Combined EGFR and c-Src Antisense Oligodeoxynucleotides Encapsulated with PAMAM Dendrimers Inhibit HT-29 Colon Cancer Cell Proliferation.

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Source

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Abstract

Colon cancer continues to be one of the most common cancers, and the importance and necessity of new therapies needs to be stressed. The most important proto-oncogen factors for colon cancer appear to be epidermal growth factor receptor, EGFR, and c-Src with high expression and activity leading to tumor growth and ultimately to colon cancer progression. Application of c-Src and EGFR antisense agents simultaneously should theoretically therefore have major benefit. In the present study, anti-EGFR and c-Src specific antisense oligodeoxynucleotides were combined in a formulation using PAMAM dendrimers as a carrier. Nano drug entry into cells was confirmed by flow cytometry and fluorescence microscopy imaging and real time PCR showed gene expression of c-Src and EGFR, as well as downstream STAT5 and MAPK-1 with the tumor suppressor gene P53 to all be downregulated. EGFR and c-Src protein expression was also reduced when assessed by western blotting techniques. The effect of the antisense oligonucleotide on HT-29 cell proliferation was determined by MTT assay, reduction being observed after 48 hours. In summary, nano-drug, anti-EGFR and c-Src specific antisense oligodeoxynucleotides were effectively transferred into HT-29 cells and inhibited gene expression in target cells. Based on the results of this study it appears that the use of antisense EGFR and c-Src simultaneously might have a significant effect on colon cancer growth by down regulation of EGFR and its downstream genes.

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