

Study uncovers genetic differences for kidney cancer that may contribute to survival disparity in African-Americans

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A University of North Carolina Lineberger Comprehensive Cancer Center-led study has identified genetic differences in tumors of African-Americans with the most common type of kidney cancer compared with whites.

The findings, published Thursday in the journal *JAMA Oncology*, could help explain lower survival rates for African-Americans with clear cell renal cell carcinoma.

"Our study suggests there are differences in the cancer biology of clear cell [kidney cancer](#) that develop in African-American patients as opposed to those that develop in white patients," said the paper's senior author William Y. Kim, MD, a UNC Lineberger member and associate professor in the UNC School of Medicine Department of Medicine, Genetics, and Urology.

Studies have shown that survival rates are lower for African-Americans with kidney cancer compared with whites, independent of age, sex, [tumor](#) stage, and other variables. A study published in the journal *Cancer* in 2013 found a more than four percentage point difference in the five-year survival rate for African-Americans and whites, with 68 percent of African-Americans living five years with the [renal cell cancer](#), and more than 72 percent of whites living five years with the disease.

"While the [genetic differences](#) we saw suggest that African-American patients have underlying biology that may contribute to their worse prognosis, we feel that access to health care and treatments also negatively impact their outcomes from kidney cancer," Kim said. "Additional research is needed to confirm this finding."

In the new study, researchers accessed genomic

data from The Cancer Genome Atlas to analyze mutations and gene expression of clear cell kidney tumors. The data included 419 clear cell [renal cell carcinoma](#) tumors from non-Hispanic white patients and 19 from non-Hispanic African-American patients. They validated their findings against a set of 125 white and 10 African American patient tumors from another publicly available data set.

The researchers found that the tumor samples from African-Americans were less likely to have inactivation of the VHL, or von Hippel-Lindau, gene. Mutations in VHL can cause higher levels of vascular endothelial growth factor, VEGF. VEGF can promote blood vessel growth, which can supply tumors with growth-enriching nutrients. There are multiple U.S. Food and Drug Administration-approved drugs used to treat kidney cancer that work by blocking the high levels of VEGF seen in kidney cancer.

Two of 12 African-American patients, or 17 percent, had VHL mutations, compared with 175 of 351 [white patients](#), or 50 percent. Gene expression analysis found down regulation of VEGF signaling pathways in African-American patients' tumors relative to tumors from whites.

Researchers hypothesize that the lower VHL mutations in African-Americans could predict lower responsiveness to treatments that target VEGF-associated pathways. However, Kim said more studies are needed to clearly show that VHL mutations truly correlate with response to VEGF inhibiting drugs, and to investigate if there are racial differences in response to these cancer drugs.

The researchers also found that the African-Americans patients more frequently had a molecular tumor subtype called ccB, which has been associated with lower survival for patients.

Fifteen of 19, or 79 percent, African-American [patients](#) had the ccB subtype, compared with 45 percent of whites.

"There are clear genetic differences in clear cell kidney tumors that develop in African-Americans compared to whites," Kim said. "While we believe that these differences could impact outcomes we don't know enough at this time to suggest that African-American's with kidney cancer should be treated differently, but it does underscore the need to investigate these findings further."

More information: Bhavani Krishnan et al. Intrinsic Genomic Differences Between African American and White Patients With Clear Cell Renal Cell Carcinoma, *JAMA Oncology* (2016). [DOI: 10.1001/jamaoncol.2016.0005](#)

Provided by University of North Carolina at Chapel Hill School of Medicine

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