HDL were elucidated: *FADS1*, *INSIG1*, *CCL4* and *LDLR*. These genes were evaluated by their capacity to affect efflux of cholesterol mediated by HDL. Knock-down of *CCL4* increased efflux of cholesterol from lipid-loaded macrophages. Knock-down of *INSIG1* diminished efflux of cholesterol. By contrast, there was no difference in the capacity of HDL particles to remove cholesterol from human THP-1 cells in which *FADS1* expression was knocked-down.
Conclusions: Thus, we have identified *CCL4* and *INSIG1* as genes involved in cholesterol efflux mediated by HDL. This work was supported by Russian Science Foundation (Grant # 14-15-00112).

P3.124
SPHINGOSINE-1-PHOSPHATE RECEPTORS S1P1 AND S1P3 REGULATE THE TRANSENDOTHELIAL TRANSPORT OF HDL AND LDL ANTAGONISTICALLY

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Objective: Lipoproteins may pass the endothelium by paracellular and transcellular routes. Sphingosine-1-phosphate (S1P) bound by apolipoprotein M (apoM) within HDL promotes the closure of interendothelial junctions. This raises the question, how S1P and its cognate receptors S1P1 and S1P3 regulate the transendothelial transport of lipoproteins.
Methods: Cultivation of human aortic endotlhelial cells (HAECs) in a transwell system. incubation of HAECs with radioiodinated lipoproteins in the presence or absence of 40x excess unlabeled lipoproteins to assess specific binding, association and transport. Use of pharmacological agonists and antagonists to to stimulate and inhibit, respectively, S1P receptors S1P1 and S1P3. Interference with the expression of candidate lipoprotein receptors with siRNAs. Inhibition of fluid-phase transport with amiloride and EIPA efficacy control by assessment of dextran transport).
Results: Pre-treatment of HAECs with inhibitors of S1P1 and S1P3 decreased the cellular binding, association and transport of ^{125}I-HDL but increased the binding, association and transport of ^{125}I-LDL. Vice-versa the pre-treatment with S1P receptor agonists increased the specific cellular binding, association and transport of ^{125}I-HDL but decreased binding, association and transcytosis of ^{125}I-LDL. The stimulatory effects of the S1P1 and S1P3 agonists on endothelial binding, association and transport of ^{125}I-HDL were abrogated by silencing of scavenger receptor BI (SR-BI). The stimulatory effect of the S1P1 inhibitor but not of the S1P3 inhibitor on endothelial association and transport of ^{125}I-LDL was decreased by treatment with the fluid-phase inhibitors amiloride and EIPA. The stimulatory effect of the S1P3 inhibitor on the cellular binding and association of ^{125}I-LDL was inhibited by silencing LDL receptor (LDLR). However, the S1P3 inhibitor continued to promote the transport of ^{125}I-LDL through HAECs with suppressed LDLR or SR-BI. Therefore, the protein mediating transcytosis of ^{125}I-LDL in response to S1P3 inhibition remains to be identified.
Conclusions: S1P1 and S1P3 regulate the transendothelial transport of HDL and LDL in an antagonistic manner. These findings emphasize that transendothelial transport of lipoproteins is a spefically regulated process which is an interesting target for therapeutic interventions with atherosclerosis.

P3.125
POLYPHENOL-RICH ARONIA BERRY EXTRACT INHIBITS TNF-α-INDUCED VASCULAR ENDOTHELIAL INFLAMMATION

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Objective: Vascular endothelial inflammation is well known to be an initial step in arteriosclerosis. Aronia berry (*Aronia meranocalpa*), known as black chokeberry, is a shrub native to North America and commonly consumed as juice, wine and jam. Aronia berry contains abundant polyphenols and recently its functionality attracts attention. Therefore, in this study, we examined the effect of Aronia berry extract on TNF-α-induced vascular endothelial inflammation.
Methods: Human umbilical vein endothelial cells (HUVECs) were pretreated with Aronia berry extract (0-25 μL) and then stimulated with TNF-α (10 ng/mL). The mRNA and protein analysis were performed by real time PCR and western blotting, respectively. Fluorescently labeled THP-1 monocytic cells were added to HUVECs, and adhesion assay was performed.
Results: Increased expression of mRNA of inflammatory cytokines (IL-1β and IL-6) by TNF-α addition was significantly suppressed by Aronia berry extract. Moreover, gp130 (IL-6ST), a signaling molecule of IL-6, was significantly suppressed by Aronia berry extract both in mRNA and protein level.
Aronia berry extract decreased the protein expression of vascular cell adhesion molecule 1 (VCAM-1), but the expression of intercellular adhesion molecule 1 (ICAM-1) was unchanged. The increase in THP-1 cells adhesion to HUVECs was inhibited by Aronia berry extract.
To investigate the mechanism of anti-inflammatory effect of Aronia berry extract, nuclear translocation of NF-κB and STAT3 was examined. Aronia berry extract inhibited phospholylation and nuclear translocation of STAT3.
Conclusions: These results showed that Alonia berry extract could exert anti-inflammatory effect through inhibition of activation of STAT3 in TNF-α-induced vascular endothelial inflammation.

P3.126
GUT DERIVED INDOLE 3-PROPIONIC ACID REGULATES ENDOTHELIAL FUNCTION IN A PXR DEPENDENT MECHANISM

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Objective: Differences in indoles derivatives were observed in the plasma of germ-free and conventionally housed murine models. Indole-3-propionic acid(IPA) is identified as one of the few derivatives expressing potent anti-oxidant property and shown to be associated with lower risk of type-2 diabetes. The objective of our work is to address the role of IPA in regulating vascular function.
Methods: PXR-/- and PXRwt/wt mice were subjected either antibiotics cocktail or IPA or in combination for a period of 2-weeks. Upon euthanasia, aortic rings were prepared and subjected to endothelium-dependent and independent relaxation. Tissues were pre-contracted with phenylephrine followed by relaxation towards acetylcholine (Muscarinic agonist) and 2-furoyl-LIGRLO-NH2 (2-fLI) PAR2-agonist were then measured by wire-myography; Further confirmation was performed in germ-free mice subjected to IPA treatment. Isolated Mouse endothelial cells were treated with IPA. Analysis of nitrite in plasma was performed to measure the nitric oxide content.
Results: Lack of PXR increased the vasorelaxation to Ach and 2-fLI by 40%. Depletion of IPA by Antibiotics treatment increased the vasorelaxation by 50% in PXRwt/wt mice. IPA treatment alone didn't restore the vasorelaxation in PXR-/- mice but in PXRwt/wt. Combination of antibiotics along with IPA protected PXRwt/wt mice from increased vasorelaxation but not in PXR-/- mice supporting PXR-dependent activation rescues impaired vasorelaxation in an endothelium-dependent manner. Nitric oxide levels in PXR-/- mice were 4-folds higher compared to PXRwt/wt mice
Conclusions: These data show the gut-derived IPA is a key player in vascular homeostasis.

P3.127
INFLUENCE OF SASKATOON BERRY POWDER ON INSULIN RESISTANCE AND INTESTINAL MICROBIOTA IN HIGH FAT-HIGH SUCROSE DIET-INDUCED OBESE MICE

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