

Abstract

J Lipid Res. 1998 May;39(5):1008-20.

Oxidized type IV hypertriglyceridemic VLDL-remnants cause greater macrophage cholesteryl ester accumulation than oxidized LDL.

Whitman SC, Sawyez CG, Miller DB, Wolfe BM, Huff MW.

Department of Medicine, Robarts Research Institute at The University of Western Ontario, London, Canada.

OBJECTIVE: We have previously shown that very low density lipoproteins (VLDL, Sf 60-400) from subjects with type IV hyperlipoproteinemia (HTG-VLDL) will induce appreciable cholesteryl ester accumulation in cultured macrophages (J774A.1). The present study examined whether copper-mediated oxidative modification of HTG-VLDL and their remnants would further enhance cholesteryl ester accumulation in J774A.1 cells.

METHODS AND RESULTS: Incubation with oxidized VLDL-remnants caused the greatest increase in cellular cholesteryl ester concentrations (54-fold) relative to control cells ($P = 0.001$). HTG-VLDL and VLDL-remnants each induced similar increases in cholesteryl ester levels (32.3- and 35.8-fold, respectively; both $P = 0.001$), whereas incubation with oxidized HTG-VLDL brought about only a 20.6-fold increase in cholesteryl ester concentrations ($P = 0.014$). The increase in cellular cholesteryl ester concentrations induced by oxidized VLDL-remnants was significantly higher ($P < \text{or} = 0.04$) than that induced by all other lipoproteins tested including low density lipoprotein (LDL) and oxidized LDL which caused a 6.7- and a 35.1-fold increase ($P < \text{or} = 0.0002$ for both), respectively. Unlike HTG-VLDL and to a lesser extent VLDL-remnants, uptake of oxidized VLDL and oxidized VLDL-remnants did not require catalytically active, cell secreted lipoprotein lipase. Co-incubation with polyinosine, which blocks binding to the type I scavenger receptor, completely inhibited the cholesteryl ester accumulation induced by oxidized HTG-VLDL, oxidized VLDL-remnants and oxidized LDL ($P < \text{or} = 0.02$).

CONCLUSION: We conclude that oxidation of VLDL-remnants significantly enhances macrophage cholesteryl ester accumulation compared to either HTG-VLDL, VLDL-remnants, or oxidized LDL. Uptake of oxidized VLDL and oxidized VLDL-remnants does not require catalytically active lipoprotein lipase, and involves a receptor that can be competed for by polyinosine.

PMID: 9610767

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