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Investigation of Methylation Changes of RASSF1A, TCF3, SNAIL2, ATGA6 and BCL-XL Genes in Breast Cancer

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Abstract

Introduction Nowadays, breast cancer is the most common cancer in women that caused by defects in the signaling mechanisms that control cell proliferation and apoptosis. Recent findings suggest that epigenetic alterations are the key factors in the development of breast cancer. Methylation changes occur within CpG islands of promoters and induce gene silencing. Abnormal methylation can be used as a potential biomarker for diagnosis of various diseases including cancer. In this study, methylation changes of RASSF1A, TCF3, BCL-XL, SNAIL2 and ITGA6 genes were assessment as epigenetic biomarkers of breast cancer.

Materials and Methods: 70 breast cancer samples and 30 normal samples were selected and identified with different Clinical and pathological data, which might be related with methylation changes. Breast cancer patients and normal blood samples were collected and DNA was extracted from white blood cells. DNA samples were digested using methylation-sensitive restriction enzymes to identify methylated sites. Unlike hypomethylated positions, hypermethylated sites were not digested using these enzymes, thus replication occurs by PCR reaction.

Results: RASSF1A and TCF3 (in some cases) were significantly hypermethylated in breast cancer cases ($P<0.05$) compared to normal samples. ITGA6 was significantly hypomethylated in breast cancer cases ($P<0.05$) compared to normal samples. According to statistical analysis, no significant correlation was observed between methylation changes and clinical factors (stage of disease, age of patients, Estrogen Receptor (ER), Progesterone Receptor (PR), and human epidermal growth factor 2 (HER2) status) in patients with breast cancer ($P>0.05$) except RASSF1A gene methylation changes that shown reverse correlation with age of patients ($P<0.05$).

Conclusions: This study demonstrated that RASSF1A, ITGA6 and TCF3 genes methylation status were changed during breast cancer and they can be used as molecular biomarkers for breast cancer diagnosis.