

Macrophage accumulation of triglycerides yields insights into atherosclerosis

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A research report appearing in the *Journal of Leukocyte Biology* helps explain how specific immune cells, called macrophages, accumulate triglycerides to support their function. Because a characteristic finding in atherosclerosis is the accumulation of fat in macrophages in the arterial wall, understanding how macrophages accumulate triglycerides may lead to new approaches toward slowing or stopping the development of atherosclerosis.

"Activation of macrophages leads to the accumulation of triglycerides in macrophages by multiple pathways that may have beneficial effects in host defense but could contribute to the accelerated atherosclerosis that occurs in chronic infections and inflammatory disease," said Kenneth R. Feingold, M.D., a researcher involved in the work from the Metabolism Section at the Veterans Affairs Medical Center in San Francisco, California. "By understanding the pathways that lead to this lipid accumulation in activated macrophages one might be able to manipulate these pathways to stimulate lipid accumulation to improve host defense or inhibit these pathways to reduce atherosclerosis depending on the clinical circumstances."

To make this discovery, scientists conducted <u>laboratory experiments</u> using a macrophage cell line, or mouse peritoneal macrophages. These cells were stimulated with various substances and the effect on macrophage glucose and fat metabolism was determined. They found that activated macrophages are more efficient at taking up glucose and use this glucose to synthesize fat. They also found that activated



macrophages are more efficient at taking up fatty acids and use the <u>fatty</u> <u>acids</u> to synthesize triglycerides. Finally, the breakdown of fat (triglycerides) is decreased in activated macrophages. Together these changes in macrophage metabolism lead to the accumulation of fat inside the macrophage itself. The fact that multiple pathways are altered suggests that the accumulation of fat in activated macrophages is important to the function of activated macrophages.

"Drilling down to understand exactly how triglycerides are used by our body should ultimately help us better treatments for diseases such as atherosclerosis," said John Wherry, Ph.D., Deputy Editor of the <u>Journal of Leukocyte Biology</u>. "This report gives us important insights into how triglycerides accumulate in key <u>immune cells</u> involved in atherosclerosis and cardiovascular disease."

More information: Heather Parker, Mike Dragunow, Mark B. Hampton, Anthony J. Kettle, and Christine C. Winterbourn. Requirements for NADPH oxidase and myeloperoxidase in neutrophil extracellular trap formation differ depending on the stimulus. *J Leukoc Biol* October 2012, 92:841-849; doi:10.1189/jlb.1211601

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