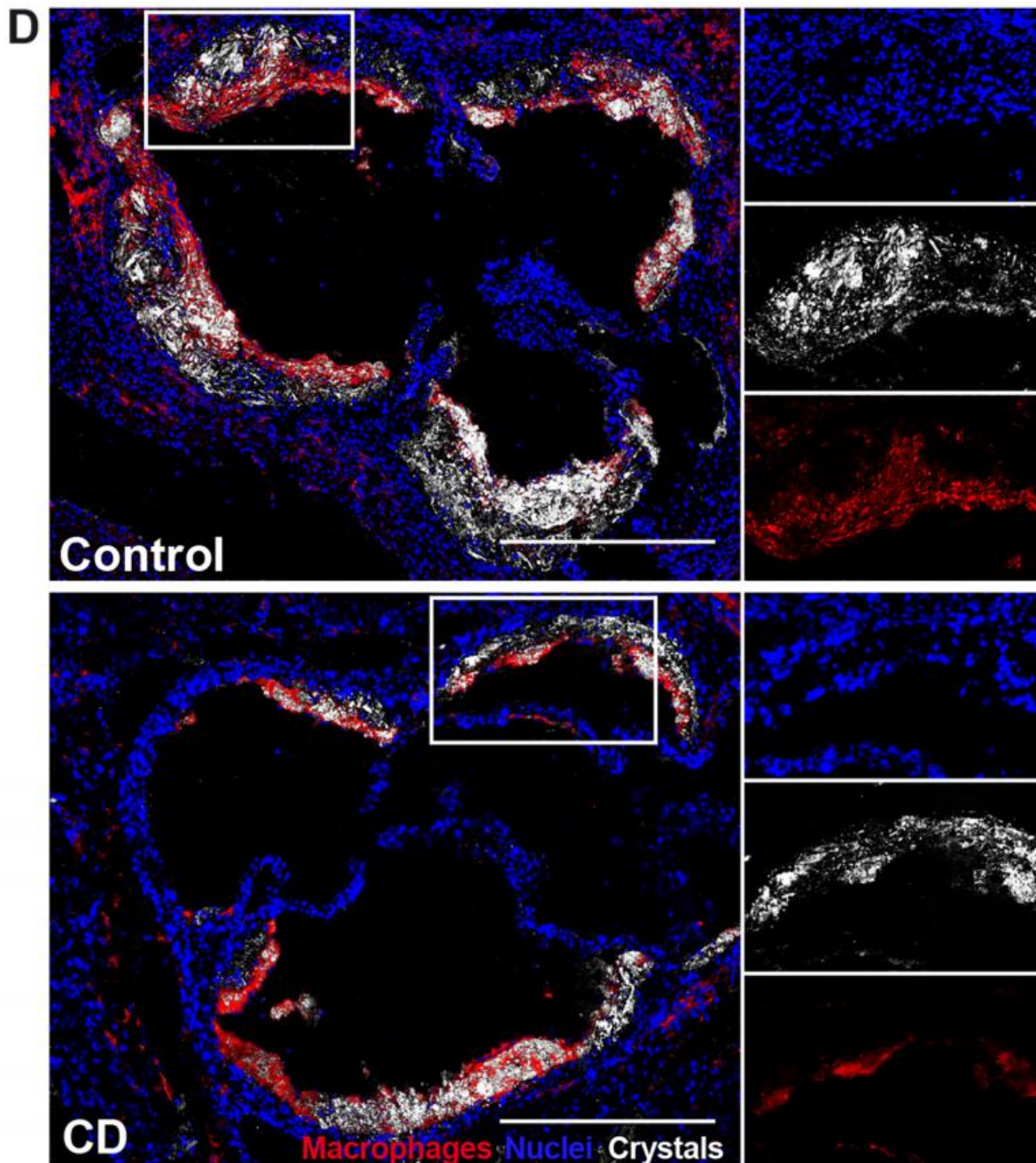


Ring-shaped sugar helps in cases of atherosclerosis

April 6 2016



Cyclodextrin (CD) treatment reduced amounts of cholesterol crystals (CCs) in atherosclerotic plaques of mice as assessed by laser reflection microscopy. Red, macrophages stained with anti-CD68 antibodies; white, reflection signal of CCs; blue, nuclei stained with Hoechst. Enlarged images are the boxed areas in the left images. Scale bars, 500 μm . Credit: S. Zimmer et al., *Science Translational Medicine* (2016)

Hardened and inflamed arteries, atherosclerosis, can be very dangerous. The consequences of atherosclerosis are among the most common causes of death in industrialized nations; in particular heart attacks and strokes. Crystalline cholesterol can contribute to this life-threatening inflammation in the arteries. An international research team of immunologists and cardiologists from the University of Bonn has now discovered that the ring-shaped sugar known as "cyclodextrin" can prevent and even reduce these dangerous cholesterol deposits. The results are now being published in the journal *Science Translational Medicine*.

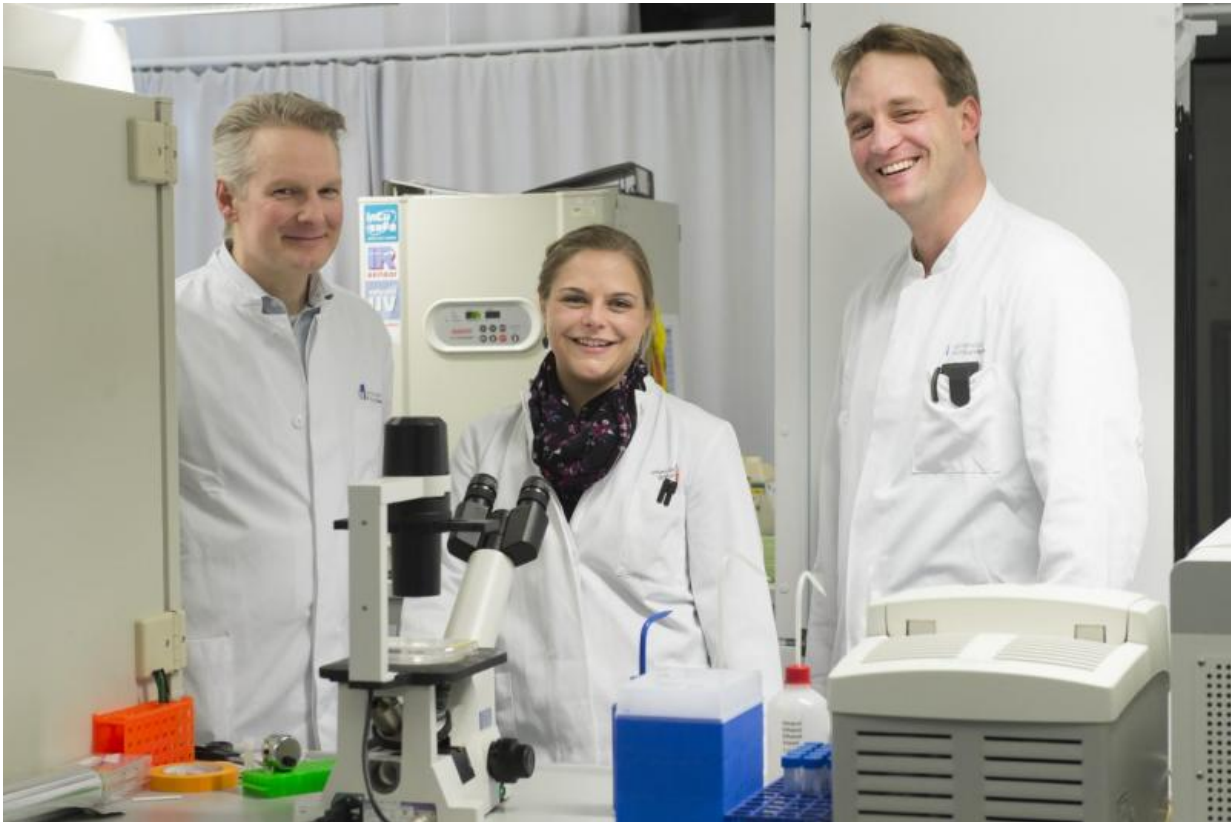
It is always a challenge for researchers to find the right approach for tackling a scientific issue. Yet sometimes people without any particular medical expertise also provide important clues which then lead to real breakthroughs. This was the case with Chris Hempel from the USA whose twin daughters suffer from the rare "Niemann-Pick type C" disease. In this disease, gene mutations cause the dysfunction of cholesterol transport in the cells. Those affected initially develop normally, but then in childhood there is a rapid worsening of neurological function, with cognitive and motor impairment. Until Chris Hempel became active, there was no treatment for Niemann-Pick C. With the aid of scientists, the mother developed a novel therapy with the

ring-shaped sugar "cyclodextrin" which leads to better elimination of excess cholesterol from brain cells. Clinical studies on this are currently being conducted in the USA.

Prof. Dr. Eicke Latz from the Institute of Innate Immunity at the University of Bonn is studying how crystalline cholesterol causes massive immune responses and leads to life-threatening inflammation in arterial walls. In 2010, he published a study in the renowned journal "Nature" on the connection between atherosclerosis and the immune system. In this study, the team of researchers working with Prof. Latz demonstrated that cholesterol crystals can activate an important receptor complex of the innate immune system and thus increase the inflammatory response in atherosclerosis. This caught Chris Hempel's attention and she reported her experiences with cyclodextrin to the immunologist.

High-cholesterol diet for mice

With an international team of researchers from Germany, the USA, Norway, Australia and Sweden, the scientists from a variety of fields from the University Hospital Bonn, under the direction of Prof. Latz, investigated whether cyclodextrin also has an effect on atherosclerosis. The researchers fed a particularly cholesterol-rich diet to mice for eight weeks and subcutaneously injected the animals with cyclodextrin. "They were far less affected by plaques in their blood vessels than a control group who did not receive any cyclodextrin," says Dr. Sebastian Zimmer from the Department of Medicine II of the University Hospital Bonn. The ring-shaped sugars apparently program the cells in a way that leads to better elimination of excess crystalline cholesterol and also to a reduction in the inflammation in blood vessels at the same time.



Prof. Dr. Eicke Latz and Alena Grebe from the Institute of Innate Immunity of the University of Bonn and Dr. Sebastian Zimmer from the Department of Medicine II from the University Hospital Bonn. Credit: (c) Photo: Barbara Frommann/University of Bonn

Cyclodextrin increases the natural breakdown of cholesterol in the cells

The transcription factor "liver-X-receptor" (LXR) is a key regulator of cholesterol metabolism and thus plays an important role in connection atherosclerosis. "If too much cholesterol is present, LXR gives a signal. As a result, genes responsible for the efflux from the cell are activated," reports Alena Grebe, doctoral student in Prof. Latz's team. "In addition, this factor downregulates inflammation." If the gene for LXR was muted

absent in mice, this signal cascade did not function and cyclodextrin did not show any effect. The ring-shaped sugar evidently fulfills the function of an intermediary which increases the natural mechanisms of [cholesterol](#) breakdown in the cells and additionally reduces the inflammatory response.

Using human atherosclerotic vessels, the team also investigated whether cyclodextrin has the same effect in humans as in mice. The researchers cultivated plaques which had been surgically removed from the carotid arteries of atherosclerosis patients in order to improve their blood flow. If cyclodextrin was mixed into the nutrient solution, the cells showed the same reprogramming as those of the rodents: the mechanisms for plaque reduction started up and the [inflammatory response](#) subsided.

The active substance is already on the market

Prof. Latz hopes that cyclodextrin can be further developed as a drug for the treatment of [atherosclerosis](#). "It is already on the market as a pharmaceutical solubilizing agent. However, costly clinical studies are needed for the new application," says the immunologist from the University of Bonn. Chris Hempel who pointed out the active substance [cyclodextrin](#) is incidentally listed as a co-author in the journal publication.

More information: "Cyclodextrin promotes atherosclerosis regression via macrophage reprogramming," *Science Translational Medicine*, [stm.sciencemag.org/lookup/doi/ ... scitranslmed.aad6100](http://stm.sciencemag.org/lookup/doi/...scitranslmed.aad6100)

Provided by University of Bonn

Citation: Ring-shaped sugar helps in cases of atherosclerosis (2016, April 6) retrieved 20 March 2024 from <https://medicalxpress.com/news/2016-04-ring-shaped-sugar-cases-atherosclerosis.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.