

Lowering cholesterol is not enough to reduce hyperactivity of the immune system

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Hypercholesterolemia is a major risk factor for cardiovascular disease. Statins are the most widely used cholesterol-lowering drugs. However, despite treatment with statins, many patients with elevated cholesterol levels will still develop cardiovascular disease.

Currently it is apparent that the immune system also plays an important role in the development of atherosclerosis, but how cholesterol and the immune system interact is still undiscovered.

A recent study from the Netherlands now provides a novel potential explanation for this residual cardiovascular risk, related to persistent activation of the immune system in patients with hypercholesterolemia who are treated with statins.

Siroon Bekkering, Radboud university medical center, Nijmegen, with colleagues from Amsterdam and Rotterdam investigated the activity of part of the immune system in individuals with and without high cholesterol levels. It appeared that specific immune cells in the blood (monocytes) were more activated in patients with high-cholesterol levels than in individuals with normal cholesterol levels; these cells produced more inflammatory molecules that are important in the development of cardiovascular disease. Subsequently, the patients with high cholesterol were treated with statins to lower their cholesterol levels and the same measurements were repeated three months later. Importantly, despite cholesterol lowering, the hyperactivity of the immune cells did not decrease at all.

Niels Riksen, professor of internal medicine from the Radboud university medical center, and coordinator of the project states that, "We



thus observed that these immune cells appear to 'remember' the high cholesterol they once were exposed to. The finding that monocytes can remember previous exposures has only recently been discovered, and has been termed 'trained immunity,' and this is the first study to demonstrate this in patients."

Riksen says it would be interesting to investigate now how long this memory lasts, and also whether the hyperactivity of the monocytes can be reduced by other drug types, such as anti-inflammatory drugs.

More information: Siroon Bekkering et al, Treatment with Statins Does Not Revert Trained Immunity in Patients with Familial Hypercholesterolemia, *Cell Metabolism* (2019). DOI: 10.1016/j.cmet.2019.05.014

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