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**Title:** Synergistic effect of LPS and 5-Fluorouracil on TLR4 expression in HCT116 colorectal cancer cell line expressing different variants of TLR4

**Authors:** Davoodi, H .1,3 *, S. R. Hashemi2, H. F. Seow3

**Abstract:** Background and Objectives: Toll-like receptors (TLRs) are a class of proteins that play a key role in the innate immune system. TLR4, which is considered one of the most important TLRs, recognizes LPS of Gram-negative bacteria. Two cosegregating single nucleotide polymorphisms (SNPs) of the human TLR4 gene, namely Asp299Gly (D299G) and Thr399Ile (T399I), have been correlated with hyporesponsiveness to inhaled lipopolysaccharide (LPS). 5-Fluorouracil (5-FU) is widely used for the treatment of patients with advanced colon cancers. Resistance to 5-FU is one of the most prominent obstacles to successful chemotherapy. The propose of this study was to investigate the effect of LPS and 5-FU on expression of TLR4 in HCT116 colorectal cancer cell line with different variants of TLR4.

**Materials and Methods:** HCT116 colorectal cancer cell line was transfected with Flag-CMV1-TLR4 wild-type (WT) and Flag-CMV1-TLR4 mutants, D299G and T399I expression plasmids. Transfected HCT116 cells were treated with different concentration of 5-FU in the presence or absence of LPS. The expression of TLR4 on 5-FU-treated HCT116 cells was analysed by FACS.

**Results:** 5 -FU significantly increased the expression of TLR4 protein on HCT116 cell line. LPS had synergistic effect with 5-FU to induce TLR4 expression. 5-FU and LPS induced TLR4 expression in wild-type cells stronger than the other cells (P<0.05).

**Conclusion:** LPS has a synergistic effect with 5-FU to induce the expression of TLR4 both in cells with wild-type and mutant TLR4 and response of the wild-type cells to 5-FU and LPS was stronger than mutants.

**Colorectal cancer, LPS, Polymorphism, TLR4**

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