Genetic variant linked with increased risk of anthracycline-related cardiomyopathy

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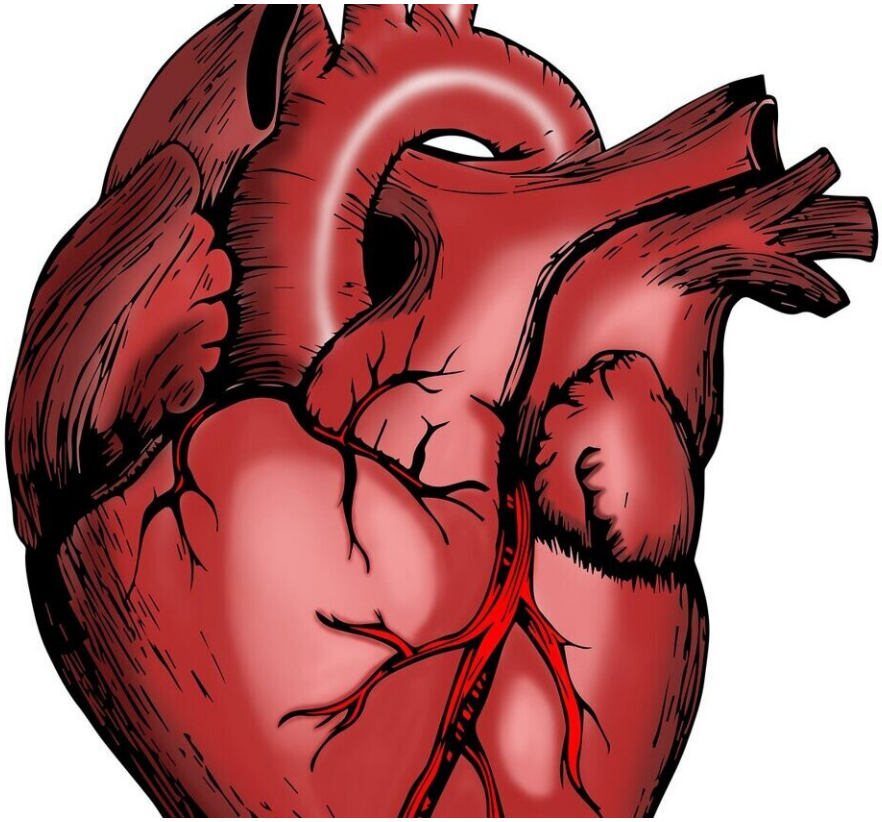

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About 60% of childhood cancer survivors have a history of anthracycline exposure, a chemotherapy that is used in the treatment of multiple childhood cancer types. Studies have shown a strong dose-

dependent association with anthracycline exposure and cardiomyopathy, a disease of the heart muscle that makes it harder for the heart to pump blood to the rest of the body. Cardiomyopathy can lead to heart failure.

In results published in the *Journal of Clinical Oncology*, researchers from the University of Alabama at Birmingham discovered an association between the genetic variant ROBO2 and an increased risk of developing anthracycline-related cardiomyopathy.

"We identified two genetic variations on the ROBO2 gene that demonstrated a significant gene-anthracycline interaction effect," said Smita Bhatia, M.D., director of the UAB Institute for Cancer Outcomes and Survivorship and senior author. "Individuals with these variations were at a twofold to eightfold higher risk of developing cardiomyopathy or heart failure."

The ROBO2 gene is a robo receptor that binds Slit guidance ligands with functions linked to cell adhesion, growth and survival. Slit-Robo signaling is involved with many aspects of heart development. It was observed that the Slit-Robo through the TGF-b1/Smad signaling pathway promoted cardiac fibrosis, which can lead to cardiac dysfunction and heart failure.

"Findings also suggest that suppressing Robo signaling and/or the TGF-b1/Smad signaling can possibly lead to a suppression of cardiac fibrosis and reduce the risk of cardiomyopathy in patients with anthracycline exposure and ROBO2 variations," Bhatia said.

More information: Xuexia Wang et al, Genome-Wide Association Study Identifies ROBO2 as a Novel Susceptibility Gene for Anthracycline-Related Cardiomyopathy in Childhood Cancer Survivors, *Journal of Clinical Oncology* (2022). DOI: 10.1200/JCO.22.01527

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