The Krembil Research Institute (Krembil) is the research arm of the Toronto Western Hospital (TWH) and one of the seven research institutes at the University Health Network (UHN). 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.

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.

Krembil is 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.

We gratefully acknowledge the work of our UHN Board of Trustees and our UHN Foundation Board, who tirelessly volunteer their time and expertise in a variety of capacities and on various committees to ensure that UHN achieves the highest standards in patient care, stewardship and accountability. Our Board members are leaders in our community who believe in and support UHN’s mission and mandate to create A Healthier World and we thank them for their commitment.

About the cover: Illustrations of the dynamic nature of science, showcasing research, care and innovation from Krembil’s three institutes. Designed by Twayne Pereira, Krembil Public Affairs and Communications.
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### Inside

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Functional brain connectivity may explain sex differences in the experience of chronic pain

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A scientist’s job is to question, to search for answers—often to fail—and to build upon existing knowledge. We do this over and over until one day, in our lifetime if we are fortunate, we finally understand the solution to a problem—and how to obtain it. In this way, we build upon humanity’s collective understanding of our world and forge new paths of discovery.

The dream of every research team at Krembil is to gain insight that will improve health and save lives. The role of science is to promote the innovation that gives rise to that insight—to power discovery.

For the past year and a half, we have seen an unprecedented pandemic ravage our world. In this time of upheaval and immeasurable suffering, science has been more important than ever.

Science helps us to better understand the context of what is happening around us. It guides us to make informed decisions about our health, and it provides a foundation on which to address the challenges we face as a society.

Without science, there would be no vaccines, no testing. Without vaccines and testing, there would be no end to the devastation caused by COVID-19 or the waves of lockdowns that have occurred.

I am proud to say that since the earliest days of the pandemic, the Krembil community has adapted to confront the global crisis. And we have done so while remaining dedicated to addressing multiple other pressing health challenges.

We have found new ways to conduct our important research into diseases of the brain and spine, bones and joints, and eyes, even as we continue to contribute to the growing body of knowledge around the SARS-CoV-2 virus and its long-term impact.

The challenges posed by COVID-19 have only strengthened our determination to work harder, smarter and more efficiently, as a team, to translate our ground-breaking research into new treatments and cures.

Inside this year’s report, you will learn about the impressive progress that our team has made, including advancing our understanding of why men and women experience chronic pain differently, validating new classification criteria for systemic lupus and developing a molecular model of the brain connections involved in visual processing that may lead to new treatments for vision loss.

At Krembil, we are building a world-class community of scientists and clinicians that is diverse in expertise, perspective and culture to address the challenges of tomorrow. On this front, we will continue to engage with future scientists from racialized and marginalized communities to ensure that our work is guided by the richness of different perspectives—a key requirement for innovation.

We will also continue to work together with our community, as partners, to share knowledge and expertise, and to ensure continued support for the life-changing work that we do.

We enter careers in science because we are insatiably curious. We stay to make a difference. At Krembil, we achieve this as one team working toward a shared goal—to improve the lives of people everywhere.

Donald F. Weaver, MD, PhD, FRCPC, FCAHS
Director, Krembil Research Institute
University Health Network
Mable Chan is a PhD candidate in Dr. Sowmya Viswanathan’s lab at the Schroeder Arthritis Institute.

“I study immune cells called macrophages and how these cells contribute to the progression of osteoarthritis—the most common form of arthritis. I am investigating whether we can reprogram patients’ macrophages to reduce joint inflammation and slow or halt the progression of their disease.

“Krembil’s unique position within UHN and its affiliated network of academic and clinician scientists enables me to conduct research in a translational space and work with disease models that are relevant to humans.

“My career goal is to continue working in the field of cell-based therapy to develop effective and affordable treatments for osteoarthritis and other diseases that currently have no cures.”

Akshay Gurdita is a PhD candidate in Dr. Valerie Wallace’s lab at the Donald K. Johnson Eye Institute.

“Transplanting light-sensitive cells, called photoreceptors, into the damaged eye is an emerging therapy for retinal diseases. I study how photoreceptors migrate to their correct positions within the retina during development. Understanding this process will enable us to improve the ability of these cells to integrate into the retina after transplantation.

“Working at Krembil means being part of a collaborative and diverse community of scientists that are striving to answer important questions and make a difference in people’s lives.

“My goal is to become a professor at a university so I can contribute to my field through mentoring students and advancing a research program.”

Alborz Noorani completed a master’s degree in Dr. Mojgan Hodaie’s lab at the Krembil Brain Institute and is now a second-year medical student at the Temerty Faculty of Medicine.

“I used advanced brain imaging to study an area of the brain known as the hippocampus, which is involved in chronic pain. Through this research, we aimed to improve therapies for patients living with this condition.

“Krembil offered me the opportunity to collaborate with and learn from world-renowned scientists and clinicians. My training has helped me understand patients’ journeys so I can focus my research on what matters to them and develop technologies to improve their health outcomes.

“As a medical student who is passionate about research, I hope my training leads me to a career as a physician–scientist at an institute as advanced as Krembil, so I can bring my research to the bedside.”
Kaitlyn Price is a PhD candidate in Dr. Cathy Barr’s lab at the Krembil Brain Institute.

“I study the genetic basis of reading disabilities and their overlap with other neurodevelopmental disorders. Reading disabilities affect 10–15% of children in North America, but their causes are poorly understood. By uncovering the molecular pathways involved in these disabilities, we hope to devise strategies to treat them.

“Krembil fosters invaluable collaboration and mentorship. The trainees are very driven and support and motivate each other. I know I will look back at my time at Krembil as an exciting and once-in-a-lifetime opportunity.

“My goal is to continue to work in the science sector, with a focus on patients and outreach. I would love to become a pediatrician or genetic counselor and work to improve the lives of children with neurodevelopmental disorders.”

Alessandra Tuccitto is a PhD candidate in Dr. Jeremy Sivak’s lab at the Donald K. Johnson Eye Institute.

“I study the underlying mechanisms of eye diseases such as glaucoma. I investigate a specific molecular pathway involved in how neurons in the eye respond to injury. By understanding this pathway, we hope to develop strategies to rescue these neurons to treat eye diseases.

“Working at Krembil has truly been an honour. I am thankful for the technologies and resources that enable me to perform cutting-edge research. I am also extremely grateful for the support that I have received from my supervisor, colleagues and the Krembil administrative team.

“In the future, I hope to continue to build on the skills that I have gained during my PhD studies and contribute to developing therapies and diagnostic tests.”

Calvin Yip is a PhD candidate in Dr. Anthony Perruccio’s lab at the Schroeder Arthritis Institute.

“My research focuses on the epidemiology of osteoarthritis, one of the leading contributors to pain and disability globally. Because there is no cure for this disease, research to understand the populations affected and advance disease prevention and management is critical.

“Working at Krembil means being a part of an intellectually stimulating, supportive and tight-knit research community. I have opportunities to collaborate with experts in arthritis research, present my research to a broad range of audiences, and attend symposia to learn from global leaders in bone and joint health.

“My goal is to work in the field of chronic disease epidemiology, conducting research to reduce the impact of disabling conditions such as osteoarthritis.”
Men and women experience chronic pain differently. Women are more likely than men to experience chronic pain, and many chronic pain conditions are more common in women.

Research led by Dr. Karen Davis and her PhD student Natalie Osborne has identified sex differences in functional brain connectivity that may explain why men and women experience chronic pain differently.

The researchers used functional magnetic resonance imaging to examine the brains of men and women with and without chronic pain caused by ankylosing spondylitis—a type of arthritis that affects the joints of the spine.

The brain scans revealed sex differences in the functional connectivity between brain regions that are implicated in acute and chronic pain. These connectivity patterns center on a particular region called the subgenual anterior cingulate cortex (sgACC), which plays an important role in how the brain responds to pain.

To identify sex differences, the team compared brain connectivity in women with and without chronic pain. They found that the sgACC of women with chronic pain was more strongly connected to brain regions that are involved in self-awareness and monitoring the body’s internal state. It was also less strongly connected to regions involved in controlling pain perception and emotional responses to pain.

In contrast, these connectivity differences were not observed when comparing men with and without chronic pain.

These findings raise questions about whether the
Researchers led by Drs. Robert Chen and Steven McCabe recently followed a patient’s recovery after hand transplantation at Toronto Western Hospital. The patient experienced a traumatic forearm and hand amputation ten years prior because of a car accident.

The researchers used non-invasive brain imaging and stimulation to map the brain region that controls movement and the sense of touch for the arm that underwent surgery. They found that this region changed following transplant to more closely resemble its pre-amputation state, and these changes began prior to the patient recovering hand function.

These findings highlight the importance of brain plasticity—including that which occurs shortly after surgery—for the restoration of hand function following transplantation.

This work was supported by the Canadian Institutes of Health Research, the Chronic Pain Network, The MAYDAF Fund and the UHN Foundation.

Dr. Sindhu Johnson jointly leads a global collaboration that is focused on developing more effective criteria for identifying individuals with systemic lupus erythematosus (SLE)—the most common type of lupus.

Lupus is an autoimmune disease in which the immune system attacks the body’s healthy tissues and organs, causing inflammation and pain.

Lupus classification systems can be assessed in terms of their sensitivity (i.e., how well they correctly identify patients with lupus) and their specificity (i.e., how well they correctly identify patients without lupus). Sensitivity and specificity are important features of disease classification systems. Existing lupus criteria are typically either highly sensitive or highly specific, but not both.

In 2019, Dr. Johnson’s team published a new lupus classification system in the journal Arthritis & Rheumatology. This system incorporates weighted criteria related to the presence of antibodies and other proteins associated with lupus, as well as other clinical factors, such as the occurrence of fevers or seizures.

The team recently validated their new criteria against sex, ethnicity and disease stage. The criteria performed exceptionally well across patient groups, with sensitivity and specificity ranging from 89 to 100% in all analyses.

This combination of excellent sensitivity and specificity is an improvement on previous criteria. For instance, criteria published in 2012 by the Systemic Lupus International Collaborating Clinics Group has 93% specificity but only 83% sensitivity for women, whereas the new classification system achieved 94% specificity and 97% sensitivity.
Many individuals with lupus experience periods of mild symptoms alternating with periods of intensified symptoms called flare-ups. Researchers led by Dr. Joan Wither have identified a biomarker that can predict the risk of flare-ups in individuals with SLE.

The team explored whether the risk of flare-ups can be predicted by levels of type 1 interferons (IFNs)—proteins that are involved in boosting the body’s immune response. Given that IFNs function by activating certain genes within immune cells, the researchers measured the activation of five of these genes in blood samples from patients.

Patients who had higher levels of IFN activity were more likely to experience recurrent flare-ups over the five-year study period. These findings suggest that IFN activity can predict lupus flare-ups and that patients with high IFN activity might benefit from close monitoring and more aggressive treatments.

The validation study also revealed that the criteria could effectively identify patients with early disease. Implementing these criteria will ensure that more patients with lupus receive early treatment and are not left out of innovative clinical trials.

The new criteria have been approved by the European League Against Rheumatism and the American College of Rheumatology, organizations that are focused on improving the care of individuals with lupus and other rheumatic diseases.

This work was supported by the European League Against Rheumatism, the American College of Rheumatology, the Intramural Research Program of the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health, and the UHN Foundation. Johnson SR, et al. Ann Rheum Dis. 2020 Oct. doi: 10.1136/annrheumdis-2020-217162.
Researchers led by Dr. Michael Reber have constructed the first computational model that describes the molecular and cellular mechanisms that drive the organization of the brain’s visual connections.

The model simulates and predicts the organization of visual connectivity and how different neural networks interact. These interactions are required to visualize and understand the world around us.

The model is based on a ‘three-step’ map alignment algorithm. The algorithm serves as a set of mathematical instructions for constructing a visual map. The benefit of this approach is that it closely mimics the three steps that are taken by the brain to process visual information.

The three steps that are defined in the algorithm and naturally followed in the brain are: 1) the formation of a visual map from information that is sent from the eye to a region of the brain known as the superior colliculus; 2) the incorporation of complementary information from the visual cortex—a brain region that is responsible for processing visual information; and 3) the ‘alignment’ of the visual information so it makes sense to the brain.

The team compared findings from the computational model with those from real-life biological models and found that the computational model could faithfully recreate errors that arise in certain neurological conditions.

“This work is essential for recreating and ultimately predicting what can go wrong in the connections between the eye and brain,” explains Dr. Reber. “Our model has the power to ‘connect the dots’ between

New molecular model of brain connections involved in visual processing

Dr. Michael Reber, Senior Scientist, Donald K. Johnson Eye Institute
Researchers led by Dr. Philippe Monnier have identified a potential target for treating inherited retinal degenerations (IRDs), eye diseases that cause progressive vision loss. Up to 1 in 2,000 individuals live with IRDs, and there are no cures or treatments to halt disease progression.

The visual impairment that are experienced by patients with IRDs results from a gradual loss of photoreceptors—light-sensitive cells in the retina. The researchers found that damaged photoreceptors in experimental models of IRDs and in the eyes of people living with an IRD contain high levels of neogenin—a protein that triggers cell death. They also found that inhibiting neogenin activity promotes photoreceptor survival and preserves vision.

These findings suggest that targeting neogenin could serve as a powerful new strategy for preserving vision in individuals with IRDs.

Full Story / Scientific Article
Our Three Institutes

**Donald K. Johnson Eye Institute**

The Donald K. Johnson Eye Institute is home to research programs that span the molecular and cellular mechanisms of retinal disease, the development of approaches for assessing retinal health and vision rehabilitation in patients with blinding eye disease.

**Schroeder Arthritis Institute**

The Schroeder Arthritis Institute is the largest multidisciplinary arthritis hub in Canada, integrating medical, surgical and basic science aspects of Hand, Orthopedics, Osteoporosis and Rheumatology with a goal of making a global impact in discovery, learning and patient care.
The Krembil Brain Institute is home to one of the world’s largest and most comprehensive teams of physicians and scientists. The neuroscience team is focused on research programs dedicated to brain and spine with a goal of alleviating debilitating chronic diseases through basic, translational and clinical research.
Alzheimer’s: Why Haven’t We Solved It Yet?

On March 30 and 31, Krembil hosted the 2021 Gairdner Symposium, ‘Alzheimer’s: Why Haven’t We Solved It Yet?’ featuring eight world-renowned experts in the field of Alzheimer’s disease research.

The goal of this event was to make dementia research accessible to everyone and to encourage public support for science.

More than half a million Canadians currently live with dementia, including Alzheimer’s, the most common type of dementia. By 2031, that number is expected to rise to more than one million.

“Alzheimer’s is quickly becoming a global health crisis that we simply cannot afford to ignore,” said Dr. Donald Weaver, Co-Director of the Krembil Brain Institute and event co-chair.

The two-day virtual event was sponsored by the Gairdner Foundation and co-organized by the Krembil Brain Institute, UHN and Johns Hopkins University. Jay Ingram, a science broadcaster and author, was the host and moderator.

Day one opened with Dr. Bradly Wouters, Executive Vice President of Science and Research at UHN. “We need our communities to be better informed about this disorder and ultimately to act as ambassadors for dementia research,” he told the audience.

Dr. Janet Rossant, Scientific Director of the Gairdner Foundation, then spoke about the organization’s mandate to raise the bar for Canadian science. “The Gairdner Foundation aims to inspire the next generation of scientists and innovators,” she said, adding that 95 winners of the Gairdner Award have gone on to win a Nobel Prize.

Day one featured four speakers. Dr. Barry Greenberg of Johns Hopkins University kicked off the talks with a discussion about why we have yet to cure Alzheimer’s, or any other neurodegenerative disease. Dr. Malú Tansey of the University of Florida then explored the role of brain immunity in identifying targets and treatments for the disease. Dr. Laura Baker of Wake Forest University presented her latest findings about lifestyle interventions that may help to prevent Alzheimer’s. Finally, Dr. Vladimir Hachinski of Western University spoke about his most recent project—the first-ever population-based study looking at the connection between heart disease, stroke and dementia. “If we can prevent the onset of stroke, can we also reduce the chances of someone developing dementia or heart disease?” he asked the audience.

On day two, Dr. Sylvie Belleville of the Université de Montréal discussed the importance of cognitive reserve and resilience in understanding the progression of Alzheimer’s. Dr. Kenneth Rockwood of Dalhousie University shared recent evidence that frailty is a major, often underestimated risk factor for the disease. Dr. Lisa Barnes of Rush University Medical Center then considered the role of diversity and equity in Alzheimer’s research. “We need to be

Reduce your risk

Avoid excessive alcohol

Manage your weight

Continue to learn
more inclusive and diverse to ensure health equity as we race for a cure for Alzheimer’s,” she told the audience. “We can’t be focused solely on one population or we will never get there.”

Dr. Weaver concluded the talks, noting that the vast number of clinical trials for Alzheimer’s treatments have failed. He suggested that a number of reasons are to blame: treatments may be tested too late in the course of the disease, the exact cause of Alzheimer’s remains unknown and there is simply a lack of funding for Alzheimer’s research.

Attendees were also treated to a video summarizing modifiable risk factors for the disease, as outlined in a 2017 publication in The Lancet.

Lively panel discussions focused on the role of inflammation in neurodegenerative disease, how looking at Alzheimer’s as a multitude of disorders instead of a single disorder may change the course of dementia research, why Alzheimer’s is more prevalent in women than men, and the impact of isolation and loneliness on disease progression.

More than a thousand people attended the symposium live and thousands more have watched online recordings of the event, which can be viewed here: day one and day two.

“We need to keep the conversation going,” said Dr. Weaver, adding that supporting homegrown research is key. “Where there is science, there is hope.”
Around the world, women continue to be underrepresented in the fields of science, technology, engineering and mathematics (STEM). In 2015, to achieve greater gender equality, the United Nations declared February 11 as the International Day of Women and Girls in Science.

To celebrate the day, Krembil partnered with the Durham District School Board to host a free livestream event for middle and high school students to spark their interest in science.

The event was moderated by Dr. Gelareh Zadeh, Co-Director of the Krembil Brain Institute and Canada’s first female Chair of Neurosurgery. “At UHN, we have countless strong, visible role models to show girls that there is a place here for them,” says Dr. Zadeh.

Drs. Mojgan Hodaie, Sowmya Viswanathan and Valerie Wallace gave inspiring presentations about their education and careers in STEM and answered questions submitted by participating students.

Guest speakers were Dr. Mayim Bialik, neuroscientist and star of television’s The Big Bang Theory, and Dr. Eugenia Addy, founder & CEO of the Toronto not-for-profit Visions of Science Network for Learning, which advances STEM engagement among youth from low-income and marginalized communities.

Krembil’s virtual Research Day brought together more than 175 investigators, trainees and staff to celebrate achievements across the Institute’s three research pillars: brain and spine, vision, and bones and joints.

The event kicked off with opening remarks from Dr. Bradley Wouters, UHN’s Executive Vice President of Science and Research, and Dr. Mary Pat McAndrews, Chair of the Krembil Trainee Affairs Committee.

“Despite the challenges that we have all faced this year, what we have accomplished is nothing short of incredible,” said Dr. Wouters.

Attendees enjoyed informative presentations from over 60 graduate students, postdoctoral fellows and staff, as well as videos featuring Krembil investigators thanking trainees for their dedication and perseverance and trainees describing what they do and why they value Research Day.

The event concluded with an inspiring message from Krembil Director Dr. Donald Weaver on the important role of science in society and the merit of scientific collaboration. “If there is one thing that I have seen and felt over the course of this pandemic, it’s the power and unifying force of the Krembil community.”
One in five Canadians has arthritis, a collection of conditions that cause inflammation of the joints. Arthritis can cause chronic pain and reduced mobility and is the global leading cause of disability.

To address the growing burden of arthritis, UHN launched the Schroeder Arthritis Institute, enabled by a generous $25 million donation from philanthropists Walter and Maria Schroeder.

Led by Co-Directors Drs. Mohit Kapoor and Robert Inman, the Institute combines arthritis research and education in four clinical programs: Hand, Orthopedics, Osteoporosis and Rheumatology.

Funds will support top scientific talent and provide critical salary and infrastructure resources for the entire research team.

“The Schroeder Arthritis Institute is Canada’s largest multidisciplinary arthritis hub,” says Dr. Kapoor. “The Institute’s recent successes include innovations in surgical interventions in orthopedics, novel treatments for rheumatic diseases, and tools to predict the outcomes of bone, joint and autoimmune rheumatic diseases.”

“This Institute is something we have long dreamed of and, with the help of Walter and Maria Schroeder, this dream has become a reality,” says Dr. Inman.

In April 2021, UHN celebrated the launch of the Max Planck–University of Toronto Centre (MPUTC) for Neural Science and Technology.

The MPUTC is the third Max Planck Centre in Canada, continuing a 50-year-long history of scientific collaboration between Canada and Germany.

Led by Co-Directors Drs. Taufik Valiante (Krembil Brain Institute) and Joyce Poon (Max Planck Institute for Microstructure Physics), the Centre brings together experts in engineering, physics, neuroscience, neuroinformatics and neuromedicine.

The centre also serves as a link between the Max-Planck-Gesellschaft, the University of Toronto, UHN, the Hospital for Sick Children and the Centre for Addiction and Mental Health.

“Cross-disciplinary research is critical to advancing brain science, and this centre brings together leading experts in neuroscience, engineering and artificial intelligence, among other fields,” says Dr. Valiante. “There is a great sense of societal urgency surrounding brain research, and we are confident that this global collaboration between world-class institutes will accelerate breakthroughs in this field.”

Unifying Research, Education and Care

Canada-Germany Research Partnership

Drs. Mohit Kapoor and Robert Inman

International collaborations foster innovation and discovery
Improving the lives of people is our mission and passion at Krembil. Delivering on this promise is a formidable undertaking and will require our scientists to be pioneers exploring new, uncharted territories as we seek the cures of tomorrow.

To facilitate this process, we have been recruiting new scientists—people with innovative ideas and the drive to translate these ideas into clinical advancements.

Krembil recently welcomed three outstanding investigators.

Dr. Brian Ballios is a clinician scientist who works at the interface between the bench and the clinic to improve vision in individuals who have eye disease.

Dr. Maurizio De Pittà is a computational scientist who develops cutting-edge mathematical tools and techniques to bear upon problems of the brain.

Dr. Olga Lucia Rojas is a neuroimmunologist who is helping to bring Krembil into the new era of brain research, which recognizes the importance of immunology and inflammation in understanding chronic brain diseases.

Moving forward, Krembil will continue to welcome new scientists to join us in making important medical breakthroughs.
Dr. Brian Ballios is an ophthalmologist and vision scientist focused on developing stem cell therapies for inherited and acquired retinal diseases.

Dr. Ballios developed the world’s first injectable biomaterial-based delivery system for transplanting stem cells into the retina. At Krembil, Dr. Ballios explores methods to generate light-sensitive cells and promote their engraftment into the damaged eye. He also investigates the unique features of different retinal diseases to improve the effectiveness of cell therapies. As a physician, he is interested in bringing the next generation of therapies to first-in-human trials.

“Coming to UHN is about joining an ecosystem of discovery,” says Dr. Ballios. “The Donald K. Johnson Eye Institute brings together outstanding clinicians and vision scientists with the common goal of improving the lives of patients.”

Dr. Maurizio De Pittà is a computational neuroscientist with expertise in the biology and function of glia—non-neuronal cells in the nervous system.

Dr. De Pittà develops mathematical models to study the interactions between glia and neurons in the healthy and diseased brain. Using these models, he has uncovered how astrocytes—a subtype of glial cell—signal and contribute to neuron activity and cognition.

At Krembil, Dr. De Pittà will clarify the role of neuron–glia interactions in information processing, learning and memory, and neurodegenerative conditions.

“My ultimate goal is to improve how we diagnose and treat brain diseases,” says Dr. De Pittà. “I look forward to working with translational scientists and clinicians at Krembil to develop a pipeline, from the surgical room to the lab, to identify disease markers and targets for therapeutic interventions.”

Dr. Olga Rojas is an immunologist studying the role of peripheral immune cells in brain inflammation and degeneration.

Dr. Rojas has identified mechanisms that underlie the body’s response to inflammation in autoimmune conditions. She found that a type of immune cell known as a B cell can travel from the gut to the brain and suppress inflammation.

At Krembil, Dr. Rojas explores how B cells affect the development and progression of neurodegenerative disorders. Her research will accelerate the development of therapies to treat these disorders, which currently have no cures.

“The opportunity for close collaborations between scientists, clinicians and patients makes Krembil the ideal setting for translating research advances into clinically useful therapeutics.”
Developing cutting-edge therapeutics for neurodegenerative diseases

Lucid Psycheuticals Inc. (Lucid), a company focused on innovative approaches to brain health, is a made-in-Ontario biomedical success story.

In May 2021, the company obtained a worldwide licence agreement with UHN, granting it exclusive rights to novel compounds for treating neurodegenerative disorders. Lucid takes inspiration from the mechanisms of action of psychoactive agents, leveraging cutting-edge medicinal chemistry approaches with the aim of helping the millions of individuals living with mental health challenges and neurological conditions.

Lucid co-founder and CEO Dr. Lakshmi Kotra and his team have decades of experience in the field of medicinal chemistry. He recently led the development of compounds that prevent the loss of an important substance in the nervous system called myelin.

Myelin surrounds components of neurons, acting like insulation on an electrical wire. When myelin is damaged, neurons are unable to communicate and eventually die. Myelin degeneration has been linked to the initiation and progression of multiple sclerosis—an autoimmune and neurodegenerative disease of the central nervous system. Dr. Kotra’s compounds have been shown to prevent and even reverse neurodegeneration in preclinical models of multiple sclerosis. These compounds could lead to a new therapy for the progressive type of the disease, for which there are currently no curative treatments.

“Lucid licensed these compounds in May 2021 and will continue to work with UHN to develop treatments for multiple sclerosis and other neurodegenerative diseases,” says Oksana Akhova, Licensing Principal with Commercialization at UHN, which brings research-related products and services to market to benefit patients. “Our goal is to have a new therapeutic for the disease on the market in seven years or less.”

Approximately 90,000 people live with multiple sclerosis in Canada, which has one of the highest rates of the disease globally. Dr. Kotra’s new compounds could greatly improve the quality of life for individuals living with multiple sclerosis and reduce the high human and economic costs associated with the disease.

“Our hope is that these compounds will prove effective not only against multiple sclerosis but also against other brain diseases,” says Dr. Kotra. “That hope, of helping patients, is what keeps me going and motivates Lucid’s investors.”

Since joining UHN in 2006, Dr. Kotra has submitted 25 invention disclosures, served as a co-inventor on four issued patent families and developed multiple therapeutic compounds that are in or nearing clinical trials. In 2021, he received the Julia Levy award from the Society of Chemical Industry in recognition of his successful commercialization in the field of Biomedical Science and Engineering in Canada. He is a Professor in the Leslie Dan Faculty of Pharmacy at the University of Toronto.
Wide-field microscope and image of the dentate gyrus. The microscope is one of many cutting-edge instruments at the Bob and Joan Wright Cell Imaging Facility at the Krembil Research Institute.
# Krembil by the Numbers

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<td>principal investigators</td>
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- 58 research fellows
- 143 graduate students
- 18 other students

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*This value represents the total research project funding expended by Krembil researchers in each fiscal year. Note that this value differs from 2021 UHN Research Report external funding amounts, which include project and organizational expenses.*
Research Articles

Normalized Citation Impact

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Research Funding

![Graph showing Research Funding from 2017 to 2021. The graph compares the contribution of non-appointed researchers (light blue) and appointed researchers (gray). The funding peaked in 2019.]

- **Contribution of Non-Appointed Researchers**
- **Contribution of Appointed Researchers**
Appointed Researcher Funding

Aligned Researcher Funding
Awards and Distinctions

Daniel Buchman
Compassion and Technology Fellow, Associated Medical Services

Karen Davis
Fellow, Royal Society of Canada

Dafna Gladman
Fellow, Canadian Academy of Health Sciences

Sidney Kennedy
Distinguished Life Fellow, American Psychiatric Association

Lakshmi Kotra
Julia Levy Award, Society of Chemical Industry

Philip Peng
John J. Bonica Award, American Society of Regional Anesthesia and Pain Medicine

Anahi Perlas-Fontana
ASRA Trailblazer Award, American Society of Regional Anesthesia and Pain Medicine

Anthony Perruccio
Distinguished Scholar Award, Association of Rheumatology Professionals

Mandeep Singh
Presidential Scholar Award, Society of Anesthesia and Sleep Medicine

Peter St George-Hyslop
Margolese National Brain Disorders Prize, University of British Columbia

Zahi Touma
Emerging Investigator Award, Canadian Rheumatology Association

Donald Weaver
2020 Harrington Scholar-Innovator, Harrington Discovery Institute

Gelareh Zadeh
2021 Top 25 Women of Influence Award, Women of Influence
Dr. Mojgan Hodaie (center) performs facial surgery for trigeminal neuralgia, reducing or completely eliminating excruciating facial pain.
Krembil Researchers

Emeritus Scientist
Charles Tator

Senior Scientists
Elizabeth Badley
Cathy Barr
Jonathan Brotchie
Peter Carlen
Robert Chen
Karen Davis
Jonathan Downar
James Eubanks
Michael Fehlings
Dafna Gladman
William Hutchison
Robert Inman
Igor Jurisica
Lorraine Kalia
Mohit Kapoor
Sidney Kennedy
Lakshmi Kotra
Gabor Kovacs
Anthony Lang
Andres Lozano
Nizar Mahomed
Rosemary Martino
Mary Pat McAndrews
David Mikulis
Philippe Monnier
Ivan Radovanovic
Michael Reber
Karun Singh
Jeremy Sivak
Frances Skinner
Antonio Strafella
Shuzo Sugita
Michael Tymianski
Murray Urowitz
Valerie Wallace
Donald Weaver
Joan Wither

Scientists
Vinod Chandran
Melanie Cohn
Nigil Haroon

Mojgan Hodaie
Suneil Kalia
Armand Keating
Milad Lankarany
Luka Milosevic
Anthony Perruccio
Olga Lucia Rojas
Zahi Touma
Kamil Uludag
Taufik Vialiante
Sowmya Viswanathan
Liang Zhang

Affiliate Scientists
Daniel Buchman
Jaskarndip Chahal
Moshe Eisenman
Brenda Gallie
Magdy Hassouna
Walter Kucharczyk
Jérémie Lefebvre
Alireza Mansouri
Massieh Moayedi
Behdhin Nowrouzi-Kia
Elise Stanley
Agnes Wong

Krembil Clinician Scientists
Michael Brent
Rajiv Gandhi
Aylin Reid

Krembil Clinician Investigators
Dimitrios Anastakis
Danielle Andrade
Heather Baltzer
Mark Bernstein
Anuj Bhatia
Yvonne Buys
Frances Chung
Hance Clarke
Robert Devenyi
Dean Elterman
Alfonso Fasano
Susan Fox
Kenneth Fung

Timothy Jackson
Timothy Leroux
Efrem Mandelcorn
Daniel Mandell
Roger McIntyre
Renato Munhoz
Laura Passalent
Fayez Quershy
Yoga Raja Rampersaud
David Rootman
Cheryl Rosen
Allan Slomovic
David Tang-Wai
Carmela Tartaglia
Christian Veillette
Mary Elizabeth Wilcox
Jean Wong
Mateusz Zurowski

Clinician Scientists
Monica Daibert Nido
Tania Di Renna
Sindhu Johnson
Timo Krings
Laurie Connie Marras
Victoria McCredie
Vitor Mendes Pereira
Sapna Rawal
Peter St George-Hyslop

Clinician Investigators
Tarek Abdelhalim
Nadine Abdullah
Ronit Agid
Paula Alcaide-Leon
Laila Alshafai
Ehtesham Baig
Venkat Bhat
Robert Bleakney
Arthur Bookman
Leslie Buckley
Esther Bui
Jennifer Calafati
Simon Carette
Leanne Casaubon
Andrea Chan
External Sponsors

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AbbVie
ActiveO
Advanced Neuro-Vision Systems
Allergan
Alpha Cancer Technologies
American Association of Neurological Surgeons
American Foundation for Surgery of the Hand
American Medical Systems
American Society of Regional Anesthesia and Pain Medicine
Amgen
Anavex
Anesthesia Patient Safety Foundation
AOSpine
ApoPharma
Arthritis Research Foundation
Assessment of SpondyloArthritis International Society
Astellas Pharma
AstraZeneca
Atuka
Aurinia Pharmaceuticals
Autism Speaks
Avicanna
Axoltis
Balt
Baycrest Health Sciences
Bayer
Biogen
Biomimetics
Bioness
Biotie Therapies
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Boston Scientific
Brain Aneurysm Foundation Of Canada
Brain Canada
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BrightFocus Foundation
Bristol-Myers Squibb
Canada Foundation for Innovation
Canada Research Chairs
Canada Research Continuity Emergency Fund
Canadian Anesthesiologists'
Society
Canadian Arthritis Network
Canadian Association of Psoriasis Patients
Canadian Blood Services
Canadian Dermatology Foundation
Canadian Initiative for Outcomes in Rheumatology Care
Canadian Institutes of Health Research
Canadian League Against Epilepsy
Canadian Open Neuroscience Platform
Canadian Stroke Consortium
Canadian Stroke Network
Cancer Research Society
CannScience Innovations
Catwalk
CDLK5 Canada
Celgene
Celxir
Centre for Addiction and Mental Health
Centre hospitalier de l’Université de Montréal
Cervical Spine Research Society
Christopher & Dana Reeve Foundation
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CorNeat Vision
Cornell University
Coviden
Cynapsus Therapeutics
DePuy Synthes
Dravet Syndrome Foundation
Dystonia Medical Research Foundation
Eisai
Eli Lilly
Emmes
Epilepsy Canada
Fisher & Paykel Healthcare
Focused Ultrasound Foundation
Fortuna Fix
Foundation Fighting Blindness
GE Canada
Genentech
Gilead Sciences
Glaucoma Research Society of Canada
GlaxoSmithKline
Healios
Health Canada
Heart and Stroke Foundation of Canada
Histiocytosis Association
Innocentive
INSIGHTEC
Insmed
IntelGenx
International Parkinson and Movement Disorders Society
International Spine Study Group Foundation
InVivo Therapeutics
Ipsen
Iveric bio
Jaeb Center for Health Research
Janssen
JSS Medical Research
Lahey Clinic Foundation
Lawson Health Research Institute
Lucid
Lundbeck
Lung Association-Ontario
Lupus Canada
Lupus Foundation of America
Lupus Ontario
Lupus Research Alliance
MaRS Innovation
Massachusetts General Hospital
McLaughlin-Rotman Centre for Global Health
Medeon
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Medi-Tate
Medtronic
Merck & Co.
Merz Pharma
Milenyi Biotec
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Ministry of Health and Long-Term Care
Ministry of Research and Innovation
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Disclaimers
All data are accurate as of March 31, 2021. Financial data are reported for the 2021 fiscal year ending on March 31, 2021.

RESEARCHER DATA provided by UHN Research Strategy and Planning. 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. Krembil–appointed and –aligned researchers are included in the Institute’s funding and publication data. STAFF & TRAINEE DATA provided by UHN People & Culture (formerly Human Resources). SPACE DATA provided by UHN Facilities Management – Planning, Redevelopment & Operations. FINANCIAL DATA provided by UHN Research Financial Services.

Research Funding represents the total research project funding expended by Krembil researchers in each fiscal year. PUBLICATION DATA provided by UHN Research Strategy and Planning. Publications include articles, reviews and proceedings papers in journals indexed in the Web of Science (WoS) Core Collection (Clarivate); those authored by more than one Krembil researcher are included once in the Institute’s total number of publications. Using Krembil publications from previous calendar years, 22 WoS subject categories were identified to represent one or more or all of Krembil’s priority areas. The publications were then allocated to represent one or all of Krembil’s priority areas based on their WoS subject category. A Medline search using priority–themed keywords was matched to the Krembil publication lists to identify relevant priority–themed publications not otherwise identified using the 22 WoS subject categories. BENCHMARKING DATA provided by UHN Research Strategy and Planning. Normalized Citation Impact is the equivalent of Clarivate’s Category Normalized Citation Impact. The publications of each institution (i.e., Krembil and comparators) were retrieved from WoS using customized search strings that included subordinate organizations. The resulting publications were then filtered by type (i.e., articles, reviews and proceedings papers) and year. Citation metrics were obtained from Clarivate’s InCites database. Normalized Citation Impact is the equivalent of Clarivate’s Category Normalized Citation Impact. Krembil and comparator publication data were retrieved within the same day to ensure citation data were contemporaneous.

Donations
To support Krembil research, please contact the UHN Foundation. Email: foundation@uhn.ca; Telephone: 416-340-3935; Toll–free donation hotline: 1–877–846–4483 (UHN–GIVE); Website: www.uhnfoundation.ca
Scientists at the Krembil Research Institute are relentlessly pursuing cures for arthritis and diseases of the brain and eye.

discoverkrembil.ca