Treatment of 6-bromo-indirubin-3'-oxime (6-BIO) attenuates inflammation of proximal tubular epithelial cells through suppression of adhesion molecules and monocyte chemoattractant protein-1 (MCP-1) in LPS-stimulated mononuclear cells

**Objectives:**

Sepsis is a clinical problem which causes an acute kidney injury (AKI) and a high risk of developing chronic kidney disease (CKD). The aim of this study was to investigate whether there was a cross-talk between tubular epithelial cells and mononuclear cells in the lipopolysaccharide induced inflammation, and whether 6-BIO, a glycogen synthase kinase-3β inhibitor, attenuated inflammation in human proximal tubular epithelial cells co-cultured lipopolysaccharide stimulated mononuclear cells.

**Methods:**

We evaluated the inflammatory response such as cytokine, chemokines, and interaction adhesion molecules in human proximal tubular epithelial (HK-2) cells co-cultured with LPS-stimulated mononuclear cells. The effects of 6-BIO on LPS-induced cytokine and chemokine, and adhesion molecules were determined using co-culture of human renal proximal tubular epithelial (HK-2) cells and human mononuclear (U937) cells. The effects of LPS and 6-BIO on cell viability were determined using EZ-CyTox assays. The protein and mRNA expression of MCP-1, cadherin, and selectin was determined by semi-quantitative immunoblotting and RT-PCR. Intracellular staining of TNF-α, INF-γ, IL-6 was determined by using flow cytometry and confocal laser microscopy.

**Results:** HK-2 cells co-cultured with LPS-stimulated mononuclear cells showed increased expression of inflammatory cytokine such as MCP-1, INF-γ, TNF-α, and IL-6 and adhesion molecule such as E-selectin, L-selectin, ICAM-1, and VCAM-1. Pre-treatment of 6-BIO in LPS-stimulated mononuclear cells and co-cultured with HK-2 cells revealed significantly attenuated the expression of cytokine, chemokine, and adhesion molecules compared with in HK-cells co-cultured with LPS-stimulated mononuclear cells without 6-BIO pretreatment.

**Conclusions:**

Glycogen synthase kinase-3β inhibitor, 6-BIO attenuated inflammation in human proximal tubular epithelial cells through suppressing the activation of cytokine, chemokines, and interaction adhesion molecules in LPS stimulated mononuclear cells.