

<https://doi.org/10.29289/259453942025V36S11101>

1101 – High co-segregation of TP53 R337H and XAF1 e134* variants in Brazilian li-fraumeni syndrome families identified through cascade screening

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Introduction: Cancer is a group of diseases characterized by uncontrolled cell growth, some of which may have a hereditary origin. In Brazil, Li-Fraumeni syndrome stands out as a genetic condition with autosomal dominant inheritance, associated with alterations in the TP53 gene, especially the R337H variant. Studies suggest that co-segregation with the E134* variant in the XAF1 gene may influence disease severity. In this context, cascade screening allows the identification of at-risk family members.

Objective: Identifying these variants is essential for genetic counseling and prevention.

Methods: In this study, seven families with primary breast cancer patients were included, referred from the Brazilian Public Health System to the Human Genetics Center of the Federal University of Goiás. Among the patients, six were female aged between 30 and 56 years, and one was a 67-year-old male. Primary patients had been previously diagnosed with Li-Fraumeni syndrome, and among the seven, only two did not show co-segregation with the E134* variant in the XAF1 gene. A total of 110 individuals were screened through cascade testing and invited to undergo genetic testing after positive results in their relatives.

Results: Of the 110 individuals tested, 37 were positive for the R337H variant in TP53, of whom 33 also carried the E134* variant in XAF1. Among the seven families, four showed 100% co-segregation, one showed 90.91%, and two showed no co-segregation. Families without co-segregation accounted for 10.81% of individuals positive for R337H. Co-segregation between the R337H variant in TP53 and E134* in XAF1 was frequent in the analyzed families, suggesting a possible influence on phenotypic expression and cancer risk.

Conclusion: These findings reinforce the importance of cascade genetic screening and contribute to more effective strategies for genetic counseling and personalized prevention.

Ethics: Research Ethics Committee Approval (CAAE 50626315.6.0000.5078).

Funding: Brazilian National Genomics and Precision Health Program (Genomas Brazil), National Council for Scientific and Technological Development (CNPq), Federal University of Goiás (UFG), The Goiás State Research Support Foundation (FAPEG) and Fundação de Amparo à Pesquisa (FAPESP) do Estado de Goiás.

Keywords: Li-Fraumeni syndrome; genetic predisposition to disease; genetic screening; genes TP53; genetic counseling.