Desialylation of blood plasma lipoproteins by exogenous sialidase.

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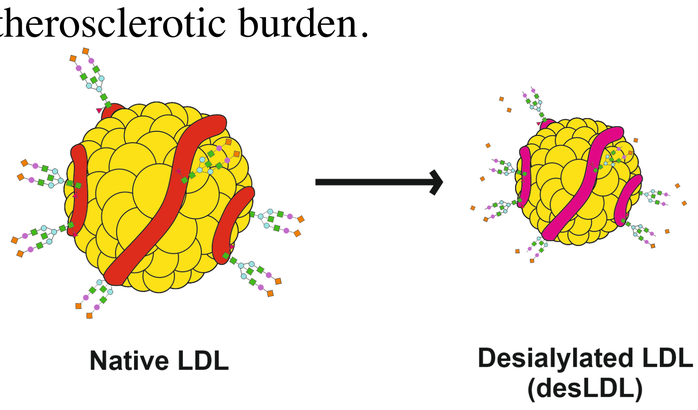
Objectives:

It has been considered that the initial link in atherogenesis is a modification of LDL. One of the types of atherogenic modification is the LDL desialylation. The aim of this study was to model the LDL desialylation in vivo. Administration of a fixed concentration of neuraminidase immobilized on IgG would allow us to model the desialylation of LDL revealed in humans.

Materials and Methods:

The control group of C57BL6 mice (n=48) was treated by a single injection of saline, while the experimental group (n=48) received *Vibrio cholerae* neuraminidase conjugated with mouse IgG. Mice were terminated at fixed periods: before and after a single injection (1-7 days). LDL was isolated from serum by ultracentrifugation. The content of sialic acid was determined according to Warren's method. Lipids of serum were measured by commercial kits. The whole aorta was stained with Oil Red O solution for quantifying atherosclerotic burden.



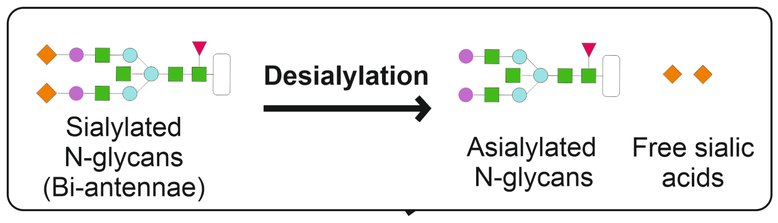


Figure 1. Desialylation of native LDL.

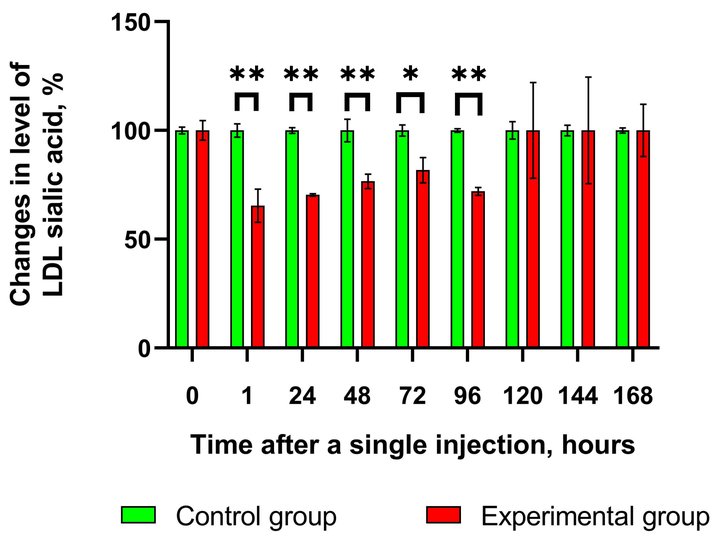


Figure 3. The values of the content of sialic acid LDL in the experimental and control groups after a single injection of neuraminidase. Significance is shown as the p value (* $p<0.05$, ** $p<0.01$, paired t test).

Results:

A significant decrease in LDL sialic acid by 30% was detected up to 4 days after the neuraminidase injection. Also, serum levels of total cholesterol, triglycerides and HDL-cholesterol in experimental mice did not differ compared with wild-type control mice. Moreover, there was no significant difference in aortic lesion surface areas of control and experimental groups.

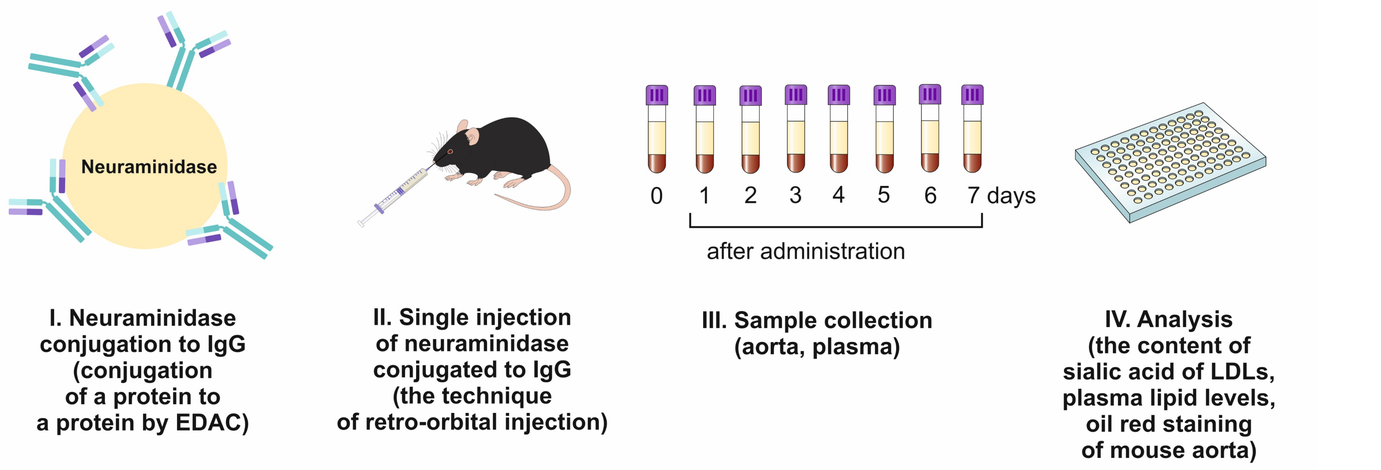


Figure 2. The stages of the experiment. The experimental modeling of LDL desialylation in mice, which was previously found in patients with atherosclerosis

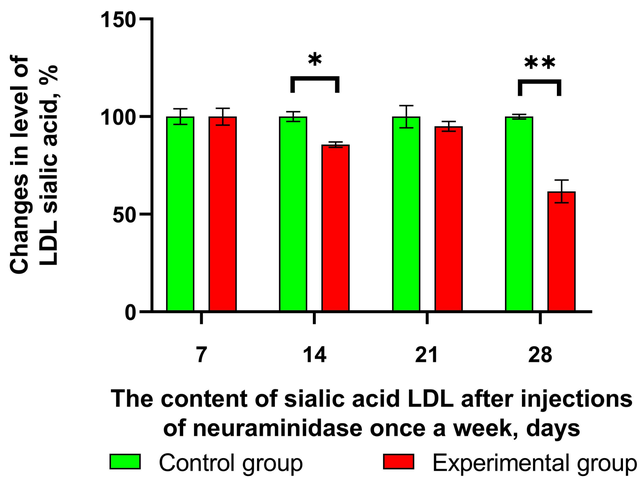


Figure 4. The values of the content of sialic acid LDL in the experimental and control groups after several injections of neuraminidase. Significance is shown as the p value (* $p<0.05$, ** $p<0.01$, paired t test).

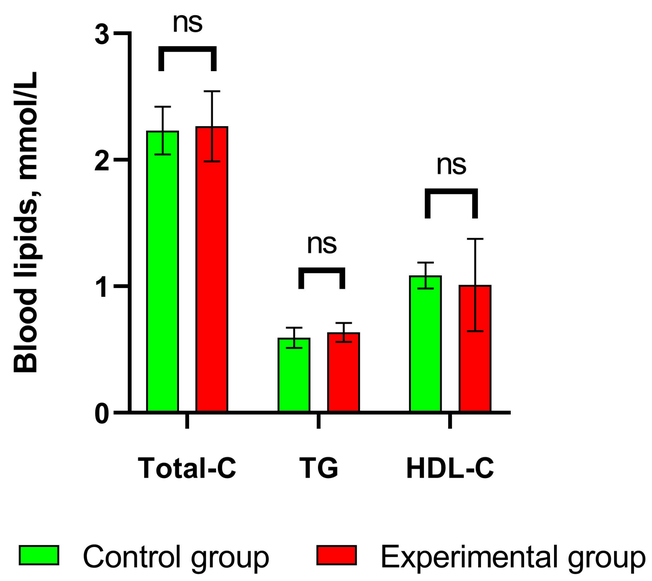


Figure 5. Blood lipid (mmol/L) response in C57BL/6 mice assigned to several injections of neuraminidase. Blood lipids including total cholesterol (TC), HDL-C and triglycerides (TG) (mmol/L). Significance is shown as the p value (ns - not significant t test).

Conclusion:

We have shown that LDL desialylation has been successfully modeled in mice, that was previously found in patients with atherosclerosis. In addition, LDL desialylation *in vivo* did not directly affect blood lipid levels and occurrence of atherosclerotic lesions in wild type mice. It is needed to do further research on the effect of LDL desialylation using a high fat diet and transgenic mice (*ApoE*-/- or *Ldlr*-/-). Research was supported by the Russian Science Foundation (grant#20-15-00264).