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Genes of colon cancer recurrence differs among blacks, whites and Asians, study finds

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The genetic makeup of colon cancer tumors and survival rates for patients with the disease differ by race, according to a study from researchers at the Mayo Clinic Cancer Center, published in the October 2015 issue of the *Journal of the National Cancer Institute*.

"These findings put the issue of race more prominently on the radar of investigators that cancer biology may contribute to race-based disparities," says the study's co-lead author, Harry Yoon, M.D., an oncologist at Mayo Clinic. "While it is too early to change the way we treat these patients, our results indicate that future studies are needed to examine potential biological drivers of these differences more closely."

According to the American Cancer Society, colon cancer is the third most common cancer in both men and women with more than 93,000 cases estimated to be diagnosed in 2015. Researchers have long known that blacks develop colon cancer at an earlier age and blacks with colon cancer are at higher risk of dying than whites. However, it has been difficult to identify why the differences in survival exist.

Researchers analyzed data from a large clinical trial of more than 3,000 patients with stage III colon cancer. The analysis revealed that tumors from whites, blacks, and Asians had different frequencies of mutations in two key cancer-related genes, BRAF and KRAS, which have been associated with worse outcomes. It also found that colon cancers were twice as likely to recur in black patients as in whites; however, the discrepancy was only evident in those under age 50.

Some of the potential reasons for this disparity include socio-economic factors, such as diagnosis at a later stage, decreased access to health care and suboptimal treatment.

"The role of the biology of colon tumors according to race has not been examined as extensively," says Dr. Yoon. "This biology can be reflected in the genetic makeup of tumors, as well as by whether and how quickly cancer returns after the patient has been treated."

Dr. Yoon and his colleagues focused their efforts on finding out if colon cancers are genetically different based on race, as well as if race-based differences exist in recurrence rates. To do this, they examined data from a large clinical trial - Alliance N0147 - which included patients with stage III colon cancer from many centers in North America who all underwent surgery to remove their cancer and chemotherapy after surgery.

As part of the trial, the patients provided a self-description of their race as either white, Asian, or black or African-American. The researchers then evaluated the tumors from these participants to see if a mutation was present in the cancer-related genes BRAF and KRAS. They also noted if the cancer had returned after treatment.

Analysis of the data showed that tumors from whites, blacks and Asians were different in terms of the frequency of mutations in the BRAF and KRAS genes. Tumors from whites were twice as likely to have BRAF mutations; whereas, tumors from blacks had the highest frequency of KRAS mutations. Tumors from Asians were the most likely to have normal copies of both genes.

The analysis also indicated that the colon cancers among blacks had more than double the risk of cancer recurrence, compared to whites. However, this discrepancy was only visible among young patients - those

under age 50. Almost half of younger black patients experienced colon cancer recurrence within five years, compared to only 22 to 35 percent of whites or Asian patients of any age.

This difference could not be explained by the genetic mutations most frequently found in the tumors of the different races. The researchers adjusted for a number of other potential confounders, such as tumor grade, the degree of lymph node involvement, depth of tumor invasion, body mass index, location of the tumor within the colon, history of smoking, and anomalies in mismatch repair genes; however, none seemed to affect the outcome for young blacks.

"Because all patients were treated and had their disease monitored in a clinical trial," says Dr. Yoon, "suboptimal treatment, differences in cancer stage, or reduced access to care cannot adequately explain the disparity."

"In addition to published data indicating that a limited number of genes are preferentially mutated in colon cancers from black versus white patients, our study revealed differences in the mutation frequencies of BRAF and KRAS oncogenes that provide prognostic information in colon cancer patients," says Frank Sinicrope, M.D., an oncologist at Mayo Clinic and co-lead author. "Our data provide further evidence that colon cancers from blacks are intrinsically different and are associated with more aggressive clinical behavior in young black patients."

More information: *Journal of the National Cancer Institute*, jnci.oxfordjournals.org/content/107/10/djv186.full

Provided by Mayo Clinic