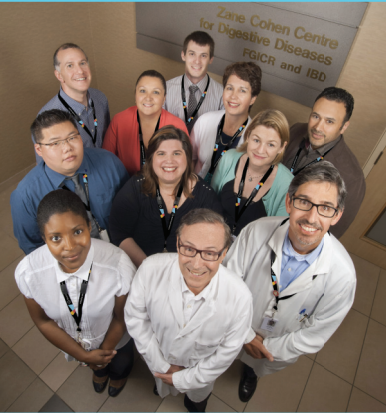




Summer 2018

Message from the ZCC Team



We invite you to partner with us as we “join the dots more quickly” to bring new knowledge into practice for better care for patients and their families. There are many ways to support our work. These include gifts of cash, stocks or existing insurance policies. Legacy gifts to the Zane Cohen Centre can also be designated in a will. To donate, visit zanecohencentre.ca/donate or contact Sarah Hurrell at 416-586-4800 x6006.

Upcoming Events

June 7-8th, 2018
3rd Annual
Sarcoma Symposium

June 12th, 2018
Zane Cohen Centre In the
Loop academic event

September 20th, 2018
Wings to Fight
Fundraising Gala



It is with a great deal of pleasure that I present the Summer 2018 Network Newsletter representing the 10th anniversary of the Zane Cohen Centre for Digestive Diseases. Since its inception in 2008, the Centre has expanded dramatically and emerged as an internationally acclaimed clinical research facility and centre for innovative medical and surgical care for the most difficult Crohn's disease, ulcerative colitis, (inflammatory bowel disease - IBD), and hereditary gastrointestinal cancer patients and their families (familial adenomatous polyposis – FAP, and Lynch syndrome).

With over 50 clinicians, geneticists, radiologists, pathologists, genetic counsellors, information systems specialists, psychologists, international fellows and students, we are well positioned to take on the challenges of these exceptionally difficult disease entities in the areas of ground breaking research, personalized therapies, surgical innovation, screening and prevention, patient education and quality of life, and remote patient care. Crohn's disease and ulcerative colitis (inflammatory bowel disease - IBD), occur in 1 in 150 Canadians. Crohn's disease in particular is on the rise in Canada and we continue to have the highest incidence of these diseases in the world. Our studies are directed at uncovering the triggers for IBD and the IBD-like inflammation that we see following restorative surgical procedures. This is done by analyzing data from the multi-institutional GEM Project and by studying biomarkers of pouchitis that occur in some patients following the pelvic pouch (J pouch) surgical procedure.

This will help us to understand the development and progression of Crohn's disease as well as Crohn's like reactions following surgical procedures. We are also expanding our role in clinical trials of newer developing agents to manage these challenging patients, and developing innovative minimally invasive surgical techniques, which has been amplified with the recruitment of two IBD surgeons – Dr. Mantaj Brar and Dr. Anthony de Buck.

We are leaders in the field of hereditary gastrointestinal cancer. New genes and new complex genetic syndromes are being discovered almost on a weekly basis. With our newly purchased genetic sequencer, we are expanding our role in identification of patients and their families with these genetic conditions and have already proven that once identified and managed and screened, the rate of colon cancer has diminished. We are thankful for all the support that we had over the years from you, our patients and our donors. We could not have reached this pinnacle without you. Please enjoy the Newsletter. If you wish to ask any questions about our Centre or any of the contents of this Newsletter please contact me directly by phoning 416-586-1555 or by emailing Zane.Cohen@sinaihealthsystem.ca. I would be happy to talk to you about all of our projects and have you partner with us as we continue to build knowledge for our patients.

Yours sincerely,

Zane Cohen, M.D., FRCS (C)
Director, Zane Cohen Centre for Digestive Diseases

this issue

| | |
|-----------------------|-----|
| Team Message | P.1 |
| Cancer update | P.2 |
| FGICR | P.3 |
| GEM & PACE | P.4 |
| IBD Bio & FAP | P.5 |
| IBD Centre & CRC risk | P.6 |



Dr. Steve Gallinger Senior Investigator

Dr. Steven Gallinger is a clinician-scientist, and surgical oncologist with an interest in gastrointestinal cancer genetics. As a Senior Investigator at the Lunenfeld-Tanenbaum Research Institute of Mount Sinai Hospital, Dr. Gallinger studies the genetics of both inherited and acquired molecular aspects of colorectal and pancreatic cancer.

Canadian Colorectal Cancer Consortium

The Canadian Colorectal Cancer Consortium (C4) is a Mount Sinai Hospital-led collaborative project funded through the Terry Fox Research Institute.

Individuals with colorectal cancer (CRC) diagnosed under age 60 and their first-degree relatives (parents, siblings, and children) were eligible for recruitment at six sites in four provinces (AB, BC, ON, QC). The C4 is looking at known genetic factors that cause CRC, such as Lynch Syndrome, assessing how family members get screened for CRC, and looking for new genes that may predispose families to an increased risk of developing CRC.

Individuals with a family history of CRC are at increased risk for this disease. Having a first-degree relative (parent, child, or sibling) with CRC approximately doubles the risk, which increases further with the number of relatives affected, particularly if they are diagnosed at younger ages (usually <50 years). Lynch Syndrome (LS) is the most common form of hereditary CRC and is caused by mutations in one of five different genes. Screening for LS in CRC patients can be done relatively easily through a tumor test performed on a patient's CRC surgical specimen. Despite recent advances in our understanding of genetic predisposition to CRC, a large fraction of high-risk Canadian LS families are not being identified and are, therefore, unknowingly missing an important

opportunity for CRC prevention, early detection, and potential novel therapeutics.

Five hundred six patients with CRC have been recruited and of those 11% had abnormal tumor screening for LS. Germline testing identified germline LS mutations in 60% of those with abnormal tumor results, 36% had LS ruled out through somatic analysis, and 4% remain unsolved. To date, five hundred and ninety one family members have also been recruited. We will be looking at how relatives follow colonoscopy recommendations and the factors that influence whether or not they participate in CRC screening. Germline next generation sequencing analysis is ongoing for families with a strong history of CRC, not due to a known genetic cause, to identify novel genes for CRC predisposition.

For more information and updates, visit www.zanecohencentre.com/c4 or speak to the TFRI Project Manager, Spring Holter



The Terry Fox Research Institute
L'Institut de recherche Terry Fox

C4

Canadian Colorectal Cancer Consortium
Consortium canadien pour le cancer colorectal



Patient-centered care in oncology

Dr. Kennedy is a colorectal surgeon at Mount Sinai and an Associate Professor in the Department of Surgery and Institute of Health Policy, Management and Evaluation at the University of Toronto. She leads a clinical research program in patient-centered care in oncology with the main focus being to develop, evaluate and implement strategies to improve patient care in terms of quality, safety and efficiency. More recently, Dr. Kennedy convened a Patient Advisory Committee and worked with this group to co-develop and implement an integrated discharge monitoring system using an interactive Mobile App to support patients at home following surgery. She is also currently leading a pan-Canadian study supported by CIHR to evaluate the safety and effectiveness of non-operative management for patients with locally advanced low rectal cancer.

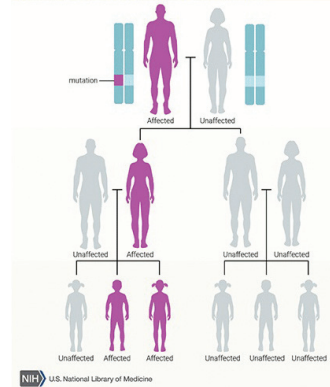


Familial Gastrointestinal Cancer Registry Update

The leadership of the Zane Cohen Centre for Digestive Diseases was showcased at three events hosted this past year by the centre's Familial Gastrointestinal Cancer Registry (FGICR). Beyond the FGICR's work as the country's only clinical and research genetics clinic specialized in gastrointestinal cancer, they provided educational opportunities for both patients and healthcare providers through these events. Supported through a generous donation of the Erika Heller Fund, the Centre's FGICR was proud to host the 2017 Hereditary Gastrointestinal Cancer Symposium at the Hyatt Regency Hotel. This event saw nearly 150 clinicians gather from across the province for an update on hereditary GI cancer syndromes and the current state of tumour and germline genetic testing within Ontario. The symposium also created working groups of genetic counsellors, physicians, pathologists and molecular geneticists, who collaborated to establish an Ontario-wide consensus on genetic testing algorithms and the use of cancer gene panels for hereditary GI cancer syndromes. Recommendations from the working groups will be presented to Cancer Care Ontario. The symposium's keynote speaker was Dr. Patrick Lynch, who presented on the evolving tools to work up the most common hereditary colorectal cancer syndrome, known as Lynch syndrome. Informative presentations were given throughout the day by Dr. Savtaj Brar on hereditary stomach cancer, Dr. Sarah Ferguson on endometrial cancer in Lynch syndrome, Dr. Uri Tabori on novel cancer therapies (immunotherapy), Dr. Robert Gryfe on new polyposis conditions, genetic counsellor Melyssa Aronson on an update for provincial testing criteria, Dr. Nancy Baxter on an update on population-based tumour testing and Dr. Aaron Pollett on a review of governmental processes for hereditary cancer protocols. The FGICR then went on to host two patient-focused education nights at Mount Sinai Hospital in November 2017; the 7th Biennial Lynch Syndrome Education Night, and the 2nd

Familial Polyposis Education Night. At one time, it was thought that all colorectal cancer followed a similar pathway to becoming cancerous, but we now know that this is not the case. Talks for families with Lynch syndrome or Familial Polyposis are tailored to the research on their unique risk, screening, inheritance and treatment of cancers in these families.

Multigenerational Conditions



The Lynch Syndrome meeting provided families with an update on genetics from geneticist Dr. Raymond Kim. As well, oncologist Dr. Uri Tabori presented exciting research on the novel use of immunotherapy to treat Lynch syndrome cancers and surgical oncologist Dr. Savtaj Brar spoke about stomach cancer screening in Lynch syndrome. At the Familial Polyposis meeting, gastroenterologist Dr. Jeffrey Mosko shared the latest on upper gastrointestinal screening, pediatric gastroenterologist Dr. Carol Durno spoke about pediatric issues in Familial Polyposis and colorectal surgeon Dr. Erin Kennedy presented research on post-surgical quality of life and support. A highlight of both meetings greatly appreciated by the audiences were the unique perspectives given by a patient with Lynch syndrome and a patient with a familial polyposis syndrome, respectively, as they shared their personal stories living with a hereditary cancer condition. Videos and presentation materials from these patient-focused meetings have since been made available through the Zane Cohen Centre website, benefitting families unable to attend these events in person.

Familial Gastrointestinal Cancer Registry (FGICR)

The FGICR focuses on the 5-10% of gastrointestinal and related cancers which occur due to a hereditary cause, where an inherited gene mutation increases a person's risk for certain types of cancer. The FGICR has been providing treatment, education, research and support to Canadian families affected with these rare hereditary cancer and polyposis conditions since 1980



Dr. Patrick Lynch
Keynote speaker
Hereditary Gastrointestinal Cancer Symposium 2017

A gastroenterologist at MD Anderson in Texas, he is an expert in hereditary cancer syndromes, including Lynch syndrome, named after his father, as well as Familial Adenomatous Polyposis (FAP) and other polyposis conditions.

The GEM Project

Mount Sinai Hospital and the Zane Cohen Centre continue to house the GEM (Genetics, Environmental and Microbial) Project with Dr. Ken Croitoru as the lead. The GEM Project has completed its ambitious goal of recruiting over 5000 individuals at high risk of developing CD. To date, 64 subjects have developed CD setting the stage to define the genetic, microbial and immune profiles that predict who will develop disease and why. It is through these efforts that we hope to develop strategies for prevention and improved treatments of IBD, if not a possible cure. The GEM Project is in the process of applying for another \$6 million of funding from Crohn's and Colitis Canada and Helmsley Charitable Trust to continue its work.

Most recently, the GEM Project team has published important findings showing there is no association between the

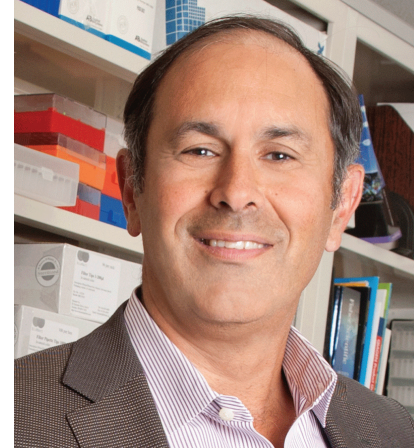


highest CD risk genes and the composition of the gut microbiome. These findings were published this month in the journal "Gut Microbes". Dr. Croitoru has been invited to present recent findings from the GEM Project to the larger scientific community this summer at the meeting Digestive Disease Week, put on by the American Gastroenterological Association which hosts over 15,000 international physicians and scientists. Ashleigh Goethel, a recent University of Toronto PhD graduate, has now joined the team as the Clinical Research Project Manager. We welcome her to the team and are confident she will bring her own strength to the team.

Promoting Access and Care through Centres of Excellence (PACE)

Through the support from Crohn's and Colitis Canada, Dr. Geoffrey Nguyen and the PACE Inflammatory Bowel Disease Telemedicine team have embarked an innovative project to improve access to quality IBD care for individuals living in rural and remote communities throughout Ontario. In less than two years, the telemedicine program has provided over 250 eVisit appointments with IBD specialists at Mount Sinai Hospital. As evaluation is a key component to PACE program, a prospective cohort study is being undertaken to compare care received via telemedicine videoconference to in-person clinic care. This study will enable objective comparison between the telemedicine group and in-person group by administering online annual questionnaires, as well as evaluating utilization of health services

at the end of the study. Patients enrolled in the study are also given access to a web-based mobile application called HealthPROMISE. Using the HealthPROMISE app, patients can complete monthly questionnaires to track their IBD symptoms and quality of life. Within the care team at Mount Sinai Hospital, an IBD nurse monitors the patient's responses and can arrange for earlier follow-up care, if there are concerns. Through the use of innovative health care technologies, the PACE IBD Telemedicine program is showing feasibility in supporting IBD patients residing in rural and remote communities.



Dr. Ken Croitoru
Gastroenterologist

Dr. Croitoru is the lead investigator of the GEM project and runs the Inflammatory Bowel Disease Clinical Translational Research Unit (IBD CTRU)

For more information including how to participate, please see:
web: gemproject.ca
twitter: @The_GEMProject



Dr. Geoffrey Nguyen
Gastroenterologist

Dr. Nguyen is an Associate Professor of Medicine at the University of Toronto and the Institute for Health Policy Management and Evaluation.



Dr. Mark Silverberg Gastroenterologist

He is currently a Professor and Clinician Scientist in the Department of Medicine and holds the Gale and Graham Wright Research Chair in Digestive Diseases. He runs a laboratory based at Mount Sinai Hospital investigating the causes of inflammatory bowel disease (IBD).

IBD Biomarkers research program

Dr. Silverberg's IBD Biomarkers research program is in its 16th year. He has a team of project managers, research assistants and coordinators, lab technicians, scientific associates and trainees. The goals of our research program are to identify susceptibility genes and biomarkers for Inflammatory Bowel Disease (IBD), which include Crohn's disease and Ulcerative colitis, and to explain the contribution of these markers to the cause and clinical course of IBD. We use a number of high-throughput methodologies such as genome-wide association studies (studying DNA and genes), whole-genome expression (studying which genes are on or off), microRNAs (small molecules that can regulate gene expression) and microbiome (gut bacteria) analysis. We also investigate serum levels of novel antibodies, biologic drug levels and their corresponding antibodies and correlate these with phenotype and how this information can be applied to clinical management. Our current projects are directed toward understanding the relationship between the microbiome in the digestive tract and host genotype or gene regulation, to gain more insight into the role of diet and how food may trigger or exacerbate IBD. We hope that ultimately, this will lead to tools that may allow clinicians to better predict who may develop IBD and also identify high-risk patients so that a more personalized approach to treatment may be employed. Dr. Silverberg and his team are participating in two international, blinded (which means we, and the patients, don't know which treatment is being received), placebo-controlled (which means a non-active substance) clinical trials on pouchitis. One trial is of a new enema medication for treating pouchitis in patients who have not responded to antibiotic treatment. We are the

leading centre and have screened 12 patients for their participation and enrolled 7 patients. Our second trial is to evaluate the efficacy of vedolizumab in patients with pouchitis. Vedolizumab is a drug administered by IV and currently approved by Health Canada for use in Crohn's disease and ulcerative colitis, but not yet for pouchitis. We are also one of the leading centres in this trial with 14 patients screened (9 enrolled). Currently, we are working hard to launch new studies in the near future, including a dietary intervention study for active ulcerative colitis patients, a prospective pouch study following patients from the time of their surgery, an ulcerative colitis relapse study following UC patients to see if we can further understand why some patients flare, as well as new clinical trials. We are also sending a large team to Digestive Disease Week (June 2018) to present our data to the international community.

This research program has been funded mainly by grants from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK/NIH), Crohn's and Colitis Canada (CCC) and Canadian Institutes of Health Research (CIHR), the International Organization for the Study of Inflammatory Bowel Disease (IOIBD) as well as generous donations.

For more information on the Silverberg Lab, please visit our lab website at: <http://research.lunenfeld.ca/silverberg>.

We are recruiting subjects for various research studies. A full listing of all clinical-translational and clinical trial research projects can be found at: <http://zanecohencentre.com/ibd/research>



Current Research

There are current trials currently operating at the Zane Cohen Centre. If you have any questions about the ongoing trials, please visit zanecohencentre.com/ibd/research or contact by phone: 1-877-586-5112 or email: zanecohencentre.msh@sinaihealthsystem.ca

Familial Adenomatous Polyposis Study

Cancer Prevention Pharmaceuticals closed enrollment for a clinical trial that is evaluating a new drug combination (eflornithine (DMFO) and sulindac) for patients with FAP (familial adenomatous polyposis). This study will determine if a combination drug treatment can work better than each drug alone in preventing the disease from getting worse. It will also look to see if this new treatment for FAP can reduce the number and/or size of colon polyps and will look at how the medication might change quality of life. There were 17 international centers participating in this trial from the United States, Germany, Spain, the UK,

the Netherlands and our Canadian Center, Mount Sinai Hospital which was one of the top recruiters of this study. Worldwide, approximately 35 patients remain on active treatment with the last completion date of approximately June 2019. When the study is published we will include these results in a future newsletter. The Zane Cohen Centre for Digestive Diseases, Mount Sinai Hospital, Dr. Steven Gallinger, Dr. Zane Cohen and Dr. Rob Gryfe would like to thank all of our patients who participated in this important clinical trial for FAP.



Innovation in Ostomy Care Exhibit & Terry Berk Library

We are proud to have established an iconic display that showcases the developmental history of innovation in Ostomy Care. In the same display is also the Terry Berk Library with dedicated reading material available to be loaned out. We would like to thank the following donors for establishing this honor; Ostomy Canada, The Toronto Ostomy Society and The Canadian Association for Enterostomal Therapy. A very special thanks to Kathryn Kozell and Diane Garde for putting together the showcase.



Dr. Tae Hart Staff Scientist

Dr. Hart's research centers on psychological factors associated with adjustment to illness in chronically-ill individuals and their spouses /partners. She investigated quality of life, psychological distress, and symptom burden in patients who have been diagnosed with cancer, multiple sclerosis, or gastrointestinal disorders.

Improving Patient Communication for families with CRC risk

Colorectal cancer (CRC) is the second most common cancer in Canada and the incidence of CRC is rising in younger people. However colonoscopy rates among families with history of CRC are quite low. Intrafamilial communication (e.g., talking about cancer within the family) is an important element to discussing cancer risk and need for colonoscopy, with the burden falling on the person diagnosed with CRC to inform their relatives. To improve adherence to colonoscopy screening, it is imperative that issues in intrafamilial communication and kin-reported barriers to CRC screening be addressed. Dr. Tae Hart, along with ZCC colleagues Spring Holter, Dr. Steve Gallinger, and Kelly McShane (Ryerson University) received a grant from the Collaborative Group of the Americas on Inherited Colorectal Cancer to conduct a study examining: 1) Why individuals with CRC do not disclose to their relatives that they are at higher risk of developing CRC and need regular colonoscopy; 2) Why lack of participation in colonoscopy screening is high among relatives at increased risk for CRC who have been informed to get regular surveillance. All participants were recruited from the Canadian Colorectal Cancer Consortium, which is a Terry Fox

Research Institute funded multi-site prospective CRC study run by Dr. Gallinger and managed by Spring Holter. Dr. Hart and colleagues recruited two sets of participants: 1) People diagnosed with CRC who had not communicated with their close relatives about their increased risk of developing CRC (16 participants) and 2) Kin who had not completed a colonoscopy within the last ten years (9 participants). Analysis of semi-structured interviews showed patients did not talk to family members about their need for CRC screening due to: worry about negative reactions from family members, not understanding why it is important to talk to family members, and the idea that younger relatives do not think about CRC screening. Among the kin participants, a number of factors influenced the decision to not obtain colonoscopy, which included: negative beliefs about colonoscopy, lack of information and understanding about their risk of CRC, including the misconception that early CRC will present with physical symptoms, and one's family physician incorrectly advising that a colonoscopy was not necessary, despite having a significant family history. Using the results from this small pilot study, the research team plans to develop tools to help patients communicate better with their family members about their CRC risk.



Dr. Hillary Steinhart Gastroenterologist

Dr. Steinhart is the Head of the Combined Division of Gastroenterology for Mount Sinai Hospital and the University Health Network. Dr. Steinhart divides his time between patient care, clinical research and teaching. His research interests are in the areas of clinical trials, outcomes assessments and the genetics of Inflammatory Bowel Diseases.

IBD Centre of Excellence

The MSH Centre for IBD continues to grow in numbers and in the breadth of expertise available at the ZCC. Dr. Vivian Huang, an expert in the area of IBD and pregnancy, has recently joined our group of expert IBD clinicians and investigators. Dr. Huang has initiated the first Preconception and Pregnancy in IBD clinical research program in Ontario. This program offers women with IBD personalized education and counselling regarding IBD, medications, and pregnancy, and offers assistance with optimizing their disease before conception and throughout pregnancy. The program will include a multidisciplinary joint clinic at MSH and a telemedicine program with networks across Ontario and in the GTA to care for pregnant women with IBD. Clinical studies include the development and testing of patient-oriented decision-aids to address patient concerns,

and innovative methods to optimize IBD disease control before conception and during pregnancy. Translational studies include investigation of the impact of maternal IBD and IBD therapies on the materno-fetal interaction, and thus on the health outcomes of the fetus and neonate. This novel MSH clinical research program will strengthen existing collaborations and will build new clinical research collaborations with multiple specialities from obstetrics to pediatrics, and from across Canada and International centres. Dr. Huang is also currently developing innovative e-health tools to improve education and health outcomes for all patients with IBD, with a special focus on expectant mothers with IBD.



Contact Us

We would love to hear from you and can be contacted:

Zane Cohen Centre
60 Murray Street L3-000
Toronto ON M5T 3L9
P: 416-586-5112
P (toll free): 1-877-586-5112
www.zanecohencentre.com