The LDL Receptor Regulates Hepatic ApoB-Containing Lipoprotein Secretion through an Intracellular Mechanism

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Abstract
Hyperlipidemia is an age-related disorder that is linked with several diseases such as diabetes, atherosclerosis, and Alzheimer’s disease. Hyperlipidemia results from defects in either the secretion or clearance of plasma lipoproteins, which is controlled primarily by the liver. It has been known that the binding of free low density lipoprotein (LDL) and other lipoproteins is mediated by the LDL receptor (LDLR). Our laboratory discovered a novel role of the LDLR in that it also controls degradation of apolipoprotein B (apoB), a protein required for the hepatic assembly of lipoproteins. In this study, we aimed to determine whether the LDLR-dependent decrease in apoB secretion occurs through an intracellular mechanism. In Ldlr-/- primary mouse hepatocytes, we expressed an LDLR wild-type (WT) or a mutant (Y807C). We found that the mutant was indeed defective in endocytosis in primary hepatocytes. However, the intracellular mechanism. In this study, we aimed to determine whether the LDLR-dependent decrease in apoB secretion occurs through an intracellular mechanism. In Ldlr-/- primary mouse hepatocytes, we expressed an LDLR wild-type (WT) or a mutant (Y807C). We found that the mutant was indeed defective in endocytosis in primary hepatocytes. However, the LDLR-dependent regulation of apoB secretion and degradation occurs through an intracellular pathway.

Research question: Can an LDLR mutant that is unable to undergo endocytosis regulate apoB secretion?

Conclusions
1. The LDLR is defective in constitutive endocytosis.
2. However, it is not defective in regulating secretion and degradation of apoB.
3. Therefore, we conclude that the LDLR-dependent regulation of apoB secretion and degradation occurs through an intracellular mechanism.

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