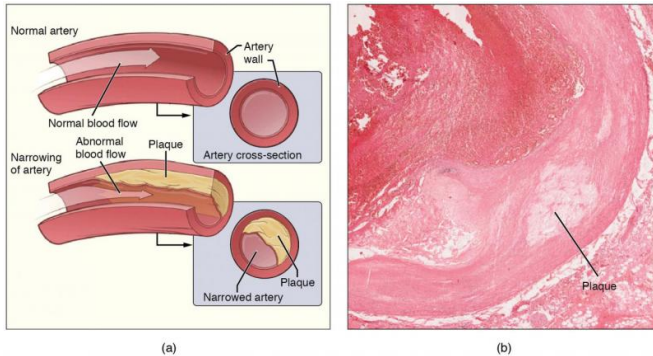


Discovery of new protein with an important role in atherosclerosis

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Atherosclerosis is a condition affecting the cardiovascular system. If atherosclerosis occurs in the coronary arteries (which supply the heart) the result may be angina pectoris, or in worse cases a heart attack. Credit: Wikipedia/CC BY 3.0

Atherosclerosis is the underlying condition that causes heart attacks and strokes. Researchers at Radboudumc in the Netherlands have discovered a protein that appears to play an important role in atherosclerosis. The protein is called Prosaposin, and its role in atherosclerosis was so far unknown. "We identified Prosaposin as a new potential target for the *Science Translational Medicine*.

Atherosclerosis is caused by cholesterol that builds up in the vessel wall and triggers [chronic inflammation](#). It has been well established that cholesterol lowering drugs help to treat [atherosclerosis](#). Recent research has shown that inhibiting inflammation can also help to prevent heart attacks and strokes. The challenge now is to find ways to inhibit inflammation specifically in atherosclerosis, without impeding the rest of the body's defenses that protect us against infections.

Increased metabolic rate

The cells primarily responsible for inflammation in

atherosclerosis are macrophages. The inflammatory activation of these cells is an energy demanding process. The cells therefore have to increase their [metabolic rate](#) considerably. "Unraveling how they do this provides insight into how we can slow down the inflammatory activity and thereby reduce atherosclerosis".

Switch off the power

An international team of researchers, led by Raphaël Duivenvoorden of the Radboudumc in the Netherlands, has investigated what happens when you "switch off the power" of macrophages. The main metabolic switch is a [protein complex](#) called mTOR. Using nanotechnology, they were able to specifically turn off this switch in macrophages and investigate its effect on atherosclerosis in a mouse model. "We saw after only a single week of treatment that atherosclerotic lesions shrank and the inflammation decreased".

New protein discovered

This result sparked their interest in unraveling the [molecular mechanism](#) underlying this potent anti-inflammatory effect. Their analyzes consistently revealed an important role for a protein called Prosaposin. Its role in atherosclerosis was so far unknown. "In additional experiments we found that Prosaposin has an important effect on macrophage's metabolism. We also observed less development of atherosclerosis and vessel wall inflammation in mice that cannot produce Prosaposin. "

Prosaposin and atherosclerosis in humans

To find out if Prosaposin also plays a role in atherosclerosis in humans, they investigated its expression in human [atherosclerotic lesions](#). "We saw substantial expression of Prosaposin by macrophages in [atherosclerotic plaques](#) and this was related to their inflammatory activity. It

confirms that Prosaposin plays a key role in atherosclerosis, and is a potential new therapeutic target for the treatment of atherosclerosis."

More information: Mandy M. T. van Leent et al, Prosaposin mediates inflammation in atherosclerosis, *Science Translational Medicine* (2021). DOI: [10.1126/scitranslmed.abe1433](https://doi.org/10.1126/scitranslmed.abe1433)

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