

The Krembil

May 2023

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 exciting news and innovative research happening at the Krembil Research Institute.

Stories in this month's issue:

- [The Don Weaver Symposium](#)
- [Excellence in Health Research](#)
- [Interrupting Interactions](#)
- [Promising New Therapy](#)
- [Why Immune Cells Attack](#)
- [An Unexplored Mechanism](#)



Jaideep Bains, PhD
Director, Krembil Research Institute
University Health Network

The Don Weaver Symposium

Krembil highlights the research, impact and legacy of its former Director, Dr. Donald Weaver.



Photos from the Don Weaver Symposium. Top left photo (L-R): Drs. Ai Jin, Gelareh Zadeh, Mohit Kapoor, Donald Weaver, Jaideep Bains, Valerie Wallace, Brad Wouters, Barbara Tate, Kevin Smith and Susan Dillon.

On May 2, 2023, the Krembil Research Institute hosted a symposium to celebrate Dr. Donald Weaver's tenure as Institute Director from 2013 to 2022.

The event, titled "*The Don Weaver Symposium - Molecules, Poetry & Exploring New Approaches in Neuroscience*" honoured Dr. Weaver's scholarship, mentorship, leadership and legacy at Krembil.

Watch a recording of the symposium [here](#).

The half-day event, hosted at the BMO Education & Conference Centre, featured remarks on the birth and evolution of Krembil, including the creation of the Krembil Brain Institute, the Donald K. Johnson Eye Institute and the Schroeder Arthritis Institute, as

well as Krembil initiatives to support trainees. The symposium also featured high-profile academic talks on the following topics:

- the burden of neurological disease;
- new directions in the treatment of Alzheimer disease;
- targeting excitotoxicity in Alzheimer disease; and
- inflammation and its expanding role as a druggable target

The event concluded with an inspiring talk from Dr. Weaver describing his latest research on Alzheimer disease as a disorder of innate immunity and what motivates him every day: the more than 10,000 patients that he has treated for the disease during his career as a neurologist.

During the symposium, Dr. Brad Wouters, UHN's Executive Vice President of Science and Research, announced a new funding opportunity established in honour of Dr. Weaver's research contributions and leadership: *The Donald Weaver Postdoctoral Researcher Fellowship in Neurodegeneration Research*.

This fellowship will provide salary support for one postdoctoral researcher working in the field of neurodegenerative diseases within the Krembil Research Institute. The deadline for submissions is Friday, June 2, 2023 at 4:00 PM. For more information about the fellowship and how to apply, email krembil@uhnresearch.ca.

Dr. Weaver was also presented with a new research chair—the Krembil Chair in Drug Discovery in Alzheimer's Research. This five-year chair will support his research into the design and synthesis of brain-penetrant, small-molecule therapies for Alzheimer disease.

"This chair represents a new level of support for Dr. Weaver's innovative approaches to drug development for Alzheimer disease and related dementias," says Dr. Wouters. "We are extremely excited about his appointment to this new chair, and we wish him continued success as he rededicates himself to research."

A very special thanks to the generous donors, the Krembil Family, the Krembil Foundation and the UHN Foundation, for making this research chair possible.

Join us in thanking Dr. Weaver for his immense contributions to the Krembil Research Institute!

Dr. Weaver is one of few individuals worldwide who co-qualified as a neurologist and medicinal chemist. He is internationally renowned for his expertise in drug discovery and translational research in Alzheimer disease and related dementias. He has published over 400 peer-reviewed articles, co-founded eight biotech companies—pioneering the concept of 'micropharma' in biotechnology—and trained over 160 students and postdoctoral researchers.

Excellence in Health Research

Neurosurgeon and Senior Scientist Dr. Gelareh Zadeh wins the Canada Gairdner Momentum Award.



The recipients of the 2023 Gairdner Awards—Canada’s most prestigious medical awards—have been announced. Among the awardees is University Health Network (UHN)’s Dr. [Gelareh Zadeh](#), who received one of two inaugural *Canada Gairdner Momentum Awards*.

The Momentum Awards were established to recognize mid-career researchers who have, over the last six years, made significant discoveries that have the potential to improve human health.

Dr. Zadeh is being recognized for her seminal contributions to improving our understanding of brain tumours. Her work has led to a new molecular classification of one of the most common types of brain tumours—an advancement that has the potential to lead to more effective treatments, models for predicting patient outcomes and biomarkers of treatment response.

Her research program integrates molecular, genomic and epigenomic techniques, together with experimental models of brain tumours, to accelerate translational research in neuro-oncology. Her work has transformed our understanding of the biology and, consequently, the management of a number of different brain tumour types—especially meningiomas, which are the most common form of brain tumour. This work has led to a

paradigm shift in the classification, predictive modelling and clinical management of these tumours.

Dr. Zadeh has also spearheaded international efforts to define the genomic landscape of neuronal tumours that have not been the focus of significant biological research, including schwannomas, peripheral nerve tumours and malignant peripheral nerve sheath tumours. These efforts have revealed novel fusion proteins and resulted in the molecular sub-classification of schwannomas.

Additionally, her team has identified two biological pathways that drive the progression of benign peripheral nerve tumours toward malignant sarcomas. These molecular pathways not only provide a better biological understanding of tumour transformation, but also provide targets that could be used to develop therapeutic strategies, including the repurposing of existing pharmaceuticals.

She has also, in collaboration with researchers at the Princess Margaret Cancer Centre, advanced the development of blood-based biomarkers that can be used to diagnose and discriminate different brain tumour types, and potentially to track response to therapy and early recurrence of disease.



Dr. Zadeh balances her clinical duties as the Head of Neurosurgery at Toronto Western Hospital with her leadership responsibilities as Chair of Neurosurgery at the University of Toronto (UofT) and Co-Director of the Krembil Brain Institute. She also leads a highly accomplished, peer-review funded, 30-member research team at the Princess Margaret Cancer Centre, where she is a Senior Scientist.

Dr. Zadeh's accomplishments have been recognized through being named the Dan Family Chair in the Division of Neurosurgery at UofT—one of the world's largest neurosurgical programs—making her the first woman in Canada to be named neurosurgery chair. Her other prestigious honours include the *William E. Rawls Prize* from the Canadian Cancer Society, the *Top 25 Women of Influence Award*, and the *Ab Guha Award* jointly awarded by the Society of Neuro-Oncology and American Association of Neurological Surgeons. She is the immediate past-President of the Society of Neuro-Oncology, which is a leading international society for brain tumour research and education. She is the current Editor-in-Chief of the open-access journal *Neuro-Oncology Advances*.

The Gairdner Momentum Award comes with a \$50,000 prize and will be presented to Dr. Zadeh during Gairdner Science Week in October 2023.

“It is such an honour to receive this award from the Gairdner Foundation,” says Dr. Zadeh. “I attribute my success in large part to the highly skilled and integrated research and clinical teams that I work with at UHN. My team's achievements in translational brain research simply would not be possible without the exceptional researchers, trainees, neuro-oncologists, surgical teams and patients that we work with every day. I hope the recognition of the work that I have done extends in impact beyond me.”

Join us in congratulating Dr. Zadeh on this momentous achievement!

To learn more about this year's recipients, read the press release [here](#).

Research

Interrupting Interactions

Researchers identify a protein interaction involved in Parkinson's and a way to disrupt it.



Drs. Suneil Kalia (left) and Lorraine Kalia (right) are Senior Scientists at the Krembil Brain Institute.

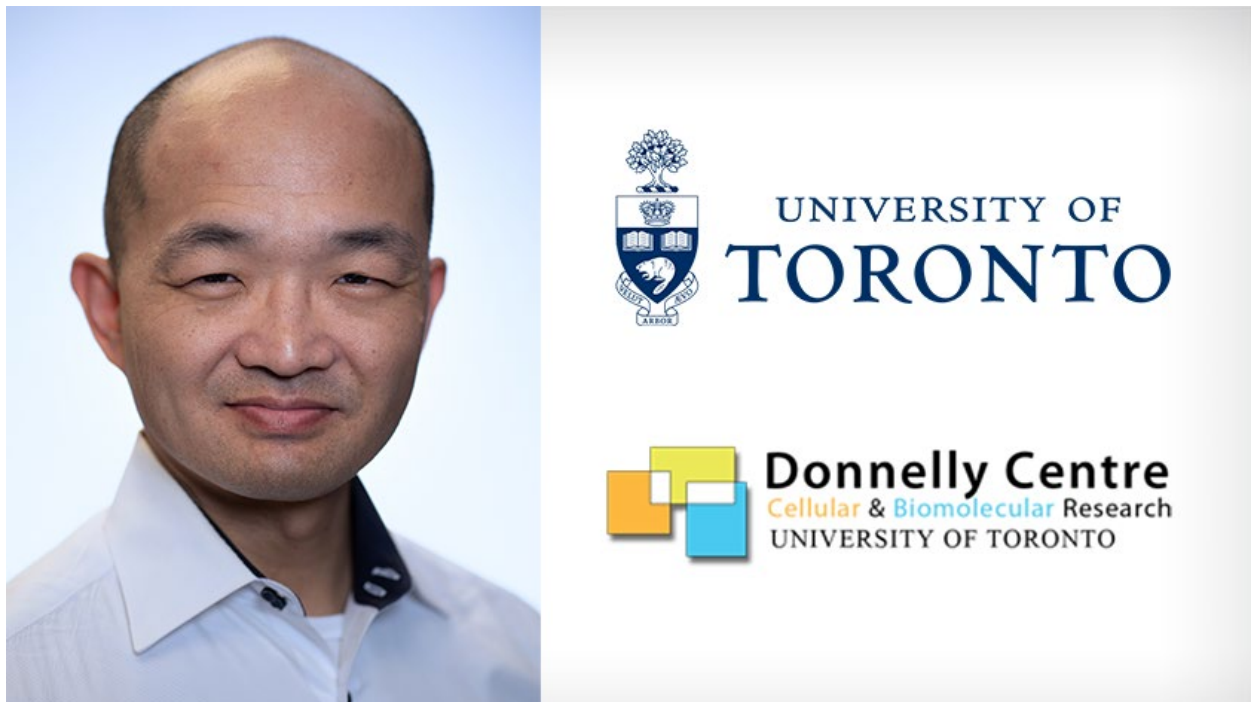
In a study published in [Nature Communications](#), a team led by Krembil Brain Institute Senior Scientists Drs. [Lorraine Kalia](#) and [Suneil Kalia](#) and University of Toronto (UofT) Professor Dr. [Philip M. Kim](#) identified a protein-protein interaction that contributes to Parkinson disease.

In the disease, a protein called α -synuclein (a-syn) accumulates in the brain and leads to cell death. Much research is currently focused on clearing a-syn with antibodies or using small molecules to prevent a-syn from aggregating. In this study, the researchers took an alternate approach by looking for protein-protein interactions that may be promoting the accumulation of a-syn.

Protein-protein interactions govern virtually all the inner workings of cells, including breaking down disease-causing proteins. Inhibiting certain interactions has emerged as a promising approach to treat diseases, such as stroke and cancer.

“We were interested in applying the approach of disrupting protein-protein interactions to Parkinson disease. However, identifying a particular interaction that contributes to a disease and then finding ways to disrupt it can be a painstaking and incredibly slow process,” explains Dr. Lorraine Kalia, who is also a Staff Neurologist at UHN and a Scientist at UofT’s Tanz Centre for Research in Neurodegenerative Diseases in the Temerty Faculty of Medicine.

According to Dr. Kim, the team took the reverse approach to expedite the discovery of potential therapies. “We developed a platform to screen molecules called peptide motifs—short strings of amino acids that can disrupt protein-protein interactions—for their ability to protect cells from a-syn. Once we identified candidate peptides, we determined which protein-protein interactions they target.”



Dr. Philip Kim is a Professor and Principal Investigator at the Donnelly Centre for Cellular and Biomolecular Research and the departments of Molecular Genetics and Computer Science at the University of Toronto. Dr. Kim’s lab applies computational and high-throughput methods to identify and design therapeutic compounds.

Through this approach, the team identified a peptide that reduced a-syn levels in cells by disrupting the interaction between a-syn and a protein subunit of the cellular machinery called ‘endosomal sorting complex required for transport III’ (ESCRT-III).

“ESCRT-III is a component of a pathway that cells use to break down proteins, called the endolysosomal pathway,” explains Dr. Lorraine Kalia. “We discovered that a-syn interacts with a protein within ESCRT-III—called CHMP2B—to inhibit this pathway, thereby preventing its own destruction.”

According to Dr. Suneil Kalia, once the group identified this interaction, they confirmed that they could use their peptide to disrupt it, preventing a-syn from evading the cell's natural clearance pathways.

“We tested the peptide in multiple experimental models of Parkinson disease, and we consistently found that it restored endolysosomal function, promoted a-syn clearance and prevented cell death.”

These findings indicate that the a-syn-CHMP2B interaction is a potential therapeutic target for the disease, as well as other conditions that involve a buildup of a-syn. The next steps for this research are to clarify exactly how a-syn and CHMP2B interact to disrupt endolysosomal activity. Ongoing studies are also determining the best approach for delivering potential therapeutics to the brain.

“This research is still in its early stages—more work is definitely needed to translate this peptide into a viable therapeutic,” cautions Dr. Lorraine Kalia. “Nonetheless, our findings are very exciting because they suggest a new avenue for developing treatments for Parkinson disease and other neurodegenerative conditions.”

This study also highlights the value of multidisciplinary collaborations in health research. “We simply could not have conducted this study in a silo,” says Dr. Suneil Kalia. “The endolysosomal pathway is underexplored, so it was not an obvious place to look for potential disease-related protein-protein interactions. Dr. Kim’s screening platform was critical for pointing us in the right direction.”

Dr. Kim says, “It is extraordinary to see this platform—which we initially used to find potential therapeutics for cancer—yielding advances in brain research. The pathways that cells use to stay healthy are fundamentally very similar across tissues, so the insights that we gain about one organ system or disease could have important implications in other contexts.”

This work was supported by the Canadian Institutes of Health Research, the Michael J. Fox Foundation for Parkinson’s Research, Parkinson’s UK, the Canada Foundation for Innovation, the Ontario Research Fund, the Krembil Research Institute and the UHN Foundation. Dr. Lorraine Kalia is an Associate Professor in the Division of Neurology, Department of Medicine, and in the Department of Laboratory Medicine and Pathobiology at UofT. Dr. Suneil Kalia is an Associate Professor in the Division of Neurosurgery, Department of Surgery, and in the Department of Laboratory Medicine and Pathobiology at UofT, and is the R.R. Tasker Chair in Stereotactic and Functional Neurosurgery at UHN. Dr. Philip M. Kim is a Professor and Principal Investigator at the Donnelly Centre for Cellular and Biomolecular Research, the Department of Molecular Genetics and the Department of Computer Science at UofT.

UofT submitted a patent application covering the composition and use of the peptides and screening methods outlined in this study, with Drs. Satra Nim, Carles Corbi-Verge, Suneil Kalia, Lorraine Kalia and Philip Kim as inventors. Drs. Suneil Kalia, Lorraine

Kalia and Philip Kim co-founded Synepark Therapeutics Inc. to commercialize aspects of this research.

Nim S, O'Hara DM, Corbi-Verge C, Perez-Riba A, Fujisawa K, Kapadia M, Chau H, Albanese F, Pawar G, De Snoo ML, Ngana SG, Kim J, El-Agnaf OMA, Rennella E, Kay LE, Kalia SK, Kalia LV, Kim PM. [Disrupting the \$\alpha\$ -synuclein-ESCRT interaction with a peptide inhibitor mitigates neurodegeneration in preclinical models of Parkinson's disease](https://doi.org/10.1038/s41467-023-37464-2). Nat Commun. 2023 April 19. doi: 10.1038/s41467-023-37464-2.

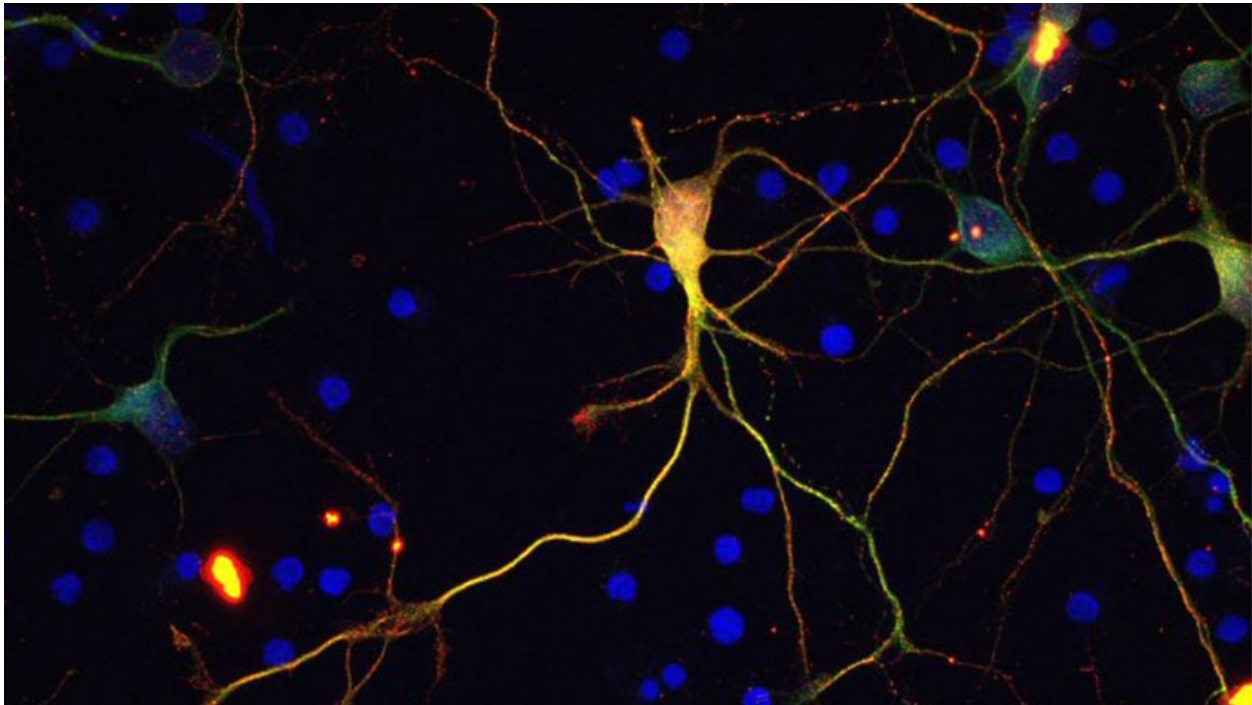


Image of a cultured neuron expressing the protein α -syn. Photo credit: Kashfia Shafiq, Kalia Labs, UHN.

Promising New Therapy

New treatment for glioblastoma prolongs patient survival in an early-phase clinical trial.



(L-R) Dr. Farshad Nassiri, a neurosurgery resident at the University of Toronto, and Dr. Gelareh Zadeh, Co-Director of the Krembil Brain Institute and Senior Scientist at the Princess Margaret Cancer Centre.

UHN neurosurgeons Drs. Farshad Nassiri and [Gelareh Zadeh](#) published the results of the Phase 1/2 clinical trial that show that a novel therapy for recurrent glioblastoma is well-tolerated and prolongs patient survival.

Glioblastoma is a notoriously difficult-to-treat primary brain cancer. Despite aggressive treatment, which typically involves surgical removal of the tumour and multiple chemotherapy drugs, the cancer often returns.

Once tumours recur, treatment options are scarce. To meet the urgent need for new treatments, Dr. Zadeh and her colleagues evaluated an innovative therapy in 49 patients with recurrent disease from 15 hospital sites across North America. UHN was the only Canadian institution and treated most of the patients enrolled in the trial.

The novel therapy involves the combination of an oncolytic virus—a virus that has been engineered to selectively infect and kill cancer cells—and type of a targeted immunotherapy called immune checkpoint inhibition.

First, the team slowly injected the virus directly into the tumour using stereotactic techniques. Patients then received a common immune checkpoint inhibitor intravenously once every three weeks, starting one week after surgery.

Immune checkpoint inhibitors are effective treatments for a variety of cancers, but they have had limited success in treating recurrent glioblastoma.

“These drugs work by preventing cancer’s ability to evade the body’s natural immune response, so they have little benefit when the tumour is immunologically inactive, as is the case in glioblastoma,” explains Dr. Zadeh, Co-Director of the Krembil Brain Institute and Senior Scientist at the Princess Margaret Cancer Centre. “Oncolytic viruses can overcome this limitation by creating a more favourable tumour microenvironment, which then helps to boost anti-tumour immune responses.”

The combination of these viruses and immune-checkpoint inhibitors results in a “double hit” to tumours: the virus directly kills cancer cells and stimulates local immune activity that makes the cancer cells more vulnerable to targeted immunotherapy.

The results, published in [Nature Medicine](#), show that the novel combination therapy is well tolerated and prolongs patient survival. The therapy had no major unexpected adverse effects and yielded a median survival of 12.5 months—considerably longer than the 6 to 8 months typically seen with existing therapies.

“We’re very encouraged by these results,” says the first author of the study, Dr. Farshad Nassiri, a senior neurosurgery resident at the University of Toronto. “Over half of our patients achieved a clinical benefit—stable disease or better—and we saw some remarkable responses, with tumours shrinking and some even disappearing completely. Three patients remain alive at 45, 48 and 60 months after starting the clinical trial.”



Dr. Farshad Nassiri examining tumour samples in the Zadeh lab.

“The findings of the study are particularly meaningful as the patients did not have tumour resection at recurrence—only injection of the virus—which is a novel treatment approach for glioblastoma,” adds Dr. Zadeh, who is also a Professor at the Department of Surgery at the University of Toronto and holds the Dan Family Chair in Neurosurgery and the Wilkins Family Chair in Neurological Brain Tumour Research.

“We believe the key to our success was delivering the virus directly into the tumour prior to using systemic immunotherapy. Our results clearly signal that this can be a safe and effective approach,” says Dr. Nassiri.

The researchers also performed experiments to define mutations, gene expression and immune features of each patient’s tumour. They discovered key immune features that could eventually help clinicians predict treatment responses and understand the mechanisms of glioblastoma resistance – the first study of its kind for brain tumors.

“In general, the drugs that are used in cancer treatment do not work for every patient, but we believe there is a subpopulation of glioblastoma patients that will respond well to this treatment,” says Dr. Zadeh. “I believe this translational work, combining basic bench science and clinical trials, is the key to moving personalized treatments for glioblastoma forward.”

The next steps for the group are to test the effectiveness of the combination therapy against other treatments in a randomized clinical trial.

This is one of the few clinical trials with promising results for glioblastoma over the last decade, and it was truly a team effort.

“The trial would not have been possible without our incredible OR teams, research safety teams and researchers—including Dr. Warren Mason at Princess Margaret Cancer Centre—and our brave patients and their families. We’re also grateful to the Wilkins Family for providing the funds to enable us to complete trials that advance care for our patients,” says Dr. Zadeh.

Click [here](#) for a video of Drs. Zadeh and Nassiri discussing the trial.

This work was supported by DNATrix Inc., Merck & Co. Inc., the Princess Margaret Cancer Centre Foundation and the UHN Foundation. Dr. Gelareh Zadeh is a Professor at the Department of Surgery at the University of Toronto and holds the Dan Family Chair in Neurosurgery and the Wilkins Family Chair in Neurological Brain Tumour Research.

Nassiri F, Patil V, Yefet LS, Singh O, Liu J, Dang RMA, Yamaguchi TN, Daras M, Cloughesy TF, Colman H, Kumthekar PU, Chen CC, Aiken R, Groves MD, Ong SS, Ramakrishna R, Vogelbaum MA, Khagi S, Kaley T, Melear JM, Peereboom DM, Rodriguez A, Yankelevich M, Nair SG, Puduvalli VK, Aldape K, Gao A, López-Janeiro A, de Andrea CE, Alonso MM, Boutros P, Robbins J, Mason WP, Sonabend AM, Stupp R, Fueyo J, Gomez-Manzano C, Lang FF, Zadeh G. [Oncolytic DNX-2401 virotherapy plus pembrolizumab in recurrent glioblastoma: a phase 1/2 trial](#). Nat Med. 2023, May 15. doi: 10.1038/s41591-023-02347-y.

Why Immune Cells Attack

New research reveals how the body generates damaging autoantibodies in lupus.



(L-R) First author, Dr. Dario Ferri, and senior author, Dr. Joan Wither.

Researchers at the Schroeder Arthritis Institute have shed light on how systemic lupus erythematosus—the most common form of lupus—develops.

Systemic lupus is an autoimmune disorder in which the body produces antibodies that attack its own tissues. These harmful self-reactive antibodies, known as autoantibodies, lead to widespread inflammation and tissue damage.

The research team, led by Schroeder Senior Scientist Dr. [Joan Wither](#), used experimental models to explore two key factors that are associated with systemic lupus: B cell tolerance and elevated levels of a protein called interferon-alpha.

“For the first time, we have shown that elevated levels of interferon-alpha in the blood disrupt immune mechanisms that maintain B cell tolerance—a key property of a healthy immune system—leading to the production of autoantibodies,” explains Dr. Wither.

B cell tolerance prevents immune cells that recognize the body from producing antibodies that would react with and harm it. Until this study, the relationship between elevated levels of interferon-alpha and B cell tolerance mechanisms was unknown.

“Our findings reveal that heightened levels of interferon-alpha have a multi-pronged effect on B cells, resulting in increased production of autoantibodies. Firstly, B cells become more activated and are more likely to produce autoantibodies. Secondly, rogue autoreactive B cells become less susceptible to destruction due to dysfunction of immune tolerance checkpoints,” says Dr. Dario Ferri, lead author of the study and a former graduate student in Dr. Wither's lab.

Notably, the team found that these effects of interferon-alpha were direct—they required interferon-alpha to bind to B cells through a receptor on the cell surface.

The study also showed that many of the effects of interferon-alpha involve helper T cells—cells that mediate immune activity by stimulating other immune cells. The researchers propose that interferon-alpha changes the ability of B cells to interact with T cells.

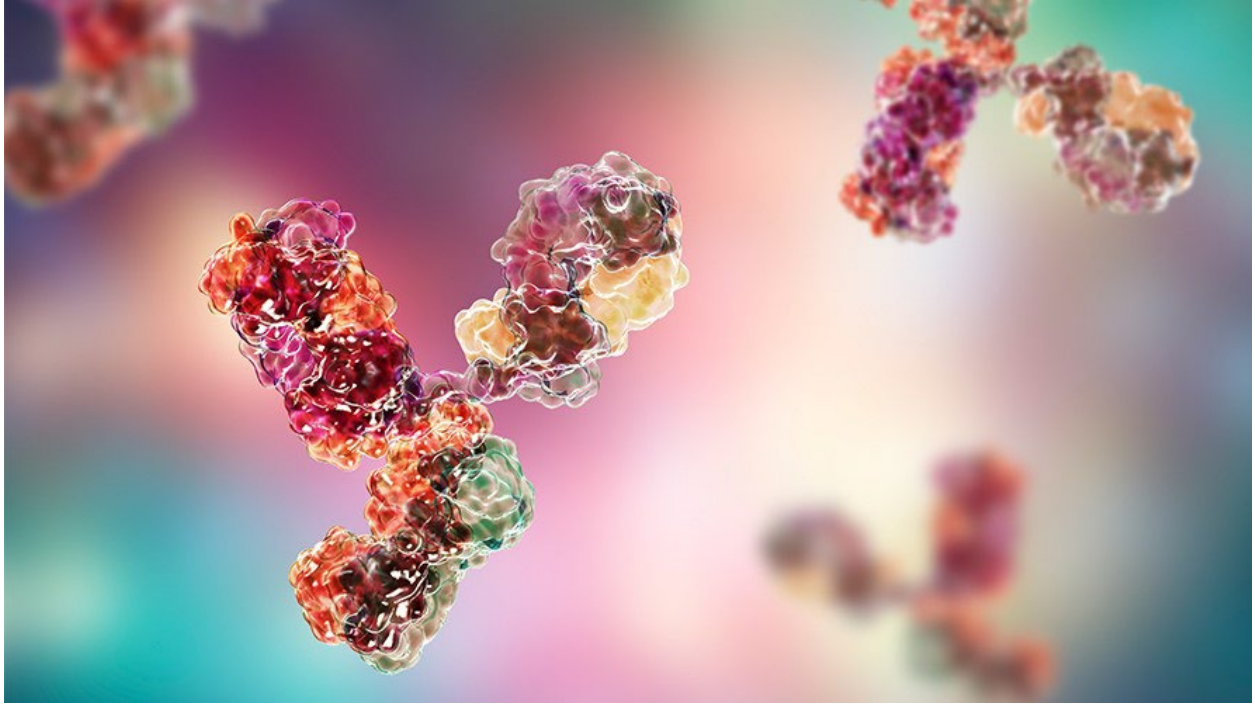
“Our work highlights the importance of interferon and the pathways through which it acts to promote autoantibody production. These pathways could serve as targets for new treatments for systemic lupus and related conditions,” concludes Dr. Wither.

This work was supported by the Canadian Institutes of Health Research, the Schroeder Arthritis Institute and the UHN Foundation. Dr. Joan Wither is a Professor of Medicine and Immunology at the University of Toronto.

Dr. Joan Wither has served on advisory boards for AstraZeneca and received a career award that was indirectly funded by Pfizer.

*Ferri DM, Nassar C#, Manion KP#, Kim M, Baglaenko Y, Muñoz-Grajales C, Wither JE. [Elevated levels of interferon-α act directly on B cells to breach multiple tolerance mechanisms promoting autoantibody production](#). *Arthritis Rheumatol*. 2023 Feb 20. doi: 10.1002/art.42482.*

#Both authors contributed equally to the work



Antibodies (illustrated above) are proteins that the immune system produces to protect against pathogens. In some cases, antibodies attack the body's own tissues, causing autoimmune diseases.

An Unexplored Mechanism

Study identifies a key cause of abnormal neuron development in 15q13.3 microdeletion syndrome.



(L-R) Drs. Brianna Unda and Karun Singh.

Researchers led by Dr. [Karun Singh](#) at UHN's Donald K. Johnson Eye Institute (DKJEI) have identified a molecular mechanism underlying brain dysfunction in 15q13.3 microdeletion syndrome.

15q13.3 microdeletion syndrome is a genetic disorder in which an individual is missing a group of genes located on chromosome 15. The syndrome is linked to multiple conditions, including autism spectrum disorder, intellectual disability, epilepsy and schizophrenia.

“Previous studies have identified DNA changes that contribute to 15q13.3 microdeletion syndrome, but we do not know how these changes result in abnormal brain function,” explains Dr. Singh, a Senior Scientist at DKJEI and the senior author of the study. “Because of this gap in our knowledge, there are no targeted treatments for 15q13.3 microdeletion syndrome, or related disorders.”

One gene that has been implicated in the microdeletion syndrome—called *OTUD7A*—stands out due to its role in neuronal maturation and connectivity and its link to brain

disorders such as epilepsy. Although researchers know that *OTUD7A* is important for brain development, its exact functions are largely unknown.

“We wanted to determine the role of *OTUD7A* in 15q13.3 microdeletion syndrome at the cellular level—how it influences proteins within neurons to cause brain abnormalities,” says Dr. Brianna Unda, a former postdoctoral researcher in Dr. Singh’s lab and the lead author of the study.

Using experimental models and patient samples, the team compared neurons with and without functional *OTUD7A* genes. They discovered that neurons defective for *OTUD7A* did not grow, mature or connect with other neurons as well as those that had an intact gene.

“This finding implicates *OTUD7A* in neuronal development and suggests that changes in this gene underlie the symptoms of 15q13.3 microdeletion,” says Dr. Unda.

To determine how *OTUD7A* contributes to neuronal development and function, the researchers developed a technique to map protein interactions within neurons. They found that *OTUD7A*—the protein encoded by the *OTUD7A* gene—interacts with Ankyrin-G—a protein that is involved in neuron function and has been linked to autism spectrum disorder and epilepsy.

Based on these results, the team took a deeper look at Ankyrin-G and discovered that neurons with 15q13.3 microdeletion had lower levels of the protein. They also found that the Ankyrin-G that was present was less stable in these cells compared to those without the microdeletion. Importantly, they could reverse the neuronal abnormalities seen in 15q13.3 microdeletion syndrome by restoring normal levels of Ankyrin-G.

These findings suggest a sort of domino effect in which 15q13.3 microdeletion leads to loss of *OTUD7A*. Loss of *OTUD7A* then leads to reduced levels and stability of Ankyrin-G. And, finally, loss of Ankyrin-G disrupts neuronal development and connectivity.

This study provides important insights into the disease mechanisms of 15q13.3 microdeletion syndrome and the role of *OTUD7A*-Ankyrin-G interactions in neuronal development.

“This is an exciting step forward for understanding neurodevelopmental disorders. By identifying key molecular pathways involved in microdeletion syndromes, our research is laying a strong foundation that could unlock future targeted therapeutics and preventative strategies,” says Dr. Singh.

This work was supported by the Canadian Institutes of Health Research, the Natural Sciences and Engineering Research Council of Canada, the Ontario Brain Institute, the Network of European Funding for Neuroscience Research and the UHN Foundation. Dr. Karun Singh is an Associate Professor in the Department of Ophthalmology and Vision Sciences at the University of Toronto.

Unda BK, Chalil L, Yoon S, Kilpatrick S, Irwin C, Xing S, Murtaza N, Cheng A, Brown C, Afonso A, McCreedy E, Ronen GM, Howe J, Caye-Eude A, Verloes A, Doble BW, Faivre L, Vitobello A, Scherer SW, Lu Y, Penzes P, Singh KK. [Impaired OTUD7A-dependent Ankyrin regulation mediates neuronal dysfunction in mouse and human models of the 15q13.3 microdeletion syndrome](#). *Mol Psychiatry*. 2023 Jan 6. doi: 10.1038/s41380-022-01937-5.



Symptoms of 15q13.3 microdeletion syndrome may be different among patients and include intellectual disability, autism spectrum disorder, epilepsy and mental illness. There are currently no specific treatments for this syndrome.