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Study of the role of siRNA mediated promoter methylation in DNMT3B knockdown and alteration of promoter methylation of CDH1, GSTP1 genes in MDA-MB -453 cell line

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Promoter methylation is one of the main epigenetic mechanisms that leads to the inactivation of tumor suppressor genes during carcinogenesis. Due to the reversible nature of DNA methylation, many studies have been performed to correct theses epigenetic defects by inhibiting DNA methyltransferases (DNMTs). In this case novel therapeutics especially siRNA oligonucleotides have been used to specifically knock down the DNMTs at mRNA level. Also many studies have focused on transcriptional gene silencing in mammalian cells via siRNA mediated promoter methylation. The present study was designed to assess the role of siRNA mediated promoter methylation in DNMT3B knockdown and alteration of promoter methylation of Cadherin-1 (CDH1), Glutathione S-Transferase Pi 1(GSTP1), and DNMT3B genes in MDA-MB-453 cell line. MDA-MB-453 cells were transfected with siDNMT targeting DNMT3B promoter and harvested at 24 and 48 h post transfection to monitor gene silencing and promoter methylation. DNMT3B expression was monitored by quantitative RT-PCR method. Promoter methylation was quantitatively evaluated using differential high resolution melting analysis. A non-significant 20% reduction in DNMT3B mRNA level was shown only after first transfection with siDNMT. Promoter methylation levels of DNMT3B, CDH1, and GSTP1 were detected at about 15%, 70% and 10% respectively, in the MDA-MB-453 cell line, with no significant change after transfection.Our results indicated that siDNMT sequence were not able to affect promoter methylation and silencing of DNMT3B in MDA-MB-453 cells. However, quantitation of methylation confirmed a hypermethylated phenotype at CDH1 and GSTP1 promoters as well as a differential methylation pattern at DNMT3B promoter in breast cancer.

Biography

Mojgan Naghitorabi is an Assistant Professor of the School of Pharmacy at Ahvaz Jundishapur University of Medical Sciences, Iran. She received her Pharm D and PhD degrees from the School of Pharmacy and Pharmaceutical Sciences at Isfahan University of Medical Sciences, Iran. Her research interests lie in the area of epigenetics, regulation of gene expression, RNA interference, and cancer. She has published four papers in her research field.

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