

A drug and a DNA variant increase heart disease risk in cancer survivors

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Scientists from St. Jude Children's Research Hospital have identified a genetic variant associated with substantially increased risk of heart disease in survivors of childhood cancer treated with the chemotherapy doxorubicin. This connection was discovered in participants in the St. Jude Lifetime Cohort Study (St. Jude LIFE) and validated in another major cancer cohort, the Childhood Cancer Survivor Study (CCSS). The results were published today in the *Journal of the*

National Cancer Institute.

"In this study, we have identified a new region in the genome that increases risk of [cardiotoxicity](#) in [childhood cancer survivors](#)," said first and corresponding author Yadav Sapkota, Ph.D., St. Jude Department of Epidemiology and Cancer Control. "This particular variant has never been identified before as a contributor to the mechanisms underlying cardiotoxicity."

Childhood cancer survivors often experience treatment-related toxicities later in life. The researchers observed that some survivors developed cardiac problems, while some did not, even when they received the same treatment. This gave them a hint that genetics may be responsible for developing cardiac problems later in life.

The heart-breaking variant and treatment combination

The scientists found a strong relationship in children with a particular genetic variant, the common chemotherapy agent doxorubicin and cardiac dysfunction later in life. Doxorubicin belongs to the anthracycline family of chemotherapy agents used to treat pediatric cancer. The newly identified genetic variant could help guide pediatric cancer treatment.

"Patients who carry this variant may not have yet developed cardiotoxicity, but they could develop cardiotoxicity in the future," Sapkota said. "When we performed the analysis among those survivors who were exposed to doxorubicin as a pediatric [cancer](#) treatment without chest radiotherapy and daunorubicin, we see that cardiotoxicity risk was much higher in somebody who carries at least one copy of this particular variant. With just a single copy, a [survivor](#) will have a 3-times larger risk of developing cardiotoxicity compared to someone else who does not have the risk allele."

"But if somebody carries two copies of the [variant](#)," he said, "Then, that person will have a 9-times higher risk for development of cardiotoxicity compared to those who did not carry the allele."

More information: Yadav Sapkota et al, A novel locus on 6p21.2 for cancer treatment-induced cardiac dysfunction among childhood cancer survivors, *JNCI: Journal of the National Cancer Institute* (2022). [DOI: 10.1093/jnci/djac115](https://doi.org/10.1093/jnci/djac115)

Provided by St. Jude Children's Research Hospital

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