The Krembil

May 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

Pitch Perfect Competition

Competition teaches presenters and audience how to craft a great pitch about their research.

Krembil's Director, Dr. Donald Weaver (first row, third from left) with the presenters and judges of the Pitch Perfect Competition.

On April 9, Krembil held its second Pitch Perfect Competition. The event was organized to help teach the Institute's members how to quickly describe their research to a listener with little to no scientific knowledge.

"It's increasingly important for researchers to be able to share their research—in an interesting and understandable way—with the general public. This will help them raise public awareness of their work and to attract philanthropic funds to support it," says Dr. Donald Weaver, Krembil's Director.

As part of the competition, 13 participants, either a Krembil trainee or staff member, presented a three-minute elevator pitch describing a recent or upcoming research project to a panel of judges from UHN Public Affairs and the audience. After each pitch, the judges provided the presenter with constructive feedback and strategies to better capture a listener's attention and interest.

At the end of the competition, the judges selected the three participants who presented the best pitches:
1. Dr. Akihiro Nakamura, a postdoctoral fellow in Dr. Nigil Haroon's lab
2. Imindu Liyanage, a technician in Dr. Donald Weaver's lab
3. Zoya Qaiyum, a technician in Dr. Robert Inman's lab

"All presenters did an excellent job. I was very impressed by their enthusiasm and their use of props and humour to engage the audience," says Heather Sherman, Senior Public Affairs Advisor at Krembil.

Of particular note, the Krembil's Public Affairs team shared a short video with the audience highlighting features and examples of successful research pitches. The video stars Dr. Kevin Smith, President and CEO of the University Health Network, and includes cameos of several Krembil researchers and trainees. View the video here.

Krembil thanks all presenters, judges and organizers for their participation and help in making Pitch Perfect 2019 a success.

Krembil Research Day 2019

Keynote speaker reveals how artificial intelligence could improve treatment of mental illness.

Krembil Research Day was attended by approximately 285 people this year.

Krembil Research Day is an annual event during which the Institute's investigators, trainees and staff come together to celebrate their research achievements.

The day was kicked off with the premiere of an inspirational and visually stunning video titled 'We are Krembil', which introduces the Institute and its mission (view the video here). It was created by Krembil's talented Public Affairs team with the help of Carley McPherson and several researchers and trainees.

Throughout the day, trainees shared their research through a variety of formats, including formal oral presentations and short elevator pitches tailored to a general audience. In addition, 80 trainees and staff presented their work through posters. At the end of the day, the best presenters were rewarded with prizes.

This year's keynote address was provided by Dr. Amit Etkin, a world-renowned psychiatrist-scientist from Stanford University who is pioneering new approaches for understanding and treating mental illness. Dr. Etkin described how his research team is combining artificial intelligence with the brain's electrical activity to improve the treatment of depression and post-traumatic stress disorder.

Dr. Donald Weaver, Krembil's Director, thanks all of the individuals who made this year's Research Day a success, including the Trainee Affairs Committee and its Chair, Dr. Mary Pat McAndrews; the Krembil administration team; and the presentation judges. In addition, he thanks Mr. Jim Leech and Ms. Deb Barrett for their generous donation that supported the event.

Congratulations to everyone who presented their work!

A complete list of presentation awardees is available here.

Keynote speaker Dr. Amit Etkin (right) speaking with Drs. Taufik Valiante (left) and Jonathan Downar (middle).

Winners of the presentation competitions, along with Dr. Donald Weaver, Director of the Krembil Research Institute (sixth from left); and Dr. Mary Pat McAndrews, Chair of the Trainee Affairs Committee (first on right).

Research

Uncovering a Hidden Risk

Undiagnosed severe sleep apnea is a major risk factor for postoperative heart complications.

Sleep apnea is diagnosed through an overnight test that measures blood oxygen, breathing, heart rate, brain waves and eye and leg movements during sleep.

A new study recently published in *The Journal of the American Medical Association* (*JAMA*) reveals that patients with severe obstructive sleep apnea have a significantly higher risk of heart-related complications.

“We found that the risk of postoperative complications related to their heart was twice as high in patients with severe sleep apnea compared to those without sleep apnea,” says Dr. Frances Chung, a Clinician Investigator at the University Health Network’s Krembil Research Institute.

Obstructive sleep apnea causes breathing to stop and start during sleep and is the most common type of sleep apnea. It is also associated with a higher risk of death, cardiac diseases and cognitive impairment in the general population.

Dr. Chung and her team initiated the study to see whether sleep apnea poses a similar risk to surgical patients.

The study enrolled over 1,200 patients that were scheduled for major noncardiac surgery. Before the surgery, patients underwent overnight sleep testing. For 30 days after the surgery, the research team took note of any heart-related complications, such as heart attack, abnormal heart rhythm, heart failure and stroke.

The study showed that two thirds of patients had unrecognized sleep apnea and about one in ten had severe sleep apnea. Furthermore, around 30% of those with severe obstructive sleep apnea experienced a heart-related complication, while only 14% of those without sleep apnea experienced similar complications.

“The key takeaway here is that if patients have symptoms of sleep apnea, perhaps they should be treated before undergoing major surgery,” says Dr. Chung. “Further study is needed to determine how best to prevent patients with severe sleep apnea from having a higher risk of heart complications.”

Source: UHN press release.

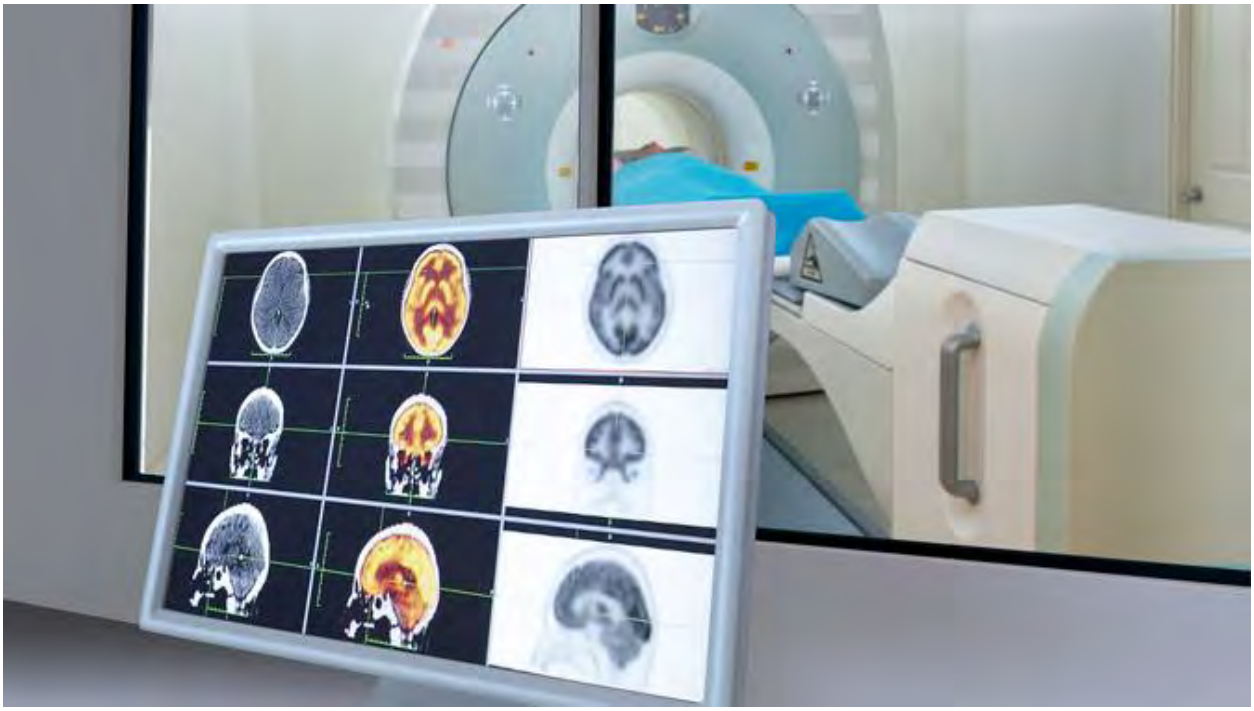
This work was supported by the Health and Medical Research Fund (Hong Kong); the National Healthcare Group-Khoo Teck Puat Hospital; the University of Malaya; the Malaysian Society of Anaesthesiologists; the Auckland Medical Research Foundation; the University of Toronto’s Department of Anesthesia and Pain Management at University Health Network and Mount Sinai Hospital; and the Toronto General & Western Hospital Foundation.

Chan MTV, Wang CY, Seet E, Tam S, Lai HY, Chew EFF, Wu WKK, Cheng BCP, Lam CKM, Short TG, Hui DSC, Chung F. Postoperative Vascular Complications in Unrecognized Obstructive Sleep Apnea (POSA) Study Investigators. JAMA. 2019 May. doi: 10.1001/jama.2019.4783.

Dr. Frances Chung, Clinician Investigator, Krembil Research Institute.

Seeing is Believing

Researchers use advanced imaging to see how a subtle gene change can alter drug effectiveness.



Positron emission tomography (PET) is an advanced imaging method that uses tiny amounts of radioactive materials that can be tailored to visualize specific parts of the body, such as dopamine receptors in the brain.

Dopamine receptors are a type of protein in the brain that are important for controlling movement, learning and decision-making. Given their wide-ranging effects, dopamine receptors are the target of several drugs used to treat a variety of diseases, including Parkinson disease and schizophrenia.

The effectiveness of these drugs can vary from one person to another and is influenced by a person's genes. The dopamine receptor (like all proteins) is made from instructions carried in a person's genetic code. Although minor changes in the gene coding for the receptor are relatively common, it is not clear how these changes could alter the effectiveness of the drugs that target the receptor.

To improve our understanding of this relationship, a team led by Dr. Antonio Strafella used advanced imaging methods, known as positron emission tomography (PET). The researchers examined PET images of dopamine receptor activity in the brain of healthy volunteers whose genes for the dopamine receptor differed by a single letter of the genetic code.

The team found that even such a small genetic change influenced the quantity and activity of dopamine receptors in the brain, especially within the ventral striatum, a brain region known to play a critical role in decision-making and processing rewards.

Understanding how genetic changes affect the distribution and activity of dopamine receptors in the brain can help scientists understand how gene variation influences treatment and a person's response to medication.

This work was supported by the Canadian Institutes of Health Research, and the Toronto General & Western Hospital Foundation. Dr. A Strafella holds the Tier 2 Canada Research Chair in Movement Disorders and Neuroimaging.

Valli M, Cho SS, Masellis M, Chen R, Rusjan P, Kim J, Koshimori Y, Mihaescu A, Strafella AP. DRD2 Genotype-Based Variants Modulates D2 Receptor Distribution in Ventral Striatum. Mol Neurobiol. 2019 Mar 8. doi: 10.1007/s12035-019-1543-0.

Dr. Antonio Strafella, Senior Scientist, Krembil Research Institute. Photo courtesy of the Globe and Mail.

Late Effects of Early Epilepsy

New study recommends that children with rare form of epilepsy be monitored for schizophrenia.

The University Health Network's Epilepsy Genetics Program cares for adult women with PCDH19-related epilepsy, the symptoms of which begin appearing in early childhood.

An international team of researchers has discovered that children affected by *PCDH19*-related epilepsy may be at higher risk of developing schizophrenia later in life.

PCDH19-related epilepsy is a rare form of epilepsy that affects girls and women and is caused by an alteration in the *PCDH19* gene. It is characterized by seizures, often trigged by a fever, that start during early childhood. Many of those affected by the disease eventually display psychiatric impairments and behavioural problems as adults.

To gain a better understanding of the types of psychiatric symptoms that affect patients and when they first appear, Dr. Danielle Andrade, Director of the Epilepsy Genetics Program and Clinician Investigator at the Krembil Research Institute, Dr. Anne Bassett, a Professor of Psychiatry at University of Toronto and Dr. Ingrid Scheffer, a Professor at the University of Melbourne, examined the medical records of 60 girls and women with the disease.

The researchers found that 21% of the patients developed a type of mental illness known as a psychotic disorder by the age of 21 years, the most common of which was schizophrenia (in 15% of patients). The prevalence of schizophrenia in the general population is only 1%.

Psychotic disorders can be severe and disabling, causing delusions and hallucinations, as well as disorganized speech, thoughts or behaviour. The symptoms can be successfully controlled through a combination of medications and counselling, especially when treatment is started early.

“Our study shows that schizophrenia and other psychotic disorders are a feature of *PCDH19*-related epilepsy that can appear during adolescence or early adulthood. Post-ictal psychosis (psychosis triggered by seizures) and antiseizure drugs’ side effects rarely cause similar behaviour problems. But now that we know that psychosis and schizophrenia are much more common in patients with *PCDH19* mutations, monitoring for these disorders should become part of routine care for girls and women with this rare form of epilepsy,” recommends Dr. Andrade. “This will ensure that, if and when symptoms appear, diagnosis can be faster and more accurate, and patients will receive the correct treatment as soon as possible.”

This work was supported by the Toronto General & Western Hospital Foundation.

Vlaskamp DRM, Bassett AS, Sullivan JE, Robblee J, Sadleir LG, Scheffer IE, Andrade DM. Schizophrenia is a later-onset feature of PCDH19 Girls Clustering Epilepsy. Epilepsia. 2019 Mar. doi: 10.1111/epi.14678. AS Bassett holds the Dalglish Chair in 22q11.2 Deletion Syndrome at the University of Toronto and the University Health Network.

Dr. Danielle Andrade, Director of the Epilepsy Genetics Program, University Health Network, and Clinician Investigator, Krembil Research Institute. Photo courtesy of the Globe and Mail.

Clearer Path to Diagnosis

Four proteins may be key to better diagnosis and management of arthritis.

Although much needed, a sensitive and reliable screening tool that can accurately diagnose patients with psoriatic arthritis is currently lacking.

A new study by Krembil researchers has uncovered a set of proteins that could help doctors diagnose two different forms of arthritis more quickly.

Psoriatic arthritis is an inflammatory condition that affects the joints, causing pain and stiffness. Clinicians who have limited experience with the disease may find it difficult to diagnose psoriatic arthritis, which is often confused with another type of arthritis known as osteoarthritis.

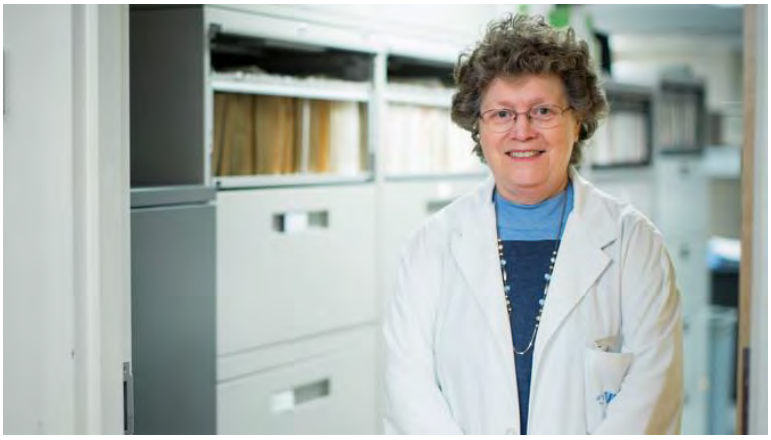
In the study, Krembil researchers sought to identify new markers that could distinguish between these two forms of arthritis. To this end, they compared the levels of different proteins in blood samples from individuals with psoriatic arthritis or osteoarthritis, as well as healthy individuals.

They identified four proteins—cartilage oligomeric matrix protein, resistin, monocyte chemoattractant protein and nerve growth factor—that were significantly higher in blood samples from patients with psoriatic arthritis. By measuring the levels of these proteins, researchers were consistently able to differentiate patients with psoriatic arthritis from those with osteoarthritis.

“Early diagnosis and treatment of psoriatic arthritis is crucial as it can prevent further joint damage and improve quality of life for patients,” says Dr. Dafna Gladman, senior author of the study. “Although further testing is needed, we believe that these markers have the potential to improve the diagnosis and care of patients with osteoarthritis and psoriatic arthritis.”

This work was supported by the Krembil Foundation and the Toronto General & Western Hospital Foundation.

Chandran V, Abji F, Perruccio AV, Gandhi R, Li S, Cook RJ, Gladman DD. Serum-based soluble markers differentiate psoriatic arthritis from osteoarthritis. Ann Rheum Dis. 2019 Mar 25. pii: annrheumdis-2018-214737. doi: 10.1136/annrheumdis-2018-214737.



Dr. Dafna Gladman, Senior Scientist, Krembil Research Institute. Photo courtesy of the Globe and Mail.