ECMC-P 2025 Conference

The 1st International Electronic Conference on Medicinal Chemistry and Pharmaceutics

01–30 November 2025 | Online

MDPI

Exogenous Neuraminidase as a Tool to Model LDL Desialylation and Accelerated Atherosclerosis in ApoE-KO Mice

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INTRODUCTION & AIM

Atherosclerosis remains the leading cause of mortality from cardiovascular diseases. It is driven by lipid accumulation within arterial walls due to retention of low-density lipoproteins (LDL). Among the atherogenic LDL modifications, desialylation — the enzymatic removal of terminal sialic acids from surface glycans — represents a critical but insufficiently studied mechanism. This study aimed to establish a novel in vivo model of sustained LDL desialylation in apolipoprotein E-knockout (ApoE-KO) mice and assess its contribution to atherosclerosis progression.

METHOD

Vibrio cholerae neuraminidase (Neu) was conjugated to murine IgG using EDAC (**figure 1a**), purified by affinity batch chromatography, sterilized by filtration and validated by PAGE (**figure 1b**).

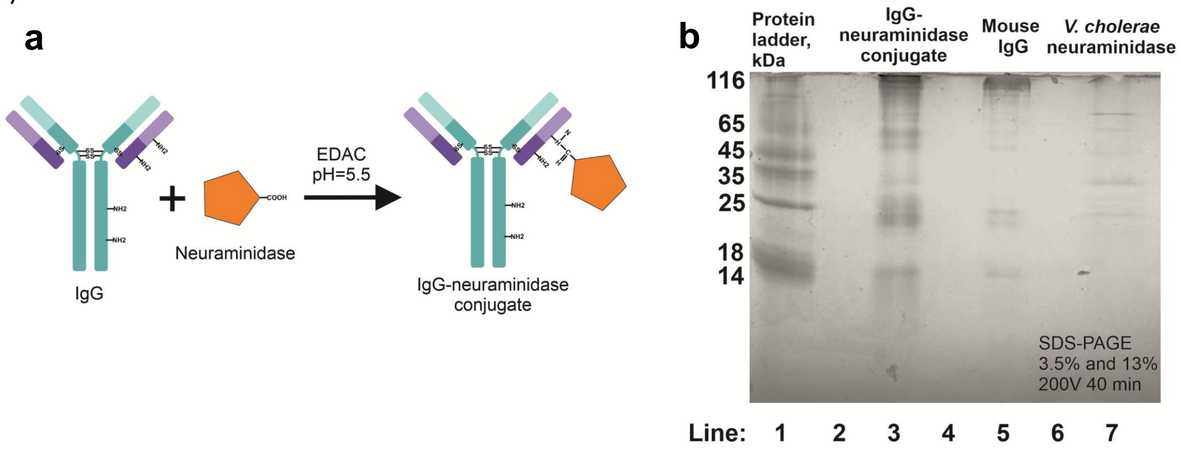

Figure 1. Conjugation of *Vibrio cholerae* (Neu) neuraminidase with mouse IgG using EDAC and PAGE of the conjugate after affinity batch chromatography.

Male ApoE-KO maintained on a chow diet received repeated Neu injections for 6 weeks (**figure 2**). LDL desialylation was quantified by the thiobarbituric acid assay. LDL atherogenicity was assessed using RAW264.7 macrophages. Morphometric analysis of aortic lesions was performed. Biochemical and hematological parameters were measured to evaluate systemic toxicity.

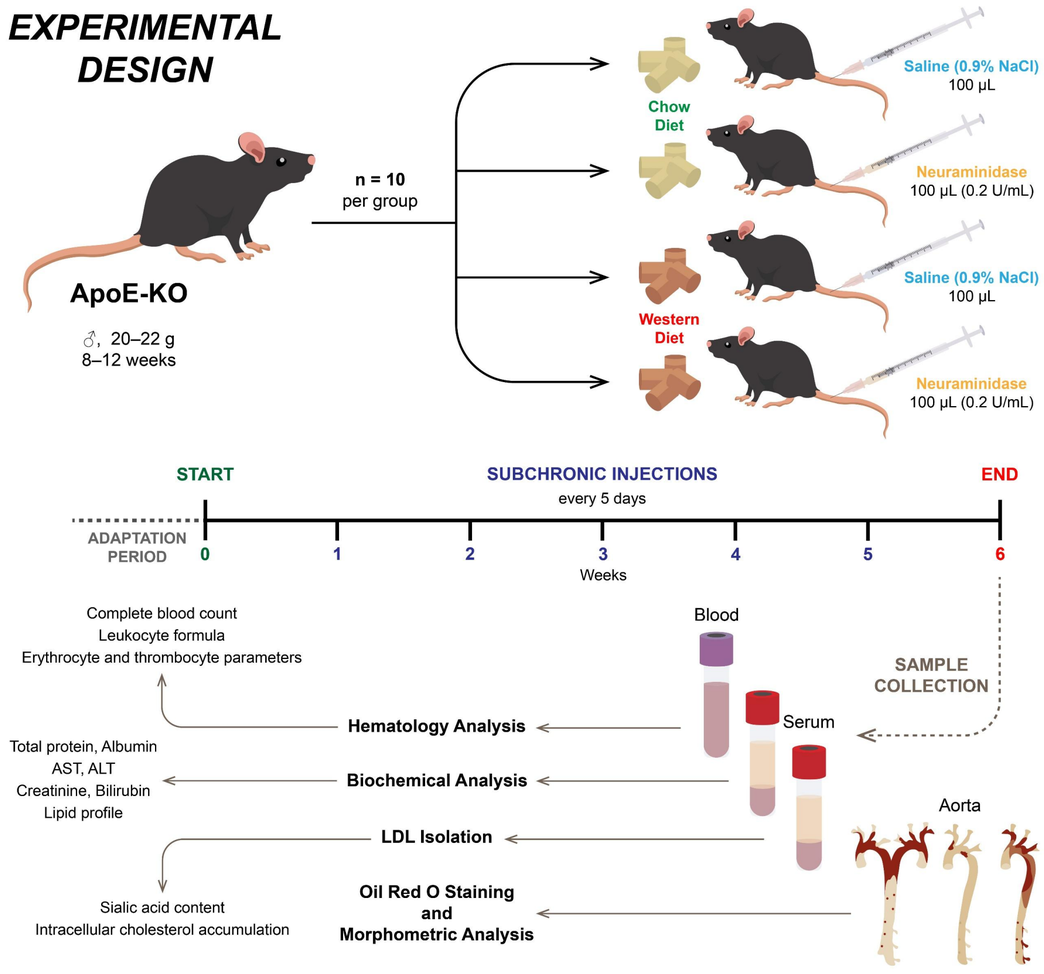

Figure 2. Schematic representation of the experimental design.

RESULTS & DISCUSSION

Neu administration significantly reduced LDL sialic acid content (**figure 3a**) and enhanced cholesterol accumulation (**figure 3b**) in RAW264.7 macrophages incubated with LDL from treated ApoE-KO mice, compared with LDL from wild-type mice.

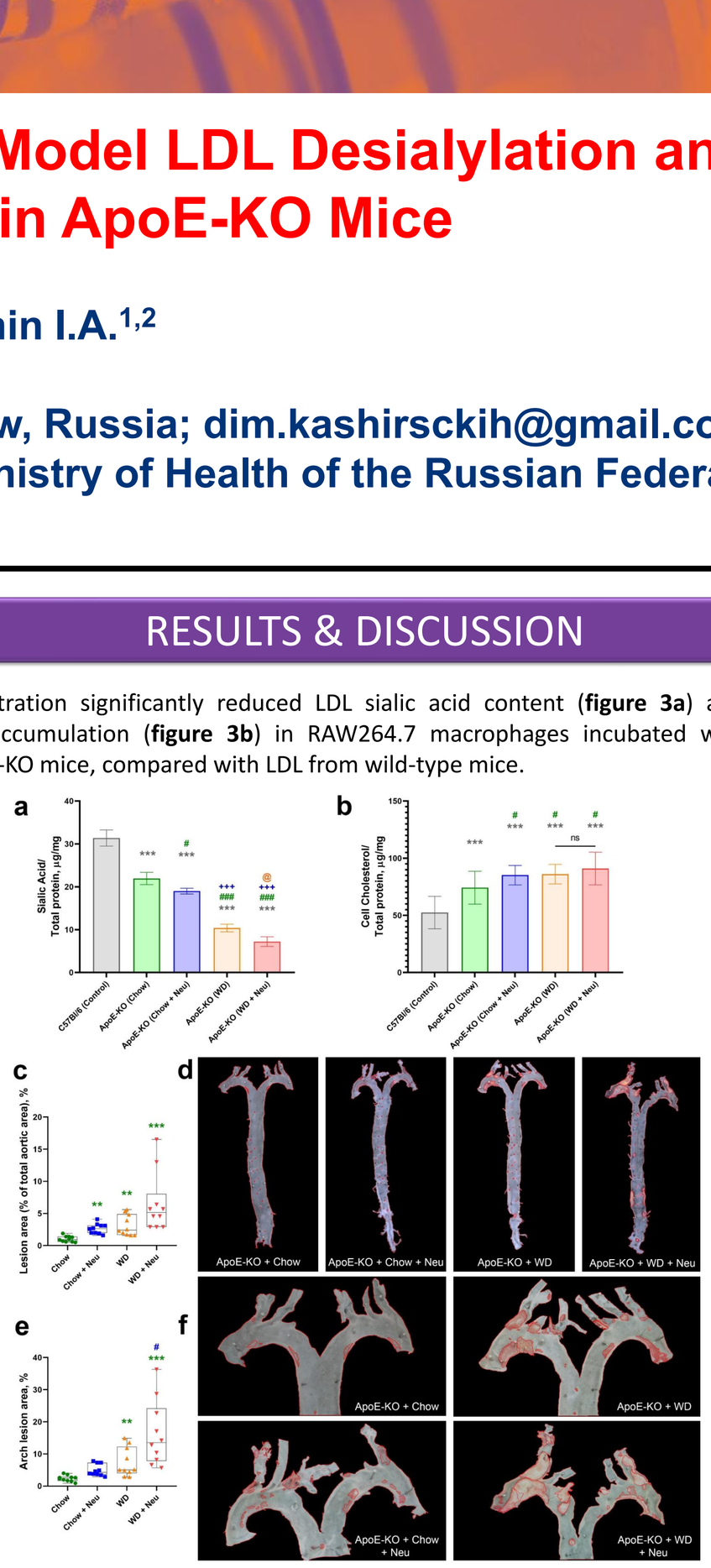

Figure 3. Exogenous neuraminidase-induced LDL desialylation enhances cholesterol accumulation in macrophages and accelerates atherosclerosis progression in ApoE-KO mice.

Treated animals exhibited elevated LDL/HDL ratio and LDL cholesterol levels (**figure 4**), and a significant enlargement of atherosclerotic lesions (**figure 3c-3f**). Importantly, Neu treatment did not induce adverse changes in biochemical or hematological parameters, indicating the absence of systemic toxicity.

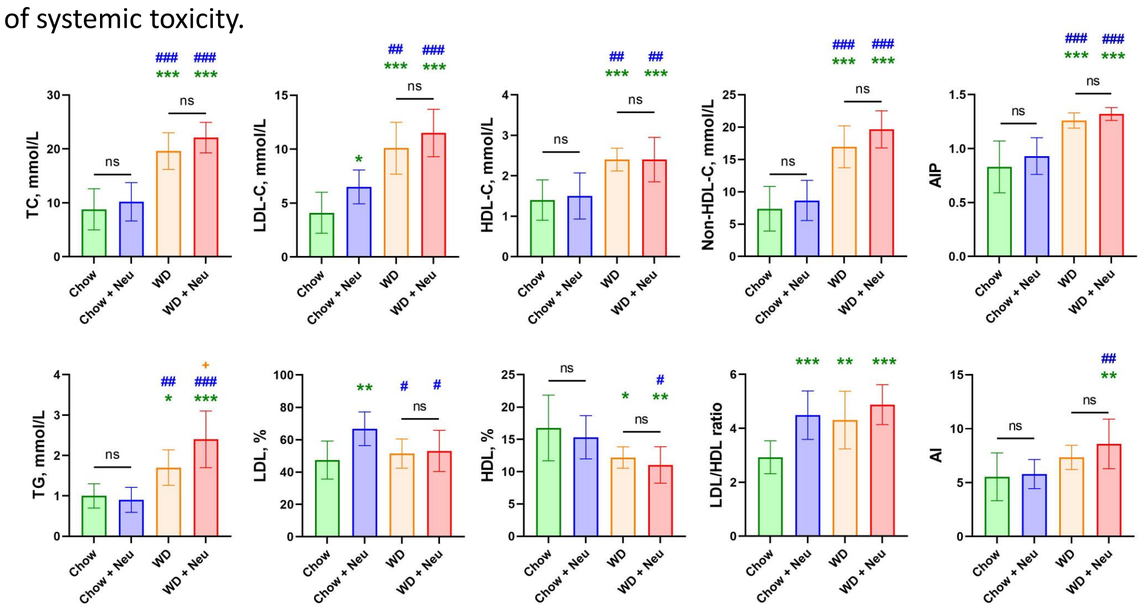

Figure 4. Plasma lipid profile parameters in ApoE-KO mice subjected to Western diet and neuraminidase administration.

CONCLUSION

We developed a novel *in vivo* model that replicates the enhanced atherogenicity of desialylated LDL and its contribution to atherosclerotic lesion progression. This study provides an experimental platform for studying glycosylation-dependent mechanisms in atherosclerosis and highlight LDL desialylation as a potential therapeutic target.