Molecular pathology in atherosclerosis: The mechanism how cholesteryl ester accumulates in atheromatous aorta.

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To study how cholesterol accumulates in atheroma, novel monoclonal antibodies were developed, using crude homogenate of atheroma as immunogens.
212D monoclonal antibody recognizing extra cellular matrix with lipid-laden deposits was selected by histochemically staining. The antigen was deduced vitronectin from cDNA library.
DLH3 monoclonal antibody recognizing oxidized LDL, epitope of which was 5- and 9-phosphatidylcholine that can form complexes with polypeptides including apoB. Significant correlations between oxidized LDL and Coronary Heart Disease (CHD) patients were observed from clinical study.
256C monoclonal antibody recognizing atheromatous lesions in human aorta was selected. Epitope must be PC-cholesterol complex which may involve in foam cell rupture. Atherogenesis will be discussed from the aspects of these antibodies.

Our working hypothesis is required to elucidate the mechanism. Denatured lipoproteins (either oxidized lipoprotein or ruptured foam cells) may induce atheroma. Oxidation of lipoprotein may be taken place both in foam cells and/or extra cellular matrix, and macrophage eliminate these denatured lipoproteins and become foam cells. The foam cells are ruptured by either apoptosis or necrosis afterward, and hydrophobic fragments of foam cells dispersed in extra cellular space, which destroys the function of biological membrane. Since biological function could be maintained by segregation of hydrophilic circumstances, macrophages uptake these fragmented material and oxidized lipoprotein to maintain the function. This vicious spiral may enhance chronically the atheroma.