Nicotinic acid blocks immune cells in atherosclerosis

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Aorta with atherosclerotic changes (red) in a mouse. © Max Planck Institute for Heart and Lung Research

Nearly all cardiac infarctions and around half of all strokes are caused by atherosclerosis. An early treatment of atherosclerosis is therefore crucial to preventing cardiovascular diseases. Stefan Offermanns' team of scientists at the Max Planck Institute for Heart and Lung Research has now demonstrated that the anti-atherosclerosis drug nicotinic acid halts the inflammation of blood vessels. Previously it had been assumed that nicotinic acid mostly alleviates atherosclerosis by reducing the concentration of LDL cholesterol and by boosting HDL cholesterol in the blood plasma.

Atherosclerosis is a chronically progressive alteration of the arteries that can develop over years and decades, in which cholesterol accumulates in the arteries and inflammation occurs. New research has shown that it is mainly the chronic inflammation of the vascular wall that promotes

atherosclerosis and may lead to acute illnesses such as a cardiac infarction. The classic treatment concept aims to lower harmful lipids such as LDL (low-density lipoprotein) cholesterol or triglycerides, and to increase beneficial lipids, such as HDL (high-density lipoprotein) cholesterol.

In genetically modified mice, Max Planck researchers were able to demonstrate that nicotinic acid strongly inhibits the progression of atherosclerosis, just as in humans. In mice that lacked the nicotinic acid receptor GPR109A, the agent had no effect on atherosclerosis. In contrast to human cholesterol levels, the cholesterol levels of mice remain constant despite the administration of nicotinic acid. "This suggests that nicotinic acid does have an anti-atherosclerotic effect via its receptor, but that this is not due to a change in the lipid concentration", says Stefan Offermanns, Director at the Max Planck Institute in Bad Nauheim.

Further studies showed that the nicotinic acid receptor is present in different immune cells. For example, the receptor was found in macrophages in atherosclerotic blood vessels. When the scientists intentionally blocked the receptor in the cells of the immune system, the effect of the nicotinic acid disappeared. This suggests that the receptor expressed by immune cells transmits the anti-atherosclerotic effect.

Finally, experiments showed that nicotinic acid keeps macrophages from entering the atherosclerotic vascular wall by activating its receptor, thereby halting chronic inflammation. Furthermore, nicotinic acid changes the gene expression in the immune cells of the vascular wall and thereby stops the inflammatory activity of these cells. They thus become more efficient at removing cholesterol stored in the atherosclerotic vascular wall.

These findings suggest that the beneficial impact of nicotinic acid, one

of the oldest agents used against atherosclerosis, inhibits inflammation in vascular walls. Targeted anti-inflammatory measures are therefore generally an efficient principle for treating atherosclerosis and preventing cardiovascular diseases. "Moreover, the effects of nicotinic acid on different cells in the immune system point to new possibilities for treating other diseases which are associated with excessive immune reactions or chronic inflammation", says Offermanns.

More information: Martina Lukasova, et al. Nicotinic acid inhibits progression of atherosclerosis through its receptor GPR109A expressed by immune cells in mice, *Journal of Clinical Investigation*, February 7, 2011

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