

**P001** The Effect of Mitogen-Activated Protein Kinase Phosphatase-2 (MKP-2) Over-Expression on LPS and Cytokine -Mediated Induction of Inflammatory Genes in Endothelial Cells

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In different cell types, including endothelial cells, LPS and cytokines stimulate a number of inflammatory genes, such as cell adhesion molecules (CAMs) and COX-2, through the activation of the mitogen-activated protein kinases (MAPK), ERK1/2, JNK and p38. It has also been shown that MKP-2, a member of the mitogen-activated protein (MAP) kinase phosphatase family, plays an important role in the feedback control of MAP kinase-mediated gene expression. Therefore, the effect of adenovirus (Adv.) wild type-MKP-2 upon LPS and cytokines stimulation of MAP kinases and inflammatory genes production was examined. In Human umbilical vein endothelial cells (HUVECs), TNF- $\alpha$  stimulated the activation of all MAPKs, whilst JNK was predominantly activated by LPS. Both stimuli lead to an increase of ICAM-1, VCAM-1 and COX-2 expression. Moreover, infection with Adv. Wild type-MKP-2 (100-300 pfu) essentially abolished JNK phosphorylation. However, surprisingly Adv. MKP-2 increased the expression of ICAM-1 and VCAM-1. Data regarding COX-2 will be presented.