



Research conducted by Dr. Armand Keating focuses on how a cell population can help injured tissue regenerate even more effectively.

Using stem cells to fight osteoarthritis at the source

Determined to find a cure, arthritis team digs into their own pockets to fund the fight against the disease

Mary Gooderham

A clinical trial involving patients with osteoarthritis (OA) taking place at the Krembil Research Institute is using stem cells to better understand and help find a cure for one of the most debilitating health problems of our day.

Supported by the Campaign to Cure Arthritis – which includes \$3 million personally donated by all of the physicians and surgeons in the Arthritis Program at Toronto Western Hospital – the vision-

ary study focuses on the evolving field of regenerative medicine to help reduce inflammation and replace lost cartilage.

The study at Krembil, the first North American mesenchymal stem cell trial for treating knee OA, could allow clinicians to repair damage biologically – at the source – rather than having to perform surgery to replace disease-ravaged joints in patients’ hips, knees, spines and shoulders.

Mesenchymal cells are found in various

tissues and fluids, are able to modulate the immune response and can support tissue regeneration.

“We want to put ourselves out of business as joint-replacement surgeons,” says Dr. Nizar Mahomed, a senior scientist at Krembil, who is also medical director of the Arthritis Program and a leading orthopaedic surgeon at Toronto Western Hospital. “We want to change the trajectory of this disease.”

The philosophy focuses on improving the knowledge of OA – which accounts for 80 per cent of arthritis cases and affects patients’ functioning, quality of life and productivity – and finding a mechanism to cure it from within. Regenerative medicine may indeed hold the key to changing the environment in which degenerative joint diseases develop and worsen.

Fundraising efforts to back arthritis research were kick-started in 2011 by 10 orthopaedic surgeons at the hospital. They felt strongly about the need to improve care for patients with arthritis, each personally donating \$125,000 over five

years, for a collective gift of \$1.25 million. And last year the surgeons – now 12 of them – renewed their commitment with new gifts totalling \$1.5 million. To date, the Campaign to Cure Arthritis has raised \$50 million – double the original target.

Dr. Mahomed, who is among the donors, performs some 300 hip and knee replacements annually, surgery he says is considered “the gold standard” for treating OA. Yet as many as one-quarter of patients continue to experience pain after the procedure. All patients experience a loss of mobility, and the devices have a finite lifespan, so they must be replaced when worn out.

Advances to date in OA research, such as developing new biomaterials and techniques for the artificial implants to alleviate pain and restore function, have focused on treating the symptoms of the disease. But this frustrates clinicians, says Dr. Mahomed, who is also the Nicki and Bryce Douglas Chair of Orthopaedic Surgery and the Smith & Nephew Chair in Orthopaedic Surgery Research. “There is no treatment that prevents, halts the progression or reverses the stage of the disease.”

Using the body’s own stem cells to reduce inflammation and regenerate the damaged osteoarthritic joint tissue, essentially restoring it back to its original healthy state, is a viable option, says Dr. Armand Keating, a Krembil scientist internationally recognized for his work in stem cell transplantation.

The research involves mesenchymal stromal cells (MSCs), which are present in the bone marrow and other tissues. These “nurturing” cells can have anti-inflammatory properties and can stimulate the regeneration of cells in damaged tissue. Dr. Keating’s research focuses on understanding more about how MSCs function to identify a cell population that can help injured tissue regenerate even more effectively.

The \$1.5 million current trial involves a dozen patients aged 45 to 65, with moderate to severe OA in the knees. In the procedure, MSCs are removed from the bone marrow in the patient’s hip and sent to the Cell Therapy Lab at UHN to be grown into larger numbers. These cells are then injected into the patient’s damaged knee joint. The trial is intended to determine whether the cell therapy is safe. It also aims to understand any changes, especially improvements, that patients experience in order to gather data for future trials.

“This is an important first step for us,”

Dr. Keating says, noting that preliminary results show that the treatment is safe. A full analysis of the study will be completed later this year when all data are available.

The trial uses autologous MSCs, meaning that the cells are harvested from the patient. Future studies, however, will use allogeneic cells, which are obtained from a donor. Dr. Keating feels allogeneic cells will prove to be a better, more practical alternative. They can be grown in greater numbers and come from healthy individuals, so they are likely to have more effective therapeutic properties. Once these cells have been identified, Krembil researchers will isolate and grow those with the most promising capacity to have restorative and anti-inflammatory properties, optimizing their impact.

“We need to tweak and modify those cells to improve that response,” says Dr. Keating, who is optimistic about the results of the research and advances in the field of cell therapy. “We hope to achieve some fairly significant milestones in the next five years.”

Krembil has the potential to become the global leader of regenerative medicine in orthopaedics, he predicts. “Funding is critical to move these studies forward. Medical science has proven that when the right resources are applied, we can make progress on ways to prevent, treat and cure these types of chronic diseases.”

Dr. Keating says that UHN’s orthopaedic surgeons “need to be commended” for undertaking, moving forward and even financing research that could make artifi-

cial joint replacements obsolete.

“It’s extraordinary – almost unprecedented. They’re really interested in finding out the best way to deal with this disease, and it might not be surgical, although that would still be quite some time in the future,” he comments, noting that even if this happened, orthopaedic specialists would still be required to deal with cases of trauma and to administer injections in joints.

Dr. Mahomed says that breakthroughs in stem cell treatments for OA would alleviate a major source of disability among Canadians, ease its impact on individuals and their families, provide clinicians with better strategies for managing degenerative joint disease and reduce the enormous cost of its management in the

healthcare budget.

“We’re going to bankrupt our system if we don’t find better ways of dealing with this problem,” he says.

Understanding the different mechanisms associated with the disease, and genetic profiles associated with the disease, including why patients respond differently to therapies, can help to tailor treatments to the individual, leading to so-called personalized medicine. This would turn standardized, one-size-fits-all treatments for osteoarthritis into a system of predictive, preventive and precise care, with the ultimate goal of being more cost-effective.

“The whole world of science in this area is evolving in a good way,” Dr. Mahomed adds. “We’ve got a problem that we need to solve, and we’re solving it.” ■



If Dr. Nizar Mahomed has his way, knee joint replacements like the one he’s holding will soon be obsolete.

“We want to put ourselves out of business as joint-replacement surgeons. We want to change the trajectory of this disease.”

– Dr. Nizar Mahomed

Personally invested in finding a cure

Physicians and surgeons in the Arthritis Program at Toronto Western Hospital have pledged \$3 million of their own money to help find a cure.

“When you get that sort of commitment, it’s hard to say no [to supporting that].”

– Tony Fell, founding co-chair of the Campaign to Cure Arthritis