Role of ox-LDL and LOX-1 in inflammation

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Oxidized LDL (ox-LDL) represents a key biomarker of oxidative vascular damage; furthermore they are strongly associated to cardiovascular disease and inflammation processes. It has been demonstrated that ox-LDL uptake, through the oxidized lipoprotein receptor-1 (LOX-1) expressed on endothelial cells surface, induces endothelial dysfunction, superoxide anions production, nitric oxide inhibition/reduction and NF-kB activation. The aim of this study was to evaluate the effect of plasma LDL and ox-LDL on IL-6 production and IL-6 role in modulation of lipoprotein receptors, as LDL-receptor (LDL-R) and LOX-1, in human microvascular endothelial cells-1 (HMEC-1). HMEC-1 were exposed 24 h to increasing doses of native LDL and ox-LDL to quantify IL-6 production. Moreover, endothelial cells were incubated 24 h with increasing doses of IL-6 to analyze LDLR and LOX-1 gene expression. Test ELISA and qRT-PCR were performed. Endothelial cells treated with LDL and ox-LDL showed a significant and dose-dependent increase of IL-6, associated with the degree of oxidation. Furthermore, treatment with increasing doses of IL-6 induced a significant raise of LDLR (up to 1 µg/ml of IL-6) and LOX-1 expression. Our data suggest the presence of a compensatory mechanism in microvascular endothelial cells during acute inflammation; indeed, IL-6 induction, mediated by LDL and ox-LDL, is responsible for a strong raise in lipid receptors expression.