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Comprehensive analysis of TWIST1 in breast cancer and other carcinomas: an association with prognosis and tumor microenvironment

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Objective: Metastasis is the main cause of death in patients with carcinomas. This process depends on a phenotypic alteration known as epithelial–mesenchymal transition (EMT), regulated by transcription factors (TFs), including TWIST1, whose increased levels have been described in several carcinomas, including breast cancer. However, a comprehensive analysis of its expression to elucidate its predictive value still needs to be performed. This study aimed to understand the prognostic value of TWIST1 expression and its biological relevance for tumor microenvironment (TME) in breast cancer and other carcinomas. **Methodology:** Initially, we conducted Kaplan-Meier analyses using patient data from TCGA of breast cancer (BRCA) and their PAM50 intrinsic subtypes, as well as the other types of carcinomas. For those groups whose TWIST1 levels were associated with a poor prognosis, we conducted the deconvolution analyses using the XCELL algorithm followed by Spearman correlation analysis ($p<0.05$) between TWIST1 levels and estimation of TME infiltrating-cell types. **Results:** Survival analysis showed that high expression of TWIST1 is associated with poor prognosis in the Luminal B breast cancer subtype (BRCA-LumB; p=0.0127), HER2 breast cancer subtype (BRCA-Her2; p=0.022), clear cell renal cell carcinoma (KIRC-ClearCell; p=0.0004), kidney renal papillary cell carcinoma (KIRP-Papillary; p=0.0002), lung adenocarcinoma (LUAD-AdenoNOS; p=0.016), stomach adenocarcinoma diffuse (STAD-Diffuse p=0.0061), and intestinal (STAD-Intestinal; p=0.0013). In addition, TWIST1 levels revealed a clear correlation with TME-infiltrating cells, demonstrating a positive correlation with cancer-associated fibroblasts (CAFs) and a negative correlation with plasma B cells in the analyzed groups. **Conclusion:** Our findings elucidated the predictive role of TWIST1 in breast cancer and other cancer types, which provided new insights exploring the possible regulatory mechanisms of TWIST1 on the TME, suggesting this TF as a potential target to develop novel diagnostic and therapeutic strategies.

Keywords: TWIST1; tumor microenvironment; prognosis, survival.