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Cyclin D_1 in breast cancer is not associated with Ki67 but with ER

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Keywords

Cancer, cyclin D_1, immunohistochemistry, Ki67, normal breast, oestrogen receptor

Context

D-type cyclins are implicated in cell cycle regulation. The cyclin D_1 gene is amplified in 15-20% of breast cancers while the protein is overexpressed in 50% of these cancers (see Additional information [1]). Overexpression of cyclin D_1 has been linked with oestrogen receptor (ER)a, because it can stimulate transcriptional functions in the absence of oestrogen (see Additional information [2]). A negative association in normal breast has been reported for ERa and Ki67 (a proliferation marker), although this relationship changes in many precancerous and ER-positive cancers. Therefore, the aim of the study was to investigate the interaction between cyclin D_1, ER and Ki67 in normal and malignant breast material.

Significant findings

The mean percentage of ER-positive cells in normal breast tissues was 20%. Approximately 50% of the cyclin-D_1-positive cells coexpressed ER. However, cyclin-D_1-positive cells were detected in 70% of ER-positive invasive ductal carcinomas (IDCs) and in 30% of ER-negative IDCs. In normal breast tissues, Ki67-positive cells accounted for 3% of the epithelial cells while only 0.3% contained cyclin D_1. In benign breast lesions no clear outcome was detected for cyclin D_1 and Ki67. Invasive cancers showed a higher percentage of Ki67-positive cells than normal tissue and this was significantly higher in ER-negative than in ER-positive carcinomas. Overall a positive correlation between cyclin D_1 and ER-positive cells was detected in normal and cancerous breast tissues, while a negative association was detected between cyclin D_1 and Ki67.

Comments

Cyclin D_1 overexpression has been associated with low grade ER-positive breast cancers (see Additional information [3]). In this study no cyclin D_1 positivity was detected in ER-negative breast cancers that contained a high percentage of Ki67-positive cells. A number of studies indicate that cyclin D_1 overexpression increases progressively from normal breast epithelium to atypical ductal hyperplasia (ADH), to ductal carcinoma *in situ* (DCIS) and to invasive cancers respectively (see Additional information [4,5]). The authors observed that cyclin D_1 was higher within in situ proliferations than in normal breasts, while in ADH cases similar values to those measured in ER-positive DCIS were seen. Therefore, they concluded that cyclin D_1 was not the ideal marker for separating benign from malignant breast lesions. Future studies should investigate further the interactions of cyclin D_1 and Ki67 expression in larger cohorts and include other histological carcinoma types.

Methods

Dual immunofluorescence immunohistochemistry

Additional information

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