

Molecular mechanisms of lipopolysaccharide-caused induction of surfactant protein-A gene expression in human alveolar epithelial A549 cells (revised)

陳大樑

Chuang CY;Chen TL;Chen RM

摘要

Abstract

Surfactant proteins (SPs) participate in the physiological and pathophysiological regulation of sepsis-induced acute lung injury. Lipopolysaccharide (LPS), a Gram-negative bacterial outer membrane component, is one of the major causes of septic shock. This study was designed to evaluate the effects of LPS on the regulation of SP-A and SP-D gene expressions in human alveolar epithelial A549 cells. Exposure of A549 cells to LPS increased SP-A mRNA synthesis in concentration and time-dependent manners without affecting SP-D mRNA production. LPS selectively enhanced translocation of transcription factor c-Jun from the cytoplasm to nuclei, but not nuclear factor kappa-B. In parallel, the DNA-binding activity of AP-1 was increased by LPS. Pretreatment of A549 cells with SP600125, an inhibitor of c-Jun N-terminal kinase, decreased c-Jun translocation, and significantly ameliorated LPS-induced SP-A mRNA production. Levels of toll-like receptor (TLR2) mRNA in A549 cells were time-dependently induced following LPS treatment. Application of TLR2 small interference (si)RNA into A549 cells significantly knocked-down the translation of this receptor, and simultaneously alleviated LPS-induced SP-A synthesis. Taken together, this study has shown that LPS selectively induces SP-A gene expression possibly through TLR2-mediated activation of c-Jun in human alveolar epithelial A549 cells.

Keywords: Alveolar epithelial cells; Lipopolysaccharide; Surfactant protein-A; Toll-like receptor 2; c-Jun