The Krembil

November 2019

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:

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

News

Science in the 6ix

Recent public event that put research across UHN in the spotlight.

Presenters at the inaugural 'Science in the 6ix' event (L to R): Jimmy Qiu (TECHNA), Dr. Nicole Woods (The Institute for Education Research), Dr. Taufik Valiante (Krembil Research Institute), Dr. Stephanie Protze (McEwen Stem Cell Institute), Dr. Bastien Moineau (KITE Research Institute), Dr. Beate Sander (Toronto General Hospital Research Institute), and Dr. Shane Harding (Princess Margaret Cancer Centre).

'Science in the 6ix: Spotlight on UHN Research' is a TED Talk-style event designed to educate and engage the public about the advanced research happening at the University Health Network (UHN) and the far-reaching impact of this work. The Krembil Research Institute organized and hosted this event.

The inaugural Science in the 6ix, held on Wednesday October 16th, provided a unique opportunity to meet and hear from UHN's trailblazing scientists, who are working on groundbreaking discoveries that will help Canadians live longer, healthier lives.

CBC's Mary Ito served as emcee and veteran journalist André Picard delivered a keynote lecture on why science needs to be a priority on the political agenda.

Research topics that were covered include:

- Stem cells as a biological alternative to cardiac pacemakers
- Smart clothing that helps patients who survived a stroke with mobility issues
- Combining cancer treatments to improve patient outcomes
- A device implanted in the brain that can stop seizures
- Computer simulations to evaluate the impact of infectious disease outbreaks
- Augmented reality tools that assist with surgical precision
- How transforming medical education can revolutionize patient care

Science in the 6ix was inspired by a similar event held at Krembil in which trainees and staff present a brief and ‘lay-friendly’ overview of their research and its importance to the Krembil community. Given the overwhelming success of the event’s 2019 installment, its organizers—Krembil’s Heather Sherman (Public Affairs) and Carley McPherson (Krembil Directorate)—offered to host a similar event in which researchers from each of UHN’s research institutes presented their work. The organizers opened up Science in the 6ix to the greater community by inviting the media, donors and the general public to attend.

If you were unable to attend, watch it here: https://youtu.be/ODfJ3KUvZqg

Hot Off the Press!

Two newly released publications showcase Krembil's research and achievements.

Publication covers (L-R): the Arthritis Magazine and the 2010 Krembil Annual Report.

Two new publications were launched this fall to promote the Krembil Research Institute's relentless pursuit of new diagnostics and therapies for chronic debilitating diseases: a magazine featuring the Arthritis Program and the 2019 Krembil Annual Report. Both include a collection of stories describing our research and achievements, interesting facts and figures and beautiful photography.

The Arthritis Magazine
Krembil has teamed up with The Globe and Mail on a special project to highlight the groundbreaking research and clinical advancements happening within the Arthritis Program at Krembil.

Inside the issue, readers will learn how our dedicated scientists and clinicians are making new discoveries and developing innovative techniques and technologies to prevent, treat and help patients recover from arthritis-related illnesses, including lupus, osteoarthritis, ankylosing spondylitis and psoriatic arthritis.

Click here to read the online version of the magazine.

2019 Krembil Annual Report
This year's report focuses on 'hope'. It includes a welcome message from Krembil's Director, Dr. Donald Weaver, which explains how hope is helping our institute achieve

its goal of improving health. It also reveals how our work is inspiring hope in others, such as our patients, their families and our generous supporters.

In addition, the report highlights some of the Krembil's most notable achievements over the past year, including:
- a discovery that could improve survival after spinal cord injury
- a recommendation that could help doctors identify and treat severe arthritis more quickly
- a new method to advance therapy for vision loss
- a new facility to accelerate the translation of research discoveries into new medicines

Click here to read the report.

Research

A Step in a New Direction

New Krembil study changes our understanding of how the brain directs the body to walk.

Adult Canadians each take an average of nearly 9,000 steps every day. Although walking does not require our full attention, our brains must still signal each step.

Dr. Michael Fehlings, a Senior Scientist at the Krembil Research Institute, and his research team have discovered a network of nerve cells that plays a key role in controlling our ability to walk. The group's findings, published in Nature Neuroscience, challenge conventional perceptions of how the brain instructs and regulates the body while walking.

Although walking may seem like an innate and straightforward action, it takes many complex processes and different regions of the brain to effect the movements involved. A full understanding of how we walk still eludes researchers.

The prevailing view has been that the motor cortex, a region of the brain that controls the planning and initiation of limb movements, directs the body to walk.

The study, led by Dr. Fehlings' former trainees Drs. Spyridon Karadimas and Kajana Satkunendrarajah, revealed that a different region of the brain, the sensory cortex, can also generate commands that trigger walking. This is surprising because the sensory cortex's main function is to process information on the internal and external environments of the body. For example, the sensation of warm sunlight on your skin is processed by the sensory cortex.

The researchers further found that the sensory cortex sends these commands directly to the spinal cord through a relay of nerve cells. This relay is distinct from and operates in parallel with the signalling route of the motor cortex.

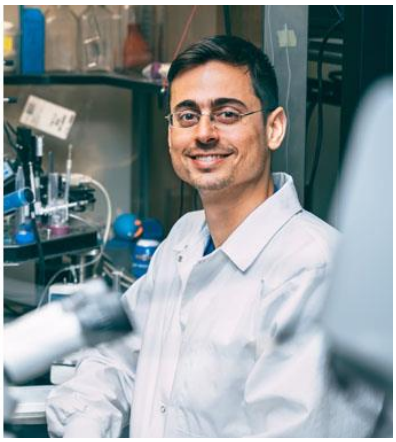
"Our data support a potential mechanism through which the sensory cortex can directly and efficiently control walking in response to the sensory information that is continuously processing," says Dr. Fehlings.

Future research will delve into the mechanisms that govern the generation of signals in the sensory cortex to deepen our understanding of how we walk.

This work was supported by the Krembil Foundation, the Canadian Institutes of Health Research, AOSpine, the Halbert Chair, the DeZwirek Foundation, the Onassis Foundation and the Toronto General & Western Hospital Foundation.

Karadimas SK, Satkunendrarajah K, Laliberte AM, Ringuette D, Weisspapir I, Li L, Gosgnach S, Fehlings MG. Sensory cortical control of movement. Nat. Neurosci. 2019 Nov 18. doi: 10.1038/s41593-019-0536-7.

Dr. Michael Fehlings, Senior Scientist, Krembil Research Institute.

Dr. Kajana Satkunendrarajah (left) is now an Assistant Professor at the Medical College of Wisconsin, and Dr. Spyridon Karadimas (right) is a neurosurgery resident at the University of Toronto.

Finding the Root Cause

Study identifies new type of immune cell in the joints of those with spinal arthritis.

Ankylosing spondylitis is a form of arthritis in which the body's immune system attacks healthy tissue in the spine. Symptoms typically first appear between ages 15 and 30.

A study led by Krembil Senior Scientist Dr. Robert Inman reveals key differences between immune cells in the joints of healthy individuals and those with a form of arthritis known as ankylosing spondylitis.

The study was initiated to shed light on why new treatments are providing mixed results. “We have made great strides in understanding the underlying cause of this form of arthritis, which affects the joints in the spine. Specifically, we have found that the immune system in the gut may drive the disease. However, new therapies that target the cross talk between the gut and inflamed spinal joints have failed to improve symptoms in all patients,” says Dr. Inman.

With the ultimate aim of refining treatment approaches, Zoya Qaiyum in Dr. Inman’s lab examined the immune cells in affected joints. She studied proteins on the surface of immune cells known as integrins. These proteins can be seen as the traffic police of the immune system: they direct immune cells as they move between different tissues.

When comparing immune cells in healthy individuals with those with ankylosing spondylitis, Zoya found heightened levels of an immune cell—known as a CD8+ T cell—in individuals with arthritis. Furthermore, these cells have a unique combination of different integrins on their surface.

“Interestingly, some of these integrins are also found on immune cells in the gut. This suggests that the CD8+ T cells that we identified may be involved in the cross talk between the gut and the spine,” says Dr. Inman.

Future research will establish the role of this unique cell population in disease with the aim of fine-tuning immune-based therapies and maximizing benefits to patients.

This work was supported by the Canadian Institutes of Health Research, the University of Toronto, and the Toronto General & Western Hospital Foundation.

Qaiyum Z, Gracey E, Yao Y, Inman RD. Integrin and transcriptomic profiles identify a distinctive synovial CD8+ T cell subpopulation in spondyloarthritis. Ann Rheum Dis. 2019 Nov. doi: 10.1136/annrheumdis-2019-215349.

Dr. Robert Inman, Senior Scientist, Krembil Research Institute.

A Surgery That Helps People Smile

Study provides new insight into how radiation relieves chronic facial pain.

Approximately 1,500 new cases of trigeminal neuralgia, a nerve disorder that causes severe facial pain, are diagnosed annually in Canada. The disorder occurs more frequently in women than men.

Trigeminal neuralgia (TN) is widely believed to be one of the most painful conditions that can affect a person. It is a nerve disorder in which mild facial stimulation—such as that caused by smiling or applying makeup—can trigger a jolt of severe pain on one side of the face.

Gamma knife radiosurgery can provide long-lasting pain relief to people suffering from TN. It involves the delivery of gamma radiation to the dysfunctional facial nerve causing the disorder. How gamma radiation affects the nerve and reduces chronic facial pain is not well understood.

To improve our understanding of this powerful treatment, Dr. Mojgan Hodaie, a Scientist at the Krembil Research Institute, led a study examining the irradiated nerve using diffusion tensor imaging (DTI). DTI is a commonly used medical imaging technique that provides information about the structure of cells in the body.

As part of the study, Dr. Hodaie and her research team studied the DTI images and medical records of 55 TN patients who underwent gamma knife radiosurgery. DTI images of the irradiated nerve up to 24 months after surgery were examined.

“In patients who experienced the highest levels of pain relief, we found evidence that radiation alters the physical structure of the cells comprising the nerve. Intriguingly, these alterations were delayed and only began appearing 12 and 24 months after treatment. In contrast, radiation did not affect the nerve structure in patients who experienced lower levels of pain relief,” explains Dr. Hodaie.

Based on their findings, the researchers postulate that radiation could be reducing pain by disrupting the nerve’s structure and its ability to transmit pain signals from the face to the brain.

“DTI appears to be an important marker for treatment response to radiation that should be incorporated into routine post-treatment care for classic trigeminal neuralgia,” says Dr. Hodaie.

This work was supported by the Canadian Institutes of Health Research and the Toronto General & Western Hospital Foundation.

Shih-Ping Hung P, Tohyama S, Zhang JY, Hodaie M. Temporal disconnection between pain relief and trigeminal nerve microstructural changes after Gamma Knife radiosurgery for trigeminal neuralgia. J Neurosurg. 2019 Jul 12. doi: 10.3171/2019.4.JNS19380.

Dr. Mojgan Hodaie, Senior Scientist, Krembil Research Institute.

A Disease with a Thousand Faces

New study shows that some symptoms of lupus are more likely to occur in groups.

Lupus is a chronic disease that affects one in a thousand Canadians, primarily young women. Its cause is still unknown and currently there is no cure.

Lupus is commonly known as ‘the disease with a thousand faces’, as it can lead to a wide variety of symptoms and clinical test results that differ from one person to another. Moreover, these features can change over time and often mimic those of other unrelated diseases.

Lupus symptoms can include—but are not limited to—fatigue, joint pain and stiffness, skin rashes, chest pain, fever and kidney failure.

Dr. Zahi Touma, a Krembil Clinician Investigator and a Clinician Scientist with the University of Toronto, recently led a large international study to better understand the relationship among the symptoms and clinical test results associated with lupus. Towards this end, Dr. Touma and his colleagues examined medical records of 389 people diagnosed with lupus from Asia, Europe and the Americas.

The researchers discovered that some features of lupus are more likely to occur together than alone. For example, it is more likely for a lupus patient to have mouth ulcers and skin rash, than to have either symptom alone. Features that tend to occur together often involved the skin, immune system or blood.

“This work was part of a much larger initiative—involving over 100 lupus experts from numerous countries and medical disciplines—that established new criteria to help researchers identify uniform groups of lupus patients for clinical research. These criteria, which were informed by our findings, will make it easier for researchers to reveal the mechanisms underlying lupus and its symptoms, as well as identify new treatments for this complex disease,” says Dr. Touma.

This work was supported by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR).

Touma Z, Cervera R, Brinks R, Lorenzoni V, Tani C, Hoyer BF, Costenbader KH, Sebastian GD, Navarra SV, Bonfa E, Ramsey-Goldman R, Tedeschi SK, Dörner T, Johnson SR, Aringer M, Mosca M; ACR/EULAR group. Associations among classification criteria items within systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2019 Sep 27. doi: 10.1002/acr.24078.

Dr. Zahi Touma, Krembil Clinician Investigator, Krembil Research Institute