




Variation in the Uncoupling Proteins Genes in Different Sports

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Abstract: Uncoupling protein (UCP) genes appear to be promising candidates for studying the effect of 'thrifty' genotypes on various aspects of modern human life, starting from susceptibility to obesity and cardiometabolic diseases and ending with sports talent. The study aims at studying directions of selection for polymorphic systems of the genes *UCP1*, *UCP2* and *UCP3* among athletes engaged in various sports. The study involved 268 people: 197 athletes (males: n=140; females: n=57) and 71 non-athletes as a control group (males: n=38; females: n=33). Buccal epithelium was used as a sample of biological material. Genomic DNA isolation and genotyping of samples for polymorphisms of *UCP1* (rs1800592), *UCP2* (rs660339), *UCP3* (rs1800849) were performed at the premises of Lytech (Moscow). Differences in the distribution of genotype frequencies of the *UCP1* and *UCP2* genes between the subgroups within the sample of athletes are statistically significant ($\chi^2 = 21.2$ p = 0.006 and $\chi^2 = 24.06$ p = 0.002, respectively). Among the athletes representing various kinds of sports, the subgroups of aerobic, mixed cyclic and team sports demonstrate the directional selection of carriers of 'thrifty' genotypes of the studied genes. The subgroup of martial arts is characterized by the opposite direction in selection.


1 INTRODUCTION

Studies in the field of molecular physiology (in particular, knockout and overexpression of UCP genes) revealed the main functions of uncoupling proteins (UCP): heat production, metabolic acceleration, and reduction of the rate of formation of reactive oxygen species (ROS) due to the uncoupling of oxidation and phosphorylation reactions in mitochondria (Toda, Diano, 2014; Victorino et al., 2015; Cardoso et al, 2014). UCPS provide controlled “leakage” of protons from the intermembrane space of mitochondria and dissipate chemical energy, stored as a proton gradient, in the form of heat. However, a high activity of UCPS is accompanied by a decrease in the efficiency of the aerobic phase of energy metabolism; i.e., the amount of synthesized ATP decreases. Mutations that reduce the activity of UCP allow more protons to pass through ATP synthase and synthesize more ATP from a similar number of substrates and oxygen, which, in turn, leads to the

storage of unspent calories as fat. Thus, a decrease in the activity of UCPS, on the one hand, leads to an increase in predisposition to obesity and, on the other hand, increases the efficiency of aerobic metabolism. In the organisms of mammals, including humans, the most common are three members of the family of uncoupling proteins: UCP1, UCP2, and UCP3. The first member of the family of uncoupling proteins, UCP1 (thermogenin), is the key player that provides heat production in nonshivering thermogenesis. Thermogenin homologs, proteins UCP2 and UCP3, have no such an explicit function and, according to several studies, regulate the formation of reactive oxygen species (ROS), protect cells from excess free fatty acids and reduce their lipotoxicity, and affect the efficiency of metabolism and its cost-effectiveness. Mutations in the *UCP* genes, which are examples of the “thrifty” genotype, are actively studied as molecular-genetic markers of increased risk of obesity, type 2 diabetes mellitus, and cardiometabolic diseases (Flouris et al., 2017). Among all members of

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the family of uncoupling proteins, UCP2 is characterized by the most widespread expression in the human body (skeletal muscles, internal organs, and adipose tissue), which is not limited, e.g., to brown adipose tissue, such as in the case of UCP1. The genes *UCP2* and *UCP3* are located side by side on the same chromosome (Solanes et al., 1997), which suggests a linkage group at least in the Russian population. It is also assumed that UCP2 and UCP3 functionally overlap each other (Bouillaud et al., 2016). The *UCP2* gene polymorphism is associated with excess weight gain, and it is also actively studied as a factor of success in sports that require high aerobic abilities of the athletes. The effect of the *UCP2* gene polymorphism on energy metabolism at rest (Astrup et al., 1999) and during exercise (Buemann et al., 2001) was studied.

The aim of the work is to study the directions of selection for polymorphic systems of UCP genes in various sports and to analyse the associations of uncoupling protein genes with the indicators of physical performance of athletes.

2 MATERIALS AND METHODS

The study involved 268 people. The surveyed sample included 197 (males: n=140; females: n=57) athletes involved in various sports and 71 non-athletes as a control group (males: n=38; females: n=33). The buccal smears were used as a sample of biological material. Biological material was collected using universal sterile disposable probes (Changzhou Chuangjia Medical Appliance Co., Ltd, China). Next, genomic DNA was isolated from the collected samples, and for each sample genotyping of polymorphic loci in the human genome was carried out: *UCP1* (rs1800592), *UCP2* (rs660339), *UCP3* (rs1800849). Genomic DNA isolation and genotyping of samples were performed at the premises of Lytech (Moscow).

The surveyed sample of athletes was divided into three subgroups, according to the prevailing source of energy supply for training and competition activities (Table 1). In turn, the group of sports with predominantly mixed energy supply was further divided into three parts: the cyclic sports subgroup, the martial arts subgroup, and the team sports subgroup.

Statistical analysis of the data was carried out using the STATISTICA 8.0 software (StatSoft, USA). Differences in the distribution of genotypes of the studied genes in the subgroups of the surveyed sample were analyzed using a nonparametric criterion

Table 1: General characteristic of the studied sample.

| Subgroup | Sports | Number |
|---------------------|--|------------|
| Control | - | 71 |
| Athletes | | 189 |
| Anaerobic | skating 500, 1000 and 1500m, sprint | 13 |
| Aerobic | biathlon 5, 7,5 and 10 km, rowing, skating 5km and all-around, ski race, swimming, modern pentathlon | 50 |
| Mixed energy supply | | 126 |
| Team sports | football, basketball | 41 |
| Cyclic sports | Short track speed skating, biathlon 3 km, | 49 |
| Martial arts | sambo, boxing, judo, taekwondo | 36 |

(χ^2). The total genotype score (TGS) was also calculated (Williams and Folland, 2008). For this purpose, we assigned a genotype score (GS) of 1 to 3 to each individual genotype (Table 2), where score 1 is for homozygous combination of the two original alleles, 2 for heterozygous and 3 for homozygous combination of “thrifty” alleles.

Table 2: Genotype scores for the *UCP*'s genes polymorphism.

| | | |
|-----------------|-----------------|-----------------|
| <i>UCP1</i> *AA | <i>UCP1</i> *AG | <i>UCP1</i> *GG |
| 1 | 2 | 3 |
| <i>UCP2</i> *CC | <i>UCP2</i> *CT | <i>UCP2</i> *TT |
| 1 | 2 | 3 |
| <i>UCP3</i> *CC | <i>UCP3</i> *CT | <i>UCP3</i> *TT |
| 1 | 2 | 3 |

The scores for all three genes were then summed up (Equation 1) and expressed as a percentage of the maximum possible ($\sum GS_{max}=9$) amount (Equation 2).

$$\sum GS \text{ (genotype score)} = GSUCP1 + GSUCP2 + GSUCP3 \quad (1)$$

$$TGS\% = (100/9) \times \sum GS \quad (2)$$

$$\sum GS9 = TGS100\% = UCP1*GG + UCP2*TT + UCP3*TT \quad (3)$$

Thus, the maximum sum of scores (Equation 3) will correspond to the greatest predisposition to excess weight gain, determined by the three uncoupling protein systems. Or, in other words, to the most effective/economical aerobic metabolism. The

average TGS values in different subgroups of the surveyed sample were compared using the median test. All subjects who participated in the study were informed of the research objectives and methods and gave their written informed consent.

3 RESULTS AND DISCUSSION

Numerical distributions and frequencies of the genotypes and alleles of the *UCP1*, *UCP2*, and *UCP3* genes in the subgroups of the surveyed sample are presented in Tables 3 to 7 and Figures 1 to 3. The distribution of genotypes in the control group conforms to the Hardy-Weinberg equilibrium for all polymorphic systems studied.

Table 3: Numerical distributions and frequencies of the *UCP1*, *UCP2*, and *UCP3* genotypes and alleles in the athletes' and control groups.

| Genotype | Athletes N (%) | Control N (%) | p-value |
|-----------------|-------------------|------------------|-----------------------------|
| <i>UCP1</i> *AA | 107 (54,3%) | 42 (60%) | $\chi^2=7,07$ p = 0,03 |
| <i>UCP1</i> *AG | 62 (31,5%) | 26 (37,1%) | |
| <i>UCP1</i> *GG | 28 (14,2%) | 2 (2,9%) | |
| <i>UCP2</i> *CC | 74 (37,6%) | 22 (31,4%) | $\chi^2 = 3,69$ p = 0,14 |
| <i>UCP2</i> *CT | 86 (43,6%) | 39 (55,7%) | |
| <i>UCP2</i> *TT | 37 (18,8%) | 9 (12,9%) | |
| <i>UCP3</i> *CC | 93 (47,2%) | 44 (62,9%) | $\chi^2 = 5,3$ p = 0,07 |
| <i>UCP3</i> *CT | 82 (41,6%) | 21 (30%) | |
| <i>UCP3</i> *TT | 22 (11,2%) | 5 (7,1%) | |

Table 4: *UCP*'s polymorphism genotype and allele frequencies amongst all participants according to their subgroup.

| Allele | Control | Athletes |
|-----------------------------|---------|----------|
| <i>UCP1</i> *A | 78,6 | 70,1 |
| <i>UCP1</i> *G [†] | 21,4 | 29,9 |
| <i>UCP2</i> *C | 59,3 | 59,4 |
| <i>UCP2</i> *T [†] | 40,7 | 40,6 |
| <i>UCP3</i> *C | 77,9 | 68 |
| <i>UCP3</i> *T [†] | 22,1 | 32 |

[†] - «thrifty» allele

Table 5: Numerical distributions of the *UCP1* genotypes in the studied subgroups.

| Subgroup | Genotype | | | p-value |
|---------------|----------|----|----|------------------------------|
| | AA | AG | GG | |
| Anaerobic | 3 | 7 | 3 | $\chi^2 = 28,9$ p = 0,001 |
| Aerobic | 26 | 12 | 12 | |
| team sports | 22 | 14 | 5 | |
| cyclic sports | 23 | 22 | 4 | |

| | | | |
|--------------|----|----|---|
| martial arts | 28 | 4 | 4 |
| Control | 42 | 26 | 2 |

Table 6: Numerical distributions of the *UCP* genotypes in the studied subgroups.

| Subgroup | Genotype | | | p-value |
|---------------|----------|----|----|------------------------------|
| | CC | CT | TT | |
| Anaerobic | 3 | 7 | 3 | $\chi^2 = 28,7$ p = 0,001 |
| Aerobic | 18 | 28 | 4 | |
| team sports | 12 | 18 | 11 | |
| cyclic sports | 15 | 20 | 14 | |
| martial arts | 24 | 7 | 5 | |
| Control | 22 | 39 | 9 | |

Table 7: Numerical distributions of the *UCP3* genotypes in the studied subgroups.

| Subgroup | Genotype | | | p-value |
|---------------|----------|----|----|-----------------------------|
| | CC | CT | TT | |
| Anaerobic | 9 | 4 | 0 | $\chi^2 = 14,7$ p = 0,14 |
| Aerobic | 24 | 20 | 6 | |
| team sports | 14 | 20 | 7 | |
| cyclic sports | 25 | 18 | 6 | |
| martial arts | 17 | 17 | 2 | |
| Control | 44 | 21 | 5 | |

Table 8: Mean values of the TGS (%) in the studied subgroups.

| Subgroup | TGS (%) |
|----------------------------|-------------|
| Control | 51.3 |
| Athletes | 56.2 |
| Aerobic | 54.9 |
| Anaerobic | 56.3 |
| Mixed energy supply | 55.9 |
| team sports | 55.8 |
| martial arts | 52.6 |
| cyclic sports | 56.2 |

Gene mutations that reduce the activity of uncoupling proteins in the past had allowed for a more efficient calorie expenditure and fat accumulation, which gave an advantage to carriers of such genes in conditions of lack of food or during long journeys. In the changed circumstances of the modern world, the 'thrifty' genotype has become a factor of increased risk of developing metabolic diseases. However, the presence of 'thrifty' variants of uncoupling protein genes in the human genome can now provide an advantage to the carriers of the original alleles when it comes to sports at an elite level. Uncoupling proteins belong to a larger family of mitochondrial anion carrier proteins (MACP). Three out of five members of this family were found to have associations with increased susceptibility to

fat accumulation and with performance indicators, that is, UCP1, UCP2 and UCP3. Physiological studies performed on animal models - knockout and overexpression of *UCPs* - suggest that the main functions are heat production, metabolism acceleration and reduction of the rate of reactive oxygen species (ROS) formation (Toda and Diano, 2014; Victorino et al., 2015; Cardoso et al., 2014).

In general, the studied group of athletes demonstrates significant differences in the distribution of frequency occurrence of genotypes from the control group of non-athletes for the UCP1 polymorphic system (Table 3). Carriers of the *UCP1*GG* genotype are four times more frequent in athletes than in the control group. The athletes also have a higher frequency of 'thrifty' alleles of *UCP1* and *UCP3* (Table 4). A generalized sample of athletes is characterized by an increased tendency to accumulate fat due to the increased frequency of occurrence of "thrifty" alleles for all studied gene systems. This actually means that, in general, athletes are characterized by lower mitochondrial uncoupling, which provides a more efficient and economical version of the aerobic phase of ATP synthesis. Despite the general direction of selection for all molecular genetic markers identified in the generalized group of athletes, the sample is not homogeneous. This group includes athletes who practice sports with different energy supply requirements and different motor activities (cyclic, acyclic, and precise). The function of uncoupling proteins allows us to reasonably assume that directional selection of "thrifty" genotypes will be observed most in those sports which require a high level of development of the aerobic component of physical performance. Therefore, an attempt was further made to study the directions of genetic selection in subgroups of athletes formed according to the principle of the prevailing source of energy supply for training and competitive activity (Table 1). The sports which have extremely high requirements on the aerobic qualities of an athlete are included in the subgroup of "aerobic" sports. In contrast, we singled out certain sports types and specializations requiring mainly strength, speed and power qualities, which formed a subgroup of 'anaerobic' sports. Those sports types and/or specializations, which are characterized by a combination of energy supply sources, or predominantly glycolytic pathway of ATP synthesis, entered the group with a mixed power supply: cyclic, team and martial arts. Thus, the group of athletes was divided into 5 subgroups (Table 1). With a certain degree of assumption, we can say that the aerobic subgroup represents long-distance

runners, the anaerobic one – sprinters, and the mixed sports subgroup consists of middle-distance runners. The analysis of the frequency of occurrence of genotypes in the subgroups within the sample of athletes revealed significant differences in the distribution of genotypes for the polymorphic systems of the *UCP1* and *UCP2* genes (Tables 3 to 7).

Differences in the distribution of genotype frequencies of the uncoupling protein 1 gene between the subgroups within the sample of athletes are statistically significant ($\chi^2 = 21.2$ $p = 0.006$). Compared to the control group, all subgroups within the sample of athletes demonstrate an increase in the number of carriers of the G allele of the *UCP1* gene, which is associated with an increased risk of obesity and a decrease in uncoupling.

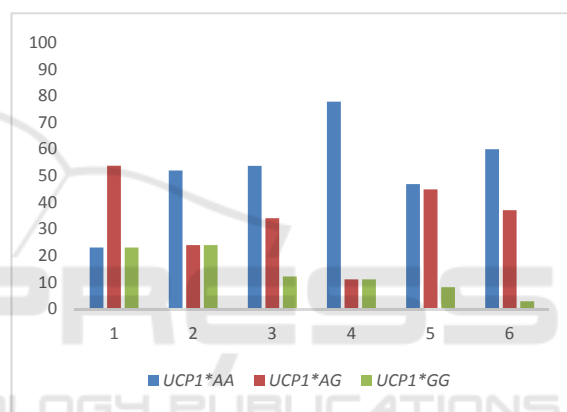


Figure 1: Frequencies (%) of genotypes of the *UCP1* gene in all subgroups within the surveyed sample.

This result is a logical one in terms of the increased energy efficiency of aerobic metabolism and the advantage of athletes carrying the 'thrifty allele' over the carriers of the 'normal' level of uncoupling. G allele carriers were reported to burn 200 Kcal/day less than the original A allele carriers (Kogure et al., 1998), and this allele also leads to a decrease in *UCP1* mRNA in BAT adipocytes (Esterbauer et al., 1998). All this suggests that the allele -3826G *UCP1* increases the efficiency of energy metabolism in BAT (brown adipose tissue) mitochondria. This genotype is most frequent in the subgroup of aerobic sports requiring a very high level of aerobic capacity. Further, directional selection of *GG*UCP1* carriers is observed due to the simultaneous decrease in the frequencies of occurrence of *AA*UCP1* and *AG*UCP1* (Fig.1). The subgroup of anaerobic sports is also characterized by a high frequency of occurrence of *GG*UCP1*; however, it should rather be referred to the selection

of heterozygous genotype carriers. The high (as compared to the control group) frequency of occurrence of genotypes containing at least one G allele found in the subgroup of anaerobic sports may indicate the existence of mechanisms supporting a high level of anaerobic performance. The molecular physiological basis for such mechanisms is uncoupling processes in BAT. The result may also be related to the small number of subjects in the subgroup of anaerobic sports.

The subgroup of martial arts demonstrates the opposite direction of selection - *AA*UCP1*, i.e. selection for the uncoupling of energy processes, although this subgroup is characterized by an increase in the number of carriers of the *GG*UCP1* genotype. The results of physiological studies on the effect of BAT activity on athletes' physical performance suggest that a sufficient level of uncoupling of oxidative phosphorylation processes in BAT adipocytes, which is determined by the A allele of the *UCP1* gene, ensures rapid utilization of lactate (Son'kin et al., 2014; Merla et al., 2010), which is formed in large quantities by muscle activity typical for martial arts. Thus, the presence of BAT adipocytes with the original level of uncoupling in athletes involved in martial arts allows them to both effectively counter acidification of skeletal muscles during the fight and quickly dispose of accumulated lactate between fights, which ensures rapid recovery of athletes. In other words, the selection of alleles observed in the martial arts subgroup which determine sufficient uncoupling of oxidative phosphorylation is apparently connected with the processes of recovery during and between fights. The greater (as compared with the control group) number of *GG*UCP1* genotype carriers in combat athletes may indicate the existence of a minor variant of selection, i.e. selection of combatants with high aerobic capabilities, who reach a high professional level due to the fight strategy based not on the speed and strength qualities, but on athlete's endurance.

Significant differences were found between the subgroups within the sample of athletes for the polymorphic system of the *UCP2* gene ($\chi^2 = 24.06$ $p = 0.002$) as well. The most pronounced differences in the distribution of occurrence frequencies of genotypes from the control group are characteristic of the subgroup of martial arts athletes (Fig.2). This group shows a pronounced selection of carriers of two original alleles of the *UCP2* gene – *CC*UCP2* – due to a decrease in the number of carriers of the heterozygous genotype. At the same time, the proportion of *TT*UCP2* genotype carriers is identical to that in the group of non-athletes. The direction of

selection for the *UCP2* system is similar to *UCP1* and, in terms of biochemistry, corresponds to the normal level of uncoupling not only in BAT adipocytes, but also in most internal organs. Subgroups of team and cyclic sports which, according to the type of energy supply, are in an intermediate position between anaerobic and aerobic sports, demonstrate the selection of carriers of the *TT*UCP2* genotype, due to a decrease in the proportion of heterozygotes. The result suggests that in such sports as basketball, football, middle-distance running advantage is gained by athletes with a more economical type of energy supply mainly in internal organ tissues. At the same time, the proportion of *CC*UCP* genotype carriers is almost identical to the control group. The anaerobic sports subgroup demonstrates the selection of carriers of the *UCP2 T* allele, due to a decrease in the proportion of *CC*UCP2* carriers. This *UCP2* allele determines a more efficient metabolism, which affects energy expenditure during exercise (Beumann et al., 2001; Kimm et al., 2002). Previously, the selection of *T*UCP2* (55Val) and *T*UCP3* allele carriers was reported in the group of Russian long-distance runners (Ahmetov et al., 2009). The aerobic sports subgroup, unlike all other sports, shows a decrease in the proportion of *TT*UCP2* carriers, with a corresponding increase in the proportions of CT and CC. It is likely that the presence of athletes with these genotypes is associated with their functional characteristics. It was reported that athletes with a heterozygous genotype have the highest rates of maximum oxygen consumption (Bondareva et al., 2018). A high-fat diet stimulates *UCP2* and *UCP3* gene expression in athletes' muscles. And the most significant increase in the concentration of *UCP2* and *UCP3* mRNA was found in muscle fibers of type IIA (fast oxidative-glycolytic fibers), which have a greater metabolic plasticity in terms of choice of oxidation sources (Schrauwen et al., 2001) and are also characteristic of the skeletal muscles of athletes in the subgroup of mixed energy supply.

We have found no statistically significant differences in the distribution of genotype frequencies of the *UCP3* gene either between the control group and the subgroups within the sample of athletes, or between the subgroups within the sample of athletes ($\chi^2 = 9.08$ $p = 0.33$). However, the results would suggest some trends in the direction of selection in different subgroups of athletes. Thus, the selection of carriers of the *UCP3 T* allele – *CT*UCP3* and *TT*UCP3* genotypes – occurs in the subgroups of aerobic, team and cyclic sports, due to a cor-

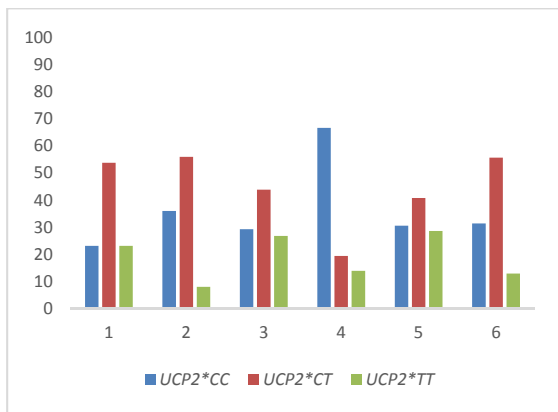


Figure 2: Frequencies (%) of genotypes of the *UCP2* gene in all subgroups within the surveyed sample.

responding decrease in the proportion of carriers of the *CC*UCP3* genotype. A similar result was obtained when studying the distribution of *UCP3* genotypes in subgroups of Italian sprinters and long-distance runners compared to the control group (Sessa et al., 2011). The anaerobic sports subgroup demonstrates the selection of the *CC*UCP3* carriers. No carriers of the two mutant alleles were found, possibly due to the advantage of carriers of a normal level of uncoupling in skeletal muscles, or because of the small number of subjects in the group. *UCP3* is expressed in skeletal muscles and myocardium, which makes it a promising marker of physical performance. The *UCP3 T* allele is associated with a more economical calorie expenditure for ATP synthesis at the aerobic stage of energy metabolism, which makes it an 'aerobic capacity allele'. Earlier we demonstrated the selection of T allele carriers in a group of football players (Bondareva et al., 2016). Therefore, the selection of *UCP3 T* allele carriers, which is observed in all subgroups except the anaerobic one, is logical. For successful training and competitive activities of the athletes included in these subgroups, the development of medium and high aerobic capabilities is necessary. An advantage is gained by the carriers of alleles allowing for the development of higher and/or more effective mechanisms for the aerobic synthesis of ATP, in the skeletal muscles and heart. In the subgroup of martial arts athletes, a directional selection of carriers of the heterozygous genotype of *CT*UCP3* was found, due to a decrease in the proportion of both homozygous genotypes. Martial arts athletes need to combine a fairly high level of aerobic capabilities, extremely high speed, strength and power qualities for rapid attacks and throws, as well as high resistance to tissue hypoxia and acidification of skeletal muscles. Therefore, the heterozygous combination of alleles

makes it possible to find a compromise between improving the energy efficiency of muscle contraction and protection against oxidative stress.

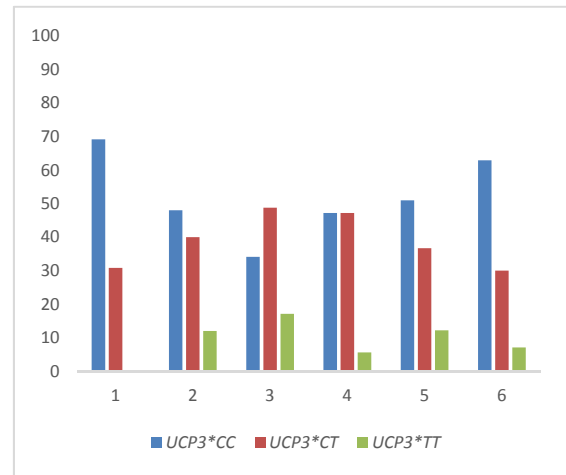


Figure 3: Frequencies (%) of genotypes of the *UCP3* gene in all subgroups within the surveyed sample.

Regular exercise and weight training reduce the level of *UCP3* mRNA and protein in mitochondria, which, in turn, is inversely proportional to BMD. All of this contributes to increasing energy efficiency in exercise (Schrauwen et al., 2005). *UCP3* exports fatty acid (FA) anions from the mitochondrial matrix preventing accumulation of excess FA in the matrix (Wang et al., 2003) and freeing CoA for continued β -oxidation of FA, thus avoiding oxidative stress and maintaining a high metabolic rate. One of the consequences of the increased concentration of uncoupling proteins 2 and 3 in cardiomyocytes, in addition to the increased uncoupling of oxidative phosphorylation, is the predominant use of FA as a substrate for the oxidation and ATP synthesis (Harmancey et al., 2013). Presumably, *UCP3* is the main regulator for the influx of energy substrates into mitochondria, since its expression is controlled by fatty acids, which is likely to play an important role in the energy supply of sports with a predominantly aerobic type of energy supply. Because during prolonged loads, typical for aerobic and team sports, fats are the main energy substrate. The observed selection of carriers of *CT*UCP3* and *TT*UCP3* genotypes may be associated with increased energy efficiency in skeletal muscle in combination with the ability to maintain a sufficient rate of entry of FA into the mitochondria of skeletal muscle. The results of animal studies suggest that one of the main functions of uncoupling proteins is to accelerate the metabolism and protect the cell from ROS. ROS have a damaging effect on both cellular and organism levels, since

uncoupling proteins are present in the mitochondria of all organs and tissues. Significant oxidative stress is observed during intense training and competition in martial arts athletes (Finaud et al., 2006). Cell survival depends on the amount of ROS: low levels of ROS trigger a cascade of reactions aimed at cell survival (Tait and Green, 2012), while high levels of ROS, which cannot be neutralized by means of cell antioxidant protection, lead to cell damage and death (Orrenius et al., 2007). The formation of ROS in mitochondria is reduced due to the soft or strong uncoupling of the electron transport chain of mitochondria and ATP synthase by means of UCPs. However, strong uncoupling leads to a lack of ATP in the cell, which causes necrosis. It is presumed that UCPs are able to “gently” uncouple oxidative phosphorylation reactions without reducing the amount of ATP (Sluse, 2012), but physiological studies are still insufficient (Shabalina and Nedergaard, 2011). Thus, a decrease in the activity of uncoupling proteins, on the one hand, makes it possible to increase the efficiency of the aerobic stage of energy metabolism, but the concentration of ROS increases simultaneously.

The above-mentioned directions of genetic selection for gene systems of uncoupling proteins were sometimes difficult to explain and differently directed for some groups of sports. However, all genetic factors act in the body and affect its phenotypic characteristics simultaneously. Therefore, we analysed the directions of selection in the formed subgroups of the surveyed sample simultaneously for all selected polymorphic systems. The results of studies on the effect of several genes on various phenotypic characteristics convincingly prove that the tendency to obesity is proportional to the number of risk genotypes/alleles present in the genome. The higher the TGS, the greater the number of alleles/genotypes that determine the accumulation of excess weight, and in the case of uncoupling proteins, this also means a more efficient ATP synthesis. Table 8 presents the average TGS calculated for the subgroups of the surveyed sample. Comparative analysis of average TGS revealed non-random statistical differences ($\chi^2 = 9.86$ $p=.02$). The lowest value (TGS=51.3%), which corresponds to the smallest number of 'thrifty' alleles/genotypes, is demonstrated by the test subjects included in the control group. Non-athletes are predominantly carriers of the original alleles of uncoupling proteins, which determine the normal level of uncoupling of oxidative phosphorylation in mitochondria, which means a small risk of obesity. All subgroups within the sample of athletes show higher TGS than the

control sample, which on the one hand is a sign of the accumulation of uncoupling protein alleles/genotypes, which increase the coupling of oxidative phosphorylation reactions in mitochondria and provides increased energy efficiency of the aerobic phase of ATP synthesis, but simultaneously increases the risk of obesity development. However, due to the increased coupling of reactions of the aerobic phase of metabolism, athletes have a reduced potential in protecting against ROS and oxidative stress. For different types of wrestling, a high glycolytic load and a high level of oxidative stress during competitions affect the selection of athletes capable of quickly disposing of lactate and effectively resisting peroxidation, both during and between fights. These properties, which are partially determined by uncoupling proteins, are leading and provide high sports achievements in martial arts. Therefore, for some systems of uncoupling proteins – *UCP1* and *UCP2* – the selection of carriers of the original alleles, rather than “thrifty” ones, occurs, opposite to the other subgroups of athletes. Previously, for another polymorphic system, the selection of carriers of alleles of resistance to tissue hypoxia among sambo athletes has already been identified (Bondareva and Godina, 2016).

4 CONCLUSIONS

Selection of carriers of 'thrifty' genotypes among the majority of subgroups of athletes allows to conclude that for most sports types and specializations, a more efficient metabolism is a factor that positively affects the success in sports. It should be noted that to a lesser extent the selection of carriers of 'thrifty' genotypes is characteristic of martial arts athletes (TGS=52.6%).

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