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The Cancer Control Challenge:
Better Understanding It to Better Face It

TP53 MUTATIONS IN BREAST CANCER: ASSOCIATIONS WITH HISTOLOGICAL AND MOLECULAR SUBTYPES

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Introduction: The tumor suppressor gene *TP53* is frequently mutated in breast cancer (BC) and is associated with poor prognosis. Identifying additional features that may assist in diagnosis, treatment, and prognostic stratification remains essential. **Objectives:** To evaluate the presence of *TP53* mutations and their association with histological and molecular subtypes of breast cancer. **Methods:** A total of 990 breast cancer samples from The Cancer Genome Atlas (TCGA) were analyzed using somatic variant data. The *maftools* package in RStudio was used to perform group comparisons via Fisher's exact test and odds ratio (OR) calculations. *p*-values were adjusted using the Benjamini–Hochberg method, with *p*adj < 0.05 considered statistically significant. **Results:** Mutations in *TP53* were associated with distinct molecular and histological subtypes of breast cancer. These variants were significant in the Luminal A subtype (*p*adj = 8.76e-31, OR = 0.095), although correlated with lower risk, consistent with this subtype's favorable prognosis. In contrast, *TP53* mutations were strongly associated with the Basal-like subtype (*p*adj = 3.45e-26, OR = 23.68), known for its aggressiveness and resistance to conventional therapies. This resistance may be driven by *TP53*-mediated molecular alterations that promote cell survival under therapeutic pressure. Histologically, *TP53* mutations were less frequent in invasive lobular carcinoma (*p*adj = 4.15e-38, OR = 0.035) and more common in invasive ductal carcinoma (*p*adj = 1.36e-25, OR = 9.13), suggesting their potential as a discriminative molecular marker. Additionally, significant co-occurrence was observed between *TP53* mutations and alterations in *CDH1*(*p*adj = 1.27e-48, OR = 0.023) and *PTEN* (*p*adj = 1.07e-05, OR = 0.226), reinforcing its integration within complex molecular networks. **Conclusion:** These findings highlight the central role of *TP53* in shaping the biological behavior of breast cancer. Its mutations are linked to greater aggressiveness, genomic instability, and disease progression, whereas their lower frequency in favorable subtypes may suggest a protective role when the gene is functionally intact. The observed associations

with *CDH1* and *PTEN* mutations further underscore *TP53*'s relevance as a prognostic biomarker and its potential utility in risk stratification and in understanding breast cancer heterogeneity.

Keywords: Breast cancer; tp53; tcga; molecular subtypes