August 2022

LIVING WITH CANCER

COLORECTAL CANCER
RESEARCH & PRACTICE UPDATES

Colorectal Cancer Canada curates monthly Research & Practice Updates to inform patients and their loved ones of new innovations in colorectal cancer care. The following updates extend from August 1st 2022 to August 31th, 2022 inclusive and are intended for informational purposes only

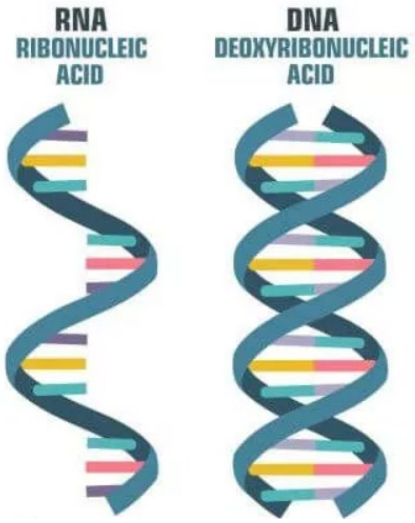
AUGUST 2022 PREVIEW

New blood test could reshape early CRC screening

August 2022

A new study published in *Gastroenterology* demonstrated how a simple blood test that scans for the presence of small pieces of RNA (microRNAs) could become a new way to screen for early age onset colorectal cancer (EAOCRC).

RNA: stands for ribonucleic acid. RNA is a type of molecule present in our cells that is structurally similar to DNA but instead of being double-stranded, it is single-stranded. RNAs are involved in carrying out different activities in the cell, including regulating the expression of genes.



In the study, the researchers identified four microRNAs that together, make up a **biomarker** that can be used to detect and diagnose the presence of CRC through a blood test in a younger population with high sensitivity and specificity. The researchers developed a laboratory test that was able to detect these four microRNAs which occur at higher levels in blood samples from EAOCRC patients compared to non-EAOCRC patients.

Biomarker: a measurable substance whose presence is indicative of a condition or disease, in this case, cancer.

To arrive at these four microRNAs, the researchers analyzed a dataset of microRNA expression from 1061 individuals to see which microRNAs were expressed at higher levels in colorectal cancer patients. They identified four microRNAs with higher expression in EAOCRC patients, and an assay was created and validated using blood samples from different EAOCRC patient populations and controls from different countries (Japan, Spain). Furthermore, the researchers found that the expression levels of these four microRNAs significantly decreased after surgical removal of the colorectal tumour - a strong suggestion that the microRNAs originate from the tumour.

The study authors commented that the test could potentially be used as a routine part of annual healthcare, or for people in high-risk families every 6 months. If the test is positive for these biomarkers, the person would undergo a colonoscopy to confirm the results. The findings are exciting as this test could address an important unmet need for a relatively inexpensive (compared to colonoscopy) and non-invasive screening method for younger populations. If approved by the FDA, the test should cost less than $100 in the US.

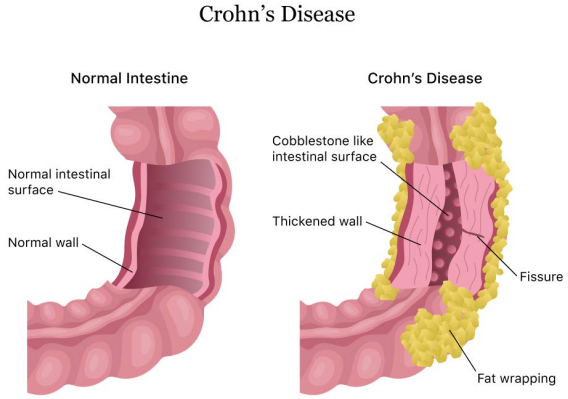
Next steps include conducting a study in a larger population to gain a better understand the performance capabilities of the test.

READ THE FULL ARTICLE

Understanding Crohn's disease: a risk factor for colorectal cancer

August 2022

Crohn's disease is a chronic (long-term) inflammatory disease that can affect any part of the gastrointestinal tract, including the mouth, throat, esophagus, stomach, small intestine, large intestine, rectum, and anus, though it usually targets the end of the small intestine or the colon (large intestine). Though experts are not certain of the exact cause of Crohn's disease, research has suggested that it could be related to the balance of good and bad bacteria in the gut microbiome[1]. Crohn's disease is associated with a reduction in microbial diversity (fewer distinct microbial types) which has been implicated in the development of the disease.



[1] https://gut.bmj.com/content/66/5/813

How common is Crohn's disease?

About 135,000 Canadians live with Crohn's disease[2], which affects people of all ages. Symptoms usually begin in childhood or early adulthood. The main symptoms are:

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Connection to colorectal cancer

Crohn's disease is an **autoimmune process** (a condition in which the body's immune system attacks and destroys body tissue that it mistakes for foreign matter) associated with an increased risk of developing colorectal cancer. The long-term injury to the gastrointestinal tract causes the inflamed areas to be in a constant state of repair and inflammation. This appears to be an important factor in **carcinogenesis** (the development of cancer) as it creates a microenvironment that is suitable for the initiation and development of tumour cells – the constant renewal of damaged cells means that an error (mutation) in the replaced cells can become more likely to occur, resulting in cancer.

Management of Crohn's disease

While there is no cure for Crohn's disease, the chronic inflammation can be controlled with medication. Furthermore, surveillance for individuals living with the disease includes regular screening exams. **If you have had Crohn's disease for 8 years or more, a colonoscopy is recommended every 1-2 years.**

Be sure to seek medical attention if you notice any gastrointestinal symptoms as soon as possible. With inflammatory bowel disease, the earlier you receive a diagnosis, the sooner symptoms can be controlled, inflammation can be minimized, and colorectal cancer risk is reduced.

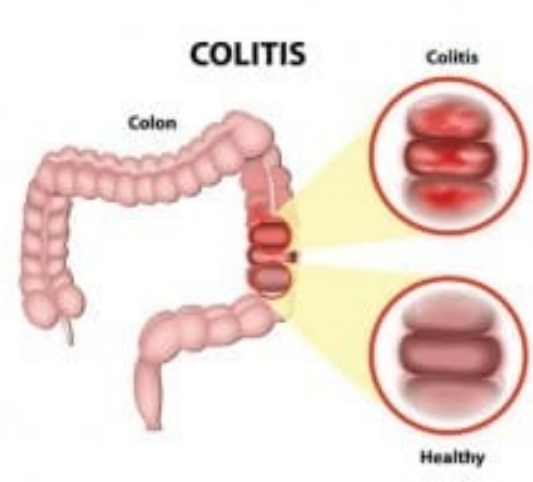
Understanding ulcerative colitis: a risk factor for colorectal cancer

August 2022

Ulcerative colitis is a chronic inflammatory bowel disease that affects the lining of the large intestine (colon and rectum). It causes inflammation and ulcers (sores) that result in the following signs and symptoms:

- Diarrhea, often with blood or pus
- Abdominal pain and cramping
- Rectal pain
- Rectal bleeding (passing small amounts of blood in the stool)
- Weight loss
- Fatigue
- Fever (in severe cases)

[2] https://academic.oup.com/jcag/article/2/Supplement_1/S6/5145703



Ulcerative colitis develops when the immune system mistakenly attacks the cells of the lining of the colon as if they were foreign invaders, causing damage over time. While the exact cause is not known, potential causes include:

- Imbalances in the populations of good and bad bacteria in the gut microbiome
- Specific genetic inherited factors have been implicated in the development of the disease, where studies have shown that 1 in 4 individuals with ulcerative colitis have a family history of the condition
- Environmental factors such as medication use, pollution, and certain types of diets have been associated with the incidence of the disease. It appears to be more common in urban areas of northern parts of western Europe and America[3]

Connection to colorectal cancer risk

Since ulcerative colitis is a chronic inflammatory condition that damages the lining of the colon over time, the inflammation and constant cell repair can result in a mutation that causes cancer. Cases of ulcerative colitis that are more severe or long-term are associated with a higher risk of developing colorectal cancer.

Reducing colorectal cancer risk

If you have been diagnosed with ulcerative colitis, you should begin getting a colonoscopy every 1-2 years beginning at 8-10 years after **onset of symptoms (not date of diagnosis).** Furthermore, it is important to keep inflammation under control with medication, which range from anti-inflammatory drugs to drugs that suppress the activity of your immune system. The medication that you take will depend on the severity of the colitis.

If an individual undergoes two colonoscopies in a row with no evidence of damage, inflammation, polyps or abnormal cells in the colon, there are considered to be in **remission**. With new types of

[3] https://www.nhs.uk/conditions/ulcerative-colitis/causes/

medication that are available today, remission is a possibility for some patients. For patients who do not respond to available medications, surgical removal of a part or all of the colon is an option. In the instance that the entire colon is removed, the patient would manage their stool through an internal or external storage pouch.

Colorectal cancer treatment and ulcerative colitis

Certain treatments for colorectal cancer, such as chemotherapy and immunotherapy, can cause irritation to mucosa including the intestinal mucosa (inner lining), resulting in digestive problems. If you are beginning treatment for colorectal cancer, it is important to notify your doctor of any chronic inflammatory bowel conditions so that they are under control before beginning treatment. This way, side effects from treatment can be minimized.

Immunotherapy-induced colitis

For patients undergoing treatment for colorectal cancer with immunotherapy agents, colitis is one of the immune-related side effects. About 45% of patients will develop colitis from immunotherapy treatment[4]. Best management of immunotherapy-induced colitis includes early recognition and timely use of immune-suppressing drugs to control symptoms.

Wholegrains, dietary fibre and colorectal cancer risk

August 2022

Based on the findings from the World Cancer Research Fund International, there is strong evidence that wholegrains and foods containing dietary fibre decrease the risk of colorectal cancer[5].

What is a wholegrain?

A wholegrain is a grain from a cereal plant such as rice, wheat, barley, or oats that has not had anything removed from it.

[4] https://www.mdanderson.org/cancerwise/does-ulcerative-colitis-affect-your-colorectal-cancer-risk.h00-159462423.html#:~:text=The%20more%20extensive%20your%20colitis,greater%20risk%20for%20colorectal%20cancer.

[5] https://www.wcrf.org/diet-activity-and-cancer/risk-factors/wholegrains-vegetables-fruit-and-cancer-risk/

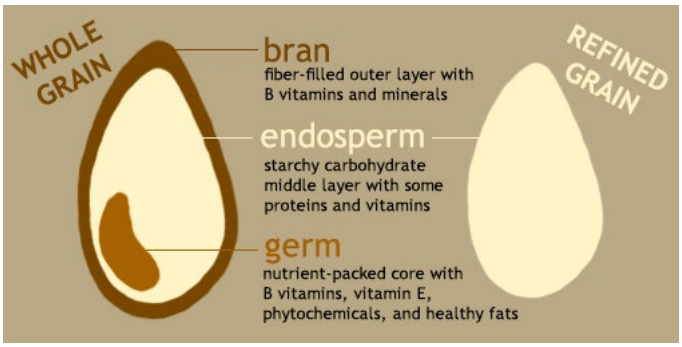


Image source : https://www.hsph.harvard.edu/nutritionsource/what-should-you-eat/whole-grains/

In addition to the starches found in the **endosperm (see diagram above)**, wholegrains contain B vitamins and other micronutrients that are mostly concentrated in the nutrient-rich **germ** and fibre-rich **bran.** Many of the nutrients and compounds found in the germ and bran of wholegrains have been shown to have anti-cancer properties, including organic compounds known as **phenolic acids.** These compounds have been shown in studies to stimulate antioxidant activities, which help to track down free radicals and neutralize their harmful effects which include making cells more susceptible to beomcing cancerous. Furthermore, wholegrains may help protect against colorectal cancer by binding to carcinogens and regulating the body's glycemic response[6].

***Glycemic index*:** a system that ranks foods from 0-100 based on how quickly and and how high thse foods cause changes to blood sugar (glucose) levels. Foods that are low on the glycemic index (GI) release glucose more slowly and gradually, while foods high on the GI release glucose rapidly.

Results from the European Prospective Investigation into Cancer and Nutrition (EPIC) Italy study investigated the associations between a carbohydrate-rich diet, resulting in high blood glucose and insulin, and the development of colorectal cancer. Among 47,749 adults recruited for the study, colorectal cancer was significantly associated with dietary glycemic index and high glycemic index carbohydrates[7].

The most common mechanism of action that connects chronically high blood glucose to cancer development is through the dysregulation of the hormone insulin[8,9]:

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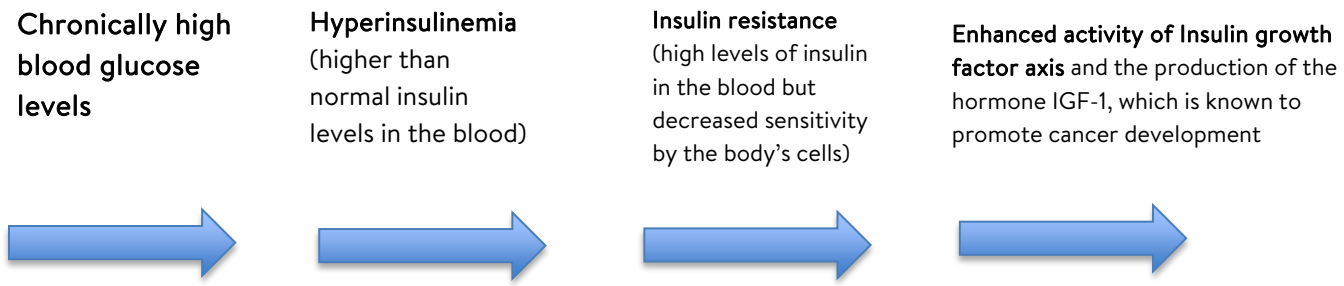
[6] https://www.wcrf.org/diet-activity-and-cancer/risk-factors/wholegrains-vegetables-fruit-and-cancer-risk/

[7] https://pubmed.ncbi.nlm.nih.gov/25403784/#:~:text=After%20stratification%20for%20waist%2Dto,increased%20risk%20of%20colorectal%20cancer.

[8] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5119990/#:~:text=IGF%E2%80%901%20is%20known%20to,%2C%20colorectal%2C%20and%20prostate%20cancer.

[9] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3308317/#:~:text=Insulin%20resistance%20is%20highly%20correlated,2%20(35%2C36).



The 2018 World Cancer Research Fund/American Institute for Cancer Research recommendations[10]:

Recommendation	Details	Goals
Eat a diet rich in whole grains, vegetables, fruits, and beans	Make whole grains, vegetables, fruits, and pulses (legumes) such as beans and lentils a major part of your usual daily diet	• Include in more meals foods containing whole grains, non-starchy vegetables, fruits, and pulses (legumes) such as beans and lentils • Eat a diet high in all types of plant foods including at least five portions or servings (at least 400 g or 15 oz in total) of a variety of non-starchy vegetables and fruits every day • If you eat starchy roots and tubers as staple foods, eat non-starchy vegetables, fruit, and pulses (legumes) regularly too if possible

What about dietary fibre?

Dietary fibre includes any indigestible parts of plant foods that our bodies cannot absorb. This is in contrast to other dietary nutrients such as carbohydrates, fats, and proteins which our bodies are designed to break down and absorb. If dietary fibre passes right through our digestive tract, why do we need it?

- It helps to add bulk to our stool, making it easier to pass and decreases the chances of constipation (difficulty in having a bowel movement)
- It helps to keep our gut healthy – not only does fibre help to "sweep out" the intestine and reduce intestinal transit time (how long food times to pass through the intestine), therefore minimizing contact between potentially harmful toxins and our digestive tract, but it also acts as a food source for the bacteria that live in our intestines, leading to the

[10] https://epi.grants.cancer.gov/wcrf-aicr-score/

production of protective by-products known as **short-chain fatty acids** that keep our intestinal cells healthy and inhibit the proliferation of colon cancer cells

- High-fibre diets (30g or more of fibre per day) are also associated with the reduction of insulin resistance, a known risk factor for colorectal cancer

The 2018 World Cancer Research Fund/American Institute for Cancer Research recommendations[11]:

Recommendation	Details	Goals
Eat a diet rich in whole grains, vegetables, fruits, and beans	Make whole grains, vegetables, fruits, and pulses (legumes) such as beans and lentils a major part of your usual daily diet	• Consume a diet that provides at least 30 g/day of fiber from food sources

Sample foods that would make up approximately 30g of fibre for one day's recommended intake:

½ cup (86g) of cooked black beans = 8g of fibre
½ an avocado = 7g of fibre
½ cup whole wheat pasta = 7g of fibre (compared to only 2g of fibre in white pasta)
1 pear = 6g of fibre
½ cup cooked oats = 4g of fibre

Source: https://www.eatingwell.com/article/2057241/top-high-fiber-foods-you-need-in-your-life/

[11] https://epi.grants.cancer.gov/wcrf-aicr-score/