Alterations and correlations of the components in the Wnt signaling pathway and its target genes in breast cancer

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Abstract

Both cyclin D1 and c-myc are key molecules in breast cancer carcinogenesis, and their transcriptional level and stability are regulated through several signaling pathways, including the Wnt signaling pathway. We performed immunohistochemical and mutational analyses of Wnt signaling components to investigate the association of Wnt signaling alterations with breast cancer carcinogenesis using 49 surgically resected primary breast cancer samples. Positive staining of cyclin D1 and c-myc was observed in 55.1% and 30.6% of the 49 breast cancer samples, respectively. Aberrant cytoplasmic expression of β-catenin, which indicates the existence of alterations in the Wnt signaling pathway, was observed in 38.8% of breast cancer samples, though no mutation was found in the β-catenin and Axin 1 genes. Reduced expression of APC was observed in 34.7% of samples. Statistical analysis revealed strong correlations between overexpression of β-catenin and that of cyclin D1 and c-myc (p=0.0001 and 0.0117, respectively). Furthermore, overexpression of β-catenin was significantly correlated with reduced expression of APC (p=0.0127). Wnt signaling alterations were frequently observed in breast cancer from the results of β-catenin immunohistochemistry, although no mutation in the components of the Wnt signaling pathway was found in the present study. Based on the statistical analyses, we speculated that reduced expression of APC leads to overexpression of β-catenin, and aberrant expression of cyclin D1 and c-myc mainly depends on alterations in the Wnt signaling pathway in breast cancer.