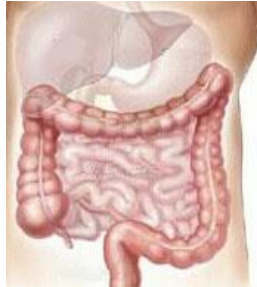


## **COLORECTAL CANCER RESEARCH UPDATES** Month Ending November 16<sup>th</sup>, 2017



The following colorectal cancer research updates extend from September 15th to November 16th, 2017 inclusive and are intended for informational purposes only.

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## DRUGS / SYSTEMIC THERAPIES

### 1. 2017 Top stories in Oncology – IDEA duration of adjuvant therapy in stage III colon cancer (Nov 6/17)

The IDEA (International Duration Evaluation of Adjuvant Chemotherapy Collaboration) study has put into question a change in standard practice to benefit patients with stage III colon cancer. The current standard of care for stage III colon cancer is 6 months of adjuvant chemotherapy which has been proven to decrease disease recurrence and improve overall survival. Thus far, the most effective therapy has been a combination of 5-FU, generally given with leucovorin and oxaliplatin (FOLFOX). An alternative therapy replaces the intravenous 5-FU/leucovorin with capecitabine (CAPOX). When administered for 6 months, however, high incidence of toxicity specifically irreversible neuropathy makes this treatment less than ideal.

Researchers from across the globe collaborated in an analysis of six randomized trials which examined 3 versus 6 months of adjuvant chemotherapy for stage III colon cancer. Objective response was 3-year disease-free survival (DFS), which correlates well with overall survival in stage III colon cancer. While there was no improvement to DFS on 3-month adjuvant chemotherapy for stage III disease overall (81.9% vs 83.5% for 3-month and 6-month therapy, respectively), researchers found a statistical noninferiority for 3 vs. 6 months on adjuvant therapy among patients with *fewer than four affected lymph nodes*, with significantly less toxicity. In other words, the 3-month treatment was not found to be any less effective than 6-month adjuvant chemotherapy among patients with less nodal involvement. Furthermore, there was higher treatment compliance with the 3-month regimen.

The IDEA study is stimulating oncologists to highly consider 3 months of adjuvant chemotherapy among patients with stage III disease in which fewer than four lymph nodes are affected. Among patients with stage III colon cancer with greater than four lymph nodes affected, the advantages and disadvantages of the 6-month treatment should be discussed with each patient in order to weigh the effects of a slightly better 3-year DFS against the greater risk of toxicities.

[http://www.practiceupdate.com/expertopinion/3093/1/1?elsca1=emc\\_eneews\\_expert-insight&elsca2=email&elsca3=practiceupdate\\_onc&elsca4=oncology&elsca5=newsletter&rid=NTU2MJ4MDA1NzQS1&lid=10332481](http://www.practiceupdate.com/expertopinion/3093/1/1?elsca1=emc_eneews_expert-insight&elsca2=email&elsca3=practiceupdate_onc&elsca4=oncology&elsca5=newsletter&rid=NTU2MJ4MDA1NzQS1&lid=10332481)

### 2. Nivolumab in advanced DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (Oct 10/17)

Based on findings from the Phase II Checkmate 142 trial, nivolumab (Opdivo) has produced lasting responses in previously treated recurrent or metastatic DNA mismatch repair-deficient (dMMR/microsatellite instability high (MSI-H) colorectal cancer. The study was in support of the recent approval of the drug in the treatment of patients 12 years or older with dMMR/MSI-H colorectal cancer that has been previously treated with a fluoropyrimidine/oxaliplatin/irinotecan regimen. In the trial, 74 patients with dMMR/MSI-H colorectal cancer received nivolumab at 3mg/kg every 2 weeks until the disease progressed, or they experienced unacceptable toxicity. All patients had undergone previous treatment with fluoropyrimidine plus oxaliplatin or irinotecan with no results. At a median follow-up of 12 months, 37.8% of patients had stable disease for 12 weeks or longer. One year progression-free survival was 50%, and 1 year overall survival was 73%. The most common treatment-related adverse events were fatigue (23%), diarrhea (21%), severe skin itching (14%), increase lipase (12%) and rash (11%). Grade 3 or 4 adverse events occurred in 20% of patients, with 7% of patients who discontinued treatment due to drug-related adverse events. Drug-related serious adverse events occurred in 12% of patients, including grade 3 or 4 adrenal insufficiency, colitis, diarrhea, gastritis, stomatitis, acute kidney injury, pain and arthritis. Four patients (5%) died of adverse events (sudden death, cardiac disorder and disease progression), though none were considered related to study treatment. In conclusion, the drug provided durable responses and disease control among pre-treated patients with dMMR/MSI-H metastatic colorectal cancer and could be a new treatment option for these patients.

<http://www.ascopost.com/issues/october-10-2017/nivolumab-in-advanced-dna-mismatch-repair-deficient-or-microsatellite-instability-high-colorectal-cancer/>

### 3. Phase I study of Cobimetinib with Bevacizumab and Atezolizumab for colorectal cancer (Oct 24/17)

In this non-randomized phase I trial, the safety, tolerability and pharmacokinetics of cobimetinib in combination with atezolizumab and bevacizumab among patients with metastatic colorectal cancer will be evaluated. Cobimetinib is an oral MEK kinase inhibitor which targets cell signalling involved in cell division and growth. Atezolizumab is an anti-PD-L1 antibody which targets the PD-L1 and PD-1 receptor to prevent suppression of the immune system against cancer cells. Bevacizumab is an antibody which interferes with the process of new blood vessel formation (angiogenesis) in cancer cells. All patients will have received at least 1 previous therapy with fluoropyrimidine and oxaliplatin or

irinotecan. Cobimetinib will be administered orally while atezolizumab and bevacizumab will be given intravenously. In the first stage of the trial, patients will receive the drug combination until the disease progresses, unacceptable toxicity or withdrawal from the trial. In the second stage of the trial, the patients will be divided into two groups. The first group will receive the drug combination and undergo repeated tumour biopsy. The second group will receive atezolizumab and bevacizumab plus the cobimetinib dose that was given in stage I. For more information regarding the study, including inclusion and exclusion criteria, locations and contact information, visit: <https://clinicaltrials.gov/ct2/show/NCT02876224>. The study is open and recruiting patients as of Oct 24, 2017 in the U.S., U.K., and Spain.

<http://www.cancertherapyadvisor.com/gastrointestinal-cancers/colorectal-cancer-phase-1-study-cobimetinib-treatment-risk-trial/article/702469/>

*Clinicaltrials.gov. Study of cobimetinib in combination with atezolizumab and bevacizumab in participants with gastrointestinal and other tumors. NCT02876224. <https://clinicaltrials.gov/ct2/show/NCT02876224>. Accessed October 24, 2017*

#### **4. Immunotherapy for metastatic mismatch repair-deficient colorectal cancer: game changer for small group of patients (Oct 10/17)**

DNA mismatch repair-deficient (dMMR) metastatic colorectal cancer tends to display a high level of microsatellite instability (MSI-H) and high tumour mutation burden. dMMR colorectal cancer tends to have a poor response to chemotherapy, with shorter overall survival than patients with mismatch repair-proficient (pMMR) metastatic colorectal cancer. Recent study findings have demonstrated that blocking certain checkpoints in the immune response can stimulate better responses to treatment among this subgroup. Nivolumab (Opdivo) is a programmed cell death protein 1 (PD-1) –blocking antibody that has demonstrated durable responses and disease control among patients with dMMR colorectal cancer in the Checkmate 142 study. As such, Nivolumab has joined pembrolizumab (Keytruda) in the immunotherapy arsenal for patients with previously treated dMMR colorectal cancer. Keytruda is another PD-1 targeted antibody which blocks the PD-1 receptor activating an immune response against tumour cells. In the Checkmate 142 study, 3mg/kg of nivolumab was given every 2 weeks in 74 patients with dMMR colorectal cancer who had progressed on or were resistant to at least one previous line of therapy. Similarly, another study examined previously treated patients who were given pembrolizumab at 10mg/kg every 2 weeks. One significant difference between the two studies was that 20.9% of the patients treated with Keytruda achieved a complete response, while no complete responses were reached with nivolumab.

The Checkmate 142 trial highlights the importance of MMR deficiency as a biomarker of response to immunotherapy in colorectal cancer. With nivolumab and pembrolizumab as two PD-1 inhibiting antibody therapies granted accelerated FDA approval, patients with metastatic dMMR/MSI-H colorectal cancer now have more treatment options with the possibility of longer-lasting responses. While these immunotherapies are important for this subgroup of patients, dMMR tumours only represent 5% of metastatic colorectal cancer. The next steps for the oncology community will be to expand the efficacy of immunotherapy to the 95% majority of patients with pMMR tumours.

<http://www.ascopost.com/issues/october-10-2017/immunotherapy-for-metastatic-mismatch-repair-deficient-metastatic-colorectal-cancer-game-changer-for-small-group-of-patients/>

## **SURGICAL THERAPIES**

#### **5. Hepatic Artery Infusion Pump (HAIP) Chemotherapy Program – Sunnybrook Odette Cancer Centre (Nov.10/17)**

The HAIP program is a first-in-Canada for individuals where colon or rectal cancer (colorectal cancer) has spread to the liver and cannot be removed with surgery. The program involves a coordinated, multidisciplinary team approach to care, with close collaboration across surgical oncology, medical oncology (chemotherapy), interventional radiology, nuclear medicine, and oncology nursing. The Hepatic Artery Infusion Pump (HAIP) is a small, disc-shaped device that is surgically implanted just below the skin of the patient, and is connected via a catheter to the hepatic (main) artery of the liver. About 95 percent of the chemotherapy that is directed through this pump stays in the liver, sparing the rest of the body from side effects. Patients receive HAIP-directed chemotherapy in addition to regular intravenous (IV) chemotherapy (systemic chemotherapy), to reduce the number and size of tumours.



Presently at Sunnybrook Odette Cancer Centre, HAIP is only being used in patients with colorectal cancer that has spread to the liver that cannot be removed surgically, and has not spread to anywhere else in the body. Patients who have few (1-5) and very small tumors in the lungs may be considered if the lung disease is deemed treatable prior to HAIP. If you believe you may benefit from this therapy and/or would like to learn more about the clinical trial, your medical oncologist or surgeon may fax a referral to **416-480-6179**.

<http://sunnybrook.ca/content/?page=colorectal-colon-bowel-haip-chemotherapy>

## 6. Living donor liver transplantation for unresectable colorectal cancer liver metastases (May 2017)

Approximately half of all colorectal cancer (CRC) patients develop metastases, commonly to the liver and lung. Surgical removal of liver metastases (LM) is the only treatment option, though only 20-40% of patients are candidates for surgical therapy. Surgical therapy adds a significant survival benefit, with a 5-year survival after liver resection for LM of 40-50%, compared to 10-20% 5-year survival for chemotherapy alone. Liver transplantation (LT) would remove all evident disease in cases where the colorectal metastases are isolated to the liver but considered unresectable. While CRC LM are considered a contraindication for LT at most cancer centers, a single center in Oslo, Norway demonstrated a 5-year survival of 56%. A clinical trial sponsored by the University Health network in Toronto will offer live donor liver transplantation (LDLT) to select patients with unresectable metastases limited to the liver and are non-progressing on standard chemotherapy. Patients will be screened for liver transplant suitability and must also have a healthy living donor come forward for evaluation. Patients who undergo LDLT will be followed for survival, disease-free survival and quality of life for 5 years and compared to a control group who discontinue the study before transplantation due to reasons other than cancer progression.



*Image Source:* <https://www.slideshare.net/AhmedAdel65/preoperative>

<https://clinicaltrials.gov/ct2/show/NCT02864485>

## 7. Antibiotics, bowel prep reduced site infections for rectal cancer surgery (Oct 29/17)

A study published in *JAMA Surgery* found that a combination of oral antibiotics and mechanical bowel preparation (MBP) helped to reduce the rate of surgical site infections (SSIs) among patients undergoing left colon and rectal cancer resections. Among patients who have undergone surgery for colorectal disease, SSIs are a common post-surgery complication and can seriously affect a patient's risk for developing other complications and death. The study was a review of 89 patients with left colon and rectal cancer resections between 2013 and 2016. Of the 89 patients, 49 had surgery with MBP only and 40 with both MBP and oral antibiotics. Patients who received oral antibiotics and MBP were younger than those who received MBP only. The overall rate of SSIs was lower in patients who received oral antibiotics and MBP compared with MBP alone (8% vs. 27%). Patients who received antibiotics had no deep or organ space SSIs or anastomotic leaks (leaks at the connection of the resected portions of the colon) compared with nine organ space SSIs and five anastomotic leaks in patients who received MBP only.

Further investigation is necessary to determine whether the same benefits could be seen among patients undergoing right colon resections. Until then, the researchers suggest that clinicians should consider using oral antibiotics and MBP for all patients undergoing left-sided colorectal cancer resections.

<http://www.cancernetwork.com/colorectal-cancer/antibiotics-bowel-prep-reduced-site-infections-rectal-cancer-surgery>



## 8. Mutant gene found to fuel cancer-promoting effects of inflammation (Oct 19/17)

Chronic inflammation in the body is known to be a trigger for colorectal cancer cell invasion. A human gene known as p53, commonly known as the “guardian of the genome” is understood to inhibit the formation and progression of tumours. In cases of mutation, however, p53 is linked to more cases of cancer than any other gene. Chronic inflammation is a long-term condition that is associated with a sustained response in the body’s immune system - a response induced in situations ranging from stress to food consumption. There is increasing evidence to support the correlation between chronic inflammation and the predisposition and progression of cancer, where some tissues such as the breast and the colon have been found to be more susceptible.

A recent study discovered a new mechanism by which mutant p53 is linked to chronic inflammation. Through large-scale genomic analyses, the researchers found that mutant p53 appears to amplify the impact of inflammation thereby increasing the invasive behaviour of cancer. In its mutant form, p53 seems to promote pro-inflammatory responses in the body’s immune system and increase cancer growth. The researchers suggest that it is very important to consider the genetic changes present in an individual’s cancer. While immune therapy is very helpful in targeting the cancer itself and decreasing tumour size, the study demonstrated how inflammatory mediators could orchestrate the growth in cancer cells with a p53 mutation. These findings may help scientists rethink the way cancer can be treated, helping to better define relevant cellular targets.

<https://www.sciencedaily.com/releases/2017/10/171019100346.htm>

*Homa Rahnamoun, Hanbin Lu, Sascha H. Duttke, Christopher Benner, Christopher K. Glass, Shannon M. Lauberth. Mutant p53 shapes the enhancer landscape of cancer cells in response to chronic immune signaling. Nature Communications, 2017; 8 (1) DOI: [10.1038/s41467-017-01117-y](https://doi.org/10.1038/s41467-017-01117-y)*

## 9. The role of genetic counselling in familial and sporadic cancer: considerations, challenges and collaboration (Oct 31/17)

Until recently, traditional genetic testing for inherited cancer risk has been limited to germline analysis for specific hereditary cancer syndromes such as DNA mismatch repair (MMR) gene testing for suspected Lynch syndrome. With increasing capability and accessibility of gene sequencing technology, commercial laboratories now offer various multigene analyses that can analyze many susceptible cancer genes at the same time. In addition, sequencing of the tumour genome enables greater precision of drug targets. As such, genetic counseling for inherited cancer risk is evolving rapidly as it incorporates these genetic discoveries and targeted technology.

<http://annals.org/aim/article-abstract/2660096/role-genetic-counseling-familial-sporadic-cancer-considerations-challenges-collaboration>

## 10. Serrated polyps plus conventional adenomas may mean higher risk for colorectal cancer (Oct 11/17)

It is known that most colorectal cancers develop from precursors known as polyps, the most common and best understood of which are conventional adenomas. Before they become cancerous, conventional adenomas progress to an intermediate step called high-risk adenomas. Another kind of polyp known as serrated polyps may be the precursor of up to 15% of colorectal cancers. While they may occur in up to 20% of adults over 50 years of age, less is known about these polyps compared to conventional adenomas. A research team from Dartmouth University aimed to examine the risk of developing future high-risk adenomas among individuals with serrated polyps. The team examined a subgroup of individuals with serrated polyps, hypothesizing that they may be at higher risk of developing future high-risk adenomas and thus colorectal cancer compared to people with high-risk adenomas alone. They found that people with serrated polyps were at higher risk for future serrated polyps, but not at risk for future high-risk adenomas. They observed, however, that people who had *both* serrated polyps and high-risk adenomas to begin with had a risk of developing future high-risk adenomas that was substantially higher than even people with high-risk adenomas alone. The research findings are significant as they identify a subgroup of individuals (who have both high-risk adenomas and serrated polyps) who may require more intense surveillance, such as more frequent colonoscopies. In the future, researchers aim to understand how risk factors such as age, sex, smoking, alcohol intake, exercise, and family history of colorectal cancer as well as molecular mutations found in individuals with both serrated polyps and high-risk adenomas can help identify others who may be at risk for having both serrated polyps and high-risk adenomas, since these individuals may have a different, higher risk profile for developing colorectal cancer.

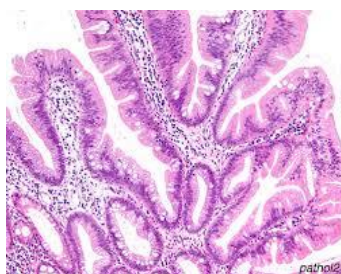


Image illustrating serrated polyp.

Source: [http://plaza.umin.ac.jp/pathol2/photo-library/index.php?now\\_position=3&first\\_category\\_id=2&second\\_category\\_id=22](http://plaza.umin.ac.jp/pathol2/photo-library/index.php?now_position=3&first_category_id=2&second_category_id=22)

## PSYCHOSOCIAL

### 11. Novel intervention may improve fear of recurrence among cancer survivors (Nov 3/17)

According to a recent study, a theory-guided intervention named ConquerFear improves the fear of cancer recurrence among survivors compared to a control intervention. Cancer survivors often suffer from fear of their cancer coming back, an issue that can seriously affect their quality of life. To date, very few trials evaluate ways to deal with this common and serious issue. In this study, survivors of breast cancer, colorectal cancer or melanoma were recruited to participate in either ConquerFear or a control intervention called Taking-it-Easy. Both interventions require therapists, but ConquerFear involves techniques focused on controlling worry among survivors and education about recurrence-prevention techniques. Taking-it-Easy involves strategies focused on helping survivors relax, including passive muscle relaxation and meditation. It was found that psychological distress and cancer-specific distress were significantly better in the ConquerFear group. The authors concluded, however, that additional research is needed in order to fine-tune the comparison between the two different interventions.

<http://www.cancertherapyadvisor.com/side-effect-management/cancer-survivor-conquerfear-novel-intervention-side-effect-recurrence/article/705336/>

### 12. Candirect research study: Learn more about a study for patients who have completed their cancer treatments and are experiencing low mood (Nov 2/17)

15% of cancer survivors are estimated to experience mood problems even one year post-treatment. The CanDirect research study aims to support cancer survivors with mood problems by providing study participants with a self-care toolkit designed to help users better manage their mood and anxiety as well as phone coaching for a maximum duration of 6 months. Participation is open to eligible adult survivors residing in Quebec and Ontario who have completed cancer treatment for a non-metastatic cancer and who are experiencing depressive symptoms. For additional information, please click on the following link :

<https://clinicaltrials.gov/show/NCT02890615>

## OTHER

### 13. New research on probiotics in the prevention and treatment of colon cancer (Sept 13/17)

An innovative new study examined how the administration of histamine-producing gut microbes to mice who lacked histamine reduced inflammation and tumour formation. Histamine is a compound released by cells in response to injury and in allergic and inflammatory reactions, causing an immune response. The study results suggest that changing the gut microbiota using probiotics could become a new preventative or therapeutic strategy for patients with inflammatory bowel conditions and colorectal cancer (CRC).

A series of experiments were conducted using mice deficient in an enzyme necessary for the production of histamine. They were administered the probiotic *Lactobacillus reuteri* 6475 which is known to contain the enzyme necessary for histamine production. The probiotic was given before and after the mice received a single dose of a colonic carcinogen and an inflammation-inducing chemical to induce tumour formation. The probiotic increased expression of the enzyme among gut bacteria and the amount of histamine in the intestines of the mice. It was observed that the mice that were given the probiotic had fewer and smaller tumours compared to untreated control mice. When researchers analyzed data from over 2000 CRC patients, results demonstrated greater survival among patients with elevated patterns of the histamine-producing enzyme and histamine receptor expression. These results suggest that histamine-generating probiotics may improve outcomes among patients with inflammatory bowel disease-associated and sporadic CRC. The role of histamine in human cancer, however, is yet to be better understood.

<https://www.sciencedaily.com/releases/2017/09/170913084437.htm>

### 14. The fascinating link between gut health and cancer treatment (Nov 3/17)

Two recent studies published in *Science* hope to shed light on why some treatments seem to work on some cancer patients and not on others. One study examined the effect of the microorganisms that live in our gut and found that a highly diverse microbiome that is full of good gut bacteria can help to maximize the effectiveness of immunotherapy treatments. Two bacteria of particular interest to researchers appear to improve efficiency of an immunotherapy drug that is used for metastatic cancer which targets a protein found on immune cells known as PD-1. Researchers collected bacterial samples from the mouth, the gut and from feces before and after therapy in cancer patients. Then they separated the study group into patients that had responded to therapy and those that did not, genetically

sequencing the bacterial samples of the patients in each group. They found that two bacteria, *faecalibacterium* and *clostridiales*, seemed to account for the difference in the number of cancer-attacking T-cells that each patient group had.

The other study found that some antibiotics can render cancer treatment less effective. The researchers examined the efficacy of PD-1 inhibitor immunotherapy among patients with kidney and lung cancer. They found that patients who had recently undergone a course of antibiotics had poorer survival rates. The antibiotics were linked to a depletion of a bacterium called *Akkermansia muciniphila*, which, when implanted into mice with microbe-free guts, increased their immune response during treatment.

These studies provide interesting insight into a potentially powerful method of improving patients' cancer treatment: examining their microbiomes to ensure that they have the necessary bacteria for treatment to be effective.

<https://qizmodo.com/the-fascinating-link-between-gut-health-and-cancer-trea-1820118334>

#### 15. It can take just one mutation for some cells to turn cancerous, one study finds (Oct 22/17)

A recent study aimed to investigate the long-standing question in cancer research: how many mutations are needed for a normal cell to become cancerous? The team of scientists from the Wellcome Trust Sanger Institute in the UK examined more than 7600 tumour samples representing 29 types of cancer in order to better understand the kind of mutations that caused them to become cancerous. They compared the kinds of genetic changes in the tumours with those in healthy tissues and between generations of individuals from different species. The study findings are the first of their kind to present precise numbers with respect to how many mutations are necessary for a cell to become cancerous. They found that about four mutations per patient on average drive liver cancers, while colorectal cancer typically require about 10 mutations. For thyroid cancer, they found that a single mutation could be all it takes to begin the cancer process. Importantly, the researchers discovered that about 50% of the mutations involved in the cancer development process occur in genes that are not yet identified as cancer genes. This research sheds light on the many genes involved in cancer that are yet to be discovered.

<https://www.sciencealert.com/number-of-mutations-needed-for-cells-to-turn-cancerous>

#### 16. Young adult colorectal cancer clinic now available at Sunnybrook (Nov.16/17)

A recent study led by University of Toronto doctors has observed a rise in colorectal cancer rates in patients under the age of 50. The study mirrors findings from the U.S., Australia and Europe. The growing colorectal cancer rates in young people come after decades of declining rates in people over 50, which have occurred most likely due to increased use of colorectal cancer screening (through population-based screening programs) which can identify and remove precancerous polyps. Patients diagnosed under the age of 50 have a unique set of needs, challenges and worries. They are unlike those diagnosed over the age of 50. **Dr. Shady Ashamalla (colorectal cancer surgical oncologist)**, and his team at the **Sunnybrook Health Sciences Centre** understand the needs of this patient population.



Dr. Ashamalla belongs to a multidisciplinary team of experts in the **Young Adult Colorectal Cancer Clinic** who will work with young colorectal cancer patients, regardless of disease stage, to create an individualized treatment plan to support each patient through their cancer journey. Their needs and concerns will be addressed as they relate to:

- Fertility concerns and issues
- Young children at home
- Dating/intimacy issues
- Challenges at work
- Concerns about hereditary cancer
- Relationships with family and friends
- Psychological stress due to any or all of the above

The team of experts consists of:

- Oncologists (medical, surgical, radiation)
- Social workers
- Psychologists
- Geneticists
- Nurse navigator

Should a patient wish to be referred to Sunnybrook, they may have their family doctor or their specialist **refer them to Sunnybrook via the e-referral form which can be accessed through the link appearing below**. Once the referral is received, the **Young Adult Colorectal Cancer Clinic** will be notified if the patient is under the age of 50. An appointment will then be issued wherein the patient will meet with various members of the team to address their specific set of concerns.

<http://sunnybrook.ca/content/?page=young-adult-colorectal-cancer-clinic>

## **NUTRITION/ HEALTHY LIFESTYLE**

### **17. Whole grains decrease colorectal cancer risk, processed meats increase the risk (Sept 7/17)**

Daily consumption of whole grains, such as brown rice or whole wheat bread, helps to reduce colorectal cancer risk according to a new report by the American Institute for Cancer Research (AICR) and the World Cancer Research Fund (WCRF). The study is the first to link whole grains as an independent factor shown to lower cancer risk. The study, "Diet, Nutrition, Physical Activity and Colorectal Cancer" also found links between regular consumption of processed meats such as hot dogs and bacon and an increased risk of colorectal cancer. The study also found that there was strong evidence to support a protective effect of physical activity against this type of cancer. The lead researchers commented that while colorectal cancer is among the most common types of cancer, the impact of diet and lifestyle have a major role in determining one's risk for the disease. Many of the ways to prevent colorectal cancer are important for the prevention of a host of diseases and promoting good health overall. The researchers examined data from over 29 million people and performed a worldwide analysis of scientific research on how diet, weight and physical activity affect colorectal cancer risk. Other factors found to increase the incidence of the disease include high consumption of red meat (over 500g cooked weight per week); being overweight or obese; and consuming two or more alcoholic drinks (30g of alcohol) per day. The study concluded that eating approximately 3 servings (90g) of whole grains per day reduces the risk of colorectal cancer by 17%, adding to previous evidence that foods containing fibre decrease the risk of this type of cancer.

Overall, the results point to the value of a plant-centered diet that is rich in whole foods. By replacing refined grains with whole grains and eating mostly plant foods such as fruits, vegetables and beans, your diet will be rich in fibre and compounds that are protective against cancer and beneficial for your overall health.

<https://www.sciencedaily.com/releases/2017/09/170907093623.htm>

### **18. High fiber intake tied to improved colon cancer survival (Nov 3/17)**

The results from an analysis of two prospective studies indicate that high fiber intake is linked to improved survival among patients with colorectal cancer (CRC), even among those who begin to increase their fiber intake after their diagnosis. The study included more than 1500 healthcare professionals who had been diagnosed with CRC. Each 5g increase in fiber per day was associated with a 22% reduction in cancer-specific mortality and a 16% reduction in overall mortality. The greatest effect was linked to whole-grain foods and vegetable fiber. Interestingly, no association with seen with daily fruit fiber intake. The maximum protective effect was seen among patients who consumed about 24g of fiber per day. Researchers suggest that the mechanism by which fiber is protective against CRC could be related to some of the effects that fiber has on insulin pathways, providing a potential target for treatment in the future. Fiber may also form a kind of probiotic substrate for gut bacteria to release anti-inflammatory compounds and metabolites. While many past studies have focused on how dietary fiber aids in the prevention of CRC, none so far have examined the impact of fiber intake on survival in patients who already have the disease. This study, however, does have limitations in its methodology (relying on personal diet logs, which are not the most reliable source of data) and in that it does identify whether it is the fiber intake that is causing the protective effect, or other protective phytochemicals in these foods. Nonetheless, the researchers suggest that the best approach would be to ensure that individuals consume a variety of grains and vegetables rather than relying on a fiber supplement.

[https://www.medscape.com/viewarticle/888006#vp\\_2](https://www.medscape.com/viewarticle/888006#vp_2)

### **19. Can the Mediterranean diet help protect against colorectal cancer? (Nov 2/17)**

Eating a plant-based diet has several benefits to our health: fewer calories, more water, more fiber and a host of protective plant nutrients. The Mediterranean diet is full of cancer-fighting phytochemicals and healthy fats that help to combat the disease as well as other health conditions such as obesity. Furthermore, it is low in red meat, alcohol and processed foods such as cold cuts and smoked meats like bacon. More than 20% of Americans 20 and older are overweight, and more than 30% are obese. According to the National Cancer Institute, obese individuals have a 30% greater risk of developing colorectal cancer than individuals with a normal weight. A study focusing on patients with early stage colorectal cancer found that when a healthy body weight, regular physical activity and a primarily plant-based diet were combined, the risk of death from the disease was reduced by 42%. Beyond the plant-based Mediterranean diet, there is epidemiological data to show that other plant-based diets, such as that found in countries such as India, coincides with a lower incidence of obesity as well as a lower incidence of colorectal cancer compared to Western countries which tend to consume greater quantities of red and processed meats.



Making the transition to a healthier diet is a gradual process. Instead of cutting out meat entirely, perhaps reducing the number of servings of red meat per week is a good start. Eating more legumes such as beans, lentils and chickpeas is a great way to get your protein needs as well as a variety of cancer-fighting phytochemicals and antioxidants. When it comes to being serious about reducing your cancer risk, none of the recommendations will work if taken isolation – eating less meat, drinking less alcohol, eating more vegetables and whole grains, and exercising more are lifestyle factors that are interconnected and work best when done together.



<https://health.usnews.com/health-care/patient-advice/articles/2017-11-02/can-the-mediterranean-diet-help-protect-against-colorectal-cancer>

**20. The anti-cancer carbs you need to know about (Oct 27/17)**

While refined carbohydrates such as white flour and white sugar provide empty calories lacking in nutritional value, there is a type of “good” carbohydrate that may play an important medicinal role in repairing damage within our gut. These carbohydrates are known as “resistant starches” and pass through our stomachs undigested. Some examples of resistant starches include bananas that are still slightly green, cooked and cooled potatoes, whole grains, beans, chickpeas and lentils. These starches arrive in the large intestine and become food for the bacteria that thrive there. In our intestine, the gut flora outnumber the body’s cells 10 to 1, including hundreds of different species with the number and type of bacteria having a significant impact on our health. The bacterial digestive process releases a short-chain fatty acid (butyrate) that serves as the main source of energy for the cells of the colon wall. Butyrate also functions to reduce inflammation and stimulate cell death of any intestinal cells that have experienced DNA damage, thereby preventing the onset of diseases like colorectal cancer. The short-chain fatty acids that are not used by the intestinal cells travel to the bloodstream, where they circulate to the rest of the body and may lead to various beneficial health effects. Furthermore, the consumption of complex starches helps to reverse insulin resistance in cases of metabolic syndrome. Some studies have found that consuming 15-30 grams of resistant starches for 4 weeks elicited a 33-50% improvement in the body’s insulin sensitivity.

<http://www.longevitylive.com/nutrition-body/healthy-eating/anti-cancer-carbs/>

**21. A Phase III study of the impact of a physical activity program on disease-free survival in patients with high risk stage II or stage III colon cancer: a randomized controlled trial (CHALLENGE) (Nov.15/17)**

The purpose of this study is to compare the disease-free survival of patients involved in a physical activity program (designed to increase physical activity participation) who also receive general health education materials (about diet and physical activity) to patients who receive the general health education materials only. This study is being done because, as of yet, there is no conclusive evidence that physical activity will decrease the likelihood of colon cancer recurrence. This study will also obtain important information about the impact of physical activity on patients’ physical functioning, body composition, quality of life, fatigue, mood, cytokines and the insulin pathway, and their influence on prognosis, as well as cost-effectiveness.

**Eligibility:** Medically fit colon cancer patients (high risk stage II and stage III) who have completed adjuvant chemotherapy within the past 60-180 days. Current physical activity levels must not meet the recommended guidelines ( $\geq 150$  minutes of moderate-to-vigorous or  $\geq 75$  minutes of vigorous exercise/week). Following registration, and prior to randomization, patients must successfully complete at least two stages of a submaximal exercise test to ensure they are able to safely exercise at a moderate to vigorous intensity.

**Participation:** Limited to invited centres.

For more information, visit the link below:

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