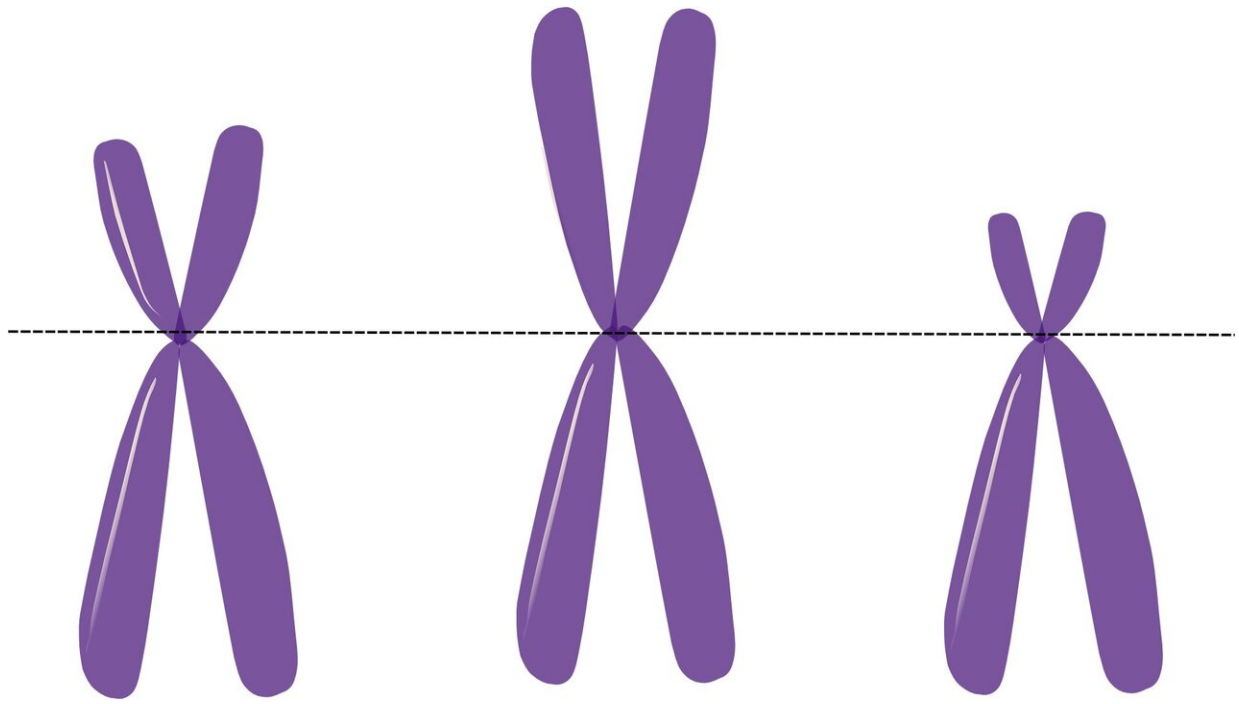
New study shows a relationship between heart disease and spontaneous loss of Y chromosome

June 27 2024



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Researchers at Boston Medical Center (BMC) and Boston University (BU) Chobanian & Avedisian School of Medicine, in collaboration with an international team of scientists, shared findings from a new study published in the American Heart Association journal, *Circulation: Heart*

Failure that explores a common cause of heart disease in older men called transthyretin cardiac amyloidosis (ATTR-CA).

The study examines the relationship between spontaneous loss of the Y chromosome (LOY), a condition in aging men where the Y chromosome is spontaneously deleted in blood cells, and ATTR-CA, a progressive disease that causes heart failure and death. The team found that men with a higher proportion of blood cells missing Y chromosomes have a higher ATTR-CA mortality rate, informing future treatment for patients with ATTR-CA. The study team included investigators from Columbia University, University of Virginia, and Osaka Metropolitan Hospital in Japan.

LOY is the most common acquired genetic mutation in men, with more than half of men in their early 90s having lost the Y chromosome in some of their blood cells according to the National Cancer Institute. While LOY has been associated with heart failure survival rates in large population studies, it has never been examined in relation to ATTR-CA. The current study suggests that men with ATTR-CA who have LOY in greater than 21.6% of their blood cells were 2.6 times more likely to not survive this form of heart disease.

"Our study suggests that spontaneous LOY in circulating white blood cells contributes both to the development of ATTR-CA in men and influences the severity of disease," said Frederick L. Ruberg, MD, Chief of Cardiovascular Medicine at BMC, Professor of Medicine at BU Chobanian & Avedisian School of Medicine, and lead researcher in this study. "Additionally, our study's findings indicate that elevated LOY may be an important reason why some patients do not respond to the ATTR-CA therapy that is typically effective."

Current treatments for ATTR-CA work well for many patients, but roughly 30 percent of patients do not respond to treatment, leading to

hospitalization and death. Findings from this study support elevated LOY as a potential barrier to treatment response. The findings could one day inform a clinician's choice in designing a treatment course for a patient with ATTR-CA and high level of LOY in hopes of a more favorable health outcome. Additionally, the findings could lead to the development of new treatments for those with heart disease, including ATTR-CA.

"Our study team represents an international collaboration that sought to explore an association between a common blood disorder and ATTR-CA that has never been previously considered," said Ruberg. "We provide evidence that these two conditions may be related, supporting a new way of understanding how ATTR-CA progresses as well as how to develop new potential targets for treatment."

More information: Mark C. Thel et al, Mosaic Loss of the Y Chromosome Is Enriched in Patients With Wild-Type Transthyretin Cardiac Amyloidosis and Associated With Increased Mortality, *Circulation: Heart Failure* (2024). DOI: 10.1161/CIRCHEARTFAILURE.124.011681

Provided by Boston Medical Center