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Anti-cancer effect of CpG ODN combined with radiotherapy is through the toll-like receptor 9 signaling pathway

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Malignant tumor is a major public health problem in China. We have recently demonstrated that synthetic oligodeoxynucleotides (ODNs) that contain unmethylated-CpG motifs (CpG ODN) may induce immune responses in cancer patients and have potent radiosensitive effect against solid tumors *in vivo*. CpG ODN may affect cancer cell behavior through the toll-like receptor 9 (TLR9) signaling pathway that mediated immune inflammation reaction in the progression of the malignant tumor. However, the mechanism of the anti-cancer effect of CpG ODN via TLR9 remains unclear. The purpose of the study is to examine the role of TLR9 in the human malignant tumor. We found that the increased level of TLR9 expression in the tumor tissue in patients with colorectal cancer (n=86) was associated with the increased level of CEA, poor-differentiation, invasion and liver metastasis. The activation of the TLR9 signaling pathway was involved in the development of human colorectal cancer. *In vitro* studies showed that CpG ODN, as a TLR9 ligand, can increase the radiosensitivity through the TLR9 that directly induced cell apoptosis and inhibited cell proliferation in human lung cancer and laryngeal carcinoma. Furthermore, we observed that the expression of TLR9 in radioresistant cells of human lung adenocarcinoma was higher than it in radiosensitive cells. Treatment of human lung cancer cells with CpG ODN combined with radiation resulted in a significant reduction of CD133 and Oct-4 expression in radioresistant cells. Moreover, our study demonstrated that CpG ODN combined with radiotherapy was able to downregulate the PD-L1 expression through the NF- κ B signaling pathway in lung cancer. Thus, our data suggests that the application of CpG ODN via the signal activation of TLR9 may have a therapeutic value for the treatment of human cancer.

Biography

Tiankui Qiao has completed his MD at Hebei Medical University. He is the Director of the Department of Oncology at Jinshan Hospital of Fudan University. His research interest is focused on clinical study of lung cancer and radiotherapy. He has published more than 40 papers in reputed journals.

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