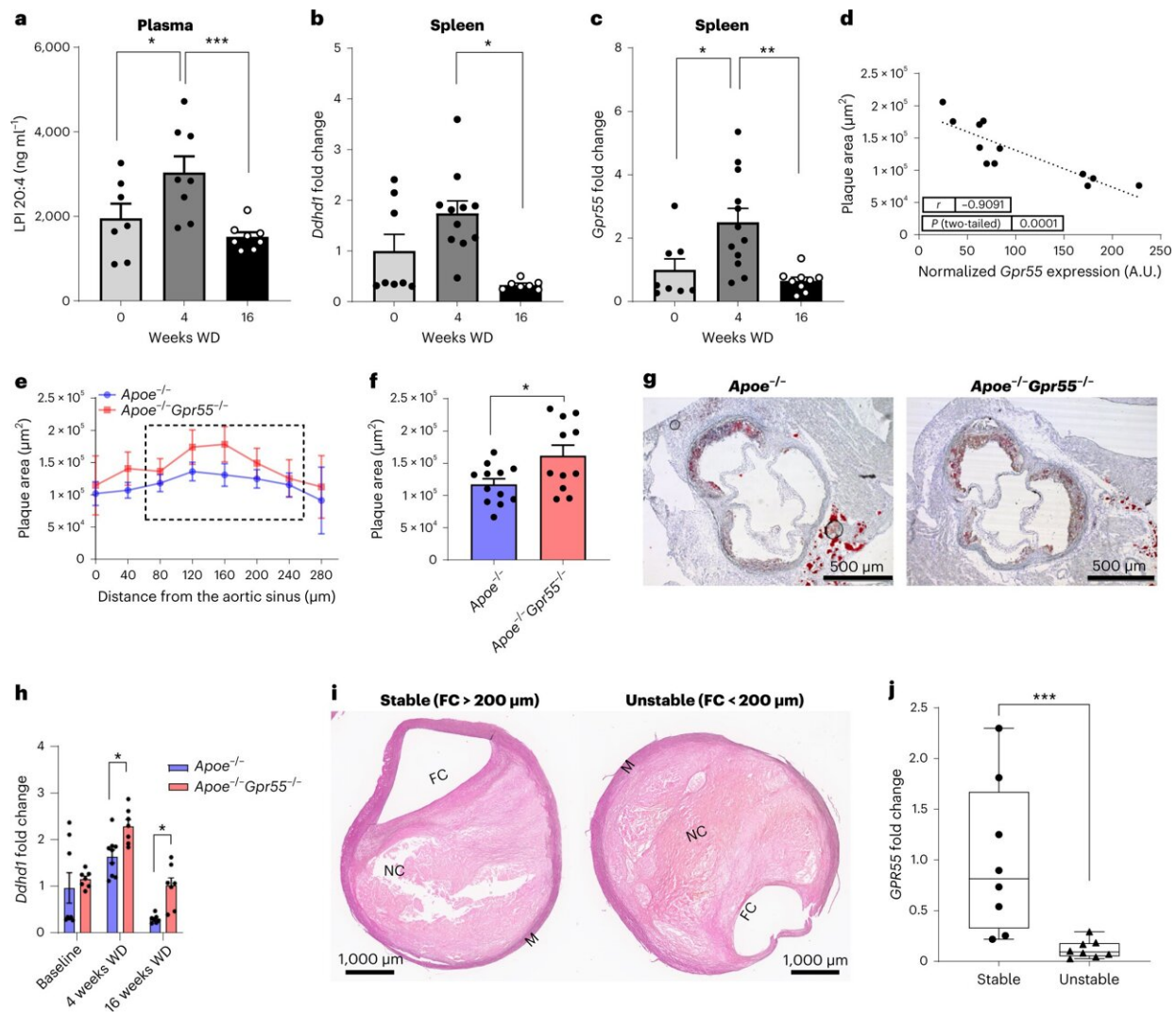


Atherosclerosis: How the body controls the activity of B cells

November 29 2022



Regulation and function of GPR55 signaling in atherosclerosis. a–d, Plasma, spleens and aortic roots were collected from ApoE^{-/-} mice at baseline or after 4 weeks and 16 weeks of WD to determine LPI plasma concentrations (n = 7–8;

*P = 0.05 and ***P = 0.0042) (a) or relative splenic mRNA expression of the gene encoding the LPI-synthesizing enzyme DDHD1 (n = 7–11; P = 0.0018) and the LPI receptor GPR55 (n = 7–12; *P = 0.019 and **P = 0.0028) (b,c). d, Splenic Gpr55 mRNA expression values of the 4-week timepoint were plotted against the aortic root plaque areas of the same mice (n = 12). e, Plaque area per aortic root section of female Apoe^{-/-} and Apoe^{-/-}Gpr55^{-/-} mice after 4 weeks of WD (n = 11–12 per group; *P = 0.023). The dotted square indicates the sections used for calculating the average plaque area per animal shown in f. g, Representative Oil Red O stains of aortic roots after 4 weeks of WD. h, Splenic Ddhd1 mRNA expression of baseline, 4 weeks and 16 weeks WD Apoe^{-/-} and Apoe^{-/-}Gpr55^{-/-} mice (for baseline n = 7–9; for 4 weeks n = 6–8 and *P = 0.04; and for 16 weeks n = 6–7 and *P = 0.035). i, Representative pictures of human stable and unstable plaques (obtained from the Munich Vascular Biobank; shown is one of the eight samples evaluated). j, Human GPR55 mRNA expression evaluated by qPCR in stable versus unstable/ruptured carotid artery plaque corrected by RPLPO used as housekeeping control (***P = 0.0006). The box plot shows the minimum to maximum value, and each dot represents one patient. Mouse data shown in a–f were combined from three independent experiments. Each dot represents one biologically independent mouse sample. All data are shown as mean ± s.e.m. Two-sided unpaired Student’s t-test or one-way ANOVA followed by post hoc Newman–Keuls multiple comparison test was used to determine the significant differences. Bivariate correlation was analyzed by Spearman’s rank correlation test. A.U., arbitrary units; FC, fibrous cap; M, media; NC, necrotic core. Credit: *Nature Cardiovascular Research* (2022). DOI: 10.1038/s44161-022-00155-0

LMU researchers have identified a protein that is involved in the regulation of immune cells and can curb the development of atherosclerosis. Their research is published in *Nature Cardiovascular Research*.

Cardiovascular diseases related to atherosclerosis are the leading cause of death worldwide. In patients, the body deposits cholesterol esters and

other fats in the inner wall of arteries. This results in the build-up of plaques, which can constrict the flow of blood so strongly that the oxygen supply to organs is impaired. Researchers have known for some time that chronic inflammatory processes occur in atherosclerosis.

A type of white blood cell known as the B cell appears to play an important role as part of the adaptive immune response. B cells have both protecting and damaging effects through the medium of antibodies. In other words, they can either promote or inhibit atherosclerosis. But how exactly does the body regulate which of these processes takes effect?

Researchers led by Prof. Sabine Steffens from the Institute for Cardiovascular Prevention (IPEK) have now identified a protein that plays a crucial role in controlling the adaptive immune response in atherosclerosis. The scientists think this protein could be suitable as a target for innovative therapies.

The role B cells play in atherosclerosis

"We wanted to understand better how B cells influence atherosclerotic diseases, with the long-term goal of developing novel therapies centered on B cells for this life-threatening condition," says Steffens, outlining the objectives of her research project. She was particularly interested in the receptor GPR55, which forwards chemical signals from the exterior to the interior of cells.

B cells in the spleen of mice produce the molecule in large quantities. For their study, the scientists investigated mouse models for atherosclerosis. If the mice received special food to trigger atherosclerosis, the receptor was upregulated after only a month—which is to say, at a rather early stage of the disease. Mice that are unable to produce GPR55 developed larger atherosclerotic plaques compared to

the wild type. In these mice, B cells were over-activated without GPR55 and inflammatory processes were promoted accordingly.

When the researchers investigated human [atherosclerotic plaques](#), they discovered that less receptor was present in unstable plaques with a high risk of triggering a stroke compared to stable plaques. "This finding indicates that the expression of the protein changes over the course of the disease," reports Steffens.

"Our results point to a protective role of the B cell GPR55 signaling pathway in atherosclerosis, which has potential relevance for human pathophysiology," says Steffens. She hopes that "GPR55 can be the starting point for novel therapies." Whether [small molecules](#) can be successfully deployed as active ingredients to stimulate the formation of GPR55 will be the work of further studies to establish.

More information: Raquel Guillamat-Prats et al, GPR55 in B cells limits atherosclerosis development and regulates plasma cell maturation, *Nature Cardiovascular Research* (2022). [DOI: 10.1038/s44161-022-00155-0](#)

Provided by Ludwig Maximilian University of Munich

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