



Research Report • University Health Network 2021

QUHN

UNIVERSITY HEALTH NETWORK

is a research hospital affiliated with the University of Toronto and a member of the Toronto Academic Health Science Network. UHN comprises four academic hospitals, an education institute and seven research institutes. Research is supported in part by the UHN Foundation and The Princess Margaret Cancer Foundation. The scope of research and complexity of cases at UHN have made it a national and international source for discovery, education and patient care.

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 work 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.

UHN 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 deliver exemplary patient care, research and education.

Featured on the front cover is Dr. Anastasia Tikhonova, a Scientist at the Princess Margaret Cancer Centre. To learn more about her research program and team members, visit her laboratory website.

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Research Committee of the Board of Trustees

WELCOME MESSAGE



Dr. Brad Wouters, Executive Vice President, Science and Research, UHN.

Science For Society

During the past year, the world's focus has been on science. The novel coronavirus called on all kinds of scientists from all over the world to delve into the unknown and rapidly find answers to the world's most pressing medical questions. The global crisis, infodemic and rapidly evolving policy recommendations were further calls to strengthen the relationship between science and society.

At UHN, our dedicated researchers serve society every day. It's our mission—through science, education and care—to create A Healthier World. Our world-class scientists rose to the challenge of fulfilling this mission and did so both inside and outside the lab. I witnessed our researchers engage with the public to provide accessible information, advocate for equitable and evidence-based public policies, and forge global collaborations to advance medical knowledge. Our science has informed and spurred changes in policy and the care that patients receive worldwide.

Because of these tireless efforts, the world is a better place.

This report highlights some of the life-changing advances that our colleagues have made this year to improve human health and wellbeing. These include a technology that can identify tumour cells from a blood sample, a deeper understanding of the brain circuitry underlying chronic pain and a recipe for generating lab-made liver cells that could serve as future therapeutics.

RESEARCH SNAPSHOT

	Research TeamUHN	4,888	
	Principal Investigators	1,153	
	Fellows Graduate Students	320 665	
	Other Students Total Trainees	317 1,302	
	Institute Staff Support Staff	2,030 183	िन्द
	Core Facilities Staff Total Staff	220 2,433	
	Publications	4,181	
	Total Funding	\$453M	
	Total Space	1.027M sq. ft.	

Photos of trainees (top left, clockwise) Mursal Nader, Ximing Li, Catherine Lin and Mark Gower in the Tikhonova laboratory.

At UHN, scientists, staff and trainees share these achievements with our academic partner, the University of Toronto, our dedicated foundations—The Princess Margaret Cancer Foundation and the UHN Foundation—as well as academic organizations, governments, private sector partners and non-profit organizations. Our successes are also shared with our patient partners, who inspire us and make our work possible.

Science is embedded within society—it underpins how we understand human health and behaviour and it responds to our shifting priorities. The relationship between science and society could not be clearer: vaccines helped to dramatically reduce COVID-19 cases so we could regain some aspects of normal life. But this success is not science's alone—empathy, communication and collaboration helped us get to this point. The pandemic reminded us all of this reciprocal relationship and the importance of engaging the public in science.

As we go forward, we will continue to work together to nurture strong public trust, help establish science-informed policies and build further support for world-class research—activities that will be key to weathering the next storm.

Leaps and Bounds

Building capacity and resilience to overcome future challenges

MONITORING LONG-HAUL SYMPTOMS

Drs. Angela Cheung and Margaret Herridge are leading the *Canada-wide COVID-19 Prospective Cohort Study*, known as CANCOV, to evaluate short-term and long-term outcomes in patients with COVID-19 and their caregivers. The study is also examining the factors that contribute to these outcomes. *> learn more*

PROTECTING PEOPLE AT RISK

Dr. Andrea Iaboni's team developed an isolation toolkit to help prevent the transmission of COVID-19 in individuals with dementia in long-term care homes. The *Dementia Isolation Toolkit* provides a framework to explore the ethics, as well as the safety and person-centered planning necessary to stop COVID-19 within this at-risk group. > *learn more*

EXPANDING TREATMENT OPTIONS

Dr. Donald Weaver's team showed in a preclinical study that an anti-inflammatory drug known as furosemide has the potential to reduce the harmful inflammation that is caused by COVID-19. A Canada-wide *clinical trial* was initiated to test the safety and efficacy of the drug in patients who require mechanical ventilation. > *learn more*

INFORMING PUBLIC HEALTH POLICY

Dr. Beate Sander's team developed the COVID-19 Resource Estimator (CORE) model to forecast the demand for resources such as ICU beds and ventilators, as well as case numbers under different public health scenarios. The modelling data supported Ontario's capacity planning and public health interventions. > learn more

PLANNING FOR UNCERTAINTY

Early on in the pandemic, personal protective equipment was in short supply and contingency plans for their reuse had to be developed. Dr. Lothar Lilge led a study to explore whether UV light can be used to sterilize N95 masks. > *learn more*

AVOIDING DANGEROUS COMPLICATIONS

Drs. Patrick Lawler and Ewan Goligher, in partnership with Dr. Ryan Zarychanski at the University of Manitoba, tested the blood thinner heparin for its effectiveness to treat COVID-19. Trial results suggest that full doses of the drug improve the chance of survival in hospitalized, moderately ill patients, but not in critically ill patients. > learn more

PRESERVING SPECIMENS FOR RESEARCH

UHN has established a COVID-19 biobank that now houses over 40,000 biological specimens from 830 participating patients. These specimens are enabling more than 15 academic and industry collaborators to conduct a broad range of research projects focused on improving our understanding of the SARS-CoV-2 virus and the body's immune response to infection. > *learn more*

LEADING THE PANDEMIC RESPONSE

• Dr. Susy Hota was recognized as one of the 2020 Women of the Year by Best Health Magazine for her leadership in preventing outbreaks in health care settings.

 Seven Clinician Investigators were named Local Heroes During COVID-19 by the Canadian Association of Emergency Physicians: Dr. Megan Landes for her research efforts to reduce health care practitioners' exposure to COVID-19; and Drs. Jennifer Bryan, Kaitlin Hayman, Dawn Lim, Nazanin Meshkat, Anna Nowacki and Erin O'Connor for their leadership and advocacy efforts.

OTHER PROGRESS

This report features other efforts to fight the pandemic: testing to show that a booster shot is safe and effective for transplant recipients (pg. 34), assessing prevalence of COVID-19 in health care workers (pg. 35) and adopting virtual visits to provide uninterrupted cancer care (pg. 22).

Moving Research Forward

Working with industry to unlock A Healthier World



2020

Today's researchers play a key role in turning their findings into treatments and technologies that benefit patients. Whether it is through launching a start-up, drug discovery activities or designing medical devices, the private sector works together with researchers to bring health care solutions to patients. This is why we commercialize.

Thanks to our world-class researchers and clinicians, UHN is now Canada's leading institution in research commercialization and the eighth top hospital in North America in research translation [AUTM Licensing Activity Survey].

Our commercialization achievements include 14 funded spin-offs since 2014, which are creating jobs in Toronto, and \$68M raised in licensing revenue in the last three years—funds that are being reinvested to further propel innovation at UHN.

Read on to see our progress over the last fiscal year, and to learn how our research discoveries are improving the health of Canadians and people around the world.

TRANSLATION HIGHLIGHTS

Oncology start-up **POINT SURGICAL INC.** launches to develop a way to instantly and accurately diagnose cancer types using laser vaporization and mass spectrometry

Cancer start-up **TCRYPTION Inc.** launches (see next page)

- **POINT BIOPHARMA** and UHN's **CANPROBE** sign an exclusive licensing agreement to develop the therapeutic compound Lu-DOTATATE, advancing options for patients with difficult-to-treat neuroendocrine cancer
- **SONA GROUP** and **VEE TECH** enter a collaboration with UHN to develop smart fabric-based wearables to improve the quality of life of individuals experiencing chronic illness, aging and disabilities
- Next-generation cancer diagnostics startup **ADELA** launches (see next page)



IN THE BLOOD

UHN precision medicine start-up Adela launched last spring with the intent to develop a simple blood test for cancer and other diseases as a new way to diagnose patients. Built on research led

TCRyption

BROADER ACCESS TO CARE

In 2020, the UHN spin-off company **TCRyption Inc.** was launched. The company is advancing a technology—known as TCR-HLA multimer staining—that enables precision cancer therapies to work in a broader base of patient populations and ethnic groups compared to existing approaches. "In addition to helping more patients, our technology also provides a way to target a wider range of cancers," says scientific co-founder Dr. **Naoto Hirano** (pictured). The technology widens the scope of a cancer immunotherapy known as T-cell receptor-based adoptive cellular therapy, which activates the body's own immune response to destroy cancer cells. by scientific co-founders Drs. Scott Bratman (pictured) and Daniel De Carvalho, Adela's proprietary platform can detect tiny amounts of tumour DNA circulating in the blood. The technology involves analyzing chemical changes to DNA known as methylation, and is paired with machine learning algorithms. Adela's goal is to replace current approaches to diagnose cancer, which often involve surgical biopsy, with a simple blood test. With UHN's unique inhouse de-risking approach and support from the Princess Margaret Cancer Foundation *Innovation Acceleration Fund*, Adela gained the confidence of five major investors, receiving the second-largest financing deal in UHN history at USD \$60M.

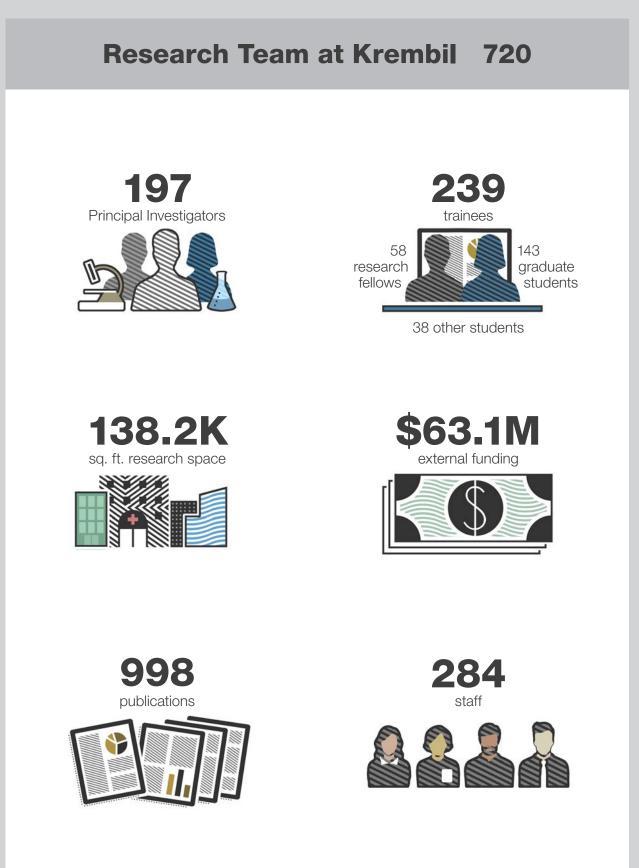


OUTSMARTING CANCER

In November 2020, a collaboration between UHN and Pfizer's *Centers for Therapeutic Innovation* was initiated. The project will screen for, identify and optimize anticancer drugs that work through a recently discovered strategy known as viral mimicry. The approach involves mimicking a viral infection in cancer cells so that the body's immune system begins to recognize and target the cancer. **Research** led by Dr. **De Carvalho** (pictured) set the stage for this new cancer treatment strategy, and his team will work closely with Pfizer to identify promising anticancer therapies.

Krembil Research Institute

KREMBIL AT A GLANCE



Wired Differently

Brain connectivity may underlie sex differences in chronic pain

Men and women experience chronic pain differently. Women are more likely to experience chronic pain and related conditions.

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 look at 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 implicated in acute and chronic pain. These connectivity patterns center on a particular region called the subgenual anterior cingulate cortex (sgACC), which plays a role in pain response.

To identify differences, the team compared brain connectivity in women with and without chronic pain. They found that in women with chronic pain, the sgACC was more strongly connected to brain regions that are involved in self-awareness and in monitoring the body's internal state. The sgACC was also less strongly connected to regions that are involved in controlling pain perception and emotional responses to pain. In contrast, these connectivity differences were not observed in men.

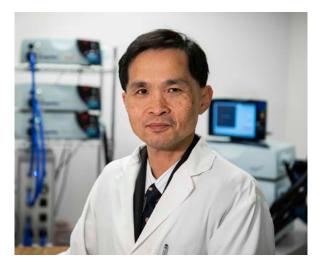


These findings raise questions about whether the unique brain circuitry seen in women with chronic pain is caused by, or contributes to, their pain condition, and whether differences in brain circuitry relate to pain severity.

Dr. Davis's team will continue to investigate the mechanisms underlying chronic pain, with the aim of developing more effective treatments that account for sex differences. "The patterns of functional connectivity that we have identified could serve as targets for new neuromodulationbased therapies such as deep brain stimulation and repetitive transcranial magnetic stimulation," says Dr. Davis.

Osborne NR, et al. Pain. 2021 Jan. doi:10.1097/j. pain.00000000002016. Supported by the Canadian Institutes of Health Research, the Chronic Pain Network, The MAYDAY Fund and the UHN Foundation.





(Top of page) Dr. Karen Davis at the Krembil Brain Institute. (Above) Dr. Robert Chen in the operating room.

Research Highlights

WELL IN HAND

Research conducted by Drs. **Robert Chen** and **Steven McCabe** demonstrated that brain regions that map to different parts of the body change in response to hand transplant surgery. They found that after transplant these regions more closely resembled the pre-amputation state. They also found that the changes began even before the patient recovered hand function. Together, these findings highlight the importance of brain plasticity for the restoration of hand function following transplantation. *Full Story / Scientific Article*

HAVING IT BOTH WAYS

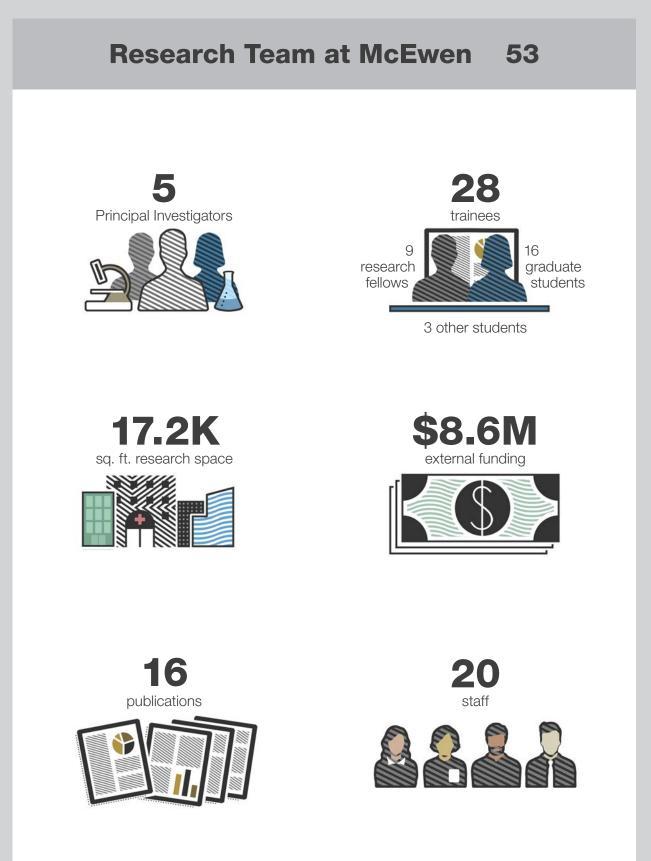
A global collaboration led by Dr. Sindhu Johnson validated a new set of criteria for diagnosing individuals with systemic lupus erythematosus the most common type of lupus. The criteria performed well among men and women of various ethnicities and patients with early disease, surpassing existing criteria in sensitivity and specificity. Implementing these new criteria will ensure that more individuals with lupus receive timely treatment and that they are not left out of innovative clinical trials. *Full Story / Scientific Article*

VISIONARY COMPUTATIONAL MODEL

Researchers led by Dr. Michael Reber constructed a computational model that describes the organization of neural networks that are involved in visual processing. The model accurately predicts interactions between neural circuits and re-creates the errors that arise in certain neurological conditions. This model could help scientists to identify neural changes that occur in leading causes of blindness such as age-related macular degeneration and diabetic retinopathy, and could yield new approaches to restoring vision. *Full Story / Scientific Article*

McEwen Stem Cell Institute

MCEWEN AT A GLANCE



Stem Cells to Liver Cells

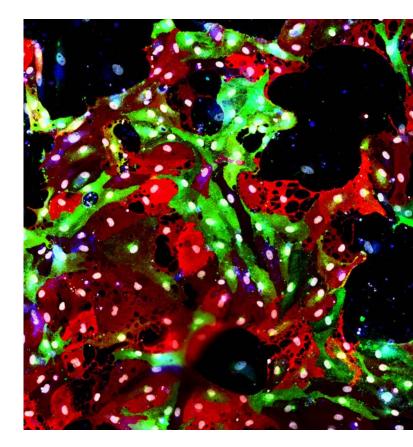
Scientists create liver cells with vital blood-clotting protein

Researchers have found a way to generate the cells that may hold the key to new treatments for hemophilia A, a genetic disorder in which the blood does not clot normally.

The cells that were produced are known as liver sinusoidal endothelial cells and are found in specific regions of the liver. The research team made the cells from human pluripotent stem cells, which can give rise to most cells in the human body.

"Individuals with hemophilia A lack a clotting factor known as Factor VIII, which is produced by these endothelial cells. We found a way to make large numbers of the precursors of these cells in the laboratory, and we were able to validate that they can make the missing clotting factor," says Dr. **Blair Gage**, a postdoctoral fellow in Dr. **Gordon Keller**'s laboratory and first author of the study.

The team first used human pluripotent stem cells to generate venous angioblasts—precursors to the endothelial cells that line the veins. Next, by transplanting these precursors into experimental models, the researchers were able to coax them to mature into sinusoidal endothelial cells that were capable of producing Factor VIII.



Dr. Keller concludes, "This finding moves us closer to understanding the role of these cells in liver function and to developing new therapies to treat a number of conditions, such as hemophilia A and chronic liver diseases."

Gage BK, et al. Cell Stem Cell. 2020 July 7. doi:10.1016/j. stem.2020.06.007. Supported by the University of Toronto's Medicine by Design Initiative, which receives funding from the Canada First Research Excellence Fund; the Canadian Institutes of Health Research; the McEwen Stem Cell Institute; and the UHN Foundation.

(Top left) Immunofluorescence image showing human pluripotent stem cell-derived liver endothelial cells. The cells are stained red and green with white nuclei. A blood factor related to Factor VIII, known as Von Willebrand Factor, is stained in blue. (Top right) Dr. Blair Gage. (Right) Dr. Alexander Mikryukov.



Research Highlight

THE WAY TO YOUR HEART

Drs. Alexander Mikryukov and Gordon Keller discovered how to produce endocardial cells—a type of cell that lines the interior of the heart—from stem cells in the laboratory.

During the earliest stages of human development, endocardial cells stimulate the growth of the first heart muscle tissue and give rise to cells that form blood vessels and the valves of the heart.

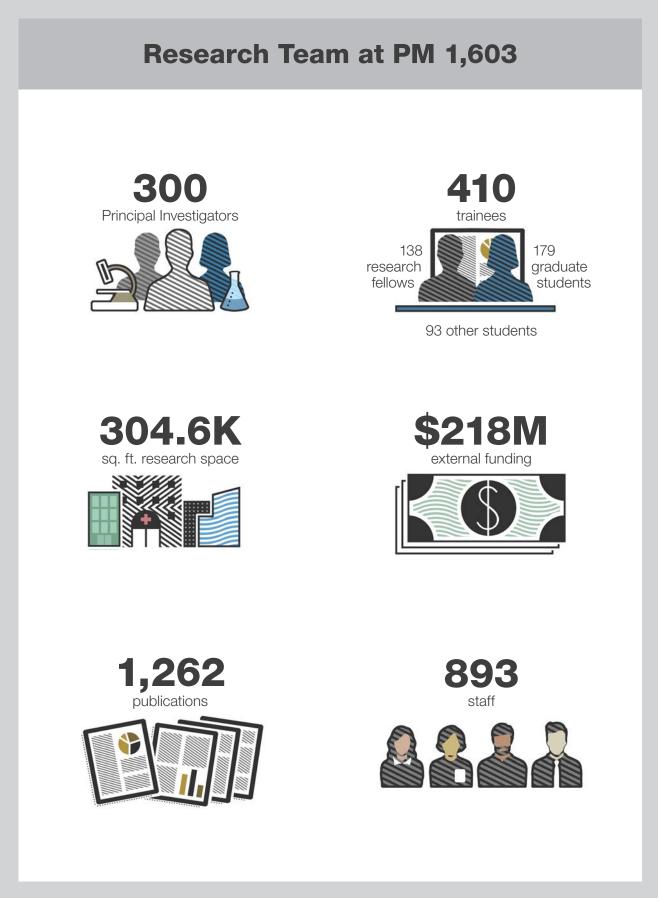
To identify how these heart cells arise in the body, the team recreated conditions for early heart development in a laboratory setting. Using human pluripotent stem cells, they showed that the protein known as BMP10 plays a key role in the development of the laboratory grown cells. Through advanced gene expression studies, the team found that the endocardial cells that were generated from stem cells share remarkable similarities with the endocardial cells in the heart.



Princess Margaret Cancer Centre

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Cancer on Pause

Cancer cells survive treatment by entering a dormant state

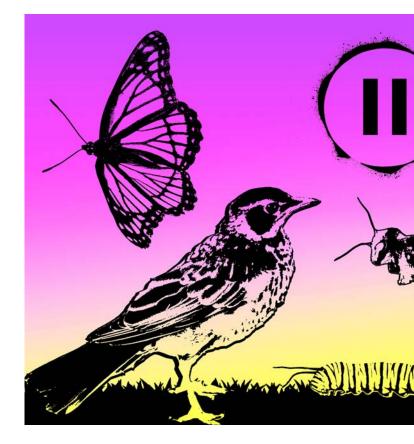
Nature has developed diverse survival strategies for harsh conditions. Cancer cells are no different in this regard and use creative ways to evade cancer-fighting drugs.

A study led by Dr. Catherine O'Brien showed that cancer cells can become dormant and enter a type of suspended animation known as a 'drugtolerant persister (DTP)' state when exposed to chemotherapy and anticancer drugs.

The research team made this discovery using experimental models of colon cancer. "When treated with chemotherapy, we found that all cells within the tumour—not just a subset of cells were capable of entering a DTP state," explains Dr. O'Brien. "Once treatment ended, the cells recovered and began growing again."

High-throughput genomic technologies were used to determine which genes were turned on and off in the DTP state. This approach helped the team identify how cancer cells survive: they use a mechanism known as diapause.

Diapause is used by animals to halt growth and development, such as pausing pregnancies in response to harsh weather, drought or food shortages. Because many chemotherapy drugs target the fast growth rate of cancer cells to kill them, by initiating diapause, which slows cell growth, the cancer cells gain protection.



The researchers found that cancer cells in the DTP state share other similarities with embryos in diapause: they rely on a mechanism known as autophagy, which enables the cells to digest portions of themselves to survive.

Taking these results further, the team searched for ways to prevent cancer cells from entering diapause. The researchers found that when cancer cells are exposed to drugs that inhibit autophagy, they can no longer enter the DTP state.

"Here we demonstrated how cancer cells have adopted an evolutionarily conserved mechanism to survive cancer treatment," says Dr. O'Brien.

"Our work lays the foundation for new strategies to target cancer cells in the DTP state—moving us one step closer to overcoming treatment failure and relapse of this disease."



Rehman SK, et al. Cell. 2021 Jan 7. doi: 10.1016/j. cell.2020.11.018. Supported by the Canadian Institutes of Health Research, the Terry Fox Research Institute, the Natural Sciences and Engineering Research Council of Canada and The Princess Margaret Cancer Foundation. M Ramalho-Santos holds a Canada 150 Research Chair in Developmental Epigenetics, TJ Pugh holds a Tier 2 Canada Research Chair (CRC) in Translational Genomics, B Haibe-Kains holds a Tier 2 CRC in Pharmacogenomics and CA O'Brien holds a Tier 2 CRC in Translational Research in Colorectal Cancer.

(Above left) Illustration showing examples of insects and animals that are known to undergo diapause. For example, monarch butterflies undergo a type of diapause, known as reproductive diapause, to conserve energy before and during their migration from Mexico to North America. (Above right) Dr. Catherine O'Brien.

Research Highlights

DETECTING IMMUNE CELLS

Dr. Naoto Hirano and his team developed a technology to detect and track certain immune cells known as T helper cells. Researchers currently study T killer cells—another type of immune cell—using a protein known as the human leukocyte antigen (HLA), which binds strongly to these cells and tags them. However, HLA only weakly binds to T helper cells. "Using advanced molecular biology techniques, we made changes to HLA proteins that increased their ability to bind to T cells by over 200-fold," says Dr. Hirano. For this innovation, Dr. Hirano was named UHN Inventor of the Year. *Full Story / Scientific Article*

USING STATINS TO FIGHT CANCER

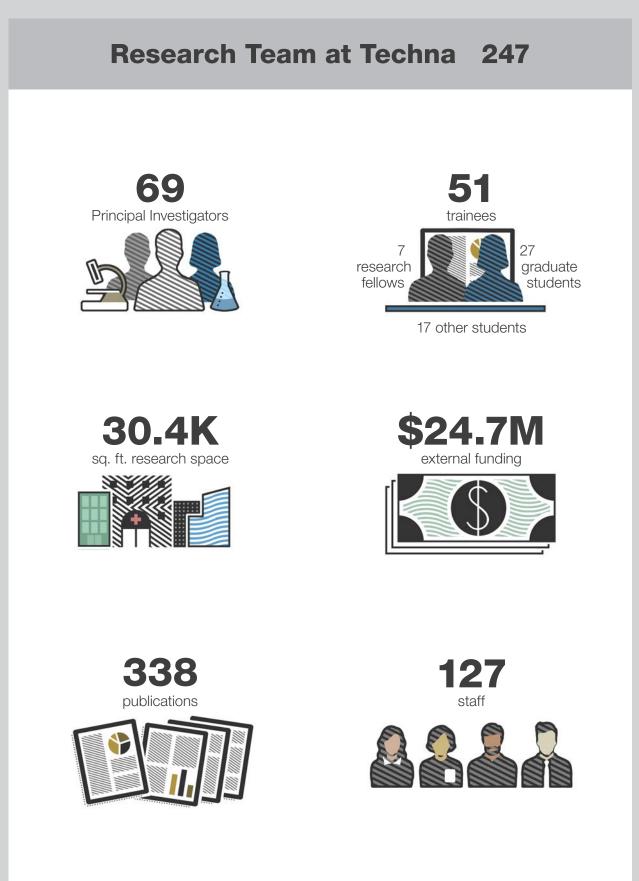
Research led by Dr. Linda Penn in collaboration with Dr. Suzanne Trudel found that statins drugs that are commonly prescribed to lower blood cholesterol—may be effective for treating some forms of multiple myeloma. Cancer cells characterized by a genetic change known as t(4;14) were more likely to die when exposed to statins. These findings set the stage for future preclinical and clinical studies to test whether cholesterollowering agents can be combined with standard therapies to treat this aggressive blood cancer. *Full Story / Scientific Article*

SPOTTING CANCER IN THE BLOOD

A revolutionary method to detect and accurately diagnose brain and kidney cancers using blood samples was developed in Dr. **Daniel De Carvalho's** laboratory. The approach is based on the detection of chemical changes to DNA known as methylation, which display different patterns in cancer cells. The findings lay the groundwork for the development of sensitive blood tests—a much less invasive approach than traditional biopsies—to diagnose cancers. *Full Story / Scientific Article 1/ Scientific Article 2*



TECHNA AT A GLANCE



Cancer Care from Home

Efforts to create virtual care provide post-pandemic benefits

When the COVID-19 pandemic struck, the Princess Margaret Cancer Centre had to quickly devise a solution for virtual visits.

Within just 12 days, several UHN teams had come together to create a custom platform that integrated with pre-existing appointment booking systems and electronic medical records. It enabled care teams to assess patients from the safety of their own home and enabled clinical workflows to continue working seamlessly.

The initiative was orchestrated by Techna's *Health Informatics Research* team and Princess Margaret Cancer Centre's *Smart Cancer Care Program*.

"Individuals with cancer often have a weaker immune system due to their disease or treatments. It was imperative to find a solution that would protect these patients," says Dr. Alejandro Berlin.

Dr. Berlin, with Dr. Monika Krzyzanowska, led a team that examined how the virtual appointments affected quality of care, patient and practitioner experience, and health care costs.

"In just under two weeks and after hundreds of hours of collective work, the team was able to launch the Virtual Care Management System. Within a month, over half of all visits—which total

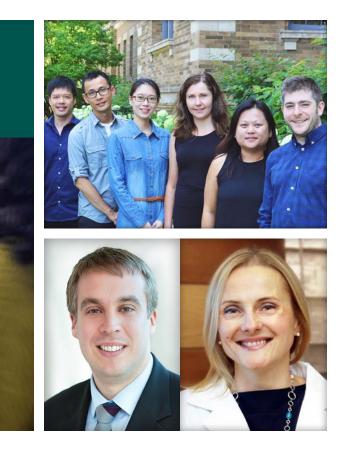
smart cancer care



about 3,900 per week—were virtual," says Tran Truong, Techna Project Director.

The system enabled a return to pre-pandemic visit volumes and the team found that there were no negative effects on the safety or timeliness of cancer care compared to standard in-person care. Furthermore, users of the system were happy with the change. The team found that 72% of practitioners and 82% of patients reported being satisfied with virtual appointments. Over the twomonth evaluation period, virtual visits also saved patients an estimated \$3M in expenses.

"Telemedicine has not only transformed how we engage and interact with patients but also provides substantial benefits," says Dr. Krzyzanowska. "Our study supports its use in our post-pandemic future."



Berlin A et al. JAMA Oncol. 2021 Jan 7. doi: 10.1001/ jamaoncol.2020.6982. Supported by The Princess Margaret Cancer Foundation.

(Top left) Photo depicting a virtual doctor's consultation. (Top right) The Health Informatics Research team at Techna, led by Project Director Tran Truong (second from the right). (Above left) Dr. Alejandro Berlin. (Above right) Dr. Monika Krzyzanowska. (Right) Screenshots of the Medly app, which is available by prescription. (Below) Dr. Patrick Ware.

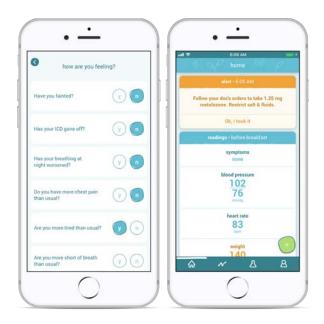


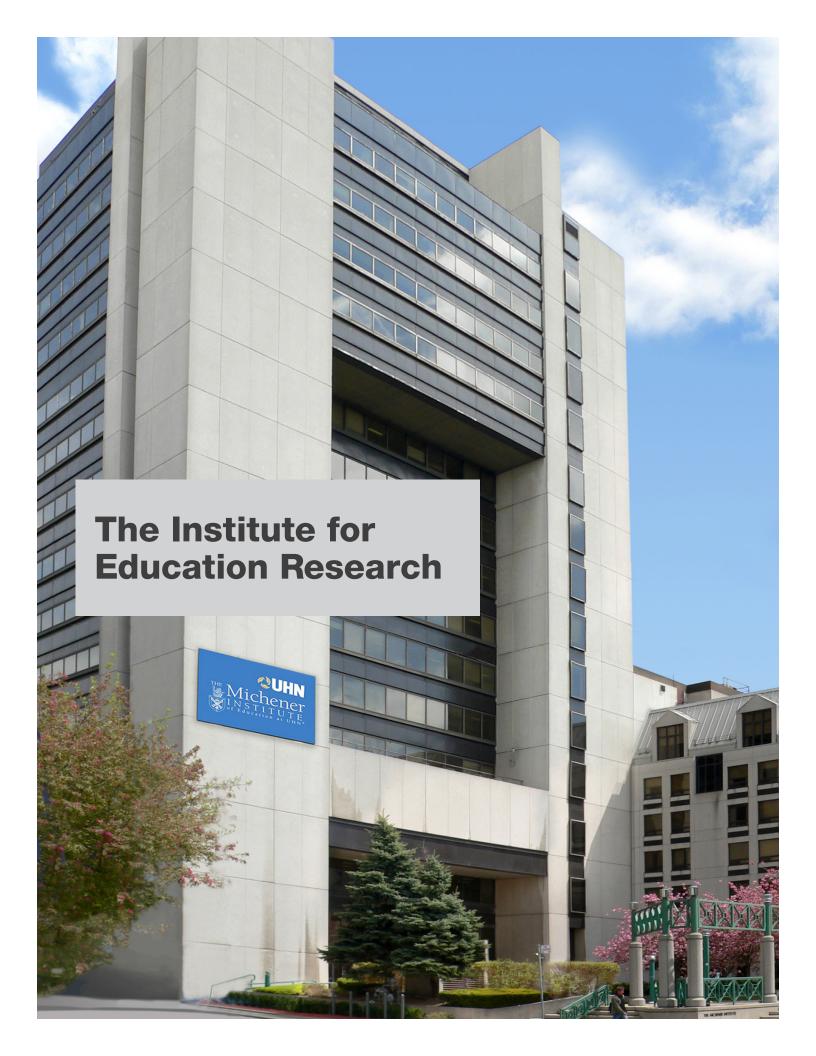
Research Highlight

DIGITAL CARE DOES A HEART GOOD

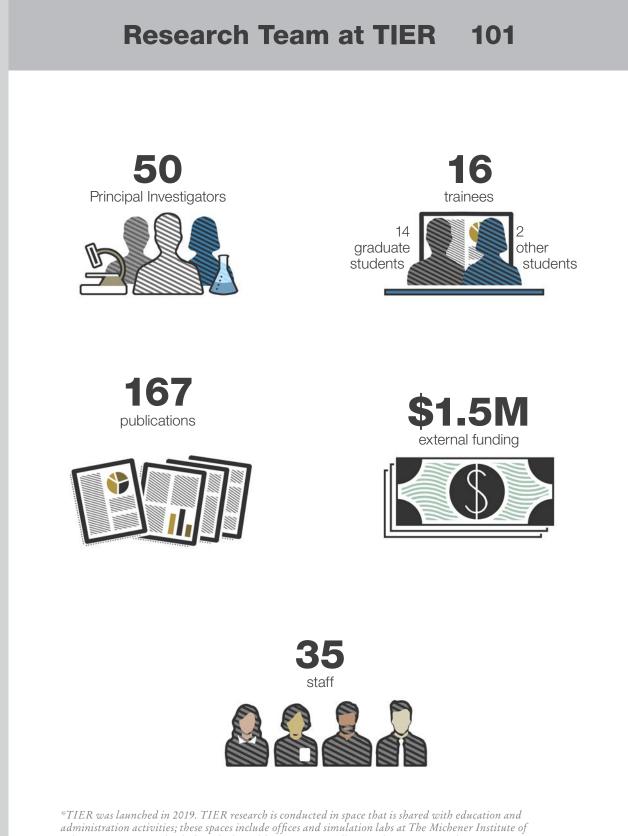
Long before the pandemic necessitated the adoption of remote care, UHN's Centre for Global eHealth Innovation and the Ted Rogers Centre for Heart Research at the Peter Munk Cardiac Centre were developing and evaluating digital health solutions, including a heartmonitoring app known as *Medly*.

The app, which is available by prescription only, collects data on patient symptoms and three measures of heart health: blood pressure, heart rate and patient weight. It analyzes the data using clinically validated algorithms to provide instant feedback to patients. It also alerts the clinical care team of serious changes to a patient's health. Dr. Patrick Ware, Program Lead at eHealth Innovation, and Dr. Emily Seto, Techna Affiliate Scientist, evaluated *Medly* in a rigorous study and found that it cuts hospitalizations in half and improves the heart health and self-care of patients. *Full Story / Scientific Article*









Education at UHN School of Applied Health Sciences, as well as at other sites across the UHN campus.

Learning From Your Mistakes

Failing can lead to better and more adaptive learning

If you have ever tackled a new challenge more easily after having failed a similar challenge in the past, then you have experienced productive failure. As a teaching strategy, it is highly effective and is known to help build problem-solving skills.

Dr. Naomi Steenhof, Education Investigator at TIER, led a study to determine whether experiencing failure can help health care professionals to learn better.

"Learning activities based on productive failure are often more difficult to design; they are also tough for students because they involve failing at an assigned task," says Dr. Steenhof. "Naturally we wondered: is it really worth the extra effort?"

For a group of pharmacy students, the research team designed two learning activities that had the same learning objective. Half of the group was not provided the correct answer and asked to generate a solution themselves—i.e., the productive failure strategy. The other half of the group was asked to contrast correct and incorrect answers from past students—a strategy that the researchers referred to as indirect failure.

The two groups showed similar performance when they were tested on the concepts that they had just learned. However, when asked to learn a new



and related concept, students in the productive failure group performed better than those in the indirect failure group. "The struggles that they had experienced in the learning activity had improved their ability to learn new concepts," says Dr. Steenhof.

Quizzes and exams are designed to evaluate how well the students understand the course material. However, students often memorize the concepts then forget the knowledge soon after.

"A high test score does not always translate to learning, and a low score does not mean that learning has not occurred," cautions Dr. Steenhof.

"Test performance and learning are not the same, and we should focus more on learning when evaluating the success of students and curricula."



Steenhof N et al. Adv Health Sci Educ Theory Pract. 2020 Dec. doi:10.1007/s10459-020-10013-y. Supported by the UHN Foundation.

(Above right) Dr. Naomi Steenhof. (Right) Dr. Janet Papadakos. (Below, left to right) Asia van Buuren, Wid Yaseen and Dr. Marcus Law.



Research Highlights

BOOSTING CONFIDENCE FOR BETTER OUTCOMES

Starting chemotherapy after a cancer diagnosis can be distressing for individuals and their caregivers. A study led by Dr. Janet Papadakos revealed that *patient education classes* preceding chemotherapy can alleviate anxiety and improve preparedness, particularly when the information is tailored to specific cancer groups. By boosting confidence and feelings of control, the classes helped patients to better manage the side effects of chemotherapy and ultimately improve their treatment outcomes. *Full Story / Scientific Article / Link to Courses*



START AS YOU MEAN TO GO ON

A study led by Dr. Marcus Law and two medical students at the University of Toronto, Asia van Buuren and Wid Yaseen, found that Canadian medical school orientations often fall short when it comes to fostering inclusion. Interviews conducted with students from five medical schools revealed that depictions of the profession during orientation did not reflect diverse identities. This caused students from underrepresented groups to feel pressured to hide their unique qualities and backgrounds. "Increasing diversity is not enough. Schools need to safeguard inclusion from the moment that students walk through the doors," says Dr. Law. *Full Story / Scientific Article*

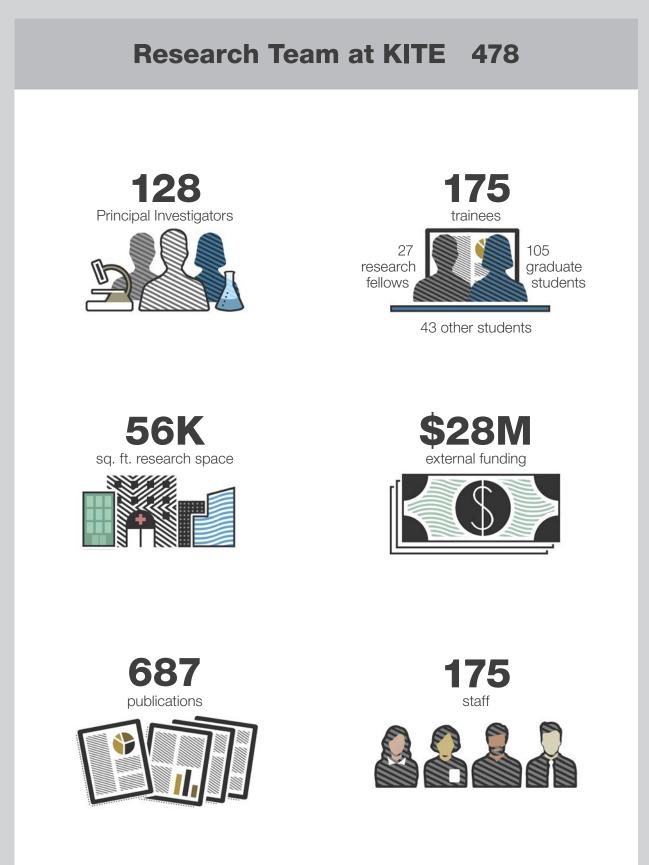
The KITE Research Institute

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Toronto Rehab

THE NUMBER ONE RENABILITATION RESEARCH CENTRE IN THE WORLD





Street Smarts

Study reveals the factors that affect older adults' acceptance

of automated cars

Self-driving cars may one day enable individuals who can no longer safely drive—to return to the freedom of the road. The technology has the potential to enhance the independence and wellbeing of these individuals, which include older adults who may no longer have adequate vision, reflexes or focus. The successful application of self-driving cars to enhance independence depends on whether older adults accept and use the technology. To explore this issue, Drs. Alex Mihailidis and Jennifer Campos tested how various factors—including the drivers' age, driving style and road conditions impacted the acceptance of the technology.

Their research team, led by PhD student Shabnam Haghzare, designed a series of driving scenarios for participants ranging in age from 65 to 90. These scenarios, which were tested using the KITE Research Institute's state-of-the-art *DriverLab* simulator, exposed the participants to challenging conditions such as heavy rain and dense traffic, as well as clear daytime roads. For each scenario, two driving sessions were completed: one that was controlled by the participant; and one that was controlled by the computer to simulate a self-driving car. By assessing feedback from the participants and their driving styles (such as their braking and acceleration), the team determined the factors that influenced the participants' comfort with and approval of automated vehicles. Participants whose driving style differed from that of the computer and those who were older had less confidence in the self-driven vehicle.

"We also saw that the participants' acceptance of the technology improved after undertaking the computer-controlled simulation," says Dr. Mihailidis. "Exposing older adults to the technology and customizing the automated driving style to match the passenger's preferences will be crucial for building trust."

Adoption of self-driving cars will improve older adults' autonomy and help to reduce motor vehicle collisions and crashes—a leading cause of unintentional injury and death in Canada.

Haghzare S, et al. Accid Anal Prev. 2021 Dec 10. doi:10.1016/j. aap.2020.105919. Supported by the Canadian Institutes of Health Research, AGE-WELL NCE, UBER Canada, the Schwartz Reisman Institute for Technology at the University of Toronto and the UHN Foundation.

(Above) The KITE Research Institute's DriverLab simulator. (Below left) Dr. Angela Colantonio. (Below right) Dr. Behrang Keshavarz.



Research Highlights

GETTING A GRIP

Drs. Tilak Dutta and Shaghayegh (Zahra) Bagheri found that winter boots that performed well on lab-based anti-slip tests reduced the risk of slips and falls for workers exposed to realworld winter conditions. The researchers used the KITE Research Institute's *WinterLab* to conduct the tests, which also revealed that winter boots made with advanced composites (i.e., two or more different materials) had superior anti-slip characteristics than boots made with conventional materials. Individuals wearing the superior labtested boots experienced approximately 70% fewer slips and 80% fewer falls. To see which footwear brands perform the best, see the *Rate My Treads* website. *Full Story / Scientific Article / Video*

BETTER WITH MUSIC

Virtual reality can be an important tool for engaging patients in rehabilitation, but many individuals can become nauseated or dizzy in a virtual environment. Research led by Dr. Behrang Keshavarz discovered that listening to music can alleviate the effects of visually induced motion sickness. The research team found that listening to music was most helpful when the listener was able to choose music that they liked. *Full Story / Scientific Article*

BRINGING VIOLENCE INTO VIEW

Stay-at-home orders to curb the spread of COVID-19 have fueled a 'shadow pandemic' of domestic abuse. Dr. **Angela Colantonio** and her former trainee Dr. **Binu Jacob**, led a study that highlighted the need for individualized care for victims of domestic violence. They found that key differences in the care sought and received by victims were associated with sex and socioeconomic factors—suggesting that customized care is important for these individuals. *Full Story / Scientific Article / Online Toolkit If you need crisis support in Ontario, call 211*

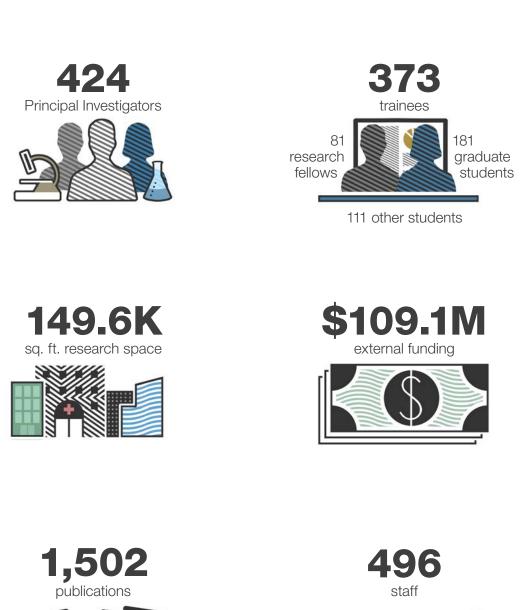
Toronto General Hospital Research Institute

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Third Time's a Charm

Clinical trial reveals that COVID-19 booster is safe and effective in transplant patients

The first randomized, placebo-controlled trial of a COVID-19 booster vaccine in transplant recipients has revealed that a third dose of the Moderna vaccine is safe and induces a robust immune response.

"We knew from previous studies that two doses of vaccines are not enough to produce a strong immune response against COVID-19 in transplant patients," says the joint-senior author of the study, Dr. Deepali Kumar.

The clinical trial was randomized, double-blind and placebo-controlled—providing a high level of rigour. A total of 120 transplant patients that had not previously contracted COVID-19 and had received two doses of the Moderna vaccine were enrolled in the trial.

At the two-month mark after their second dose, half of the participants received a third shot, while the other half received a placebo. The findings revealed that the booster shot increased antibodies against the spike protein to levels that are believed to provide at least 50% protection against developing COVID-19. After three doses, only 18% of the participants in the placebo group showed this response, whereas 55% of those in the



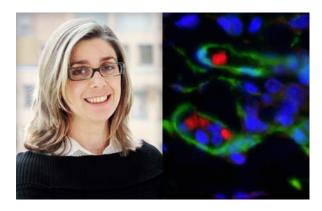
vaccine group met these antibody levels. The research team also found that the booster led to the production of T-cells and neutralizing antibodies, both of which specifically target and neutralize the virus. In the Moderna group, 60% tested positive for at least some ability to neutralize the virus, compared to only 25% of participants on placebo.

In terms of safety, the booster vaccine was well tolerated, associated with only mild side effects and did not lead to organ rejection. "We found that the third dose was safe and increased immune responses in transplant patients. These findings are quite definitive and tell us that third doses should be given to this vulnerable population to help prevent COVID-19," says Dr. Atul Humar, Medical Director of the UHN Ajmera Transplant Centre, and the joint-senior author of the study.



Hall VG, et al. N Engl J Med 2021 Aug 11. doi:10.1056/ NEJMc2111462. Supported by the Ajmera Transplant Centre, the Di Poce Transplant Fund, the Government of Canada's COVID-19 Immunity Task Force and the UHN Foundation

(Above, left to right) Drs. Atul Humar and Deepali Kumar. Photo: Tim Fraser Photography. (Below left) Dr. Sara Vasconcelos. (Below right) Immunofluorescence image showing adipose-derived microvessels (green) after being transplanted. Cell nuclei are stained blue and red blood cells are stained red.



Research Highlights

COVID-19 IN HEALTH CARE WORKERS

Drs. Atul Humar and Deepali Kumar have also helped to define the rate of asymptomatic carriers of the SARS-CoV-2 virus. Along with Scientific Associate Dr. Victor Ferreira, they identified the percentage of health care workers at UHN who did not show symptoms despite being infected with the virus. They found that for every seven workers with symptoms, there was around one who was asymptomatic, emphasizing the benefits of routine screening. *Full Story / Scientific Article*

UNRAVELLING GOOD FROM THE BAD

The most commonly used immunosuppressant used to prevent organ transplant rejection—a drug known as tacrolimus—comes at a cost: it can make transplant recipients more susceptible to infections. A research team co-led by Dr. **Mamatha Bhat** discovered that tacrolimus reduces the activity of a group of genes in immune cells known as Kupffer cells. These cells capture and kill bacteria in the blood as it is filtered through the liver. "By exploring how tacrolimus works at the molecular level, our findings suggest that there may be a way to protect Kupffer cells and prevent this unwanted side effect," says Dr. Bhat. *Full Story / Scientific Article / Video of Kupffer Cells Catching Bacteria*

GROWTH AND REPAIR

While cell therapies capable of replacing damaged heart tissue after a heart attack are under development, challenges remain. One major hurdle is to ensure that the transplanted cells survive. Dr. Sara Vasconcelos, with Research Associate Dr. Xuetao Sun and other UHN collaborators, helped to address this challenge by transplanting blood vessels harvested from fat tissue along with the heart muscle cells—a strategy that improved heart function by promoting the survival of the transplanted cells. *Full Story / Scientific Article / Lab Website*

Awards and Distinctions

Selected honours awarded to UHN researchers



Dr. Cheryl Arrowsmith Fellow, Royal Society of Canada

Dr. Anne Bassett

2020 Lieber Prize for Outstanding Achievement in Schizophrenia Research, Brain & Behavior Research Foundation

Dr. Jennifer Bell

2020 Early Career Investigator Award, Canadian Association of Psychosocial Oncology

Dr. Sandra Black

2020 Lifetime Achievement Award, Society for Behavioral and Cognitive Neurology

Dr. Michael Brudno

Canada CIFAR Artificial Intelligence Chair, Canadian Institute for Advanced Research

Dr. Angela Colantonio

2020 William Fields Caveness Award, Brain Injury Association of America2020 John Stanley Coulter Award, American Congress of Rehabilitation MedicineTier 1 Canada Research Chair in Traumatic Brain

Injury in Marginalized Populations (new)

Dr. Marcelo Cypel

2020 Academy Award, Academia Sul-Rio-Grandense de Medicina

Dr. Tirone David

2020 Lifetime Achievement Award, American Association for Thoracic Surgery

Dr. Karen Davis

Fellow, Royal Society of Canada

Dr. John Dick

Member, National Academy of Medicine

Dr. Geoff Fernie

Member of the Order of Ontario, Government of Ontario Fellow, The Canadian Academy of Engineering

Dr. Andrea Furlan

2020 Pain Excellence Award, Pain Society of Alberta

Dr. Herbert Gaisano

Tier 1 Canada Research Chair in Diseases of the Exocrine and Endocrine Pancreas (new)

Dr. Dafna Gladman

Fellow, Canadian Academy of Health Sciences

Dr. Benjamin Haibe-Kains

Tier 2 Canada Research Chair in Computational Pharmacogenomics (new)

Dr. Kathryn Howe

2020 Wylie Scholar, Vascular Cures

Dr. Doris Howell

2020 CAPO Lifetime Achievement Award, Canadian Association of Psychosocial Oncology

Dr. Harry Janssen

2020 Research Excellence Award, Canadian Association for the Study of the Liver

Dr. Michael Jewett Member of the Order of Canada, The Governor General of Canada

Dr. Jennifer Jones 2020 CAPO Award for Research Excellence, Canadian Association of Psychosocial Oncology

Dr. Gordon Keller 2020 Bloom Burton Award, Bloom Burton & Co.

Dr. Shaf Keshavjee

2020 Governor General's Innovation Award, Rideau Hall Foundation

Dr. Rama Khokha Fellow, Royal Society of Canada

Dr. Ana Konvalinka

2020 CST Research Excellence Award, Canadian Society of Transplantation

Dr. Lakshmi Kotra

2021 Julia Levy Award, Society of Chemical Industry

Dr. Kulamakan Mahan Kulasegaram

2020 Outstanding Achievement Award in the Evaluation of Clinical Competence, Medical Council of Canada

Dr. Sonya MacParland

2020 Early Career Researcher Award, Canadian Society for Virology

Dr. Tak Mak

2021 Szent-Györgyi Prize for Progress in Cancer Research, National Foundation for Cancer Research

Dr. Katherine McGilton Fellow, Canadian Academy of Health Sciences

Dr. Maria Cristina Nostro

2020 Innovation & Science Award, Italian Chamber of Commerce of Ontario

Dr. Catherine O'Brien

Tier 2 Canada Research Chair in Translational Research in Colorectal Cancer (new) Dr. Brian O'Sullivan

2020 Gold Medal Award, American Society for Radiation Oncology

Dr. Anahi Perlas Fontana 2020 ASRA Trailblazer Award, American Society of Regional Anesthesia and Pain Medicine

Dr. Anthony Perruccio

2020 Distinguished Scholar Award, Association of Rheumatology Professionals

Dr. Trevor Pugh

2020 Canada's Top 40 Under 40, Caldwell

Dr. Ravi Retnakaran Fellow, Canadian Academy of Health Sciences

Dr. Peter St. George-Hyslop

2020 Margolese National Brain Disorders Prize, University of British Columbia Faculty of Medicine

Dr. Darrell Tan

Tier 2 Canada Research Chair in HIV Prevention and STI Research (new)

Dr. Paaladinesh Thavendiranathan

Tier 2 Canada Research Chair in Cardio-Oncology (new)

Dr. Zahi Touma

2021 Emerging Investigator Award, Canadian Rheumatology Association

Dr. Ming-Sound Tsao

Fellow, Royal Society of Canada

Dr. Rebecca Wong

2020 Academic Leadership Award, Canadian Nuclear Isotope Council

Dr. Azadeh Yadollahi

Tier 2 Canada Research Chair in Cardiorespiratory Technologies (new)

Dr. Gelareh Zadeh

2021 Top 25 Women of Influence Award, Women of Influence

Above and Beyond

Donors remain committed to fueling cancer research in uncertain times

The past year highlighted one unwavering truth: cancer remains a top priority for our supporters. Generous donors went above and beyond to support life-saving cancer research, helping us grant \$113M to the Princess Margaret Cancer Centre—a new record! Here are just some of the ways in which our supporters are enabling the biggest and brightest minds in science to tackle one of our world's greatest challenges.

TAKING ON GRAND CHALLENGES

The Princess Margaret Cancer Foundation, in partnership with generous donors, provided funds to support bold, high-impact research through the inaugural *Princess Margaret Grand Challenges*. Four grants of \$500,000 were awarded in the areas of early detection, high-definition therapeutics, digital intelligence and human touch in cancer care. Through these investments, scientists are exploring the use of liquid biopsies in the early detection and targeted treatment of lung cancers. They are also testing whether the Hexoskin smart shirt—currently used to monitor astronauts— can be used to evaluate quality of life and treatment responses, and estimate life span in palliative patients. A sincere thank you to Canadian gold mining company **Agnico Eagle**, who pledged an outstanding \$10M to fund in part the *Grand Challenges* competitions in the areas of early detection and high-definition therapeutics.

INVESTING IN RESEARCH

Through the *Invest in Research* program, donors get a front-row seat to the future of cancer care and vote on which research project they believe will have the greatest impact on conquering cancer. Thanks to their exceptional generosity, three scientists received funding for their transformative research: Dr. **Geoffrey Liu** for advancing the early detection of lung cancers and relapsing tumours; Dr. **Catherine O'Brien** for identifying ways to target colorectal cancer cells that evade treatment by entering a dormant state; and Dr. **Anna Spreafico** for finding ways to detect and monitor skin cancer cells that persist after treatment.

TRANSFORMING THERAPIES AND CANCER CENTRE SPACE This year, the Longo's *Charitable Family Foundation* made a landmark gift of \$2.5M towards two major areas of impact—UHN's *Tumour Immunotherapy Program* and the cancer centre's *Space Transformation* initiative. Funding emerging research in immunotherapy is part of the philanthropic vision of the Longo family (pictured below). This generous donation will advance targeted treatments to increase survival rates in the years ahead.





Selected winners of the inaugural Grand Challenges Awards: Dr. Natasha Leighl (above left), who is advancing a blood test capable of detecting lung cancer; Dr. Jennifer Croke (top right), who is working with a team of UHN researchers to develop tools to support cancer patients and their care givers; and Drs. Philip Wong and Aisling Barry (bottom right), who are testing the Hexoskin smart shirt.

GAMERS UNITE AGAINST CANCER

A global initiative was launched to enable the gaming community to use their love of conquering games to raise money to conquer cancer. Learn more at *QuestToConquerCancer.ca*.

WORLD-CLASS MUSIC, WORLD-CLASS

SPACE A virtual concert was performed by the Toronto Symphony Orchestra to celebrate the completion of the first phase of our *Space Transformation* project. To watch, *click here* or on the video below.





Stronger Together

UHN Foundation launched to support the full spectrum of research

On April 1, 2021, the UHN Foundation was born through the amalgamation of the Toronto General & Western Hospital Foundation and the Toronto Rehab Foundation. By leveraging the strengths of each, this merger enhances the foundation's ability to support the full spectrum of research conducted at six of UHN's seven research institutes, including fundamental discoveries, new therapies, clinical care and rehabilitation.

In the last fiscal year, the foundation exceeded its fundraising goals by securing approximately \$212.7M. This achievement is particularly exceptional given the challenges posed by the COVID-19 pandemic. Despite the need for lockdowns and physical distancing, which made it impossible to hold galas or bring people into the hospital for informational tours and events, there has been an outpouring of support.

Exceptional donors came forward on their own because they saw a great need. Some gave extraordinary gifts. Those who donated over

LANDMARK SUPPORT FOR ARTHRITIS RESEARCH

Walter and Maria Schroeder provide a \$25M donation that enables the launch of the Schroeder Arthritis Institute

\$1M included Leo and Sala Goldhar, Juan and Stefania Speck, Melanie Munk, Loretta A. Rogers, the FDC Foundation and the New Hope Foundation—thanks to all for making a difference!

Over \$13.3M of these funds supported COVID-19-related projects, with \$5M going to research.
Supported projects include the following:
Establishment of the COVID-19 Preserve
Biobank, a vital resource that will support a wide range of research into ways to predict the course of the disease, develop new vaccines and test new treatments. Led by Dr. Sharon Walmsley.

• Evaluating the effectiveness of interferon therapy for the treatment of COVID-19. Led by Drs. Jordan Feld and Atul Humar.

• Testing the effect of inhaled **nitric oxide therapy for the treatment of advanced COVID-19**. Led by Drs. Atul Humar and **Marcelo Cypel**.

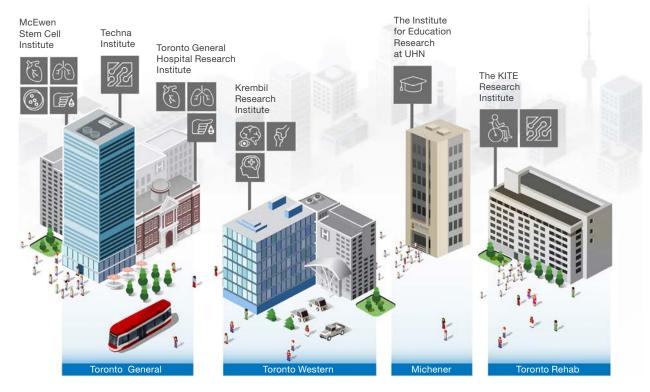
• Development of an intubation shield to protect frontline health care workers from COVID-19. Led by Dr. Ian McGilvray.

VISIONARY GIFT

An anonymous \$10M gift for vision research enables Dr. Jeremy Sivak (pictured) to lay the foundation for a translational research program at the Donald K. Johnson Eye Institute

Schroeder Arthritis Institute





The name UHN Foundation was chosen based on extensive research, including feedback from our donor and volunteer communities, stakeholders and the general public. The name reflects an expanded fundraising mandate that covers six UHN research institutes (listed above near grey logos representing the research areas of focus) and four of UHN's main sites (listed above in blue bars).

LASTING LEGACY

The Krembil Foundation provides \$3.38M for ongoing support of the Krembil Research Institute (pictured: the Krembil Discovery Tower)

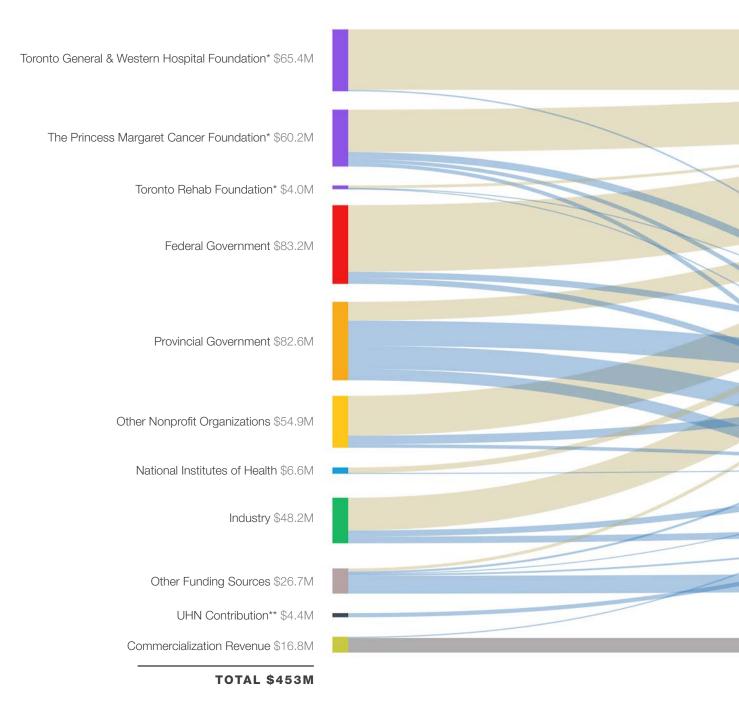
TACKLING LUNG DISEASE

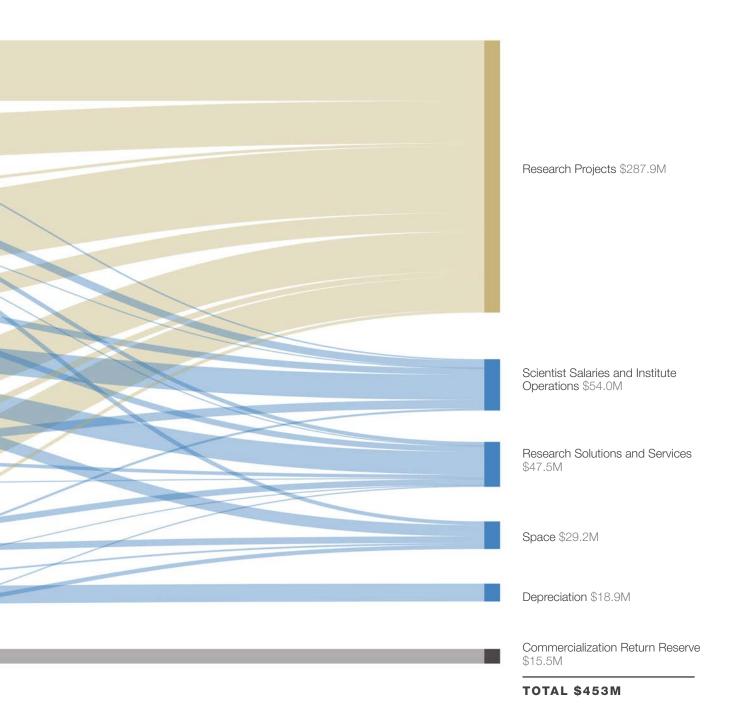
Donald K. Jackson provides \$2M to Drs. Keshavjee and Waddell (pictured, center) to support research into new treatments for idiopathic diseases of the lung

Krembi Relentless.

Financials

Flow of research funding by source for the 2020/2021 fiscal year





The above diagram shows how research funding was utilized towards UHN's research mission for the fiscal year ending on March 31, 2021. Values are rounded to the nearest \$100,000. *These values are based on expenses incurred at UHN and categorized according to research-specific spending; note that on April 1, 2021, the Toronto Rehab Foundation and the Toronto General & Western Hospital Foundation were amalgamated into the UHN Foundation. **These funds do not originate from the Ontario Ministry of Health and Long-Term Care. For UHN's audited financial statements, please visit www.UHN.ca.

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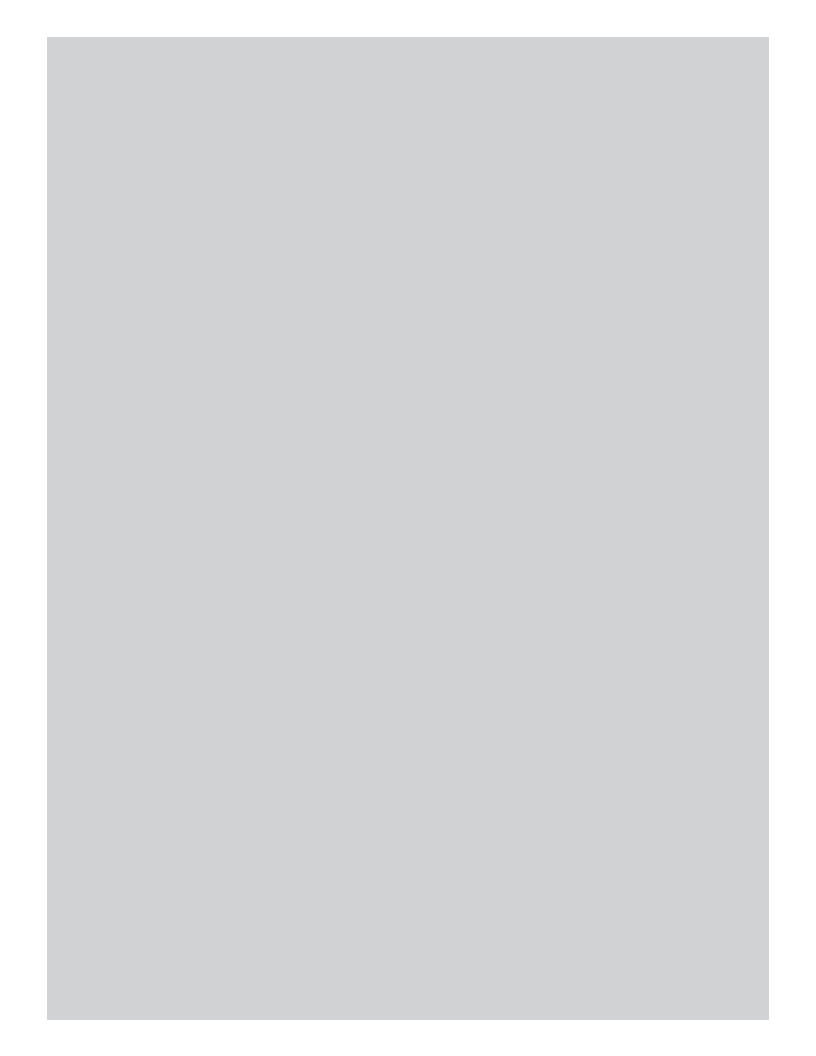
Darlene Dasent Brian Hodges Sheryl Seidman Brad Wouters

Disclaimers: All data are accurate as of March 31, 2021. Publication data is reported for the previous calendar year. Financial data is reported for the 2020/21 fiscal year ending on March 31, 2021.

Research Snapshot Metrics reported for UHN (page 2) and individual research institutes (pages 9, 13, 17, 21, 25, 29, 33) include data for all Principal Investigators (PI). PIs either have a formal appointment at a UHN research institute or are aligned to a UHN research institute as either a clinician scientist or a clinician investigator. PIs affiliated with two or more institutes are included only once in the total Research Snapshot for UHN.

PI Data provided by UHN Research Strategy and Planning. **Publication Data** provided by UHN Research Strategy and Planning. Publications include articles, reviews and proceeding papers indexed in the Web of Science Core Collection that were published in the previous calendar year with at least one UHN PI in the author list. Those authored by more than one UHN PI are included once in the UHN and institute Research Snapshots. **Staff and Trainee Data** provided by UHN People & Culture (formerly Human Resources). Trainee values reflect the number of students whose primary supervisor is appointed at UHN. **Space Data** provided by UHN Facilities Management - Planning, Redevelopment & Operations (FM-PRO). Institute space values include institute-specific space only. UHN space values include all institute space, as well as core research facilities, Research Solutions and Services (RSS) space, and external companies and programs on UHN premises. **Financial Data** provided by UHN Research on page 43. Research institute external funding data are calculated based on the institute affiliations of PIs.

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