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#4389 siRNA mediated knockdown of Bcl-2 and low-dose taxol treatment in human glioblastoma U251MG cells induces apoptosis, inhibits cell invasion, angiogenesis, and tumor growth in nude mice. Joseph George, Naren L. Banik, Swapan K. Ray. Medical University of South Carolina, Charleston, SC.

RNA interference using siRNA is a powerful tool to knockdown the mRNA and thus protein level of a target gene. Taxol is an anti-cancer drug that binds to β-tubulin to prevent tumor cell division; however, higher doses of taxol may be toxic to normal cells. The anti-apoptotic molecule Bcl-2 is upregulated in cancer cells for protection from apoptosis. The aim of our present study was to downregulate Bcl-2 expression using cognate siRNA in a highly invasive glioblastoma cell line (U251MG) during a low-dose taxol treatment and to examine apoptosis, inhibition of cell invasion, angiogenesis, and tumor growth. Human glioblastoma U251MG cells were treated with 100 nM taxol or 100 nM Bcl-2 siRNA or both for 72 h. Semiquantitative reverse transcription-polymerase chain reaction (RT-PCR) and Western blotting demonstrated around 80% knockdown of Bcl-2 mRNA and protein levels. Fluorescent activated cell sorting (FACS) analysis and the terminal deoxynucleotidyl transferase mediated dUTP nick end labeling (TUNEL) assay demonstrated apoptosis in almost 60% of cells after combination treatment with taxol and Bcl-2 siRNA. Matrigel invasion studies demonstrated a significant decrease in cell invasion after treatment with taxol and Bcl-2 siRNA. In vivo angiogenesis assays in immunocompromised mice showed complete inhibition of neo-vasculature after treatment with both agents. The combination treatment with taxol and Bcl-2 siRNA further demonstrated a remarkable decrease in growth of both subcutaneous and intracerebral tumors in nude mice. Taken together, the results of our study indicated that the combination treatment with taxol and Bcl-2 siRNA effectively induced apoptosis and inhibited cell invasion, angiogenesis, and tumor growth. Therefore, this combination therapeutic strategy offers a potential tool for the controlling the growth of human glioblastoma. This work was supported by the R01 CA-91460 grant from the NCI.

Citation Format

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