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# Inhibition of JAK/STAT Pathway Ameliorates LPS-induced Cell Adhesion Molecule Expression and Myocardial Dysfunction

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## Inhibition of JAK/STAT Pathway Ameliorates LPS-induced Cell Adhesion Molecule Expression and Myocardial Dysfunction

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Vascular endothelial cells play an important role in leukocyte trafficking during inflammatory process. Pro-inflammatory cytokines activate the endothelial cells to express cell adhesion molecules. Janus kinase/signal transducers and activators of transcription (JAK/STAT) is one of the major intracellular cytokine signaling and involved in pathogenesis of renal ischemia/reperfusion injury, diabetic nephropathy. The purpose of our study is to investigate the mechanism of LPS-induced cell adhesion molecule and myocardial dysfunction by regulation of JAK/STAT pathway in the human umbilical vein endothelial cells (HUVECs) and endotoxemic mice.
JAK3 inhibitor, JANEX-1, decreased TNF-$\alpha$-induced ICAM-1, VCAM-1 and fractalkine expression in the HUVECs. JAK3 inhibitor mediated downregulation of adhesion molecule expression was mediated through suppression of NF-$\kappa$B activation and STAT3 phosphorylation. JANEX-1 inhibited monocyte adhesion to HUVECs stimulated by TNF-$\alpha$. In endotoxemic mice, JANEX-1 decreased LPS-induced ICAM-1 and MCP-1 expression and myocardial dysfunction.
These results demonstrated that inhibition of JAK/STAT pathway by JANEX-1 ameliorates LPS-induced cell adhesion molecule expression and myocardial dysfunction.

**Key Words:** 내독소, 패혈증 모델, JAK/STAT pathway
Endotoxin, Sepsis, JAK/STAT pathway