

Genetic variants linked to heart health in African American childhood cancer survivors

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Scientists at St. Jude Children's Research Hospital recently identified genetic variants in childhood cancer survivors of African ancestry that increase their risk of treatment-related heart problems. The findings, which have implications for how the health of these survivors is monitored, were published online today in *Cancer Research*, a journal of the American Association for Cancer Research.

"Childhood [cancer](#) survivors are a unique population," said corresponding author Yadav Sapkota, Ph.D., of the St. Jude Department of Epidemiology and Cancer Control. "But within that group, survivors of African ancestry are an even more specific population, who until now have generally been excluded from studies looking into the genetic mechanisms behind health outcomes among pediatric cancer survivors."

Cardiomyopathy occurs at significantly higher rates in survivors of [childhood](#) cancer than the general population. However, research into the effect of genetic variants on patients' health among racial and [ethnic groups](#) is lacking, often because of the rarity of patient data. Researchers at St. Jude used the St. Jude Lifetime Cohort study, a large cohort of [childhood cancer survivors](#) followed over time, to study risk of cardiomyopathy in childhood cancer survivors of African ancestry.

The findings showed that when compared to survivors of European ancestry, childhood cancer survivors of African ancestry are 2.5 times more likely to develop cardiomyopathy. The results accounted for known cardiovascular risk factors such as hypertension, diabetes, dyslipidemia, physical activity, alcohol consumption and smoking.

After establishing that African American childhood cancer survivors are at a higher risk of developing cardiomyopathy, the researchers looked for biologic mechanisms that could account for the difference. The scientists identified two distinct genetic variants associated with cardiomyopathy in African American survivors.

"As a group, childhood cancer survivors represent a highly heterogenous population with respect to type of cancer and treatment exposures. Thus, it is often important to investigate treatment-related risks within well-defined subgroups," said author Leslie Robison, Ph.D., chair of the St. Jude Department of Epidemiology and Cancer Control. "The genetic variants identified in this study demonstrate the importance of

considering associations within racial or ethnic subgroups."

On chromosome 15q25.3, the variant (rs9788776) occurs only in survivors of African descent and increases cardiomyopathy risk by 4.5 times. On chromosome 1p13.2, the variant (rs6689879) increases cardiomyopathy risk in survivors of African descent by 5 times. The rs6689879 variant does occur in survivors of European descent, but only increases their cardiomyopathy risk by 1.3 times. Additional findings suggested a mechanism by which the 1p13.2 variant leads to cardiomyopathy by up-regulation of the gene PHTF1, a transcription factor.

This study has implications for long-term follow-up and surveillance of childhood cancer survivors of African ancestry.

"All childhood cancer survivors should be monitored for cardiac late effects, but as we gain a more granular understanding of [cardiomyopathy](#) risk among different populations, we can start to focus interventions on those individuals with the greatest need," said author Melissa Hudson, M.D., St. Jude Cancer Survivorship Division director.

More information: "Genetic variants associated with therapy-related cardiomyopathy among childhood cancer survivors of African ancestry," *Cancer Research* (2020). [DOI: 10.1158/008-5472.CAN-20-2675](https://doi.org/10.1158/008-5472.CAN-20-2675) , [cancerres.aacrjournals.org/use ... 008-5472.CAN-20-2675](https://cancerres.aacrjournals.org/use...008-5472.CAN-20-2675)

Provided by St. Jude Children's Research Hospital

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