

Cholesterol microdomain deposition by cholesterol-enriched macrophages.

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Accepted on August 22, 2017

Within atherosclerotic plaques, both intracellular and extracellular cholesterol accumulate. However, the origin and fate of extracellular cholesterol in atherosclerosis is far less understood compared with intracellular cholesterol. There are several reasons why accumulation of extracellular unesterified cholesterol is important to the development of atherosclerotic plaques: 1) unesterified cholesterol accumulates within the extracellular space of atherosclerotic lesions; 2) unesterified cholesterol is the form of cholesterol that cells typically excrete when eliminating excess cholesterol; 3) at high concentrations unesterified cholesterol can be cytotoxic; and 4) when not solubilized unesterified cholesterol forms crystals that can promote inflammation [1].

During cholesterol enrichment of macrophages with cholesterol, macrophages take up and store much of the cholesterol within lipid droplets. However, we have discovered that at the same time, the macrophages deposit unesterified cholesterol into the surrounding extracellular space [2-5]. We have detected these extracellular unesterified cholesterol deposits using a unique

monoclonal antibody that detects cholesterol microdomains [6]. The human M-CSF differentiated monocyte-derived macrophages in this image were enriched with cholesterol by incubation for 1 day with acetylated low-density lipoprotein (Figure 1). The green color in this image indicates the extracellular deposition of cholesterol microdomains. The blue color shows macrophage nuclei. Characterization of these unique extracellular cholesterol microdomains is currently under investigation.

Similar extracellular unesterified cholesterol microdomains occur in human atherosclerotic plaques [4]. Thus, it will be important to learn how these extracellular deposits of cholesterol contribute to cholesterol trafficking within plaques and to the pathogenesis of atherosclerosis.

Acknowledgment

This work was supported by intramural funds from the National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health, USA.

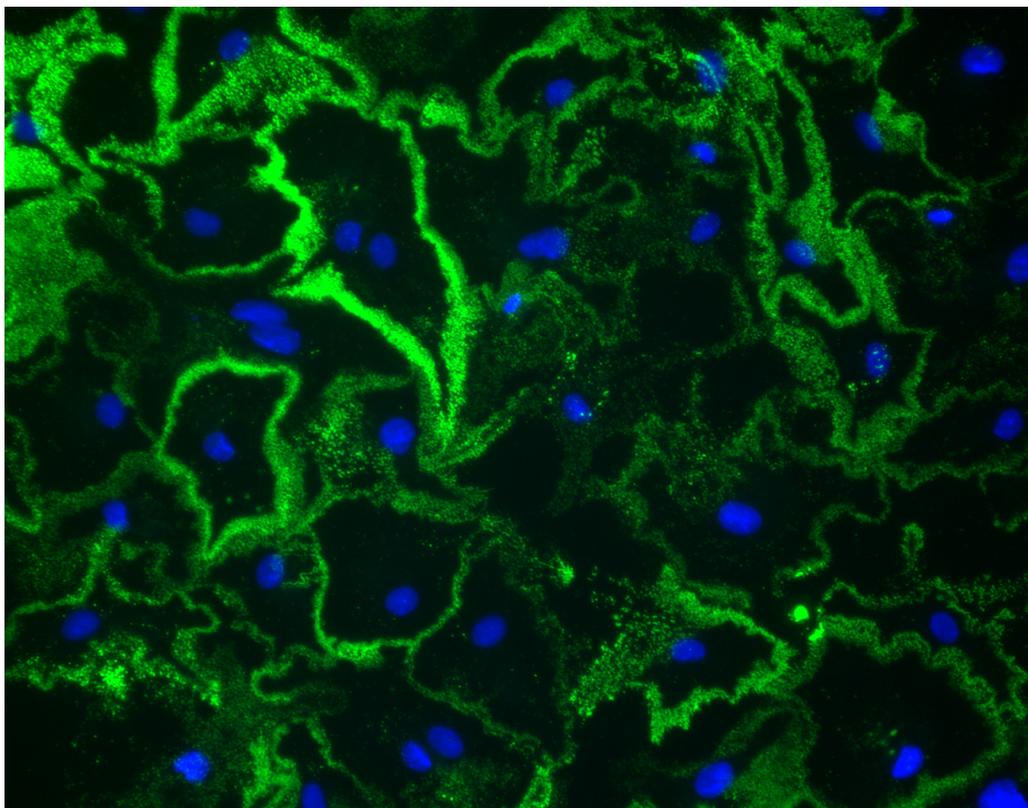


Figure 1. Fluorescence of Cholesterol deposition.

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