



Zane Cohen Centre for Digestive Diseases

Sinai Health System

NETWORK NEWSLETTER



Spring 2016

A Message from the Director

The Zane Cohen Centre for Digestive Diseases (ZCC) is a clinical research facility and internationally acclaimed as a leader in the understanding and treatment of gastrointestinal diseases. The Centre's research focus is to determine the causes of hereditary familial cancers and Inflammatory Bowel Diseases (ulcerative colitis and Crohn's disease), with an emphasis on their genetic basis. It is because our investigators are clinicians; the Centre prides itself in being able to quickly and efficiently bring new research findings into the medical setting for more tailored treatment and better patient care.

The ZCC is proud of its collaborative team structure consisting of gastroenterologists, surgeons, psychiatrists, psychologists, pathologists, radiologists, molecular and clinical geneticists, researchers, genetic counsellors, epidemiologists, pediatricians and IT specialists. We invite you to take advantage of the resources we offer through this newsletter.

IBD Centre of Excellence update

The Mount Sinai Hospital Centre for Inflammatory Bowel Disease (IBD) was established as one of the hospital's five clinical Centres of Excellence at the end of 2010 following the release of the hospital's Strategic Plan for 2010 - 2013. The primary goal of the Centre for IBD has been to improve integrated team care and clinical outcomes for our patients with Crohn's disease and ulcerative colitis. Although the focus of the Centre of Excellence is on clinical care and outcomes, many of the goals are closely aligned with the activities of the Zane Cohen Centre (ZCC) through the application of clinical and translational research advances at the ZCC to improve the care of our patients. The Centre for IBD has undertaken a number of initiatives to improve the patient experience, enhance quality of care and safety and improve access to care and efficiency of care. The institution of Best Practices in General Surgery, which was first introduced in the province at Mount Sinai Hospital, has been championed across the rest of the province by one of our surgeons, Dr. Robin McLeod. These best practices have resulted in improved patient outcomes.



Dr. Hillary Steinhart

The Centre is also taking a leading role in a program that has been designed to improve the care of IBD patients across Canada. This program, entitled Promoting Access and Care through Centres of Excellence (PACE) is intended to improve IBD patient outcomes and address current gaps through clinical care and research. More information about the PACE project can be found inside.



Dr. Zane Cohen
Director,
Zane Cohen Centre

We Build Knowledge
To Improve Treatment



Brenda O'Connor

IBD Support Network Update

Treatment of IBD involves more than diagnosis, prescribing medication or undergoing surgery. When confronted with illness, patients seek professional help and advice from their physician, nurse, social worker and also rely on support from family members, peers and fellow patients. Our support groups are an excellent opportunity for patients, family members and friends to gain information on all aspects of their IBD journey. The groups also provide a safe forum to meet and share on living well with the diseases and receive peer support. The Daytime support group meets monthly at 2pm on the 14th floor classroom on the last Wednesday of the month: April 27, May 25, September 28, October 26, November 28 and December 14 for 2016. The Evening support

group starts at 7pm in the 18th floor auditorium: May 25, September 26, and November 26 for 2016.

For information about the support groups and speakers, please access <http://zanecohencentre.com/ibd/for-patients/ibd-supportnetwork>.

If you have any questions, please contact Brenda O'Connor at 416-586-4800 x8349 or email boconnor@mtsinai.on.ca. If you are not in the Toronto area or are unable to attend the IBD support meeting and would like to become a peer support person or receive peer support, please email Brenda directly.



Dr. Rebecca Gladdy

Abdominal Sarcoma Program

Sarcoma is a rare cancer that arises from connective tissues (e.g. muscle, fat, bone) and affects both children and adults. In adults, approximately 1% of all cancers are sarcoma. There are over 40 different types of sarcoma, with less than half of all sarcomas occurring in the abdomen. Mount Sinai Hospital is the Centre of Excellence for Sarcoma in Canada in collaboration with Princess Margaret Cancer Centre. The Abdominal Sarcoma Research Team has adopted a multidisciplinary approach to patient care as sarcoma can be treated by a combination of radiation, chemotherapy and surgery, depending on the type of sarcoma. The Abdominal Sarcoma Clinical Research Program was established in 2009 by Dr. Rebecca Gladdy and Dr. Carol Swallow, Surgical Oncologists at Mount Sinai Hospital and Princess Margaret Cancer Centre, who also have research programs at the Lunenfeld-Tanenbaum Research Institute (LTRI).

This program was developed to address a 'bench to bedside' approach in Abdominal Sarcoma, where the clinical research team continues to provide an essential link between the laboratory ("bench") and the point of patient care, be it hospital ("bedside"), physician's office or outpatient clinic.

Recent Research Developments in the Abdominal Sarcoma Program include:

- MSH Abdominal Sarcoma Database
- Sarcoma Tissue and Cell Line Biorepository
- Participation in International Sarcoma Research
- Development of Selective Therapies for Sarcoma
- Upcoming events: 2nd Toronto International Sarcoma Symposium, June 10th 2016 at the Park Hyatt, Toronto

For more information, please visit our site: www.zanecohencentre.com/gi-cancers/stsrp



Dr. Steven Gallinger

Ontario Pancreas Cancer Study

The Ontario Pancreas Cancer Study (OPCS) was created in 2002 with the hopes of identifying and characterizing causes of pancreas cancer, including genetic, environmental, and lifestyle factors, as well as what treatments are available to patients with this disease. To date, the OPCS has family history and risk factor questionnaires on approximately 2000 patients and blood and/or saliva and plasma from approximately 1800 patients. The main goals of the OPCS are to foster local and multisite collaborative research in classical epidemiology and genetic epidemiology (including both average risk and high risk genetics).

Using our large case/control OPCS resource, we

have contributed to both local and international single and multisite projects exploring potential risk factors such as family history, allergies, alcohol consumption, dietary patterns, pancreatitis, obesity, diabetes, reproductive factors, and genetic variants on pancreas cancer susceptibility. The OPCS staff have also abstracted and characterized exhaustive clinicopathologic data from cases enrolled in the International Cancer Genome Consortium (ICGC), most of which are dual-enrolled in the OPCS. In addition, the OPCS pancreas cancer screening study will hopefully determine the effectiveness of contrast-MRI (magnetic resonance imaging) for early detection of pancreatic cancer in high-risk families.



IBD PACE Project

Optimal care for IBD patients most often involves a multidisciplinary team and is ideally delivered at a Centre of Excellence equipped to deliver such care. Despite evidence that early gastroenterology intervention is associated with reduced IBD complications, there are substantial geographic inequalities in access to specialists. Moreover, the overuse of chronic steroids remains a widespread issue. Crohn's and Colitis Canada (CCC)'s Promoting Access and Care Through Centres of Excellence (PACE) Project aims to improve quality of life for patients living with Crohn's disease and ulcerative colitis by addressing these healthcare gaps. This unique, four-year collaboration will be led by Dr. Geoffrey Nguyen of the Zane Cohen Centre for Digestive Diseases and has been funded by CCC and its pharma partners. PACE's \$2.5 million budget will support four initiatives to be carried out at five IBD Centres of Excellence across Canada.

In addition to acting as the Principal Investigator for the broader project, Dr. Nguyen will lead the PACE Mount Sinai initiative, focusing on the delivery of telemedicine outreach to geographic regions in Ontario currently underserviced by IBD specialists. He and his team will identify geographic regions in Ontario in which IBD patients are underserviced, develop a patient-centric IBD telemedicine network centered around IBD nodes of care driven by IBD-trained nurses, and evaluate the intervention through a cluster randomized trial using



Psychosocial Aspects of CRC

Study on Colorectal Cancer History

Colorectal cancer (CRC) is the second most common type of cancer in Canadian men and the third most common cancer in Canadian women. Treatment for CRC, such as surgery, chemotherapy, and radiation can cause lasting and sometimes severe symptoms that endure for years, such as bowel and urinary dysfunction, sexual dysfunction, fatigue and emotional distress and low quality of life (QOL). Existing CRC survivorship studies are limited by short follow-up, often not exceeding five years, and the lack of a comparable group of unaffected controls. Without information about QOL, symptoms and other health conditions in an age- and gender-matched control group, it is unclear to what extent problems reported by survivors are due to cancer or to comorbidity and/or older age. Dr. Tae Hart, along with Drs. Steve Gallinger, Michelle Cotterchio, Nancy Baxter and Zane Cohen, examined the degree to which presence or absence of CRC history was associated with long-term self-reported physical functioning, QOL, and psychological well-being. This study was funded by an operating grant from the Canadian Institutes of Health Research, with Dr. Hart as the Principal Investigator. This was a population-based sample of CRC survivors (N=296) and their age- and gender-matched controls (N=255) who were recruited from the Ontario Familial Colorectal Cancer Registry.

Dr. Tae Hart

health administrative data to measure improvements in patient outcomes.

Once piloted in Ontario, telemedicine outreach will be rolled out at all participating PACE sites. PACE-funded initiatives at the other participating Centres of Excellence will focus on :

- i) Developing an electronic clinical care pathway to provide a standardized approach to minimizing repeated use of, and complications related to, chronic steroid use. (University of Alberta: Dr. R. Fedorak, University of Calgary: Dr. R. Panaccione)
- ii) Using an electronic platform to facilitate the communication of patient-reported outcomes to guide disease management and empower patients to be actively involved in their care, support. (McMaster University: Drs. J. Marshall, N. Narula, W. Reinisch);
- iii) Measuring the effectiveness of the PACE Project based on quality indicators. (McGill University: Dr. A. Bitton).

The CCC PACE Project will launch in April 2016.

For more information, please contact:

Dr. Nguyen: gnguyen@mtsinai.on.ca

Natasha Kachan: nkachan@crohnsandcolitis.ca.



Survivors were an average of 15 years post-diagnosis. Survivors were compared to controls on QOL, using the Functional Assessment of Cancer Therapy-General Scale. Symptom severity (bowel function, urinary function, and fatigue) and depression were also assessed, using validated measures. Survivors and controls were compared to one another after adjusting for income, education, and comorbid medical conditions. CRC survivors reported good emotional, functional, physical and overall QOL that was comparable to unaffected controls. Fatigue and urinary functioning also did not differ significantly between survivors and controls. Survivors reported significantly higher social QOL and significantly lower depression compared to unaffected controls. The one area survivors reported significantly worse deficits were in bowel dysfunction, but the magnitude of differences was relatively small. The overall message is encouraging: CRC survivors appear to have comparable QOL and in some aspects, better well-being than people who have never had cancer. Our data show that overall QOL can be expected to be very good in the long term after treatment for colorectal cancer. Health care providers should be aware that bowel dysfunction may be an ongoing issue for CRC survivors, even 15 years after diagnosis. Dr. Hart and colleagues have submitted these findings for publication in a scientific journal and are also working on providing this information to survivors and organizations such as the Colorectal Cancer Association of Canada and the Colon Cancer Canada.



Left to Right: Melyssa Aronson, Spring Holter, Dr. Zane Cohen, Kara Semotiuk, Laura Winter

Familial Gastrointestinal Cancer Registry

The genetic clinic at the ZCC, consisting of 4 genetic counsellors and a geneticist, offers education, support, genetic counselling and testing to families with hereditary cancer and GI polyp conditions. We have expanded the support we offer patients by formalizing a "buddy system" which matches people with the same genetic conditions so they can share experiences. We have also designed patient friendly pamphlets for 7 hereditary conditions including Lynch syndrome and FAP, and held two patient education evenings in the past year, one for Lynch syndrome families and the other for families with FAP and MAP. Both were attended by over a hundred patients and family members. A special thanks to Ann McLaughlin and Joe Aiello, and the Erika Heller Quality of Life Fund for generously sponsoring the Lynch syndrome and Familial Polyposis education nights, respectively.

Genetic research is conducted under the umbrella of the Familial Gastrointestinal Cancer Registry (FGICR) which was established in 1980 to collect biospecimen (blood and tissue) as well as family and medical history to better understand the causes of hereditary cancer and polyp conditions and improve treatment, diagnosis and prevention of cancer in families. This Registry follows hundreds of families in Ontario, and across Canada with strong family histories of cancer and colorectal polyps as well as those with confirmed hereditary conditions. Research in the past year has focused on many different issues including: a) Quality of life - looking at the relationship between individuals with Lynch syndrome and their physician and the impact it has on uncertainty and cancer worry; looking at long term psychological adjustments to receiving genetic results; and examining cancer worry in families with stomach cancer b) Cancer risk and screening – determining the risk of a second cancer after colon surgery in young individuals with colorectal cancer; examining the risk of GI cancer and polyps in children who have a rare genetic condition known as BMMRD; determining the risk of cancer in individuals with both IBD and Lynch syndrome; evaluating treatment of brain cancer in children with a hereditary condition, c) Policy development – assessing the needs and availability of testing in the province of Ontario, and the criteria development to test families for hereditary GI cancer, and d) Genetic test evaluation – determining the efficacy of genetic testing in Ontario families to find genetic causes. The FGICR is an international leader in hereditary GI cancer and continues to lead research and collaborate with other Registries around the world.

Biallelic Mismatch Repair Deficiency

The unrecognized syndrome

Biallelic mismatch repair deficiency (BMMRD) is caused when two mutations in the mismatch repair genes are inherited, compared to one mutation inherited in Lynch syndrome. This is a rare syndrome with a phenotype distinct from Lynch Syndrome. Patients have characteristic skin findings called café-au-lait macules. One of our goals is to raise awareness of BMMRD among gastroenterologists, oncologists, dermatologists and pediatricians. In contrast to other colorectal cancer predisposition syndromes such as Lynch Syndrome or Familial Adenomatous Polyposis the family history in BMMRD is often non-contributory therefore a high index of suspicion is paramount. Patients with BMMRD are at risk of a number of cancers. We developed a surveillance protocol to detect polyps and other tumors before they develop into cancer. The surveillance protocol is used at hospitals around the world. Over the past fifteen years we have been monitoring BMMRD patients and collecting data to advance our understanding of the natural history of the gastrointestinal features of this syndrome. Recently we published, "Gastrointestinal Findings in the Largest Series of Patients with Hereditary Biallelic Mismatch Repair Deficiency Syndrome: Report from the

International Consortium" in The American Journal of Gastroenterology (Aronson et al). The lifetime risk of gastrointestinal cancer among BMMRD patients is the highest reported of all gastrointestinal cancer predisposition syndromes, and the age at diagnosis of tumors can be very young. The rate of progression of adenomas among BMMRD patients appears accelerated and more rapid than in Lynch Syndrome. Patients with BMMRD undergo surveillance of the small intestine for polyps. Video capsule endoscopy (VCE) is a noninvasive technology which can be used to visualize the duodenum, jejunum and ileum. A pill sized video camera is swallowed and takes pictures of the small bowel as it passes through. The pictures are sent to a small recording device. The video is reviewed by a specialist to evaluate for polyps. We initiated the first study, an international multicentre project, to determine if VCE is an effective technology to identify polyps of the small bowel in BMMRD patients. Results from this VCE trial will be presented at the upcoming World Congress of Pediatric Gastroenterology Meeting in Montreal, October 2016.



Dr. Carol Durno

STUDY UPDATES

Dr. Carol Swallow



Hereditary Gastric Cancer

The Zane Cohen Centre has a strong and dedicated team committed to better understanding the genetics of stomach cancer, screening and prevention. The most common hereditary condition causing stomach cancer is Hereditary Diffuse Gastric Cancer Syndrome, and because of the high risk, treatment to remove the stomach is needed to prevent stomach cancer. Dr. Carol Swallow has performed over 20 of these preventative surgeries and in almost all cases; early cancer was found which was prevented from becoming invasive cancer. Melyssa Aronson, genetic counsellor, has been working with patients to better understand the decision-making and impact of having this surgery. Their next goal is to write a booklet for those contemplating surgery with helpful hints and Q & A. Much work still needs to be done in understanding the genes that cause stomach cancer to develop. The ZCC has offered genetic testing to about 100 families that presented with high-risk family histories, and the genetic cause for the stomach cancer was discovered in less than 20% of these high-risk families. This means there are probably other genes to be discovered, or better techniques needed to find the genetic mutations so families can better understand their risk and take steps to prevent cancer. Dr. Sav Brar and Dr. Anand Govindarajan are actively involved in screening individuals at high risk for stomach cancer, but better screening techniques are needed to find stomach cancer at an early stage.



Ulcerative Colitis

We are currently Recruiting Subjects for Ulcerative Colitis (March 2016)

- 1) Etrolizumab in UC
 - a) etrolizumab/placebo for anti-TNF naïve patients
 - b) etrolizumab/placebo for patients who are refractory/intolerant to TNF inhibitors
- 2) APD334-003 (S1P1 receptor antagonist) in UC
- 3) Humira (open label) and Methotrexate in UC

Crohn's Disease

We are currently Recruiting Subjects for Crohn's Disease (March 2016)

- 1) Etrolizumab in CD
- 2) RHB-104 in CD

The other studies we are currently involved in are in the maintenance phases and not recruiting new patients. If you are interested in any of the above studies please call Shelley at 416-586-4800 x4989 from Monday-Thursday or e-mail smikolainis@mtsinai.on.ca. We are happy to be pre-screening over the telephone as each study has many inclusion/exclusion criteria. More details about the study can be found online at: <http://zanecohencentre.com/ibd/research>

Pouchitis Research Study

Mount Sinai Hospital is participating in a clinical trial that is looking at the safety and effectiveness of a new enema medication for treating pouchitis in patients who have previously and/or currently not undergone an IPAA procedure and currently experiencing pouchitis (inflammation of the pouch lining) and have not responded to antibiotic treatment. For more information please contact Ajani Jeyakumar (Study Coordinator) at 416-586-4800 x5953 or Dr. Mark Silverberg (Principal Investigator) at 416-586-4800 x8236.

Drug Trial for FAP

The Zane Cohen Centre (ZCC) is participating in an international clinical drug trial on polyp development in Familial Adenomatous Polyposis (FAP). Individuals with FAP can develop hundreds to thousands of adenomatous polyps in the colon, rectum, and first part of the small bowel (duodenum), which leads to an increased cancer risk in these organs. These individuals typically require surgical removal of their colon to prevent cancer, as well as lifelong monitoring of remaining tissue. The study is examining whether two drugs, called CPP-1X (eflornithine HCl) and sulindac, reduce the number and/or size of adenomas in the colon, rectum and duodenum. Study enrollment closed in March 2016. The ZCC recruited 17 patients with FAP, placing them amongst the top of the 21 international enrolment centres. Patients are receiving active treatment for 24 months. A request was submitted to the hospital's Research Ethics Board to extend those patients near the end of the 24 month treatment period for an additional year. The ZCC is also working to participate in a new FAP polyp study in the near future.

Best Practice in General Surgery (BPIGS)

The BPIGS group was developed in 2006 with the aim of standardizing general surgical procedures across the University of Toronto affiliated hospitals. The group has developed six clinical practice guidelines, available online at <http://www.bpisgs.ca/> and is currently developing further guidelines as they transition from the BPIGS to Best Practice in Surgery.



Staff of the Zane
Cohen Centre
thank you for your
continued support

Our research leadership

Making genetic, environmental and microbial discoveries

Family history and genetic predisposition are known risk factors for IBD – in just the past 15 years, more than 190 gene variants have been linked to IBD. But genetics alone cannot explain the booming epidemic. To treat IBD, scientists must also decode the synergistic role of our environment, including factors like diet and exposure to chemicals. Dr. Kenneth Croitoru is unraveling this delicate balance of genetics, environment and gut microbes. He leads the GEM (Genetic, Environmental and Microbial) Project, a major, multi-centre clinical research study with its headquarters at Mount Sinai. The GEM Project examines how the interplay of genetics and environmental factors influence the microbiome (gut bacteria), to understand the role of each in triggering Crohn's. Tracking more than 4,000 people from hospitals across Canada, the United States, the United Kingdom, Israel and New Zealand, Dr. Croitoru and his colleagues are studying individuals with Crohn's disease and their healthy relatives. The GEM Project findings will reveal how genetics, diet, chemical exposures and lifestyle factors play a role in affecting the microbiome, to slow or accelerate the development of Crohn's disease. Study recruitment remains open to individuals diagnosed with Crohn's disease and their healthy relatives age 6 to 35. More information regarding the GEM Project can be found online at www.gemproject.ca. The GEM Project is generously supported by the Crohn's and Colitis Foundation and has recently secured a very prestigious \$6 million match grant from the US-based Helmsley Foundation. The team must raise another \$4 million to unlock the grant and complete their work. Their discoveries will lead to new and better ways to prevent and treat IBD.



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 online: www.zanecohencentre.ca/donate
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