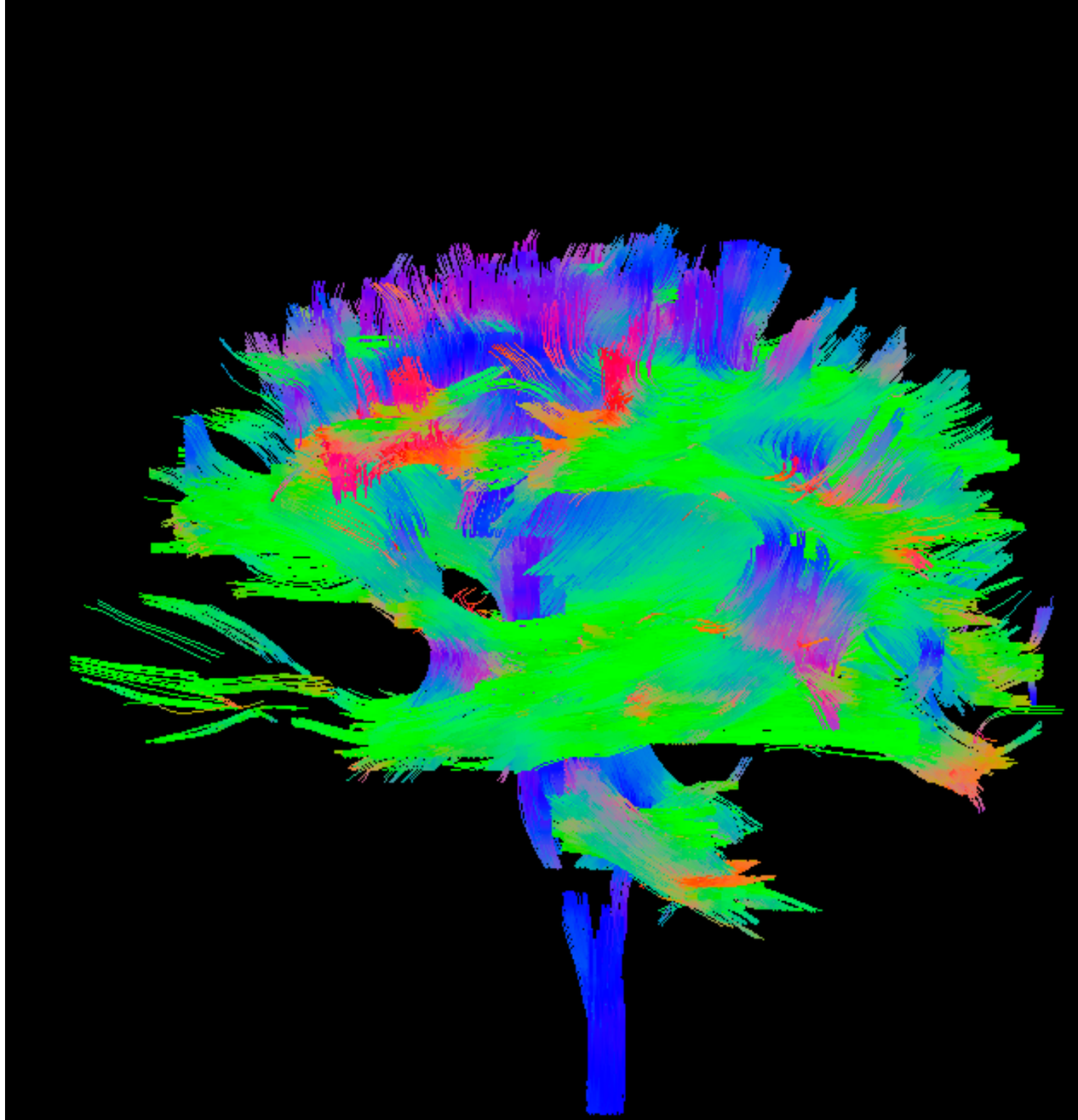
Philippe Monnier
Mel Mitzel Research Excellence Award, Glaucoma Research Society of Canada

Yoga Raja Rampersaud
Chiropractic Champion Award, Ontario Chiropractic Association

Zahi Touma
Lupus Canada Catalyst Award, Lupus Foundation of America

Sowmya Viswanathan
Top 10 Research Advances of 2021, Arthritis Society Canada
The Biologic Association's Summit 2021 Research Award, American Orthopaedic Society for Sports Medicine

Starlee Lively, Sequencing Specialist; Krembil Research Institute



Diffusion tensor imaging of the brain showing neuronal fibre pathways. Provided by Mia Mojica, postdoctoral fellow; Slaight Family Centre for Advanced MRI

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

Dr. Lyanne C. Schlichter
Former Krembil Senior Scientist

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

Dr. Mohit Kapoor
Krembil Senior Scientist

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

Dr. Valerie Wallace
Krembil Senior Scientist

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