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Stimulation of LDL Receptor Activity in Hep G2 Cells and Isolated Human Hepatocytes by High Density Serum Fractions

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In contrast with fibroblasts, in Hep G2 cells the LDL receptor activity was increased 3-fold upon increasing the concentration of normal whole serum in the culture medium from 20 to 100% by volume. Incubation of the Hep G2 cells with physiological concentrations of LDL resulted in a maximally 2-fold decrease in LDL receptor activity as compared with incubation under serum-free conditions (10-fold decrease in fibroblasts). Incubation with physiological concentrations of HDL with density between 1.16 and 1.20 g/ml (heavy HDL; 250 μ g apo A-I/ml) resulted in an about 7-fold increase in LDL receptor activity (1.5-fold in fibroblasts). Simultaneous incubation of Hep G2 cells with LDL and heavy HDL (both 200 μ g/ml) resulted

in a 3-fold stimulation of the LDL receptor activity as compared with incubation in serum-free medium without any addition (10-fold decrease in fibroblasts). Cultured human hepatocytes behaved similarly to Hep G2 cells with respect to weak reduction and strong stimulation of the LDL receptor activity by incubation with respectively LDL and heavy HDL. Incubation of Hep G2 cells with LDL or heavy HDL did not influence Hep G2 cells' capacity to synthesize and secrete apolipoprotein A-I and E. Modification of heavy HDL by lecithin: cholesterol acyltransferase (LCAT) enhanced the capability of heavy HDL to stimulate the LDL receptor activity. However, the presence of active LCAT in the culture medium was no requirement for the observed stimulation. We suggest that the plasma level of heavy HDL together with its modification by LCAT are important determinants of receptor-mediated catabolism of LDL by the liver in vivo.

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