Original Paper DOI: 10.5604/942738 Biol. Sport 2011;28:101-106

POLYMORPHISM OF THE α-ACTN3 GENE IN INDIVIDUALS PRACTISING DIFFERENT SPORTS DISCIPLINES

Accepted for publication 21.12.2010

AUTHORS: Holdys J.[1], Kryściak J.[1], Stanisławski D.[2], Gronek P.[1]

[1]Department of Physiology, the University School of Physical Education in Poznań, Poland
[2]Computer Laboratory of the Faculty of Animal Breeding and Biology, the University of Life Sciences in Poznań, Poland

Reprint request to:
Joanna Holdys
Department of Physiology
Laboratory of Genetic Analyses
University School of Physical Education in Poznań
61-871 Poznań
Królowej Jadwigi 27/39
e-mail: strelka@wp.pl

ABSTRACT: In this study the R577X polymorphism of the α-actinin-3 (*ACTN3*) gene was analysed in relation to physical fitness measured with maximal oxygen uptake (VO_2max). The studies were carried out in a group of 154 men and 85 women, students of the University of Physical Education in Poznań and professional athletes representing various sports and fitness levels. In our research physiological and molecular procedures were used, i.e. direct measurement of maximum oxygen uptake (VO_2max) and R577X *a-ACTN3* genotyping by PCR-RFLP. The results do not confirm some literature data concerning a statistically significant association of R577X polymorphism in the *ACTN3* gene and the level of maximal oxygen uptake (VO_2max). A trend was observed for higher VO_2max values to be found in individuals with the *XX* and *RX* genotypes as well as the predominance of the *RR* genotype in the group of individuals practising speed and power disciplines.

KEY WORDS: ACTN3 polymorphism, maximum oxygen uptake

INTRODUCTION

Alpha-actinins are cytoskeletal proteins belonging to the spectrin superfamily, exhibiting high evolutionary conservation [9]. In humans four actinin-encoding genes have been identified, i.e. *ACTN1-ACTN4.* The *ACTN1* and *ACTN4* genes are non-muscle isoforms, while *ACTN2* and *ACTN3* are expressed in myocytes, being responsible for the binding of actin myofilaments to the Z-disc in the muscle sarcomere. Actinin 2 is found in all fibre types, whereas actinin 3 is expressed only in muscle fibres type IIA and IIX, used in short-term effort of high intensity (1). Apart from the mechanical functions they serve, ACTN2 and ACTN3 also participate in numerous metabolic pathways and in signalling processes [7].

In 1999 North et al. identified a nonsense mutation, substitution C→T in position 1747 (C1747T) in exon 16, resulting in the formation of a stop codon (X) in the arginine site (R) in position 577 of the protein chain, which results in the interruption of translation and the formation of inactive protein forms. Individuals with the 577XX genotype do not have actinin 3 in their fast-twitch fibres. North estimated that approx. 16% of the population worldwide (from 25% of Asians, 18% of Europeans to less than 1% of African Bantu) are devoid of this protein in their muscles, and since there is no phenotypic effect in the form of a disease syndrome it was assumed that it does not play any key role [11]. In 2003 Yang et al. proposed a hypothesis on the compensatory effect of actinin 2 in individuals with the 577XX genotype. However, the high conservatism of the *ACTN3* gene suggests that it has survived in the genome due to a function other than that served by *ACTN2* and most probably mutation R577X appeared for the first time in humans [9,19].

The phenomenon of opposition in the case of speed and strength vs. endurance fitness imposes considerable limitations on the development of effort tolerance [5]. This is manifested in athletes practising the decathlon, in whom the result of competitions requiring considerable muscle strength, such as the 100 m run, the shot put, the long jump or the 110 m hurdle race, is negatively correlated with the result of the 1500 m run, in turn requiring aerobic capacity and engagement of fatigue-tolerant muscles [16]. Analysis of the occurrence of the R577X polymorphism in the *ACTN3* gene among representatives of the Australian national teams in different sports disciplines showed a significant correlation between the elite

status and the character of practised disciplines. Sprinters of both sexes had allele R in their genotype more frequently than it was recorded in the controls, which indicates a significant role of actinin 3 in the functioning of fast-twitch fibres and which seems evolutionarily advantageous for this type of exercise. In women practising sprint running the RX genotype was observed more often than it had been expected, while a lower than anticipated frequency was found for the RX genotype among women practising endurance disciplines. A lack of a similar dependency among men suggests that the *ACTN3* genotype affects fitness in athletes in a slightly different way in men and in women due to involvement of androgens in response to training [19]. Also studies by Niemi and Majamaa on a group of leading Finnish athletes of the endurance profile and in sprinters showed a higher frequency of the 577RR genotype in sprinters, in contrast to the XX genotype, recorded more frequently in "endurance"-type athletes. None of the examined leading sprinters represented the XX genotype [10].

The association of the R577X polymorphism with the elite athlete status and fitness suggests that a lack of actinin 3 affects the functioning of muscle fibres type IIA and IIX. In *ACTN3* knock-out mice MacArthur et al. observed significant changes in fast-twitch fibres, i.e. a reduction of their diameters, enhanced activity of many enzymes in oxidative pathways, changes in contractility, faster elimination of fatigue, and thus transition towards properties of slow-twitch fibres, characterized by aerobic metabolism, resulting in an increase in endurance capacity [8]. The composition of muscle fibres analysed by Vincent et al. showed a much higher number and area of IIA and IIX fibres in RR than XX genotype individuals, which would indicate a relationship between the R577X *ACTN3* polymorphism with regulation of fibre proportions in muscles [17].

The aim of this study was to analyse polymorphism in the *alpha-ACTN3* gene, which in terms of muscle metabolism may affect the parameter of physical efficiency of the organism, such as the maximal oxygen uptake ($\dot{V}O_2$max) in the group of young individuals, both practising sports disciplines differing in terms of the nature of energy metabolism, and those less physically active. At the time the investigations within this study were initiated, this problem to the best of our knowledge had not been addressed in the Polish population and no results from completed studies on this problem were available.

MATERIALS AND METHODS

Experimental group and biological material. Biological material for genetic analyses comprised samples of peripheral blood collected from students of the University School of Physical Education in Poznań, both those actively practising sports, as well as those less active, and athletes training for different sports disciplines, representing different sports classes, including representatives of the Polish national teams. The research was approved by the Commission of Bioethics no. 1060/05 at the Karol Marcinkowski University of Medicine in Poznań.

The group subjected to physiological and genetic analyses comprised 239 individuals (154 men and 85 women) aged 18-26 years. Due to the fact that $\dot{V}O_2$max is a sex-dependent parameter, all statistical analyses were performed separately for women and men.

In order to verify the effect of polymorphism in the analysed gene on maximal oxygen consumption depending on the level of physical activity, participants in this study were divided into a group of individuals involved in training (119 men and 37 women) and those who did not do any sport training (35 men and 48 women). Moreover, the group of training individuals was divided into three subgroups in terms of sports disciplines, depending on the character of exercise metabolism, into: (i) speed and strength disciplines (disciplines with predominating anaerobic energy metabolism, such as short-distance running, high jump, long jump, discus) denoted as Sp-St (24 men, 11 women), (ii) endurance-speed-strength disciplines (disciplines with an intermediate character of energy metabolism, such as field hockey, tennis, rugby, soccer, volleyball, basketball, handball, rowing, canoeing, kickboxing, taekwondo) denoted as E-Sp-St (63 men, 9 women), and (iii) endurance disciplines (those with predominating aerobic energy metabolism, such as triathlon, medium and long-distance running, race walking, skiing, long-distance swimming, mountaineering) denoted as E (33 men, 17 women). A detailed division of disciplines was conducted based on the classification according to Bellotti et al. [2].

Physiological analyses

Physiological analyses were conducted at the Laboratory of Functional Examinations of the University School of Physical Education in Poznań, a holder of the Certificate of Quality Management System ISO 2000:9001 (no. 956-2007-AQ-GDA-RvA) with respect to design, organization and implementation of research.

The index of maximal oxygen uptake in the participants of the experiment was determined using the direct method during exercise tests on a moving track with the use of an Oxycon Mobile spiroergometer (Jeager). In the course of exercise the composition of air inhaled and exhaled by a given individual ($\dot{V}O_2$, $\dot{V}CO_2$) was analysed and their heart rate (HR) was monitored using a pulsometer (Polar). The test comprised exercise with increasing load, starting from running speed of 8 km/h, increasing the load by 2 km/h every 3 min, until the moment the maximum individual load was reached.

Genetic analyses

Genetic analyses were conducted at the Laboratory of Genetic Analyses, the University School of Physical Education in Poznań, a holder of the Certificate of Quality Management System ISO 2000:9001 (no. 956-2007-AQ-GDA-RvA) with respect to design, organization and implementation of research.

DNA was isolated from 5 ml of peripheral blood (leukocytes) collected from the examined individuals onto an anticoagulant (EDTA). DNA isolation was performed using the method with guanidine isothiocyanate (GTC). The R577X polymorphism of *ACTN3* was genotyped by the PCR–RFLP method (polymerase chain reaction and restriction fragment length polymorphism) with *HpyF3I* enzyme.

DNA was amplified in a volume of 20 μl. Genomic DNA, from each examined individual was placed in a separate test tube in the amount of 4 μl (200 ng) and 16 μl of reaction mixture was added, containing 50 mM KCl, 10 mM Tris-HCl (pH 8.3), 1.5 mM $MgCl_2$, 0.25 mM dNTP, 7.5 pmol each primer and 0.5 unit of Taq polymerase. The primer sequence was F- TCA gTT CAA ggC AAC ACT gGC, R- Agg Tgg CAC TgA CCA TAT CC [19]. The 30-cycle reaction was run in a Biometra T-personal thermocycler. The standard cycle comprised initial denaturation at 95°C for 10 min., denaturation at 95°C for 30s, annealing at 55°C for 30 s, synthesis at 72°C for 30 s and final synthesis at 72°C for 10 min.

PCR products 176 bp long were subsequently digested with *HpyF3I* (Fermentas Life Sciences) restriction endonuclease in the conditions recommended by the supplier. The digested products were then electrophorised in a 10% polyacrylamide gel at current intensity of 70 V for 16 hours. Results were visualized by silver staining.

Statistical analyses

Statistical calculations were performed at the Computer Laboratory of the Faculty of Animal Breeding and Biology, Poznań University of Life Sciences, using statistical software SAS ver. 9.1.

The χ^2 test was used to verify the goodness of fit for genotype distributions and the consistency of values of maximal oxygen uptake with the Hardy–Weinberg principle. Homogeneity of variance was determined using the Bartlett's test. Association of the R577X polymorphism of the *ACTN3* gene with the maximal oxygen uptake ($\dot{V}O_2max$) recorded for the participants of the experiment was verified using the one-way analysis of variance (ANOVA) – a parametric *t* test.

RESULTS

Table 1 presents the general characteristics of the experimental group, taking into consideration mean values of anthropometric characteristics, i.e. body weight and height as well as age, with standard deviations.

The highest value of $\dot{V}O_2max$ in the group of men was found for a triathlete (79.0 ml/kg·min^{-1}), the lowest for a field hockey player (40.3 ml/kg·min^{-1}), while among women the highest value was recorded for a triathlete (59.8 ml/kg·min^{-1}) and the lowest for an individual not involved in sports (30.6 ml/kg·min^{-1}). The mean ± SD value of oxygen uptake obtained by the group of men and women was 55.1 ± 7.06 ml/kg·min^{-1} and 45.6 ± 6.63 respectively.

TABLE 1. GENERAL CHARACTERISTICS OF THE EXPERIMENTAL GROUP. MEAN ± STANDARD DEVIATION VALUES OF BODY WEIGHT, BODY HEIGHT AND AGE IN THE GROUP OF WOMEN AND MEN

Sex	N	Body weight (kg)	Body height (cm)	Age (years)
F	85	59.7±5.71	169.4±6.28	21.4±1.67
M	154	76.2±8.14	180.3±10.58	20.9±2.12

Note: N - population size

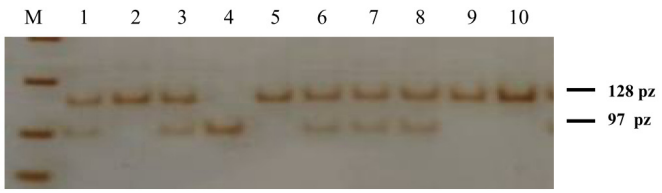

FIG. 1. AN EXAMPLE OF THE RESULT FOR GENOTYPING OF RESTRICTION SITE FOR *HpyF3I* WITHIN THE *ACTN3* GENE USING PCR-RFLP.

Note: Electrophoresis of products was performed in 10% silver-stained polyacrylamide gel. Lanes 2, 5, 9, 10 – genotype of homozygote 577R/R (HpyF3I -/-); lanes 1, 3, 6, 7, 8 – genotype of heterozygote 577R/X (HpyF3I+/-); lane 4 – genotype of homozygote 577X/X (HpyF3I +/+); M – size marker Ultra Low Range GeneRuler DNA Ladder.

Men and women were divided into groups of individuals actively practising sports and not involved in training, as well as in terms of the character of energy metabolism connected with the practised sports discipline. As it had been expected, women had lower values of $\dot{V}O_2max$ in relation to men, and individuals not practising sports had lower values than those practising them. Mean ± SD values of $\dot{V}O_2max$ for training and non-training women were 49.9 ± 5.9 ml/kg·min^{-1} and 42.3 ± 5.2 ml/kg·min^{-1} respectively. In the group of men obtained mean values of $\dot{V}O_2max$ were 50.7 ± 4.3 ml/kg·min^{-1} for non-training and 56.4 ± 7.2 ml/kg·min^{-1} for involved in training.

In the group of individuals involved in training the highest values of maximal oxygen uptake were recorded for representatives of endurance disciplines (51.5 ± 6.9 ml/kg·min^{-1} for women and 62.4 ± 9.0 ml/kg·min^{-1} for men) while the lowest were observed for representatives of endurance-speed-strength disciplines (47.5 ± 4.5 ml/kg·min^{-1} for women and 53.8 ± 4.2 ml/kg*min^{-1} for men).

Results of molecular analyses

An example of the result for genotyping of the R577X *ACTN3* polymorphism is presented in Figure 1.

Association analysis of the examined gene with the volume of $\dot{V}O_2max$

Within this study an analysis was conducted on the association of the investigated polymorphism with the volume of maximal oxygen uptake recorded for examined individuals. In the experimental group the frequency of alleles and genotypes and the distribution of $\dot{V}O_2max$ values were analysed. The χ^2 test confirmed that the investigated parameter was characterized by the normal distribution, while the frequency of *ACTN3* genotypes was found within genetic equilibrium ($\chi^2_{tab;\ n-1=2,\ \alpha=0.05} = 5.991 > \chi^2$ calc. = 1.3113). Homogeneity of variance was verified using the Bartlett's test. Differences in the values of maximal oxygen uptake recorded for different polymorphic variants of the examined gene were determined on the basis of one-way ANOVA – with the parametric *t* test. Descriptive statistics and the comparative analysis of maximal oxygen uptake recorded for individual polymorphic variants of the investigated gene are presented in Table 2. Differences between mean values of maximal oxygen uptake observed in the three groups with different genotypes turned out to be statistically non-significant.

TABLE 2. DESCRIPTIVE STATISTICS AND COMPARATIVE ANALYSIS OF MAXIMAL OXYGEN UPTAKE ($\dot{V}O_2max$ in ml/kg·min^{-1}) BETWEEN GENOTYPES OF THE R577X ACTN3 POLYMORPHISM

ACTN3	RR			RX			XX		
sex	N	$\bar{x}$ ± SD	Min - Max	N	$\bar{x}$ ± SD	Min - Max	N	$\bar{x}$ ± SD	Min - Max
F	31	45.51 ± 6.13	32.30 – 59.00	35	46.16 ± 7.59	30.60 - 59.80	19	44.75 ± 5.70	33.80 - 54.20
M	63	54.90 ± 6.82	40.30 - 76.80	70	54.96 ± 6.99	41.10 - 79.00	21	56.38 ± 8.17	42.30 - 74.90

Note: Analysis of variance did not show statistically significant differences between mean values of recorded maximal oxygen uptake in groups represented by RR, RX and XX genotypes.

TABLE 3. DESCRIPTIVE STATISTICS AND COMPARATIVE ANALYSIS OF MAXIMAL OXYGEN UPTAKE ($\dot{V}O_2max$ in ml/kg·min^{-1}) BETWEEN GROUPS WITH VARIED GENOTYPES OF R577X ACTN3 POLYMORPHISM AMONG WOMEN AND MEN TRAINING AND THOSE NOT PRACTISING SPORTS

Sex	ACTN3	Non-training			Training		
		N	$\bar{x}$ ± SD	Min - Max	N	$\bar{x}$ ± SD	Min - Max
F	RR	15	42.07 ± 4.92	32.30 – 50.50	16	48.74 ± 5.45	39.30 – 59.00
	RX	21	41.90 ± 5.81	30.60 – 58.40	14	52.56 ± 5.03	41.30 – 59.80
	XX	12	43.27 ± 4.49	34.20 – 50.70	7	47.29 ± 6.97	33.80 – 54.20
M	RR	11	51.45 ± 4.94	42.70 – 62.20	52	55.62 ± 6.97	40.30 – 76.80
	RX	18	49.87 ± 2.48	45.70 – 55.40	52	56.72 ± 7.19	41.10 – 79.00
	XX	6	52.02 ± 7.03	42.30 – 59.30	15	58.13 ± 8.14	49.80 – 74.90

Note: Analysis of variance did not show statistically significant differences between mean values of recorded maximal oxygen uptake in groups represented by genotypes RR, RX and XX.

TABLE 4. DESCRIPTIVE STATISTICS AND A COMPARATIVE ANALYSIS OF MAXIMAL OXYGEN UPTAKE ($\dot{V}O_2max$ in ml/kg·min^{-1}) BETWEEN GROUPS WITH DIFFERENT GENOTYPES OF THE R577X ACTN3 POLYMORPHISM IN THE GROUP OF WOMEN AND MEN PRACTISING DISCIPLINES WITH DIFFERENT CHARACTER OF ENERGY METABOLISM AND THOSE NOT INVOLVED IN TRAINING

Sex	ACTN3	Sp-St			E-Sp-St			E			Non-training		
		N	$\bar{x}$ ± SD	Min - Max	N	$\bar{x}$ ± SD	Min - Max	N	$\bar{x}$ ± SD	Min - Max	N	$\bar{x}$ ± SD	Min - Max
F	RR	6	48.60 ± 5.16	39.30 - 53.60	4	47.48 ± 5.45	40.20 - 52.00	6	49.73 ± 6.48	39.90 - 59.00	15	42.07 ± 4.92	32.30 - 50.50
	RX	3	53.20 ± 2.52	51.50 - 56.10	4	47.98 ± 4.84	41.30 - 51.60	7	54.90 ± 4.50	47.50 - 59.80	21	41.90 ± 5.81	30.60 - 58.40
	XX	2	46.35 ± 2.05	44.90 - 47.80	1	46.10 ± -	-	4	48.05 ± 9.69	33.80 - 54.20	12	43.27 ± 4.49	34.20 - 50.70
M	RR	14	55.61 ± 6.51	48.20 - 71.50	28	52.93 ± 4.65	40.30 - 62.00	10	63.18 ± 7.95	52.10 - 76.80	11	51.45 ± 4.94	42.70 - 62.20
	RX	8	53.78 ± 5.29	41.10 - 58.10	25	54.50 ± 3.79	45.80 - 61.30	19	60.87 ± 9.36	42.30 -79.00	18	49.87 ± 2.48	45.70 - 55.40
	XX	2	54.20 ± 5.37	50.40 - 58.00	9	54.86 ± 3.97	49.80 - 61.90	4	67.45 ± 9.99	52.80 - 74.90	6	52.02 ± 7.03	42.30 - 59.30

Note: Analysis of variance did not show statistically significant differences in maximal oxygen uptake between RR, RX and XX genotypes within the established subgroups.

In order to verify whether there are differences in the volume of maximal oxygen uptake for different genotypes depending on the degree of physical activity, women and men participating in the study were divided into groups of training individuals and those not practising sports. The distribution of genotypes and values of maximal oxygen uptake (minimum, maximum and mean value) in the subgroups for individual polymorphisms are presented in Table 3. No statistically significant differences were observed.

Results were also analysed in terms of differences in the volume of maximal oxygen uptake recorded for individuals with different genotypes of examined polymorphisms, depending on the character of energy metabolism predominant in the practised sports discipline. A list of mean values of maximal oxygen uptake for the polymorphism in the analysed gene in the subgroups of individuals practising disciplines of speed-strength, endurance-speed-strength, endurance character and those not practising sports are presented in Table 4. Analysis of variance did not show statistically significant differences in the volume of $\dot{V}O_2max$ depending on the genotype.

DISCUSSION

High individual variation in the observed effort tolerance in the overall population, but also in the population of athletes alone, indicates the advisability to describe factors modifying this capacity, which are obviously many due to the complex character of the trait, such as physical fitness.

The R577X *ACTN3* polymorphism, identified in 1999 by North et al., was selected for the investigations as there were scarce publications on the subject, concerning mainly the Finnish population [10,19]. To the best of our knowledge this is the first original study on this polymorphism in the Polish population in the context of a search for genes determining physical fitness.

Actinin 3 is a structural protein of type II muscle fibres, both IIA (fast-twitch oxidative-glycolytic fibres) and IIX (fast-twitch glycolytic

fibres), responsible for the generation of high power by muscles in short-term effort, e.g. short-distance run. Results from different research centres indicate a higher frequency of allele R (functional actinin 3) in speed-strength athletes than in endurance athletes, in whom allele X predominates (a lack of actinin 3) [5,10,12].

The distribution of alleles and genotypes of *ACTN3* in comparative studies by Yang et al. on African marathon runners (Kenyans and Ethiopians) and sprinters (Nigerians) showed a very low frequency of allele X in Kenyans and Nigerians and a higher one in Ethiopians, which did not correspond to the higher number of endurance athletes. The authors concluded that a lack of actinin 3 is not the primary cause for the commonly known, high endurance capacity of Africans [20].

For the R577X *ACTN3* polymorphism no statistically significant differences were found in the volume of maximal oxygen uptake depending on the genotype. There is a trend in men with the XX genotype to obtain higher values of maximal oxygen uptake in relation to the other *ACTN3* genotypes. A similar distribution of results may be observed in case of the division into the groups of training individuals and those not practising sports, except for training women, among whom the highest maximal oxygen uptake was recorded for individuals with the RX genotype. The trend for higher $\dot{V}O_2$max values in individuals with the XX or RX genotypes is maintained in most subgroups of the detailed division into disciplines of different character. The fact that higher values of maximal oxygen uptake are recorded for individuals with the XX genotype, which is characterized by a lack of actinin 3 in muscle fibres, is consistent with the mechanism of development of physical fitness towards the aerobic type in case of a lack of predisposition to generate high power by muscles, which was proposed by MacArthur [8]. It is of interest that among the 11 women and 24 men practising speed-strength disciplines as many as 6 women and 14 men had the RR genotype, while only 2 individuals in each group had the XX genotype. In the subgroups of disciplines with the predominance of aerobic metabolism and those not involved in sports the numbers of individuals with particular genotypes were closer to the normal distribution, with the predominance of RX heterozygotes, while in the subgroup of disciplines with mixed type energy metabolism genotypes with the speed-strength allele R (RR and RX) also predominated. The more frequent incidence of the RR and RX genotypes in soccer players (a discipline with mixed effort metabolism) was also observed by Santiago et al. in their studies on the distribution of *ACTN3* genotypes in athletes [14]. Among analyses on the R577X *ACTN3* polymorphism only a few concern the effect on maximal oxygen uptake. A study by Lucia et al. on a group of elite cyclists did not confirm the difference in the distribution of genotypes between the group of athletes and the control group. Moreover, values of $\dot{V}O_2$max recorded between individual *ACTN3* genotypes among cyclists were not significant [6]. Results obtained in this study on the one hand are consistent with the results reported by Lucia et al. in terms of the effect of this polymorphism on the level of maximal oxygen uptake, while on the other hand there is an observable trend for the characteristic distribution of the RR and XX genotypes depending on the character of practised sports disciplines, which in turn is consistent with most results of studies on different populations worldwide [4,10,12,19].

Studies aiming at the search for genotypes determining physical fitness are developing at a fast rate. Analysis of associations of individual polymorphisms at present is considered to be a relatively ineffective method to search for the genetic background of complex traits. Genetic models are being formed, taking into consideration several polymorphisms in order to create an optimal profile characterization of athletes practising a sports discipline with the predominance of a specific type of effort metabolism [13,18]. For this reason several analyses need to be performed, covering spatially a narrower range of the genome, subjecting to complex analysis a specific aspect of efficiency, e.g. cardiorespiratory efficiency or efficiency of cell respiration, in order to systematically create the database of genetic profiles advantageous for professional sports.

CONCLUSIONS

No statistically significant effect of the R577X *ACTN3* polymorphism on maximal oxygen uptake was found. A trend was observed for higher values of $\dot{V}O_2$max to be reached by individuals with the *XX* and *RX* genotypes and a predominance of the RR genotype was found in the group of individuals training for speed-strength disciplines.

REFERENCES

1. Beggs A.H., Byers T.J., Knoll J.H.M., Boyce F.M., Bruns G.A.P., Kunkel L.M. Cloning and characterization of two human skeletal muscle alpha-actinin genes located on chromosomes 1 and 11. J. Biol. Chem. 1992;267:9281-9288.
2. Bellotti P., Benzi G., Dal Monte A., Donati A., Matteucci E., Vittorio C. Fizjologiczna klasyfikacja dyscyplin sportu (Physiological classification of sports disciplines). Sport Wyczyn. 1982;10:214 (in Polish).
3. Clarkson P.M., Hoffman E.P., Zambraski E., Gordish-Dressman H., Kearns A., Hubal M., Harmon B., Devaney J.M. ACTN3 and MLCK genotype associations with exertional muscle damage. J. Appl. Physiol. 2005;99:564-569.
4. Druzhevskaya A.M., Ahmetov I.I., Astratenkova I.V., Rogozkin V.A. Association of the ACTN3 R577X polymorphism with power athlete status in Russians. Eur. J. Appl. Physiol. 2008;103:631-634.
5. Garland T. Jr, Bennett A.F., Daniels C.B. Heritability of locomotor performance and its correlates in a natural population. Experimentia 1990;46:530-533.
6. Lucia A., Gómez-Gallego F., Santiago C., Bandrés F., Earnest C., Rabadán M., Alonso J.M., Hoyos J., Córdova A., Villa G., Foster C. ACTN3 genotype in professional endurance cyclists. Int. J. Sports Med. 2006;27:880-884.
7. MacArthur D.G., North K.N. A gene for speed? The evolution and function of alpha-actinin-3. Bioessays 2004;26:786-795.
8. MacArthur D.G., Seto J.T., Raftery J.M., Quinlan K.G., Huttley G.A., Hook J.W., Lemckert F.A., Kee A.J., Edwards M.R., Berman Y., Hardeman E.C., Gunning P.W., Easteal S., Yang N., North K.N. Loss of ACTN3 gene function alters mouse muscle metabolism and shows evidence of positive selection in humans. Nat. Genet. 2007;39:1261-1265.

9. Mills M.A., Yang N., Weinberger R.P., Vander Woude D.L., Beggs A.H., Easteal S., North K.N. Differential expression of the actin-binding proteins, alpha-actinin-2 and -3, in different species: implications for the evolution of functional redundancy. Hum. Molec. Genet. 2001;10:1335-1346.
10. Niemi A-K, Majamaa K. Mitochondrial DNA and ACTN3 genotypes in Finnish elite endurance and sprint athletes. Eur. J. Hum. Genet. 2005;13:965-969.
11. North K.N., Yang N., Wattanasirichaigoon D., Mills M., Easteal S., Beggs A.H. A common nonsense mutation results in alpha-actinin-3 deficiency in the general population. Nat. Genet. 1999;21:353-354.
12. Roth S.M., Walsh S., Liu D., Metter E.J., Ferrucci L., Hurley B.F. The ACTN3 R577X nonsense allele is under-represented in elite-level strength athletes. Eur. J. Hum. Genet. 2008;16:391-394.
13. Ruiz J.R., Gómez-Gallego F., Santiago C., González-Freire M., Verde Z., Foster C., Lucia A. Is there an optimum endurance polygenic profile? J. Physiol. 2009;587:1527-1534.
14. Santiago C., González-Freire M., Serratosa L., Morate F.J., Meyer T., Gómez-Gallego F., Lucia A. ACTN3 genotype in professional soccer players. Br. J. Sports Med. 2008;42:71-73.
15. Suminaga R., Matsuo M., Takeshima Y., Nakamura H., Wada H. Nonsense mutation of the alpha-actinin-3 gene is not associated with dystrophinopathy. Am. J. Med. Genet. 2000;92:77-78.
16. Van Damme R., Wilson R.S., Vanhooydonck B., Aerts P. Performance constraints in decathletes. Nature 2002;415:755-756.
17. Vincent B., De Bock K., Ramaekers M., Van den Eede E., Van Leemputte M., Hespel P., Thomis M.A. ACTN3 (R577X) genotype is associated with fiber type distribution. Physiol. Genomics 2007;32:58-63.
18. Williams A.G, Folland J.P. Similarity of polygenic profiles limits the potential for elite human physical performance. J. Physiol. 2008;586:113-121.
19. Yang N., MacArthur D.G., Gulbin J.P., Hahn A.G., Beggs A.H., Easteal S., North K. ACTN3 genotype is associated with human elite athletic performance. Am. J. Hum. Genet. 2003;73:627-631.
20. Yang N., MacArthur D.G., Wolde B., Onywera V.O., Boit M.K., Lau S.Y., Wilson R.H., Scott R.A., Pitsiladis Y.P., North K. The ACTN3 R577X polymorphism in East and West African athletes. Med. Sci. Sports Exerc. 2007;39:1985-1988.