Gene variant may contribute to increased cancer risk in African-Americans

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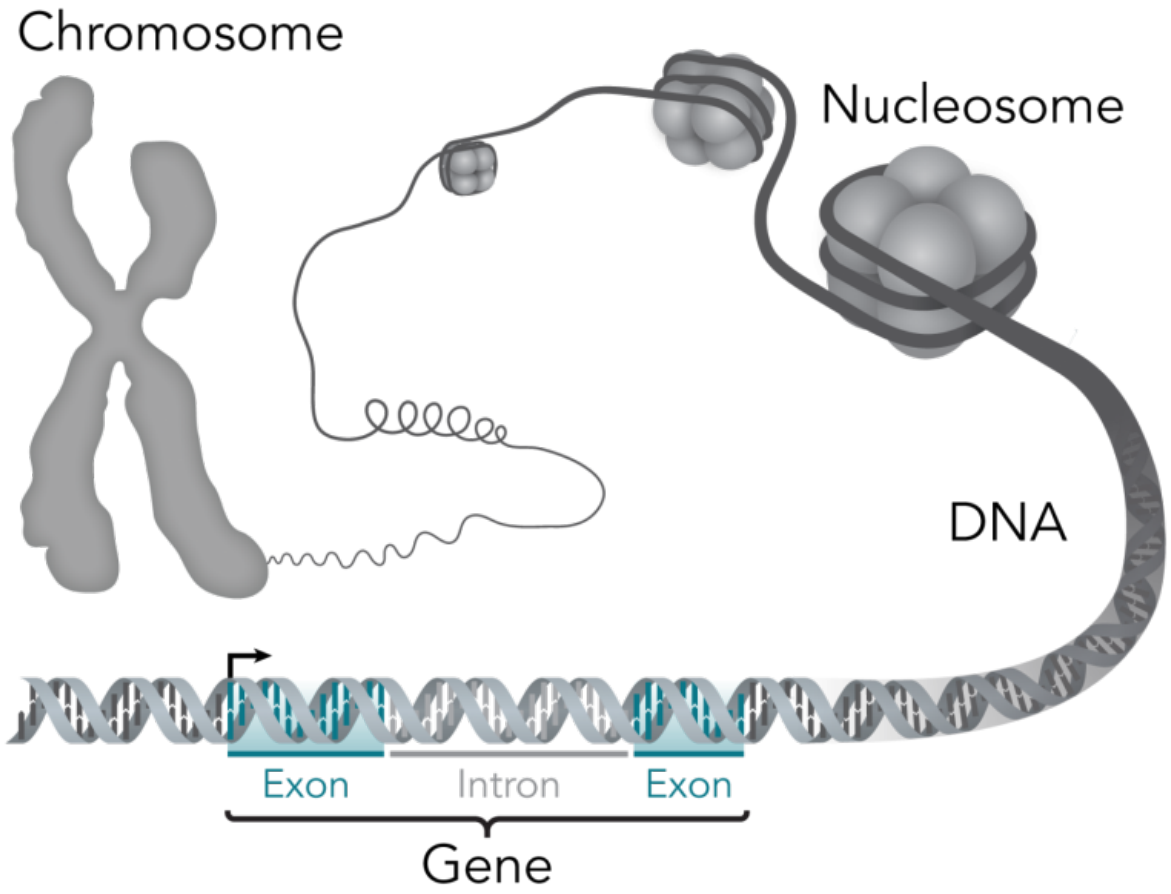

This stylistic diagram shows a gene in relation to the double helix structure of DNA and to a chromosome (right). The chromosome is X-shaped because it is dividing. Introns are regions often found in eukaryote genes that are removed in the splicing process (after the DNA is transcribed into RNA): Only the exons encode the protein. The diagram labels a region of only 55 or so bases as a gene. In reality, most genes are hundreds of times longer. Credit: Thomas

For years, clinical data have shown that African Americans have a higher death rate and shorter period of survival among patients with commonly diagnosed cancers. While studies have focused on whether socioeconomic factors contribute to these statistics, researchers have been diligently trying to determine a genetic basis for these disparities.

Now, new research from The Wistar Institute has pinpointed a single variant in a gene that is only found in Africans and African Americans, which makes cancer resistant to cell death and may contribute to increased cancer risk. Study results are published in the journal *Genes and Development.*

"We may finally have a truly genetic explanation for why African Americans are more prone to a variety of cancers," said Maureen Murphy, Ph.D., professor and program leader in the Molecular and Cellular Oncogenesis program at The Wistar Institute and senior author of the study. "This is a variant that has never been observed in Caucasian populations, so identifying people who have this variant may be crucial for providing improved prognosis and personalized treatment that will lead to better outcomes."

Murphy and her colleagues studied the S47 variant of p53, a tumor suppressor gene that is mutated and activated in the vast majority of cancers. This particular variant is restricted to people of African descent, occurring in approximately 2 percent of African Americans and up to 8 percent of Africans. The Murphy lab created a mouse model containing the S47 variant to study the impact of this variant in otherwise genetically-identical organisms. Wistar's business development team is dedicated to making this physiologically relevant model system widely

available to researchers investigating new treatments for patients having the S47 genetic variant and partners that can help develop new diagnostic and efficacious treatment regimens.

While they were not surprised to find that this form of p53 is impaired at some functions, the researchers were surprised to find that spontaneous cancer occurred in 80 percent of the mice with the variant. Liver cancer, lymphoma and colorectal cancer occurred most frequently in the mice with the S47 variant. Liver cancer is more common in African Americans, and colorectal cancer is responsible for approximately 9 percent of all newly diagnosed cases of any type of cancer in African Americans.

"Validation of these results in humans will require a large population to determine the significance it has on cancer risk among those of African descent," Murphy said. "However, we now have some of the strongest evidence ever obtained for a genetic basis for this disparity and a larger, population-based study is warranted."

Provided by The Wistar Institute