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LPS stimulates MUC5AC expression in human biliary epithelial cells: whether there exists a possible pathway of PKC/NADPH/ROS?

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Abstract Previous studies have shown that lipopolysaccharide (LPS) can upregulate MUC5AC in airway epithelial cells. However, the relationship and mechanism between bacterial infection and altered mucus secretion in the biliary tract remains unclear. Human biliary epithelial cells were induced by LPS, H_2O_2 production in the cell supernatants were detected by specific kit and expression of MUC5AC were detected by real-time PCR, Western blot, and immunohistochemistry. H_2O_2 production increased in a dose-dependent manner, LPS upregulate MUC5AC expression in both mRNA and protein level while specific inhibitors can reduce this high expression. Reactive oxygen species participates in the process of LPS by upregulating MUC5AC secretion. Moreover, PKC and NADPH oxidase regulate MUC5AC production in LPS-challenged human biliary epithelial cells.

Keywords LPS · MUC5AC · ROS · PKC · NADPH oxidase

Introduction

Brown pigment stones are major calculi in hepatolithiasis, and bacterial infection is thought to be crucial to their formation. Bile is normally sterile. Nevertheless, bacteria are frequently found in the bile of patients with intrahepatic cholelithiasis [1]. The most common bacteria found in bile are *Escherichia coli* followed by *Klebsiella* [1, 2]. Lipopolysaccharide (LPS), a Gram-negative bacterium endotoxin, is a major outer surface membrane component of Gram-negative bacteria such as *E. coli*. Previous studies have shown that LPS plays an important role in Gram-negative bacterial infection and pathogenesis.

Hyperplasia cholangitis of the intrahepatic biliary tree, which is responsible for mucin production, is thought to be another significant factor involved in lithogenesis. The biliary tree and secretory glands of hyperplasia cholangitis patients are pathologically characterized as chronically inflamed and hyperplastic. Most of the hyperplastic secretory gland maintains the ability to secrete mucin, and the aberrant secretion of mucin forms a microenvironment that facilitates lithogenesis. Mucin distribution in epithelial mucosae functions to lubricate and protect the epithelial surface. Mucin production shows tissue-specific and cell-specific expression and distribution in humans. To date [3–6], more than 20 types of mucin have been reported, and six of them (MUC1, MUC2, MUC3, MUC5AC, MUC5AB, and MUC6) have been found in the biliary tract. Normally, MUC5AC is marginally present in bile, whereas much more MUC5AC is observed in the context of hepatolithiasis [7]. Recent studies have shown that the overexpression of mucin may be related to the development of biliary diseases such as hepatolithiasis [8].

The relationship between bacterial infection and overexpression of MUC5AC has been shown in the respiratory tract. Several studies have shown that LPS can induce the overexpression of MUC5AC in human airway epithelial cells. These studies showed that the PKC–NADPH oxidase (Nox) pathway, EGFR-p38/JNK pathway as well as AQP5, MMP-9, phorbol-12-myristate 13-acetate (PMA), neutrophil elastase, and cigarette smoke can increase the secretion of MUC5AC [9–20].

Min Li and Yu Tian have contributed equally to this study.

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