atherothrombotic stroke. We aimed to compare the lipid profile and HDL's characteristics between asymptomatic and recently symptomatic patients with CA in order to assess the putative contribution of these factors to plaque vulnerability.
Methods: Prospective study of consecutive patients with CA causing ≥50% degree of stenosis who underwent carotid endarterectomy in our center between 2021 and 2024. CA patients were divided into asymptomatic (CA-A, n=30) and symptomatic (CA-S, n=67). A control group of patients with cardioembolic stroke was also included (CE group, n=30). Plasma lipid profile and apolipoproteins were evaluated by autoanalyzer. PAF-AH and PON enzymatic activities associated to HDL were measured in the serum apoB-depleted fraction. HDL was isolated from plasma by ultracentrifugation and then incubated with macrophages derived from THP1-CD14 monocytes. HDL-induced cytokine release and gene expression in macrophages were assessed by ELISA and real-time PCR, respectively.
Results: Patients with CA had lower HDL-C and apoA-I plasma concentrations than CE patients, with CA-S patients showing lower values than CA-A patients. PAF-AH and PON activities associated with HDL were significantly lower in CA than in CE patients. PON activity was decreased in CA-S compared to CA-A patients. In macrophages, HDL isolated from the 3 group of patients induced IL1β and IL6 release and gene expression. HDL from CA-S elicited higher IL6 release and IL1β gene expression than HDL from CA-A. Plasma IL6 levels were elevated in CA-S compared to CA-A.
Conclusions: Patients with CA, particularly CA-S, have lower levels of HDL-C and apoA-I, and HDL with less antioxidant properties than CE. HDL from the 3 groups shows inflammatory potential, with that from CA-S promoting the highest IL-6 release and IL1β gene expression in macrophages.

P159 / #1133
Poster Topic: *AS02 LIPIDS AND LIPOPROTEINS / AS02.03 HDL*
The lack of apoA-I in apoE-KO mice affects the liver transcriptome

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Background and Aims: Liver is the major organ involved in apoA-I synthesis and HDL-C turnover, but the impact of apoA-I/HDL on the hepatic transcriptome has never been investigated before. In the present study, a transcriptomic analysis by high-throughput RNA-seq was conducted in the liver of atherosclerosis-prone mice, with the aim of identifying new genes/pathways modulated by apoA-I/HDL with a potential effect on atherosclerosis development.
Methods: Eight-week-old apoE knockout (apoEKO) mice lacking apoA-I/HDL (DKO) and with physiological levels of apoA-I/HDL (DKO/hA-I) were fed either a standard rodent diet (SRD) or a Western diet (WD) for 22 weeks.
Results: After both dietary treatments, DKO mice were characterized by lower cholesterol levels, but increased atherosclerosis development, compared to DKO/hA-I mice. The liver transcriptome of DKO and DKO/hA-I mice fed SRD diverged in a relatively small number of genes, suggestive of a greater activation of the PPAR signaling pathway and the retinoid metabolism pathway in DKO/hA-I mice. Following WD, transcriptomic analysis highlighted in both genotypes an upregulated expression of immune/inflammatory genes and a reduced activation of the retinoid metabolism. The evaluation of the hepatic response of the two genotypes to the dietary switch from SRD to WD revealed strong divergences in genes involved in metabolic pathways only in the presence of apoA-I/HDL, with reduced endogenous sterol biosynthesis and glutathione metabolism, together with increased glucose metabolism.
Conclusions: The presence or absence of apoA-I expression differently alters hepatic pathways involved not only in cholesterol metabolism, but also in those of glutathione and glucose metabolism.

P160 / #24
Poster Topic: *AS02 LIPIDS AND LIPOPROTEINS / AS02.03 HDL*
Novel bioactive lipids enhance HDL-mediated cholesterol efflux and provide protection against LDL oxidation

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Background and Aims: Introduction: Enhancing HDL's functionality and overall quality is anticipated to attenuate atherosclerosis and lower the risk of cardiovascular disease (CVD). We extracted a newly bioactive compound, Lyso-DGTS, from Nannochloropsis microalgae, which improved the activities of paraoxonase 1-PON1, the primary antioxidant enzyme linked to HDL. Our aim is to thoroughly investigate the structural aspects of these lipid components, delineating their significance in HDL-mediated cholesterol efflux and preventing LDL oxidation.
Methods: we investigated the effect of synthesized lipid derivatives and endogenous analogs of lyso-DGTS on PON1 lactonase activity through the dihydrocoumarin assay, and LDL oxidation was monitored by measuring the formation of conjugated dienes at 234 nm; furthermore, the effect of the bioactive lipids on HDL-mediated cholesterol efflux from macrophages was examined, and the mechanism was explored using fluorescent sterol BODIPY-cholesterol. The effect of lyso-DGTS derivatives and analogs on the surface polarity of HDL was examined using the Laurdan generalized polarization (GP) assay.
Results: Six lipids significantly elevated recombinant PON1 (rePON1) lactonase activity in a dose-dependent manner. Using a tryptophan fluorescence-quenching assay and a molecular docking method, lipid–PON1 interactions were characterized. An inverse correlation was obtained between the lactonase activity of PON1 and the docking energy of the lipid–PON1 complex. Furthermore, five lipids increased the LDL oxidation lag time and inhibited its propagation. Lyso-DGTS and lyso-PAF increased HDL-mediated cholesterol efflux from macrophages dose-dependently, mainly via the ABCA1-mediated cholesterol efflux pathway and by enhancing apolipoprotein A1 binding to the ABCA1 receptor. A reverse Pearson linear regression was obtained between Laurdan GP values and HDL-mediated cholesterol efflux.
Conclusions: Novel bioactive lipids based on Lyso-DGTS derivatives interact selectively with HDL components, altering their structure and functions. Improving HDL functions using Lyso-DGTS and its derivatives might be a novel approach for reducing atherosclerosis development and decreasing CVD risk.

P161 / #913
Poster Topic: *AS02 LIPIDS AND LIPOPROTEINS / AS02.03 HDL*
Low residence time of exogeneous HDL is associated with preserved renal function in rats treated with $HgCl_2$ and accumulation of HDL-protein in adipose tissue

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Background and Aims: Previous studies demonstrated that therapeutic administration of exogeneous HDL limits the tissue damage induced by $HgCl_2$ in rats without plasma HDL-lipids concentrations increases, suggesting an extravasation of HDL for tissue repair. The aim of this study was to demonstrate the capacity of HDL to preserve the viability of cultured cells challenged with $HgCl_2$ and determine whether and increased catabolic rate of exogenous HDL explains