

# Researchers find gene mutations lead to more aggressive colon cancer in African Americans

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Case Comprehensive Cancer Center researchers, a research collaboration which includes University Hospitals Seidman Cancer Center and Case Western Reserve University, who last year identified new gene mutations unique to colon cancers in African Americans, have found that tumors with these mutations are highly aggressive and more likely to recur and metastasize. These findings partly may explain why African Americans have the highest incidence and death rates of any group for this disease.

The study is published online and will be printed in the December 2016 issue of the *Journal of the National Cancer Institute* (JNCI) by members of a research team that a year ago found 15 genes in African Americans that are rarely or never detected as mutated in colon cancers from Caucasians. The current study investigated the outcomes associated with these mutations in African American [colorectal cancer](#).

The researchers examined 66 [patients](#) who had stage I - III colorectal [cancer](#) and found those patients positive for the mutations had an almost three times higher rate of metastatic disease, and stage III patients positive with mutations were nearly three times more likely to relapse compared to patients without the mutations.

"This study is significant because it helps shed further light on why colorectal cancers are more aggressive in African Americans compared to other groups," said the study's senior author Joseph E. Willis, MD, Chief of Pathology at University Hospitals Case Medical Center and

Professor of Pathology at Case Western Reserve School of Medicine. "While mortality rates for Caucasian men with colorectal cancer have decreased by up to 30 percent, they have increased by 28 percent for African American men since 1960," said Dr. Willis, who is also director of tissue management in the Case Comprehensive Cancer Center.

These findings and the earlier study only became possible because of technological advances in gene sequencing and computational analysis. These studies ultimately involved review of 1.5 billion bits of data.

"This study builds on our previous genetic research on colorectal cancer," said Sanford Markowitz, MD, PhD, a co-author and principal investigator of the \$11.3 million federal gastrointestinal cancers research program (GI SPORE) that includes this project. "It illustrates the extraordinary impact that dedicated, collaborative teams can make when they combine scientific experience and ingenuity with significant investment."

Announced in 2011, this GI SPORE program is one of just five in the country. Dr. Markowitz, Ingalls Professor of Cancer Genetics at Case Western Reserve School of Medicine and a medical oncologist at UH Seidman Cancer Center, included studies of the disease's behavior in minority patients as part of his team's original grant application. The disparity between colorectal cancer rates in African Americans and other groups has long existed; the most recent federal statistics, for example, put age-adjusted incidence at 46.8 cases for every 100,000 African Americans, and 38.1 cases for every 100,000 Caucasian Americans. Yet scientists have struggled to determine what factors—biological, economic, environmental, or others—account for this disparity.

From the very start, Dr. Markowitz and colleagues believed the answer to this question would be found through genetic analysis.

"Identifying gene mutations has been the basis of all the new drugs that have been developed to treat cancer in the last decade," Dr. Markowitz said. "Many of the new cancer drugs on the market today were developed to target specific genes in which mutations were discovered to cause specific cancers."

"We wondered if [colon cancer](#) is the same disease molecularly in African American individuals as it is in Caucasian individuals. Or could colon cancer be the same disease behaving differently in one population compared to another," he said. "This study gave us our answer. Colon cancer in African American patients is a different disease molecularly."

The scientists made their discovery by using DNA sequencing to compare 103 colorectal cancer samples from African American patients with 129 colorectal cancer samples from Caucasian patients, all of whom had received care at UH Case Medical Center in Cleveland. The scientists examined 50 million bits of data from 20,000 genes in every cancer.

**More information:** Zhenghe Wang et al. Adverse Clinical Outcome Associated With Mutations That Typify African American Colorectal Cancers, *Journal of the National Cancer Institute* (2016). [DOI: 10.1093/jnci/djw164](#)

Provided by University Hospitals Case Medical Center

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