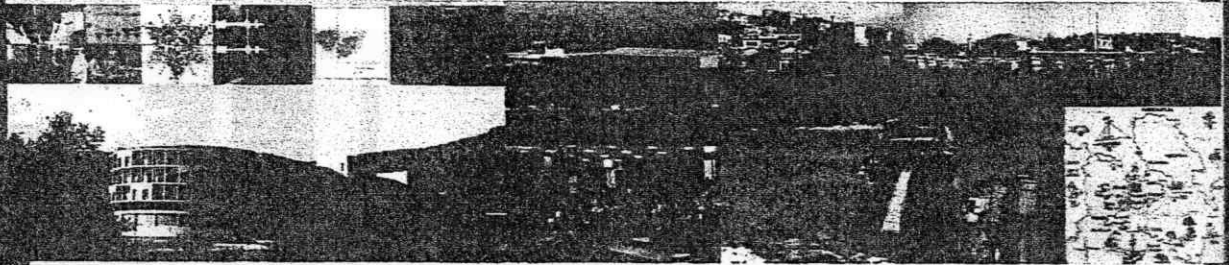


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P110. Association of DNAMethylationofp16^{INK4a}(CDKN2A)andMGMT Genes Andhistopathological Features OfBreast Cancer

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Abstract

Breast cancer (BC) is the most common tumor in women, and the second leading cause of death. Histopathology plays an important part in determining the treatment strategy for women with BC. DNA methylation is an important regulator of gene transcription [1,2]. p16^{INK4a} can block G₁-S-phase progression and that mutant p16^{INK4a} proteins are nonfunctional in cell cycle arrest or Cdk inhibition suggests that p16^{INK4a} plays an important role in negative growth control. O⁶-methylguanine-DNA methyltransferase (MGMT) is involved in direct cleavage of mutagenic alkyl adducts within DNA (direct DNA repair). In this study the promoter methylation levels of p16^{INK4a} and MGMT genes which are associated with BC were investigated by Methylation-Sensitive PCR. We analysed primary tumor core biopsies from 96 high-risk primary BC patients and their histopathologic types were associated with the methylation levels. In our study the promoter hypermethylation status were observed at different rates; p16^{INK4a} and MGMT methylation frequencies were 43.8% and 34.4% respectively. The promoter hypermethylation levels of the genes found to be significant with ER positivity (+), PR (+), HER2/neu (+), E-Cadherin (+) and Ki-67 (<30%). In conclusion, our study shows that DNA methylation is a frequent event in BC and that different genes are methylated in BCs with different histopathological features.

Keywords: Breast cancer, Methylation, P16, MGMT, Histopathology

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P111. The Correlation between Lymph Node Metastasis and Methylation in Breast Cancer

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Abstract

Breast cancer (BC) is one of the most common malignancies with a high mortality rate among women. Invasion and metastasis are two important hallmarks of malignant tumors associated with complex genetic and epigenetic alterations that allow tumors to disseminate throughout lymphatics or blood vessels, giving rise to the colonization and growth of metastatic cells in distant organs. Considering that tumor dissemination is an early event in BC, genetic and epigenetic analysis of tumors and metastatic lesions could provide results for biomarker discovery and may improve diagnosis, prognosis and proper management of the treatment for BC patients. The contribution of aberrant DNA hypermethylation of cancer related genes to the transcriptional silencing and carcinogenesis has been demonstrated in different diseases including different cancer types [1]. We investigated the DNA methylation of MGMT, BMP6, p16^{INK4a}, RINT1, THBS1 and TIMP3 genes by Methylation Sensitive PCR. DNA methylation analysis of the candidate genes showed higher methylation proportion in the primary tumor tissue than that of the matched adjacent normal tissue from the same BC patients and the differences were significant for the p16^{INK4a} and RINT1 promoter regions ($P < 0.05$). MGMT and BMP6, ($P < 0.01$). THBS1 ($P < 0.001$). Our results showed methylation heterogeneity between primary tumors and metastatic lesion. The contribution of aberrant methylation alterations of BMP6, MGMT and THBS1 in lymph node metastasis might provide a further clue to establish useful biomarkers for screening metastasis.

Keywords: Breast cancer, Methylation, Lymph Node

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