ABSTRACT

Evaluation of Neuropilin-1 & 2 polymorphisms and their Expression in Breast Cancer

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Breast cancer is the fifth most common cause of cancerous mortality worldwide. In India, the age-standardized breast cancer incidence, and mortality rates are 25.8 and 12.7 per 100 000 respectively. Breast cancer is multifactorial and heterogeneous disease, which varies from one individual to another with significant difference in the expression and functionalities of the specific genes and proteins in the tumor cells. These differences in the tumors can be attributed to genetic variations which are responsible for differential outcome of the disease in different individuals. Neuropilin 1 & 2 act as co-receptors for VEGFA and TGFβ1 and play major role not only in physiological but also in pathological pathway of angiogenesis, apoptosis etc. Genetic variation in genes encoding neuropilin 1 & 2 may contribute to individual differences in the outcome and severity of the disease. The present study aimed to evaluate the role of NRP1 C/T (rs10082) & NRP2 T/C (rs10090) polymorphisms and their expression in breast cancer tissue. A total of 100 breast cancer patients and 100 healthy controls were considered for the study. The genotyping was carried out by allele specific PCR method and quantitative RT-PCR was performed to measure NRP1 (n=15) and NRP2 (n=15) expression in breast cancer tissue and surrounding unaffected tissue. Statistical analysis was performed to test the significance of the results. The genotypic and allelic distribution of NRP1 C6719T (co-dominant model: $\chi 2$=0.655, p=0.722) and NRP2 T-470C (co-dominant model: $\chi 2$=3.80, p=0.149) polymorphisms in breast cancer and controls did not show any statistically significant difference. However, NRP1 expression in breast cancer tissue is significantly elevated compared to unaffected tissue (t= 3.57, p=0.023*) and there was no significant difference in expression of NRP2 (t=23.4, p=0.45). The increased expression of NRP1 might contribute in enhanced tumor angiogenesis and promote tumorigenesis. Thus, NRP1 could be a potent biomarker and a target for cancer therapy. However, an increase in sample size might strengthen the evidence of NRP1 as biomarker for breast cancer.