African Americans face highest risk for multiple myeloma yet underrepresented in research

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Though African-American men are three times more likely to be diagnosed with multiple myeloma, a type of blood cancer, most

scientific research on the disease has been based on people of European descent, according to a study led by researchers at the Keck School of Medicine of USC.

That trend is problematic considering that African-Americans—the most at-risk population for multiple myeloma—have different genetics that can affect how this type of cancer progresses and what kind of targeted therapies are most effective, said Zarko Manojlovic, lead author of the study.

For example, in the study, multiple myeloma patients of European descent were six times more likely than their African peers to have mutations in the TP53 gene, a tumor suppressor that helps prevent cancer. African-Americans, on the other hand, experienced heightened mutations in BCL7A, a different tumor suppressor gene.

"A cancer therapy that targets TP53 would not be as effective for African-Americans with multiple myeloma as it would be for a white population because doctors would be trying to fix the wrong mutated gene," said Manojlovic, assistant professor of research translational genomics at the Keck School of Medicine.

The study was published on Nov. 22 in *PLOS Genetics*. Researchers analyzed the genetic sequencing data of 718 multiple myeloma patients and found that African-Americans had increased mutations in the genes BCL7A, BRWD3 and AUTS2, while white people had more mutations in the genes TP53 and IRF4.

The study is the largest and most ethnically diverse genomics study of multiple myeloma to date, the researchers said.

The scientists genetically analyzed the ancestry for all patients and found that 127 patients were of African descent and 591 were of European

descent.

"There are clearly molecular differences between African-American and Caucasian multiple myeloma cases, and it will be critical to pursue these observations to better improve clinical management of the disease for all patients," said John D. Carpten, senior author of the study and chair of the Department of Translational Genomics at the Keck School of Medicine.

Higher incidence rate and lower survival rates for African-Americans

Multiple myeloma is a cancer of plasma cells in the blood that causes tumor growths in bone marrow. About 30,280 people will be diagnosed with the cancer this year, and about half of them will survive longer than five years, according to the National Cancer Institute.

African-Americans are two times more likely than white people to die from multiple myeloma, the study stated.

"In the past decade, new treatments for the disease have spurred a remarkable improvement in survival for myeloma patients, but those benefits have disproportionately increased survival rates for Caucasian patients," Carpten said. "African-American multiple myeloma patients have higher incidence rates and lower survival rates than their Caucasian peers despite this being a relatively easy-to-treat cancer.

"We in the cancer genomics community have a responsibility to ensure that our studies represent true population diversity so we can understand the role of ancestry and biology in health outcomes. The new candidate myeloma genes we identified in the African-American population may have been overlooked because of the lack of diversity in previous genomic efforts."

Jonathan Keats director of Bioinformatics at the Translational Genomics Research Institute in Arizona and a co-author of the study, added: "This study provides a unique view on the genetic differences of multiple myeloma in African-American and Caucasian populations that is only possible in studies like the Multiple Myeloma Research Foundation CoMMpass study, which was designed to collect a patient cohort reflective of the demographics of the United States population."

David W. Craig from the Keck School of Medicine; Austin Christofferson, Winnie Liang, Jessica Aldrich, Megan Washington, Shukmei Wong and Jonathan Keats from the Translational Genomics Research Institute; Daniel Rohrer and Scott Jewell from the Van Andel Research Institute; and Rick Kittles and Mary Derome from the Multiple Myeloma Research Foundation also contributed to the study. Researchers used data from the Multiple Myeloma Research Foundation's CoMMpass Study.

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