

Association of nestin with anti-apoptotic and tumor suppressor factors in human breast cancer

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Human breast carcinoma is a heterogeneous disease embracing different phenotypes with different biological characteristics. Transcriptional profiling has identified five breast cancer subtypes, of which the "basal epithelial" is the most aggressive, with a predilection for younger women, and correlates with poor prognosis.

Nestin, an intermediate filament protein, was originally identified as a marker of neuroepithelial stem/progenitor cells in the brain. Recently, it was observed that nestin is expressed in basal/myoepithelial cells of the normal mammary gland and was also later found in cancer stem like cells of many tumors. Some studies showed that nestin is robustly immunohistochemically expressed in basal epithelial and triple negative breast tumors and that its expression correlates with survival patients.

The increased expression of survivin, a member of the inhibitor-of-apoptosis (IAP) protein family, has been demonstrated to be associated with resistance to apoptosis. It has been reported that survivin and other IAP proteins cooperate to activate kinase cascades that control cell motility, thus stimulating tumour cell invasion and promoting metastasis. This mechanism seems to play a central role in breast cancer progression and resistance to treatment.

The p53 protein represents the final effector of the p14CDKN2A/MDM2 pathway; in majority of human cancers, the TP53 gene is functionally inactivated. Lack or reduced expression levels of the p53 protein seem to be associated with a defective apoptotic response to genotoxic damage and, thus, to anticancer agents.

In this study, we evaluated the immunohistochemical expression of nestin in association with an anti-apoptotic protein, such as survivin, and a tumor suppressor factor, such as p53, and with Ki-67 proliferation index in bioptic samples of T4 breast tumors. The results will be discussed.

Keywords: breast cancer, nestin, survivin, p53, Ki-67