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Since the inception of the McMaster Stem Cell and Cancer Research Institute (SCC-RI) in 2006, a world-class team of investigators in the Michael G. DeGroote Centre for Learning and Discovery, have achieved countless critical discoveries that have had extraordinary impact. Today, this globally-renowned research powerhouse leads in several important areas, including the development of stem cell technologies that can treat blood and neural diseases, chronic pain, autism, brain tumours and aging.

We remain grateful for the ongoing support of our donors and funders, including Michael G. DeGroote, the Marta and Owen Boris Foundation and Mr. David Braley. These gifts enabled McMaster to recruit Dr. Mick Bhatia, already a worldwide recognized expert in the biology of stem cells. Dr. Bhatia set up the SCC-RI, which quickly became one of the top stem cell research institutes in the world and has attracted and continues to attract remarkable scientists. The initial focus on human stem cells and their expansion proved prescient. Dr. Bhatia and his team proved that with complex genetic modification it was possible to differentiate a number of different cells in the body into completely different cells.

The recent interest of Dr. Bhatia and other members of the SCC-RI in commercializing some of their discoveries is timely as the Faculty of Health Sciences is currently enhancing entrepreneurship and commercialization.

With over a decade of discovery, SCC-RI researchers continue to deepen our understanding of some of the most complex issues related to human health, while mentoring and training our next generation of biomedical researchers. We salute them for their dedication and commitment.

McMaster has earned its reputation as a global research powerhouse on the strength of its researchers. The talent that resides in the McMaster Stem Cell and Cancer Research Institute is a case in point.

They’re recognized worldwide for their individual and collective contributions to the advancement of stem cell research. And what’s more: Their commitment to basic discovery is matched by their potential to translate their research results into treatments that can – and will – improve the health and well-being of Canadians and citizens around the world.

With over a decade of discovery, SCC-RI researchers continue to deepen our understanding of some of the most complex issues related to human health, while mentoring and training our next generation of biomedical researchers. We salute them for their dedication and commitment.

Rob Baker
Vice-President, Research, Faculty of Health Sciences, McMaster University
2017 marks the first year since the unveiling of our new brand and vision for the future direction of the SCC-RI. Our aim was to reflect the evolution of the institute over the past decade as well as the exciting directions we are embarking upon.

SCC-RI research programs are now focused on specific areas of cancer biology and treatment, understanding blood formation and how we can improve life-saving bone marrow transplants towards better outcomes for patients, and have expanded to include new endeavours to identify and model therapeutic targets in neurological disorders. As always, SCC-RI programs continue to employ human model systems, to assure more immediate translation of our work to the clinic.

This year’s report highlights the importance of relationships between the laboratory and the clinic; scientists and physicians; researchers from other disciplines; and also, the contributions of our committed students and postdoctoral fellows that are a cornerstone of our success. We hope that our trainee’s stories will inspire other young people to embark on a path to exciting and diverse career opportunities that begin with the training provided in the SCC-RI’s collaborative and dynamic research environment.

Of course, without the support of the selfless people who dedicate their time to better understand what we do and make informed contributions to support innovative projects, trainee scholarships and the creation of state-of-the-art research facilities, we could not continue to make the inroads necessary to achieve our central goal of improving human health. We would like to acknowledge all of SCC-RI’s friends and supporters that have brought us closer to this purpose. In particular, I would like to take this opportunity to remember Ellie Voortman and Jim Kennedy. Their commitment to the SCC-RI has truly made a difference to our graduate students and empowered them to do their best work. Their lives and legacy are an inspiration to all of us at the SCC-RI.

Mick Bhatia, PhD
Scientific Director
Killing cancer cells indirectly by powering up fat cells in the bone marrow, could help acute myeloid leukemia patients according to a new study from the Bhatia Lab at McMaster’s Stem Cell and Cancer Research Institute.

In collaboration with Hamilton Health Sciences, Ottawa Health Research Institute and London Health Sciences, researchers in the Bhatia lab found that boosting adipocytes, or fat cells, located in the bone marrow suppressed cancerous leukemia cells but – in a surprise to the translational team – induced the regeneration of healthy blood cells at the same time.

The production of healthy red blood cells is critical for those with acute myeloid leukemia but is sometimes overlooked as conventional treatments focus on killing the leukemia cells alone. Patients with this disease suffer from anemia and infection due to the failure of healthy blood production, all of which are leading causes of hospitalization and death from the disease.

The study was published in the journal *Nature Cell Biology* in October 2017.

“Our approach represents a different way of looking at leukemia and considers the entire bone marrow as an ecosystem, rather than the traditional approach of studying and trying to directly kill the diseased cells themselves,” said Allison Boyd, postdoctoral fellow with the research institute and first author of the study.

“These traditional approaches have not delivered enough new therapeutic options for patients. The standard-of-care for this disease hasn’t changed in several decades.”

The McMaster-led study was conducted over the past three and half years and started from observations of leukemia patients. This led to the collection of bone marrow samples from larger cohorts of patients with The Ottawa Hospital, as well as those from Western University and Hamilton Health Sciences, for the next steps of investigation. This included detailed study and imaging of individual leukemia cells compared to healthy cells residing in the bone marrow, which revealed the effects of targeting fat cells.

A drug commonly used to moderate diabetes that induces fat cell production in the bone marrow was used and was found to help foster red blood cell production as well as suppress leukemic disease.

“The focus of chemotherapy and existing standard-of-care is on killing cancer cells but instead we took a completely different approach which changes the environment the cancer cells live in,” said Mick Bhatia.

“This not only suppressed the “bad” cancer cells, but also bolstered the “good” healthy cells allowing them to regenerate in the new drug-induced environment.”

“The fact that we can target one cell type in one tissue using an existing drug makes us excited about the possibilities of testing this in patients.”

“We can envision this becoming a potential new therapeutic approach that can either be added to existing treatments or even replace others in the near future. The fact that this drug activates blood regeneration may provide benefits for those waiting for bone marrow transplants by activating their own healthy cells.”

Funding for the study came from the Canadian Cancer Society and the Marta and Owen Boris Foundation.

“With nearly one in two Canadians expected to be diagnosed with cancer in their lifetime, the need to find new and more effective treatments has never been more urgent,” said Lynne Hudson, president and CEO of the Canadian Cancer Society.

“We’re thrilled that we could fund Dr. Bhatia and his team on this exciting project. The double-duty treatment they have discovered could lead to a whole new approach to treating leukemia.”
Allison Boyd is a postdoctoral fellow in the Bhatia Lab and lead author on the *Nature Cell Biology* study. We asked Allison about her experience at the SCC-RI and how she has been supported in her quest to address complex biological questions that will help us better understand cancers like leukemia.

When I was searching for a research position to study cancer biology, the Bhatia lab at the SCC-RI was the obvious choice. It is rare to find a research program that brings together diverse ideas to understand the blood system all the way from its embryonic origins to regulation in adults, and unfortunate dysregulation in leukemic disease. I was curious to study blood cancer, because I found the biology of a liquid tumor less intuitive to understand compared to solid tumors. Unlike a solid mass that clearly invades and damages neighboring tissue, leukemia cells are not fixed in place and they do not permanently destroy the normal blood system. Patients with leukemia still have healthy blood stem cells, but for some reason these cells stop functioning to produce the normal red and white blood cells that the body needs, causing life threatening symptoms. It was not well understood why this happens, and this became my central research question.

Working with Mick has taught me the importance of looking at the big picture to understand biology. While many researchers study leukemia cells by growing them in a culture dish, analyzing the diseased cells by themselves could not explain how they affect the rest of the body and disrupt normal blood production. Mick is a leading expert in the technique of grafting human blood tissue to grow in mice, which is the best way to examine human leukemia cells in a realistic living environment. This approach is what led us to the observation that leukemia stifles normal blood production by disturbing the “habitat” in the bone marrow, where healthy stem cells live. Specifically, we found that leukemia causes fat cells to disappear from bone marrow, and by treating mice with drugs that trigger fat cell formation, we could reverse the effects of disease and boost healthy blood production. The project gained momentum when I started working with another student who was directly analyzing bone tissue from leukemia patients. The lab has a great culture of collaboration that promotes the exchange of ideas and observations, and when we noticed strong parallels between human patients and our experimental mouse system, this gave us confidence that we were moving in the right direction. Beyond the strong teamwork atmosphere within the lab, we also benefitted from regular feedback from medical doctors who specialize in the treatment of leukemia patients. Not many training environments provide this level of contact with the clinic while also offering such sophisticated laboratory techniques, and this shaped the way we approached our research.

The significance of fat cells in the bone marrow has been overlooked for a long time and our work now shows that these cells participate in a meaningful way to regulate blood production, and we can use them to our advantage to fight leukemic disease. It has been so fulfilling to arrive at a new understanding of the blood system that I would never have predicted, while successfully addressing the question that originally brought me to the lab. I would have traveled anywhere for my PhD studies, but as a Canadian I am very proud to have worked with the best scientists to pursue such an important research topic, right here at home.
Last year Dr. Kristin Hope, leader of the SCC-RI’s Blood Program, published an important paper on the role of a RNA-binding protein, called Musashi, in expanding blood stem cells in the top scientific journal *Nature*. More recently we spoke with Kristin to see what her lab has been up to in the year since this study was published:

**The Nature study was your first major publication as an independent investigator. This must have been a tremendously exciting time for you and your lab….**

Yes, it has been quite a rollercoaster ride since we first received word that our work had been accepted to *Nature*. I had just been informed that, while we were close, we had unfortunately missed out on receiving important, highly competitive funding. Literally the next day, we received the news from *Nature*. It was both a low point and high point of my career in the same week. Fortunately, the OICR funding that supports my position and research program was in place at the time to enable me to continue to build upon our initial findings. We were also awarded a Stem Cell Network Impact Grant to further our work and strengthen the provisional patent we filed that covers the methods developed for the *Nature* study.

And I can also report that my former PhD student Stefan Rentas and lead author on the study, was accepted into a prestigious fellowship program at the University of Pennsylvania to pursue his dream of becoming a clinical genetecist.

**How has your research program evolved since this work was first published?**

The lab has leveraged what we have learned about healthy hematopoietic stem cells, and flipped it to see if we could apply it to an unhealthy, leukemic, situation. We know that the protein Musashi is important for normal hematopoietic stem cells (higher levels of Musashi result in higher production of stem cells), and we also know that in leukemia, a high expression of Musashi is implicated in disease progression and poor prognosis. So, we are now trying to determine if we can treat leukemia by turning Musashi off. We are already seeing some promising results using this strategy.

**When we last spoke you also mentioned that your group would be exploring other RNA-binding proteins like Musashi-2. How is that going?**

We are now collaborating with Dr. Daniel Schramek, a screening expert at the Lunenfeld-Tanenbaum Research Institute, on studying a subset of RNA-binding proteins we have identified that are much more elevated in leukemia stem cells than they are in other leukemia cells. Laura De Rooij, a PhD candidate in my lab has designed a screen to test which RNA-binding proteins are necessary regulators of leukemia stem cells and ultimately control how the disease functions in the body.

**How does the collaborative environment at the SCC-RI enhance your work?**

What I’ve always really liked about the environment here is the mix of perspectives. Sharing the same space and working collaboratively allows me to engage with other researchers with differing views first-hand and integrate them into my own lab. These interactions lead to the development of new ideas and experimental approaches. The positive discussions that happen on a daily basis really elevate the work—something that rarely happens in traditional research environments.
Lead the Way
Branavan Manoranjan, MD PhD Candidate

In our “Lead the Way” series, we introduce you to SCC-RI trainees who are transitioning into exciting and diverse careers and poised to be the next generation of leaders to advance human health.

We asked MD PhD candidate, Branavan Manoranjan, to reflect on his path towards earning his advanced degrees, and his time as a trainee at the SCC-RI. Hear from him in his own words, about his journey from eager high school student to scientist and medical trainee…

I am overcome with nostalgia for my last semester of high school every time I hear the words, “It was all a dream” from the song “Juicy” by the Notorious B.I.G. I experienced what Malcolm Gladwell would consider my “tipping point” during those final 5 months in high school. Through an inner-city mentorship program, I had the opportunity of a lifetime to conduct translational research on injury prevention and traumatic brain injuries with neurosurgeon, Dr. Michael Cusimano at Toronto’s St. Michael’s Hospital. Indeed, it was all a dream! The placement not only introduced me to medical research but also instilled a sense of social responsibility within me for conducting translational “bench-to-bedside” research. I was surrounded by clinician-scientists who were motivated to not only treat their patients but to go one step further and determine the underlying factors that may influence their patients’ health outcomes.

During my placement, I had the privilege of meeting two additional mentors who have played critical roles in my MD/PhD pursuits: Dr. Kalman Kovacs and Dr. Sheila Singh. Dr. Kovacs is an endocrine pathologist who has made seminal contributions to the study of pituitary adenomas. I had the opportunity to work on a project with Dr. Sheila Singh when she was on Dr. Cusimano’s service as a neurosurgical resident at the University of Toronto. Seeing Dr. Singh’s motivation for her research, all the while managing her busy schedule as a resident, gave me a realistic picture of the dedication, patience, and optimism needed to thrive as a clinician-scientist.

Fast forward to 2017, I am now in the fifth year of the MD/PhD program at McMaster University, wrapping up my PhD in Dr. Sheila Singh’s laboratory. While an undergraduate trainee in Dr. Singh’s lab in the SCC-RI, I had no doubt in my mind that she would be the perfect mentor for completing my MD/PhD training. Dr. Singh is an influential role model in the clinician-scientist community and fosters a close-knit and supportive team environment. Supplementation of the SCC-RI’s unique training environment in which researchers with diverse interests may collaborate and ask some of the most provocative questions to address the knowledge gaps in stem cell and cancer biology.

In taking advantage of the many opportunities made available throughout my training, I have been fortunate to have been awarded a CIHR Vanier Canada Graduate Scholarship, travelled internationally to present my research, co-authored several manuscripts, and most importantly, built relationships with the families of patients who have supported my research and served as an unyielding source of motivation.

After receiving my MD/PhD, I plan to pursue residency training in neurosurgery combined with a post-doctoral fellowship. My long-term goal is to merge my academic interest in neuro-oncology with a clinical career in neurosurgery focused on the treatment and management of patients with brain tumours. My proudest professional achievement during my time at the SCC-RI has been in working with my peers to motivate and engage local high school students to consider a career in science and research. Through our annual Stem Cell Talks event, the SCC-RI graduate students have played an instrumental role in encouraging the next generation of stem cell and cancer biologists.

As we all embrace the challenges encountered throughout our journey to provide better care for our patients as clinician-scientists, we’re reminded that we stand on the shoulders of the likes of Drs. Cusimano, Kovacs, and Sheila Singh who serve as lighthouses during our voyage. Mentorship plays a critical role in cultivating the minds of future medical researchers, and I am immensely grateful to all the clinician-scientists who inspired me to work towards making this dream a reality.
Ryan Mitchell began his training in the SCC-RI as a co-op student. After completing his PhD, he began a postdoctoral fellowship in the Bhatia lab. Now focused on a career path that blends science and business, Ryan gave us his thoughts on why it is so important to translate and commercialize discoveries made in the lab.

Translation and commercialization are two terms that are often mentioned together, and I think it’s critical to understand the difference between them if you want to appreciate their importance. Translation refers to the process of bringing a product, procedure, or practice from the “bench” in the lab, to the “bed side” in the hospital. Commercialization is the process of taking your product or service to market where it can be sold to turn a profit. It is easy for scientists and the public alike to understand why translating is important, because there is a direct link to a person in need of this new product or service. However, commercialization of science is often vilified by scientists and the public, on the feeling that companies are profiting from the misfortunes of others. Although profits are made, this line of thinking ignores the largest benefit of commercialization, which is that it is often the very vehicle that enables the widespread distribution of critical medical products and services that alter and save the lives of millions of people. Without commercialization, many of the medicines and medical services that people rely on today would not be accessible.

What advice would you give to a new trainee that wanted to develop their commercialization skills?

If they have not decided on a lab already, I would recommend applying to supervisors that have demonstrated competency in commercialization before, or at least a willingness to do so, should the opportunity arise. Being surrounded by entrepreneurial culture can provide very unique and rewarding learning experiences. Get in touch with your University’s technology transfer office and seek out networking events with other entrepreneurs. You should never perform science with the intent to commercialize, but you can prepare yourself by making the right connections in case your academic pursuits should lend themselves to doing so.

What is your ideal role when you leave the SCC-RI?

I have always wanted to work at the interface between business and science. In fact, this was the reason I joined Mick’s lab, it was engrained in all of the projects I worked on, and it became my final quest during my post doc. With this in mind, I pursued and have now accepted a position in scientific consulting within the healthcare investment banking sector.
The last time we spoke with Yannick Benoit a postdoctoral fellow trainee in the lab of SCC-RI Scientific Director, Dr. Mick Bhatia, he had been awarded the prestigious Cancer Research Society Scholarship for the Next Generation of Scientists. In that very popular SCC-RI blog post, the discussion focused on how the CRS scholarship would support Yannick’s research goals and prepare him for future success. He revealed that he was working towards finding a faculty appointment and wanted to establish his own lab within 3 years. We recently caught up with Yannick and asked him how it feels to have achieved his goal…

It feels awesome! This is the beginning of a great new adventure for the curious and passionate scientist that I am. The road to get here has been long, and competition for a faculty position was fierce, as great candidates from the best research institutes around the world were also interviewing for those jobs. In the end, I was presented with multiple opportunities and opted for the University of Ottawa. The support and the bilingual environment offered by the University of Ottawa made my decision very easy.

**Can you tell us about your new position at the University of Ottawa?**

I am now a tenure-track Assistant Professor in the Department of Cellular and Molecular Medicine, which is part of the Faculty of Medicine. This department includes over 40 faculty members performing cutting-edge research in cancer, cardiovascular disease, and various topics in neuroscience. I am very proud to be part of such a world-renowned group of scientists. Dr. David Lohnes, the chairman of the department, and all of my new colleagues quickly made me feel like part of the team and everybody here has been very supportive as I launch my career as an independent investigator. I recently recruited my very first graduate student, so I am very excited about the future!

**What will your research program focus on?**

I am going back to my “comfort zone,” in the sense that I will resume working on a topic that I studied during my Ph.D. and first post-doctoral fellowship: human colon cancer. More specifically, I will study the contribution of epigenetics, or the way “chromosome folding” is influencing gene expression in the development and maintenance of cancer stem cell populations within human colon tumors. I will be working to identify and characterize new chemical compounds with the capacity to target key epigenetic aberrations in colon cancer stem cells. In the long run, I hope to develop new molecular therapeutic strategies to eradicate these deadly populations of cells in human colorectal tumors, which lead to the deaths of over 9,000 Canadians every year.

**How has your time at the SCC-RI prepared you to lead your own lab?**

The training that I received at the SCC-RI over the last 4 years was absolutely priceless. When I decided to come back to Canada after my training at the Weill Cornell Medical College in New York, I knew that if I wanted to bring my research to the next level, I needed to learn from one of the best scientists in the country, so I was happy to secure a position in Mick Bhatia’s lab. Having the opportunity to work in such an established lab allowed me to be involved in groundbreaking projects and to contribute to multiple scientific publications in stellar journals. Authorships in journals like *Cancer Cell*, *Nature Communications*, *Cell Chemical Biology*, and *Cell Reports* mean so much for a young investigator like myself when it comes time to compete for research funding at the national level. I’ve also gained invaluable knowledge in the areas of cancer stem cells and drug discovery which will be fundamental to my independent research program. Above all else, though, Dr. Bhatia’s approach to research and the culture of excellence he promotes in his lab inspires young trainees to get the best out of themselves. In this environment, I developed the skills and self-confidence that will help me to overcome challenges in this next phase of my career.
Dr. Eva Szabo is getting to the heart of how genetics play a role in the early onset of cardiac disease in some patients. In collaboration with Dr. Guillaume Paré, Director of the Genetic and Molecular Epidemiology Laboratory at the Population Health Research Institute (PHRI), her lab is working to learn how specific genetic mutations may impact endothelial (blood vessel) cells and lead to the early progression of disease.

Dr. Paré has identified one such mutation, DHX34, shared by a subset of patients enrolled in a long-term study conducted at PHRI. These patients have a median age between 32 and 40, a family history of cardiovascular disease and display early signs of disease themselves but importantly, have none of the usual risk factors such as high cholesterol, diabetes or Familial Hypercholesterolemia (FH).

The Szabo lab uses blood samples obtained from patients in the PHRI study and transforms them into induced pluripotent stem cells (iPSCs) which can be differentiated into blood vessel cells. The lab can then test how these cells form vessels and respond to inflammatory signals, key factors implicated in diseases such as atherosclerosis. They are also employing advanced gene editing technology called CRISPRs, to insert the identified mutations into healthy cells to test if the cell’s response to injury is delayed. This would indicate that the regeneration potential of these cells with the mutation is slower than for a normal healthy cell without the mutation.

This work which is funded by the Heart and Stroke Foundation is novel in its “medicine by design” approach. Employing stem cell models such as iPSC, allows investigators to examine the causes of disease at an individual level which could lead to better, targeted therapies specific to the patient. Currently those identified with early onset cardiac disease that appears to be genetically-linked, are treated in the same way as older patients with cardiac disease resulting from lifestyle and environmental factors. The Szabo lab ultimately wants to know if these genetic mutations can be corrected through early intervention to lessen the metabolic impact or enhance the regenerative capacity of these cells.

Dr. Szabo’s PhD student, Alexandria Afonso is the lead researcher on this study. Alexandria is a recipient of the prestigious Frederick Banting and Charles Best Canada Graduate Scholarship awarded by the Canadian Institutes of Health Research. She is very enthusiastic about the project and she thinks that identification of a new risk gene for heart disease would really help to expand our knowledge on how the disease progresses in patients. Alexandria expressed that “having a better understanding means that we can find better treatment and preventative methods to hopefully lower the number of lives lost to cardiovascular disease every year.”
SCC-RI Principal Investigator and neurosurgeon, Dr. Sheila Singh is uniquely positioned to tackle the problem of glioblastoma (GBM), a particularly aggressive form of brain cancer.

As a paediatric neurosurgeon at McMaster Children’s Hospital, Dr. Singh sees firsthand how tumours like glioblastoma affect the lives of her patients and their families and where the course of treatment has succeeded or failed.

As a research scientist with unique clinical insights, Dr. Singh is changing how we approach the problem of GBM. Instead of looking at the initial occurrence of the cancer, Dr. Singh is concerned with what is ultimately killing patients: relapse. When GBM is treated, patients may go into remission for a time, but the cancer inevitably comes back, and when it does it’s practically unrecognizable. The genomic landscape of the cancer has changed, and strategies that may have worked when treating the initial occurrence no longer apply.

Dr. Singh knows that to really address the problem of recurrent glioblastoma, she needs to look at the cancer stem cells that are escaping therapy and driving the cancer’s ability to reestablish itself. However, she also understands that this is a big problem that requires a team of researchers uniquely qualified to do this. To this end, Dr. Singh has partnered with Drs. Jason Moffat and Sachdev Sidhu at the Donnelly Centre, University of Toronto who bring their sizeable expertise in genomics, proteomics and cell signaling to form the ultimate GBM ‘dream team’. In 2016, the team was awarded $2.25M from the Terry Fox Research Institute (TFRI), New Frontiers Program.

Dr. Singh has acknowledged that the TFRI project is a major component of this initiative is providing opportunities for cross-training to prepare the next generation of scientists to tackle these big, complex research questions. As part of this mandate, trainees participate in exchanges with the other labs. Chirayu Chokshi, a graduate student in the Singh lab participated in one such exchange, joining the Moffat lab in Toronto for several months. While there, he gained valuable hands-on experience in CRISPR (gene-editing) techniques that he brought back to the Singh lab, and in turn, shared his knowledge of human stem cell models and protocols with the Moffat lab.

With phase 1, novel target discovery, nearing completion, Team GBM is now analyzing and collating large datasets to generate a list of prioritized hits. In the late fall, after presenting their data at the Annual Terry Fox meeting, they will launch phase 2, the engineering of new immunotherapies directed against the lead hits.

Sheila hopes that ultimately the efforts of the TFRI team will lead to better treatments that will improve the outcomes of her patients and others with GBM.

“Our main goal is to get new therapies into patients as soon as possible,” says Dr. Singh, noting that it is her own patients that will be directly benefitting from new brain cancer therapies. “Our team also has the ability to commercialize, to bring industry partners in and help us actually develop drugs based on the antibodies we design…through collaboration and interaction, we can be the whole package.”
The collaboration between Drs. Karun Singh and Stephen Scherer was born out of a recognition of the potential of their distinct yet complementary approaches to demystifying the complex set of neurodevelopmental disorders known as Autism Spectrum Disorder (ASD).

With the support of Google and Autism Speaks, Dr. Scherer, a world-leading geneticist at the Hospital for Sick Children, has used next generation sequencing to sequence the genomes of more than 5,000 Canadian families with ASD towards the goal of 10,000. His team has compiled this data into a cloud-based format that can be accessed by researchers the world over. The database, called MSSNG (a nod to the gaps in our knowledge about ASD), is one of the largest autism genome sequencing programs. So far, it has resulted in the identification of dozens of genes implicated in ASD – and they’re just getting started.

SCC-RI Principal Investigator and Neural Program Leader, Dr. Karun Singh recognized the potential of the big data being generated from the MSSNG project to further his own work in ASD. He believes his expertise as a neuroscientist and strengths in human stem cells, a skillset acquired at the SCC-RI, is ideal for modelling the genetic causes of autism towards drug discovery and improved pre-screening for clinical trials.

Karun’s lab is now using blood samples from MSSNG participants to convert them into neural cells that possess the individual’s unique genetic profile. They then analyze how specific genetic mutations may be contributing to ASD in that individual.

Merely identifying the genes responsible for ASD is not enough for Karun. Once his lab has modelled an individual’s form of ASD and identified potential genetic causes, they intend to screen these cells in the SCC-RI’s established high content drug discovery platform.

“Our goal is to find out what is going wrong in the patient’s brain cells, and move towards a drug screen to find out if we can find a compound that can correct it,” explained Dr. Singh.

The team is working to find drugs that can be matched to certain classes of mutations, so therapies can be tailored for different genetic forms of autism.

While this is one of the ultimate goals of this collaboration, another more immediate objective is to improve the design and implementation of clinical trials for ASD. By better characterizing underlying common genetic factors, trial participants could be stratified to receive experimental therapies that are better predicted to work for their specific form of autism.

Karun expressed that, “Given the lack of drugs to treat ASD, our collaboration is unique in Canada, and is urgently needed to discover specific medications for each type of Autism, providing better outcomes for Clinical Trials”.

“Many ideas grow better when transplanted into another mind than the one where they sprang up”

– Oliver Wendell Holmes
Idiopathic pulmonary fibrosis (PF) is a progressively debilitating and ultimately deadly respiratory disease that arises later in life, and currently has no cure. There are a wide range of environmental factors, such as exposure to dusts and particulates, that can contribute to the emergence of PF. However, it is becoming increasingly clear that a genetic component could play an important role in the onset and progression of disease. The study of families in which multiple members are affected by a condition, such a pulmonary fibrosis, can provide important genetic clues that enable the identification of genes that cause susceptibility to the disease.

In a study funded by the Ontario Thoracic Society and the Canadian Pulmonary Fibrosis Foundation, Dr. Jonathan Draper, in collaboration with clinician Dr. Martin Kolb at the Firestone Institute for Respiratory Health (FIHR), is working to identify genetic components that make certain individuals susceptible to pulmonary fibrosis.

Gene sequencing of the affected individuals, performed with the assistance of Dr. Guillaume Paré, Director of the Genetic and Molecular Epidemiology Laboratory at the Population Health Research Institute (PHRI), has identified several candidate gene mutations that Amos Lim, a graduate student in Dr. Draper’s group, is now testing for their contribution to the onset of PF disease symptoms. The long-term goals are to identify risk genes that increase the likelihood that some patients will develop PF, in addition to revealing the genetic mechanisms that operate during the onset and progression of the disease. Although still some way off, building an understanding of how genetics contributes to PF could ultimately allow for targeted therapeutic strategies that help in the prevention or treatment of this disease.
In the News

SCC-RI researchers are hard at work to advance scientific discoveries that will ultimately lead to new and improved therapies for patients with cancer and other devastating conditions. Key findings are regularly featured in the media which helps to inform our stakeholders about our research and how their contributions whether through tax dollars or private donations, are being put to good use. Here are a few of the recent SCC-RI discoveries that were featured in the news in 2017:

New insights made into cellular signalling pathway linked to cancer and other diseases

The laboratory of Brad Doble has revealed important insights into the regulation of the cell signalling pathway Wnt, which is important for normal stem cell function and is strongly implicated in the development of colon and several other types of cancer. PhD candidate Steven Moreira was the first author on this study published in the journal *Cell Reports*.

New genes discovered regulating brain metastases in lung cancer patients

Sheila Singh’s laboratory has identified new regulators of brain metastases, the genes called SPOCK1 and TWIST2, in patients with lung cancer. This is a significant finding as brain metastases are the most common brain tumour in adults and the leading cause of death in cancer patients. PhD candidate, Mohini Singh was the first author on this study which was published in the journal *Acta Neuropathologica*.

Discovery by McMaster team provides key for targeted cancer treatment

The laboratory of Mick Bhatia has been working to figure out why certain drugs work for some cancer patients but not others. They have identified a protein in cancer stem cells called Sam68 that appears to be responsible. When this protein is absent, some cancer drugs do not work. Dr. Bhatia believes that this discovery ‘has the potential to make a profound difference for patients.’ As a result, the Bhatia team is now looking to replicate this approach to find out why other drugs only work in some patients. This work was published in the scientific journal, *Cell Chemical Biology*. Postdoctoral Fellow, Dr. Yannick Benoit now a Principal Investigator at the Ottawa Hospital Research Institute, was the first author on this study.

McMaster study gives greater understanding to autism’s root cause

Karun Singh’s team has identified and ‘on button’ on a strand of protein that instructs brain cells to form connections during development and isolated the genetic changes that keep this button ‘turned off’ in some people who have autism. Dr. Singh hopes this work published in *Cell Reports* will one day lead to the identification of safe and effective treatments that can help restore brain cell synapse growth and activity in individuals with certain forms of autism.
SCC-RI in the Spotlight

Stefan Rentas from the Hope Lab was the first author on a groundbreaking study published in the top science journal, Nature in 2016. Shortly after receiving his PhD, Stefan received a Clinical Genetics Fellowship at the Children’s Hospital Philadelphia, University of Pennsylvania School of Medicine. This program is highly competitive and typically only accepts physicians who have already completed training in a clinical specialty. Stefan hopes to apply this knowledge towards establishing his own genetics research program in the future.

Muluken Belew started as a technician in the Hope Lab and then decided to pursue his PhD in order to dedicate himself to research. Muluken’s hard work and focus has been rewarded and after successfully defending his thesis, he was offered a position as a Hematopoietic Stem Cell Research Scientist at the Novartis Institute for Biomedical Research in Cambridge, Massachusetts.

Borhane GuezGuez completed his postdoctoral training under the supervision of Dr. Mick Bhatia and is now leading his own research group at the German Cancer Research Centre. His program will focus on the regulatory mechanisms of the bone marrow niche in order to develop new immunotherapy treatments for leukemia.

Alumni News

Graduate students and postdoctoral fellows who complete their training at the SCC-RI go on to pursue postgraduate studies and careers in science, medicine and industry. In 2017, former postdoctoral fellows have taken up academic positions at prestigious institutes in Canada and Germany and represent the next generation of scientists pursuing their own research questions. Some will continue their medical training and soon become clinician-scientists that will treat patients and use their clinical observations to explore the underlying biology in their own research labs. The SCC-RI’s drive towards translation of basic research into clinical and commercial outcomes can lead our graduates into fields they may not have initially envisioned when they began their training. SCC-RI alumni are now working in the private sector in areas such as biotechnology start-ups, healthcare investment, scientific equipment and drug development. Below are a few examples of SCC-RI trainee success stories from 2017:

Trainee Travels

Sonam Bhatia, PhD candidate in the laboratory of Dr. Jon Draper, was awarded the NSERC-CIHR Michael Smith Foreign Study Supplement which aims to promote international scientific collaborations. With this award, Sonam was afforded the opportunity to work in the laboratory of Dr. Aki Minoda at Japan’s renowned Riken Institute to acquire new bioinformatics skills important for her work at the SCC-RI. Sonam was struck by the Riken’s ‘harmonization of people with varied scientific backgrounds…biologists, mathematicians, statisticians, engineers, software developers…all working together towards the same goals’. She also expressed her gratitude for the ‘opportunity to learn so much and experience Japanese culture and traditions’.
SCC-RI in the Spotlight

Awards and Scholarships 2017-18

SCC-RI trainees are some of the best and brightest young researchers at McMaster and across the country which is reflected by the impressive list of scholarships awarded to our graduate students in 2017:

<table>
<thead>
<tr>
<th>Recipient</th>
<th>Program</th>
<th>Award</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solen Abdulla</td>
<td>MSc</td>
<td>GSA Travel Assistance Grant</td>
</tr>
<tr>
<td>Alexandria Afonso</td>
<td>PhD</td>
<td>CHIR (Canadian Institutes of Health Research) CGSD (Graduate Scholarship Doctoral)</td>
</tr>
<tr>
<td>David Bakhshinyan</td>
<td>PhD</td>
<td>CIHR CGSD (Canadian Graduate Scholarship Doctoral)</td>
</tr>
<tr>
<td>Derek Chan</td>
<td>MD/PhD</td>
<td>MD/PhD CIHR Doctor Studentship</td>
</tr>
<tr>
<td>Xiaoxiao Deng</td>
<td>MSc</td>
<td>NSERC (Natural Sciences and Engineering Research Council) CGSM (Canadian Graduate Scholarship Master’s)</td>
</tr>
<tr>
<td>Diana Golubeva</td>
<td>MSc</td>
<td>Ontario Graduate Scholarship; Jan’s Graduate Scholarship in Stem Cell Research</td>
</tr>
<tr>
<td>Victor Gordon</td>
<td>PhD</td>
<td>Ontario Graduate Scholarship</td>
</tr>
<tr>
<td>Michelle Kameda</td>
<td>PhD</td>
<td>Ontario Graduate Scholarship</td>
</tr>
<tr>
<td>Ava Keyvani Chahi</td>
<td>PhD</td>
<td>Michael G. DeGroote Doctoral Scholarship of Excellence</td>
</tr>
<tr>
<td>Vickie Kwan</td>
<td>PhD</td>
<td>Impact Award</td>
</tr>
<tr>
<td>Lina Liu</td>
<td>PhD</td>
<td>International Excellence Award</td>
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<tr>
<td>Nadeem Murtaza</td>
<td>PhD</td>
<td>Fred and Helen Knight Enrichment Award</td>
</tr>
<tr>
<td>Deanna Porras</td>
<td>PhD</td>
<td>Ontario Graduate Scholarship; Michael G. DeGroote Doctoral Scholarship of Excellence; The Lee Neilson Roth Award</td>
</tr>
<tr>
<td>Maleeha Qazi</td>
<td>PhD</td>
<td>CIHR CGSD</td>
</tr>
<tr>
<td>Jennifer Reid</td>
<td>PhD</td>
<td>CIHR CGSD; Michael G. DeGroote Doctoral Scholarship of Excellence; The Thomas Neilson Scholarship; The Betty Horricks Research Endowment Fund Award</td>
</tr>
<tr>
<td>Nazanin Tatari</td>
<td>PhD</td>
<td>Michael G. DeGroote Doctoral Scholarship of Excellence</td>
</tr>
<tr>
<td>Damian Tran</td>
<td>MSc</td>
<td>Ontario Graduate Scholarship</td>
</tr>
<tr>
<td>Brianna Unda</td>
<td>PhD</td>
<td>Ontario Graduate Scholarship</td>
</tr>
</tbody>
</table>
Research Funding

In 2017, SCC-RI investigators were awarded a total of $2.75M in operating funds to support their research programs from various funding agencies such as the Canadian Institutes for Health Research, Natural Sciences and Engineering Research Council of Canada (NSERC), Heart and Stroke Foundation, Ontario Lung Association and the Ontario Institute for Cancer Research:

Drs. Bhatia, Hope and Singh were awarded a total of $718K in funding from the Ontario Institute for Cancer Research to pursue translational research initiatives focused on Acute Leukemia and Glioblastoma Multiforme (GBM).

Dr. Bhatia was awarded $1M+ over five years to study “rilSCs” a new population of Acute Myeloid Leukemia (AML) patient cells identified by his group. They have discovered a new protein on these cells to be tested for therapeutic targeting to prevent relapse in patients.

Dr. Sheila Singh was awarded $255K from LongBow Therapeutics to target patient-derived glioblastoma cells using a combination of radiation and drug therapy.

Dr. Eva Szabo was awarded $223K to model Early Onset Coronary Artery disease by the Heart and Stroke Foundation of Canada. Read more about this study on Page 9.

Dr. Sheila Singh was awarded the Tier 1 Canada Research Chair (CRC) in Human Brain Cancer Stem Cell Biology. The CRC program provides funding to attract and retain accomplished researchers like Sheila, in Canada. This award will provide $1.4M over seven years to McMaster University.

Dr. Singh’s research is focused on the characterization of genetic abnormalities of brain tumour initiating cells (BTICs), with the intent of developing targeted therapies. Targeting BTICs holds great promise to alleviate brain tumours in children, a form of cancer that remains difficult to cure and often leads to death despite surgical advances.
Publications


On the Cover…


