

KREMBIL

Krembil Research Institute | Arthritis

IT'S A YOUNG PERSON'S PROBLEM, TOO

Arthritis affects thousands of teenagers and young adults every year

A HELPING HAND

How doctors are repairing damaged hands

CAN AI FIND A CURE?

Leading researchers talk tech in a roundtable Q&A



No more
Pain

Krembil researchers are on a mission to cure arthritis.

Toronto Western
Hospital 



Dr. Mohit Kapoor

Dr. Robert Inman

THE STATISTICS ARE STAGGERING, AND THEY'RE GETTING WORSE

One in five adult Canadians is currently living with arthritis, a painful, debilitating chronic health condition that affects the mobility of joints and bones. By 2040, that number is expected to rise by 50 per cent, affecting nearly a quarter of our population.

These shifting demographics currently leave our aging population with increasing levels of disability, which in turn limits earning potential in the most productive years, affects relationships with family and friends, and even impacts mental health. Arthritis hits us where it hurts the most.

This is a crisis, and we at the Krembil Research Institute are on the front line. It's time to invest in our future, by empowering scientific research, so that we can help more people, sooner.

University Health Network's (UHN) Arthritis Program, based at Toronto Western Hospital, incorporates rheumatology, orthopedics, hand and osteoporosis programs under one roof. The program has evolved with the changing needs of our society.

We have assembled a team of the world's most innovative arthritis clinicians and researchers. We have given them the tools, the resources and the support they need to push the boundaries of discovery and to translate those discoveries into advanced patient care.

New technologies – such as sophisticated imaging and biological profiling with immune and inflammatory markers, as well as predictive analytics and artificial intelligence – allow us to diagnose patients earlier, customize their treatment and track their progress in real time.

This interdisciplinary approach helps us to break down silos in order to speed up progress. Our quest for answers has led us to discover, innovate and improve patient care for those who need it most.

It's patients like Jill Miller, Susan Rivers and Everton Williams, all featured in this magazine, who inspire and energize us. We are driven by a passion to make a difference in their lives – to diagnose them earlier and provide them with effective treatments, to help them better manage their symptoms and improve their mobility. Ultimately, we want to help them achieve productive and fulfilled lives, free of pain and disability.

Today, there is no cure for arthritis, but we're envisioning one for tomorrow.

Let's all work together to make this dream a reality.

Dr. Robert Inman
Medical director, UHN Arthritis Program
Senior scientist, Krembil Research Institute

Dr. Mohit Kapoor
Research director, UHN Arthritis Program
Senior scientist, Krembil Research Institute

Krembil Research Institute

By the numbers

Incidences of arthritis have ballooned, and it's only going to affect more people in the future. Here are some numbers – about arthritis and University Health Network's Arthritis Program – to put things into perspective.

350 million



People living with arthritis around the world – it's a leading cause of disability
(Global RA Network)

\$35 billion +



Cost of arthritis, injuries and musculoskeletal-related diseases to the Canadian health care system
(Canadian Institutes of Health Research)

50%

Canadians living with arthritis who are under 65.
(Arthritis Society)

20 years



until the number of Canadians living with arthritis increases by 50%
(Arthritis Society)

6 million

Canadians currently living with arthritis
(Arthritis Society)

UHN'S ARTHRITIS PROGRAM

80,000+

Patients treated annually

1,200+

JOINT REPLACEMENT procedures performed every year



150,000+

TISSUE SAMPLES

from ankylosing spondylitis, lupus, osteoarthritis and psoriatic arthritis – in Krembil's arthritis biobank, one of the largest of its kind in North America



Researchers at the Krembil Research Institute were the **FIRST TO DISCOVER microRNA TISSUE BIOMARKERS** associated with spine osteoarthritis

LARGEST MULTIDISCIPLINARY ARTHRITIS RESEARCH PROGRAM IN CANADA, integrating medical, surgical and basic science aspects of arthritis

5

Number of **international research networks** studying arthritis that are headquartered at Krembil

KREMBIL

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A look at how far University Health Network's Arthritis Program has come.

BACK in the GAME

More and more athletes are returning to competitive sports after ACL injuries

By Wendy Haaf



EVERTON WILLIAMS HAD ALWAYS WANTED to become a professional football player. But at 24, just as he was finishing university, he tore the ACL ligament in his knee. Williams, an offensive lineman, missed training camp for Canadian Football League prospects that year, but then signed with the Hamilton Tiger-Cats, crediting early intervention, including knee reconstruction surgery, for helping him recover months ahead of schedule. “It’s like brand new,” he says.

Williams is one of about 5,000 people in Ontario who undergo ACL repair each year. Some do so because non-surgical treatments haven’t sufficiently restored normal function; others, like Williams, are athletes intent on resuming sports and want to avoid further joint damage. “Surgical intervention prevents knee buckling, and secondary damage to knee joint structures that can occur with pivoting and twisting motions associated with sport,” explains Dr. Jas Chahal, an orthopedic surgeon and Krembil Research Institute clinician scientist. He adds that people of all ages and activity levels can benefit from ACL surgery if non-operative care isn’t effective.

Currently, Dr. Chahal is investigating whether leg position during surgery affects patient outcomes. If it does, then health professionals may be able to customize the surgical and rehabilitation process to each individual. “With an appropriate treatment program including surgery and physiotherapy, athletes like Everton can recover from their injuries and continue to play competitive sports at the highest levels,” explains Dr. Chahal.

Williams is just one of many players, including Tom Brady and Kyle Lowry, who haven’t missed a step post-surgery. “I’m feeling great and looking forward to getting back in the game,” he says.

Osteoporosis’ effect on astronauts

Krembil researchers are helping NASA come up with better bone strength guidelines

By Wendy Haaf

DR. ANGELA CHEUNG isn’t just a renowned osteoporosis researcher; you might say her expertise is out of this world. She and her team pioneered research to better understand how various factors affect bone health, which then helped NASA create guidelines for more accurately measuring bone strength in astronauts. The space agency wants to ensure the bone loss that occurs in space flight doesn’t place them at risk of potentially dangerous fractures after returning to Earth. A hip fracture, for instance, can lead to permanent disability, including arthritis, and the need for long-term care.

A living tissue, bone is continually being remodelled by two teams of cells: osteoclasts, which tear it down, and osteoblasts, which rebuild it. If the “demolition crew” outpaces the “bricklayers,”

bone becomes weak, which is what happens in osteoporosis. (Weight-bearing exercise, like walking, prods the bricklayers to keep working, which is why low gravity causes bone loss.)

Typically, doctors use what’s called dual X-ray absorptiometry to measure bone density, but it can’t “see” whether the framework inside the bone is sturdy or spindly; soundly or shoddily constructed. However, high-resolution peripheral quantitative computer tomography (HR pQCT), which uses low-dose CT and sophisticated software, can provide information about a bone’s structure, says Dr. Cheung.

Scanning may be a better way to evaluate astronauts, as you need both bone structure and mineral content to determine bone strength, she says. HR pQCT is sensitive enough to monitor whether bone loss treatments, such as medication, work in space flight.

Recently, NASA incorporated Dr. Cheung’s recommendations into their guidelines for evaluating bone integrity – which are more important than ever with the advent of long-duration missions. So, thanks to Dr. Cheung and her colleagues, astronauts and osteoporosis patients alike will benefit from this research, and can be more confident about their future bone health.



Dr. Angela Cheung

Meet your future researchers

Soon-to-be scientists come to Krembil to train

Promising trainees come to Krembil from around the world to study with top scientists and physicians, and participate in leading-edge arthritis research. Here are four early-career researchers who are already on their way to becoming superstars in the field.



HELAL ENDISHA
PhD
United Kingdom

RESEARCH GOAL

“Current therapies for osteoarthritis only ease symptoms like pain; our goal is to develop a disease-modifying tool that can stop cartilage destruction. In obesity, which is the number-one risk factor for osteoarthritis after aging, fat cells release harmful inflammatory molecules that can target the joints. I’m looking at the influence of obesity on osteoarthritis; specifically whether a molecule that we previously found is present at high levels in the joint fluid of people with advanced-stage osteoarthritis and contributes to joint destruction.”

KEY ACCOMPLISHMENTS

Found a common link between obesity and osteoarthritis – abnormalities in the production of a molecule that contributes to cartilage destruction.



ERIC GRACEY
PhD
New Zealand

RESEARCH GOAL

“My goal is to understand spondyloarthritis in order to develop more effective treatments. In this type of arthritis, which starts when people are in their 20s or 30s, you get destruction of joints in the spine and limbs, but you also get fusion of the joints. The drugs we have now reduce symptoms, but they don’t prevent joint fusion.”

KEY ACCOMPLISHMENTS

Discovered that an immune cell involved in inflammatory bowel disease plays a role in spondyloarthritis and pinpointed a potential target for treatment – a specific type of white blood cell.



AKIHIRO NAKAMURA
Rheumatologist,
PhD candidate
Japan

RESEARCH GOAL

“I’m working on finding a new therapeutic target in ankylosing spondylitis. Ankylosing spondylitis has two main features – inflammation and abnormal bone formation in the joints of the spine. Currently, we don’t have treatments that stop bone formation.”

KEY ACCOMPLISHMENTS

Co-discovered a small molecule that is now being tested as a prospective treatment for osteoarthritis in the spine and knees.



MEITAL YERUSHALMI
PhD candidate
Israel

RESEARCH GOAL

“About 30 per cent of patients with psoriasis will eventually develop psoriatic arthritis. I’m looking at whether the skin microbiome – the community of bacteria on the surface of the psoriatic lesions – could be involved in triggering psoriatic arthritis.”

KEY ACCOMPLISHMENTS

Found an association between the diversity of surface skin bacteria on psoriatic lesions and inflammation severity, as well as a link between microbiome diversity and a gene that predisposes people to psoriasis.

NO MORE PAIN



While she still feels the effects of osteoarthritis, long-time weightlifter Jill Miller continues to train and compete.

Osteoarthritis afflicts one in six Canadians – and the painful disease is only going to affect more people in the future. Scientists at the Buchan Arthritis Research Centre at Krembil Research Institute are hoping to stop it before it starts

By Sarmishta Subramanian

When Jill Miller competed at the Pan American Masters Weightlifting Championships in Orlando, Fla., in late May 2019, hoisting an 88-lb barbell over her five-foot-two-inch frame, people watching would never have guessed she was due in a Toronto operating room five weeks later, for surgery on her arthritic right knee. Miller, who is 68 years old, has a high pain threshold. She could weather the tightness in the joint, but she also describes sudden pangs of “a knife-like pain.” During the operation to repair her meniscus – the C-shaped disk of cartilage that cushions the knee and that breaks down in arthritis – her surgeon removed seven floating fragments of bone, adding up to some 13.5 centimetres. These fragments would get stuck in her joint, locking it. “A lot of the time it wouldn’t hurt,” Miller recalls. “But when one of those pieces of bone shifted, eeoowww!”

And that was the good knee. Diagnosed with arthritis in 2012, Miller had the same surgery on her left knee last year – on top of cortisone shots, an injection of stem cells taken from her lumbar area and platelet-rich plasma to trigger healing. She shouldn’t even have been walking, her orthopedic surgeon, Dr. Darrell Ogilvie-Harris, at Toronto Western Hospital, told her. Four days after her July surgery, she was off the anti-inflammation drugs. Within a couple of weeks, she had returned to her gym in Collingwood, Ont., where she would gradually work up to her usual level. Walking long distances is challenging, and it still hurts to travel up and down stairs, but in late July she was in Peru, refereeing a weightlifting championship. “If I wasn’t a bit of a Pollyanna,” Miller admits, “I couldn’t do any of this. I wake up in the morning and it hurts.”

A LURKING EPIDEMIC

Miller is as typical as she is exceptional. One in six Canadians suffer from osteoarthritis (OA). By 2035, it will be one in four. In OA, the cartilage that cushions the bones in the body’s joints degenerates, leaving them

to grind against each other. Knees, hips and spines are all common sites, but OA can hit elbows, shoulders, even thumbs and toes. Age-related changes to joint function – cartilage becoming brittle, the loss of muscle mass – make people more susceptible, but typically there is also a genetic predisposition or another factor such as obesity, a sedentary lifestyle or repeated injury.

Millions of Canadians live with OA – most of whom are not athletes like Miller. It lurks in many more, who may not yet feel its telltale signs: pain or stiffness in the joints, swelling and crackling sounds. By the time there is a diagnosis through X-ray or MRI, the disease has progressed, and the loss of mobility may eventually demand surgery, perhaps the replacement of a hip or knee. There is no way to reverse its damages; treatments only ease the pain.

However, as game-changing research from Krembil shows, long before this point, there are hints of OA at the cellular level: certain molecules, called microRNAs, floating undetected in joint tissue cells. As they increase, they wear down cartilage. If those molecules can be detected so disease can be averted in the first place, it could transform lives. Early detection – and a treatment that modifies the disease, rather than just addresses the symptoms – is the Holy Grail among researchers. And the Arthritis Program at University Health Network is making significant headway. Dr. Mohit Kapoor, the program’s research director and a senior scientist at Krembil, puts it succinctly: “Our mandate is to find a cure.”

In 2016, a team led by Dr. Kapoor, and included spinal surgeon Dr. Raja Rampersaud and rheumatologist Dr. Akihiro Nakamura, identified two significant microRNA molecules in tissue samples of patients with





Dr. Mohit Kapoor's research on microRNAs could help prevent OA from occurring.

“You have to get super lucky to discover something, but you also have to have the infrastructure in place – and patience.”

Dr. Mohit Kapoor
Research director, UHN Arthritis Program

OA of the spine. If DNA molecules contain the cell's genetic blueprint, RNA molecules are the messengers that translate that genetic information into protein production. MicroRNAs are tiny RNAs; they regulate gene expression by silencing or activating certain genes. With funding from the Campaign to Cure Arthritis, Dr. Kapoor's team identified two microRNAs by studying the tissue of patients with mild, moderate and severe arthritis – an ambitious undertaking made possible by specialized technology at Krebil and by its massive arthritis biospecimen biobank, one of the world's largest, with some 150,000 tissue and fluid samples.

One molecule, microRNA 181-5p, proved promising:

the worse the osteoarthritis, the higher its levels were. To learn why, the researchers conducted a series of patient-cell studies and pre-clinical studies. “We started to understand that this molecule is produced in the cartilage, but breaks down the cartilage,” says Dr. Kapoor. Production is triggered by “an inflammatory sort of insult” to the cartilage – that is, injury, a pathological trigger or repeated strain. “And massive production of this molecule starts to damage the cartilage.”

This is what Miller would have been feeling when she went to her doctor with knee pain, as well as pain in her back and legs following an injury. That led to a diagnosis of arthritis of the back and knee. By the time she saw Dr. Ogilvie-Harris in Toronto, her back issues had improved greatly thanks to intensive physiotherapy and her own training – but she still had pain and loss of motion in the left knee.

THE ATHLETE'S DILEMMA

Miller has faced both the reward and risk associated with intensive sports: almost three decades of Olympic-style weightlifting have kept her healthy and fit. But being an athlete might have made her more vulnerable to OA due to injuries, including a partial tear of her ACL. As a past team physician for the Toronto Maple Leafs, Dr. Ogilvie-Harris has had many patients tear an ACL and end up with OA later in life.

Some researchers, including Dr. Kapoor's lab, are pursuing ways to restore or regenerate the cartilage eroded by arthritis. In the three years since identifying microRNA 181-5p, the team has developed a blocker that relies on “anti-sense technology,” which essentially disables the molecule. The blocker has a comb-like structure that locks onto the molecule, preventing it from functioning. The hope is to one day inject it into patients' joints. If it works, it will be the first treatment for OA that halts its progression. It has been effective in pre-clinical studies.

The Kapoor lab's researchers, in conjunction with their orthopedic colleagues, are also working on a diagnostic blood test. “If you have a biomarker that can tell you that you are either at risk or you have osteoarthritis,” says Dr. Kapoor, “it's like having a glucose test [for diabetes].” A blood test could also help doctors determine whether a surgical approach or physiotherapy, for instance, is best. To help develop this test,

QUICK TIPS TO PREVENT OA

- Early diagnosis equals better prognosis
- Keep weight down and make nutrition a priority
- Exercise and avoid injury

Krebil researcher Dr. Amanda Ali is examining blood samples to understand which microRNAs are present in which patients. The next step will be for Dr. Ali to collaborate with orthopedic surgeons, including Dr. Ogilvie-Harris, to study patients with an ACL tear. “We're going to look at the microRNA piece before and after the surgery, and over the next six months to year, to see if we can predict which patients are going to run into trouble with arthritis,” says Dr. Ogilvie-Harris.

“If we can predict that, then we can show these changes in the blood.”

To do this, Dr. Ali is also applying cutting-edge next-generation sequencing – the technology, funded by the Campaign to Cure Arthritis, that sequenced the human genome – to hundreds of patients' blood samples. She's looking at known microRNAs, but also entirely new, undiscovered ones. Dr. Ali, whose first post-doctoral project involved working with seniors with

arthritis in London, Ont., is interested in how lab research translates into the real world. “It's very important to me that the work I'm doing has some kind of relevance to helping people.”

THE FOOD FACTOR

A lot about osteoarthritis remains a mystery. We know that exercise, by building muscle strength, helps ward off OA, and that sports injuries correlate with higher rates of the disease. Some people tear an ACL, have it repaired and still get arthritis later. Others with the same injury don't. With early arthritis, there's a lot of inflammation, Dr. Ogilvie-Harris notes, and with later arthritis, that inflammation disappears. What does that mean? And why is obesity a major risk factor?

Dr. Kapoor and his colleagues, including Drs. Poulami Datta, Jason Rockel and Rajiv Gandhi, have identified four harmful molecules that occur at higher levels in the blood following consumption of a high-fat diet. “Somebody who's consuming a high-fat diet regularly is more likely to have production of these destructive molecules,” says Dr. Kapoor. Indeed, cardiovascular and other ailments cluster with obesity-related OA.

Understanding how biomarkers interact could lead to better treatments, but it takes time. “You have to get super lucky to discover something,” says Dr. Kapoor. “But you also have to have the infrastructure in place – and patience.” Investment, too, is vital for this phase, says Dr. Ogilvie-Harris. He was among a group of surgeons who personally contributed a collective \$2.5 million as part of the Campaign to Cure Arthritis, which launched in 2011 and has raised \$64 million to date.

For now, there is one option available to the millions who might face OA: prevention. Studies point to the role of physical activity, and strength building in



Building muscle strength may help ward off arthritis, says Dr. Ogilvie-Harris.



Understanding which microRNAs are present in a patient could help Dr. Amanda Ali predict who might get arthritis.

particular, in warding off arthritis. “Muscle weakness often precedes the development of arthritis,” Dr. Ogilvie-Harris notes. Part of the landmark U.S. Framingham Heart Study looked at arthritis of the knee and found that patients with strong quadricep muscles were far less likely to get arthritis. Starting exercise at any age, he says, can significantly improve joint health. Stopping it can trigger a decline.

Miller started weightlifting at age 40. When she stops, the effects are immediate: “When I train hard, my back is completely discomfort free,” she says. “Right now, because I can’t lift, it’s worse. But I have never considered giving it up.” She won’t compete again this year, but in January, she and her husband will go to Brazil in search of sun and hard training.

Next June, she wants to compete in the Pan American games. After that, a year of travel: Spain, Morocco, Egypt, Turkey and India. At age 70, she plans to compete in the World Masters Weightlifting Championships in Japan, where she’ll be among the youngest in her age category and where, she says, “I just might win.”

| OSTEOARTHRITIS PREVENTION |

Learning to move improves OA

International program GLA:D (Good Life with osteoArthritis: Denmark) can help people with osteoarthritis (OA) improve their symptoms through exercise and education. Dr. Aileen Davis, epidemiologist and Krembil senior scientist, explains

By Wendy Haaf



Dr. Aileen Davis

Q: WHAT IS GLA:D?

Aileen Davis: We’ve long known that patient education, exercise and weight control can prevent or at least slow the progression of symptoms and functional problems experienced by people with hip and knee osteoarthritis. GLA:D Canada is a community-based, supervised, targeted program that incorporates these elements. It was developed in Denmark, and in partnership with Bone and Joint Canada we’ve brought it to Canada, and moved it from a research project into a national clinical program.

Q: HOW DOES PATIENT EDUCATION HELP?

AD: We spend a lot of time educating people about this paradox that, while it can hurt to be active, in the long run, exercise improves pain. We can help people learn how to manage their pain, and help them understand how much pain during and after exercise is OK. They then lose the fear of damaging their joints and feel more comfortable exercising.

Q: WHY IS EXERCISE IMPORTANT?

AD: When people have pain, they unconsciously change the way they move. That decreases muscle strength, and it can change joint alignment, which increases stress on the joints. Doing the right exercises can ease the load on the knee or hip by strengthening the muscles that support it. We also work on keeping people’s joints properly aligned during activities, like getting out of a chair and going down stairs.

Q: HOW WELL IS THE GLA:D PROGRAM WORKING?

AD: GLA:D has now been implemented in more than 150 clinics across Canada, and results indicate that people are achieving a reduction in pain intensity of about 33 per cent, and have improved function and quality of life. That’s a huge benefit for people.

In good hands

Bridging research with her clinical work, Dr. Heather Baltzer is treating more patients with severe hand injuries than almost any other doctor in Canada

By Tamar Satov



Craig Burgen is thrilled to be back at work after nearly losing his thumb in a workplace accident.

OCTOBER 23, 2018, IS A DATE Craig Burgen won’t soon forget. The 48-year-old industrial mechanic was in the midst of a repair, removing a massive eight-foot steel roller at the Woodbridge, Ont., plastic sheeting company where he works, when one side of it slipped and came down on his left hand like a guillotine. His thumb was severed between the two knuckles, left to hang perilously from a small piece of skin. “I held my thumb in my right hand and started to freak out,” recalls Burgen.

In shock, he didn’t feel any pain. Paramedics took him directly to Toronto Western Hospital, which performs the largest number of hand and finger replacements in the province.

“I felt like I was going to be in good hands, so to speak,” he says, reflecting on the experience. “You don’t realize how much you need your thumb until you don’t have use of it anymore.”

Hand injuries are extremely common, sending more Canadians to the emergency room annually than any other cause. In Ontario alone, research suggests that there are more than 100,000 cases of traumatic hand injuries every year – including fractures, dislocations and amputations.

These injuries can be life-changing. Arthritis, for example, is extremely common in hand-injury patients and can cause long-term health consequences, even if the damaged

joint was treated properly. As well, many patients find themselves struggling with mental health and addiction issues after a traumatic hand injury, according to research conducted by Dr. Heather Baltzer, a hand surgeon and interim director of the Hand Program, and a clinician investigator at Krembil. “Hand trauma is an unrecognized public health issue that has a profound impact on the patient, limiting the ability to carry out activities of daily living,” she says.

In an attempt to shed more light on hand trauma and improve patients’ lives, Dr. Baltzer and other researchers are looking at the economic burden of hand and wrist injuries, how



Dr. Ryan Paul wants to make the recovery process smoother for patients with hand injuries.

different delivery-of-care models affect patient outcomes, and whether preventive measures such as improved workplace safety standards could reduce the incidence of hand injuries.

Using population health data, Dr. Baltzer identified two-million emergency department (ED) visits in Ontario for hand trauma over the past decade, with 500,000 being repeat visits. More than a third of surgical hand trauma patients access mental health and addiction services after their surgeries, compared to 10 per cent of the general population. The average length of an ED visit due to hand trauma is two and a half hours, which translates into over 1,300 hours of ED health care per day. That may be contributing to emergency room congestion.

With hand injuries potentially causing arthritis later in life, Dr. Baltzer and other Krembil researchers are looking at the different inflammatory profiles of patients with hand osteoarthritis. Their research could help identify personalized forms of treatment that could then reduce the progression of the disease.

By the time Burgen arrived at the hospital, he was starting to feel a bit of pain. Within about 10 minutes, before it could really take hold, the nurses hooked him up to an IV with a morphine drip. “Next thing I know, I’m waking up in my hospital bed in my room with my arm suspended,” he says.

What seemed like no time at all to Burgen was more than six hours of surgery performed by Dr. Baltzer and her team. They started by thoroughly cleaning his hand and wound, which was still greasy from the machinery he had been handling, then spent about an hour finding and tagging the tiny blood vessels in his thumb and hand they would need to reattach. “We put a very fine suture – a little blue stitch – in each one at the start, so we could easily see them later when we’d been in surgery for hours,” says Dr. Baltzer.

Next was an hour of what she calls heavy work, or fixing the bones with wires, plates and screws, so they had a stable base on which to do the delicate repair of nerves, arteries and veins. After about 40 minutes of repairing tendons, which allowed the thumb to bend, they moved on to the nerves and arteries. Some of the blood vessels, which are only 0.5 millimetres in diameter, had parts that were crushed, so those parts needed to be removed to open up blood flow. They used high-magnification microscopes and



Dr. Heather Baltzer is one of the busiest hand surgeons in the province.

micro-equipment – forceps, dilators and sutures finer than a piece of hair – to perform the painstaking work, one of the reasons why hand surgeries take as long as they do.

Another hour was spent harvesting a vein from Burgen’s arm to replace a segment of a badly damaged artery in his hand. It took one hour to set the vein, allowing blood to flow into his thumb. “I wasn’t sure how it was going to go, but his thumb pinked right up,” says Dr. Baltzer. Finally, they closed the skin and bandaged his hand.

Staff had to check Burgen’s circulation every hour in the days following the surgery to make sure his thumb was getting enough blood. If circulation was poor, they would have to return to the operating room, since fingers can only last about six to 12 hours without adequate blood supply.

Thankfully, that didn’t happen, and he was released – with his thumb intact – a week later. But leaving the hospital wasn’t the end of the story for Burgen, nor is it for most patients who undergo hand surgery.

“One of the biggest challenges we face is the length of recovery, which in certain cases can be in excess of six months to a year, and the fact that patients require a lot of post-operative care and therapy to restore motion and strength,” says Dr. Ryan Paul, an orthopedic surgeon in the hand surgery group at Toronto Western Hospital. That includes battling stiffness after surgery, as well as the emotional fallout from experiencing a trauma and loss of dexterity. “Even small deficits are really felt because we use our hands so frequently,” he explains.

In response to these challenges, Toronto Western Hospital’s Hand Program has set up a pilot project to help patients through the recovery process. A psychologist and pain management team screen patients to see who might benefit from additional treatment, such as group therapy or other mental health and addiction services. “The more we can identify individual needs, the better their outcomes will be,” says Dr. Baltzer.

For Burgen, recovery is ongoing. He’s back

in the machine shop and has been in physiotherapy since January, but many everyday tasks, such as doing up zippers, buttons and spreading butter on toast, are challenging.

In July, nearly nine months after his accident, he had a second surgery to help regain the sensation on the inside of his thumb where it meets the index finger. A third surgery, yet to be scheduled, will improve movement of his thumb, as the joint has become scarred and stiff.

Burgen is grateful for the care he’s received from Dr. Baltzer and the rest of the team at Toronto Western Hospital, and he’s doing what he can to help with his recovery. “I’m trying to lead a more stress-free life,” he says.

That’s music to Dr. Baltzer’s ears, who wants nothing more than to help her patients live their best lives, both through her actions as a clinician and as a researcher. “When someone has had part of their hand function taken away, and I can give it back to them, that’s an excellent feeling.”

Back pain breakthrough

Nearly everyone feels back pain at some point, with many experiencing chronic pain. Krembil Research Institute researchers hope that new tools and tests can alleviate, if not eliminate, the suffering

By Wendy Glauser



ABOUT SIX YEARS AGO, Aki Tanaka felt her first pangs of back pain. It was intermittent at first, with water aerobics, Pilates and visits to physiotherapists helping to keep the pain at bay. Over the next few years, though, things worsened. By 2016, she needed a walker and had to bend forward slightly when she moved. If she stood for too long, she'd feel a stabbing pain in her back and especially down her leg. Tanaka also had to give up her job as an engineer at a non-profit organization and said goodbye to gardening, her passion. She couldn't even help her university-aged sons settle into their new homes. "There was a lot of lying down," she says. "I was in my sixties, but my life was like I was in my eighties. It felt like my life had been stolen from me."

Then, in the fall of 2016, a breakthrough. She was referred to the Inter-professional Spine Assessment and Education Clinic (now called the Rapid Assessment Clinic), which was launched in 2012 by a team at UHN led by Dr. Raja Rampersaud, an orthopedic surgeon and clinician investigator at Krembil, to help pain sufferers get assessed and treated faster. After several tests, she finally received a long-awaited diagnosis: osteoarthritis (OA) and spondylo- listhesis in the lower back. One of the vertebrae in Tanaka's spine had slipped over the bone below it, which made her spine unstable and pinched her nerves.

Doctors think age and osteoarthritis caused the muscles supporting the spine to wear down, allowing the disc to slip. In 2017, Dr. Rampersaud surgically stabilized her spine, and Tanaka soon started feeling like her old self again. "By about a year, I thought, 'Wow, this is pretty good,'" she recalls.

Although Tanaka's situation is less common, debilitating back pain unfortunately is not. In any

Aki Tanaka gave up gardening when her back pain became too severe. Now that her pain has improved, she's back to doing what she loves.



With more than 20 per cent of Canadians living with arthritis and that number expected to grow, Dr. Anthony Perruccio says more research is critical.

given year, one in three people will experience life-altering back pain. While the problem can disappear with time, exercise and posture improvement, many people can't shake the pain no matter what they do. In a study published in early 2019, Dr. Mayilee Canizares from Dr. Rampersaud's research team looked at data from 13,000 Canadians over a 16-year period and found that almost half of these people reported back pain to a practitioner at least once. Of those, nearly 20 per cent said their back pain continued to persist, while almost a third said their pain, whether occasional or persistent, worsened over time.

While it's clear that back pain is a major issue among Canadians, it's often an invisible struggle. Worse still, back pain, which can be caused by severe forms of arthritis, has received little research attention. A review done by Dr. Anthony Perruccio, a scientist at Krembil, found that at major North American public health and epidemiology conferences, less than one per cent of the

tens of thousands of studies that have been presented focused on musculoskeletal issues, "even though musculoskeletal conditions, like osteoarthritis, are among the most common chronic conditions and the leading cause of disability in the population," he says. With more than 20 per cent of Canadians living with arthritis – a number this is expected to grow – more research is critical, says Dr. Perruccio.

Fortunately, Krembil researchers are facing this growing problem head on. They're trying to find ways of predicting the types of back pain that are likely to be persistent or worsen over time. That way, clinicians can pinpoint who would benefit the most from specialized diagnostic tools and early treatment. Drs. Perruccio and Rampersaud have studied how factors like age, sex, and severity of pain and disability relate to different patterns of back pain – whether it's back-dominant or leg-dominant, intermittent or constant. By identifying differences between subgroups of patients with back

DID YOU KNOW?

People with arthritis are more likely to experience anxiety, mood disorders, poor mental health and difficulty sleeping, compared to those without arthritis.



→ **80%**
 Canadians who experience debilitating back pain at least once in their life
(Bone and Joint Canada)

Dr. Raja Rampersaud says identifying axial spondyloarthritis in patients early can help prevent devastating impacts and side effects.

pain, more targeted interventions are possible. Inflammation can also influence back pain, but its impact isn't uniform. For instance, studies by Dr. Perruccio and colleagues have found that some inflammation-related proteins are associated with pain and multi-joint osteoarthritis in women, but not in men, and vice versa. By narrowing in on the specific contributors to inflammation and pain, researchers might one day develop different anti-inflammatory medications for men and women, says Dr. Perruccio. "The more we can tease apart different groups of back pain and osteoarthritis patients, the faster we can get moving toward personalized treatments," he says. Treating back pain earlier is key for Laura Passalent, a clinician investigator at Krembil and a physiotherapist with advanced training in arthritis, as she's seen the difference the right diagnosis can make. "If we can identify patients with specific types of back pain early in the disease process, they can receive appropriate treatments early, which ultimately improves their overall function



For physiotherapist Laura Passalent, early detection is key.

and quality of life," she explains. Passalent and colleagues found that screening patients for axial spondyloarthritis – a particularly painful type of inflammatory arthritis that affects the back – by physiotherapists with advanced training can speed up the diagnosis by three years. In her research, physiotherapists conducted a comprehensive assessment including a detailed history, a physical exam and appropriate investigations. They would then refer those they suspected of having spondyloarthritis to a rheumatologist who specializes in the disorder. According to Passalent's study, these physiotherapists are comparable to rheumatologists in accurately identifying patients with axial spondyloarthritis. While early and accurate diagnosis is always important, it's especially critical in axial spondyloarthritis, where the immune system attacks the ligaments and tendons around the spine over many years, leading to swelling that can erode the bone and cause it to grow back abnormally. As Dr. Rampersaud puts it, "We want to identify patients earlier so we can actually do something to prevent some of the chronic destructive changes that can happen in the joints and bones." It's also important to treat pain early because it can snowball and affect other areas of health, including sleep and mood. Due to inactivity, patients with arthritic back pain also have a potentially higher likelihood of dying or ending up in a nursing home, says Dr. Rampersaud. It's been two years since Tanaka's surgery, and her pain is no longer dictating her life. She can now laugh and talk with her 99-year-old mother at her nursing home; before her surgery, her visits were limited to giving instructions to the care providers. She's also become a climate change activist, speaking at local libraries and community centres, and she's back to gardening. "I cultivate milkweed, and it's a favourite home for caterpillars that will become beautiful butterflies," she says. It's a fitting metaphor for Tanaka, who is now spreading her wings, after what seemed like an impossibly long wait. ☪

→ **Circle of care**



Dr. Rajiv Gandhi

ALTUM HEALTH IS A NEW KIND OF CLINIC

Nestled inside Toronto Western Hospital sits one of the country's most revolutionary rehab clinics: Altum Health. The clinic, which is headquartered at the hospital but also has satellite clinics across Ontario, is focused on early intervention and an integrated delivery of care. Unlike in the past, when a patient might receive care from a single practitioner, people who come to Altum Health can be seen by a variety of specialists, such as physiotherapists, chiropractors and massage therapists who work together to come up with a highly tailored treatment program for that person. That team approach helps patients receive better, and often more effective, care. "A lot of patients come for back pain assessment and find that a good course of physiotherapy can fix their problem," explains Dr. Rajiv Gandhi, an orthopedic surgeon at Toronto Western Hospital and medical director of Altum Health. When it comes to surgery patients, Altum Health provides "prehab" before an operation and then rehab after it, because "the stronger you are going into surgery, the faster you recover," says Dr. Gandhi. Once it's over, Altum's surgeons and specialists will create a detailed recovery plan. "Patients feel a sense of confidence knowing that all of their health providers are on the same page, and they're talking to each other and learning from each other," he says.



It's a young person's problem, too

Most people don't realize arthritis affects thousands of teenagers and young adults. Here's why that matters and what Krembil Research Institute scientists are doing about it

By Elizabeth Chorney-Booth

Susan Rivers was just 10 when she experienced "growing pains." It turned out to be a form of arthritis, which she's learned how to manage over time.

The back and leg pain started when Susan Rivers was just 10 years old. Her family doctor – followed by a succession of other physicians – told her parents the aches were a simple side effect of growing. But as other kids' "growing pains" dissipated, Rivers' back issues got progressively worse. Both she and her family believed it went beyond normal adolescent discomfort. Yet, it never occurred to Rivers' physicians that she could be suffering from arthritis, a condition commonly associated with old age.

By the time Rivers graduated from high school in Parry Sound, Ont., she had spent nearly half her life in often debilitating pain. The sporadic stiffness and aching she'd experienced as a child had grown more frequent, and Rivers could no longer ignore it or shake it off. "I felt old, but I wasn't old," she says. "It was very frustrating."

At the age of 18, Rivers was referred to a rheumatologist, who diagnosed her with ankylosing spondylitis (AS), a form of arthritis that triggers inflammation of the vertebrae, causing severe pain. If it goes untreated, AS can also cause permanent damage to the spine, limiting mobility. "My first reaction to the diagnosis was, 'I'm not crazy,'" says Rivers, now 38. "It was something this whole time."

When Rivers first met Dr. Robert Inman, a rheumatologist and medical director of the Arthritis Program at University Health Network, as well as a researcher at the Krembil Research Institute, 20 years ago, she was struggling. She had started attending university, but she couldn't climb stairs or walk more than short distances, and her medical team had a hard time finding drugs that worked without causing unacceptable side effects, such as nausea, headaches and dizziness. Rivers withdrew from her friends and found it difficult to pay attention in class because it hurt to sit. It took her 10 years to complete her degree. "I went through an extreme depression," she says. "I was

in a lot of pain and thought, what is the point of living if you can't live your life?"

IMPACT ON THE YOUNG

Rivers is far from alone in her story. Dr. Nigil Haroon, co-director of the Spondylitis Program at Toronto Western Hospital and a scientist at Krembil, says that spondyloarthritis – a group of inflammatory diseases that impact the joints, along with the sites where tendons and ligaments attach to bones – affects just over one per cent of the population, or more than 300,000 Canadians, nearly all of whom get it when they are between 15 and 40.

People are usually surprised by the diagnosis. But young people suffer from a variety of arthritis types – rheumatoid arthritis has similar occurrence rates as AS, and osteoarthritis, which is typically associated with aging, can also affect the young. Dr. Haroon hopes that by educating the medical community about recent advances in diagnosing AS, especially in primary care, this may help to reduce wait times for patients to receive a diagnosis.



After my treatment started, I improved so much, I thought I was cured. I could even jump on the trampoline with my sister's kids."

Susan Rivers
Arthritis Program patient

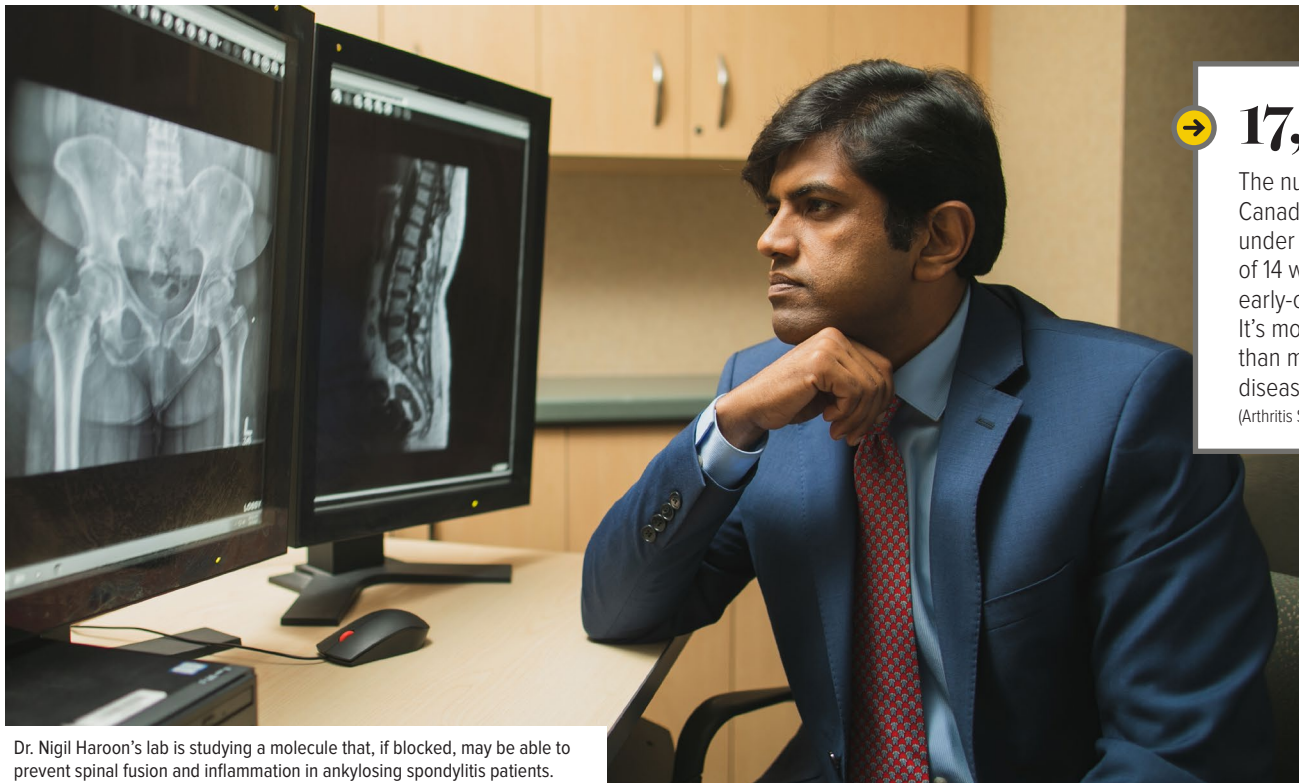


Dr. Vinod Chandran (centre) and his team are hoping to identify a blood marker that can help diagnose psoriatic arthritis.

Some of the signs of AS include morning stiffness that improves with activity and nighttime pain that interrupts sleep. The trouble is those symptoms can also point to other, more easily explained ailments, which means physicians often don't consider a diagnosis of AS and refer to a rheumatologist.

Another complicating factor is that AS comes with no obvious physical signs of inflammation in the back, making it harder to diagnose than, say, rheumatoid arthritis, which produces visible swelling of the joints. There are some telltale clues, however, such as inflammation in the eye or inflammation in the gastrointestinal tract, which could represent an inflammatory bowel disease such as Crohn's disease, says Dr. Inman.

This is all related, because Crohn's and eye inflammation are, like AS, rooted in a patient's immune system. Rheumatologist and Krembil researcher Dr. Vinod Chandran specializes in what's called psoriatic arthritis – a form of arthritis that is either preceded or accompanied by psoriasis, a chronic skin disease that causes itchy scales to form on the skin. Such autoimmune issues are often hereditary, though they might manifest with differing symptoms, which means primary-care physicians should delve into a patient's family history in search of similarities. "You could also see patients in a family where one person has psoriasis, another has Crohn's disease and a third person has ankylosing spondylitis," Dr. Chandran explains. "They're all in the same family of diseases." Dr. Chandran wants to identify blood markers and develop a blood test to help diagnose psoriatic arthritis.



Dr. Nigil Haroon's lab is studying a molecule that, if blocked, may be able to prevent spinal fusion and inflammation in ankylosing spondylitis patients.

➔ **17,400**

The number of Canadian children under the age of 14 who have early-onset arthritis. It's more common than most chronic diseases in children (Arthritis Society)

THE IMPORTANCE OF EARLY DIAGNOSIS

Anything doctors can do to diagnose a young patient faster will impact their quality of life. According to Dr. Inman, studies show that AS patients experience back pain for an average of five years before getting a diagnosis. It's not just five years of pain, either: AS and other forms of early-onset arthritis often cause significant fatigue, and many patients – like Rivers – experience depression as they watch their peers build careers and have families. “It certainly impacts patients’ recreational activities and has a very significant impact on work productivity,” Dr. Inman says.

Typically, AS is diagnosed with an X-ray that shows changes in a patient’s sacroiliac joint in the pelvis, but new research has shown an MRI can confirm an AS diagnosis before those changes even start happening. That’s crucial, because Dr. Inman is seeing evidence that early diagnosis can slow down the progression of the disease, which can cause significant disabilities as patients age. If left unchecked, chronic arthritis of the spine can cause the spine to fuse together, meaning patients end up with very limited mobility and a deformed posture.

Fortunately, there are treatments available. Exercise and physiotherapy, along with anti-inflammatory drugs, can help alleviate symptoms. Krembil researchers are also studying the use of biologic drugs that work to slow the progression of the disease. Dr. Haroon pub-

“Studies show that ankylosing spondylitis patients experience back pain for an average of five years before getting a diagnosis. Many experience fatigue and depression.”

Dr. Robert Inman
Medical director, UHN Arthritis Program

lished a landmark study in 2018 that showed drugs that target a molecule in the blood called TNF can decrease the chance of AS progression by 50 per cent.

But there’s a short window of opportunity for achieving optimum results, says Dr. Haroon. The potential to slow progression is at its highest if treatment is started within the first few years of symptoms appearing. Dr. Haroon hopes that, one day, AS can be stopped altogether. “My lab is studying a molecule that can drive both inflammation and bone formation,”

he says. “If we are successful in blocking this molecule, we hope we can directly block both spinal fusion and inflammation in AS patients.”

All of this is great news for patients like Rivers. Through a clinical trial with Dr. Inman, she was able to find a biologic drug that alleviated many of her symptoms with no significant side effects. “After my treatment started, I improved so much, I thought I was cured,” she says. “I could even jump on the trampoline with my sister’s kids. I could work more hours and make money, rather than depending on my family to help.”

There have been hiccups: In 2007, UHN’s Dr. Rod Davey performed a double hip replacement because Rivers’ joints were already damaged so much that she could feel bone grinding on bone. But she recovered quickly, thanks in part to her age, and in the intervening years she has gone from a young woman struggling with chronic disease with little hope for a pain-free future to an active person who is able to fully participate in work and family life.

Where once Rivers needed assistance to perform routine physical tasks, she now has two jobs — working in administration at the front desk of a local hospital and as a part-time waitress. Her condition hasn’t disappeared, but finding the right treatment means she can look forward to a good quality of life for years to come. “I never thought children could get arthritis,” says Rivers. “It turns out, that’s what I had this whole time.”

“If we can catch arthritis earlier in patients, then ultimately, we should be able to cure it.”

Drs. Igor Jurisica and Christian Veillette hope to improve treatments and eventually stop arthritis from developing in patients. How? With data and analysis

By Bryan Borzykowski



Drs. Igor Jurisica (left) and Christian Veillette, two leading AI researchers, share their thoughts on how the technology is being used to better treat arthritis.

For Drs. Igor Jurisica and Christian Veillette, AI isn't just a buzzword.

The two have been using AI and machine learning algorithms to analyze arthritis-related information and create rich data sets, which will help doctors diagnose arthritis earlier and treat the disease more effectively.

Q: DR. JURISICA, YOU BEGAN YOUR CAREER USING PREDICTIVE ANALYTICS FOR CANCER RESEARCH. WHAT DREW YOU TO FOCUS ON ARTHRITIS?

Dr. Igor Jurisica: With cancer, we usually have one sample per patient, and we're trying to predict where it's coming from and where it's going. With arthritis we have at least a few samples, so we can, on a molecular level, analyze where the disease was before surgery, what changes were made during the surgery and how it's changing as a response to treatment over time. We started to develop computational tools to analyze these individual data sets, which gives us so much more opportunity to study what happens to these patients in their recovery, and long term, it can help us personalize treatments for individuals.

Dr. Christian Veillette: It was our samples that caught Igor's attention. We have a large and well-documented repository for clinical samples – called a biobank – that we've built up over the years, using pre- and post-op samples from arthritis patients. We have tissues from the hand, wrist, knee and spine, including synovial fluid, blood samples and more. We've amassed thousands of samples, and the collection continues to expand in numbers and richness. It's really incredible to have access to such a wealth of high-quality data. You don't have as much data with cancer, and especially not longitudinal samples from the same patient.

Q: WHAT'S THE BENEFIT OF INCORPORATING AI INTO MEDICINE?

CV: One of the main reasons for incorporating AI into medicine is to create efficiencies in order to help people get better faster. In 2007, when I joined University Health Network, I was involved in getting rid of all paper-based outcomes, such as the questionnaires people filled out in the clinic, and creating an electronic platform. This is one example of how using AI can help create an infrastructure, which allows you to capture data that you can then use to help drive decisions.

IJ: AI isn't new in medicine, but it's evolved. We now have faster computers so we can perform large-scale image analysis, using visualization and simulation to make more accurate outcome predictions. When I did my PhD, I had access

to 700 patient samples from an in vitro fertilization clinic. At that time, this was considered a huge data set for machine learning algorithms. Now, we have tens of thousands of highly characterized patient samples with tens of thousands more data points, and hundreds of clinical parameters and lab measurements. In our Arthritis Data Integration Portal (ADIP, developed with funding from the Krembil Foundation), when we combine clinical information and molecular profiles, we have more than 11,000 patient samples.

Q: HOW ARE YOU USING ALL OF THAT DATA?

IJ: We participate in multiple collaborations where the data and our algorithms help us understand a complex spectrum of diseases. And we use it in our own studies to look for new treatments for arthritis, such as repurposing existing drugs for other diseases and modifying lifestyle factors specific to each patient, to increase their response to the treatment. For example, we used these data to predict a novel treatment for osteoarthritis, and we expect we'll be able to validate it using pre-clinical models and eventually translate that into the clinic.

CV: On the clinical side, the data is helping us with the prediction of patient outcomes. So, basically, we're saying, "This person has this per cent chance of having a good outcome," or "These are the modifiable factors, such as exercise, surgery or therapeutics, that we should change in order to improve their chance of having a successful outcome." That's where we've started taking the data we've been capturing from the biobank and from the clinic, and we're now able to bring that full circle into actually making and assisting with decisions.

DID YOU KNOW?

UHN's Arthritis Program, funded by the Campaign to Cure Arthritis, was the first in North America to safely inject a patient's own stem cells into knee joints for OA treatment.

Q: ONE OF THE TOOLS YOU'VE DEVELOPED IS CALLED MIRDIP. HOW DOES IT HELP YOU ANALYZE INFORMATION?

CV: MirDIP is a data integration portal developed by Igor that helps researchers pull up information on microRNAs (small molecules that play an important role in arthritis and other diseases, and identify which genes they regulate). When we started taking in data, we had a lot of questions. How do we annotate it? How do we understand what all this is? How do we help impact actual decisions? I started looking into data integration platforms, which is when I came across some of the work Igor had done on cancer. Data integration portals are enabling us to integrate different data sets on arthritis and identify novel, previously missed connections.

IJ: We can benefit from experiments done in multiple laboratories around the world, which expands the variety of patient samples we can use. Integrating data from different experiments also provides richer information about the context or conditions of the experiment. Com-

bined, we can identify more accurate prognostic and predictive biomarkers, and better determine who will respond to what therapy and find new drug targets for developing new therapies.

CV: Essentially, it's about understanding all the different interactions that happen within a person's body and within the cells, at different levels. These portals help us organize all that information so we can see those interactions, which will help us better predict a patient's final outcome. Igor and his group have been able to study different types of microRNAs to see how they're working, and which ones are going to provide a benefit and which ones are harmful. They can now see that drugs that had previously been used for other diseases might work well for arthritis. There are different ways to use these different integration portals in order to find answers.

Q: ARE THERE ANY RISKS TO ALL THIS DATA COLLECTION AND ANALYSIS? HOW DO YOU MAKE SURE YOU'RE DOING IT RIGHT?

CV: If you don't do it properly, you can come up with incorrect decisions or predictions. One thing we've learned is that integration across the team – having that clinical information and clinical knowledge paired with technical, analytic knowledge – is key to mitigating those risks and not generating erroneous results.

IJ: We go through multiple steps to ensure that what we are following is not just smoke and mirrors, but hopefully something actionable. Integrating data into networks enables us to separate signal from noise and build explainable models.

Q: IS EARLY DIAGNOSIS THE GOAL?

CV: That's what it really boils down to. If we can catch the disease earlier in patients, then ultimately, we should be able to cure it. Or at least minimize its impact.

IJ: I'm fascinated by how medicine is changing from being reactive to proactive or predictive. If somebody has specific joint damage from a sports-related injury, maybe that's the time when stem cells should be injected instead of waiting until the cartilage degrades. With an earlier diagnosis, you have more options for treatment, and you can generate better outcomes at a reduced cost to the patient and to society. ↻

World-class researchers



DR. IGOR JURISICA, a senior scientist at Krembil Research Institute, combines integrative computational biology with advanced AI and data mining algorithms to tackle chronic diseases. In 2019, analytics agency Deep Knowledge Analytics named him one of the Top 100 AI leaders in drug discovery and advanced health care, and he has won numerous awards and distinctions, including an IBM Faculty Partnership, an IBM Shared University Research Award and a Tier 1 Canada Research Chair in Integrative Cancer Informatics.



DR. CHRISTIAN VEILLETTE is division head of Orthopedic Surgery at UHN and a clinician investigator at Krembil. He has also been recognized internationally for his work with AI technology and informatics, including winning the Edit This award for the most innovative and best use of the Confluence enterprise wiki platform, and an award from the Canadian Orthopedic Association recognizing his leadership and innovation in orthopedic informatics.



Liz Attfield's lupus nearly prevented her from having a child. Her daughter, Molly, is now eight years old.

Living with lupus

Krembil researchers have studied lupus for half a century. They're now looking at new ways of treating, and potentially stopping, this debilitating disease

By Anna Sharratt

THIS SUMMER, LIZ ATTFIELD hopped into her car and drove for two hours to Muskoka, a cottage community north of Toronto. The Rolling Stones were playing a rare outdoor show, and she wasn't going to miss it. However, attending a concert under the blazing sun and with thousands of other people isn't easy for Attfield. She suffers from lupus erythematosus, a chronic autoimmune disease in which the body can attack the joints, skin, kidneys, blood cells, brain, heart and lungs.

Indeed, the event led to a flare-up. "I was outside all weekend – and the sun isn't good for lupus," she says. "I only have so much energy, and I have to be careful about expending it."

As one of the 35,000 Canadians who have lupus – it usually

strikes between the ages of 15 and 44 – Attfield is well versed in pain management. She's been dealing with symptoms since she was 14. "I had gone trick-or-treating and I could barely walk up the stairs," says the now 44-year-old marketing and fundraising executive.

Since she was diagnosed at age 17, Attfield has been treated by Dr. Murray Urowitz, director of the Lupus Clinic at Toronto Western Hospital and a senior scientist at the Krembil Research Institute. She has received corticosteroids and drugs to suppress her immune system, which have effectively controlled the disease.

Still, life with lupus has challenges. Attfield never thought she could have a child, as lupus patients have high-risk pregnancies. "I knew there was a chance I wouldn't be able to keep the pregnancy," she says. "That was the hard part."

And she did have trouble conceiving. Fortunately, in 2011, she delivered a healthy baby girl. "She was three weeks early," recalls Attfield. "But I had a great medical team. I am so grateful for my daughter."



We understand much more about lupus than we did 10 years ago, but this complicated disease requires a tailored approach."

Dr. Dafna Gladman

Senior scientist, Krembil Research Institute

A POTENTIALLY FATAL DISEASE

Many people don't realize how serious lupus can be. It can cause severe joint pain, skin lesions, extreme fatigue and organ damage, as well as fatal strokes and heart attacks. In fact, it is one of the leading causes of death in young women. New treatments and medications are sending the condition into remission, giving new hope to patients.

Krembil's researchers are working to identify biological molecules in blood and urine that may predict how lupus will develop. They're looking at ways to deliver earlier treatments

to help reduce irreversible organ damage, and they're gathering information related to the long-term health complications, such as premature cardiovascular disease, osteoporosis, bone damage and cognitive impairment.

However, lupus presents differently in every patient. Examining a patient's genetic, environmental and lifestyle factors can help predict which organs could be impacted and how responsive the disease may be to different treatments. "We understand much more about lupus than we did 10 years ago," says Dr. Dafna Gladman, a rheumatologist and senior scientist at Krembil. "But this complicated disease requires a tailored approach."

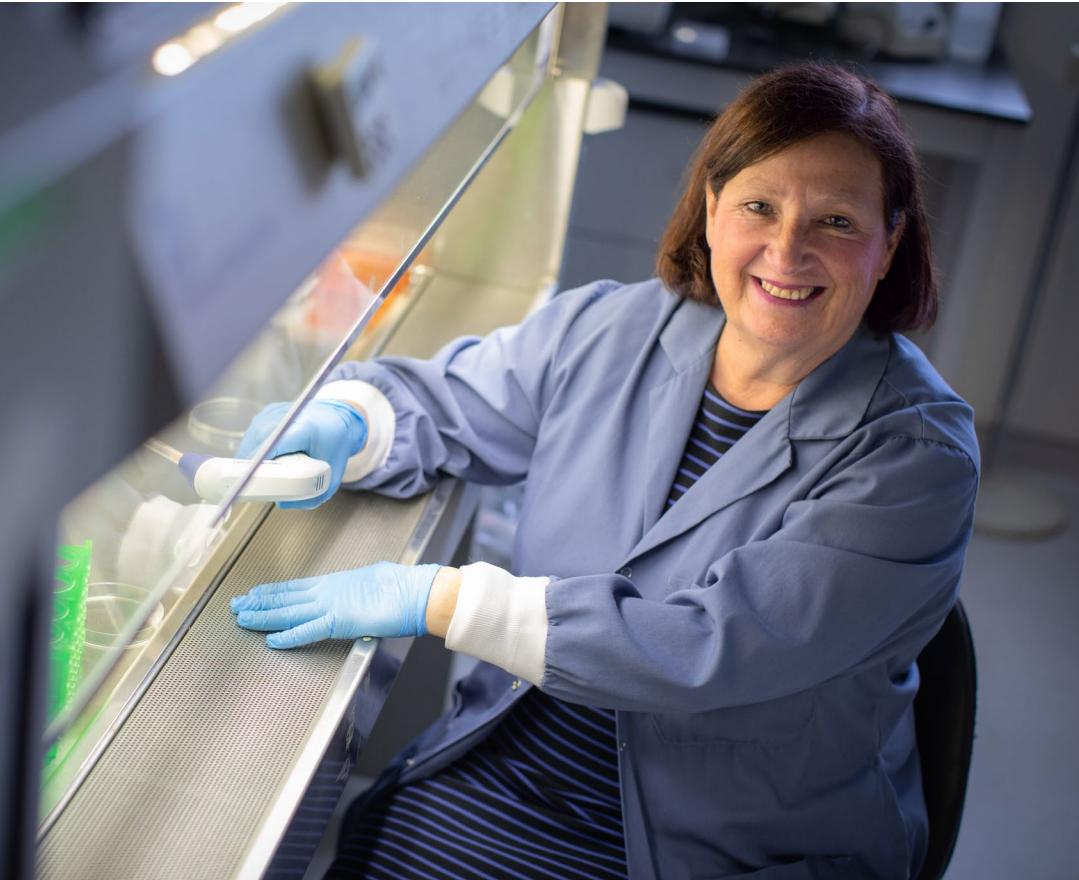
THE DISEASE OF MANY FACES

Lupus can present as any number of diseases that occur due to immune system dysfunction, says Dr. Urowitz. Since many of the 90 genes that have been linked to lupus are also found in healthy people, scientists are looking at how these genes interact with one another and produce the disease. "A specific gene might predispose a person to lupus, but only if it is present with other lupus-related genes or specific environmental triggers," says Dr. Joan Wither, a Krembil senior scientist. She's studying how Type 1 interferons, proteins that are elevated in lupus patients, disrupt immune function and interact with other types of lupus-predisposing genes. If Dr. Wither discovers a link between these proteins and the onset of lupus, stopping their formation or blocking their



Rheumatologist Dr. Dafna Gladman wants to help lupus patients get the treatment that works best for them.

Fighting arthritis for 40+ years



Dr. Joan Wither hopes that by stopping specific proteins from disrupting immune function, she can prevent lupus' onset.

function could possibly halt the disease's progression.

Dr. Wither's studies into the immune basis of lupus also extend into other systematic autoimmune rheumatic diseases, such as scleroderma and Sjögren's syndrome. Dr. Sindhu Johnson is director of UHN's scleroderma clinic. Dr. Johnson is also playing a leadership role globally in defining criteria that enable doctors to accurately classify such rheumatic diseases.

A unique multidisciplinary Sjögren's syndrome clinic has been established by Dr. Arthur Bookman. This clinic provides one-stop care for this autoimmune disease, incorporating experts from rheumatology, dentistry, ENT and ophthalmology.

MORE DATA, BETTER OUTCOMES

Dr. Zahi Touma, a clinician investigator with Krembil, has enrolled more than 300 lupus patients into a screening program that uses computer questionnaires and performance-based tests to detect cognitive changes, such as a decline in memory and thinking speed, attention and planning abilities. Another platform, PROMIS (Patient-Reported Outcomes Measurement Information System), will help doctors assess the different aspects of a patient's quality of life, explains Dr. Touma.

This data has led to many advancements in lupus research over the past 20 years, and will help doctors better understand how the disease progresses and how different treatments might work on specific patients. This can allow for a more personalized treatment regimen, adds Dr. Urowitz.

There's also been significant progress in treating pregnant lupus patients, like Attfield. Researchers have found that patients have the best chance for success when they're clinically inactive before getting pregnant, if they're put on the right medications and if they're monitored regularly. The Lupus Clinic has so far helped more than 450 patients have healthy babies. "This is why we do what we do," says Dr. Urowitz.

Attfield is happy that her lupus hasn't defined her life. "I've had a successful career, and I have my daughter," she says. "I think I've done a pretty good job of having a normal life." ☺

→ **5 million**

People worldwide who have a form of lupus
(Lupus Foundation of America)



Dr. Murray Urowitz leads the Lupus Clinic at Toronto Western Hospital.

FOR MORE THAN FOUR DECADES, University Health Network's Arthritis Program has been a global leader in arthritis-related research and treatments. Naturally, it's taken years of hard work by numerous medical and scientific teams working together with patients and volunteers to get to this point. "It has involved many champions over the years," says Dr. Mohit Kapoor, research director of the Arthritis Program.

The program has taken a multidisciplinary approach to research, education and clinical care, with a focus on orthopedics, rheumatology, hand and osteoporosis. This "complete approach," as Dr. Kapoor puts it, has been a recipe for success. "One day we will stop arthritis in its tracks."

The Campaign to Cure Arthritis, started in 2011, has been instrumental in fast-tracking discoveries and accelerating their translation to improve care for patients. Philanthropy has played a huge role in the success of the Arthritis Program. Every full-time doctor in the program has pledged a donation to the Campaign to Cure Arthritis. Their dedication has inspired hundreds of people living with arthritis and their loved ones to donate generously to the program, too. "These donations help us to continue our work as world leaders in arthritis research, education and patient care," says Dr. Kapoor. "We are so grateful."

Campaign to Cure Arthritis

Join us on our mission to cure arthritis at cureforarthritis.ca

