

Expression of Functional TLRs in Human Uterine Myocytes

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ABSTRACT:

INTRODUCTION: Infection and/or inflammation are commonly associated with preterm delivery (PTD), especially preceding 30 weeks of gestation. To better understand these phenomena, murine and other animal models have been utilized to replicate the inflammatory events that trigger PTD. Research has shown activation of the innate immune response triggers PTD in 24 hours or less in the pregnant mouse. Lipopolysaccharide (LPS) and other pathogen associated molecular pattern molecules (PAMPs) have been shown to stimulate Toll-like receptors (TLRs) and trigger PTD in these animal model. LPS, the ligand/agonist for the TLR4 receptor, is found in the membrane capsule of gram-negative bacteria. Previous studies have demonstrated TLR4 expression in whole uterine tissue; however, none of these studies have determined if functional TLR4 receptors are actually present on smooth muscle myocytes.

METHODS: This study sought to assess if human smooth muscle myocytes express TLRs and are responsive when stimulated with PAMPs. Specifically, these studies were performed using in vitro cultures of human uterine myocytes. Control and stimulated cells (containing 1 - 100 ng/mL of LPS) were incubated in 6-well plates for 12, 24, and 48 hours. Subsequently, the culture media underwent ELISA analysis for the IL-6 cytokine (released upon stimulation of the TLR4 receptor).

RESULTS: Based on multiple sets of experiments, these studies demonstrated significantly increased expression of IL-6 in the culture media corresponding to increasing concentration of LPS treatment and allotment of time. These data are consistent with the presence of functional TLR4 receptors on the surface of human smooth muscle myocytes.

CONCLUSIONS: Based on these results, it may be possible to use the information gathered to reveal alternate methods involving the inhibition of TLR4 signaling to prevent preterm delivery.