The Research Institute of St. Joe's Hamilton

2018 Annual Report

Introduction

The Research Institute of St. Joe's — Hamilton oversees the work of over 600 researchers, learners, and staff members as they carry out clinical, translational, evaluative, and fundamental research to improve diagnostics, care, and treatment for patients in our community and around the globe.

Since its inception in 2014, the Research Institute has become a leader in collaborative, translational research. Known as the bench-to-beside approach, this innovative method of conducting research allows scientists working in our labs to make the latest advancements available to clinicians for patient care, all within the walls of our hospital.

The Research Institute is an integral partner within Hamilton's health care community. Our researchers have transformed the way medicine is practiced, helping to improve the quality of life and the quality of care provided by health care professionals.

The Research Institute of St. Joe's Hamilton

St. Joseph's HEALTH SYSTEM

Publication Credits

Managing Editor:
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Author & Designer:
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Photos:

Page 7: Courtesy of JD Howell / McMaster University

Page 13: Courtesy of Dr. Martin Stämpfli

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A word from Dr. Gail Martin

It has been a prodigious year – both at home and abroad – for the Research Institute. In Hamilton, we have further developed synergistic interactions with our key partners across the city's health innovation landscape. Across Canada and beyond, our researchers have collaborated with preeminent scholars, clinicians, and institutions as they lead state-of-the-art projects in their respective fields.

The mandate of the Research Institute is to foster innovation and discovery in order to transform patient care. By creating collisions between innovators, advancing opportunities for research participation, and gaining efficiency across multiple levels of research administration – study recruitment, finance, contract negotiation, and regulatory compliance, to name a few – we continue to increase our capacity to conduct groundbreaking studies.

The creation of the new Genitourinary research program in 2018, made possible through the generosity of our donors, reinforces our position as a premier research centre in the area of urological oncology. Using a translational approach, this program connects basic scientists and clinicians to study various urologic cancers at the molecular and genetic levels, with the goal of developing novel methods for early diagnosis and effective treatment.

At St. Joe's, researchers practice across an array of distinct fields, yet they all share the same goal of enhancing patient quality of life through improvements in treatment and care. I am pleased to present this year's report that highlights – in the voices of our researchers, our clinicians, and our patients – just some of the major advancements made at our organization.

Gail Martin, PhD, BSc
Executive Director, The Research Institute of St. Joe's — Hamilton

A word from Dr. Jack Gauldie

As an academic, patient-centered research hospital, St. Joseph's Healthcare Hamilton continues to be at the forefront of groundbreaking discoveries that have significant impact on patient treatment and care. Our connections to McMaster University, the Michael G. DeGroote School of Medicine, and affiliated institutions in the city and beyond have enabled us to develop a vast, collaborative network of research professionals.

The Mission of Discovery has long been part of our hospital's core values, and this emphasis on research is flourishing as we continue to grow as an organization devoted to serving our community. The accomplishments of our researchers over this past year have bolstered our commitment to improving patient care, with an outpouring of enthusiasm from senior leadership at St. Joseph's Healthcare Hamilton and St. Joseph's Health System. Fittingly, the Research Institute is aiming its sights higher than ever before.

As we move forward, the Research Institute is working to remove barriers and provide greater opportunities for research participation to our patients and the community. By connecting patients to research possibilities, we increase the accessibility and quality of new therapies and world leading clinical trials conducted in our hospital.

Our researchers have proven that they are capable of world-class, groundbreaking work. Together, we will continue to revolutionize the research enterprise. I hope you will be inspired by the stories contained within these pages, and excited for the future of scientific inquiry at St. Joe's.

Jack Gauldie, CM, PhD, DSc
Scientific Director, The Research Institute of St. Joe's — Hamilton
VP Research, St. Joseph's Healthcare Hamilton

Improving treatment for Canadians living with PTSD

“Under Dr. McKinnon’s leadership, the national Trauma Research Network represents the future of PTSD research and treatment in Canada. Our patients and clients will benefit tremendously from the work of this new network.”

Jagoda Pike
President & CEO
Homewood Health

The majority of Canadians will be exposed to traumatic stress at some point in their lives, but only some of those who experience trauma will develop post-traumatic stress disorder (PTSD).

“Some people show resilience and do not develop symptoms of PTSD, but 10 to 25 percent of individuals exposed to a traumatic event are expected to develop PTSD as a result of that exposure,” explains Dr. Margaret McKinnon, who studies PTSD and other mood disorders at St. Joseph’s Healthcare Hamilton.

The symptoms that are commonly associated with PTSD include hyper-arousal or hyper-vigilance, being easily startled, and heightened irritability.

“But PTSD is more than just a fear-based disorder,” says Dr. McKinnon, “it also involves feelings of being numbed-out, not being connected with others, and feeling disconnected from one’s body or one’s surroundings.”

Dr. McKinnon studies special populations who have experienced traumatic events causing PTSD, including veterans and emergency first-responders.

Though general awareness of various mental health issues has grown and stigma is in decline, much more work remains to be done to improve mental health treatment and outcomes.

To address the need for more translational research in this field, a new partnership was formed in April 2018 between the Homewood Research Institute, McMaster University, and the Research Institute of St. Joe’s. Central to this partnership – designated the Homewood-McMaster Trauma Research Network – is the inaugural appointment of Dr. McKinnon as the Homewood Research Chair in Mental Health and Trauma.

“We can help to create living laboratories to explore questions surrounding PTSD,” notes Dr. McKinnon. “We also need to better understand how emotional trauma has a physical impact on the brain.”

Dr. McKinnon is hoping to grow the partnership to explore the causes and consequences of mental illness, with a particular focus on PTSD. By bringing together several mental health centres, the new collaborative network will leverage collective expertise in novel treatment interventions, clinical innovation, and evaluation and knowledge exchange, as a means to improve treatment and outcomes for people experiencing PTSD.

“We also need to better understand how emotional trauma has a physical impact on the brain.”

“This is an important national development,” says Dr. Paul O’Byrne, Dean and Vice President of the Faculty of Health Sciences at McMaster, further adding that the partnership will “advance this important area of care faster than any of us could do alone.”

Ultimately, the collaborative network, which has its foundations in Ontario, will aim to expand across Canada to include other mental health institutions.

Dr. Margaret McKinnon

Through the haze: advancing the science of medical cannabis

"The guiding principle of the DeGroote Centre for Medicinal Cannabis Research is putting evidence first. A key part of that is making sure health care providers and the public are aware of what we do and don't know about medical benefits and potential harms. We want to help people separate fact from fiction when it comes to cannabis. Equally important is leading the next generation of studies that will provide the critical evidence we need about this exceptionally complex drug."

Dr. James MacKillop
Director, Michael G. DeGroote Centre for Medicinal Cannabis Research

A vast number of questions related to medicinal and recreational cannabis flourish across the web, each with their own fair share of conflicting answers. Are teens more susceptible to the effects of cannabis on the brain compared to adults? Can cannabis lead to the development of psychological disorders? How common is addiction to cannabis? How severely does cannabis affect one's ability to drive? Depending on where the answer is coming from, the responses to each question may be dramatically different. Too often, personal opinion and anecdotal evidence leads to misinformation about cannabis that is presented and repeated as fact.

The Canada-wide legalization of recreational cannabis in October 2018 highlighted the urgent need for effective and evidence-based public communications, as well as the need for further research into cannabis.

Evidence-based communications may be the only remedy to combat the myths and misinformation surrounding medicinal and recreational cannabis. As part of its mandate to provide a public knowledge portal, the Michael G. DeGroote Centre for Medicinal Cannabis Research (CMCR) promotes evidence-based information that has been curated by cannabis research experts and comes directly from primary research.

The CMCR is a partnership between St. Joseph's Healthcare Hamilton and McMaster University. Housed within St. Joe's West 5th Campus, researchers are investigating the nature of cannabis use for treating pain, and more broadly, as a novel treatment for a variety of clinical conditions.

One major priority of the CMCR is pursuing the scientific evidence supporting (or not supporting) therapeutic uses of cannabis. Another critical aspect of medicinal and recreational cannabis use involves understanding the associated risks and harms. To that end, the CMCR's second major priority involves understanding the unintended consequences associated with recreational cannabis use, including Cannabis Use Disorder, the clinical diagnosis of addiction to cannabis.

For a small subset of the population, cannabis use can lead to Cannabis Use Disorder – a clinical diagnosis of cannabis addiction combined with significant impairment. Cannabis Use Disorder ranges from mild to severe, and may be associated with comorbid conditions, such as mood and anxiety disorders, and other psychiatric conditions. The importance of understanding the development of Cannabis Use Disorder, along with other cannabis-related conditions, is paramount.

For researchers at the CMCR, building a body of cannabis knowledge is only half the battle. Effective public communication that translates new knowledge into actionable policies for communities, families, and individuals will continue to be a key priority for the CMCR.

Learn more about medicinal and recreational cannabis online at **research.stjoes.ca/cannabis**.

St. Joseph's Healthcare Hamilton – West 5th Campus

Helping the world breathe better

Bench to Bedside

Theresa has been living with a respiratory illness for years, visiting clinic after clinic. Doctors could not agree on a diagnosis – was it COPD? Emphysema, perhaps?

"After learning about the Firestone Regional Chest Clinic at St. Joe's, I immediately asked my family doctor for a referral," notes Theresa.

The dual role of the Firestone Institute for Respiratory Health as a clinic and research centre enables us to utilize translational research practices – that is, the ability to connect advancements made in the research lab directly to patient care in our clinic. This allows diagnostic methods to quickly become available to the patient population.

"I've had more tests at Firestone in the last week than I have in the last three years at the other clinics," says Theresa, glad that she has access to clinicians equipped with the latest advances in respiratory diagnostics.

A staggering 2.4 million Canadians over the age of 12 have been diagnosed with asthma, a respiratory illness characterized by constriction of the bronchial tubes in the lungs. Asthma causes chest tightness, shortness of breath, coughing or wheezing attacks, trouble sleeping, and can even lead to hospitalization and death.

Mild asthma makes up 50 to 75 percent of all asthma cases in Canada. Despite its name, mild asthma still has a considerable impact on the overall quality of life for patients. In fact, 40 percent of asthma exacerbations that require emergency care come from those with mild asthma.

For years, physicians have prescribed inhaled medications to treat mild asthma. A typical regimen includes two inhaled medicines: terbutaline, used as-needed for immediate symptom relief, and budesonide, a twice-daily maintenance drug to help minimize symptoms in the long-term.

Juggling multiple inhalers is a challenge for patients, especially when symptoms are not always present. Adherence to multiple inhaler regimens in cases of mild asthma is around 20 percent – only 1 in 5 people are taking their medications on the prescribed schedule.

"When patients have very mild disease, and don't have symptoms every day, they tend not to use the medication as prescribed," explains Dr. Paul O'Byrne, a clinician-researcher in the Firestone Institute for Respiratory Health at St. Joe's.

Maintenance budesonide, an inhaled corticosteroid, is effective at treating asthma symptoms when taken regularly. However, patient concerns over possible side effects associated with regular doses of corticosteroids is a major factor that contributes to low drug adherence.

Patient concerns over possible side effects associated with regular doses of corticosteroids is a major factor that contributes to low drug adherence.

This leaves as-needed terbutaline as the only asthma medication that many patients end up taking. Unfortunately, terbutaline does not help mitigate the long-term risk of asthma exacerbation – it merely provides short-term relief of symptoms once they occur.

In 2018, the results of two landmark clinical trials led by Dr. O'Byrne were published in the New England Journal of Medicine. Researchers determined that a single combination inhaler containing a mixture of budesonide and formoterol, taken as-needed, was superior to as-needed terbutaline in controlling asthma exacerbations. As well, the combination inhaler provides a similar effect as maintenance budesonide, but at a much lower corticosteroid dosage.

Clinicians who face adherence challenges with their patients' medications will now be better equipped with the knowledge to help Canadians breathe better, through the superior, single-inhaler approach.

Dr. Paul O'Byrne

Building research capacity across the globe

“The Firestone Institute for Respiratory Health is increasing its research capacity by collaborating with clinicians and scientists in China and around the world. This growth will enable further concurrent research projects in many areas of respiratory health. Such projects are of critical importance to an aging population.”

Dr. Martin Kolb
Research Director
Firestone Institute for Respiratory Health

The adverse health effects of cigarette smoking are well known. About half of all smokers will develop a serious smoking-related illness, such as chronic obstructive pulmonary disease (COPD), cardiovascular disease, or cancer. Despite widespread awareness of the health risks associated with smoking, the number of cigarettes sold around the world has steadily increased since 1980. While global prevalence of smoking has decreased since that time, with a rising population coupled with aggressive marketing of cigarettes in emerging markets such as China, more people are smoking today than ever before. In fact, almost half of all adult males in China smoke.

Chinese researchers at the Guangzhou Institute for Respiratory Health (GIRH) are attempting to get ahead of this problem. Since 2012, GIRH has been collaborating with researchers at the Firestone Institute for Respiratory Health (FIRH) at St. Joe’s.

Dr. Martin Stämpfli, a researcher at FIRH, studies how cigarette smoke affects the immune system and its role in the development of various respiratory diseases, including COPD. Dr. Stämpfli has been working with his colleague, Professor Rongchang Chen, for several years. This productive collaboration between GIRH and FIRH has yielded multiple peer-reviewed publications and presentations at international meetings.

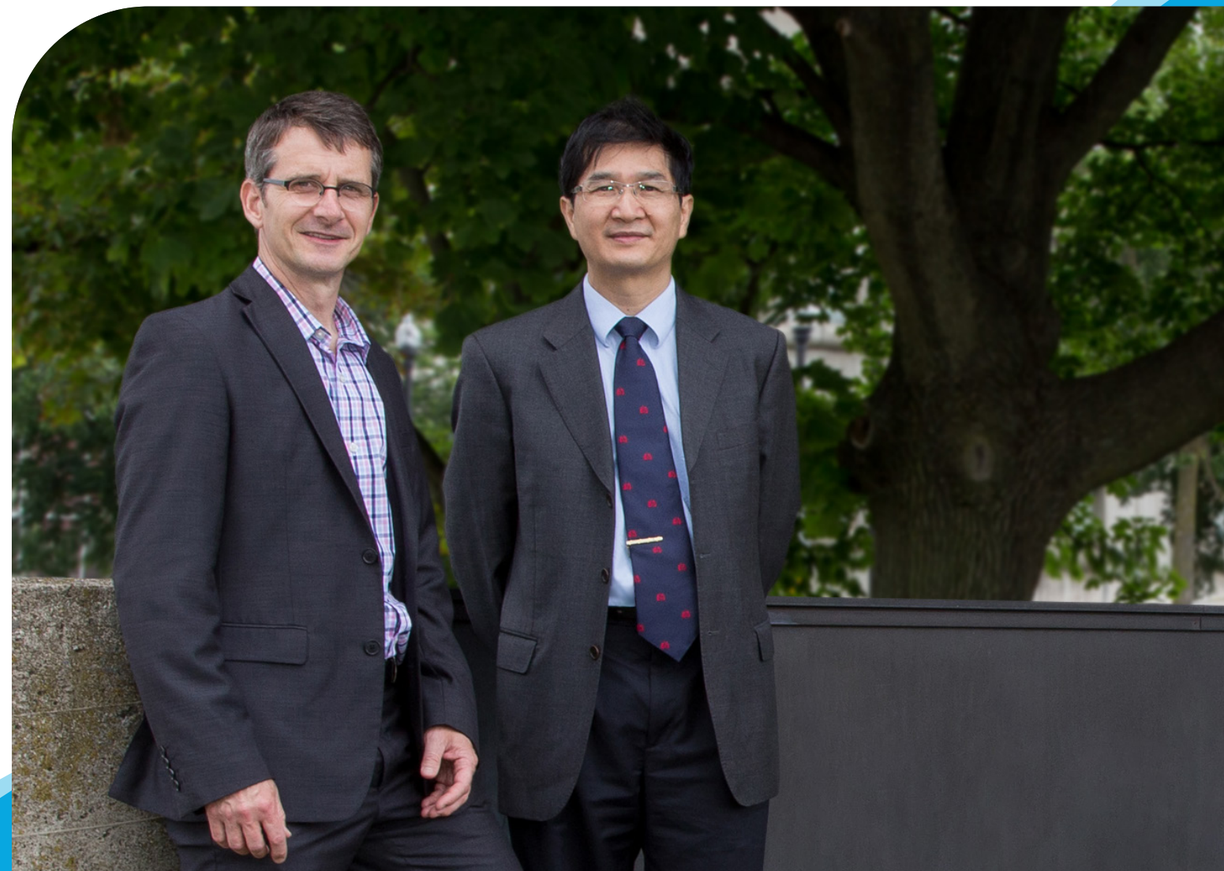
In July 2018, the collaboration entered its next phase as Dr. Stämpfli began a year-long research leave in Guangzhou, China. His goal is to expand his collaborations and establish a clinical research program in Guangzhou that will facilitate future translational studies. The program will feature graduate students and post-doctoral fellows who are aiming to tackle this growing threat to public health.

Dr. Stämpfli hopes to translate preclinical laboratory observations to clinical studies and investigate clinical observations in mechanistic laboratory studies. This bench-to-bedside and bedside-to-bench research will foster scientific discovery, with the hopes of translating novel observations into clinical trials. The partnership will allow FIRH to leverage its 40 year history of respiratory innovation with Guangzhou’s excellence in basic and clinical science.

To date, Dr. Stämpfli has successfully initiated a number of new research projects with Professor Chen and established new collaborative ties with several research faculty members at GIRH, as well as the State Key Laboratory of Respiratory Disease (SKLRD) in Guangzhou, the premier respiratory research facility in China. The success of these collaborative projects is rooted in the enthusiasm of our Chinese collaborators to further basic and clinical research. These are exciting opportunities for Dr. Stämpfli and FIRH, as the Research Institute continues to expand this productive collaboration in China.

Smoking remains a global epidemic. Thankfully, the collaborative work of Drs. Stämpfli and Chen is creating the capacity to conduct novel and exciting research that is urgently needed in the fight for respiratory health.

Dr. Martin Stämpfli and Dr. Rongchang Chen



A Year in Numbers

Total # of Researchers

185 + **493**

Research Staff & Learners

Total Publications

1132

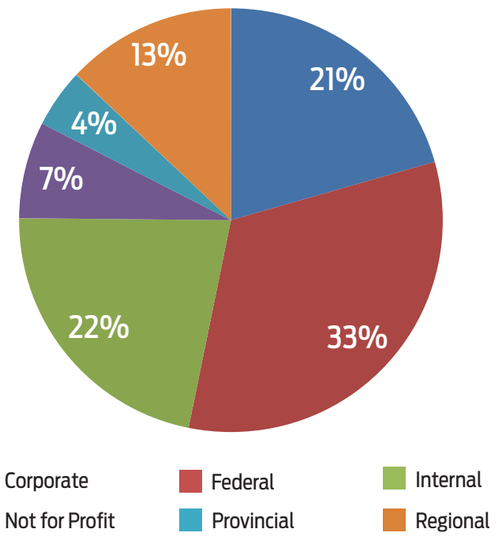
Events Hosted

20

Research Event

116 Clinical Research Projects Started This Year

Funding Source by %



72,981 ft²

Dedicated Research Space

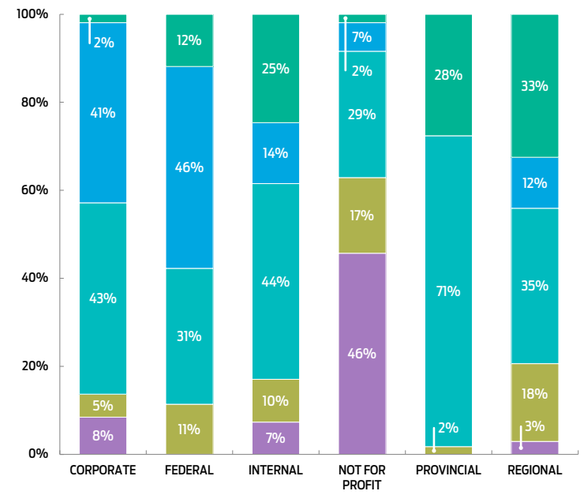
1 Refreshed Identity

1 New Pillar

Average Research Funding Per Investigator Per Program

Mental Health & Addiction	$ 118,981
Lungs & Chest	$ 296,390
Father Sean O'Sullivan Research Centre	$ 175,604
Kidney	$ 187,779
Genitourinary	$ 370,345

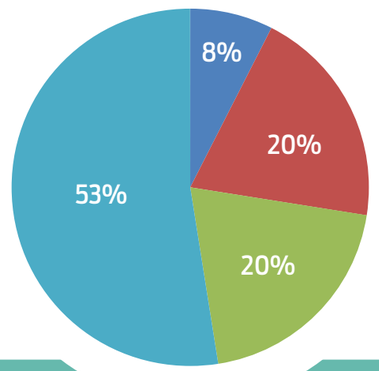
Funding Source by % per Program



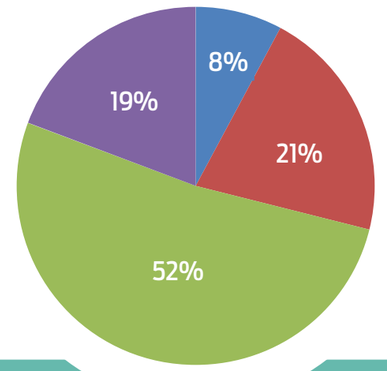
Total Funding

$25,073,216

40 New Clinical Trials



166 Ongoing Clinical Trials



Cartilage culture: a new hope for knees

"It's been 6 months since the procedure and though I'm still recovering, I'm very pleased with the results so far. My range of mobility has improved significantly and my knee feels a lot better than before the surgery."

Salim Lakhi
Patient & Research Participant

The World Health Organization estimates that by 2020, osteoarthritis will become the fourth-leading cause of disability globally. Around 10 percent of Canadians over the age of 15 already suffer from osteoarthritis. The condition is typically brought on by age-related degenerative changes, but can also arise following a traumatic episode.

When 20-year-old Salim Lakhi from Kitchener, Ontario was rock climbing during a trip to South Africa, he fell from a height of about 3 metres and injured his knee. Salim felt a sharp pain and was unable to walk for a few days, but he assumed his injuries would heal over time.

As his knee pain persisted, he would soon discover the magnitude of the damage caused by the fall. Due to the severity of his case, Salim was referred to Dr. Anthony Adili and Dr. Moin Khan – renowned orthopedic surgeons at St. Joseph's Healthcare Hamilton.

"These aren't great injuries to have as a young individual," says Dr. Adili, explaining that within 10 to 15 years, "it likely will develop into a very arthritic compartment, if not arthritic knee, without intervention."

St. Joe's doctors had discovered that Salim had a large injury to his knee cartilage. The standard treatment method involves the use of a microfracture in which small holes are made in the bone to stimulate the formation of scar cartilage.

"Unfortunately, microfracture results in the formation of fibrocartilage or 'scar cartilage,' which does not have the same properties as native, hyaline cartilage," says Dr. Moin Khan. "The ideal scenario would be to replace the injured cartilage with his own native cartilage."

Luckily for Salim, Dr. Adili and Dr. Khan are collaborating on a randomized controlled trial comparing the outcomes between microfracture and the latest in cartilage transplant surgery. Specifically, the study is examining autologous chondrocyte transplant, where tissue is taken from the same individual who receives the transplant.

Dr. Adili and Dr. Khan informed Salim of this novel procedure, one that was still being studied at various centres in the United States. It would involve harvesting a tiny, healthy sample of Salim's cartilage, which would be used to grow sheets of the patient's own cartilage in a laboratory. The lab-grown cartilage would then be fitted to the injury, and transplanted back into Salim's knee.

Optimistic about the potential for a better treatment outcome, Salim decided to participate in the study. In August 2018, a small sample of his cartilage was sent to a lab in the United States. The following month, the newly-grown cartilage was surgically inserted into Salim's knee. This was the first time this form of cartilage transplant was performed in Canada.

"Our goal from the surgery was to prevent Salim from developing osteoarthritis later in life," explains Dr. Adili, "thereby avoiding the need for knee replacement surgery."

By collaborating with other institutions, clinician-researchers at St. Joe's are helping to develop the next generation of orthopedic treatments for knee joint preservation.

Dr. Anthony Adili and Dr. Moin Khan

Look and listen: using ultrasound to catch arthritis sooner

"I was diagnosed with rheumatoid arthritis (RA) in my hands. The treatment for RA involves corticosteroid injections to reduce the inflammation that causes pain. To avoid further discomfort, Dr. Larché numbs my hands before the procedure. Her use of ultrasound to pinpoint the problematic spots of my hands allows her to find the best place for each injection, improving the effectiveness of the treatment. Dr. Larché has given me the use of my hands, which has greatly improved my quality of life."

Margaret Clark
Patient & Research Participant

Rheumatoid arthritis (RA) is an auto-immune disease that affects approximately 1 in 100 Canadians. Unlike osteoarthritis, which is caused by wear-and-tear or trauma to the joint cartilage, RA is caused by a malfunction of the body's own immune system. The disease is characterized by joint inflammation that causes pain, stiffness, and swelling. Joint degradation occurs as a result of the immune system's attack on the lining of the joints.

Early signs of this auto-immune disease can be vague, such as feeling tired and unwell, accompanied by sore joints. As the disease progresses, more joints may become affected, usually in a symmetrical pattern throughout the body.

Detecting RA in its early stages is a major factor in the successful treatment of the disease. The window to achieve remission, thereby preventing permanent damage to the joints, is an estimated 6-12 months. With a limited number of RA specialists, this narrow timeframe presents a challenge.

Dr. Maggie Larché is a clinician-researcher at St. Joseph's Healthcare Hamilton and an Associate Professor of Medicine at McMaster University. Her research and clinical practice focus on rheumatoid arthritis, systemic sclerosis (commonly known as scleroderma), and other inflammatory, auto-immune diseases.

For years, Dr. Larché has been at the forefront of advancing the use of ultrasound in the diagnosis and treatment of RA. In fact, she is a founding member of the Canadian Rheumatology Ultrasound Society (CRUS), a group that advocates for the use of ultrasound for diagnosing the disease. Dr. Larché continues to teach musculoskeletal ultrasonography to medical trainees and clinicians in an effort to expand access to this diagnostic technique.

"We know that ultrasound can detect rheumatoid arthritis sooner than clinical methods, and an earlier diagnosis can have a significant impact on a patient's recovery and overall quality of life," explains Dr. Larché. "Through the CRUS, my colleagues and I have promoted the use of ultrasound in diagnosing and monitoring patients with inflammatory arthritis, as well as increased the access to ultrasound training for health care providers in Canada."

Overall, there are many advantages of using musculoskeletal ultrasound over other imaging methods. Ultrasound is a non-invasive, radiation-free, portable, and inexpensive tool for diagnosing RA. In addition, diagnosis occurs in real-time with the patient, unlike an MRI or CT scan.

Research on the feasibility of ultrasound for RA diagnosis conducted by Dr. Larché and her colleagues is transforming the field of rheumatology in Canada. Though the technique may require longer clinical visits for patients at the point of care, its ability to enhance early detection and monitoring will help more Canadians start treatment sooner and avoid permanent damage to their joints. Not only does this reduce the health care resources needed to treat chronic RA, it assists in improving patient quality of life.

Dr. Maggie Larché

Designing high quality research from start to finish

From mental health and addiction studies to clinical trials for complex airway diseases – research at St. Joe's occurs across a wide variety of disciplines.

The Research Institute's Biostatistics Unit is one of the key components of our research enterprise, working to ensure the high-quality of research generated at St. Joe's. With such a large and diversified volume of active research, it is critical that the work of our researchers is not only ethically sound, it must also be designed to effectively answer the research questions. Housed within the Father Sean O'Sullivan Research Centre at St. Joe's, the Biostatistics Unit collaborates with researchers within and outside of St. Joe's in order to ensure the study design, methodology, and data collection are optimized from the beginning of any research study.

The Biostatistics Unit is strategically placed within the walls of the hospital in order to facilitate better understanding of clinical operations that will affect study design and outcomes. The team is made up of researchers affiliated with McMaster University's Department of Health Research Methods, Evidence, and Impact (HEI).

Dr. Lehana Thabane, Director of the Biostatistics Unit and Associate Chair of HEI, describes himself as a practical methodologist rather than a statistician. According to Thabane, the Biostatistics Unit specializes in translating clinical problems into researchable questions and designing the best studies to answer these questions.

To optimize the quality of research, collaboration with the Biostatistics Unit ideally begins at the initial conception of any research study. Salvaging data from a poorly designed study is a very inefficient method of doing research, and often may not be possible. Thankfully, Biostatistics researchers are available to collaborate from initial concept through to publication — providing leadership on various forms of studies that include **pilot studies** designed to assess feasibility of larger studies; **interventional studies** aimed at assessing the benefits and harms of therapies and procedures among in-hospital, ambulatory, or primary care patients; and **clinical effectiveness research studies** aimed at using scientific evidence to understand the effectiveness, benefits, and harms of different options to prevent, diagnose, treat, and monitor clinical conditions and improve the delivery of service.

In fact, recognizing the significance of effective study design to research outcomes, institutions from around the world have sought the services of the Biostatistics Unit at St. Joe's. Dr. Thabane estimates that he and his team have collectively visited nearly 50 countries to develop high quality studies or to build biostatistics capacity in institutions of higher learning. Their work continues to place St. Joseph's Healthcare Hamilton, McMaster University, and Canada in the forefront of scientific innovation and sophistication in health research methodology, leading to advances in health care delivery locally, nationally, and internationally.

The Biostatistics Unit at St. Joe's is an essential component of any research team, one that both veteran and novice researchers continue to utilize to help navigate the complexities of data analysis and study design.

Research in Action

In the summer of 2018, as part of the Carnegie African Diaspora Fellowship Program, Dr. Lawrence Mbuagbaw, a research methodologist in the Biostatistics Unit at St. Joe's, travelled to Cape Town, South Africa. His goal was to help Stellenbosch University build capacity within their recently established graduate program in biostatistics.

"Biostatistics capacity is in short supply on the African continent and many efforts are underway to train more biostatisticians. They are critical members of any research team," says Dr. Mbuagbaw. "I try to take these opportunities to collaborate in Africa whenever I can."

Overall, these efforts will enhance the career growth of students in the MSc Biostatistics Program at Stellenbosch University.

St. Joe's Biostatistics Unit

Could atherosclerosis be an auto-immune disease?

"Our laboratory scientists are working on the frontiers of the human body and its mysteries. It is these groundbreaking studies, ones that force us to rethink our understanding of diseases, which have immense impacts on the long-term development of live-saving medicines and treatments."

Dr. Tom Stewart
President & CEO
St. Joseph's Health System

The growth of plaque lesions in blood vessels, known as atherosclerosis, is the underlying cause of cardiovascular disease in the developed world. Complications that may result from cardiovascular disease can include stroke, heart attack, aneurism, and other cardiovascular problems.

Earlier research has shown that various forms of LDL – the so-called "bad" cholesterol – can cause stress to the endothelial cells that line the inside of the blood vessels. However, previous research did not provide a clear picture of what happens at the cellular level that leads to increased cellular stress and plaque build-up.

Fortunately, in December 2018, Drs. Richard Austin and Ali Al-Hashimi published their research on a protein called GRP78 and its connection to atherosclerosis. They had discovered a significant link between the acceleration of plaque lesion growth and the body's own immune system.

Normally, GRP78 resides inside the endothelial cells where it helps to fold and transport other proteins. St. Joe's researchers found that GRP78 is abnormally transported to the surface of endothelial cells when they experience stress caused by cholesterol and other factors.

When GRP78 appears on the cell surface, the immune system considers it a foreign entity and responds by producing autoantibodies. The binding of these immune antibodies to surface GRP78 initiates a domino effect – adhesive proteins are released, further trapping immune cells and the "bad" cholesterol, which induces more cellular stress. This feedback loop ultimately accelerates the growth of plaque lesions.

"Now that we have a clearer understanding of the complex process that links surface GRP78 to autoantibodies and accelerated lesion build-up, we can identify new drugs that disrupt this interaction," notes Dr. Austin.

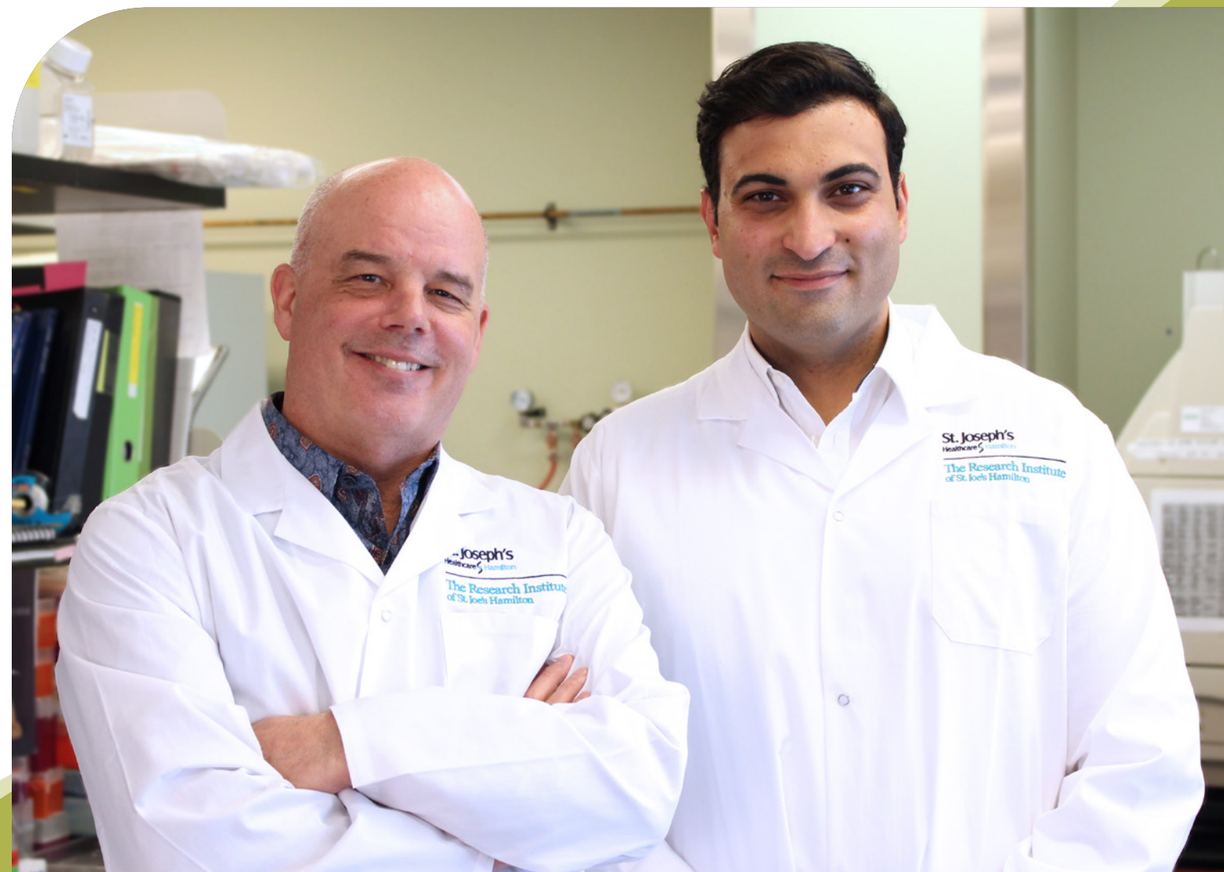
The role of the immune system in the acceleration of plaque build-up has scientists reconsidering whether atherosclerosis is, in fact, an auto-immune disease. This new conception of the disease has researchers considering novel treatment pathways.

This new conception of the disease has reseachers considering novel treatment pathways.

So far, researchers have found that enoxaparin, a form of the blood-thinning drug heparin, is able to block the interaction between surface GRP78 and the immune system autoantibodies in mouse models. The next step for St. Joe's researchers will be identifying other compounds or biologics that can function like enoxaparin, but without its blood-thinning properties.

The development of such a medication would be a major step in preventative treatments for atherosclerosis and cardiovascular disease – that's why scientists in the Research Institute's Kidney program are dedicated to exploring the minutia of the body's cellular workings.

Dr. Richard Austin and Dr. Ali Al-Hashimi



A giant leap in the fight against urological cancer

A Helping Hand

In 1998, John Ribson was diagnosed with bladder cancer. Unsure of his future, he put his trust in physicians at St. Joe's. At the time, there were few options for treating urological cancers. However, research has since increased cure rates and uncovered better disease management strategies. John got the treatment he needed.

Twenty years after he was first diagnosed, John Ribson is helping St. Joe's researchers establish a new Urological Oncology Research Centre through a generous gift of $1 million.

"I believe it is important to support causes that are close to our hearts and ones that can have an impact in our community," says Mr. Ribson. "I am thankful to be able to give back to the hospital, the physicians, and the researchers that helped save my life and to hopefully help them save even more lives through new research."

Each year, over 35,000 Canadians are diagnosed with kidney, bladder, or prostate cancer. In fact, 1 in 7 men will be affected by prostate cancer at some point in their lifetime.

Until now, urology research at St. Joseph's Healthcare Hamilton has mostly been in the form of clinical trials, in support of diagnosis and disease management. Advances in robotic surgery at St. Joe's have helped us become a leader in this growing field. Today, St. Joe's is making the next big leap in urological research by expanding collaboration between basic scientists and clinical researchers through the formation of the Urological Oncology Research Centre.

Dr. Anil Kapoor, a urologic surgeon and researcher, has been named the Centre's director. Dr. Kapoor envisions a research enterprise that will utilize translational research practices.

Translational research is a specialty of St. Joe's – it allows our researchers to take their discoveries from the lab bench to the clinical bedside, all within our hospital. This bench-to-bedside approach is tremendously successful in other research areas at St. Joe's. Researchers at the new Urological Oncology Research Centre hope to benefit from these translational practices that connect basic scientists in our laboratories to clinicians caring for patients.

For example, basic scientists working at St. Joe's, including Dr. Richard Austin and his team, have identified several biomarkers that are correlated with various urological cancers in animal models and in humans.

Over the next few years as the new Urological Oncology Research Centre progresses, Dr. Kapoor's goal is to link discoveries that are being made through groundbreaking lab work, including the identification of specific biomarkers and genetic testing, to clinical diagnostics and patient care.

"The next step will be to check for these biomarkers in a clinical setting," says Dr. Kapoor. By searching for biomarkers in patients, Dr. Kapoor and his team hope to be able to determine a patient's risk of cancer reoccurrence. This foresight will be a powerful tool in the fight against kidney, bladder, and prostate cancer – allowing doctors to plan a tailored follow-up for each patient.

By searching for biomarkers in patients, Dr. Kapoor and his team hope to be able to determine a patient's risk of cancer reoccurance.

Thanks to the philanthropic leadership of patient donors like Mr. John Ribson, St. Joseph's Healthcare Hamilton now has the resources to take the next step in urological cancer research. The Urological Oncology Research Centre will launch early 2019, with the goal of transforming care for patients with genitourinary cancer.

Dr. Anil Kapoor and Mr. John Ribson

Supporting discovery: one patient's message of hope

"Cancer is an equalizer and something that will only be beat by the next big advance uncovered through extensive research. I believe it is up to all of us to make whatever contribution we can to research to help search for a solution to cancer."

Mr. Jim Bullock
Grateful St. Joe's Patient
& Philanthropist

In 2013, Jim Bullock was referred to St. Joseph's Healthcare Hamilton in the hope he would qualify to participate in a cancer treatment clinical trial. The prognosis from his referring health care team was grim. The trial was an attempt to keep his kidney cancer at bay and allow him time with family and friends. That was his sole hope until he met St. Joe's urologist, Dr. Anil Kapoor.

"You wouldn't think a person would be happy to know they didn't qualify for a clinical trial but, in my case, it was the best news because it was delivered along with a new idea – an idea that was more aggressive and would be delivered by one of the leading urology specialists around," says Jim. "When Dr. Kapoor told me he didn't believe the kidney cancer was as aggressive as originally suspected and he was confident that I qualified for a robotic-assisted laparoscopic surgery procedure that would be less invasive than traditional surgery, I was for the first time in a long time hopeful."

Jim's hope was not misplaced. After the robotic assisted surgery, Dr. Kapoor confirmed Jim's kidney was removed cleanly. Dr. Kapoor began monitoring Jim every month, but as Jim continued to improve, those visits were extended to every four months and now, every six. All along, Jim had some small tumours on his lungs, which Dr. Kapoor explained were slow-growing kidney cancer tumours, not lung cancer. Jim quickly received "pencil-precision radiation" and both his outlook and prognosis remained positive.

"I'm proof that our health care system works very well. I got the expert care I needed when I needed it, but few would disagree that our health care system is on the edge of chaos," says Jim. "I know that if our system is stretched, there certainly won't be funding available for research into what the next innovation will be. And that's exactly why I have made a donation to research in urological oncology at St. Joe's."

St. Joe's urological oncology program is one of the best in Canada. The hospital has the expertise and reputation and now, thanks to donor generosity, it will also be one of Ontario's leading urological research sites. Under the leadership of Dr. Kapoor, teams will uncover life-saving treatments and preventions for patients like Jim and so many others.

"It remains stunning to me that everyone – young, old, female, male and from all cultures and backgrounds – is represented in Dr. Kapoor's waiting room," notes Jim. "Cancer is an equalizer and something that will only be beat by the next big advance uncovered through extensive research. I believe it is up to all of us to make whatever contribution we can to research to help search for a solution to cancer."

Jim joined other grateful patient donors and made a generous contribution to the establishment of a Urological Oncology Research Centre. After donating $250,000 to the Centre, Jim is encouraging others to give, too – Jim will match any donations made to the Centre of $10,000 or more to a maximum of $750,000. Learn more and make a donation today by visiting St. Joseph's Healthcare Foundation's website, **stjoesfoundation.ca**.

Mr. Jim Bullock

Every gift to St. Joe's *inspires*

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