potential confounders. Our results, implies that rs2737190 may be useful marker for the genetic study of sepsis.

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E-P05 Cardiovascular disorders

E-P05.02
Targeting sequencing in Russian families with arrhythmogenic right ventricular cardiomyopathy: first results

M. A. Fedyakov[1], O. E. Veleslavova[2], S. V. Apalko[1,2], O. V. Romanova[1], N. Y. Shved[1,2,3], Y. V. Shubik[2], S. D. Rud[4], T. E. Ivaschenko[3], A. M. Sarana[1,2], S. G. Scherbak[1,2], O. S. Glotov[1,2,3]

[1]City Hospital № 40, Saint-Petersburg, Russian Federation, [2]Saint-Petersburg University, Saint-Petersburg, Russian Federation, [3]FSBSI "The Research Institute of Obstetrics, Gynecology and Reproductology named after D.O.Ott", Saint-Petersburg, Russian Federation, [4]Military Medical Academy named after S.M.Kirov, Saint-Petersburg, Russian Federation

Introduction: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a hereditary progressive cardiac muscle disease characterized by fibrofatty myocardial dysplasia, ventricular arrhythmia, and sudden cardiac death. In Russia, most studies are targeted at hypertrophic and restrictive cardiomyopathy, with insufficient data on ARVC. Materials and Methods: In this study we analyzed a cohort of 43 patients from 13 ARVC families. The diagnosis was established according to the Task Force Criteria of the European Society of Cardiology revised in 2010. The assay was performed on the MiSeq (Illumina, USA), panel TruSight Cardiomyopathy Target Genes. Coding regions of 46 genes associated with the development of inherited cardiomyopathies, including genes *PKP2, PLN, DSP, DSC2, DSG2, JUP, TMEM43, DES, TTN, LMNA* associated with the development of the hereditary form of ARVC were sequenced. Results: At present 35 patients from 10 families are tested. Pathogenic mutations were confirmed in 1 family. We have found new frameshift mutation c.355delT in the *PKP2* in the patient with a definite diagnosis of ARVC. Subsequent family assessment showed that all three of the proband's children also carried this mutation. Data of remaining 8 patients are processed. Current mutation detection rate was 1/10 (10%). Conclusions: The first results of our work suggest that Russian ARVC population is not similar to same European populations. Mutation detection rate is significantly lower than expected. More comprehensive gene panel or exome sequencing is needed to explore new variants and genes potentially involved in ARVC pathogenesis. This study was supported by Russian Science Foundation grant №14-50-00069.

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E-P05.03
The contribution of genetic variants to plasma lipid composition related to the atherosclerotic status

E. V. Butenko, S. Timofeeva, E. Derevyanchuk, T. Shkurat

Southern Federal University, Rostov-on-Don, Russian Federation

Introduction. Lipid metabolism is determined by genes, which mutations can lead to modulation in enzyme activity with lipid profile change consequently. This study was carried out to estimate the contribution of lipid metabolism gene variants related to the atherosclerotic status and their association with lipid indicators in Russian population.

Materials and Methods. The study involved 124 people older than 55 years divided into 3 age- and sex-matched groups according to the values of intima - media thickness. Lipid profiling was measured by homogeneous enzymatic colorimetric test. SNPs in *ApoE* (rs769452), *APOC3* (rs5128), *LIPC* (rs2070895) and *LPL* (rs328) genes were detected by allele-specific real-time polymerase chain reaction method using commercial kits.

Results. The distributions of genotype and allele frequency between patients with atherosclerosis and the controls were equal for *ApoE, APOC3* and *LPL* genes polymorphism. Wildtype *LIPC* genotype was associated with increased risk of severe atherosclerosis development (OR = 2,88; 95%CI 1,02 - 8,13). *LIPC* −250A genotype homozygote carriers showed decreased total cholesterol and low density lipoprotein levels. Heterozygous carriers of *LPL* Ser447Ter polymorphism had lower atherogenic index then non-carriers. Heterozygous carriers of ApoE Leu28Pro polymorphism had lower triglycerides blood level then non-carriers. No associations between *APOC3* genotypes and blood lipid levels were observed.

Conclusion. Natural polymorphic genes variants with protective effect such as *LIPC* −250A could be a prototype

for the predictive gene therapy of multifactorial diseases including atherosclerosis.This research was supported by the Russian Science Foundation grant No: 15-15-10022

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E-P05.05
Next generation sequencing revealed new mutations in Bulgarian patients with hyperthrophic cardiomyopathy

E. Marinova[1], V. Penchev[1], M. Rizov[1], G. Nikolov[1], I. Gruev[2], I. Dimova[3]

[1]Office for Technology Transfer in the area of Molecular Genetics and Diagnostics, Medical Centre "ReproBioMed" Ltd., Sofia, Bulgaria, [2]Clinics of Cardiology, NMTB, Sofia, Bulgaria, [3]Department of Medical Genetics, Medical University of Sofia, Sofia, Bulgaria

Background: Hyperthrophic cardiomyopathy is the most common genetic heart disorder, affecting 1 in 500 people worldwide. It is characterized by inappropriate myocardial hypertrophy that occurs in the absence of an obvious inciting hypertrophy stimulus. The genetic basis of the disease include defects in several of the genes encoding for the sarcomeric proteins, such as myosin heavy chain, actin, tropomyosin, and titin. With the advances of genomic technologies multiple mutations have been identified, with genotype-specific risks for mortality and degree of hypertrophy. Materials and methods: We have analysed 5 patients meeting criteria for familial hyperthrophic cardiomyopathy by using next generation sequencing of panel of genes connected to cardiac function. First, we filtered the detected gene alleles based on their frequency according to the existing data bases - ExAC_all, ExAC_NFE, 1000g_all, 1000g_eur. Then six variant prediction programs were used for estimation of non-annotated genetic variants discovered in the genes - ClinVar Effect, SIFT, Polyphen2 HDIV, Polyphen2 HVAR, MutationTaster, FATHMM. Results: In 4 of 5 analysed patients (80%) we found new genetic variants predicted as pathogenic from at least 3 prediction programs, they are presented in the following table:

Gene	Location	Aminoacid and nucleotide change
PATIENT1		
MYH7	chr14:23893238exon23:c.G2800A:p.A934T	
PATIENT2		
MYBPC3	chr11:47364607exon14:c.G1316A:p.G439D	
MYBPC3	chr11:47369975exon6:c.G772A:p.E258K	
PATIENT3		
MYBPC3	chr11:47353740exon32:c.C3697T:p.Q1233X	
PATIENT5		
ACTN2	chr1:236906268exon11:c.C1180T:p.R394W	

Conclusion: Gene panel analysis by next generation sequencing becomes gold standard in evaluation of genetic basis for hyperthrophic cardiomyopathy. Data collection and clinical follow-up will allow us to improve prognostic risk stratification in our patients.

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E-P05.06
Study of polymorphic genes relevant to folic acid metabolism in pregnant women from West Ukraine with prenatally diagnosed fetal heart defects

Y. Sharhorodska, H. Makukh, H. Akopyan, I. Haiboniuk, I. Kovaliv

Institute of Heredetary Pathology NAMS, Lviv, Ukraine

The purpose of study was to investigate genetic variations in MTHFR and MTHFD1 genes in pregnant women from West Ukraine in cases of prenatally diagnosed fetal heart defects. Genotyping of *MTHFR* 677 C > T, *MTHFR* 1298 A > C and *MTHFD1* 1958G > A polymorphisms was performed in 35 pregnant women with prenatally diagnosed congenital heart defects in fetus and in 30 healthy women. The molecular genetic analysis was performed by PCR and RFLP. The frequency of mutant *MTHFR* 677 T allele was significantly higher among the women with fetal heart defects comparable to controls (47% and 28% respectively, $p = 0.04$), while the frequency of mutant *MTHFR* 677 TT genotype was almost identical (14% and 10% respectively, $p = 0.27$). Probable cause of revealed difference appeared to be a significant increase in the frequency of heterozygous carriers of mutant *MTHFR* 677 T allele among the women with fetal heart defects (65,7% and 36,7%, p = 0,04; [OR = 3.31 (95% CI: 1.07 - 10.51)]. The frequency of *MTHFR* 677CC genotype was significantly more often in controls (53% and 20%; p = 0.02), that is associated with 4-fold decreased risk to having offspring with congenital heart defects [OR = 0.22 (95% CI: 0.06 - 0.74)]. In cases of *MTHFR* 1298 A > C and *MTHFD1* 1958G > A polymorphisms the frequencies of alleles and genotypes were not significantly different in women with fetal heart defects comparable to controls (p > 0,05). In conclusion, the carrying of *MTHFR* 677 T allele seems to be highly probable risk factor for Ukrainian women to have a child with