

**Title:**

Modulation of CD36 Scavenger Receptor Expression by Curcumin and Vitamin E Affects Cellular Uptake of Lipids and Bacteria

**Authors:**

Jean-Marc Zingg, Kyotaka Nakagawa, Angelo Azzi, Mohsen Meydani

**Presented by:**

Jean-Marc Zingg

**Department:**

Vascular Biology Laboratory, Jean Mayer USDA Human Nutrition Research Center on Aging

**Abstract:**

**Introduction:** Atherosclerosis is associated with inflammation and oxidative- and lipid-mediated damage in the vascular system: the risk of these events progressively rises with age. At the molecular level, hyperlipidemia and bacterial infection have been linked as causal triggers that accelerate atherosclerosis. The CD36/FAT scavenger receptor/fatty acid translocase mediates the uptake of fatty acids in various tissues. Other molecules that are recognized and/or taken up by CD36 include oxLDL, fibrillar  $\beta$ -amyloid, apoptotic cells, erythrocytes infected with *Plasmodium falciparum*, and Gram-negative and Gram-positive bacteria. Recent research also links CD36 with several signal transduction cascades leading to inflammasome activation with sterile and non-sterile triggers. CD36 associates with Toll-like Receptors 2, 4 und 6, interacts with bacterial lipids and modulates signal transduction required for native immunity and for inflammatory processes in response to bacterial pathogens. Mice homozygous for CD36 deletion are hyperlipidemic and hypersusceptible to *Staphylococcus aureus* infection. In cell culture, CD36 mediates uptake of *Escherichia coli* and *Staphylococcus aureus*. The ability of nutritional components to affect the expression of CD36 and to change the inflammatory and phagocytic response to lipids and bacteria in monocytes/macrophages is largely unknown and could be an important regulatory event modulating inflammation and atherosclerosis in response to lipids and microbial pathogens.

**Results:** Here we show that curcumin, a natural polyphenol from turmeric spice, increases the surface and gene expression of CD36 leading to increased lipid uptake in THP-1 monocytes/macrophages. The curcumin metabolite, tetrahydrocurcumin (THC), has no effect, most likely since it is not efficiently taken up into cells. In contrast, CD36 surface expression and lipid uptake is decreased by alpha-tocopherol and more so by alpha-tocopheryl phosphate. Interestingly, phagocytosis of inactivated *Staphylococcus aureus* (Wood strain), as AlexaFluor 488® or 595® conjugate bioparticles is affected by these compounds in a similar manner as

observed for lipids, suggesting that binding and uptake of lipids and bacteria may share common molecular mechanisms.

**Conclusions:** It is concluded that the cellular lipid uptake and the phagocytic response to bacteria in monocytes/macrophages are modulated by curcumin and vitamin E and involve altered expression of CD36 at the cellular surface. Thus, these dietary components may not only directly modulate the cellular anti-microbial and inflammatory response but also indirectly by influencing the host-microbiome interaction. Supported by USDA contract #58-1950-014.