

PCSK9 inhibitors have unexpected anti-inflammatory effects

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PCSK9 inhibition is a new therapeutic strategy for atherosclerosis which is known to lower LDL cholesterol. Research from Karolinska Institutet, presented at the ESC Congress last year and now published in the *Journal of Internal Medicine*, shows that PCSK9 inhibitors could ameliorate cardiovascular disease by immune mechanisms that are independent of LDL lowering.

Atherosclerosis is a chronic inflammatory process involving cells of the immune system such as T cells and [dendritic cells](#). Lipid-lowering statins are commonly used to treat the condition, and in recent years a new class of atherosclerosis drugs which inhibit the enzyme PCSK9 (proprotein convertase subtilisin kexin 9) has reached the market. PCSK9 is known to target the LDL receptor, resulting in increased levels of low-density lipoprotein (LDL).

Researchers at Karolinska Institutet have examined how [immune cells](#) from human atherosclerotic plaques are affected by PCSK9. Using a new experimental system, they found that oxidised LDL, a central player in atherosclerosis, induced PCSK9 and promoted the maturation of dendritic cells. These dendritic cells then mediated the activation of T cells into a pro-inflammatory phenotype. PCSK9 inhibition reversed the effects of oxidised LDL on immune activation.

Could be anti-atherosclerotic

"This anti-inflammatory effect was unexpected and could potentially be anti-atherosclerotic, suggesting that the benefits of PCSK9 inhibition extend beyond lowering LDL cholesterol," says lead author Johan Frostegård, Professor at the Institute of Environmental Medicine, Karolinska Institutet.

More information: Anquan Liu et al. PCSK9 plays a novel immunological role in the oxidized LDL-induced dendritic cell maturation and T cell activation from human blood and atherosclerotic plaque, *Journal of Internal Medicine* (2018). [DOI: 10.1111/joim.12758](https://doi.org/10.1111/joim.12758)

Provided by Karolinska Institutet

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