HER2 amplification is associated with higher TMB in breast cancer

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Abstract

Background: HER2 gene amplification is a frequent event in breast cancer, which is followed by expression of HER2 protein (HER2-P) and activates ErbB2/HER2 signaling pathway. However, the association between HER2 amplification and tumor mutational burden (TMB) level is still unclear. In order to better understand the role of HER2 amplification in the therapeutic response and prognosis of breast cancer, we aimed to explore the relationship between HER2 amplification and TMB in breast cancer.

Methods: Whole-exome sequencing (WES) and targeted sequencing (TGS) data from 366 breast cancers from TCGA cohort and 335 breast cancers from clinical cohort were analyzed using the online SNPlio tool to obtain the somatic non-synonymous mutations and TMB level. HER2 gene amplification (HER2 copy number ≥ 2 and HER2/PDGFRB copy ratio ≥ 2) was co-occurrence with the TMB in breast cancer.

Results: HER2 gene amplification was significantly associated with higher TMB in breast cancer, which were confirmed in both TCGA and clinical cohort (P = 0.010). In addition, HER2 amplification was also associated with higher TMB level in HER2-negative breast cancer (P = 0.041). Patients with HER2-negative breast cancer and high TMB level had worse overall survival either in the entire study population or in HER2-positive patients. In the HER2-positive cohort, patients with HER2 amplification and low TMB level had worse overall survival compared with those with HER2 amplification and high TMB level (P = 0.045), while in de novo breast cancer patients, there was no statistical difference in overall survival.

Conclusions: HER2 amplification is a biomarker for TMB in breast cancer, which may assist the selection of breast cancer patients likely to benefit from immunotherapy.

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