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Immunoliposomes for Co-Delivery of Doxorubicin and Ribonucleotide Reductase M2 Sirna Inhibit of Gastric Cancer Growth

Authors : Jie Gao

Abstract : The combination of chemotherapy with gene therapy is highly effective in cancer therapy. To achieve combined therapeutic effects in human gastric cancer over expressing EGFR, we developed targeted LPD (liposome-polycation-DNA complex) conjugated with anti-EGFR (epidermal growth factor receptor) Fab' for co-delivery of doxorubicin (DOX) and ribonucleotide reductase M2 (RRM2) siRNA (DOX-RRM2-TLPD). The results showed that EGFR was over expressed in several gastric cancer cell lines and gastric cancer tissues. Gene Expression Omnibus (GEO) results showed that RRM2 expression was significantly higher in gastric cancer than in non-gastric cancer tissue, and RRM2 siRNA inhibited the proliferation of several gastric cancer cells, indicating that RRM2 is a candidate target for gastric cancer therapy. Confocal studies and flow cytometry showed that DOX-RRM2-TLPD delivered DOX and RRM2 siRNA to EGFR over expressing gastric cancer cells specifically and efficiently both in vitro and in vivo, resulting in enhanced therapeutic effects (cytotoxicity and apoptosis) compared with single-drug loaded or non-targeted controls, including DOX-NC-TLPD (targeted LPD co-delivering DOX and negative control siRNA), RRM2-TLPD (targeted LPD delivering RRM2 siRNA) and DOX-RRM2-NTLPD (non-targeted LPD co-delivering DOX and RRM2 siRNA). The in vivo antitumor assay showed that the average weight of the gastric cancer in mice treated with DOX-RRM2-TLPD was significantly lighter than that of mice treated with other controls. DOX-RRM2-TLPD represents an effective approach for combined therapy of gastric cancer over expressing EGFR.

Keywords : gene therapy, chemotherapy, immunoliposomes, gastric cancer
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