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Interaction of CpG-Oligodeoxynucleotides with Toll Like Receptor 9 Induces Apoptosis and Modulates Metaloproteinase-2 Activity in Human Intestinal Epithelium

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Abstract:

Recent reports have indicated different effects of immunostimulatory sequences containing CpG-Oligodeoxynucleotides (ODN) on various immune cells. However, the exact role of CpG-ODN in the human gut is unclear.

In the present study, we assessed potential effects of CpG-ODN on non lymphoid cell (intestinal epithelial cell line HT-29) on a dose-response and time-course basis. Intestinal epithelial cell line HT-29 was treated with CpG-ODN (CpG 2006) and lipopolysaccharide (LPS) at 5, 10, 25, 50 µg/ ml and 1, 5, 10 µg/ ml concentrations, respectively. Following treatments, dose- response and time-course cytotoxicity using a colorimetric method, Metaloproteinase-2 (MMP-2) activity (using gelatin zymography) and apoptosis (using annexin-v flowcytometry method) assays were performed. Chloroquine treatment was also used for its inhibitory effect on endosomal acidification process to verify specific CpG-ODN and Toll Like Receptor 9 (TLR9) interactions.

Cytotoxicity analysis of CpG-ODN showed that CpG-ODN increased significantly the proliferation of CpG-ODN treated cells, as compared to untreated cells, at concentrations of 10-25 µg/ml ($p < 0.05$). Overall MMP-2 activity analysis showed significant differences between treated and untreated cells. However, minimal changes were observed when MMP-2 activity was assessed per cell. Moreover, CpG-ODN treated cells demonstrated an increasing apoptosis rate of 0.8 %, 6.46 % and 14.21% at concentrations of 5, 10, 25 µg/ml, respectively.

Collectively, our data indicated that intestinal epithelial cell line HT-29 is highly responsive to CpG effect in vitro and exhibits modified activities. The direct CpG-ODN and TLR-9 interactions in HT-29 cells could provide new approaches in malignant tumor therapeutic strategies.

Keywords:

CpG-ODN ، HT-29 ، TLR9

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