

A genetic-based algorithm for personalized resistance training

AUTHORS: Jones N¹, Kiely J², Suraci B³, Collins DJ², de Lorenzo D^{4,5}, Pickering C⁶, Grimaldi KA⁶

¹ DNA Sports Performance Ltd, Manchester, UK

² Institute of Coaching and Performance, University of Central Lancashire, Preston, UK

³ Suraci Consultancy, Portsmouth, UK

⁴ Departament de Ciències Experimentals i de la Salut, Universitat Pompeu Fabra, CEXS-UPF-PRBB, Barcelona, Catalonia, Spain

⁵ Centro de Estudios en Genómica y Nutrición-CESGEN, Parc Científic i Tecnològic Agroalimentari de Lleida-PCiTAL, Lleida, Catalonia, Spain

⁶ Exercise and Nutritional Genomics Research Centre, DNAFit Ltd, London, UK

ABSTRACT: Association studies have identified dozens of genetic variants linked to training responses and sport-related traits. However, no intervention studies utilizing the idea of personalised training based on athlete's genetic profile have been conducted. Here we propose an algorithm that allows achieving greater results in response to high- or low-intensity resistance training programs by predicting athlete's potential for the development of power and endurance qualities with the panel of 15 performance-associated gene polymorphisms. To develop and validate such an algorithm we performed two studies in independent cohorts of male athletes (study 1: athletes from different sports (n=28); study 2: soccer players (n=39)). In both studies athletes completed an eight-week high- or low-intensity resistance training program, which either matched or mismatched their individual genotype. Two variables of explosive power and aerobic fitness, as measured by the countermovement jump (CMJ) and aerobic 3-min cycle test (Aero3) were assessed pre and post 8 weeks of resistance training. In study 1, the athletes from the matched groups (i.e. high-intensity trained with power genotype or low-intensity trained with endurance genotype) significantly increased results in CMJ (P=0.0005) and Aero3 (P=0.0004). Whereas, athletes from the mismatched group (i.e. high-intensity trained with endurance genotype or low-intensity trained with power genotype) demonstrated non-significant improvements in CMJ (P=0.175) and less prominent results in Aero3 (P=0.0134). In study 2, soccer players from the matched group also demonstrated significantly greater (P<0.0001) performance changes in both tests compared to the mismatched group. Among non- or low responders of both studies, 82% of athletes (both for CMJ and Aero3) were from the mismatched group (P<0.0001). Our results indicate that matching the individual's genotype with the appropriate training modality leads to more effective resistance training. The developed algorithm may be used to guide individualised resistance-training interventions.

CITATION: Jones N, Kiely J, Suraci B et al. A genetic-based algorithm for personalized resistance training. *Biol Sport*. 2016;33(2):117–126.

Received: 2016-02-29; Reviewed: 2016-03-06; Re-submitted: 2016-03-07; Accepted: 2016-03-08; Published: 2015-04-01.

Corresponding author:

Nicholas Jones

DNA Sports Performance Ltd,
Manchester, UK

E-mail: nicholasjones@

dna-sports-performance.com

Key words:

DNA

Polymorphism

Genotype

Personalized training

Power

Endurance

INTRODUCTION

Resistance exercise training is widely used to enhance general fitness and athletic potential/capacity across many sporting disciplines including power, strength and endurance events [1, 2]. When properly performed and combined with adequate nutrition, resistance training leads to increases in strength, power, speed, muscle size, local muscular endurance, coordination, and flexibility and reductions in body fat and blood pressure [3].

Effective resistance exercise prescription involves manipulation of several variables specific to the targeted goals, such as intensity or load per repetition (i.e. percentage of one repetition maxi-

mum (1 RM)), volume (total number of sets and repetitions), training frequency, muscle action (concentric vs. eccentric), rest intervals between sets, repetition velocity and others [3, 4]. Furthermore, resistance training can be categorized into two common types: low-intensity (~30% of 1 RM and high repetitions) and high-intensity (~70% of 1 RM and low repetitions) resistance training. Low-intensity resistance training is effective for increasing absolute local muscular endurance [5], explosive power [6, 7] and preferential hypertrophy of slow-twitch muscle fibres [8, 9], while high-intensity training (also known as classic strength training) leads to in-

creases in absolute strength [3] and the hypertrophy of all types of muscle fibres [10, 11].

There is a large variability in both muscle size and strength gains in response to resistance training between individuals [4]. In a large study of 585 subjects, Hubal *et al.* [12] have shown that men and women exhibited wide ranges of strength gain (1 RM: 0 to +250%) and skeletal muscle hypertrophy (cross-sectional area: -2 to +59%) in response to 12 weeks of resistance training, indicating individual training responses may vary widely dependent on factors such as genetic heritage. Accordingly, the level of adaptation experienced by

each individual will be dependent on the interaction between specific training performed and genotype. Indeed, there is a general consensus that resistance training programs should be individualized, but little information exists to accurately discern how best to personalize training program design to maximize outcomes [3, 4, 12, 13].

Muscle fiber composition is a heritable (~45%) trait [14], with large variability between individuals. For example, slow-twitch (Type I) content of vastus lateralis ranges from 5-90%. This variability, in turn, may determine individual's potential to perform different types of resistance training. Accordingly, data show that Type I muscle

TABLE I. List of genetic variants analysed by DNAFit Peak Performance Algorithm™

Gene	Full name	Functions and associated phenotypes	Polymorphism	Endurance or power related allele	References
<i>ACE</i>	Angiotensin I converting enzyme	Regulates circulatory homeostasis through the synthesis of vasoconstrictor angiotensin II and the degradation of vasodilator kinins.	Alu I/D (rs4646994)	Endurance: I Power: D	[20, 21]
<i>ACTN3</i>	α -actinin-3	Stabilizes the muscle contractile apparatus in fast-twitch muscle fibres.	Arg577Ter (rs1815739 C/T)	Endurance: 577Ter (T) Power: Arg577 (C)	[20, 22]
<i>ADRB2</i>	β -2 adrenoreceptor	Plays a pivotal role in the regulation of the cardiac, pulmonary, vascular, endocrine and central nervous system.	Gly16Arg (rs1042713 G/A)	Endurance: 16Arg (A)	[23, 24]
			Gln27Glu (rs1042714 C/G)	Endurance: Gln27 (C)	[25]
<i>AGT</i>	Angiotensinogen	Angiotensinogen is an essential component of the renin-angiotensin system that regulates vascular resistance and sodium homeostasis, and thus determining blood pressure.	Met235Thr (rs699 T/C)	Power: 235Thr (C)	[26, 27]
<i>BDKRB2</i>	Bradykinin receptor B2	Involved in the endothelium-dependent vasodilation.	rs1799722 C/T	Endurance: T	[24]
<i>COL5A1</i>	Collagen, type V, α 1	Encodes the pro- α 1 chain of type V collagen, the rate-limiting component of the of type V collagen trimer assembly.	rs12722 C/T (BstUI)	Endurance: T	[28, 29]
<i>CRP</i>	C-reactive protein, pentraxin-related	Involved in several host defense related functions based on its ability to recognize damaged cells and to initiate their elimination in the blood.	rs1205 A/G	Endurance: A	[30, 31]
<i>GABPB1 (NRF2)</i>	GA binding protein transcription factor, β subunit 1 (nuclear respiratory factor 2)	Encodes a transcriptional regulator of genes involved in activation of cytochrome oxidase expression and nuclear control of mitochondrial function.	rs7181866 A/G	Endurance: G	[32, 33]
<i>IL6</i>	Interleukin-6	IL-6 is a pleiotropic cytokine expressed in immune and muscle cells. Involved in a wide variety of biological functions, including regulation of differentiation, proliferation and survival of target cells.	-174 C/G (rs1800795)	Power: G	[34, 35]
<i>PPARA</i>	Peroxisome proliferator-activated receptor α	Regulates liver, heart and skeletal muscle lipid metabolism, glucose homeostasis, mitochondrial biogenesis, cardiac hypertrophy.	rs4253778 G/C	Endurance: G Power: C	[36, 37]
<i>PPARGC1A</i>	Peroxisome proliferator-activated receptor γ coactivator 1 α	Regulates fatty acid oxidation, glucose utilization, mitochondrial biogenesis, thermogenesis, angiogenesis, formation of muscle fibers.	Gly482Ser (rs8192678 G/A)	Endurance: Gly482 (G)	[38, 39]
<i>TRHR</i>	Thyrotropin-releasing hormone receptor	Stimulates the release of thyroxine, which is important in developing skeletal muscle.	rs16892496 A/C	Power (muscle mass): C	[40]
<i>VDR</i>	Vitamin D receptor	Involved in sustaining normocalcemia by inhibiting the production of parathyroid hormone and has effects on bone and skeletal muscle biology.	BsmI A/G (rs1544410)	Power: A	[41, 42]
<i>VEGFA</i>	Vascular endothelial growth factor A	Growth factor active in angiogenesis, vasculogenesis and endothelial cell growth.	rs2010963 G/C	Endurance: C	[43, 44]

fibres have high resistance to fatigue and are thus suited for low-intensity resistance or aerobic (endurance) training, IIA fibres are better suited for medium-term anaerobic exercise, and type IIX fibres are adapted for high-intensity (power and strength) exercise [8, 13, 15]. It should be noted that although muscle fibre composition is an informative biomarker, muscle biopsies are highly invasive. Subsequently, the potential value of non-invasive exercise prescription tools, such as genetic profiling, seems worthy of investigation.

Association studies have linked dozens of genetic variants to training responses and sport-related traits, such as strength, skeletal muscle mass, recovery ability and muscle fibre composition [16-19]. However, no intervention studies prescribing training on the basis of a genetic profile of athletes have been carried out. Here we evaluate an algorithm that facilitates training prescription by using a panel of 15 gene polymorphisms associated with physical performance and muscle-specific traits to predict an athlete's potential for development of power and/or endurance qualities (Table 1). These polymorphisms are located within the genes involved in the regulation of muscle fibre type composition and muscle size, cytoskeletal function, muscle damage protection, metabolism, circulatory homeostasis, mitochondrial biogenesis, thermogenesis and angiogenesis.

The aim of the present work therefore was to test, in two independent studies, the hypothesis that genetically matched athletes (i.e. high-intensity trained with power genotype or low-intensity trained with endurance genotype) show greater improvements in explosive power (countermovement jump) and aerobic fitness (aerobic 3-min cycle test) in response to high- or low-intensity resistance training compared to mismatched athletes (i.e. high-intensity trained with endurance genotype or low-intensity trained with power genotype).

MATERIALS AND METHODS

Study participants. In Study 1, 55 Caucasian male University athletes, all aged 18-20 years, volunteered for the study, and 28 of them (height 180.7 ± 1.5 cm, weight 77.0 ± 2.1 kg) successfully completed it (27 athletes had not completed all aspects of the study due to either injury or illness). Each participant was a member of first or second team, actively competing in British Universities and Colleges Sports (BUCS) leagues. The athletes competed in squash ($n = 1$), swimming ($n = 7$), running ($n = 1$), ski/snowboard ($n = 4$), soccer ($n = 1$), lacrosse ($n = 2$), badminton ($n = 1$), motorsport ($n = 1$), cycling ($n = 4$), cricket ($n = 2$), volleyball ($n = 1$), fencing ($n = 1$) and rugby union ($n = 2$).

In study 2, 68 male soccer players, all aged 16-19 years, volunteered to participate in the study, and 39 of them (height 176.1 ± 1.0 cm, weight 68.9 ± 1.5 kg) successfully completed it (29 participants were withdrawn from the study due to non-adherence of set training volumes over the 8 weeks, or injury). Each subject was a member of college soccer academy who actively competed in BUCS leagues.

Ethical approval

The two-stage study was approved by the University of Central Lancashire Ethics Committee according to the Declaration of Helsinki. Each participant gave written informed consent after procedures were fully explained. Each participant was free to withdraw from the studies at anytime.

Study design

Study design utilised a time series trial as explained by Batterham and Hopkins [45]. Participants of both studies were randomly allocated to an eight-week high- or low-intensity resistance-training program, after undergoing performance tests for both explosive power and endurance. Participants transitioned from their normal training plan to the designed 8-week intervention followed by an eight-week wash-out period. The study was double blinded, in that all were unaware of their 'genetic potential status', as determined by the DNAFit Peak Performance Algorithm™. This also included the lead investigator who coached the participants during the 8 weeks of resistance training.

Prior to involvement in the study, all participants had undertaken weekly strength and conditioning programs, supervised by an accredited strength and conditioning coach, for a minimum of six months and maximum of two and half years. These sessions took place in a free weights facility where technique and adherence was closely monitored at all times. Participants engaged in a minimum of one, and maximum of two (preferentially), sessions per week. No other form of resistance training was undertaken during this time, and participants were actively partaking in other sport-specific training sessions and competitive games in parallel to the intervention. The investigator selected the same exercises for both groups: deadlift, pulldowns, front squat to 90 degrees, dumbbell flat press, step ups to medium high box and vertical jump single effort.

Each group self-selected training loads for each session, were monitored for progressive increases in perceived exertion, using a modified Borg scale, and loads were recorded to ensure progression. The only differences between the training programs were volume modifications. The high-intensity resistance training program consisted of ten sets of two reps over the eight-week study. This gave a total volume of one hundred and twenty reps per session. The low-intensity resistance training program consisted of three sets of ten reps for first two weeks, three sets of fifteens reps for the next three weeks and three sets of twenty for the last three weeks. This gave a total volume of one hundred and eighty reps in the first two weeks, two hundred and seventy in the next three weeks and three hundred and sixty reps in the last three weeks.

Physiological measurements

All participants undertook a pre- and post-test measure of explosive power and aerobic fitness (endurance performance); namely, a countermovement jump (CMJ) and Aerobic 3-min Cycle test (Aero3), using a Optojump (Microgate, Italia) and Wattbike Pro (Wattbike, Not-

tingham, UK), respectively. Participants performed a standardized warm up before every testing session with the CMJ preceding the Aero3. Subjects were requested to arrive for testing in a rested and hydrated state and to refrain from caffeine intake for at least 12 hours before testing. Testing took place on the same time and weekday on each occasion, to ensure a consistent placement within the subject's usual schedule.

Genotyping

Upon enrollment into study each participant volunteered a saliva sample, which was collected through sterile and self-administered buccal swabs. Samples were sent to IDna Genetics laboratory (Norwich, UK) within thirty-six hours, where analysis of the genes detailed in Table 1 was undertaken. DNA was extracted and purified using the Isohelix Buccalyse DNA extraction kit BEK-50 (Kent, UK). DNA samples were amplified by real-time PCR on an ABI7900 real-time thermocycler (Applied Biosystem, Waltham, USA).

Calculation of power/endurance ratio

Following the analysis, the DNAFit Peak Performance Algorithm™ was used to determine percentage power/endurance score (P/E) ratio, similar to the research conducted by Egorova *et al.* [46]. Initially, each allele was given a point (0, 1, 2, 3 or 4) depending on the effect of the polymorphism on performance (power/muscle hypertrophy or endurance with respect to response to training). The strength of the rating was based on the evidence from cumulative literature results averaged over time. The total points for the P/E were expressed as a percentage of P/E and then combined to give the balance percentage. A percentage-ranking list was then compiled using this score. Every other participant on the list then undertook high- or low-intensity resistance training. To clarify, someone who is 75% power but does low-intensity resistance training would be doing mismatched genotype training, while a participant rated as 75% endurance that completed low-intensity resistance training would be doing matched genotype training. A threshold for 50% was used as the splitting value in this process.

Statistical analysis

Statistical analysis was conducted in SPSS, Version 20 (Chicago, IL). The required sample size for this study was validated using the Mann-Whitney test. The chi-square test was used to test genotype distributions for deviation from Hardy-Weinberg equilibrium. The non-parametric 2-sample paired test was performed matching "before" and "after" measurements from each individual tested. A 2-sided Mann-Whitney test for 2 independent samples was used to compare gains in CMJ and Aero3 between groups. Differences in phenotypes between different genotype groups were analysed using ANOVA or unpaired *t* test. Spearman's (non-parametric) correlations were used to assess the relationships between the genotype score and performance tests. The squared correlation coefficient R^2 was used as a measure of explained variance. Bonferroni's correction for multiple testing was

performed by multiplying the P value with the number of tests where appropriate. All data are presented as mean (standard deviation; SD). Statistical significance was set at a P value < 0.05.

RESULTS

Efficiency of different training modalities. All performance parameters increased significantly (<0.001) in response to low- and high-intensity resistance training when the results of two studies were combined. No significant differences in explosive power (CMJ: 5.4 (5.0) vs. 4.6 (6.1)%, $P = 0.547$) and aerobic fitness (Aero3: 4.3 (3.8) vs. 4.3 (3.7)%, $P = 0.711$) gains were observed between low- and high-intensity resistance training groups, indicating that i) both training modalities can be used to improve these performance parameters and ii) results of responses to both training types can be combined for the analysis where appropriate.

Association analysis between genotypes and phenotypes

With some exceptions for the *GABPB1* and *VDR* gene polymorphisms in Study 2 (due to the low sample sizes in terms of population genetics), genotype distributions of 15 gene polymorphisms amongst all athletes of both studies were in Hardy-Weinberg equilibrium (Table 2).

To assess the association between each polymorphism and performance parameters we used the combined data of two studies. After Bonferroni's correction for multiple testing the results were considered significant with $P < 0.0033$ (i.e. $0.05/15$). In accordance with the literature data (Table 1), we found that athletes with the *ACE* DD ($P > 0.1$ for CMJ, $P > 0.1$ for Aero3), *ACTN3* Arg/Arg ($P = 0.065$ for CMJ, $P = 0.0038$ for Aero3), *CRP* rs1205 GG ($P > 0.1$ for CMJ, $P = 0.0833$ for Aero3), *PPARGC1A* Ser/Ser ($P = 0.065$ for CMJ, $P = 0.0499$ for Aero3) and *VDR* AA ($P > 0.1$ for CMJ, $P > 0.1$ for Aero3) genotypes demonstrated a tendency to have greater gains in one or two performance tests compared with the opposite genotype carriers after high-intensity resistance training, while the latter (except for the *PPARGC1A* polymorphism) better responded to the low-intensity training (*ACE* II: $P > 0.1$ for CMJ, $P = 0.0355$ for Aero3; *ACTN3* Ter/Ter: $P > 0.1$ for CMJ, $P > 0.1$ for Aero3; *CRP* rs1205 AA: $P = 0.0224$ for CMJ, $P > 0.1$ for Aero3; *VDR* GG ($P > 0.1$ for CMJ, $P = 0.0311$ for Aero3). No significant differences in CMJ and Aero3 gains were observed between different genotype groups with respect to the other polymorphisms (data not shown). However, given that the latter 10 polymorphisms have recently been reported to be associated with endurance, power and muscle-specific traits, and the fact that each contributing gene can explain only a small portion of the observed interindividual differences in training-induced effects, we felt justified in retaining all 15 genetic markers for further analysis.

Effect of different training modalities and genetic profiles on performance parameters

Based on power/endurance genotype score (see Methods), in two studies we identified 39 athletes (58.2%) with endurance genotype

TABLE 2. Genotype distributions and minor allele frequencies of candidate genes in athletes of two studies.

Gene and variation	Study	Genotypes						MAF, %	PHW	
		AA	AB	BB						
ACE rs4646994 I/D	S1	DD	10	ID	11	II	7	I	44.6	0.2776
	S2		14		16		9		43.6	0.3005
ACTN3 rs1815739 C/T	S1	CC	8	CT	10	TT	10	T	53.6	0.1356
	S2		12		21		6		42.3	0.5199
ADRB2 rs1042713 G/A	S1	GG	16	GA	10	AA	2	A	25.0	0.8011
	S2		21		13		5		29.5	0.2153
ADRB2 rs1042714 C/G	S1	CC	5	CG	15	GG	8	G	55.4	0.6572
	S2		14		16		9		43.6	0.3005
AGT rs699 T/C	S1	TT	9	TC	15	CC	4	C	41.1	0.5723
	S2		17		17		5		34.6	0.8171
BDKRB2 rs1799722 C/T	S1	CC	9	CT	14	TT	5	T	42.9	0.9122
	S2		15		17		7		39.7	0.5745
COL5A1 rs12722 C/T	S1	TT	8	TC	17	CC	3	C	41.1	0.1784
	S2		13		17		9		44.9	0.4576
CRP rs1205 A/G	S1	GG	12	GA	12	AA	4	A	35.7	0.7243
	S2		21		12		6		30.8	0.0828
GABPB1 rs7181866 A/G	S1	AA	27	AG	1	GG	0	G	1.8	0.9233
	S2		36		2		1		5.1	0.0031*
IL6 rs1800795 C/G	S1	GG	10	GC	13	CC	5	C	41.1	0.8289
	S2		17		16		6		35.9	0.4977
PPARA rs4253778 G/C	S1	GG	21	GC	5	CC	2	C	16.1	0.0736
	S2		26		11		2		19.2	0.5653
PPARGC1A rs8192678 G/A	S1	GG	7	GA	18	AA	3	A	42.9	0.0982
	S2		15		17		7		39.7	0.5745
TRHR rs16892496 A/C	S1	AA	14	AC	9	CC	5	C	33.9	0.1342
	S2		15		17		7		39.7	0.5745
VDR rs1544410 A/G	S1	GG	11	GA	16	AA	1	A	32.1	0.1009
	S2		16		11		12		44.9	0.0073*
VEGFA rs2010963 G/C	S1	GG	13	GC	11	CC	4	C	33.9	0.5126
	S2		18		18		3		30.8	0.6028

Note: MAF - minor allele frequency; S₁ - Study 1; S₂ - Study 2. *P_{HW} < 0.05 - not consistent with Hardy-Weinberg equilibrium.

and 28 athletes (41.8%) with power genotype profiles. Changes in CMJ and Aero3 tests of athletes with predominantly endurance or power genotype profiles from both studies after 8 weeks of low- and high-resistance training are presented in Tables 3 and 4. In both studies it was shown that athletes with endurance genotype profile had greater benefits from the low-intensity resistance training, while athletes with power genotype profile better responded to the high-intensity resistance training. As expected, the outcomes were more prominent in the Study 2 with homogeneous cohort (i.e. soccer players). Furthermore, we found that power genotype score (%) of athletes from both studies was positively correlated with CMJ ($r = 0.56$; $P = 0.0005$) and Aero3 ($r = 0.39$; $P = 0.0199$) increases (%) in response to high-intensity training, while endurance genotype score (%) was positively correlated with CMJ ($r = 0.37$; $P = 0.0399$) and Aero3 ($r = 0.51$; $P = 0.0032$) increases (%) in response to low-intensity training, indicating that power genotype score explained 14-32% of the variation in physiological parameters of athletes. In accordance with power/endurance genotype score and training

modality, 34 athletes performed matched training (high-intensity training with power genotype ($n=15$) or low-intensity training with endurance genotype ($n=19$)), while other 33 athletes completed mismatched training (high-intensity training with endurance genotype ($n=20$) or low-intensity training with power genotype ($n=13$)). In study 1, the athletes from the matched group have significantly increased their results in CMJ ($P=0.0005$) and Aero3 ($P=0.0004$). On the other hand, athletes from the mismatched group have shown non-significant improvements in CMJ ($P=0.175$) and less prominent results in Aero3 ($P=0.0134$) (Table 5). In study 2, soccer players from the matched group have also demonstrated significantly greater ($P<0.0001$) performance changes in both tests compared to mismatched group (Table 5).

Determinants of variability in response to resistance training

With respect to the changes in CMJ gains (%), the athletes from both studies ($n = 67$) were divided into tertiles: high responders (increase in CMJ from 7.4 to 19.4%; $n = 23$), moderate responders (increase

TABLE 3. Intergroup comparisons of CMJ increases (%) in response to high- or low-intensity training

Group	Increase in CMJ, %				P ₁
	Low-intensity RT	P ₂ (paired test)	High-intensity RT	P ₂ (paired test)	
Study 1					
All athletes (n = 28)	6.4 (5.8)	0.0009*	4.1 (8.1)	0.131	0.369
Athletes with P genotype (n = 11)	3.8 (5.0)	0.156	7.0 (6.7)	0.125	0.429
Athletes with E genotype (n = 17)	8.2 (5.9)	0.0078*	2.2 (8.8)	0.813	0.067
	P ₃ = 0.272		P ₃ = 0.353		
Study 2					
All athletes (n = 39)	4.6 (4.3)	0.0056*	5.0 (4.7)	<0.0001*	0.932
Athletes with P genotype (n = 17)	1.0 (4.6)	0.578	7.1 (5.9)	0.0059*	0.0046*
Athletes with E genotype (n = 22)	7.1 (1.0)	0.002*	3.2 (2.5)	0.0005*	0.0008*
	P ₃ = 0.0002*		P ₃ = 0.0056*		
Studies 1 and 2					
All athletes (n = 67)	5.4 (5.0)	<0.0001*	4.6 (6.1)	0.0002*	0.547
Athletes with P genotype (n = 28)	2.3 (4.8)	0.1465	7.1 (5.9)	0.0006*	0.0052*
Athletes with E genotype (n = 39)	7.6 (4.0)	<0.0001*	2.8 (5.7)	0.051	0.0012*
	P ₃ = 0.0022*		P ₃ = 0.0098*		

Note: *P < 0.05 - statistically different values between groups; P - power; E - endurance, RT - resistance training. P₁ - comparison between athletes with different training types (i.e. low-intensity vs. high-intensity); P₂ - significant increases in CMJ (paired test); P₃ - comparison between athletes with different genotype profiles (i.e. power genotype vs. endurance genotype) of the same training modality

TABLE 4. Intergroup comparisons of Aero3 increases (%) in response to high- or low-intensity training

Group	Increase in Aero3, %				P ₁
	Low-intensity RT	P ₂ (paired test)	High-intensity RT	P ₂ (paired test)	
Study 1					
All athletes (n = 28)	2.6 (3.1)	0.0103*	4.4 (4.4)	0.0017*	0.618
Athletes with P genotype (n = 11)	2.0 (4.3)	0.3125	6.0 (3.9)	0.0625	0.178
Athletes with E genotype (n = 17)	3.0 (2.2)	0.0078*	3.4 (4.6)	0.0391*	0.541
	P ₃ = 0.776		P ₃ = 0.284		
Study 2					
All athletes (n = 39)	5.8 (3.7)	<0.0001*	4.2 (3.3)	<0.0001*	0.218
Athletes with P genotype (n = 17)	1.7 (0.5)	0.0156*	6.8 (2.5)	0.002*	0.002*
Athletes with E genotype (n = 22)	8.7 (1.6)	0.002*	2.1 (2.3)	0.0161*	<0.0001*
	P ₃ = 0.0001*		P ₃ = 0.002*		
Studies 1 and 2					
All athletes (n = 67)	4.3 (3.8)	<0.0001*	4.3 (3.7)	<0.0001*	0.711
Athletes with P genotype (n = 28)	1.8 (2.8)	0.0171*	6.5 (2.9)	<0.0001*	0.0004*
Athletes with E genotype (n = 39)	6.0 (3.5)	<0.0001*	2.6 (3.3)	0.0004*	0.0013*
	P ₃ = 0.0004*		P ₃ = 0.0026*		

Note: *P < 0.05 - statistically different values between groups; P - power; E - endurance, RT - resistance training. P₁ - comparison between athletes with different training types (i.e. low-intensity vs. high-intensity); P₂ - significant increases in Aero3 (paired test); P₃ - comparison between athletes with different genotype profiles (i.e. power genotype vs. endurance genotype) of the same training modality

in CMJ from 2.7 to 7.2%; n = 22) and non- or low responders (increase in CMJ from -8.4 to 2.5%; n=22). There was a significant linear trend for the proportion of matched-trained athletes among the high responders (82.6%), moderate responders (50.0%) and non- or low responders (18.2%) ($\chi^2=18.7$, P < 0.0001). Similarly, when considering increases of Aero3 (%), we found a significant

linear trend for the proportion of matched-trained athletes among the high (increase in Aero3 from 6.0 to 13.2%; n = 22) responders (86.4%), moderate (increase in Aero3 from 2.0 to 5.9%; n = 23) responders (47.8%) and non- or low (increase in Aero3 from -6.1 to 1.9%; n = 22) responders (18.2%) ($\chi^2=20.5$, P < 0.0001). In other words, among non- or low responders to any type of resistance

TABLE 5. Comparisons of CMJ and Aero3 increases (%) in response to resistance training between matched and mismatched groups.

Study	Group				P ₃
	Matched athletes		Mismatched athletes		
Study 1	n =14	P ₁ (paired test)	n = 14	P ₂ (paired test)	
Change in CMJ, %	7.8 (5.9)	0.0005*	2.9 (7.2)	0.175	0.0596
Change in Aero3, %	4.0 (3.1)	0.0004*	2.8 (4.3)	0.0134*	0.2456
Study 2	n =20		n = 19		
Change in CMJ, %	7.1 (4.1)	<0.0001*	2.4 (3.5)	0.0053*	<0.0001*
Change in Aero3, %	7.7 (2.2)	<0.0001*	1.9 (1.8)	0.0004*	<0.0001*
Studies 1 and 2	n =34		n =33		
Change in CMJ, %	7.4 (4.9)	<0.0001*	2.6 (5.3)	0.0152*	<0.0001*
Change in Aero3, %	6.2 (3.2)	<0.0001*	2.3 (3.1)	<0.0001*	<0.0001*

Note: *P₁ and P₂ < 0.05 - significant increases in CMJ and Aero3 (paired test); *P₃ < 0.05 - significant difference between matched and mismatched groups. Matched athletes - high-intensity trained with endurance genotype or low-intensity trained with power genotype; mismatched athletes - high-intensity trained with power genotype or low-intensity trained with endurance genotype.

training, 82% of athletes (both for CMJ and Aero3) were from the mismatched group, while high responders were predominantly matched athletes (83% and 86% for CMJ and Aero3, respectively; $P < 0.0001$ for the comparison between non- or low responders and high responders). Accordingly, after 8 weeks of resistance training the odds of achieving more favorable outcomes in CMJ and Aero3 were 21 and 28.5 times, respectively, greater ($P < 0.0001$) for matched than mismatched genotype training (when first and third tertiles were compared).

DISCUSSION

To the best of our knowledge, this is the first study to examine the efficacy of using genetic profiling methods to target training of both power and endurance qualities of athletes. The results of our study demonstrated that all performance parameters increased significantly in response to 8-weeks of either low- or high-intensity resistance training without differences between the two training modalities, however, the magnitude of training effects was strongly related to the association between genetic profile and training modality. Our main finding is that matching individual genotype with the appropriate mode of training led to more substantial resistance training benefits, for both power and endurance matched participants. More specifically, in the first athletes from the matched group demonstrated significantly enhanced results in explosive power and aerobic fitness, while the gains realized by the mismatched athletes were of lesser magnitude. Importantly, these results were replicated in the second study, using a homogenous cohort of athletes.

There was also a positive correlation between power genotype score of athletes and performance changes in response to high-intensity training, as well as a positive correlation between endurance genotype score and increases in performance tests in response to low-intensity training: findings suggesting that the commonly observed heterogeneity in resistance training-induced explosive power and

aerobic fitness responses may be partly explained by genetic factors and selected training modalities. Another important finding was that among non- or low responders to resistance training, most athletes were from the mismatched group, while high responders were predominantly matched athletes. These results suggest personalized training prescription based on genetic profiling may help some individuals overcome unresponsiveness to resistance training.

Exercise training response is influenced by a multitude of determinants including genetics, environmental factors, measurement errors and others. Studies suggest that muscle strength and explosive power are under moderate to high genetic control with heritabilities ranging between 30 and 84% [17, 47]. Numerous studies reported the association between individual differences in strength/anaerobic power phenotypes in response to resistance/anaerobic power training and gene variations [16, 17]. Accordingly, several gene polymorphisms in our study were found to be individually linked with training responses. For instance, the II genotype of the *ACE* and XX (Ter/Ter) genotype of the *ACTN3* genes (known as endurance markers) were associated (or tended to correlate) with increases in aerobic fitness in response to low-intensity resistance training, while the *ACE* DD and *ACTN3* RR (Arg/Arg) genotypes (known as power/strength markers) carriers demonstrated greater improvement of performance parameters in response to high-intensity resistance training, which is consistent with previous findings [48-51].

The likely mechanism through which the polygenic profile (i.e. profile composed of 15 polymorphisms) of athletes was associated with training responses could be the link between genetic variations and skeletal muscle characteristics, such as muscle fibre composition. Of note, 5 of 15 gene polymorphisms (*ACE* I/D, *ACTN3* rs1815739 C/T, *PPARA* rs4253778 G/C, *PPARGC1A* rs8192678 G/A and *VEGFA* rs2010963 G/C) included in our panel, have recently been reported to be associated with muscle fibre type [18]. It is well known that slow-twitch muscle fibres better respond to low-intensity resis-

tance or aerobic (endurance) training, while fast-twitch muscle fibres are better suited for high-intensity (power and strength) training [8, 13, 15]. Consequently, elite endurance athletes have a remarkably high proportion of slow-twitch muscle fibres, whereas muscles of top sprinters and weightlifters predominantly consist of fast-twitch muscle fibres [15]. Interestingly, Sukhova *et al.* [52] have shown that speed skaters whose muscle fibre composition did not correspond to their distance specialty (*i.e.* speed skaters with increased proportion of slow-twitch muscle fibres who performed sprint training and speed skaters with predominantly fast-twitch muscle fibres who performed endurance training) had destructive alterations of their muscles (with possible negative effect on physical performance), indicating that individuals should train and select sports in accordance with their genetic potential. One might speculate that non- or low-responders to different training modalities in our study genetically were not suited for selected resistance training types. On the other hand, there are many more factors at the molecular, cellular, tissue and organ system levels that may determine individual responses to resistance training. For instance, Petrella *et al.* [53] have demonstrated that extreme responders (in terms of hypertrophy of muscle fibres) to a 16-week resistance training program showed a markedly higher activation of their satellite cells and greater myonuclei addition compared with moderate responders and non-responders.

Our study has some limitations, which have to be pointed out. Firstly, this was a relatively small study: only 28 athletes from Study 1 and 39 athletes from Study 2 completed the resistance training programs. However, the power calculation suggested that the sample size was sufficient to adequately fulfill the study's main objective. Secondly, the sample was taken from a wide range of sporting disciplines, all of which were commonly exposed to different forms and levels of training and competition stresses: a factor which could conceivably influence training responses. Furthermore, the low number of weekly training sessions, which were by necessity completed in tandem with sport-specific training, may well have confounded the experimental manipulation. However, athletes from Study 2 were all soccer players and thus represented the homogeneous group with more significant results. Further studies involving untrained (*unfit*) subjects and strength athletes with more carefully controlled total training loads are warranted. Third, the subjects of our studies performed a short-term, nonperiodized resistance training. It has been shown that systematically varying volume and intensity (*i.e.* periodized training) is most effective for long-term progression compared with programs with the stable training variables [3]. Therefore, although we have shown that genetically matched nonperiodized training was

effective during resistance training program, one might speculate that even in this case the manipulation of training variables is necessary for long-term resistance training progression. Fourth, the results of our study may be applicable only for specific training goals, such as improvement of explosive power and aerobic performance with one of two different modalities. Although loads of < 45% of 1 RM (*i.e.*, performed with very high repetitions) may increase strength in untrained individuals [54], whereas trained weightlifters appear responsive only to heavier loading [55]. Further research analyzing genetic determinants of improvement of absolute strength and skeletal muscle hypertrophy is needed. Finally, in our study we have used a validated panel of a limited number ($n=15$) of gene polymorphisms associated with power/strength, endurance and other muscle-specific traits, which could explain only 14-32% of the variation in *physiological parameters* of athletes in our study. Undoubtedly there are likely to be many more genetic variants associated with responses to different modalities of resistance training that remain to be identified. Therefore, it is logical to conclude that the picture we see in the future may become clearer as more genetic markers are included in the panel.

CONCLUSIONS

In conclusion, our results suggest that using genetic profiling to better match individual genotype with appropriate training modality may be a powerful tool to aid more personalized, and precise, resistance training prescription in the future.

Acknowledgements

The authors would like to acknowledge the University of Manchester's Sport Department and Athletic Union as well as the Portsmouth College for the allowing their students/athletes the chance to volunteer as participants in the study. Also thanks must go to all the coaches of DNA Sports Performance Ltd and Suraci Consultancy who took part in data collection and training for the participants. DNAFit™ supported this original research by providing all genetic testing. Finally the authors would also like to acknowledge the hard work and effort of the participants in this study, who without their hours and hours of testing and training these results would have remained hidden from the world.

Conflict of interests: the authors declared no conflict of interests regarding the publication of this manuscript.

REFERENCES

1. American College of Sports Medicine. American College of Sports Medicine position stand. Progression models in resistance training for healthy adults. *Med Sci Sports Exerc.* 2009;41(3):687-708.
2. Vikmoen O, Ellefsen S, Trøen Ø, Hollan I, Hanestadhaugen M, Raastad T, Rønnestad BR. Strength training improves cycling performance, fractional utilization of VO₂ max and cycling economy in female cyclists. *Scand J Med Sci Sports.* 2015 Apr 18. doi: 10.1111/sms.12468.
3. Kraemer WJ, Ratamess NA. Fundamentals of resistance training: progression and exercise prescription. *Med Sci Sports Exerc.* 2004;36(4):674-688.
4. McGlory C, Phillips SM. Exercise and the Regulation of Skeletal Muscle

- Hypertrophy. *Prog Mol Biol Transl Sci.* 2015;135:153-173.
5. Campos GE, Luecke TJ, Wendeln HK, Toma K, Hagerman FC, Murray TF, Ragg KE, Ratamess NA, Kraemer WJ, Staron RS. Muscular adaptations in response to three different resistance-training regimens: specificity of repetition maximum training zones. *Eur J Appl Physiol.* 2002;88(1-2):50-60.
 6. Wilson GJ, Newton RU, Murphy AJ, Humphries BJ. The optimal training load for the development of dynamic athletic performance. *Med Sci Sports Exerc.* 1993;25(11):1279-1286.
 7. McBride JM, Triplett-McBride T, Davie A, Newton RU. The effect of heavy- vs. light-load jump squats on the development of strength, power, and speed. *J Strength Cond Res.* 2002;16(1):75-82.
 8. Ntetreba AI, Popov DV, Liubaeva EV, Bravyi IaR, Prostova AB, Lemesheva IuS, Vinogradova OL. Physiological effects of using the low intensity strength training without relaxation in single-joint and multi-joint movements. *Ross Fiziol Zh Im I M Sechenova.* 2007;93(1):27-38.
 9. Mitchell CJ, Churchward-Venne TA, West DW, Burd NA, Breen L, Baker SK, Phillips SM. Resistance exercise load does not determine training-mediated hypertrophic gains in young men. *J Appl Physiol (1985).* 2012;113(1):71-77.
 10. Fry AC. The role of resistance exercise intensity on muscle fibre adaptations. *Sports Med.* 2004;34(10):663-679.
 11. Kosek DJ, Kim JS, Petrella JK, Cross JM, Bamman MM. Efficacy of 3 days/wk resistance training on myofiber hypertrophy and myogenic mechanisms in young vs. older adults. *J Appl Physiol (1985).* 2006;101(2):531-544.
 12. Hubal MJ, Gordish-Dressman H, Thompson PD, Price TB, Hoffman EP, Angelopoulos TJ, Gordon PM, Moyna NM, Pescatello LS, Visich PS, Zoeller RF, Seip RL, Clarkson PM. Variability in muscle size and strength gain after unilateral resistance training. *Med Sci Sports Exerc.* 2005;37(6):964-972.
 13. Pipes TV. Strength training and fiber types. *Scholastic Coach.* 1994;63:67-70.
 14. Simoneau J-A, Bouchard C. Genetic determinism of fiber type proportion in human skeletal muscle. *FASEB J.* 1995;9:1091-1095.
 15. Andersen JL, Schjerling P, Saltin B. Muscle, genes, and athletic performance. *Sci Am.* 2000;283(3):48-55.
 16. Bray MS, Hagberg JM, Pérusse L, Rankinen T, Roth SM, Wolfarth B, Bouchard C. The human gene map for performance and health-related fitness phenotypes: the 2006-2007 update. *Med Sci Sports Exerc.* 2009;41(1):35-73.
 17. Hughes DC, Day SH, Ahmetov II, Williams AG. Genetics of muscle strength and power: polygenic profile similarity limits skeletal muscle performance. *J Sports Sci.* 2011;29(13):1425-34.
 18. Ahmetov II, Vinogradova OL, Williams AG. Gene polymorphisms and fiber-type composition of human skeletal muscle. *Int J Sport Nutr Exerc Metab.* 2012;22(4):292-303.
 19. Ahmetov II, Fedotovskaya ON. Current Progress in Sports Genomics. *Adv Clin Chem.* 2015;70:247-314.
 20. Ma F, Yang Y, Li X, Zhou F, Gao C, Li M, Gao L. The association of sport performance with ACE and ACTN3 genetic polymorphisms: a systematic review and meta-analysis. *PLoS One.* 2013;8(1):e54685.
 21. Wang G, Mikami E, Chiu LL, DE Perini A, Deason M, Fuku N, Miyachi M, Kaneoka K, Murakami H, Tanaka M, Hsieh LL, Hsieh SS, Caporossi D, Pigozzi F, Hillel A, Lee R, Galloway SD, Gulbin J, Rogozkin VA, Ahmetov II, Yang N, North KN, Ploutarhos S, Montgomery HE, Bailey ME, Pitsiladis YP. Association analysis of ACE and ACTN3 in elite Caucasian and East Asian swimmers. *Med Sci Sports Exerc.* 2013;45(5):892-900.
 22. Yang N, Arthur DG, Gulbin JP, Hahn AG, Beggs AH, Eastale S, North K. ACTN3 genotype is associated with human elite athletic performance. *Am J Hum Genet.* 2003;73(3):627-631.
 23. Wolfarth B, Rankinen T, Mühlbauer S, Scherr J, Boulay MR, Pérusse L, Rauramaa R, Bouchard C. Association between a beta2-adrenergic receptor polymorphism and elite endurance performance. *Metabolism.* 2007;56(12):1649-1651.
 24. Tsianos GI, Evangelou E, Boot A, Zillikens MC, van Meurs JB, Uitterlinden AG, Ioannidis JP. Associations of polymorphisms of eight muscle- or metabolism-related genes with performance in Mount Olympus marathon runners. *J Appl Physiol (1985).* 2010;108(3):567-574.
 25. McCole SD, Shuldiner AR, Brown MD, Moore GE, Ferrell RE, Wilund KR, Huberty A, Douglass LW, Hagberg JM. Beta2- and beta3-adrenergic receptor polymorphisms and exercise hemodynamics in postmenopausal women. *J Appl Physiol (1985).* 2004;96(2):526-530.
 26. Gomez-Gallego F, Santiago C, González-Freire M, Yvert T, Muniesa CA, Serratos L, Altmäe S, Ruiz JR, Lucia A. The C allele of the AGT Met235Thr polymorphism is associated with power sports performance. *Appl Physiol Nutr Metab.* 2009;34(6):1108-1111.
 27. Zarębska A, Sawczyn S, Kaczmarczyk M, Ficek K, Maciejewska-Karlowska A, Sawczuk M, Leońska-Duniec A, Eider J, Grenda A, Cięszczyk P. Association of rs699 (M235T) polymorphism in the AGT gene with power but not endurance athlete status. *J Strength Cond Res.* 2013;27(10):2898-2903.
 28. Posthumus M, SchwelInus MP, Collins M. The COL5A1 gene: a novel marker of endurance running performance. *Med Sci Sports Exerc.* 2011;43(4):584-589.
 29. Brown JC, Miller CJ, Posthumus M, SchwelInus MP, Collins M. The COL5A1 gene, ultra-marathon running performance, and range of motion. *Int J Sports Physiol Perform.* 2011;6(4):485-496.
 30. Obisesan TO, Leeuwenburgh C, Phillips T, Ferrell RE, Phares DA, Prior SJ, Hagberg JM. C-reactive protein genotypes affect baseline, but not exercise training-induced changes, in C-reactive protein levels. *Arterioscler Thromb Vasc Biol.* 2004;24(10):1874-1879.
 31. Kuo HK, Yen CJ, Chen JH, Yu YH, Bean JF. Association of cardiorespiratory fitness and levels of C-reactive protein: data from the National Health and Nutrition Examination Survey 1999-2002. *Int J Cardiol.* 2007;114(1):28-33.
 32. He Z, Hu Y, Feng L, Lu Y, Liu G, Xi Y, Wen L, McNaughton LR. NRF2 genotype improves endurance capacity in response to training. *Int J Sports Med.* 2007;28(9):717-721.
 33. Eynon N, Sagiv M, Meckel Y, Duarte JA, Alves AJ, Yamin C, Sagiv M, Goldhammer E, Oliveira J. NRF2 intron 3 A/G polymorphism is associated with endurance athletes' status. *J Appl Physiol (1985).* 2009;107(1):76-79.
 34. Ruiz JR, Buxens A, Artieda M, Arteta D, Santiago C, Rodríguez-Romo G, Lao JI, Gómez-Gallego F, Lucia A. The -174 G/C polymorphism of the IL6 gene is associated with elite power performance. *J Sci Med Sport.* 2010;13(5):549-553.
 35. Eider J, Cieszczyk P, Leońska-Duniec A, Maciejewska A, Sawczuk M, Ficek K, Kotarska K. Association of the 174 G/C polymorphism of the IL6 gene in Polish power-orientated athletes. *J Sports Med Phys Fitness.* 2013;53(1):88-92.
 36. Ahmetov II, Gavrilov DN, Astratenkova IV, Druzhevskaya AM, Malinin AV, Romanova EE, Rogozkin VA. The association of ACE, ACTN3 and PPARA gene variants with strength phenotypes in middle school-age children. *J Physiol Sci.* 2013;63(1):79-85.
 37. Lopez-Leon S, Tuvblad C, Forero DA. Sports genetics: the PPARA gene and athletes' high ability in endurance sports. A systematic review and meta-analysis. *Biol Sport.* 2016;33:3-6.
 38. Lucia A, Gómez-Gallego F, Barroso I, Rabadán M, Bandrés F, San Juan AF, Chicharro JL, Ekelund U, Brage S, Earnest CP, Wareham NJ, Franks PW. PPARGC1A genotype (Gly482Ser) predicts exceptional endurance capacity

- in European men. *J Appl Physiol* (1985). 2005;99(1):344-348.
39. Maciejewska A, Sawczuk M, Cieszczyk P, Mozhayskaya IA, Ahmetov II. The PPARGC1A gene Gly482Ser in Polish and Russian athletes. *J Sports Sci*. 2012;30(1):101-113.
 40. Liu XG, Tan LJ, Lei SF, Liu YJ, Shen H, Wang L, Yan H, Guo YF, Xiong DH, Chen XD, Pan F, Yang TL, Zhang YP, Guo Y, Tang NL, Zhu XZ, Deng HY, Levy S, Recker RR, Papasian CJ, Deng HW. Genome-wide association and replication studies identified TRHR as an important gene for lean body mass. *Am J Hum Genet*. 2009;84(3):418-423.
 41. Wang P, Ma LH, Wang HY, Zhang W, Tian Q, Cao DN, Zheng GX, Sun YL. Association between polymorphisms of vitamin D receptor gene Apal, Bsm1 and TaqI and muscular strength in young Chinese women. *Int J Sports Med*. 2006;27(3):182-186.
 42. Windelinckx A, De Mars G, Beunen G, Aerssens J, Delecluse C, Lefevre J, Thomis MA. Polymorphisms in the vitamin D receptor gene are associated with muscle strength in men and women. *Osteoporos Int*. 2007;18(9):1235-1242.
 43. Prior SJ, Hagberg JM, Paton CM, Douglass LW, Brown MD, McLenithan JC, Roth SM. DNA sequence variation in the promoter region of the VEGF gene impacts VEGF gene expression and maximal oxygen consumption. *Am J Physiol Heart Circ Physiol*. 2006;290(5):1848-1855.
 44. Ahmetov II, Khakimullina AM, Popov DV, Missina SS, Vinogradova OL, Rogozkin VA. Polymorphism of the vascular endothelial growth factor gene (VEGF) and aerobic performance in athletes. *Hum Physiol*. 2008;34:477-481.
 45. Batterham AM, Hopkins WG. A decision tree for controlled trails. *Sportsci*. 2005;9:33-39.
 46. Egorova ES, Borisova AV, Mustafina LJ, Arkhipova AA, Gabbasov RT, Druzhevskaya AM, Astratenkova IV, Ahmetov II. The polygenic profile of Russian football players. *J Sports Sci*. 2014;32(13):1286-93.
 47. Calvo M, Rodas G, Vallejo M, Estruch A, Arcas A, Javierre C, Viscor G, Ventura JL. Heritability of explosive power and anaerobic capacity in humans. *Eur J Appl Physiol*. 2002;86(3):218-225.
 48. Montgomery HE, Marshall R, Hemingway H, Myerson S, Clarkson P, Dollery C, Hayward M, Holliman DE, Jubb M, World M, Thomas EL, Brynes AE, Saeed N, Barnard M, Bell JD, Prasad K, Rayson M, Talmud PJ, Humphries SE. Human gene for physical performance. *Nature*. 1998;393(6682):221-222.
 49. Folland J, Leach B, Little T, Hawker K, Myerson S, Montgomery H, Jones D. Angiotensin-converting enzyme genotype affects the response of human skeletal muscle to functional overload. *Exp Physiol*. 2000;85:575-579.
 50. Pescatello LS, Kostek MA, Gordish-Dressman H, Thompson PD, Seip RL, Price TB, Angelopoulos TJ, Clarkson PM, Gordon PM, Moyna NM, Visich PS, Zoeller RF, Devaney JM, Hoffman EP. ACE ID genotype and the muscle strength and size response to unilateral resistance training. *Med Sci Sports Exerc*. 2006;38(6):1074-1081.
 51. Pereira A, Costa AM, Izquierdo M, Silva AJ, Bastos E, Marques MC. ACE I/D and ACTN3 R/X polymorphisms as potential factors in modulating exercise-related phenotypes in older women in response to a muscle power training stimuli. *Age (Dordr)*. 2013;35(5):1949-1959.
 52. Sukhova ZI, Ivanitskaia VV, Makarova LF, Poluéktova BP, Iazvikov VV. Features of the ultrastructural organization of the muscles of skaters in relation to their sport specialization and muscle fiber composition. *Arkh Anat Gistol Embriol*. 1985;89(12):87-90.
 53. Petrella JK, Kim JS, Mayhew DL, Cross JM, Bamman MM. Potent myofiber hypertrophy during resistance training in humans is associated with satellite cell-mediated myonuclear addition: a cluster analysis. *J Appl Physiol* (1985). 2008;104(6):1736-42.
 54. Stone WJ, Coulter SP. Strength/endurance effects from three resistance training protocols with women. *J Strength Cond Res*. 1994;8:231-234.
 55. Häkkinen K, Komi PV, Alén M, Kauhanen H. EMG, muscle fibre and force production characteristics during a 1 year training period in elite weightlifters. *Eur J Appl Physiol Occup Physiol*. 1987;56(4):419-27.

