Study finds colon cancer driven by hereditary gene mutations in 1 in 6 patients

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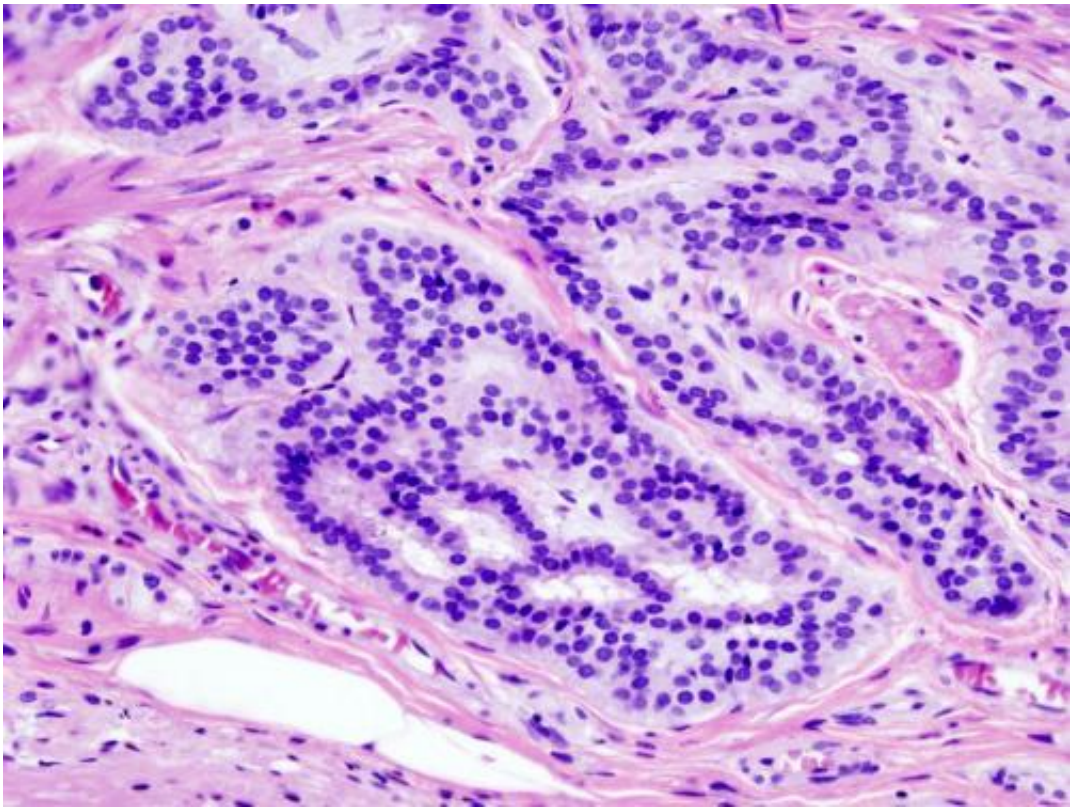

Cancer—Histopathologic image of colonic carcinoid. Credit: Wikipedia/CC BY-SA 3.0

A new Mayo Clinic study bolsters evidence that colorectal cancer is often imprinted in family genes and passed on from one generation to the next.

In the study, published in *Clinical Gastroenterology and Hepatology,* researchers within the Mayo Clinic Center for Individualized Medicine found 1 in 6 patients with colorectal cancer had an inherited cancer-related gene mutation, which likely predisposed them to the disease. In addition, the researchers discovered that 60% of these cases would not have been detected if relying on a standard guideline-based approach.

"We found that 15.5% of the 361 patients with colorectal cancer had an inherited mutation in a gene associated with the development of their cancer," says Niloy Jewel Samadder, M.D., a Mayo Clinic gastroenterologist and hepatologist, who is the study's senior author. "We also found that over 1 in 10 of these patients had modifications in their medical or surgical therapy based on the genetic findings."

The patients were tested with a sequencing panel that included more than 80 cancer-causing or predisposing genes. In comparison, standard panels for colorectal cancer only include 20 or fewer genes.

The patients with colorectal cancer were part of a larger cohort of 3,000 patients involved in the two-year Interrogating Cancer Etiology Using Proactive Genetic Testing (INTERCEPT) study, and were newly diagnosed with various cancers at Mayo Clinic Cancer Center locations in Arizona, Florida and Minnesota.

"Through the INTERCEPT study, the Center for Individualized Medicine has addressed a question of relevance to all cancer patients," says Aleksandar Sekulic, M.D., Ph.D., associate director of the Center. "The findings published by Dr. Samadder and colleagues shed a new light on the role our genes play in the development of colon cancer."

The colorectal cancer study emphasizes that uncovering hidden inherited genetic mutations using a universal testing approach and broader gene panels could lead to opportunities for cancer management in families

and targeted cancer therapies that can save lives.

Colorectal cancer is the second leading cause of cancer death in the U.S., according to the American Cancer Society. Unlike many other cancers that are difficult to uncover in early stages, colon cancer begins as a polyp, which can be detected in a colonoscopy screening and removed to prevent cancer from developing and spreading. The American Cancer Society recommends people at average risk of colorectal cancer start regular screenings at age 45.

"Colorectal cancer screening is an important modality to prevent this deadly disease and many resultant unnecessary deaths," Dr. Samadder says. "Screening can be performed with a colonoscopy, stool tests or even specialized CT scans."

In the study, Dr. Samadder and his team examined gene variants (mutations) with which the patient was born and that predisposed them to developing cancer. Mutations are abnormal changes in the DNA of a gene. A gene mutation can affect the cell in many ways, including interfering with proteins or causing a gene to be activated.

Although many mutations that cause colorectal cancer happen by chance in a single cell—including from environmental factors, diet, smoking and alcohol use—the study confirms many are inherited mutations that set off a cycle of events that can lead to cancer.

"Though the most common mutations were found in genes typically associated with colorectal cancer, we found that a substantial number of mutations were present in genes typically associated with breast and ovarian cancer," Dr. Samadder explains. "This may lead to novel targeted therapies based on the cancer's unique genetic basis. For example, where a breast cancer drug can be used in a patient with colon cancer."

Equally important to the discovery of a patient's inherited cancer mutation is the potential for patients to share the heritable cause of their disease with their blood relatives, allowing family members to pursue care for earlier disease detection and cancer management.

"The power of genetics is that we can foresee the cancer that will develop in other family members," Dr. Samadder says. "This can allow us to target cancer screening to those high-risk individuals and hopefully prevent cancer altogether in the next generation of the family."

In the study, all blood-related family members of patients found to have a genetic mutation were offered free genetic testing. Overall, just 16% of these family members underwent testing, which may suggest there are nonfinancial barriers to genetic testing.

Dr. Samadder says the next steps will be to incorporate the study findings into the care of all patients with cancer at Mayo Clinic.

"Steps are being taken to ensure all patients are offered genomic sequencing to better understand the genes that led to the development of their cancer, and how to precisely target treatment and improve survival," Dr. Samadder says.

Genetic sequencing, deletion and duplication analysis, and variant interpretation were performed at Invitae Corp. in San Francisco. Dr. Nussbaum is the chief medical officer of Invitae. Support for this project was provided by the Mayo Transform the Practice Grant, Mayo Clinic Center for Individualized Medicine, Desert Mountain Members' CARE Foundation, and David and Twila Woods Foundation.

Provided by Mayo Clinic