

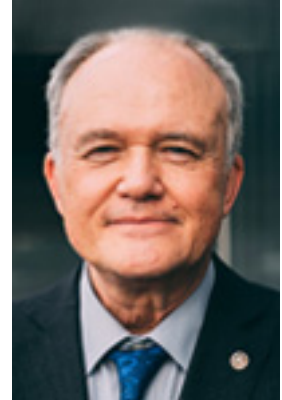
The Krembil

May 2021

The Krembil is the official newsletter of the Krembil Research Institute. It informs the Toronto Western Hospital community, external stakeholders and interested community members about the exciting news and innovative research happening at the Krembil Research Institute.

Stories in this month's issue:

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

Canada-Germany Research Partnership

Introducing the Max Planck–University of Toronto Centre for Neural Science and Technology.



On Wednesday, April 14, 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 successful scientific collaboration between Canada and Germany.

Led by Co-Directors Dr. [Taufik Valiante](#) (Krembil Brain Institute) and Dr. [Joyce Poon](#) (Max Planck Institute for Microstructure Physics), the Centre brings together experts in the fields of engineering, physics, neuroscience, neuroinformatics and neuromedicine. It also serves as a link between the Max-Planck-Gesellschaft, the University of Toronto, University Health Network and participating hospitals—the Hospital for Sick Children and the Centre for Addiction and Mental Health.

“The partnership between these research institutions and hospitals will support the development of new tools and experiments that are relevant to the human brain,” says

Dr. Valiante. “There is a great sense of societal urgency surrounding brain research, and we are confident that the MPUTC will accelerate breakthroughs in this field.”

Graduate trainees will have the opportunity to enroll in a joint PhD program at the MPUTC. This program will enable students to spend the first year of their PhD studies at the University of Toronto followed by up to three additional years at a participating Max Planck Institute.

Krembil has committed to funding three joint PhD program studentships, during which students will be supervised by Krembil Brain Institute scientists.

For more information, visit the Centre’s website [here](#).

Embracing Emotions

Krembil celebrated Mental Health Week with online resources to promote emotional well-being.



Mental and emotional health are closely intertwined.

Having good mental health does not mean that you feel happy all the time. One key to maintaining good mental health is learning to recognize, accept and deal with your emotions—both positive and negative.

With hard-hitting waves of COVID-19 and continued disruptions to our daily routines, 2021 has been a remarkably stressful year. A nationwide survey conducted by the Canadian Mental Health Association, in partnership with UBC researchers, found that approximately 40% of Canadians have experienced deteriorated mental health since the start of the COVID-19 pandemic.

To promote mental health, the Krembil Research Institute shared daily resources to help faculty, staff and trainees recognize their emotions and deal with feelings of stress, anxiety and depression.

Mental Health Week may be over, but maintaining good mental and emotional well-being is a life-long process. The resources compiled by Krembil staff are still available and are listed below.

[30-minute mindfulness session](#)

YouTube video

Led by Jenna McLeod, team lead at the Poul Hansen Family Centre for Depression at UHN

[Resiliency in Uncertain Times](#)

YouTube video, 1 hour

By Dr. Robyne Hanley-Dafoe, multi-award-winning psychology and education instructor and author of “Calm Within the Storm”

[Good Food, Good Mood](#)

Krembil Cookbook in PDF format (UHN sign-in required)

A collection of recipes that are sure to pick you up after a tough day

For more information about Mental Health Week, visit <https://mentalhealthweek.ca>.

Research

Taking the High Road

Study settles the dispute over whether low dose steroids are effective for lupus nephritis.



Systemic lupus erythematosus, the most common form of lupus, affects women more than men. Up to 50% of individuals with lupus develop lupus nephritis, which, if left untreated, can lead to kidney failure.

A study led by Krembil researchers reveals that currently recommended doses of the steroid medication prednisone are more effective at treating the disease than lower doses.

Prednisone is the most common drug prescribed to treat lupus nephritis—an autoimmune disease in which the body’s immune system attacks the kidney. The disease causes inflammation at sites in the kidney—known as glomeruli—that filter and cleanse the blood.

Because steroid drugs can cause a number of serious side effects, such as cataracts, diabetes and osteoporosis, efforts are underway to minimize the amount of prednisone

that is prescribed to individuals with lupus. Two recent studies have suggested that low doses of the drug might be effective at treating lupus nephritis.

“These studies were preliminary. They enrolled very few participants and did not fully establish the link between drug dose and symptom improvement, so we saw the need for a larger and more thorough investigation,” says Dr. [Murray Urowitz](#), senior author of the study and Senior Scientist at UHN’s Schroeder Arthritis Institute.

Working with a team of Krembil researchers that included Senior Scientist [Dafna Gladman](#), Dr. Urowitz led a study involving 206 individuals with lupus nephritis. The researchers split the participants into two groups based on their prednisone dose: a medium dose group (30 mg/day or less) and a high dose group (40 mg/day or more). The two groups were matched for demographic features, lupus disease factors and other therapies used.

The study followed the patients over three years. As is standard for treatment with prednisone, doses were lowered over time. The dose reductions were not the same for both groups: the drug levels in high dose group were lowered to a greater extent so that, by one year after the start of treatment, prednisone levels were lower in this group than in the original medium dose group.

The results revealed that around 62% of individuals in the high dose group experienced complete remission (i.e., disappearance of the signs of disease) at the one-year mark—versus only around 38% in the medium dose group. Furthermore, there was no difference observed between the two groups in terms of harmful side effects.

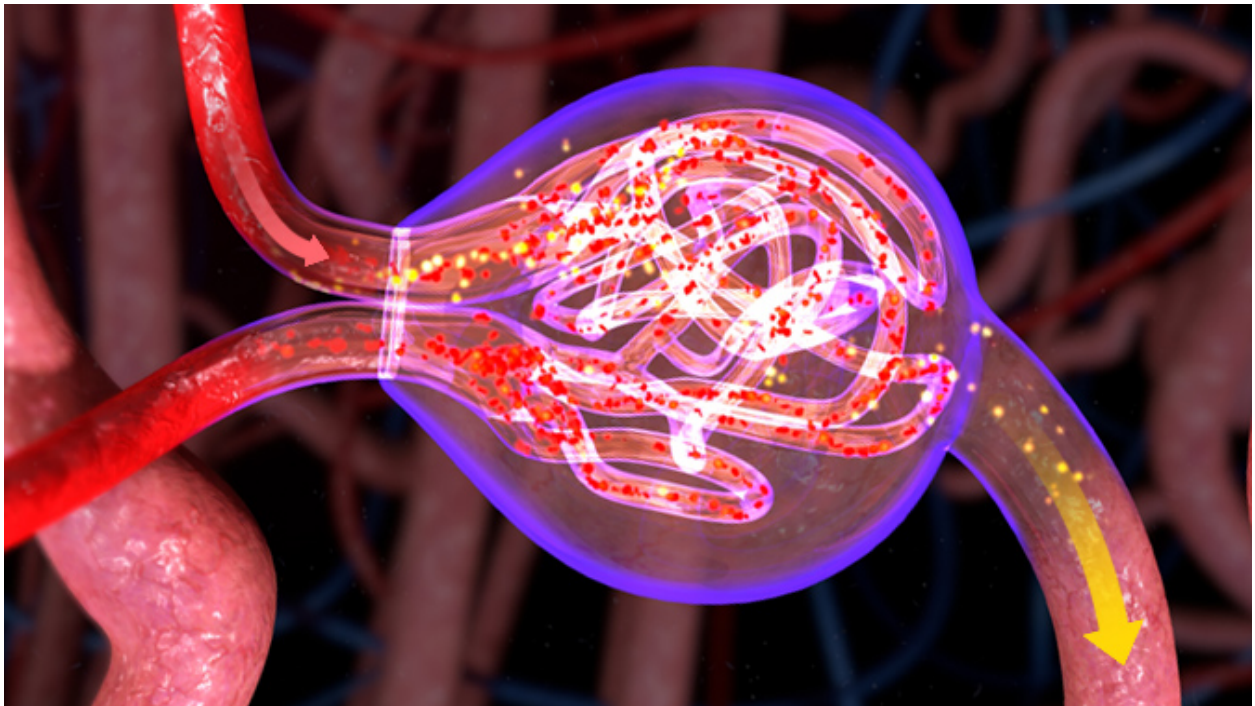
“Our findings reveal that high prednisone doses—40 mg or more per day—within the first six months are beneficial for treating lupus nephritis, and that lower doses do not provide additional benefits or fewer side effects,” concludes Dr. Urowitz.

This work was supported by the Canadian Institutes of Health Research, the Lou and Marissa Rocca Family, the Mark and Diana Bozzo Family, Lupus Canada and the UHN Foundation.

Tselios K, Gladman DD, Al-Sheikh H, Su J, Urowitz MB. [Medium versus high initial prednisone dose for remission induction in lupus nephritis: A propensity score matched analysis](#). *Arthritis Care Res (Hoboken)*. 2021 Mar 4. doi: 10.1002/acr.24592.



Dr. Murray Urowitz, lead author of the study and Senior Scientist at the Schroeder Arthritis Institute.



In the kidney, glomeruli serve as microscopic filters: blood (red arrow) enters the glomerulus and is filtered through a tightly packed network of vessels to produce urine (yellow), which flows to the bladder.

An Eye for Innovative Treatments

Customized prosthetic device improves vision in individuals with corneal conditions.



The cornea is the clear outermost layer at the front of the eye. In addition to protecting the eye, the cornea plays an important role in vision by helping to focus light.

Vision researchers at the Donald K. Johnson Eye Institute have shed light on patient experiences surrounding a prosthetic device-based treatment for complex corneal conditions.

Corneal conditions, such as irregularly shaped corneas and corneal degeneration, are a leading cause of eye disease and vision loss. These conditions cause eye discomfort and impaired vision, and are commonly treated with artificial tears, anti-inflammatory drugs and specialized contact lenses. Patients with severe conditions that do not respond to traditional treatments have recently benefitted from a new therapy called PROSE—Prosthetic Replacement of the Ocular Surface Ecosystem.

PROSE involves daily use of a custom-designed lens that covers the cornea and rests on the white of the eye, called the sclera. The space between the lens and the cornea is filled with saline solution, which the patient replaces each time they insert the lens. PROSE treatment reduces eye discomfort, improves vision and promotes cornea healing.

PROSE is a relatively new treatment in Canada, and research is needed to better understand patient experiences surrounding PROSE device fitting and use.

A research team led by Krembil Clinician Investigators Drs. [Allan Slomovic](#) and [Clara Chan](#) analyzed medical records from 78 adults who underwent PROSE device fitting at the Kensington Eye Institute in Toronto. The team analyzed what symptoms and diagnoses led to PROSE treatment, previous devices used and vision improvements that patients experienced with PROSE.

The researchers found that doctors recommended PROSE for patients with a variety of complex corneal conditions. Prior to PROSE treatment, patients commonly experienced blurry vision, light sensitivity, eye pain and glare and saw rainbows around lights. Most patients had previously tried conventional contact lenses, but these lenses often failed to improve vision or were uncomfortable.

In addition to identifying common diagnoses and symptoms leading to PROSE treatment, the researchers found that PROSE significantly improved visual acuity—the sharpness or clarity of one’s vision. The researchers also found that patients could comfortably wear the PROSE device for long periods of time, often for at least five hours each day.

“PROSE is an effective treatment for patients who do not benefit from traditional therapies,” says Dr. Chan. “Reducing the debilitating eye pain and vision loss associated with corneal diseases can dramatically improve patients’ quality of life.”

This work was supported by the UHN Foundation.

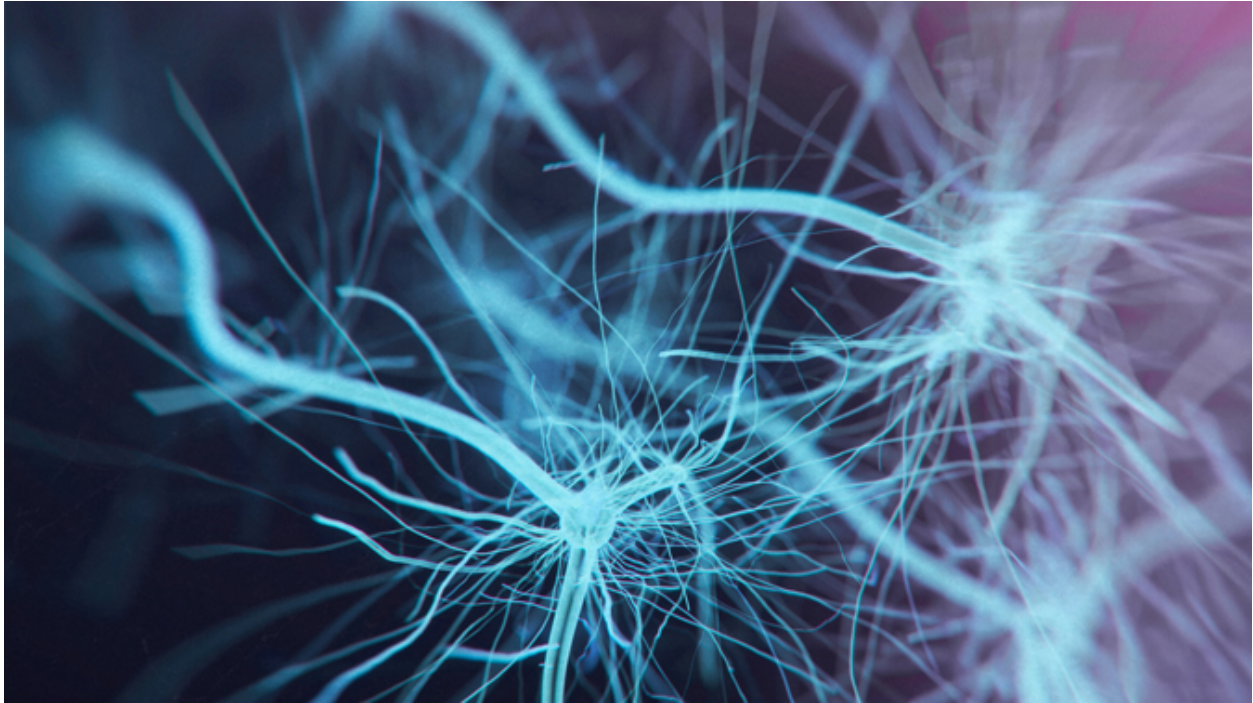
Wong BM, Garg A, Trinh T, Mimouni M, Ramdass S, Liao J, Chandrakumar M, Chan CC, Slomovic AR. [Diagnoses and Outcomes of Prosthetic Replacement of the Ocular Surface Ecosystem Treatment-A Canadian Experience](#). *Eye Contact Lens*. 2021 Mar 16. doi: 10.1097/ICL.0000000000000779.



Dr. Allan Slomovic (left) and Dr. Clara Chan (right) are Clinician Investigators at the Donald K. Johnson Eye Institute.

Snowflakes All the Way Down

A rare look at living human brain tissue reveals a high degree of cellular diversity.



Neurons are specialized cells whose electrical signals are critical to brain function. Much of what we know about human neurons has come from experimental models rather than living human tissue.

Everyone's brain is unique, but are brains unique combinations of similar building blocks, or are the building blocks themselves—the brain cells—also unique? A study by UHN's Krembil Brain Institute and the Centre for Addiction and Mental Health found a remarkably high degree of diversity of human brain cells.

Pyramidal neurons are one of the more common types of cells in the neocortex, the outermost region of the brain. Neurons in this region are organized into six distinct layers, and the physical and electrical properties of these neurons influence brain activity. Understanding the properties of these neurons is critical to understanding changes in brain function that underly disorders such as epilepsy.

The research team, led by Krembil Scientist Dr. [Taufik Valiante](#), studied brain tissue that was donated by patients who underwent brain surgery to treat epilepsy or cancer. With extreme care, Dr. Homeira Moradi, Krembil Scientific Associate, and the other researchers kept the delicate tissue alive after the surgery and studied various features of the neurons.

Little is known about the structure and function of adult human neurons because it is very rare to obtain living human brain tissue. “There are few opportunities beyond brain surgery for researchers to examine living human neurons,” says Dr. Valiante. “This study was only possible because of the very large and active epilepsy program at UHN’s Krembil Brain Institute.”

The researchers used microscopic electrodes to characterize the electrical properties of over 200 neurons from 61 patients. This painstaking work was the product of almost a decade of collaboration from a multidisciplinary team including neurosurgeons and neuroscientists, patients who were willing to participate in the study and ethicists who ensured patient rights and safety.

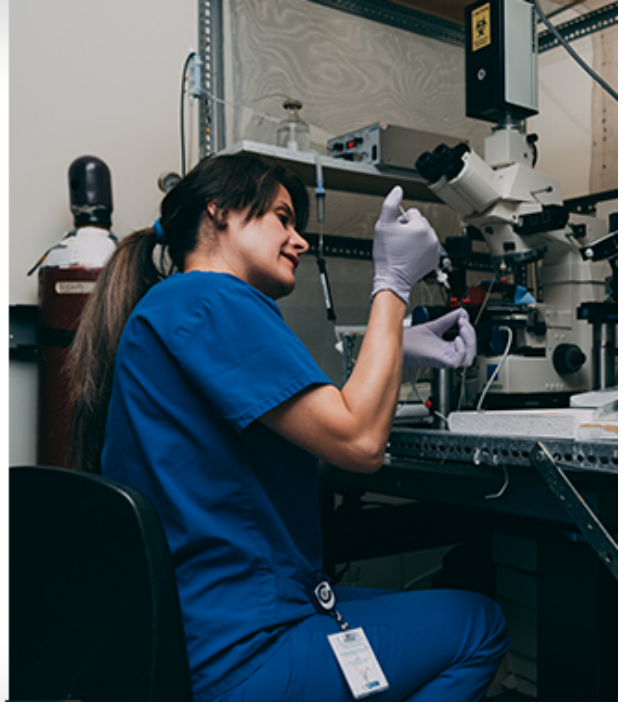
The study revealed the impressive variability and distinct features of neurons located within different cortical layers. Specifically, neurons in deeper layers had unique electrical properties and shapes—and more variation in those shapes—compared to those in more superficial layers. These features suggest that deep layer neurons may drive communication across layers.

“Our findings are quite different from what we expected based on past studies that used pre-clinical models,” explains Dr. Valiante. “The findings provide further evidence for the unique physiology and specializations of the human brain.”

This study represents one of the largest studies of human neurons. The resulting data will serve as a valuable resource for improving computer simulations of brain function—simulations that will enable researchers to better model neocortical neurons and shed light on neurological disorders such as epilepsy.

This work was supported by the Centre for Addiction and Mental Health Discovery Fund, the National Institutes of Health, the Natural Sciences and Engineering Research Council, The Kavli Foundation and the UHN Foundation.

Chameh HM, Rich S, Wang L, Chen FD, Zhang L, Carlen PL, Tripathy SJ, Valiante TA. [Diversity amongst human cortical pyramidal neurons revealed via their sag currents and frequency preferences](https://doi.org/10.1038/s41467-021-22741-9). *Nat Comm*. 2021 May 3. doi: 10.1038/s41467-021-22741-9.



Dr. Taufik Valiante (left) is a Scientist at the Krembil Brain Institute, a staff neurosurgeon and the Director of the Surgical Epilepsy Program at Toronto Western Hospital. Dr. Homeira Moradi (right) is a Scientific Associate at Krembil.

More Power to You

Study finds that the Manage My Pain app can engage and empower patients towards better health.



The Manage My Pain app has more than 50,000 users and was the first pain-management app available for Android mobile devices.

Digital health apps are helping to connect patients with their health care teams. These apps enhance the ability of patients to manage their health while providing their care teams with real-time feedback, alongside standard care; however, their benefits are not always fully apparent.

A recent study led by Dr. [Anuj Bhatia](#), a Clinician Investigator at the Krembil Brain Institute, assessed the [Manage My Pain](#) app, which was designed specifically for people experiencing chronic pain.

“Although digital tools can help us to better connect with our patients, we need to thoroughly understand an app’s real-world use in order to maximize its benefits,” says Dr. Bhatia.

Manage My Pain was first launched in 2011 by the Toronto-based company ManagingLife, who have since collaborated with UHN and other partners to refine the app. A patient can track their pain, activity and medication use by submitting daily reflections and detailed pain reports. The app automatically creates graphs and tables

that help the patient and their remote care team monitor what makes the pain worse or better and whether treatments are working.

To evaluate Manage My Pain, the research team analyzed app use by patients with chronic pain and compared the users' progress against patients who used conventional paper questionnaires to record their pain episodes. Because individuals' lifestyles differ according to where they live, the study included patients from urban settings and from rural settings, where remote health care solutions are even more valuable.

The researchers first assessed whether patients were receptive to the app and would use it over the long term. The team found that, in comparison to other mobile health apps, a greater proportion of patients accepted Manage My Pain and stuck with it. Nearly four times as many patients continued to use Manage My Pain after one month.

Next, the researchers examined whether the app improved patient outcomes. The results indicated that app users not only received benefits from conventional care but also experienced lower levels of anxiety and reduced feelings of helplessness or devastation related to their pain.

"We think that the benefits experienced by patients who use Manage My Pain are the result of how it enables them to monitor their symptoms, which leads to feelings of empowerment," says Dr. Bhatia. "This empowerment could lead to fewer in-person visits with health care teams and less misuse of pain medication."

This study is particularly timely given the restrictions to in-person visits to clinics and hospitals that have been put in place to curb the spread of COVID-19. Tools such as Manage My Pain are invaluable for ensuring that care continues without disruption and for making health care more accessible to remote communities.

This work was supported by the Department of Anesthesia and Pain Medicine at UHN, the Iroquois Falls Family Health Team and the UHN Foundation. Co-author J Katz holds a Tier 1 Canada Research Chair in Health Psychology.

Bhatia A, Kara J, Janmohamed T, Prabhu A, Lebovic G, Katz J, Clarke H. [User Engagement and Clinical Impact of the Manage My Pain App in Patients With Chronic Pain: A Real-World, Multi-site Trial](#). JMIR Mhealth Uhealth. 2021 Mar 4. doi: 10.2196/26528.



Dr. Anuj Bhatia, Clinician Investigator at the Krembil Brain Institute.