**Effective utilization of genetic information for athletes and coaches: focus on ACTN3 R577X polymorphism**

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**INTRODUCTION**

Physical resistance and endurance training have beneficial effect on fitness and athletic performance for the general population and athletes [1,2]. Resistance and endurance training variants such as type, intensity, and duration of exercise can be selected according to individual aims and fitness assessment. Recently, various resistance and endurance training methods have been used for muscle hypertrophy and VO2max improvement. However, genetic factors such as polymorphisms have not been considered for athletic- and fitness-related candidate genes.

Genetic variation may contribute to inter-individual differences in athletic performance and fitness assessments. Recent reviews have noted that variants of more than 200 genes are associated with fitness-related phenotypes [3]. There is an association between genetic polymorphism and athletic performance [4]. One of the most potent athletic performance-related genotypes is α-actinin-3 (ACTN3) R577X. It is associated with muscle fiber composition [5], muscle strength [6], structural factor in type II fibers [7], and elite performance [8-10]. Factors such as muscle composition and muscle tension can affect the response to resistance training with regard to muscle hypertrophy and the development of strength and power. The purpose of this review is to summarize current knowledge on training protocols for muscle hypertrophy and VO2max improvement, genetic polymorphism (especially the ACTN3 R577X genotype), and fitness phenotypes in athletes and the general population so that we can provide a proposal for effective utilization of genetic information to improve physical training. Effective utilization of genetic information may provide a suitable response of high and low responders to physical training (Fig. 1). Characteristics of ACTN3 R577X are summarized in Table 1. These characteristics based on recent primary findings are discussed in details.

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**Training protocols for muscle hypertrophy and VO2max improvement**

Current guidelines for resistance training state that loads of ≥ 65% one-repetition maximum (1RM) are necessary to elicit favorable increases in hypertrophy. Higher loads are
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Table 1. Characteristics of individuals with different ACTN3 R577X genotypes

| Characteristic                      | RR genotype | RX genotype | XX genotype | References |
|-----------------------------------|-------------|-------------|-------------|------------|
| Athletic status                   |             |             |             |            |
| Sprint/power status               | High frequency | High frequency | Unknown | [10,24,28,29,33,45-53] |
| Endurance status                  | Unknown     | Unknown     | High frequency | (Limited evidence) | [10,34,49,51,54-56] |
| Mixed events                      | Unknown     | Unknown     | Unknown | [57] |
| Physiological phenotype           |             |             |             |            |
| Strength                           | High        | High or Moderate | Low | [6,35,58-61] |
| Power                             | High        | High or Moderate | Low | [38,44,62-66] |
| Aerobic performance               | Unknown     | Unknown     | High (Limited evidence in humans) | [60,67,68] |
| Muscle mass                       | High        | High        | Low         | [36,69] |
| Muscle composition (Type IIx)     | High        | -           | Low         | [5,58,70] |
| Muscle damage (CK) after eccentric exercise | Low | Low | High | [39,71,72] |
| Muscle stiffness                   | High        | Moderate    | Low         | [73] |
| Sex hormone (testosterone) after resistance training | High | High | Low | [74] |
| Strength training response         | High (Limited evidence) | High (Limited evidence) | Low (Limited evidence) | [43,68,75-77] |

needed to maximize the strength [1,11]. It has been postulated that heavy loading is required to fully recruit higher-threshold motor units [11]. These data suggest that strength and hypertrophy can be optimized via complete motor unit activation using heavy loads. However, a recent study has suggested that low-intensity exercise such as 30-40% 1RM can induce a similar level of muscle hypertrophy as high-intensity resistance training [12-14]. Mitchell et al. [12] have demonstrated an effect of resistance training with low loads (30% 1RM) and high repetitions on muscle hypertrophy. They examined subjects who performed 10 weeks of unilateral knee extension resistance training. Each leg was randomly assigned in a counterbalanced fashion to one of three possible unilateral training conditions: 1) one set of knee extensions performed until voluntary failure at 80% of 1RM, 2) three sets of knee extensions performed to the point of fatigue at 80% of 1RM, and 3) three sets performed to the point of fatigue at 30% of 1RM. Similar results were observed between the 3 sets at 80% 1RM group and the 3 sets at 30% 1RM group with respect to muscle hypertrophy. However, improvement in the one set and 3 sets groups at 80% 1RM was higher than that in the 3 sets at 30% 1RM group after training. Schoenfeld et al. [13] have examined the effect of low-load and high-load training on muscle strength and hypertrophy in well-trained men. They divided subjects into two groups: a low-load training group (n = 9) and a high-load training group (n = 9). They found that low-load training was an effective method to increase muscle hypertrophy in the extremities of well-trained men. These results suggested that there is a different optimal load and method for obtaining muscle hypertrophy.
between high-load (70-85% 1RM) and low-load (30-40% 1RM) resistance training.

VO\textsubscript{2max} is an important factor in endurance performance. Successful athletic training involves the manipulation of training intensity, duration, and frequency to maximize the performance and related physiological characteristics. Endurance athletes normally use a high-volume low-intensity training approach incorporated with moderate volumes of high-intensity training. Recently, Gibala and Jones [15] have reported that high-intensity interval training (HIT) can enhance aerobic capacity and muscle endurance performance similar to traditional endurance training with a markedly lower exercise volume and training-time commitment. These studies demonstrated significant improvements in peak oxygen uptake at a substantially reduced training volume. In fact, the weekly training volume for sprint interval training was ~90% lower than that in the continuous endurance training group (i.e., 225 vs. 2,250 kJ) [16]. From an athletic viewpoint, HIT is also an effective strategy to improve endurance performance when used as a supplement to high training volumes in well-trained athletes normally use a high-volume low-intensity training approach incorporated with moderate volumes of high-intensity training. Recently, Gibala and Jones [15] have reported that high-intensity interval training (HIT) can enhance aerobic capacity and muscle endurance performance similar to traditional endurance training with a markedly lower total training volume. In fact, the weekly exercise volume and training-time commitment. These studies demonstrated significant improvements in peak oxygen uptake at a substantially reduced training volume. In fact, the weekly training volume for sprint interval training was ~90% lower than that in the continuous endurance training group (i.e., 225 vs. 2,250 kJ) [16]. From an athletic viewpoint, HIT is also an effective strategy to improve endurance performance when used as a supplement to high training volumes in well-trained endurance athletes [17]. The observed increase in VO\textsubscript{2max} after HIT with low-volume training is similar to that observed in subjects who perform traditional low-intensity high-volume endurance training [15,16].

These previous studies suggest novel training protocols can vary depending on parameters such as intensity, repetition, and duration. They can differ dramatically from traditional training protocols. Previous studies considering twins and families have suggested that genetic factors can affect the trainability and training responses [18,19]. In a well-known family study, Bouchard et al. [19] estimated that the heritability of VO\textsubscript{2max} training response was 47% (Health, Risk Factors, Exercise Training, and Genetics; HERITAGE). However, athletes and coaches do not consider genetic factors such as polymorphisms in athletic- and fitness-related candidate loci in the development of training programs. We will discuss one of the most extensively studied genetic polymorphisms associated with these phenotypes, ACTN3 R577X, in the next section. Potential genotype-based training protocols are also proposed.

**Effect of ACTN3 R577X polymorphism on athletic performance and muscle phenotypes**

ACTNs (actin binding proteins) are major structural components of Z-line in skeletal muscles [20]. Two ACTN isoforms (ACTN2 and ACTN3) encoded by ACTN2 and ACTN3 are expressed in human skeletal muscles [21,22]. ACTN3 is expressed only in fast-twitch skeletal muscle fibers [22]. It is important for anchoring actin. It also plays a regulatory role in the coordination of muscle fiber contraction [23]. ACTN3 is absent in approximately 18% of the European population and 25-29% of the Japanese population. These individuals are homozygous for an allele encoding a premature stop codon at R577X (rs1815739, C-to-T transition at nucleotide position 1729 in the ACTN3 open reading frame) [22,24]. The ACTN3 577XX genotype associated with a complete deficiency of α-actinin-3 occurs in approximately 1.5 billion people worldwide. The ACTN3 XX genotype (complete α-actinin-3 deficiency) is not associated with any disease phenotype possibly due to compensatory upregulation of its closely related isoform α-actinin-2. At amino acid level, human α-actinin-2 and α-actinin-3 are 80% and 90% similar to ACTN3, respectively [21]. The specialized expression pattern and strong sequence conservation of α-actinin-3 over 300 million years suggests that it plays a specific role in fast-twitch skeletal muscle fibers [21,25].

In the first study on ACTN3 R577X genotype, Yang et al. [10] have suggested that RR and RX genotypes are associated with sprint/power performance while the XX genotype is associated with endurance performance in Australian athletes. Interestingly, the XX genotype was not observed in elite sprint/power athletes who participated in the Olympic Games [10]. The ACTN3 R allele and RR genotype are associated with top-level power-oriented athletic performance in a broad variety of ethnic groups [26-30]. In a meta-analysis, Alfred et al. [31] have reported that the ACTN3 RR genotype is more common among European sprint/power athletes than in non-athletes. Another meta-analysis [32] also revealed a positive association between ACTN3 RR and RX genotypes and sprint/power athletic status in Europeans but not in Asians or Africans. Recently, a few studies have evaluated the association between the ACTN3 R577X genotype and athletic status in Asian athletes such as wrestlers, track athletes, and field athletes [24,33]. In our recent study [30], the frequency of RR and RX genotypes was positively associated with the level of athletic status (i.e., regional < national < international) for sprint/power track and field athletes and wrestlers. However, we did not detect carriers of the XX genotype in a sample of Olympic wrestlers [30], similar to the results of Yang et al. [10]. In replication studies considering independent cohorts of elite endurance athletes, the X allele and the ACTN3 XX genotype were associated with elite endurance performance in some studies, but not all studies [34]. Although it has been reported that the ACTN3 RR genotype is associated with endurance performance [34], the role of ACTN3 R577X genotype in endurance performance remains unclear.
The relationship between the *ACTN3* R577X genotype and muscular phenotypes in the general population and in athletes belonging to several ethnic groups has been examined extensively [35-38]. Previous studies have suggested that the XX genotype is associated with smaller thigh-muscle cross-sectional area and lower muscle function than the RR or RX genotype in adult Japanese population [35,36]. In addition, individuals with the *ACTN3* XX genotype (complete ACTN3 deficiency) have higher creatine kinase activities after eccentric training than individuals with the *ACTN3* RR genotype [5]. Soccer players with the XX genotype also exhibited higher creatine kinase activities and higher levels of α-actin and cortisol than those with the RR genotype [39]. The possible mechanisms underlying the association between ACTN3 and structural advantage in type II fibers have been discussed in details [7]. The proportional surface area and number of type IIX fibers are greater in subjects with the RR and RX genotypes than in those with the XX genotype [5]. In addition, muscles of Actn3-knockout mice have reduced force generation associated with response to muscle disuse [6,40,41]. Therefore, *ACTN3* R577X genotype affects structural factors of type II fibers.

Previously, we have found that athletes with the *ACTN3* RR or RX genotype have higher peak power in the 30-s Wingate anaerobic performance test (WAnT) than those with the XX genotype [44]. We also found that 4.6% of variability in the relative peak power in WAnT among male Japanese athletes was due to the *ACTN3* R577X genotype [44]. Massidda et al. [42] have reported that the *ACTN3* R577X genotype accounts for 8.0% of the variation in squat-jump performance of elite soccer players. In the general population, the *ACTN3* R577X polymorphism is responsible for 1-2% of the variation in muscle strength [37,43]. These results suggest that the *ACTN3* R577X genotype has an apparent contributing role in competitive athletes, particularly elite athletes compared to that in the general population.

There are conflicting results regarding the association between the *ACTN3* R577X genotype and sex differences in muscle phenotypes, e.g., muscle strength and power [35,37,44]. Yang et al. [10] have reported that the *ACTN3* XX genotype is associated with endurance performance only in female athletes. We detected a positive relationship between the *ACTN3* R577X genotype and relative peak power in WAnT of Japanese male athletes but not in female athletes [44]. However, another study showed that the absence of ACTN3 negatively influenced peak isokinetic torque during knee extension in middle-aged women but not in middle-aged men [37]. We can only speculate on possible reasons responsible for the conflicting results between male and female subjects in these *ACTN3* R577X genotype studies. Sex hormones are associated with muscle volume and stiffness. For example, estrogen may affect results. In addition, absolute muscle mass and fiber type distribution may be associated with differences in muscle phenotypes between *ACTN3* genotypes. Future studies are necessary to determine the sex-dependent effect of *ACTN3* R577X genotype on muscle phenotypes.

**Proposal for effective utilization of ACTN3 R577X polymorphism for physical training**

**Strength training**

In resistance training for hypertrophy, we propose that individuals with *ACTN3* RR or RX genotypes who have relatively high strength and power should choose high-load, low-repetition resistance training. In contrast, individuals with the XX genotype of *ACTN3* should prefer a low load with high repetitions. Our proposal for genotype-based training protocols is based on the observation that the *ACTN3* R577X genotype affects structural factors in type II fibers and muscle strength as well as power output [35-38]. Individuals with the RR genotype have increased muscle strength and higher tolerance for muscle damage. However, previous studies on the *ACTN3* R577X genotype used resistance training with a relatively high load (e.g., 10RM or 70-75% 1RM). Therefore, it is necessary to investigate the association between the *ACTN3* R577X genotype and training response using various training types such as low-load resistance and short intervals to obtain useful genotype-based training protocols.

**Endurance training**

In endurance training to improve VO2max, we propose that individuals with the RR or RX genotypes of *ACTN3* should choose HIT. Individuals with the RR and RX genotypes of *ACTN3* R577X polymorphism are more resistant to muscle damage resulting from high-intensity training than athletes with the XX genotype [39]. In addition, there is a positive relationship between *ACTN3* RR or RX genotype and the relative peak power in the Wingate test for Japanese athletes [44]. MacArthur et al. [6] have reported that Actn3-knockout mice (animal model of α-actinin-3 deficiency) have skeletal muscle with higher oxidative capacity than the skeletal muscle of the wild-type mice. In addition, Actn3-knockout mice are able to run 33% farther than wild-type mice in a treadmill endurance test. Individuals with the XX genotype are completely deficient in the α-actinin-3 protein. They will exhibit inferior skeletal muscle function in terms of force generation from contraction and poor ability to recover from high-intensity intermittent exercise. Therefore, individuals
with the ACTN3 XX genotype will have higher oxidative capacity. They should choose the traditional endurance training, i.e., low intensity and high volume. However, the role of the ACTN3 XX genotype in endurance capability remains unclear. It is necessary to investigate the association between the ACTN3 R577X genotype and endurance capability or training response using various training types to determine useful genotype-based training protocols.

**Concluding remarks and future studies**

This review examined the evidence regarding the effect of ACTN3 R577X genotype on athletic performance and muscle phenotypes. We provided a proposal for effective utilization of ACTN3 R577X polymorphism for physical training. Many previous studies have reported that the ACTN3 R577X genotype is associated with athletic performance, especially with sprint/power athletic performance and muscle phenotypes in several ethnic populations. Individuals with the ACTN3 RR or RX genotypes have higher muscle strength and power as well as stronger structural factors in type II fibers than individuals with the ACTN3 XX genotype. Other novel or known genetic variants require additional testing in multiple cohorts, similar to studies on ACTN3 R577X genotype.

As described above, most case-control studies of athletic performance compared the frequency of genetic polymorphisms between athletes and controls. This method using definitions of sporting performance based on Olympic or world championship appearances or various event types (e.g., sprints/power events, endurance events, mixed-type events, etc.) is utilized by researchers worldwide to identify genes associated with sporting performance. Recently, genome-wide association studies have enabled exhaustive searches for genes related to athletic phenotypes. However, these searches have not yielded a narrow list of candidate genes. It is important to carry out studies on the effect of genes and a range of environmental factors on sporting performance. This may clarify the effect of genes on sporting performance and the effectiveness of training.

The ACTN3 R577X polymorphism is the only genetic factor that is conclusively related to sports performance and muscle phenotypes. Individuals with the ACTN3 XX genotype are completely lack of α-actinin-3. Follow up research utilizing an Actn3-knockout mouse model to mimic individuals with the XX genotype may provide additional mechanistic insight into the development of phenotypes associated with the loss of α-actinin-3. These genetic factors might predict various aspects of response to training, thus providing useful information for athletes and their coaches.

**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;41:687-708.
[2] Garber CE, Blissmer B, Deschenes MR, Franklin BA, Lamonte MJ, Lee IM, Nieman DC, Swain DP. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Med Sci Sports Exerc. 2011;43:1334-59.
[3] Bray MS, Hagberg JM, Perusse 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;41:35-73.
[4] Ahmetov II, Fedotovskaya ON. Current progress in sports genomics. Adv Clin Chem. 2015;70:247-314.
[5] Vincent B, De Bock K, Ramaekers M, Van den Eede E, Van Leemputte M, Hespel P, Thomis MA. ACTN3 (R577X) genotype is associated with fiber type distribution. Physiol Genomics. 2007;32:58-63.
[6] MacArthur DG, Seto JT, Chan S, Quinlan KG, Raftery JM, Turner N, Nicholson MD, Kee AJ, Hardeman EC, Gunning PW, Cooney GJ, Head SI, Yang N, North KN. An Actn3 knockout mouse provides mechanistic insights into the association between alpha-actinin-3 deficiency and human athletic performance. Hum Mol Genet. 2008;17:1076-86.
[7] Norman B, Esbjornsson M, Rundqvist H, Osterlund T, von Walden F, Tesch PA. Strength, power, fiber types, and mRNA expression in trained men and women with different ACTN3 R577X genotypes. J Appl Physiol. 2009;106:959-65.
[8] Gomez-Gallego F, Santiago C, Gonzalez-Freire M, Muniesa CA, Fernandez Del Valle M, Perez M, Foster C, Lucia A. Endurance performance: genes or gene combinations? Int J Sports Med. 2009;30:66-72.
[9] Juffer P, Furrer R, Gonzalez-Freire M, Santiago C, Verde Z, Serratosa L, Morate FJ, Rubio JC, Martin MA, Ruiz JR, Arena J, Gomez-Gallego F, Lucia A. Genotype distributions in top-level soccer players: a role for ACE? Int J Sports Med. 2009;30(5):387-92.
[10] Yang N, MacArthur DG, Gulbin JP, Hahn AG, Beggs AH, Eastal S, North K. ACTN3 genotype is associated with human elite athletic performance. American journal of human genetics. 2003;73:627-31.
Optimizing exercise based on ACTN3 polymorphism

[11] Kraemer WJ, Ratamess NA. Fundamentals of resistance training: progression and exercise prescription. Med Sci Sports Exerc. 2004;36:674-88.

[12] 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. 2012;113:71-7.

[13] Schoenfeld BJ, Peterson MD, Ogbonn D, Contreras B, Sonmez GT. Effects of low- versus high-load resistance training on muscle strength and hypertrophy in well-trained men. J Strength Cond Res. 2015, in press.

[14] Schoenfeld BJ. Is there a minimum intensity threshold for resistance training-induced hypertrophic adaptations? Sports Med. 2013;43:1279-88.

[15] Gibala MJ, Jones AM. Physiological and performance adaptations to high-intensity interval training. Nestle Nutr Inst Workshop Ser. 2013;76:51-60.

[16] Burgomaster KA, Howarth KR, Phillips SM, Rakobowchuk M, Macdonald MJ, McGee SL, Gibala MJ. Similar metabolic adaptations during exercise after low volume sprint interval and traditional endurance training in humans. J Physiol. 2008;586:151-60.

[17] Laursen PB, Jenkins DG. The scientific basis for high-intensity interval training: optimising training programmes and maximising performance in highly trained endurance athletes. Sports Med. 2002;32:53-73.

[18] Bouchard C. Genomic predictors of trainability. Exp Physiol. 2012;97:347-52.

[19] Bouchard C, An P, Rice T, Skinner JS, Wilmore JH, Perusse L, Leon AS, Martin RM, Moran CN, Sayer AA, Smith GD, Harriss SE, Kumari M, Martin RM, Moran CN, Pitsiladis YP, Ring SM, Yamin C, Meckel Y, Rutigzin VA, The ACTN3 R577X polymorphism with power athlete status in Russians. Eur J Appl Physiol. 2008;103:631-4.

[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:e54685.

[21] Mikami E, Fuku N, Murakami H, Tsuchie H, Takahashi H, Ohiwa N, Tanaka H, ACTN3 R577X genotype is associated with sprinting in elite Japanese athletes. Br J Sports Med. 2010;44:649-52.

[22] North K. Why is alpha-actinin-3 deficiency so common in the general population? The evolution of athletic performance. Twin Res Hum Genet. 2008;11:384-94.

[23] Blanchard A, Ohanian V, Critchley D. The structure and function of alpha-actinin. J Muscle Res Cell Motil. 1989;10:280-9.

[24] Kikuchi N, Ueda D, Min SK, Nakazato K, Igawa S. The ACTN3 XX genotype's underrepresentation in Japanese elite wrestlers. Int J Sports Physiol Perform. 2013;8:57-61.

[25] MacArthur DG, North KN. A gene for speed? The evolution and function of alpha-actinin-3. Bioessays. 2004;26:786-95.

[26] Yevon N, Duarte JA, Oliveira J, Sagiv M, Yamin C, Meckel Y, Sagiv M, Goldhammer E. ACTN3 R577X polymorphism and Israeli top-level athletes. Int J Sports Med. 2009;30:695-8.

[27] Niemi AK, Majamaa K. Mitochondrial DNA and ACTN3 genotypes in Finnish elite endurance and sprint athletes. Eur J Hum Genet. 2005;13:965-9.

[28] Papadimitriou ID, Papadopoulos C, Kouvaris TA, Triantaphyllidais C. The ACTN3 gene in elite Greek track and field athletes. Int J Sports Med. 2008;29:352-5.

[29] Druzhevskaya AM, Ahmetov, II, Asratenevova IV, Rogozkin VA. Association of the ACTN3 R577X polymorphism with power athlete status in Russians. Eur J Appl Physiol. 2008;103:631-4.

[30] Kikuchi N, Ueda D, Min SK, Nakazato K, Igawa S. The ACTN3 XX genotype's underrepresentation in Japanese elite wrestlers. Int J Sports Physiol Perform. 2013;8:57-61.

[31] Alfred T, Ben-Shlomo Y, Cooper R, Hardy R, Cooper C, Deary IJ, Gunnell D, Harris SE, Kumari M, Martin RM, Moran CN, Pitsiladis YP, Ring SM, Sayer AA, Smith GD, Starr JM, Kuh D, Day IN, HALCyon study team. ACTN3 genotype, athletic status, and life course physical capability: meta-analysis of the published literature and findings from nine studies. Human Mutation. 2011;32:1008-18.

[32] 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:e54685.

[33] Mikami E, Fuku N, Murakami H, Tsuchie H, Takahashi H, Ohiwa N, Tanaka H, ACTN3 R577X genotype is associated with sprinting in elite Japanese athletes. Br J Sports Med. 2014;35:172-7.

[34] Ahmetov, II, Druzhevskaya AM, Astra Tenkova IV, Popov DV, Vinogradova OL, Rogozkin VA. The ACTN3 R577X polymorphism in Russian endurance athletes. Br J Sports Med. 2010;44:649-52.

[35] Kikuchi N, Yoshida S, Min SK, Nakazato K, Iwaga S. The ACTN3 XX genotype's underrepresentation in Japanese elite wrestlers. Int J Sports Physiol Perform. 2013;8:57-61.

[36] Zempo H, Tanabe K, Murakami H, Iemitsu M, Maeda S, Kuno S. ACTN3 polymorphism affects thigh muscle...
area. Int J Sports Med. 2010;31:138-42.

[37] Walsh S, Liu D, Metter EJ, Ferrucci L, Roth SM. ACTN3 genotype is associated with muscle phenotypes in women across the adult age span. J Appl Physiol. 2008;105:1486-91.

[38] Moran CN, Yang N, Bailey ME, Tsiokanos A, Jamurtas A, MacArthur DG, North K, Pitsiladis YP, Wilson RH. Association analysis of the ACTN3 R577X polymorphism and complex quantitative body composition and performance phenotypes in adolescent Greeks. Eur J Hum Genet. 2007;15:88-93.

[39] Pimenta EM, Coelho DB, Cruz IR, Morandi RF, Cruz IR, Morandi RF, de Azambuja Pussiedi G, Carvalho MR, Silami-Garcia E, De Paz Fernandez JA. The ACTN3 R577X polymorphism in soccer players in response to acute eccentric training. Eur J Appl Physiol. 2012;112:1495-503.

[40] Seto JT, Chan S, Turner N, MacArthur DG, Raftery JM, Berman YD, Quinlan KG, Head S, Yang N, North KN. The effect of alpha-actinin-3 deficiency on muscle aging. Exp Gerontol. 2011;46:292-302.

[41] Garton FC, Seto JT, Quinlan KG, Yang N, Houweling PJ, North KN. alpha-Actinin-3 deficiency alters muscle adaptation in response to denervation and immobilization. Hum Mol Genet. 2014;23:1879-93.

[42] Massidda M, Corrias L, Ibba G, Scoreu M, Vona G, Calo CM. Genetic markers and explosive leg-muscle strength in elite Italian soccer players. J Sports Med Phys Fitness. 2012;52:328-34.

[43] Clarkson PM, Devaney JM, Gordish-Dressman H, Thompson PD, Hubal MJ, Urso M, Price TB, Angelopoulou TJ, Gordon PM, Moyna MN, Pescatello LS, Visich PS, Zoeller RF, Seip RL, Hoffman EP. ACTN3 genotype is associated with increases in muscle strength in response to resistance training in women. J Appl Physiol. 2005;99:154-63.

[44] Kikuchi N, Nakazato K, Min SK, Ueda D, Igawa S. The ACTN3 R577X polymorphism and female endurance athletes in China. Int J Sports Med. 2010;31:913-6.
Optimizing exercise based on ACTN3 polymorphism

[58] Norman B, Esbjornsson M, Rundqvist H, Osterlund T, von Walden F, Tesch PA. Strength, power, fiber types, and mRNA expression in trained men and women with different ACTN3 R577X genotypes. J Appl Physiol. 2009;106:959-65.

[59] Shang X, Zhang F, Zhang L, Huang C. ACTN3 R577X polymorphism and performance phenotypes in young Chinese male soldiers. J Sports Sci. 2012;30:255-60.

[60] Pimenta EM, Coelho DB, Veneroso CE, Barros Coelho EJ, Cruz IR, Morandi RF, De a Pussieldi G, Carvalho MR, Garcia ES, De Paz Fernandez JA. Effect of ACTN3 gene on strength and endurance in soccer players. J Strength Cond Res. 2013;27:3286-92.

[61] Ruiz JR, Fernandez del Valle M, Verde Z, Díez-Vega I, Santiago C, Yvert T, Rodriguez-Romo G, Gomez-Gallego F, Molina JJ, Lucia A. ACTN3 R577X polymorphism does not influence explosive leg muscle power in elite volleyball players. Scand J Med Sci Sports. 2011;21:e34-41.

[62] Massidda M, Corrias L, Ibba G, Scorcu M, Vona G, Calo CM. Genetic markers and explosive leg-muscle strength in elite Italian soccer players. J Sports Med Phys Fitness. 2012;52:328-34.

[63] Orysiak J, Busko K, Michalski R, Mazur-Rozycka J, Gajewski J, Malczewska-Lenczowska J, Sitkowsi D, Pokrywka A. Relationship between ACTN3 R577X polymorphism and maximal power output in elite Polish athletes. Medicina. 2014;50:303-8.

[64] Hanson ED, Ludlow AT, Sheaff AK, Park J, Roth SM. ACTN3 genotype does not influence muscle power. Int J Sports Med. 2010;31:834-8.

[65] Santiago C, Rodriguez-Romo G, Gomez-Gallego F, Gonzalez-Freire M, Yvert T, Verde Z, Naclerio F, Altmae S, Esteve-Lanao J, Ruiz JR, Lucia A. Is there an association between ACTN3 R577X polymorphism and muscle power phenotypes in young, non-athletic adults? Scand J Med Sci Sports. 2010;20:771-8.

[66] Garatachea N, Verde Z, Santos-Lozano A, Yvert T, Rodriguez-Romo G, Sarasa FJ, Hernandez-Sanchez S, Santiago C, Lucia A. ACTN3 R577X polymorphism and explosive leg-muscle power in elite basketball players. Int J Sports Physiol Perform. 2014;9:226-32.

[67] Pasqua LA, Bueno S, Artioli GG, Lancha AH, Jr., Matsuda M, Marquezini MV, Lima-Silva LA, Saldiva P, Bertuzzi R. Influence of ACTN3 R577X polymorphism on ventilatory thresholds related to endurance performance. J Sports Sci. 2015;5:1-8.

[68] Silva MS, Bolani W, Alves CR, Biagi DG, Lemos JR, da Silva JL, de Oliveira PA, Alves GB, de Oliveira EM, Negrao CE, Krieger JE, Dias RG, Pereira AC. Influences of ACTN3 R577X variant in oxygen uptake are eliminated by endurance training in healthy individuals. Int J Sports Physiol Perform. 2015;10:636-41.

[69] Bell W, Colley JP, Evans WD, Darlington SE, Cooper SM. ACTN3 genotypes of Rugby Union players: distribution, power output and body composition. Annals Hum Biol. 2012;39:19-27.

[70] Ahmetov, II, Druzhkevskaya AM, Lyubaeva EV, Popov DV, Vinogradova OL, Williams AG. The dependence of preferred competitive racing distance on muscle fibre type composition and ACTN3 genotype in speed skaters. Exp Physiol. 2011;96:1302-10.

[71] Vincent B, Windelinckx A, Nielen H, Ramaekers M, Van Leemputte M, Hespel P, Thomis MA. Protective role of alpha-actinin-3 in the response to an acute eccentric exercise bout. J Appl Physiol. 2010;109:564-73.

[72] Venckunas T, Skurvydas A, Brazaitis M, Kamandulis S, Snieckus A, Moran CN. Human alpha-actinin-3 genotype association with exercise-induced muscle damage and the repeated-bout effect. Appl Physiol Nutr Metab. 2012;37:1038-46.

[73] Broos S, Malisoux L, Theisen D, Francaux M, Deldicque L, Thomis MA. Role of alpha-actinin-3 in contractile properties of human single muscle fibers: a case series study in paraplegics. PloS ONE. 2012;7:e49281.

[74] Ahmetov, II, Donnikov AE, Trofinov DY. Actn3 genotype is associated with testosterone levels of athletes. Biol Sport. 2014;31:105-8.

[75] Delmonico MJ, Zmuda JM, Taylor BC, Cauley JA, Harris TB, Manini TM, Schwartz A, Li R, Roth SM, Hurley BF, Bauer DC, Ferrell RE, Newman AB, Health ABC and MrOS Research Groups. Association of the ACTN3 genotype and physical functioning with age in older adults. J Gerontol A Biol Sci Med Sci. 2008;63:1227-34.

[76] Gentil P, Pereira RW, Leite TK, Bottaro M. ACTN3 R577X Polymorphism and Neuromuscular Response to Resistance Training. J Sports Sci Med. 2011;10:393-9.

[77] Norman B, Esbjornsson M, Rundqvist H, Osterlund T, Glenmark B, Jansson E. ACTN3 genotype and modulation of skeletal muscle response to exercise in human subjects. J Appl Physiol. 2014;116:1197-203.