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ApoA-I deletion or overexpression in apoE deficient mice alters lipid deposition in peripheral tissues

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The reverse cholesterol transport is a multistep process whereby excess cholesterol is conveyed by HDL from the peripheral tissues to the liver for excretion. In this study, the impact of the genetic manipulation of HDL/apoA-I levels on lipid deposition in intestine, liver, kidney and adrenals was investigated.

Mice with extremely low plasma HDL levels, deficient for both murine apoA-I and apoE (DKO), were compared with mice characterized by elevated HDL, deficient for both apoA-I/apoE, but overexpressing human apoA-I (DKO/hA-I). Mice, both female and male, were fed a standard rodent diet until one year of age. Plasma lipids were quantified by enzymatic methods. Intestine, liver, kidney and adrenal morphology was evaluated by light microscopy on frozen sections.

Plasma total cholesterol concentration in DKO mice was comparable with that of wild-type mice and 3-fold lower than that observed in DKO/hA-I mice. Plasma HDL-C was almost absent in DKO mice and strongly elevated in DKO/hA-I mice. The H&E-stained sections did not reveal the presence of morphological alterations in the tissues analyzed: intestinal villi and crypts were regular, steatosis in liver parenchyma, as well as foam cells in renal glomeruli were absent and adrenal size was comparable in both genotypes. The neutral lipid-specific staining with Oil Red O showed instead interesting differences. The intestine did not exhibit HDL-mediated effects on lipid deposition. On the contrary, in the hepatic parenchyma, an increased accumulation of lipids around the centrilobular vein was observed in DKO/hA-I mice only. In addition, within the glomeruli and the adrenal cortex of DKO/hA-I mice, lipid accumulation was significantly higher than in DKO.

On summary, although DKO mice are almost completely devoid of HDL and prone to atherosclerosis development, they do not exhibit signs of abnormal lipid accumulation in liver, kidney and adrenals, as in DKO/hA-I mice, characterized by elevated HDL levels.