

Colorectal cancers in black patients have molecular differences, Cleveland research team discovers



A team of researchers at Case Western Reserve University has identified new gene mutations that are unique to colon cancers diagnosed in black American patients. (Associated Press)

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CLEVELAND, Ohio – Researchers at the Case Comprehensive Cancer Center at Case Western Reserve University have identified how **colorectal cancer** on the molecular level is different in black Americans than in other racial and ethnic groups.

The discovery could one day help identify who is at risk for the disease and need to be screened earlier and more frequently. Even more long term, the discovery could one day lead to new drug development.

The findings, published Monday in the journal **Proceedings of the National Academy of Sciences**, come from a study that is part of the five-year GI SPORE (Specialized Program of Research and Excellence) program, created with **an \$11.3 million grant from the National Institutes of Health**. The purpose of GI-SPORE is to conduct studies on the prevention and cure of gastrointestinal cancers, a group of cancers that include colon cancer. The program in Cleveland is one of only five such programs in the country.

Funds from that program, along with gifts from several foundations, paid for the research.

Trying to understand colon cancer in black Americans has been one of the key projects of the GI SPORE program, said **Dr. Sanford Markowitz**, principal investigator of the GI-SPORE program and one of the study's authors.

Black Americans have the highest incidence and death rates of colon cancer than any other group. The most recent federal statistics put age-adjusted incidence at 46.8 cases for every 100,000 black Americans, compared with 38.1 cases for every 100,000 white Americans.



Dr. Sanford Markowitz
CWRU

"I think the presumption was that the difference in cancers in minority communities could be explained by differences in health care [access]," Markowitz, professor of cancer genetics at CWRU School of Medicine and a medical oncologist at UH Seidman Cancer Center, told The Plain Dealer. "Although that's certainly a reality, it would be cavalier to think that it explained everything."

"We were the outliers," Markowitz said of the study's focus, which used gene sequencing and computational analysis to look at colorectal cancer samples from patients who had been treated at University Hospitals Case Medical Center. "Other folks didn't think there was something to be found."

Led by Markowitz and Dr. Joseph Willis, both known for being part of a team that sequenced the colon cancer genome, the research team compared 103 colorectal cancer samples from black patients with 129 colorectal cancer samples from white patients. Their starting point was more than 1,500 tumor tissue samples, from which they identified what would be studied further.

What they found:

- Twenty new gene mutations in the colorectal cancers of black Americans that never before had been seen in patients with this disease. The researchers confirmed that 15 of the mutations affected primarily black patients; just over 40 percent of colorectal cancers in black patients carried mutations in one or more these genes. In addition, they found that the mutations were more than three times more common in black patients than in white patients.
- Researchers focused on mutations in two of the 15 genes, EPHA6 and FLCN. The mutations, which show up exclusively in black patients, are known to raise the risk of certain cancers. In this study, the researchers became the first to link the EPHA6 gene mutation with colorectal cancer.

"This study gave us our answer," Willis, associate professor of pathology at the CWRU School of Medicine and director of tissue management at Case Comprehensive, said in a statement. "Colon cancer in African-American patients is a different disease molecularly."



Dr. Joseph Willis
CWRU

With that knowledge, further research is now needed to get at the answers to more questions, Markowitz said. Why are these mutations – which he describes as "genetic accidents" that happen during the course of a person's life – happening in black people and not in white people? Are the mutations associated with cancers that are more lethal? And where are those differences coming from? The environment? Lifestyle? And can those mutations be changed or even prevented?

The next step will be to collaborate with other medical centers across the country. Markowitz said he hopes those larger studies, needed to confirm the findings here in Cleveland, will begin in the next 12 months.

The study findings are the second in what Markowitz said he hopes will be a series of "high-impact observations," with the first being a study published last April that showed the **benefits of aspirin to reduce the risk of colorectal cancer in certain people**.

"We're beginning to see the fruits of our efforts," he said. "We took a very big and very expensive gamble. So I think we are all breathing a bit of a sigh of relief that our hunch has proved correct."