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Investigating the role of nitric oxide on DNA methylation in breast cancer cells

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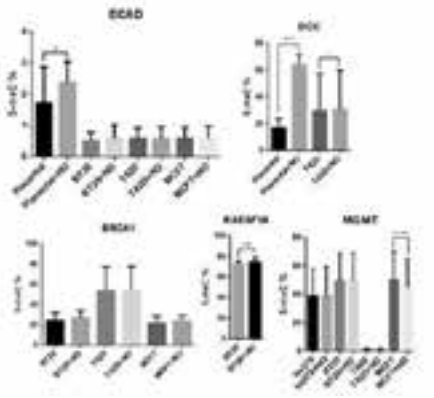
Introduction & Aim: Breast cancer is a predominant neoplastic disease among women and regardless of the disease subtypes it has been proposed that genetic mutations and epigenetic alterations caused by environmental factors may affect tumor development and growth. Nitric Oxide (NO), a free radical, is a well-known antioxidant has various roles in normal physiology. However, NO is also an important element in tumor microenvironment and has been linked to tumor growth. NO production is elevated in various human tumors including breast cancer. NO dependent gene regulation and histone methylation has been shown in cancer cells. As NO promoted deamination of 5-meC, it can be hypothesized that NO exposure can induce C-T transition in cancer cells. To exploit this hypothesis, we aimed to evaluate gene promoter methylation of BT-20, T42D and MCF-7 cell lines upon NO treatment.

Materials & Methods: Placental cell line was used for normal cell control. E-Cadherin (ECAD), Deleted in Colon Cancer (DCC), Breast Cancer 1 (BRCA1), Secreted Frizzled Related Protein 1 (SFRP1), Ras-association domain family 1 (RASSF1A), O-6-Methylguanine-DNA Methyltransferase (MGMT) promoter methylations were assessed before and upon no treatment using ion torrent next-generation sequencing system after bi-sulfite conversion. Promoter methylation was determined as percentage of cytosine reads of the total cytosine and thymine reads of each CpG site. To compare differences between groups, student t-test was applied.

Results: In control cell line, the effect of NO on DNA methylation was evaluated only for ECAD and DCC genes as the reading counts were below 100 for other genes. We found that NO exposure increased promoter methylation percentage of ECAD and DCC genes in placental cells ($p<0.05$). However, no significant change was seen on other cell lines for ECAD. DCC gene promoter methylation was found higher in T42D cells compared to placental cells and the methylation was increased upon NO exposure in both cell lines ($p<0.05$). We didn't find any significant chance in BRCA1 gene promoter methylation upon NO treatment in all cell lines. RASSF1A gene methylation in BT-20 cells and SFRP1 gene methylation in T42D cells were significantly increased upon NO treatment ($p<0.05$).

Conclusion: Our results can be further expanded using different cancer cell lines and interpreting the gene expression levels. We believe our results will contribute to the studies to further investigate the role of NO in regulation of gene expression in cancer cells.



Biography

Berna Demircan Tan has completed her PhD degree in Biochemistry. She completed her Postdoctoral training in USA in 2006-2010. Her research efforts have focused on the epigenetic basis of cancer, particularly DNA methylation. She has publications and book chapters on her research field. Currently, she is working as an Associate Professor at Istanbul Medeniyet University, Istanbul, Turkey.

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