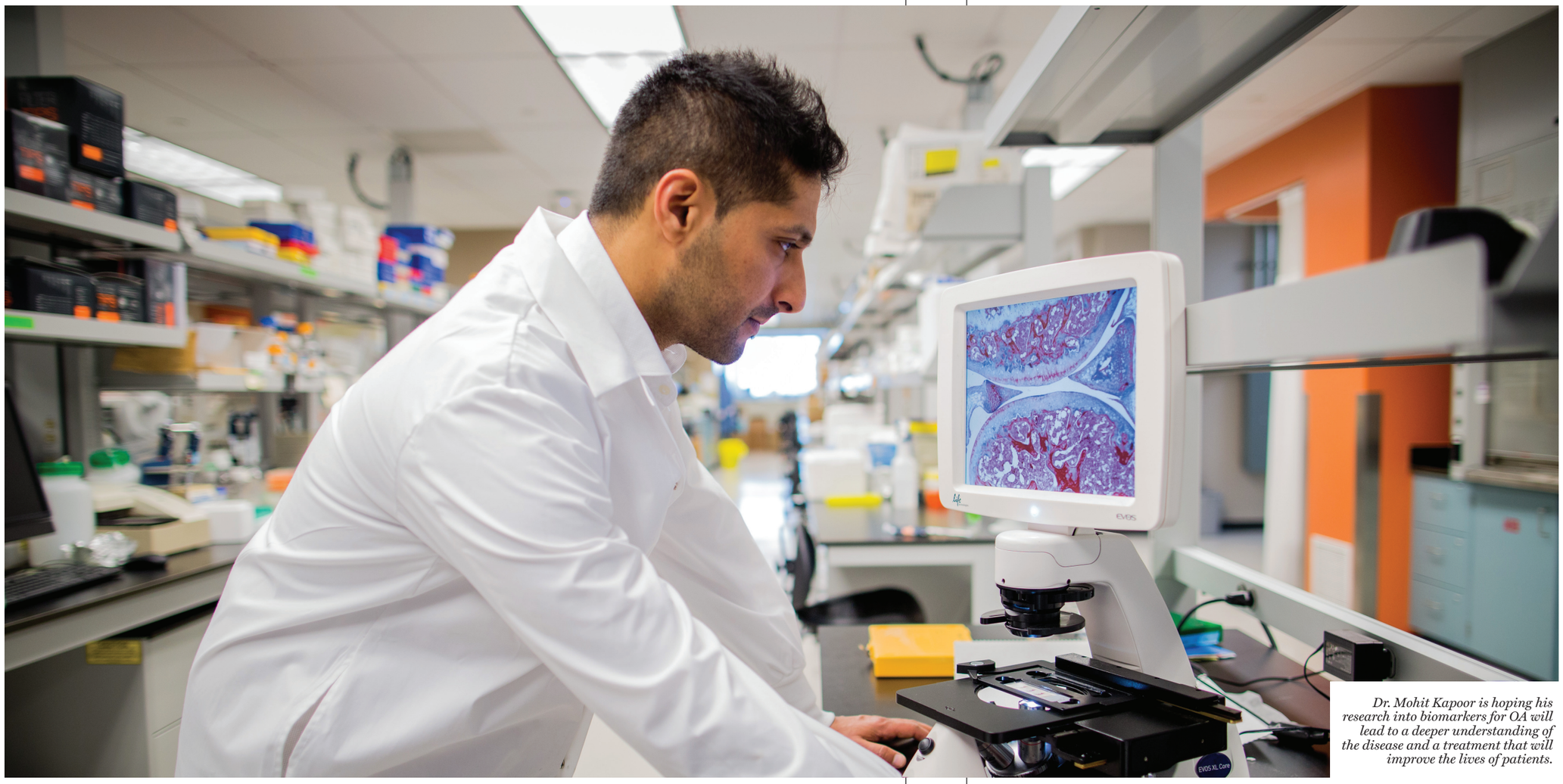

Dr. Mohit Kapoor is hoping his research into biomarkers for OA will lead to a deeper understanding of the disease and a treatment that will improve the lives of patients.

The mission to cure osteoarthritis

Dr. Mohit Kapoor and his team believe their discovery of two biomarkers could lead to better tracking and treatments

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"We're on the cusp of developing a blood test to diagnose OA, along with injectable treatments to repair damaged cartilage."

– Dr. Mohit Kapoor

Osteoarthritis (OA) is a debilitating disease that affects more than one in 10 Canadian adults – a number expected to rise to one in four by 2040 as the country's population ages. In this chronic condition, cartilage between bones is destroyed, and the fluid that cushions and lubricates joints breaks down and loses viscosity.

By the time OA shows up on X-rays or even through magnetic resonance imaging (MRI), there isn't much for doctors to do except manage its symptoms, which include stiffness and pain in the joints. In many cases, the symptoms of OA – which are often compounded by significant weight gain as patients become less active – get worse over time to the point where the affected joint must be operated on and replaced.

"There's no cure for osteoarthritis," explains Dr. Mohit Kapoor, senior scientist and Research Director of the Arthritis Research Group at the Krembil Research Institute. "As of today, there are no approved drugs in the world that can stop this disease from progressing."

This could soon change, thanks to a discovery at Krembil of a pair of biological markers for OA in the spine. About three years ago, Dr. Kapoor and his research team at the Buchan Arthritis Research Centre – comprising postdoctoral fellow Dr. Akihiro Nakamura along with Dr. Raja Rampersaud, a spine surgeon at Toronto Western Hospital and one of Dr. Kapoor's research partners – began studying tissue biopsies taken from 55 patients with various stages of spine OA.

Using a tool developed at Krembil, the study looked at 2,100 microRNAs – small ribonucleic acid (RNA) molecules throughout the body that control almost 60 per cent of our genes – and spotted two particular microRNAs that increased significantly as destruction of the cartilage got worse.

"These two biomarkers – known as microRNA-181a-5p and microRNA-4454 – contribute directly to cartilage destruction and increased inflammation," says Dr. Kapoor. "What we also found was that they depleted collagen – the most important component of cartilage – and

promoted the death of cartilage cells," he says.

"When you look at the relationship between the levels of these two [bio]markers and compare this to the clinical imaging using MRI, the MRI and the levels of the [bio]markers show a significant correlation."

So what does this all mean for patients with OA? "We're on the cusp of developing a blood test to diagnose OA, along with injectable treatments to repair damaged cartilage," Dr. Kapoor says.

Dr. Rampersaud says that knowing the biomarkers for OA can help scientists and clinicians answer three critical questions.

"Can we track arthritis, can we monitor response to treatment better and can we leverage this knowledge to develop a drug where a blocker of this molecule can be used in the treatment?" he says. "This is a significant finding, and a great example of research that has clinical relevance and could actually change the lives of patients with osteoarthritis."

Dr. Kapoor says being able to analyze the tissue of patients with various stages of OA was critical to the study.

"We had a spectrum of patients, ranging from those at very early stages of the disease with very mild degeneration of cartilage to patients with severe degeneration. And we also found a subset of patients who had other spinal problems, but did not have cartilage degeneration," he says. "This allowed us to screen for [bio] markers. If you didn't have all stages of the disease represented, you really cannot do this study."

The 55-patient study was the initial phase of this research project, says Dr. Kapoor. He and his team are now working on the next phase, which involves more than 250 patients. They are also developing two new tools: one to detect OA biomarkers in patients' blood and another to block the microRNAs that contribute to OA.

"The blockers, to turn off these destructive microRNAs, are designed to be injected into the joint," says Dr. Kapoor. "Once they show promise, we will then move forward into the clinical phases."

With a biomarker panel for blood testing and blockers to stop the culprit microRNAs, doctors will find it easier to diagnose OA in its early stages and halt the progression of the disease, says Dr. Kapoor.

"This test is not meant to replace clinical imaging, but rather to be a complementary tool for diagnosing the nature of the arthritis and to tell if your disease is early stage or advanced, so your doctor can decide on the most appropriate intervention," says Dr. Kapoor.

Dr. Rampersaud says the biomarker panel will also allow for a more effective and tailored approach to treatment. For instance, doctors who might normally recommend exercise could instead send a patient for surgery consideration more quickly because of biomarker panel results.

"If somebody has a really high level of biomarkers and is not likely to respond to conservative treatment such as exercise, then the doctor could say, 'Let's consider surgery sooner, rather than later,'" says Dr. Rampersaud. "Otherwise, a doctor could be prescribing exercise for years, while the OA keeps getting worse. So what we're working on now is a way of refining the prognosis."

Dr. Rampersaud says the Krembil team is also looking at how the biomarker panel can be used to assess patients' progress after surgery or drug therapy. This would open the door to truly personalized medicine where treatment is fine-tuned based on each patient's biological response to therapy.

"So the next step is researching how we can better track patients' response to treatment," says Dr. Rampersaud. "It's a very exciting project – one that I think is going to change the life of OA patients, hopefully in the near future." ■