cular disease (CVD). However, FH patients are underdiagnosed and undertreated. So, public cholesterol screening is essential to find individuals with FH and prevent cardiovascular disease in these patients. In this study, we aim to investigate the percentage of patients with FH in an hospital cholesterol screening program and the characterization of their cardiovascular risk.
Methods A total of 1575 LDL cholesterols were screened. Finally, 56 suspected FH patients (DCLN score ≥ 4) were selected to perform genetic analysis. The diagnosis of FH was supposed using the Dutch Lipid Clinic Network (DLCN) criteria and confirmed by pathogenic genetic variants presence. Familial Hypercholesterolemia Genetic Analysis (SEQPRO LIPO) detected variants associated with Autosomal Dominant Hypercholesterolemia (ADH) and Autosomal Recessive Hypercholesterolemia (ARH). To confirm probably or possibly pathogenic status of the novels genetic variants, the in silico prediction of the LDLR, APOB and PCSK9 genes missense mutations effect was performed using PolyPhen-2 and SIFT Human Protein refined SIFT. Mean common carotid intima media thickness (IMT) were assessed using consensus criteria in subjects without history of cardiovascular disease (CVD).
Results. The detection rate of FH was 1.64% (one in 61). All FH patients had a pathogenic genetic variants. FH patients had higher mean IMT than non-exposed subjects (0.73±0.14 vs. 0.68±0.1mm, $p<0.05$). In addition, in a multiple linear regression, IMT was associated with corneal arcus and/or tendon xanthomas presence ($p<0.01$) and age ($p<0.01$).
Conclusions. In clinical practice, detecting FH patients by screening serum lipid levels is useful to find new cases of FH. In addtion FH patients in primary prevention had higher mean IMT than non-FH subjects. Finally, corneal arcus and/or tendon xanthomas presence is associated with early carotid atherosclerotic injury in subject with higher LDL value.

BIGLYCAN EXPRESSION IN CARDIOVASCULAR RISK CONDITIONS: ARTERIAL HYPERTENSION AND CIGARETTE SMOKING

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Background. Biglycan (BGN), a small leucine rich proteoglycan, plays a pivotal role in initiating the deposition of lipids in the arterial subintimal space by its ability to bind and retain apoB-containing lipoprotein, including LDL, VLDL and IDL. Moreover, BGN acts as an endogenous ligand of Toll-like receptors mediating innate immunity and inflammation.
Patients, Methods and Results. Evaluating patients affected by arterial hypertension (AH) we found that BGN expression is increased, and that Angiotensin II can mediate BGN expression. The treatment by an Angiotensin receptor blocker, Losartan, administrated at standard dose of 50 mg/day, significantly reduced BGN expression with respect to baseline. IL-6, TNF-alpha, CRP, and fibrinogen were also significantly reduced. These results suggest that Losartan can reduce BGN expression in monocytes from AH patients and that the effects of AngII on BGN expression in monocytes may be modulated, in part, by an Angiotensin receptor blocker.
We also investigate whether cigarette smoking (CS) may enhance monocyte BGN in subjects without additional cardiovascular risk factors (CVRFs). Fibrinogen Il-6, CRP, carotid-femoral pulse wave velocity (cf-PWV) and intima media thickness (cIMT) were also evaluated. BGN was increased in young smokers, as compared to controls, and appears associated with increased fibrinogen, CRP, and IL-6, lower HDL-C, and altered AS and cIMT. Last, we evaluated whether monocyte BGN may decrease after smoke cessation. Anthropometrics, laboratory profile, cf-PWV, cIMT, and BGN were evaluated during active CS, and 12 months after smoke cessation.
We found that BGN, IL-6, CRP, fibrinogen, HDL-C, and cf-PWV were significantly improved as compared to baseline. These data show that BGN expression may be reversibly induced by CS, and also by AH.
Conclusions. Overall, these data suggest that BGN represents a link between proatherogenic status induced by CS or AH and the development and progression of vascular damage.

INTEGRATED HIGH-THROUGHPUT MIRNOMICS AND LIPIDOMICS OF WILD-TYPE, PCSK9 AND LDLR KNOCKOUT MICE AS A TOOL TO DISSECT MIRNA TO MOLECULAR LIPID LEVELS CORRELATIONS

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Aim. Pcsk9 and LDL receptor knockout mice are two sides of the same coin, showing profound changes in lipid metabolism related to wild-type mice. We leveraged on these different genotypes to reconcile differences in miRNA expression and lipid levels.
Methods. Wild type, Pcsk9- and Ldlr-knockout mice were fed both chow and Western diets for 16 weeks. MicroRNAs were high-throughput sequenced in liver, aorta, white adipose tissue, duodenum, jejunum, ileum and brain; 387 molecular lipid species were quantified by high-throughput mass-spectrometry in liver, aorta and plasma. An algorithm to reconcile and integrate the two datasets was developed; background correlations were calculated against 1,000 randomized datasets.
Results. Expression levels for each miRNA were tested for correlation with each lipid measurement, permuting all possible combinations of samples. ~150 miRNAs showed more correlations with lipid values than those expected from background expectation; 48 miRNAs showed at least thrice (*Fig. 1A*). We found that liver and small intestine (ileum, especially) are the tissues where the number of such correlations are higher (*Fig. 1B*). The analysis could identify established miRNAs related to lipid metabolism (like miR-33, miR-210 and miR- 21a) and also find novel miRNAs with similar association patterns. For example, hepatic miR-33 associates strongly with cholesteryl esters levels in the liver, as does previously unre-