A. actinomycetemcomitans LPS Enhances Foam Cell Formation Induced by LDL

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Abstract  The objective of this study was to examine whether native low-density lipoprotein (LDL) induces foam cell formation by macrophages and to examine the effect of lipopolysaccharide (LPS) on native LDL-induced foam cell formation by macrophages in vitro. RAW 264.7 cells were cultured with LDL or high-density lipoprotein (HDL) in the presence of LPS derived from Aggregatibacter actinomycetemcomitans. Foam cell formation was determined by staining with Oil-red-O to visualize cytoplasmic lipid droplet accumulation. The expression of LDL-receptor and the degree of internalization of FITC-conjugated LDL in RAW 264.7 cells were examined by immunofluorescence microscopy. The images were digitally recorded and analyzed with Image J software. Statistical analysis was performed by JMP software. **Foam cell formation was induced by the addition of native LDL** in dose- and time-dependent manners, whereas HDL showed no effect. **LPS enhanced the foam cell formation induced by native LDL.** In addition, LPS stimulated the expression of LDL-receptor protein on RAW 264.7 cells **and enhanced the internalization of LDL.** The enhancement of foam cell formation induced by LPS and LDL was inhibited by the depolymerizing agent nocodazole and amiloride analog 5-(N-ethyl-N-isoprophy) amiloride (EIPA). Our findings indicate that LPS plays an important role in foam cell formation by LDL-stimulated macrophages.
Foam cell
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Foam Cells are fat-laden immune cells of the type macrophage. They are an indication of plaque-build up, or atherosclerosis, which is commonly associated with increased risk of heart attack and stroke.

Foam cells are formed when the body sends macrophages to the location of a fatty deposit on the blood vessel walls.[1] The macrophage surrounds the fatty material in an attempt to destroy it. The cell becomes filled with lipids (fats). The lipids surrounded by the macrophage give it a “foamy” appearance.

In chronic hyperlipidemia, lipoproteins aggregate within the intima of blood vessels and become oxidized by the action of oxygen free radicals generated either by macrophages or endothelial cells. The macrophages engulf oxidized low-density lipoproteins (LDLs) by endocytosis via scavenger receptors, which are distinct from LDL receptors. The oxidized LDL accumulates in the macrophages and other phagocytes, which are then known as foam cells.[2] Foam cells form the fatty streaks of the plaques of atheroma in the tunica intima of arteries.

Low-density lipoprotein (LDL) cholesterol is contained by a foam cell. LDL is also known as “bad” cholesterol. It becomes a marker for atherosclerosis. Foam cells are the body’s way of trying to get rid of bad cholesterol from the blood vessels. Foam cells do not give off any explicit signs or symptoms, but they are part of the origin of atherosclerosis. Foam
cells are very small in size and can only be truly detected by examining a fatty plaque under a microscope after it is removed from the body. HDL cholesterol is good cholesterol and it removes harmful bad cholesterol from where it does not belong. If foam cells are present, standard treatments for atherosclerosis are an appropriate treatment.

Foam cells are not dangerous as such, but can become a problem when they accumulate at particular foci thus creating a necrotic centre of atherosclerosis. If the fibrous cap that prevents the necrotic centre from spilling into the lumen of a vessel ruptures, a thrombus can form which can lead to emboli occluding smaller vessels. The occlusion of small vessels results in ischemia, and contributes to stroke and myocardial infarction, two of the leading causes of cardiovascular-related death.

Atherosclerosis is the hardening and narrowing of the arteries, due to the formation of plaques in the blood vessel. Atherosclerosis is the usual cause of heart attacks, strokes, and peripheral vascular disease. Together, these diseases are called “cardiovascular disease.”

**Atherosclerosis**

- A condition in which patchy deposits of fatty material develop in the walls of medium-sized and large arteries, leading to reduced or blocked blood flow
- Caused by repeated injury to the walls of arteries
- Factors that contribute to injury include: high blood pressure, tobacco smoke, diabetes, and high levels of cholesterol in the blood
- First symptom is pain or cramps
- Preventions include: stop using tobacco, improve diet, exercise regularly, and maintain control of blood pressure and diabetes
- Causes complications such as a heart attack or stroke
- Leading cause of illness and death in most developed countries
- Can affect the medium-sized and large arteries of the brain, heart, kidneys, other vital organs, and legs
- Three types- atherosclerosis (large and medium arteries/ most common form), arteriolosclerosis, (small arteries and arterioles) and Mönckeberg’s arteriosclerosis (muscular arteries)
- Treatment: drugs that include statins and aspirin or other antiplatelet drugs
- May also be linked to autoimmunity.

**Risk factors for Atherosclerosis**

1. advancing age
2. sex (males and post-menopausal females)
3. hyperlipidaemia
Arteriosclerosis is defined by thickening and loss of elasticity of the arterial walls. There are 3 patterns (arteriosclerosis is used as a generic term for all patterns above):

1. Atherosclerosis: large and medium sized arteries
2. Mönckeberg medial calcific sclerosis: muscular arteries
3. Arteriolosclerosis: small arteries and arterioles

Autoimmunity occurs when the body starts attacking itself. The link between atherosclerosis and autoimmunity is plasmacytoid dendritic cells (pDCs). PDCs contribute to the early stages of the formation of atherosclerotic lesions in the blood vessels. Stimulation of pDCs leads to an increase of macrophages present in plaques.

Additional images

A micrograph showing foam cells in the vascular papillae of papillary renal cell carcinoma. H&E stain.

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