TLR4/NF-κB signaling pathway-mediated and oxLDL-induced up-regulation of LOX-1, MCP-1, and VCAM-1 expressions in human umbilical vein endothelial cells

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ABSTRACT. This study aimed to investigate the function and signaling pathway of Toll-like receptor 4 (TLR4) in oxidized low-density lipoprotein (oxLDL)-induced up-regulated expressions of oxidized LDL receptor 1 (LOX-1), monocyte chemoattractant protein 1 (MCP-1), and vascular cell adhesion molecule 1 (VCAM-1) in human umbilical vein endothelial cells (HUVECs). HUVECs were incubated with different oxLDL concentrations (0, 20, 40, 60, and 80 µg/mL) for 24 and 48 h. The influence of oxLDL on TLR4, LOX-1, MCP-
1, and VCAM-1 expressions in HUVECs was detected by real-time polymerase chain reaction and Western blot analysis. HUVECs were transfected with small interfering RNA targeting TLR4 (siTLR4), in which protein expressions of LOX-1, MCP-1, and VCAM-1, and the nuclear translocation of NF-κB (P50) were detected by Western blot. After 48 h of processing HUVECs with pyrroldine dithiocarbamate (PDTC), protein expressions of TLR4, LOX-1, MCP-1, and VCAM-1 were detected by Western blot. OxLDL induced a concentration-dependent up-regulation of mRNA and protein expressions of TLR4, LOX-1, MCP-1, and VCAM-1 in HUVECs (P < 0.001). siTLR4 significantly reduced protein expressions of LOX-1, MCP-1, VCAM-1, and reduced the NF-κB (P50) nuclear translocation (P < 0.001). PDTC significantly inhibited protein expressions of TLR4, LOX-1, MCP-1, and VCAM-1 (P < 0.001). Results of this study demonstrate that the TLR4/NF-κB signaling pathway has an important function in the up-regulation of oxLDL-induced expressions of LOX-1, MCP-1, and VCAM-1 in HUVECs.

Key words: Oxidized low-density lipoprotein (LDL); NF-κB; Toll-like receptor-4; Lectin-like oxidized LDL receptor-1; Vascular cell adhesion molecule-1; Monocyte chemotactic protein-1