Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand; [8] *Hormonal And Metabolic Disorders Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand*

Background and Aims : Thai Familial Hypercholesterolemia (FH) registry has been established to characterize Thai FH subjects, identify treatment gaps, and raise awareness of the disease.

Methods: Subjects with clinical diagnosis of FH by the Dutch Lipid Clinic Network (DLCN) criteria were recruited and clinical data were collected. Blood specimens were obtained for whole exome sequencing (WES).

Genetic results of Thai subjects with Familial Hypercholesterolemia by whole exome sequencing

	ALL (N = 27)	PROBABLE FH (N = 10)	DEFINITE FH (N = 17)
DLCN score		6-8	>8
Number of subjects with mutations found, n (%)	8 (30)	1 (10)	7 (41)
LDLR mutations	5	p.Asn428Lys	p.Glu208Ter p.Asn428Lys p.Leu568Val c.695-1G>A
APOB mutations	2	-	p.Arg3527Trp
PCSK9 mutations	1	-	p.Arg93Cys

Results: As of June 2021, 154 subjects with probable or definite FH (DLCN score ≥6) were recruited. The mean age was 51 years old and 63% were women. Mean LDL-C was 4.07 mmol/L. Only 7% had history of premature coronary artery disease (CAD) and 19% had family history of premature CAD. Around 49% were given lipid-lowering medications. Among 27 subjects who underwent WES, eight (30%) were found to harbour six pathogenic variants. Four variants in the *LDLR* gene (c.622G>T, c.695-1G>A, c.1284C>G, and c.1702C>G) were found in five subjects. A missense variant in the *APOB* gene (c.10579C>T, p.Arg3527Trp) was identified in two cases and a missense variant in the *PCSK9* gene (c.277C>T, p.Arg93Cys) was also found.
Conclusions: Our first preliminary report of the Thai FH registry showed that history of premature CAD was less prevalent than that of the regional or global data. Only half currently received lipid-lowering medications, allowing us to identify treatment gaps in care of these subjects. Majority of patients did not carry pathogenic variants in coding regions of genes known to cause FH.

EP506 / #166, TOPIC: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-13 GENOMICS, GWAS AND POPULATION GENETICS; MENDELIAN RANDOMIZATION*, POSTER VIEWING SESSION.
THE BLOOD PROTEO-GENOMIC ARCHITECTURE OF VENOUS THROMBOEMBOLISM

A. Girard [1], E. Abner [2], H.D. Manikpurage [1], E. Gagnon [1], É. Gobeil [1], C. Couture [1], P. Mathieu [1,3], T. Esko [2], B.J. Arsenault [1,4]. [1] *Cardiology, Quebec Heart and Lung Institute, Québec, Canada;* [2] *Estonian Genome Center, Uniersity of Tartu, Tartu, Estonia;* [3] *Department Of Surgery, Université Laval, Québec, Canada;* [4] *Département De Médecine, Université Laval, Québec, Canada*

Background and Aims : Genome-wide association studies (GWAS) have identified dozens of genetic loci associated with venous thromboembolism (VTE) susceptibility. The functional impact of these genetic variants is not completely characterized. We hypothesized that VTE susceptibility loci have an important influence on the human blood proteome.

Methods: We performed two new GWAS in the Estonian Biobank (12,569 cases and 164,827 controls) and in the UK Biobank (13,722 cases and 393,364 controls) and used GWAS summary statistics from FinnGen (9176 cases and 209,616 controls) to perform a genome-wide association meta-analysis of these three cohorts totaling 35,467 cases and 766,807 controls. Using a Bayesian genetic colocalization method, we mapped genome-wide significant hits at 26 loci from that GWAS meta-analysis and from previously published GWAS to blood proteins using GWAS summary statistics on 2925 blood proteins from 3301 participants of the INTERVAL cohort. Genetic variants with a posterior probability of genetic colocalization (PPH4)>0.80 were considered as colocalized.
Results: When taking into consideration trans-pQTL, this method identified 382 blood proteins (313 blood proteins after excluding the ABO locus) that colocalized with at least one VTE variant. A total of 32 VTE variants were transacting only, while 4 variants had both cis and trans effects (31 trans-acting only and 2 cis and trans-acting after exclusion of the ABO locus).
Conclusions: We mapped 26 VTE susceptibility loci to hundreds of blood proteins. Most of these associations were driven by trans-acting SNPs, thereby highlighting the complexity of the genetic architecture of VTE.

EP507 / #282, TOPIC: *ASA03 - DYSLIPIDEMIA AND RISK FACTORS / ASA03-13 GENOMICS, GWAS AND POPULATION GENETICS; MENDELIAN RANDOMIZATION*, POSTER VIEWING SESSION.
MITOCHONDRIAL HETEROPLASMY VARIANTS ASSOCIATED WITH SUBCLINICAL ATHEROSCLEROSIS

T.V. Kirichenko [1], S.J. Urazalina [2], A.N. Orekhov [3], I.A. Sobenin [1], S. Kozlov [4]. [1] *Laboratory Of Medical Genetics, National Medical Research Center of Cardiology, Moscow, Russian Federation;* [2] *Department Of Cardiology, JSK Scientific-Research Institute of Cardiology and Internal diseases, Almaty, Kazakhstan;* [3] *Laboratory Of Cellular And Molecular Pathology Of Cardiovascular System, Research Institute of Human Morphology, Moscow, Russian Federation;* [4] *Laboratory Of Problems Of Atherosclerosis, National Medical Research Center of Cardiology, Moscow, Russian Federation*

Background and Aims : The level of mitochondrial heteroplasmy increases with age and may play an important role in the development of atherosclerotic lesions. Previously we determined several variants of mitochondrial heteroplasmy associated with atherosclerotic lesions in aortal intima and carotid intima-media thickness (cIMT) in Russian population. In present study, these variants of mitochondrial heteroplasmy were analysed in Kazakh subjects with subclinical atherosclerosis.

Methods: The study included 70 participants free of cardiovascular disease aged 50-70 years old. DNA was isolated from blood leukocytes by phenol-chloroform extraction. Mitochondrial heteroplasmy levels were determined by pyrosequencing of mtDNA PCR-amplificated fragments. B-mode ultrasound scanning of carotid arteries was performed to measure cIMT. Statistical analysis was performed by SPSS ver.27.0.
Results: The mean age of study participants was 62.0(4.5) years old, the mean cIMT – 0.806(0.097) mm. The following levels of pro-atherosclerotic mitochondrial heteroplasmy variants were determined: 13513G>A – 11.7(6.4)%; 12315G>A – 29.3(6.2)%; 5178C>A – 22.5(8.2)%; 14459G>A – 13.2(11.2)%; 14846G>A – 18.9(4.9)%. The significant association of cIMT with mitochondrial heteroplasmy variants m.13513G>A and m.12315G>A was found. Mitochondrial heteroplasmy 13513G>A correlated negatively with cIMT (r=-0.526, p=0.036); 12315G>A correlated positively with cIMT (r=0.696, p=0.025).
Conclusions: Thus, atherosclerosis-related variants of mitochondrial heteroplasmy were found in subjects from Kazakh population, however, further search in larger cohorts of genetically diverse populations is needed to estimate the role of mitochondrial heteroplasmy in atherosclerosis development. This work was supported by the Russian Science Foundation (Grant #22-15-00134).