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Abstracts

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A multi-stage genome-wide association study of elite endurance athlete status

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Endurance athlete status is a complex phenotype subject to the influence of both environmental and genetic factors. The aim of the study was to identify SNPs associated with elite endurance athlete status in Russians using a multi-stage GWAS approach (HumanOmni1-Quad BeadChips). The study involved 223 endurance athletes, 67 elite power (sprinters and speed/strength athletes) athletes and 173 controls. VO2max (major indicator of aerobic capacity) was measured in 71 endurance (41 males and 30 females; 26 long distance and 45 middle distance) athletes. Initially, we performed GWAS in 4 subgroups (all and elite long distance athletes, all and elite middle distance athletes) of endurance athletes and controls, and found replications of associations with endurance athlete status in all subgroups for 93 SNPs with P<10-4, but none of them reached genome-wide significance level. Adding three criteria, i) an increase of the frequency of effect allele with increase of the level of achievement of endurance athletes; ii) significant differences in allelic frequencies between 56 elite endurance athletes and 67 elite power athletes (second case-control study); iii) positive correlation of the effect allele with high values of aerobic capacity, resulted in remaining five SNPs (effect alleles: CAMK1D rs11257754 A, CPQ rs6468527 A, GRM3 rs724225 G, SGMS1 rs884880 A, L3MBTL4 rs17483463 A) associated with elite endurance athlete status. These SNPs are located in the genes involved in the regulation of carbohydrate metabolism (CAMK1D), synthesis of thyroxine (CPQ), glutamatergic neurotransmission (GRM3), sphingomyelin and diacylglycerol metabolism (SGMS1) and chromatin modification (L3MBTL4).

J18.25

FREQUENCY OF ALL FORMS CONGENITAL MALFORMATIONS OF NEWBORNS BY BASED ON GENETIC REGISTER „UMIT» AND EUROPEAN INTERNATIONAL REGISTER EUROCAT

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According to the International Centre for EUROCAT, which unites more than 20 countries of the European Economic Community, the cumulative incidence of PPS varies widely - from 10.3 to 32.3 per 1,000 live births. This may be due to the peculiar environmental conditions surveyed regions, the difference in accounting methods congenital malformations, quality and principles of diagnosis, the difference in years of research. The study group was isolated malformations to be counted according to the list of the International Registry of congenital malformations (21 nosology), and analyzed in comparison with the data of our register. The overall frequency of these birth defects was 10.6 per 1,000 live births, which corresponds to the average values of the International Registry. The results of the research in our database, in comparison with the data EUROCAT more common Downs syndrome, multiple congenital malformations, congenital heart disease and malformations such as hydrocephalus, diaphragmatic hernia, Spina bifida. When comparing the frequency of congenital malformations in our case with those in the EUROCAT was found that the prevalence of a number of malformations of the central nervous system (anencephaly, encephalocele) and microtia, renal agenesis and bladder exstrophy 2-3 times lower. These types of birth defects, anophthalmia and microphthalmia as are found in our region is 3 times less than on the data recorded by the European register.

J18.26

Genome-wide association study of elite power athlete status

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The aim of the study was to identify SNPs associated with elite power athlete status in Russians using a GWAS approach (HumanOmni1-Quad BeadChips). The study involved 176 power (89 sprinters, 38 speed/strength athletes and 49 strength athletes; 102 elite and 74 sub-elite) athletes, group of athletes with speed/strength component (n=204; 64 wrestlers, 42 rugby players, 98 rowers/kayakers/canoeers), 223 endurance athletes and 173 controls. Initially, we performed seven analyses using GWAS data (elite power athletes vs. controls, all sprinters vs. controls, elite sprinters vs. controls, all speed/strength athletes vs. controls, elite speed/strength athletes vs. controls, all strength athletes vs. controls, elite strength athletes vs. controls) and found 68 SNPs which were associated with power athlete status (with P value from 0.001 to 1.345e-05) and replicated in all three subgroups of power athletes (regardless of their level of achievement). The comparison of allelic frequencies of these SNPs between the large cohort of power athletes (n=380; i.e. power athletes plus group of athletes with speed/strength component) and endurance athletes (as a second control group) resulted in remaining eight SNPs (PPARGC1B rs10060424 C, NRG1 rs17721043 A, ZNF423 rs11865138 C, RC3H1 rs767053 G, IP6K3 rs6942022 C, HSD17B14 rs7247312 G, CALCR rs17734766 G, COTL1 rs7458 T) associated with power athlete status. These SNPs are located in the genes involved in the regulation of muscle fiber composition and carbohydrate/lipid metabolism (PPARGC1B), growth and development (NRG1, ZNF423), mRNA deadenylation and degradation (RC3H1), metabolism of inositol hexakisphosphate (IP6K3), metabolism of steroids (HSD17B14), calcium homeostasis (CALCR) and actin cytoskeleton (COTL1).

J18.27

The mutation spectrum of the MEFV gene of the Southern Russia population

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Familial Mediterranean fever (FMF) is typical for populations living around the Mediterranean basin, it is also affects the Southern Russia population. Different clinical course may be caused by different mutations. Recent study reports the mutation spectrum of the FMF gene (MEFV) in the Southern Russia population.

Blood samples were collected from a cohort of 105 FMF patiens (52 male, 53 female; age: 4 to 88 years), inhabiting in the South region of Russia. The sequencing of the exon 10 in MEFV gene was performed by using a sequencer ABI PRISM 3500.

The six mutations were investigated in the exon 10 in MEFV gene in 67 patients: *M694V* - 58,3%, *V726A* - 19,1%, *M680I* - 14,8%, *R761H* - 6%, *A744S* - 0,9%, *K695R* - 0,9%.

Results of genotype analysis are shown in Table.

Genotype		Patients	%
Compound heterozygote	*M680I© / M694V*	11	16,42%
	M694V / V726A	10	14,93%
	M680I / V726A	3	4,48%
	M680I / R761H	1	1,49%
	M694V / K695R	1	1,49%
	M694V / R761H	1	1,49%
	V726A / R761H	1	1,49%
	Total	28	41,79% ± 9,32
Homozygote	*M694V / M694V*	15	22,39%
	V726A / V726A	2	2,99%
	R761H / R761H	2	2,99%
	M680I / M680I	1	1,49%
	Total	20	29,85% ± 10,23
Heterozygote	*M694V / N*	14	20,90%
	V726A / N	4	5,97%
	A744S / N	1	1,49%
	Total	19	28,36% ± 10,34
Total:		67	100%

This results can be discussed as a background to the search of new diagnostics and population research.

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J18.28

The genetic basis of the relationship between reproduction and longevity : a study on common variants of three genes in steroid hormone metabolism (CYP17, HSD17B1, COMT).

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Evolutionary theories of aging predict an antagonistic relationship between