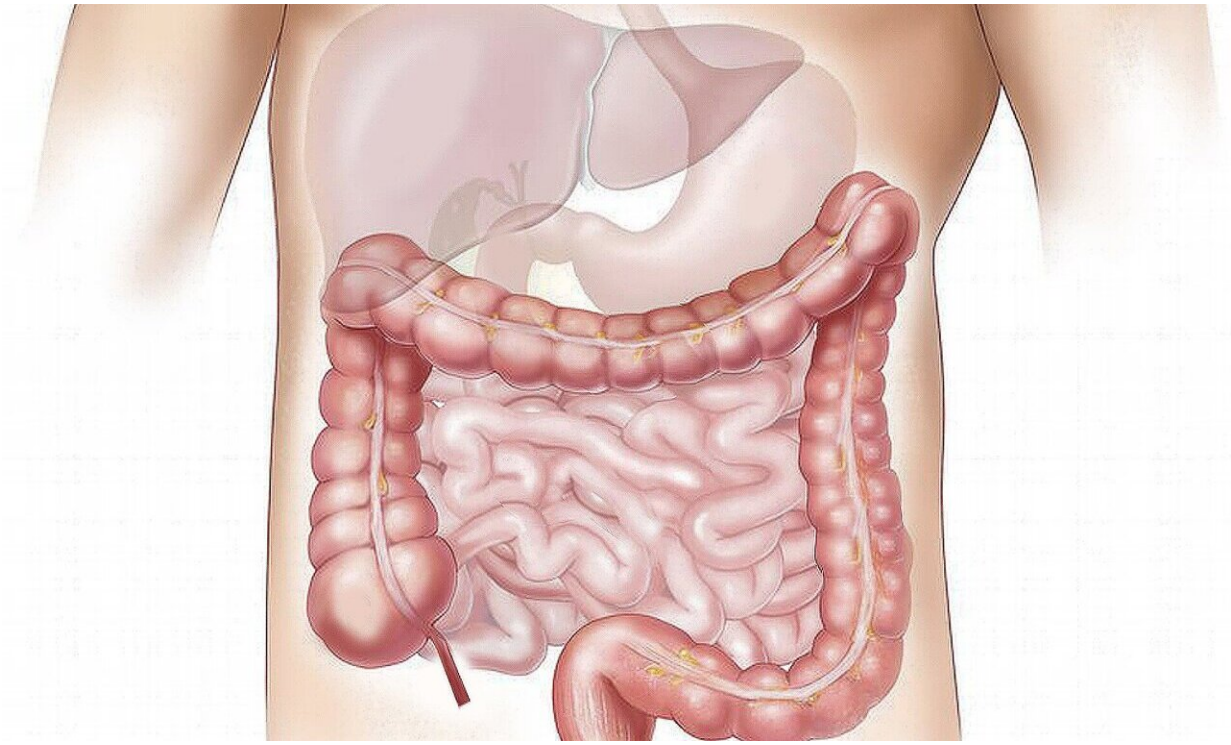
Microbial signature of colorectal cancer-associated mutations identified

April 4 2024



Credit: CC0 Public Domain

For about 40% of people diagnosed with colorectal cancer (CRC), the tumor carries a mutation in a gene called KRAS. Many of those mutations have been linked to shorter survival and more aggressive forms of disease. The onset and growth of CRC tumors has also been associated with imbalances in the gut microbiome, but the interplay

between these two characteristics—gut dysbiosis and KRAS mutations—remains poorly understood.

In a study, published in *Microbiology Spectrum*, researchers in China have identified microbiota signatures associated with KRAS mutations in people diagnosed with colorectal cancer. The findings suggest that gut microbes may serve as a kind of non-invasive biomarker for identifying subtypes of CRC and may inform personalized approaches to therapy, said Zigui Huang, a medical student at Guangxi Medical University Cancer Hospital who worked on the study.

The study was led by oncologist Weizhong Tang, M.D., at the same hospital, whose research focuses on harnessing molecular knowledge of CRC for better diagnosis and treatment of the disease.

"Our new work contributes to the growing body of evidence highlighting the significance of microbiota-driven mechanisms in cancer pathogenesis," Tang said.

Nearly 2 million people are diagnosed with colorectal cancer each year worldwide, and more than 900,000 die from the disease, according to the World Health Organization. Globally, it's the third most common cancer and the second leading cause of cancer-related deaths. Previous studies have connected gut bacterial imbalances to the formation and spread of CRC, suggesting that a closer study of the gut microbial populations in the context of CRC could yield new insights about diagnosis and treatment.

"Understanding the specific associations between different types of KRAS mutations and CRC is vital for several reasons," Huang said. Those include elucidating the molecular mechanisms that drive the development of CRC and identifying biomarkers for diagnosis and disease progression.

For the new study, the researchers analyzed stool samples from 94 individuals with CRC using 16s rRNA sequencing. Out of the 94, 24 had mutations in the KRAS gene and the rest had the "wild-type," or non-mutated, form of the gene.

Sequencing revealed 26 different types of gut microbiota that were present in one group but not the other. The genera Fusobacterium, Clostridium and Shewanella were all abundant in the mutant group. Fusobacterium is a Gram-negative microbe found in the GI tract and the oral cavity, and previous studies have connected it to the development of CRC. All three of these, the researchers noted, should be considered as non-invasive biomarkers to determine a patient's KRAS status.

Bifidobacterium and Akkermansia were abundant in the samples from patients without a KRAS mutation. Bifidobacterium is a probiotic, and Akkermansia has shown some probiotic activities in previous studies, including suppression of pro-inflammatory factors in the colon. Based on this finding, the researchers speculate that the presence of these bacteria may reduce a person's chance of developing a KRAS mutation and, to an extent, slow the progression of CRC.

In the same paper, the researchers introduced a machine learning model that could use this information to guide personalized treatment recommendations based on microbiota signatures. However, Huang said, the model requires data from a larger cohort to improve its efficacy. The group plans to conduct larger studies to validate the findings and better understand the significance of the gut microbiota they've identified, in hopes of improving treatment for CRC patients.

"This study aligns with our broader research focus on understanding the intricate interplay between genetic mutations, the tumor microenvironment and gut microbiota in colorectal cancer," Tang said.

More information: journals.asm.org/doi/10.1128/spectrum.02720-23