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Reversal of hypermethylation and reactivation of glutathione S-transferase pi 1 gene by curcumin in breast cancer cell line

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Abstract

Background

One of the mechanisms for epigenetic silencing of tumor suppressor genes is hypermethylation of cytosine residue at CpG islands at their promoter region that contributes to malignant progression of tumor. Therefore, activation of tumor suppressor genes that have been silenced by promoter methylation is considered to be very attractive molecular target for cancer therapy. Epigenetic silencing of glutathione S-transferase pi 1, a tumor suppressor gene, is involved in various types of cancers including breast cancer. Epigenetic silencing of tumor suppressor genes can be reversed by several molecules including natural compounds such as polyphenols that can act as a hypomethylating agent. Curcumin has been found to specifically target various tumor suppressor genes and alter their expression. To check the effect of curcumin on the methylation pattern of glutathione S-transferase pi 1 gene in MCF-7 breast cancer cell line in dose-dependent manner.

Material and Methods

To check the reversal of methylation pattern of hypermethylated glutathione S-transferase pi 1, MCF-7 breast cancer cell line was treated with different concentrations of curcumin for different time periods. DNA and proteins of treated and untreated cell lines were isolated, and methylation status of the promoter region of glutathione S-transferase pi 1 was analyzed using methylation-specific polymerase chain reaction assay, and expression of this gene was analyzed by immunoblotting using specific antibodies against glutathione S-transferase pi 1.

Results

A very low and a non-toxic concentration (10μM) of curcumin treatment was able to reverse the hypermethylation and led to reactivation of glutathione S-transferase pi 1 protein expression in MCF-7 cells after 72h of treatment, although the IC50 value of curcumin was found to be at 200μM. However, curcumin less than 30μM of curcumin could not alter the promoter methylation pattern of glutathione S-transferase pi 1.

Conclusion

Treatment of breast cancer MCF-7 cells with curcumin causes complete reversal of glutathione S-transferase pi 1 promoter hypermethylation and leads to re-expression of glutathione S-transferase pi 1, suggesting it to be an excellent non-toxic hypomethylating agent.

Biography

Dr. Umesh Kumar has done his doctoral thesis entitled "Epigenetic Regulation in Breast Carcinogenesis" in Dr. B. R. Ambedkar Center for Biomedical Research (ACBR), Delhi University (North Campus) in 2013. From his thesis he was able to publish his interesting findings in peer reviewed international journals of repute. He has received excellent training in various molecular biology techniques including DNA, RNA and protein preparation, PCR, single strand conformation polymorphism (SSCP), Automated DNA sequencing, Next-Generation Sequencing, methylation specific PCR, RT-PCR, western blotting, EMSA, ELISA, mammalian cell culture, Immunohistochemistry, FISH, FACS and other associated advanced molecular biology techniques.

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