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Prognostic marker for breast cancer

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p16 protein is a tumour suppressor gene and a major target of carcinogenesis. It is downregulated in many cancers like melanoma, oesophageal cancer, breast cancer, brain cancer, ovarian cancer, etc. The p16 protein is an inhibitor of cyclin dependant kinase (CDK) which blocks the G1-S phase of the cell cycle by inhibiting cyclin D-CDK 4/6 complex formation by binding to CDK. The p16-Cdk 4/6 complex then inhibits pRb phosphorylation (tumour suppressor gene) eventually resulting in G1 arrest. p16 promoter methylation and protein expression have been studied in breast cancer and this data has been correlated to the expression of hormone receptors like ER (oestrogen receptor), PR (progesterone receptor) and HER2 (human epidermal growth factor receptor-2). A case study was conducted with 114 cases of histological/cytological confirmed cases of breast carcinoma. Age, type of tumour, grade, lymph node status and hormonal receptor status (ER/PR/HER2) was recorded in each case. Age is an important independent prognostic factor in breast cancer. The age of patients ranged from 24 to 80 years. Research has shown that hereditary breast cancers were seen to have higher ER and 70% of cases of sporadic cancers were found to be ER positive. ER is overexpressed in 20-30% of breast cancer cases. p16 shows a significant association between ER and PR statuses but no association with clinicopathological factors like age, menopause, lymph node or HER2 status. Moreover, strong p16 expression was found with increasing tumour grade. Additionally, epigenetic changes included methylation of DNA which involved methylation of the CpG islands in the perimeter. Methylation-specific PCR studies revealed that p16 methylation showed a significant association with ER positive and PR positive cases. In addition to this, p16 methylation also showed an association with the grade of the tumour. In conclusion, p16 may be involved in breast cancer carcinogenesis in the majority of sporadic cases and hence can be used as a prognostic marker to predict treatment response to hormone therapy.

Keywords: p16, Methylation, Breast cancer, Oestrogen receptor, Progesterone receptor, Hormone receptor

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