Genes Expressed in Monocyte/Macrophage Cell Differentiation and Atherosclerotic Plaques in WHHL Rabbits

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Genetic defects in the LDL receptor give rise to hypercholesterolemia and lead to atherosclerosis in humans and rabbits. Although the LDL receptor pathway clearly demonstrated how hypercholesterolemia is induced by a defect in the receptor, the mechanism by which hypercholesterolemia causes atherosclerosis remains to be elucidated. To elucidate the process of atherosclerotic plaque formation, we isolated cDNAs for mRNAs either induced or suppressed during the monocyte/macrophage differentiation. In addition, we have also obtained a cDNA for the mRNA specifically expressed in WHHL rabbit aorta.

Methods

Differential hybridization screening was used to isolate cDNAs encoding mRNAs either induced or suppressed during monocyte/macrophage differentiation. Differential hybridization screening was also performed to isolate cDNAs for mRNA specifically expressed in WHHL rabbit aorta.

Results

Treating THP 1 human monocyctic leukemia cells with retinoic acid leads to monocyte/macrophage differentiation. By differential hybridization, several cDNA clones encoding mRNAs either induced or suppressed during the differentiation of the cells were isolated and characterized. The results revealed that the mRNAs for light and heavy chains of ferritin were induced and the mRNAs for beta and gamma cytoskeletal actins, heterogeneous nuclear ribonucleoprotein A1, ribosomal protein S6 were down-regulated during differentiation. We also carried out differential hybridization screening to obtain cDNAs for the mRNAs specifically expressed in the aorta of WHHL rabbits. By this procedure, we obtained a cDNA clone for the mRNA predominantly expressed in the aorta of WHHL rabbits. We could not detect this mRNA in the normal aorta. The levels of mRNA were closely related to the incidence of atherosclerotic plaques in WHHL rabbit.