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Novel hyper methylated miRNA genes and its potential targets in breast cancer

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Epigenetic mechanisms including DNA methylation and interaction between miRNAs and mRNAs are the most dynamic mechanisms of genes deregulation in cancer. The aim of the study was to identify novel miRNA genes, regulated by DNA methylation, and target genes involved in the apoptosis, in breast cancer (BC). We used 58 paired (tumor/normal) BC samples, methylation-specific PCR, and quantitative PCR. Algorithms *of miR*Walk 2.0 database and the IBM SPSS statistics base 20 software package were used. We observed hyper methylation of 9 miRNA genes, and for the first time – *of MIR-127, -132, -1258* and *-193a*, and hypo-methylation *of MIR-191*. Using qPCR, we established a strong correlation between promoter methylation and expression levels for 10 miRNA genes, demonstrating the functional importance of altered methylation patterns. A strong association between hyper methylation *of MIR*-127 and *MIR-125b-1* and BC progression, particularly metastasis was found. The negative correlations were revealed between expression level alterations of 3 genes and 6 potential regulatory miRNAs for the following pairs: *BCL2* – miR-124-3p, -212-3p, -24.2-5p; *DAPK1–miR-127*-5p, miR-9; *RASSF1 (A)*–miR-375 (Rs=-0.43 - -0.32, $p \leq 0.01$, $p \leq 0.05$). The results of transfection of MCF7 cell line with miR-124-3p duplex oligonucleotide analogues strengthened the hypothesis on the direct or indirect interaction of this miRNA with mRNA of the *BCL2* gene. Thus, novel hyper methylated miRNA genes and potential interactions of *DAPK1*, *BCL2*, and *RASSF1 (A)* mRNAs with a number *of miR*NAs were identified that could be useful as markers and potential targets in combined BC therapy.

Biography

Eleonora A Braga has completed her PhD at Lomonosov Moscow State University, Bioorganic Chemistry Department. She has taken part in Russian Human Genome Project and HUGO. She was an Invited Principle Investigator at Karolinska Institute (Stockholm, Sweden, 1999-2000). She has completed her full Dr. of Biology Sc. at Engelhardt Institute of Molecular Biology in 2007. She is a head of Laboratory of Pathogenomics and Transcriptomics at Institute of General Pathology and Pathophysiology, Moscow, Russia. She has published more than 70 papers in reputed Journals.

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