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Short Communication

Modified LDL particles activate inflammation and ER-stress in monocyte-derived macrophages

Chegodaev E.S

Institute of General Pathology and Pathophysiology, Russian Federation

Abstract

Aim: Cholesterol accumulation in arterial cells triggers atherogenesis at the cellular level. The aim of this work was to identify the genes responsible for cholesterol accumulation caused by modified LDL.

Methods: Monocytes were isolated from the blood of healthy individuals and futher differentiated into macrophages. Intracellular cholesterol accumulation was induced by incubation of cultured cells with native and modified LDL: oxidized, desialylated and acetylated. Total RNA was sequenced using Illumina HiSeq 3000. The role of identified by Genexplain platform genes in cholesterol accumulation were evaluated by siRNA.

Results: Modified LDL caused significant 1.5- to 3-fold increase in intracellular cholesterol level as compared with native LDL. Treatment of macrophages with modified LDL resulted in up-regulation of genes involved in the inflammation and immune responses, without affecting the activity of known cholesterol metabolism-regulating genes. Integrated promoter-pathway analysis was performed to identify the master-regulators not only associated but also responsible for cholesterol accumulation. We identified that PERK/eIF2/CHOP signaling pathway inducing by ER-stress is highly responsible for intracellular cholesterol accumulation. Moreover, the knockdown of gene PERK in human macrophages totally canceled the cholesterol accumulation under the treatment by modified LDL.

Conclusions: We assume that ER-stress-induced inflammation could play the critical role in foam cell formation.

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Biography

Chegodaev is PhD-student working in Laboratory of Angiopathology, Institute of General Pathology and Pathophysiology, Moscow, Russian Federation.

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