

## Abstract

# Aberrantly Expressed Long Non-Coding RNAs and mRNAs in Breast Cancer and Their Interaction <sup>†</sup>

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<sup>†</sup> Presented at the 4th International Electronic Conference on Cancers, 6–8 March 2024; Available online: <https://sciforum.net/event/IECC2024>.

**Keywords:** long non-coding RNAs; mRNAs; breast cancer; apoptosis; epigenetic regulation

According to the latest global statistics for 2020, breast cancer (BC) has taken first place in the incidence of epithelial tumors, ahead of lung cancer, and is the main cause of mortality from cancer pathology among women around the world. Recently, the critical role of non-coding RNAs (ncRNAs) in the regulation of genes and signaling pathways in cancer pathogenesis, particularly apoptosis, has been identified.

The aim of our work was to identify new aberrantly expressed long non-coding RNAs and mRNAs in BC, as well as to study their possible interactions in BC.

**Materials and Methods.** Total RNA was isolated from paired breast cancer samples according to the standard method. Reverse transcription was performed using the MMLV RT kit # SK021 (Evrogen, Moscow, Russia), and qPCR was performed on a Bio-Rad CFX96 Real-Time PCR Detection System (Bio-Rad, Hercules, CA, USA) using the qPCRMix kit -HS SYBR (Evrogen, Moscow, Russia) according to the manufacturer's protocol. Data were analyzed using relative quantification based on the  $\Delta\Delta C_t$  method. Changes in the expression levels of lncRNAs and mRNAs were considered less than 2 times ( $|\Delta\Delta C_t| \leq 2$ ) as 'no changes'. qPCR was performed in three technical replicas.

**Results.** Changes in the expression level of the lncRNA ADAMTS9-AS1, OIP5-AS1, and mRNA of genes associated with apoptosis, such as APAF1, BAX, BAK1, BIM, and BCL2, were studied in breast cancer. We found decreased expression levels of ADAMTS9-AS1, OIP5-AS1, and APAF1 and BAX in 60 breast tumor samples compared with paired norms ( $p = 0.05$ ). The level of BCL2 expression is significantly ( $p = 0.001$ ) higher in breast tumors compared to the paired norm. A high statistically significant correlation was established between the expression of BIM and BAX ( $R_s = 0.48$ ,  $p = 0.01$ ). This result may indicate that the mRNA pairs may be involved in common processes of breast carcinogenesis. A highly significant positive correlation of expression was established for the pairs ADAMTS9-AS1–BAX ( $R_s = 0.67$ ,  $p = 0.01$ ), OIP5-AS1–BAK1 ( $R_s = 0.52$ ,  $p = 0.01$ ), and OIP5-AS1–BIM ( $R_s = 0.51$ ,  $p = 0.01$ ), suggesting a direct or indirect activating interaction of these pairs in breast cancer. The obtained data on coexpression are confirmed by the data obtained from correlation analysis carried out on a dataset showing differential expression levels of lncRNAs in breast cancer, selected from and complementary to the TCGA Tumor/TCGA Normal libraries.

**Conclusions.** lncRNAs and mRNAs that are differentially expressed in breast cancer have been identified; a positive correlation has been established in mRNA-mRNA and



**Citation:** Filippova, E.; Lukina, S.; Pronina, I.; Burdenny, A.; Kazubskaya, T.; Loginov, V.; Braga, E. Aberrantly Expressed Long Non-Coding RNAs and mRNAs in Breast Cancer and Their Interaction. *Proceedings* **2024**, *100*, 5. <https://doi.org/10.3390/proceedings2024100005>

Academic Editor: Stephen Geoffrey Ward

Published: 27 March 2024



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mRNA-lncRNA pairs in breast cancer, which indicates their participation in common signaling pathways in breast cancer. Determining new lncRNAs involved in the pathogenesis of BC and in the deregulation of apoptosis genes is one of the priority tasks of modern molecular oncology.

**Author Contributions:** Conceptualization, E.B. and E.F.; methodology, I.P.; T.K. and V.L.; performing experiments, S.L., I.P. and A.B.; data analysis, E.F. and A.B.; writing, E.F. All authors have read and agreed to the published version of the manuscript.

**Funding:** This work was supported by the Russian Science Foundation grant no. 22-75-00132.

**Institutional Review Board Statement:** The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of the Institute of General Pathology and Pathophysiology (protocol №1 03.03.2022; protocol №4 31.08.2023).

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** The data presented in this study are available on reasonable request from the corresponding author.

**Conflicts of Interest:** The authors declare no conflict of interest.

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