

Types of bacteria vary widely in tumors of people with early vs. late-onset colorectal cancer

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Researchers at Georgetown University's Lombardi Comprehensive Cancer Center studied the microbiome of people with colorectal cancer and found the make-up of the bacteria, fungi and viruses in a person's tumor varied significantly depending on whether they were diagnosed with early-onset disease (age 45 or younger) or late-onset disease (age 65 or older). These results may help answer the riddle of why more young people are developing colorectal cancer, particularly those who have no known identifiable risk factors for the disease.

The findings will be presented at the American Society of Clinical Oncology 2023 annual meeting in Chicago in June.

Colorectal cancer incidence rates have been declining for several decades in people over 55, in part because of the increased use of screening for the disease, particularly with colonoscopy which can find and remove polyps before they become cancerous. But nearly double the number of young adults under 55 are being diagnosed with colorectal cancer compared to a decade ago, with an increase in the incidence rate going from 11% in 1995 to 20% in 2020.

"Younger people with colorectal cancer have more biologically aggressive cancers and whatever survival benefit they have by being younger is outweighed by the more aggressive tumor biology. We also know, that for the most part, genetics doesn't explain the recent rise in young-onset disease," said Benjamin Adam Weinberg, MD, an associate professor of medicine at Georgetown Lombardi. "But we have trillions of bacteria residing in our body, including in our gut, some of which are



implicated in the development of colorectal cancer, hence we think the microbiome may be an important factor in the development of the disease as it is involved in the interplay between a person's genetics, environment, diet and immune system."

Scientists have known for a while that certain microbes can disturb the lining of the colon and promote tissue inflammation. This can result in mutations to the DNA of cells in the colon and lead to cancer. Researchers also know that one type of bacteria, *Fusobacterium nucleatum* (*F. nuc*), can promote cancerous growth by suppressing immune responses in the colon.

To better understand the role of the microbiome and how its influence varies depending on a person's age of onset of colorectal cancer, Weinberg and colleagues looked at the DNA and the microbiome of tumors from 36 patients with colorectal cancer who were diagnosed before age 45 as well as specimens from 27 people who were diagnosed after age 65.

Overall, the investigators detected 917 unique bacterial and fungal species in the tumors. One of the most common bacteria found was F. nuc, which appeared equally in about 30% of both early and late-onset tumors. Differences were seen in Cladosporium sp., which was found more commonly in early-onset disease, whereas Pseudomonas luteola, Ralstonia sp., and Moraxella osloensis were seen more commonly in late onset disease. In terms of composition, Clostridium perfringens, Escherichia coli, Leptotrichia hofstadii, Mycosphaerella sp., Neodevriesia modesta, Penicillium sp., and Leptosphaeria sp., each made up 11% of the microbiome in people with late-onset disease.

Weinberg says with the current data, and with future efforts to collect more samples, they anticipate expanding their research efforts to



continue exploring the relationship between the microbiome and other factors that contribute to colorectal <u>cancer</u>.

"Because we have tumor <u>genetic data</u> and diet questionnaire results from many of our patients, we hope to explore more relationships and other aspects of how the microbiome impacts <u>colorectal cancer</u> progression in the future," said Weinberg. "We are also interested in the circulating <u>microbiome</u>, such as bacteria that could be picked up in a <u>blood sample</u>, and how this correlates with bacteria in the gut and in the <u>tumor</u>."

More information: Comprehensive study of the intratumoral microbiome in early- vs. late-onset colorectal cancer: Final analysis of COSMO CRC., American Society of Clinical Oncology 2023.

Provided by Georgetown University Medical Center

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