Background and Aims : Delayed cerebral vasospasm (DCV) is the leading cause of mortality after subarachnoid hemorrhage (SAH). There is increasing evidence that inflammation, specifically leukocyte-endothelial cell interactions, plays a role in the pathogenesis of DCV. High-density lipoproteins (HDL) are biological molecules that prevent the expression of cell adhesion molecules induced by pro-inflammatory agents in endothelial cells, thus inhibiting leukocyte adhesion. In pathological conditions, HDL undergo quantitative and qualitative changes that have been associated with loss of physiological function. However, the role of HDLs in DCV has not been studied, hence the novelty of the present work.

Methods: Plasmatic HDL were isolated from 26 patients with or without DCV, as well as 24 healthy controls. We analyzed their anti-inflammatory activity and examined the HDL-associated proteins by LC-MS-MS.
Results: We observed that SAH patients had significantly lower levels of HDL in plasma compared to controls. Furthermore, HDL isolated from patients lost the ability to prevent adhesion of THP-1 monocytes to endothelial cells (HUVEC), and the effect was more pronounced in patients with DCV. The unadjusted differential expression analysis showed eleven proteins (AGT, APOH, C3, CRP, ITIH4, LRG1, SAA1, SAA2, SAA4, SELL, SERPINA3) were overexpressed in patients, while three (APOA4, APOC2, ITIH1) were lower compared to controls. Between patients, LRG1, SAA1, and SAA2 were associated with the presence of DCV.
Conclusions: The study of HDL in the pathophysiology of DCV after SAH is needed since HDL can be considered a novel therapeutic approach to the treatment of the inflammatory response that participates in the onset of DCV after SAH.

EP215 / #399, TOPIC: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-04 LIPOPROTEIN RECEPTORS*, POSTER VIEWING SESSION.
SILENCING OF PCSK9 BY SIRNA-FUNCTIONALIZED RHDL AS TOOL TO UPREGULATE LDLR EXPRESSION IN HEPATOCYTES

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Background and Aims : Cardiovascular disease (CVD) is the leading cause of death worldwide and is often related to high plasma concentrations of low-density lipoprotein cholesterol (LDL-c). Many approaches have been carried out to deal with high cholesterol levels in plasma, statins and antibodies targeting PCSK9 among others. Although the use of antibodies has been proven to be an efficient treatment against PCSK9 effect, they are not effective for GOF variants with intracellular activity. Recently, the use of siRNA that impair the PCSK9 synthesis has been proposed as an alternative to antibodies. Therefore, the aim of this work has been to develop a new therapeutic strategy based on siRNA delivery within recombinant HDL (rHDL) to downregulate PCSK9 expression.

Methods: siRNA targeting PCSK9 was incorporated onto rHDL. Uptake of the nanoparticles, their effect on LDL uptake and LDLr expression was determined by flow cytometry. *PCSK9* mRNA levels were determined by qPCR. PCSK9 expression was measured by western blot and ELISA
Results: siRNA targeting PCSK9 delivered by rHDL significantly reduces *PCSK9* mRNA levels and PCSK9 expression, as well as increases *LDLR* expression and LDL uptake.
Conclusions: The inhibition of PCSK9 by rHDL-mediated delivery of siRNA is an effective method to reduce the deleterious effect of PCSK9 *in vitro*. This approach could also useful against PCSK9 variants with intracellular activity.

EP216 / #1371, TOPIC: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-04 LIPOPROTEIN RECEPTORS*, POSTER VIEWING SESSION.
MICRORNA 33A CONTROLS SREBP-2 AND LXR DEPENDENT REGULATION OF THE LDL RECEPTOR PATHWAY

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Background and Aims : Coordinated cellular mechanisms that regulate LDLR transcription and degradation remain largely obscure. We sought to assess the effect of miR-33a on the LDLR pathway given the concerted action of SREBP-2 and miR-33a in elevating cellular cholesterol levels.

Methods: The role of miR-33a in LDLR expression and (V)LDL-uptake was assessed in a series of gain and loss of function studies. Post-transcriptional inhibition through direct binding to target mRNAs was determined and validated by vector-based and Par-Clip assays. The effect on plasma cholesterol and triglyceride levels was evaluated in DIO, *Ldlr*$^{+/-}$ and E3L.CETP mice.
Results: MiR-33a-3p/5p modulated LDLR protein abundance and LDL uptake without a change in mRNA. Intrinsic binding sites predominantly positioned within the PCSK9 coding sequence and IDOL 3'-UTR, facilitated inhibition and interrupted sustained LDLR repression in hepatocytes. MiR-33a-3p, but not 5p, also directly inhibited ANGPTL3 expression. Liver-targeted miR-33a-3p mimic reduced hepatic and circulating PCSK9 levels and lowered LDL levels. In E3L.CETP mice, it also attenuated postprandial TG and non-HDL-C levels as a consequence of increased triglyceride-derived fatty acid uptake by white adipose tissue and subsequent hepatic uptake of lipoprotein remnants, accompanied by reduced plasma ANGPTL3.
Conclusions: Our findings reveal a compensatory control mechanism in the LDLR pathway and highlights miR-33a-3p mimics as alternative therapeutic inhibitors of LDL-cholesterol in hypercholesterolemia.

EP217 / #1373, TOPIC: *ASA02 - LIPIDS AND LIPOPROTEINS / ASA02-06 CHOLESTEROL EFFLUX AND REVERSE CHOLESTEROL TRANSPORT*, POSTER VIEWING SESSION.
MOROCCAN POMEGRANATE (SEFRI VARIETY) POLYPHENOLS PREVENT HYPERLIPIDEMIA, OXIDATIVE STRESS AND ENHANCE CHOLESTEROL EFFLUX PROCESSES

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Background and Aims : The present study aimed to investigate the effect of phenolic-rich extract from pomegranate peels (PEPP) and arils (PEPA) on lipid profile in high fat-high fructose diet (HFFD) induced hyperlipidemia in *Wistar* rats and to provide a molecular explanation for their effects.

Methods: Potent antioxidative and antiatherogenic effects of pomegranate phenolic-rich extracts against lipid peroxidation in whole plasma were