SIALYLATION OF HUMAN PLASMA LIPOPROTEINS AS A KEY DETERMINANT OF BIOLOGICAL FUNCTION

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Background and Aims

Human plasma lipoproteins contain multiple oligosaccharide moieties, whose composition and functional importance remain incompletely characterised.

Our aim was to assess:

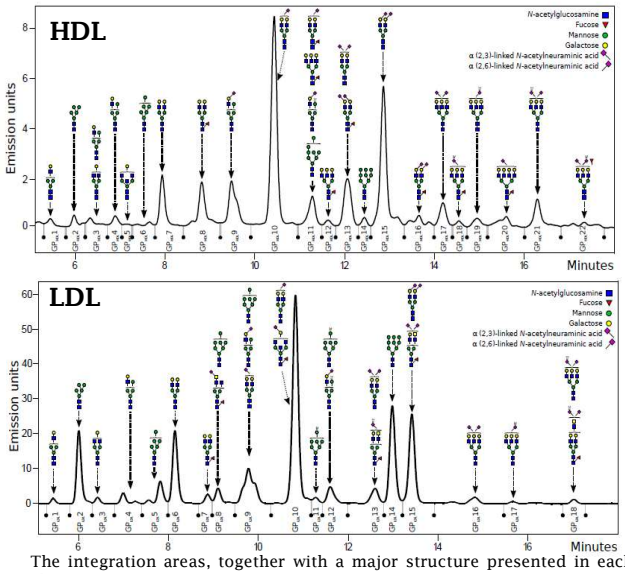
- glycomic profiles of human plasma high-density lipoprotein (HDL) and low-density lipoprotein (LDL), and
- the role of the lipoprotein glycome in cellular cholesterol metabolism.

Methods

HDL and LDL were isolated from normolipidemic human plasmas (n=6) by isopicnic density gradient ultracentrifugation. Glycomic profiles of native and neuraminidase-treated HDL and LDL were obtained using HILIC-UPLC/MS approach. The capacity of HDL to mediate cellular efflux of cholesterol and the capacity of LDL to induce cellular accumulation of cholesterol esters were evaluated in macrophage-like human THP-1 cells.

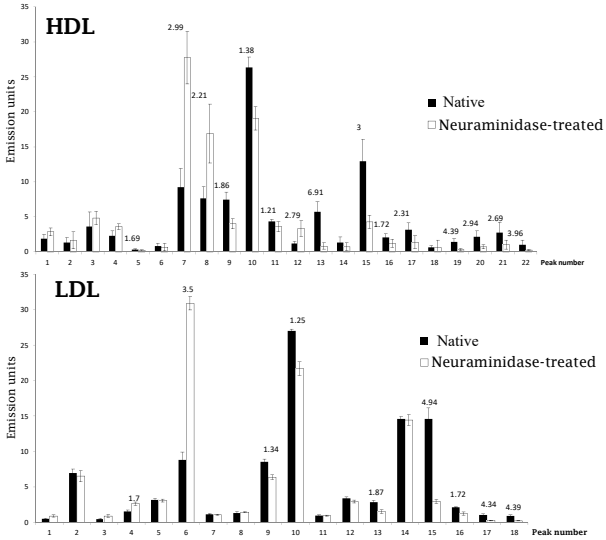
Results

1. Representative chromatogram of 2-AB labeled N-linked glycans released from native HDL and LDL and separated by HILIC-UPLC: *High glycan sialylation*



The integration areas, together with a major structure presented in each glycan group are given.

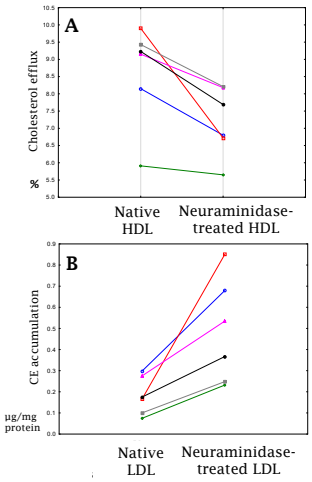
2. Relative abundance of individual glycan peaks in native and neuraminidase-treated human HDL and LDL: *Removal of sialic acid residues by the enzyme*



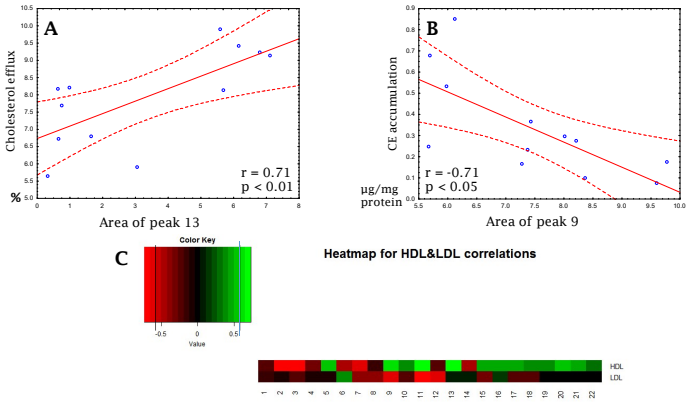
Numbers at the bars denote fold differences in case of significant difference. For peak numbers see Figure 1.

3. Influence of the treatment with neuraminidase on biological properties of human HDL and LDL: *Decrease in cholesterol efflux capacity mediated by HDL and increase in cholesterol ester accumulation induced by LDL*

Cellular cholesterol efflux capacity of native and neuraminidase-treated human HDL in macrophagic THP-1 cells (A) and accumulation in THP-1 cells of cholesterol ester derived from native and neuraminidase-treated human LDL (B) are shown. Mean values ± SDs of 6 experiments performed with 6 individual plasma samples are 8.63 ± 1.45 vs. 7.21 ± 1.00 % ($p<0.05$) in the non-treated and treated with neuraminidase HDL, respectively (A), and 0.18 ± 0.09 vs. 0.49 ± 0.25 μg/mg protein ($p<0.05$) in the non-treated and treated with neuraminidase LDL, respectively (B).



4. Relationships between the glycome and biological properties of HDL and LDL: *Role of sialic acid residues*



Correlations between cellular cholesterol efflux capacity of HDL and area of the peak 13 (A) and between cellular cholesterol ester accumulation induced by LDL and area of the peak 9 (B) are shown together with a heatmap representing correlation coefficients of the glycome (as peak numbers shown in Figure 1) with the cholesterol efflux capacity of HDL and cellular total cholesterol accumulation induced by LDL (C). Values of correlation coefficients corresponding to p = 0.05 are shown as straight lines (C).

Conclusions

Sialylation of human plasma HDL and LDL represents a key determinant of their biological function.

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