

Methylation role of lncRNAs in breast cancer pathogenesis

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Epigenetic mechanisms, as promoter CpG islands methylation play a pivotal role in genes expression regulation, including long noncoding RNA (lncRNA) genes that involved in the pathogenesis of breast cancer (BC). The aim of this study was to assess the methylation status of 7 lncRNA genes in BC and the relationship with the morphological features of the tumor.

Methylation analysis was performed using quantitative methylation-specific PCR in 30 paired (tumor/normal) breast cancer samples. The significance of the results was assessed by the R statistics (Mann-Whitney U-test, Kolmogorov-Smirnov test, SPSS 20; $p < 0.05$).

The analysis of 7 lncRNA genes methylation level (MEG3, SEMA3B-AS1, HAND2-AS1, ZNF667-AS1, TINCR, MALAT, SNHG1) revealed statistically significant ($p < 0.001$) hypermethylation for MEG3, SEMA3B-AS1, HAND2-AS1, ZNF667-AS1; moreover, results for SEMA3B-AS1 and ZNF667-AS1 in breast cancer was shown for the first time. We also found the statistically significant ($p < 0.001$) increase of MEG3, SEMA3B-AS1, HAND2-AS1, ZNF667-AS1 methylation level on late stages (III-IV). A significant ($p < 0.001$) correlations between changes in the methylation level of the HAND2-AS1 lncRNA gene with tumor cells high size (T3/T4), the presence of lymph node metastases (NxMx) and a decrease level of differentiation (G3) were determined.

Thus, our results supplement the “molecular portrait” of breast cancer and contribute to understanding its pathogenesis. The revealed methylation features of the studied genes can be applicant for new approaches to the prognosis, prevention and treatment tactics for breast cancer.

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