Clearance of fetuin-A–containing calciprotein particles is mediated by scavenger receptor-A.

Fetuin-A is a liver-derived plasma protein involved in the regulation of calcified matrix metabolism. Biochemical studies showed that fetuin-A is essential for the formation of protein-mineral complexes, called calciprotein particles (CPPs). CPPs must be cleared from circulation to prevent local deposition and pathological calcification. We studied CPP clearance in mice and in cell culture to identify the tissues, cells, and receptors involved in the clearance. In mice, fetuin-A-containing CPPs were rapidly cleared by the reticuloendothelial system, namely Kupffer cells of the liver and marginal zone macrophages of the spleen. Macrophages from scavenger receptor-A/II (SR-A)-deficient mice cleared CPPs less efficiently than macrophages from wild-type mice, suggesting that SR-A/II is involved in CPP binding and endocytosis. Accordingly, we found reduced clearance of CPPs in SR-A/MARCO-deficient mice. We could demonstrate that fetuin-A-containing CPPs facilitate the clearance of mineral debris by macrophages via SR-A. Since the same receptor also contributes to the uptake of modified low-density lipoprotein particles in atherosclerosis, defective endocytosis of both types of particle may impinge on lipid as well as mineral debris clearance in...
calcifying atherosclerosis.

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