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Co-segregation analysis of the XAF1-E134* variant in patients with pathogenic variants in the TP53 gene: its relationship with the clinic

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Introduction: Variant co-segregation refers to a genetic inheritance pattern in which alterations in different genes are transmitted simultaneously through generations with high frequency. In this context, the co-segregation of the XAF1-E134 and TP53-R337H variants was recently reported in the literature as a likely factor associated with increased aggressiveness of the tumor phenotype, in addition to being associated with clinical heterogeneity. **Objective:** The aim of this study was to identify the XAF1-E134 variant associated with a more aggressive cancer phenotype of Li-Fraumeni Syndrome. **Methods:** All patients treated at the Human Genetics Center of the Federal University of Goiás (CEGH-UFG) since 2022, who underwent genetic sequencing for TP53 gene analysis, were included in the present investigation. To date, of the 348 general patients, 30 were found who presented pathogenic variants associated with TP53, specifically c.455C>T and c.1010G>A. Of these positive cases, 11 corresponded to primary patients and 19 to family members who were previously screened due to kinship with the diagnosed individuals. **Results:** Of the 30 samples with identified variants, 18 were submitted to quantitative polymerase chain reaction (qPCR) for validation and additional analysis. Among them, 14 cases presented positive results, distributed in seven different families. These findings highlight the importance of family genetic screening and the use of complementary methodologies, such as qPCR, to deepen the molecular characterization of TP53 variants and their correlation with cancer predisposition. **Conclusion:** A high prevalence of the XAF1-E134 variant associated with the TP53 gene was observed. Given the relevance of these variants and their clinical implications in the aggressiveness and heterogeneity of hereditary cancer in Brazil, it is essential to develop research in this area, aiming to expand scientific knowledge and contribute to the advancement of personalized clinical treatment and prevention strategies.

Keywords: hereditary breast and ovarian cancer syndrome; breast cancer.