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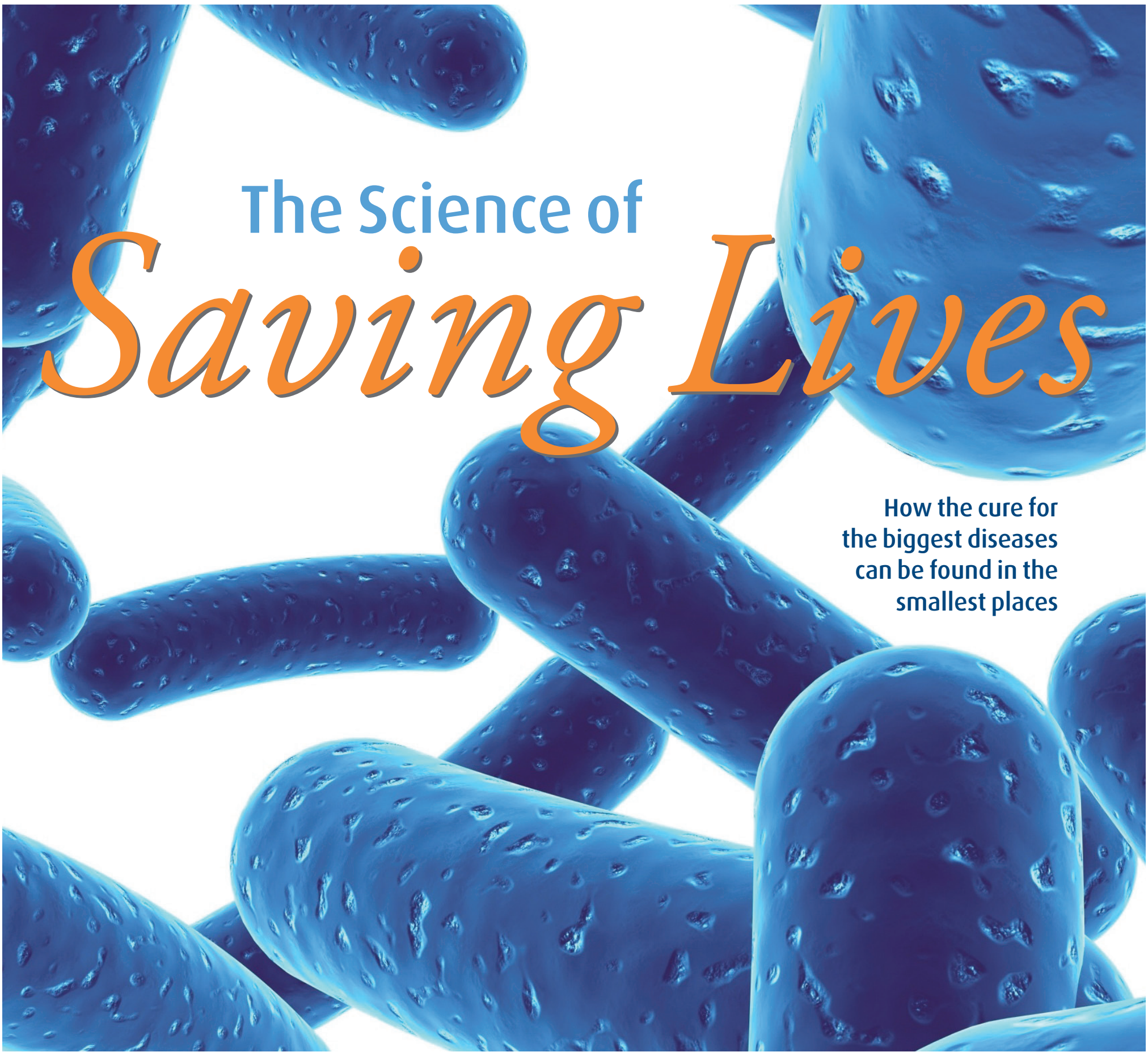
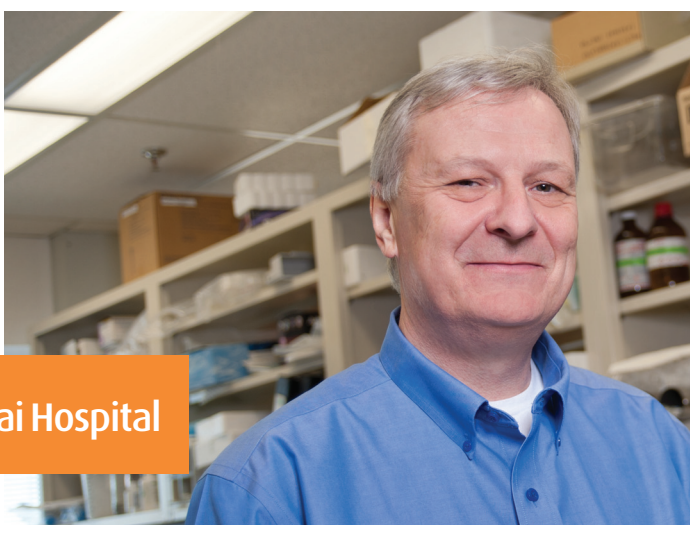


How Research Impacts *Your Health*



By *Dr. Jim Woodgett*, Director, Samuel Lunenfeld Research Institute of Mount Sinai Hospital

We are fortunate to live during an age of evidence-based medicine, where scientists are working to solve the mysteries of the human body and some of the most pressing chronic diseases of our time, including diabetes, cancer, mental health and autoimmune conditions such as arthritis and inflammatory bowel disease. Scientists who collaborate closely with physicians in academic hospital settings have the advantage of asking questions that connects their research with patient care being delivered by physicians, so that their lab discoveries can get to the patient's bedside sooner.

From the vantage point of one of the world's leading research institutes, all of us at Mount Sinai Hospital's Samuel Lunenfeld Research Institute get to peek at the future of medicine while simultaneously recognizing how much more work there is left to do.

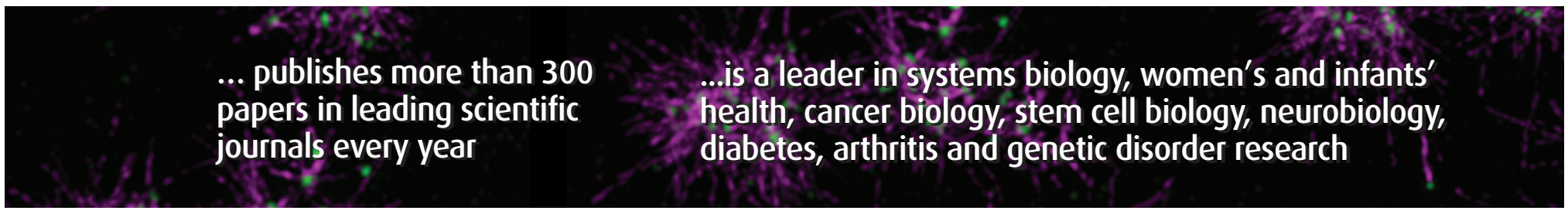
The beauty of biology is that it represents one of the last great frontiers of discovery offering us revelations of how our cells and tissues actually work and how we might employ this knowledge to improve our health.

Over a third of The Lunenfeld's 40 research scientists hold Canada Research Chairs, ranking among the highest proportion of any research institute in the country and an indicator of the stature that they hold in this country. Housed within Mount Sinai Hospital, we have consistently punched above our weight, ranking in the top 2.5 per cent of research institutes worldwide in quality of science. Our researchers are experts in systems biology, women's and infants' health, cancer biology, stem cell biology, neurobiology, diabetes, arthritis and genetic disorder research.

Patients benefit tremendously from close collaborations between scientists and physicians throughout the Hospital because scientific discovery is driven by the hunger for transformative treatments that help people live better, healthier lives. For example, diabetes already has an enormous impact on our society and health-care system and this will only increase with obesity rates. But did you know that high levels of insulin also increases the risk of breast and other cancers? Dr. Pamela Goodwin, both a clinician and a researcher at Mount Sinai Hospital, was among the first to demonstrate this connection and is now leading a large multi-national trial to test whether diabetes medications that reduce blood sugar can protect against breast cancer recurrence.

In seeking to understand the causes of disease and to develop treatments, our scientists explore the remarkable similarities between species to uncover new mechanisms by which our own biology is controlled. This "fundamental science" leverages the relative simplicity of fruit flies and nematode worms (they are still extraordinarily complicated!) to discover which genes and proteins are important for ensuring the right connections are made to avoid cancer and other chronic diseases. Indeed, we believe that the cures for the biggest diseases will emerge from these tiniest of organisms, which are revealing so many of the mysteries of biology.

Medical students facing the task of five to ten years of specialist training often ask me whether there will still be important discoveries to be made when they emerge from their studies. My answer is always the same - "Why, of course!" Indeed the breadth of our understanding is dwarfed by the depth of our lack of knowledge and within those chasms lie better treatments, preventative strategies and technologies that will ultimately benefit our health.



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A Portable *Insulin Factory*

Islets only make up about 2 per cent of the mass of the human pancreas, but they are the key to producing insulin.

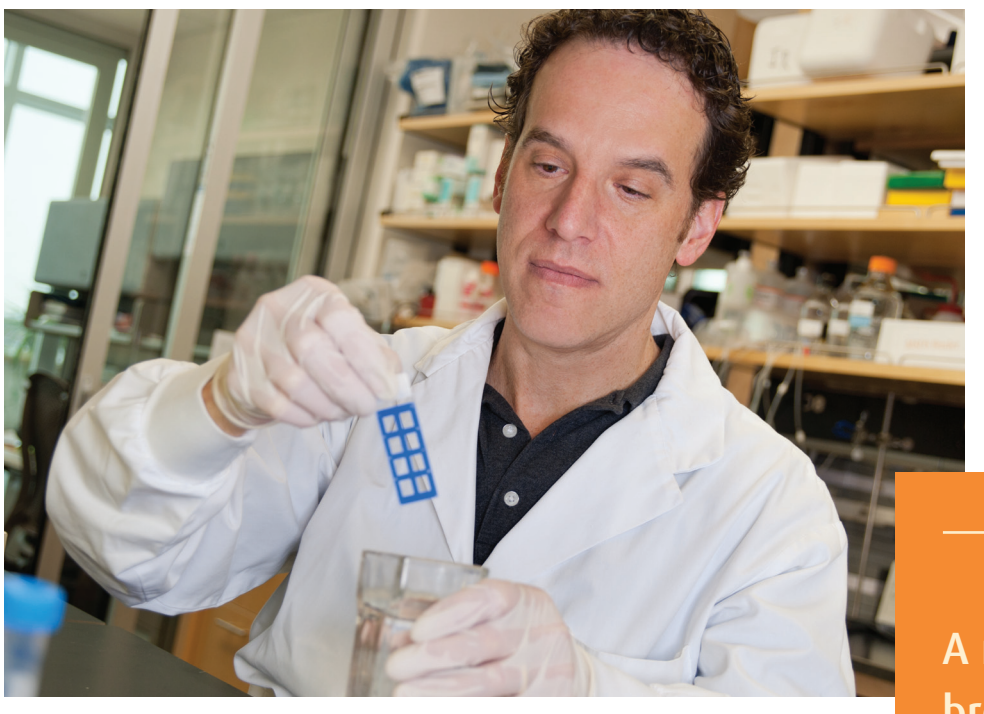
In a small five-millimetre area on a square gel foam that resembles soft Styrofoam packaging material, millions of insulin-producing cells – called islets – are grown and harvested by Dr. Ian Rogers' team at Mount Sinai's Samuel Lunenfeld Research Institute. By simulating and manipulating these cells they will ultimately perform the powerhouse blood sugar regulating function of a pancreas. It's not quite growing a pancreas in a Petri dish, but it's the next best thing. It is here, in one of The Lunenfeld's largest labs, located in one of Toronto's most respected hospitals, that the promise of a more effective and simple treatment of type 1 diabetes is being played out.

The premise of this research is simple – recreate the function of the pancreas, which in diabetics, does not function properly, so that patients can begin to live normal, healthy lives. Dr. Rogers hopes to one day be able to package these lab-grown islets into a medium about the size of a lima bean that could be inserted just under the skin of a type 1 diabetic patient to help regulate blood sugar levels. Decades of fluctuating blood sugar levels often leads to major health issues in diabetics such as kidney and eye disease.

While clinical trials of this research are a few years away, Dr. Rogers has a clear vision of how his discovery could work. "We would expect patients will still have to monitor their blood sugar and take some insulin injections in the first generation of this therapy, but it should reduce or even eliminate the need for both eventually," Rogers says. "More importantly, it should help regulate the spikes in blood sugar and reduce the associated complications," he adds.

The assumption is that the lab-grown islets would take about three months after implantation before they became fully functional because they would reach maturity as they were nourished by a patient's own blood supply. The islets would then remain active in a person's body for six months to a year before the individual would require a replacement.

"There is a real need for more manageable diabetes treatments out there," says Rogers. "The other day a mother of a 16 year old said to me: "Teenagers don't listen - they don't take their injections. If you gave me six months of peace of not having to nag my son to take his injections, I'd be so happy."



Dr. Ian Rogers
Associate Scientist, Samuel Lunenfeld Research Institute of Mount Sinai Hospital

At the heart of the islet production is research Rogers began about ten years ago on blood cells extracted from umbilical cords. "We came up with a way to change them, so they would become more than just plain blood cells. They started acting more like multi-potential cells." These cells, reprogrammed through culturing, can then be further stimulated and grown into various different cells with specialized functions, such as insulin-producing cells. Four years ago Rogers progressed to creating the three dimensional insulin-producing islet-like cells of a pancreas. Islets only make up about two per cent of the mass of the human pancreas, but they are the key to producing insulin.

Rogers said he is driven to work towards a direct application in the research he pursues. But he stressed that upfront financial investment and support of basic science is critical because all clinical therapies start out as a basic research question. "Groundbreaking quantum leaps have to come from fresh ideas inspired by basic research," he says. "I always emphasize that the goal in my lab is for our discoveries to make their way to the clinic, to be directly translated into therapies to help patients."

"My lab is targeting specific ways for diabetics to manage their disease in a way that will improve their quality of life. That's what motivates me – the impact that our research has on a patient's ability to live a better, healthier life," Rogers says.

A research breakthrough that would allow my body to even temporarily produce and regulate insulin would be like a dream come true.

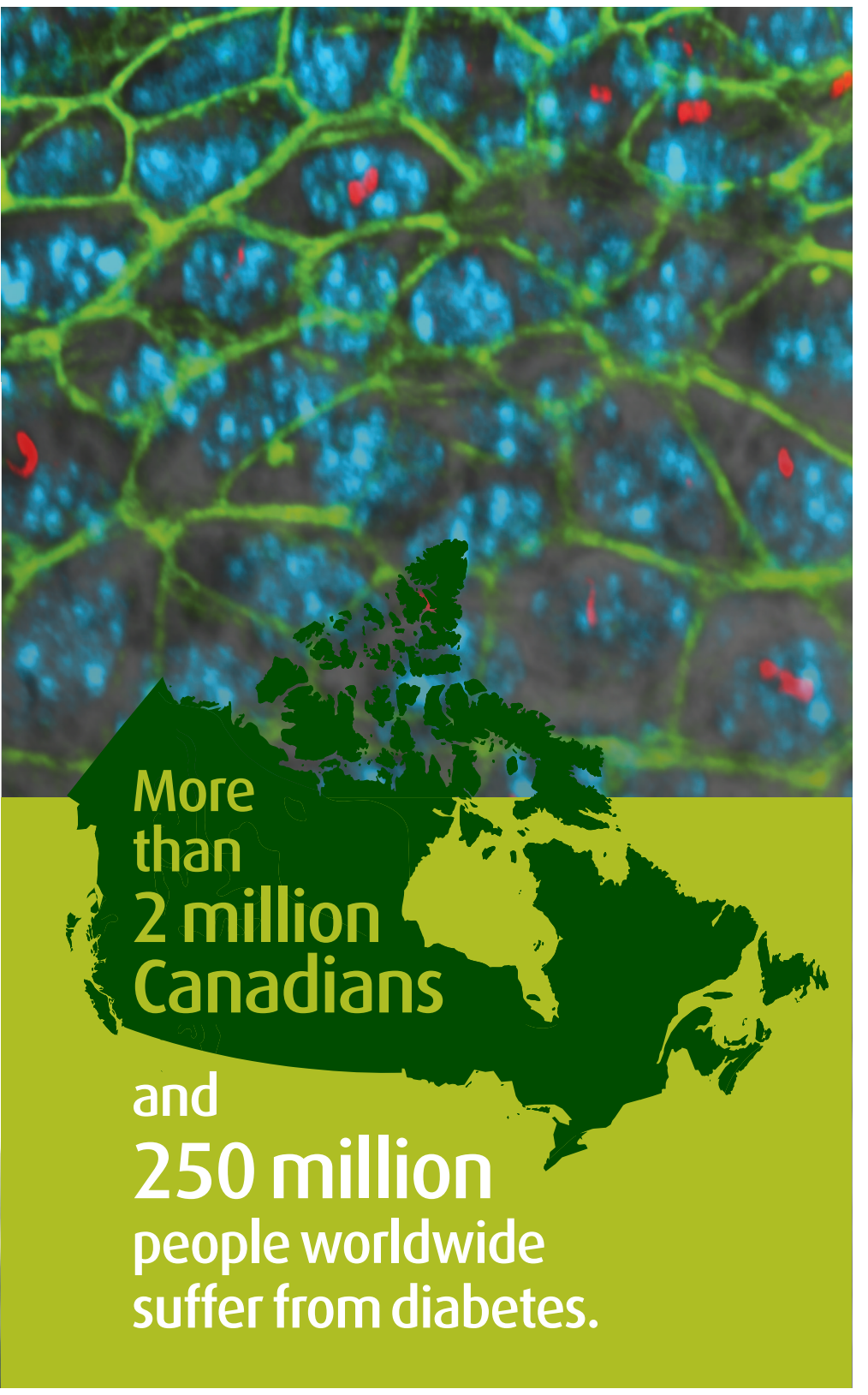
Debbi Ross, type 1 diabetes patient.

Connection Between Insulin and Breast Cancer *Discovered*

While one group of researchers at Mount Sinai Hospital is breaking new ground in the regulation of insulin production and its potential impact on diabetics, in another corner of the Hospital, Dr. Pamela Goodwin, the Marvelle Koffler Chair in Breast Research, has made a major discovery linking insulin levels with a woman's risk of recurrence in breast cancer. Dr. Goodwin's pivotal research has found that high levels of insulin stimulate the growth of tumours and increases the likelihood of breast cancer returning. She is leading the largest worldwide clinical trial of a common diabetes medication – Metformin – to examine its ability to reduce the recurrence of breast cancer and improve the survival for women with early stages of the disease.

This is an example of how collaboration is ultimately an advantage of conducting scientific research in a hospital setting. Discoveries and insights gained about the progression and treatment of one disease can profoundly enlighten and guide the course of treating another. So, the impact of the original investment in the research is multiplied.

Redefining *Treatment* and *Quality of Life* for People with Diabetes



Bayview Village resident Debbi Ross has been living with type 1 diabetes for 60 years. Over the years, the mother of two and grandmother of four has developed complications that impact her eyes and her kidneys. She takes four injections of insulin a day, constantly monitors her blood sugar, plans what she can eat, how much exercise she can do and must be prepared to respond quickly to low or high blood sugar if she doesn't get it right. Debbi is one of more than two million Canadians and 250 million people worldwide who suffer from diabetes.

As an international leader in both diabetes research and patient care, Mount Sinai Hospital's top scientists and physicians work closely together to make cutting-edge discoveries that are translated into improved treatments for patients. One of those scientists is Dr. Daniel Drucker, whose work was critical in developing new, effective drug treatments for type 2 diabetes. In 2011 he was awarded the Canadian Institutes of Health Research – Canadian Medical Association Journal Award for top achievements in health research and in 2012, he received the Claude Bernard Lecture/ Award of the European Association for the Study of Diabetes.

Here Dr. Drucker shares his thoughts about the impact of research on the treatment of diabetes.

What is the scope of diabetes as a health issue?

We are facing a worldwide epidemic of diabetes. We're seeing type 2 diabetes that we used to see in elderly people, but now the disease is being detected in kids as young as 15. That's really what is scary. We're going to see more complications in people decades earlier than we used to. It's a looming public health crisis.

What brought you into this field of study?

I had the opportunity to do some fundamental basic science research at Harvard in 1984 in an area very few people worked on at the time. It was an area that I'll call gut hormones, which may not sound very glamorous, but these hormones have an important link to diabetes.

What breakthrough discovery did you make in linking gut hormones and the control of diabetes?

In 1987, I pinpointed the action of a digestive hormone – glucagon-like peptide 1 or GLP 1 – which regulates the production of insulin. By studying this hormone over the last 25 years, my lab was able to identify its role in regulating food intake, digestion and body weight. Our research here at The Lunenfeld, along with the work of other leading scientists, also identified an enzyme that can inhibit the proper functioning of the GLP 1 hormone. New diabetes drug therapies that better regulate insulin production and discourage overeating have been developed as a result of this research.

Are these drugs a game changer for diabetics?

The two approved drug therapies based on our work represent the first medications for diabetes that not only control blood sugar, but also tell people when they're not hungry anymore. They work in what I call a smart manner, meaning they lower your blood sugar when it is high, but the moment it comes back to normal, they stop working.

What does that mean to patients with diabetes?

People with diabetes taking traditional medications must constantly monitor their blood sugar levels and adjust their dosage. The number one side effect of these medications is low blood sugar– hypoglycemia, because the medications continue to work even when the blood sugar levels drop. When you have a smart medication, you don't have this side effect.

Are these new *smart* drugs currently available?

Several options are currently available and a monthly and annual dosage are in development. Imagine the lifestyle impact if a person with diabetes only had to get a single annual injection to keep their blood sugar under control!

How does the urgency around diabetes as a global health issue affect your work?

It's immensely satisfying to collaborate with Mount Sinai's physicians who are prescribing medications based on discoveries that originated in our lab. Since Mount Sinai is a leader in diabetes, our patients are among the first to benefit from clinical trials based on new advances developed here.

What future hopes do you have for these *smart* drugs?

There are about eight huge studies involving patients with diabetes – several are being carried out here at the Leadership Sinai Centre for Diabetes – that we call cardiovascular outcome studies. It may well turn out that these *smart* medications not only lower blood sugar, but may also reduce the number of heart attacks and strokes in diabetic patients. That's the thing about basic medical discovery – it's all connected. A single breakthrough can have enormous impact in areas that you never imagined.

Dr. Daniel Drucker

Senior Investigator, Samuel Lunenfeld Research Institute of Mount Sinai Hospital

The Good, the Bad and the Ugly: *What Your Gut Says About You*

Dr. Kenneth Croitoru
Associate Scientist, Samuel Lunenfeld Research Institute

Dr. Kenneth Croitoru is focused on identifying the unique combination of bacteria in people's guts. While that may sound a little off putting, Croitoru says this exciting work may hold the key to personalizing effective treatments for individuals suffering with inflammatory bowel disease (IBD), a debilitating condition that affects about 200,000 Canadians.

IBD refers to a group of disorders including Crohn's disease and ulcerative colitis that cause the lining of the intestines to become inflamed and develop ulcers, often leading to severe diarrhea and chronic pain. Through its Centre for Inflammatory Bowel Disease, Mount Sinai Hospital is an international leader in research and advancing treatments for patients coping with these diseases and the associated diminished quality of life.

Most people typically view bacteria as dangerous organisms posing a threat to their health. However, there are many 'friendly' bacteria that co-exist in our bodies and assist with functions like digestion and the balance of these organisms help to keep us healthy. "IBD is an example of a disease where something has gone wrong in the interaction between the immune system and the gut microbiome, which is a collection of bacteria present in everyone," Croitoru says.

"We know that genetic risk factors exist, but it doesn't guarantee that you will get IBD. So, there is an environmental trigger that we're looking for that alters the microbiome and how it interacts with the immune system to cause chronic inflammation, ulcers and other symptoms in some people," says Croitoru, who is a clinician-scientist in Mount Sinai's Zane Cohen Centre for Digestive Research, Associate Scientist with Mount Sinai's Samuel Lunenfeld Research Institute, and a Professor of Medicine in the Division of Gastroenterology at the University of Toronto. Dr. Croitoru is one of the leads in a recently announced partnership with the University of Toronto that will see the opening of Canada's largest IBD clinical research unit located at Mount Sinai Hospital.

"By studying the good and bad bacteria in people's bodies, we want to deduce a personalized profile of a patient's risk of developing the disease and determine their specific triggers based on their immune responses," Croitoru explains. "The results may tell us that you will be better off with antibiotics, and perhaps not anti-inflammatory drugs, or we may be able to prescribe types of bacteria to reconstitute your microbiome to a healthy state if you have this disease. Five years ago this was more like science fiction, but we're beginning to see a glimmer of this becoming the future of patient care."

IBD is a debilitating condition that affects about 200,000 Canadians.

New Hope for IBD Patients

As a parent you'd rather be the one to have pain than to see your children suffer. The great work being done at Mount Sinai Hospital to pinpoint the triggers of IBD and customize solutions gives us hope that better treatments, and ultimately, a cure will be found in my children's lifetime.

Ruth Scully is mother to a 22-year-old daughter and a 20-year-old son living with IBD.

Genetics and Environment Shape *Your Baby's Health*

If there was anything I could do right now to help my child have a better chance of being healthier in 25 or 30 years, naturally I would do it in a heartbeat.

Lise Phaneuf, a Mount Sinai Hospital patient, is due to deliver her second child in the spring.

Dr. Stephen Lye believes it's never too soon to start preventative health care. In fact, Lye, the Associate Director of Research at Mount Sinai Hospital's Samuel Lunenfeld Research Institute and Mount Sinai Hospital Auxiliary Chair in Women's and Infants' Health Research, is out to revolutionize the notion of preventative care by focusing on the genetic and environmental factors that begin in the womb.

By observing the health of pregnant women, tracking the progress of developing fetuses and monitoring early infancy into childhood, Dr. Lye is convinced that he and his colleagues at Mount Sinai Hospital can discover the recipe to avoid many chronic diseases in later life.

This premise is at the heart of the Ontario Birth Study, which is being led by Dr. Lye's collaborator, Dr. Alan Bocking, a physician in Mount Sinai's Department of Obstetrics and Gynaecology. "Everyone wants their children to grow up healthy, happy and do well in their lives," says Lye, a leading expert in developmental health. "Our genetic makeup is essentially a blueprint, but it's a flexible blueprint. What we are exposed to in the womb, the nutrition of pregnant mothers, our experiences throughout infancy and early childhood, all interact with our genetic makeup and can impact our health throughout our lives."

The innovative Ontario Birth Study recently began rolling out at Mount Sinai Hospital in collaboration with the University of Toronto where Lye is also Executive Director of the Fraser Mustard Institute for Human Development.

Lye is working closely with Lunenfeld colleagues like Dr. Laurent Briollais, who was the principal investigator of a recently published study which revealed that exclusively breastfeeding (for at least three months) infants who carry a gene which predisposes them to obesity can help reverse the impact of their genetic risk.

"Our real interest is to improve people's lives. We want to progress to the point where we have a wide range of information to adapt preventative treatment to a person's individual risk, which is a very personalized approach to health care," Lye explains. "Whether the risk factors are genetic or environmental, we will be able to reduce the incidence of chronic diseases by investigating and gaining more knowledge about the earliest stages of human development."

Mount Sinai's Samuel Lunenfeld Research Institute

Back to Basics: *Discovering the Fundamentals of Your Health*

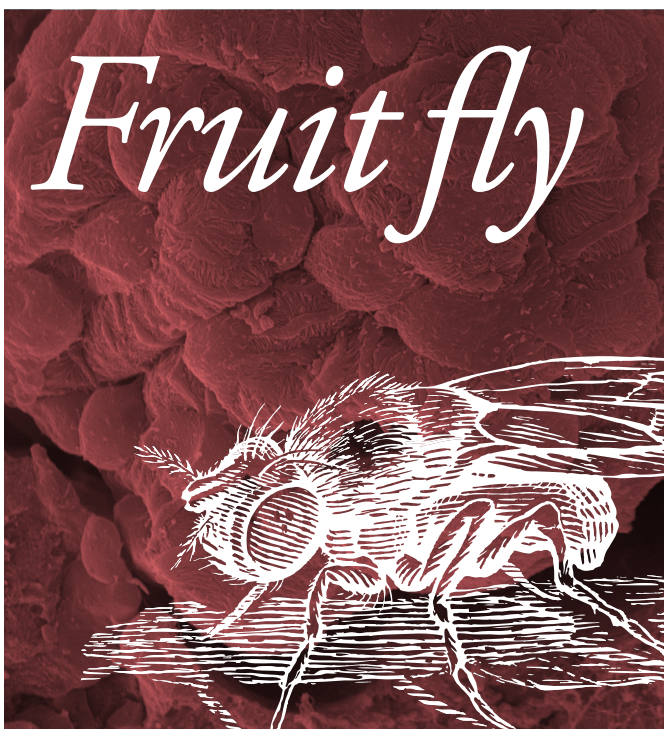
What do a microscopic worm, a fruit fly and yeast microorganisms have to do with your health? They are helping researchers at Mount Sinai Hospital's renowned Samuel Lunenfeld Research Institute unlock the key to discoveries that will one day have profound impact on the treatment of conditions like cancer, kidney disease and neurodegenerative disorders.

It may be years before pivotal secrets are uncovered that will lead to new medical treatments, but every major medical breakthrough began with a scientist peering into a microscope, trying to decipher the mysteries in a Petri dish, conducting countless experiments and spending a lifetime of unraveling, for example, the neurological pathways of a worm. The cure for major diseases can be found through the study of small and simple organisms. Basic science holds the key to changing the face of medicine and improving the health of millions.

"Basic science is like building a vast root system. It must be in place before a plant can grow and be harvested," says Dr. Mei Zhen, a Lunenfeld Senior Investigator and Lawrence and Judy Tanenbaum Research Chair in Developmental Neuroscience, who is one of many scientists at The Lunenfeld who are applying their knowledge and expertise to basic science. "When people see a successful medical treatment, it's just the fruit. What they don't see are the years of work that have gone into creating the roots of the advancement."

The Lunenfeld's Dr. Jim Woodgett emphasizes the importance of the early investment in basic science. "When you hear about a new medical breakthrough, it's the culmination of exceptional scientific talent, visionary leadership, steadfast government support and a passionate philanthropic commitment from community members who are as committed to discovery as the scientists themselves."

Here is a snapshot of three of the leading-edge basic science projects using the smallest of organisms currently taking place at Mount Sinai's Samuel Lunenfeld Research Institute.



Number of kidney/ kidney-like cells

Fruit Fly: dozens

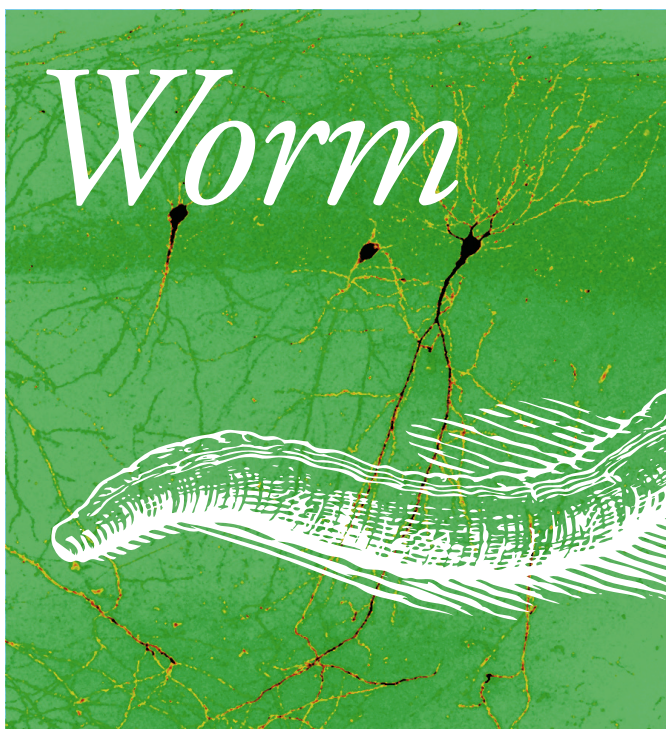
Human: millions

For most people, fruit flies are annoyances, but for Dr. Helen McNeill these flying insects are helping her to pursue her life's work.

"My lab is studying how cells organize and co-ordinate themselves. We're trying to find answers such as why some cells stop growing, while others will grow out of control," McNeill says. "We're using fruit flies because you find almost all of the same biological processes in a fruit fly as in a human being."

McNeill's breakthrough discovery a few years ago on a gene known as FT showed that when the gene mutates it causes cells to grow out of control, resulting in the cellular pathway that it regulates to trigger an overgrowth of tumours. McNeill's collaborators have found FT pathway mutations in patients with breast cancer, liver cancer and kidney disease.

"The more we know about how things go wrong the easier we can eventually find ways to treat them," McNeill says. "I am 100 per cent confident that our understanding of FT biology is essential to eventually treating cancer and kidney disease."



Number of synapses

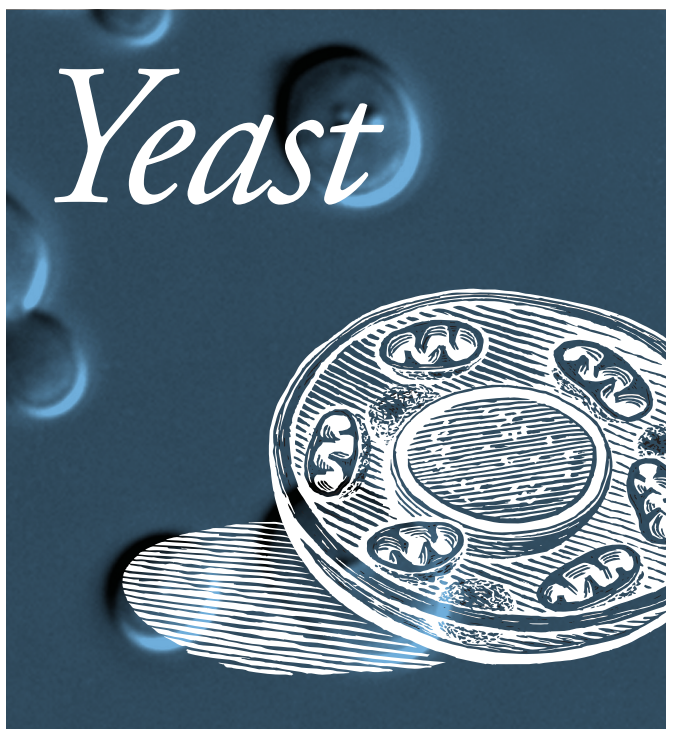
The *C. elegans worm*: fewer than 10,000

Human: billions

Dr. Mei Zhen is fascinated by how a worm moves. To be specific, she is studying the movements of the *C. elegans worm*, a microscopic creature that is used as a model for understanding the nervous system.

The focus of Zhen's research at The Lunenfeld is to determine what neurons in the worm are controlling specific movements. Her goal is to uncover how our brains direct and control movement and other functions so that we can one day treat devastating diseases such as Parkinson's and other chronic diseases that affect motor skills.

"A human being is a complex jigsaw puzzle, but a worm, being a simpler version of this puzzle, can help us understand how behaviour or memory is being controlled at the individual cell level," Zhen says. "I hope that this work will help us figure out how to re-establish the communications and command controls in the motor system, so that we can improve the quality of life for patients who are losing their mobility either during the aging process or because of a neurodegenerative disorder."



Number of genes

Yeast: 6,000

Humans: 24,000

"Humans share a common ancestor with yeast, a microorganism that most people associate with bread baking and beer," says Dr. Frederick Roth, a genomics expert at The Lunenfeld, and an international leader in genomics research. "You just have to go back about a billion years, but it turns out that about half of the genes in yeast still correspond to genes in human beings," he explains.

In collaboration with international researchers, Dr. Roth's team is taking known disease mutations such as cancer from human genes and transferring them into yeast to understand how disease-causing mutations function.

DNA in yeast is the same chemical structure as in human cells, so when it breaks, it often breaks in similar ways. Yeast, which grows and divides quickly and can be easily manipulated in experiments, is the optimum model for Roth's research. "You can go from a single cell of yeast to a colony of millions of cells in two days," he says.

He adds, "For mechanics to fix a car they need to know what is under the hood, what all the parts are and how they work together. We're getting close to a complete list of the parts that contribute to disease, but now we must understand how the parts fit and work together so that more medically focused research can move forward with better treatments and prevention."

Dinner with Scientists: *Healthy Discussion Saves Lives*

Over 150 guests had the opportunity to experience a unique event that celebrated Mount Sinai Hospital's research talent and to learn first hand how their work will impact health care for generations to come. On March 5, Dinner with Scientists, an annual event held by Leadership Sinai, Mount Sinai's growing group of young philanthropists, celebrated these life-changing discoveries and the individuals who have given generously to make them possible.

Hosted by CTV news reporter Alicia Markson and held at the Eglinton Grand, the event was an incredible evening of gourmet food and groundbreaking ideas. Each guest table included a researcher from Mount Sinai's Samuel Lunenfeld Research Institute who offered guests a glimpse of what the future holds for the treatment of some of the most prevalent diseases of our time.

Perhaps the most entertaining part of the evening was asking some of the world's most brilliant scientific minds to summarize their life's work into a two minute presentation called a "lightning round". For example, Dr. Ken Croitoru valiantly did his best to explain, in layman's terms, his extensive and complex research in inflammatory bowel disease. Five minutes may not have been enough time to explain everything that we know about genetics and the environmental factors of the disease, but it did leave guests wowed by the possibilities that lay ahead for those who suffer from the debilitating condition and was certainly fodder for provoking discussions throughout the evening.

As Co-Chairs of the event for the past two years, Leadership Sinai board members Lucas Atkins and Bill Arvanitis have bolstered the event's goal of raising awareness and understanding of

Left to right: Lucas Atkins, Alicia Markson, Bill Arvanitis, Shawn Mecklinger

The Lunenfeld's groundbreaking work. "This event continues to amaze me. Getting an inside look at the research is incredibly inspiring," says Lucas. "It reinforces our commitment to funding their research because it allows us to draw a straight line from their work to patient care – and how they are literally transforming peoples lives. It's also a real treat to be in a room with so much brain power!" adds Bill.

Kevin Goldthorp, Mount Sinai Hospital Foundation's new President and Hospital Senior Vice-President of Advancement, was thrilled with the evening: "I would like to personally thank our Leadership Sinai volunteers for their incredible commitment and vision for this event. It was particularly gratifying to see a room full of donors and volunteers sharing in the excitement about medical discoveries with our scientists.

Support leading edge research at Mount Sinai Hospital's Samuel Lunenfeld Research Institute today.

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