Expression of ACYL-Coenzyme A:Cholesterol Acyltransferase-1 (ACAT-1) Protein in Human Atherosclerotic Lesions and Cultured Monocytes-Macrophages

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Summary

The ACAT gene was first cloned in 1993 (Chang et al., J. Biol. Chem. 1993;268:20747-20755; designated as ACAT-1). Using affinity purified antibodies raised against N-terminal portion of human ACAT-1 protein, we performed immunohistochemical localization studies, and showed that the ACAT-1 protein was highly expressed in the atherosclerotic lesions of human aorta. We also performed cell-specific localization studies using double immunostaining, and showed that ACAT-1 was predominantly expressed in macrophages, but not in smooth muscle cells. We then used cell culture system *in vitro* to monitor the ACAT-1 expression in differentiating monocytes-macrophages. The ACAT-1 protein content increased by up to 10-fold when monocytes spontaneously differentiate into macrophages. This increase occurred within the first two days of culturing the monocytes, and reached a plateau level within four days of culturing, indicating that the increase in ACAT-1 protein content is an early event during the monocyte differentiation process. The ACAT-1 protein expressed in the differentiating monocytemacrophages was shown to be active by enzyme assay *in vitro*. The high levels of ACAT-1 present in macrophages maintained in culture can explain the high ACAT-1 content found in the atheroslerotic lesions. Our results thus support the idea that ACAT-1 plays an important role in the differentiating monocytes, and in forming the macrophage foam cells during the development of human atherosclerosis.

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