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Evaluating the Influence of the *ACTN3* rs1815739 Gene Polymorphism on the Performance of Physically Active Adult Males in the Arrowhead Agility Drill Test

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Abstract

The alpha actinin-3 gene (*ACTN3*) is a significant candidate gene among genetic markers that determine athletic ability. The *ACTN3* gene is responsible for the creation of the actin protein in fast-twitch muscle fibers, which is associated with muscle power and speed. The objective of this study was to analyze the changes in performance of the arrowhead agility drill test and the distribution of genotype variants in the *ACTN3* rs1815739 gene polymorphism in physically active adult males after a 6-week training period. The research will focus on a cohort of 58 male students, aged 19-24, who are enrolled in the Faculty of Sports Sciences and participate in swimming activities. Genomic DNA was extracted from swab samples obtained from participants using the Buccalyse DNA Extraction Kit from Isohelix, following the manufacturer's supplied technique. The study findings revealed that there was no statistically significant difference between all three genotypes when comparing the pre-test and post-test values of the sample group in terms of left and right foot characteristics. Within this framework, it is acknowledged that the outcomes derived from our investigation could potentially influence the research findings. These aspects include the restricted sample size and the incapacity to regulate individual variances such as concentration and motivation during the pre-test and post-test sessions. Nevertheless, it is believed that the results obtained from our study could potentially enhance future research and literary works in the same field.

Introduction

The field of sports genomics gained traction with the examination of human DNA structure and the identification of the initial DNA alterations (*ACE*, *ACTN3*, *AMPD1*, *PPARD*, and *PPARGC1A* gene variants) associated with athletic performance (2002-2003). Subsequently, research on this topic started to proliferate globally (Akhmetov, Astranenkova and Rogozkin, 2007; Bray et al., 2009; 1000 Genomes Project Consortium, 2015).

Due to the extensive implementation of genotyping technology, numerous research have been conducted to investigate the genetic status control of candidate gene variants. These studies have reported linkages with being an exceptional athlete, however these connections have not been fully confirmed (Ahmetov and Fedotovskaya, 2015).

By the end of 2020, researchers had identified around 220 DNA polymorphisms linked to sports genomics. Among these genetic markers, 97 were shown to be associated with athlete status, with 35 related to endurance, 24 to strength, and 38 to power *(Ahmetov et al., 2022)*. Around 20 of these genes have been discovered to be linked to the performance of outstanding athletes (Pitsiladis et al., 2013; Bulğay et al., 2021).

The alpha actinin-3 gene (*ACTN3*) is a significant genetic marker in determining athletic performance. The *ACTN3* gene polymorphisms are a crucial genetic marker linked to speed, power, and strength characteristics (Ma et al., 2013; Guilherme et al., 2020). The *ACTN3* gene affects muscle power and speed by expressing the actin protein in fast-twitch muscle fibers. A-actinins are the essential components of α-actinin protein, which is located in the sarcomeric Z line of skeletal muscle fibers. The proteins create a cage-like structure that guarantees the connection of thin filaments, known as actin, to one another and maintains the stability of the contraction mechanism. *ACTN3* is a specific form of α-actinin that is only found in fast-twitch muscle fibers, which are responsible for rapid contractions and generating powerful forces. The *ACTN3* gene is responsible for encoding α-actinin-3, which is a protein present in muscle fibers and plays a role in enhancing contractile strength. There is a genetic variation at location 11q13.1 of this gene, specifically a C-T mutation in exon 16 known as rs1815739 R577X. This variation causes a stop codon (X) to be produced instead of arginine (Arg or R) at amino acid 577.

The presence of the 577X allele (XX genotype) results in a lack of the α-actinin-3 protein in affected persons. Protein deficiencies is less common among strength/sprint athletes, but is more prevalent among athletes with the RR genotype (or Arg577 allele) (Yang et al., 2003).

The *ACTN3* TT (XX) genotype codes for a shortened form of the functional α-actinin-3 protein. This genotype is linked to power performance and points towards endurance. Conversely, sprint performance is associated with the *ACTN3* CC (RR) genotype *(Ulucan et al., 2013).* Athletes with the 577R (C) R allele and CC (RR) genotype are compatible with power/speed-oriented sports performance, while those with the 577X (T) X allele and TT (XX) genotype are acceptable with endurance-oriented sports performance, as indicated by certain *ACTN3* gene studies. Numerous research have revealed that top athletes and sedentary individuals differ substantially in their genotype distributions, *ACTN3* gene allele development levels, and physical performance (such as strength, speed, and endurance) (Bulgay et al., 2020; Varillas-Delgado et al., 2022).

The aim of this study was to examine changes in male active adults' performance on the arrowhead agility drill test and the genotype distributions of the *ACTN3* rs1815739 gene polymorphisms after six weeks of conditioning. This study is also expected to offer an alternative viewpoint on the literature on sports genetics and could guide similar future research endeavors.

Material and Methods

Ethical approval

The study was conducted in accordance with the declaration of Helsinki, and approval was obtained from the Lokman Hekim University Non-Interventional Clinical Research Ethics Committee with decision number 2023-248/1.

Study population and sample collection

The research will focus on a cohort of 58 male adults, aged 19-24, who are students of the Faculty of Sports Sciences and have a keen interest in swimming sports. The sample size was calculated through voluntary participation, with a confidence level of 95% and a margin of error of 0.05. There were a total of 50 male students included in the sample *(Cingi., 1994).*

Evaluation methods for exercise and performance

The principal and assistant researchers conducted the data collecting and analysis techniques in the study. Task allocation was implemented in order to minimize measurement inaccuracies. The application was conducted through scheduled appointments, following a predetermined pattern that aligned with the students' educational calendar. The participants were provided with information regarding the measurement process and the study one week prior. Students who satisfied the requirements for participating in the study were provided with both oral and written information regarding the procedures. Participants were requested to provide their signature on the "Informed Voluntary Consent Form". Prior to the test, samples of swabs and oral epithelial tissue swabs (also referred to as Buccal Swabs) were collected from the study participants in order to identify and assess the *ACTN3* gene polymorphism. In addition, the Arrowhead Agility Drill test was administered both at the start and conclusion of the 6-week trial to assess aerobic power, anaerobic performance, and recovery levels. Every participant actively participated in a training program that lasted for six days a week. The program includes workouts designed to improve anaerobic and aerobic capacity, intermuscular and intramuscular coordination, as well as speed and plyometric training loads.

Data collection tools

Arrowhead agility drill test

The Arrowhead agility test is an assessment that quantifies athletes' agility, explosiveness, and ability to change direction. The initial purpose of this test was to assess the athletic capabilities of football players, but it has subsequently been employed in other sports that prioritize agility. The test assesses the participant's proficiency in speed, explosive strength, body control, and the ability to execute turns at various angles and directions. To conduct the test, both a photocell and a funnel are necessary (Lockie and Jalilvand, 2017).

ACTN3 rs1815739 polymorphism analysis

The molecular tests in Sport Science Faculty Cadets were carried out at the Damagen Genetic Diagnosis Center in Ankara. Genomic DNAs from oral swabs were isolated using the Buccalyse DNA Extraction Kit (Isohelix, UK), according to the supplier’s instructions.

The DNA concentration was determined using a Nano Drop spectrophotometer (Thermo Fisher Scientific, Waltham, MA, USA). The genotyping of the single-nucleotide polymorphism (SNP) was performed using the KASP genotyping method (LGC Genomics, Beverly, CA, USA). In brief, the KASP assay mixture contained three oligos that were assay-specific and unlabeled, including two allele-specific forward and a common reverse primer. The main focus of concern within the SNP is the *ACTN3* gene, specifically the variant *rs1815739*. The KASP Master Mix (2X) was purchased as a ready-to-use solution containing the universal fluorescent dyes FAM and VIC in the

presence of ROX passive dye. After adding the SNP-specific KASP primers and the universal KASP Master mixture to the DNA samples, PCR reaction was performed on the 7500 Real-time PCR System (Applied Biosystems, Foster City, CA, USA) device. Then, fluorescence readings were taken, and the obtained data were analyzed according to the previous reports (He et al., 2014).

Statistical analysis

Mac Excel and Statistical Package for the Social Sciences (SPSS) for Windows version 23.0 software programs used for data analysis and statistical calculations. A total of 29 computer programs were utilized to conduct statistical analysis on the research data. Descriptive statistics, including percentage, mean, and standard deviation, were employed to thoroughly assess the dataset. The Shapiro-Wilk and Kolmogorov-Smirnov tests were conducted to analyze the skewness and kurtosis values. Within this context, the skewness and kurtosis values, as defined by George (2011), was considered to be within the range of -2 to +2. Based on this, it was concluded that the distribution followed a normal pattern. The Paired Samples t-Test was employed in this context to ascertain the disparities between the pre-test and post-test measurements of the subject group. The hypotheses were evaluated using a 95% confidence interval and a significance level of 0.05 (George, 2011).

Results and discussion

The following section presents the results gained by analyzing the differences between the measurements obtained on the study participants and the evaluations of these findings. According to the findings in Table 1, the study analyzed the pre-test and post-test values of the subject group in relation to the left foot variable. The analysis revealed that there was no statistically significant difference among all three genotypes (CC genotype t (-0,303) = p> 0.05, CT genotype t(-0,779) = p > 0.05, TT genotype t(-0,691) = p > 0.05).

Upon evaluating the pre-test and post-test values of the subject group in the study, it was found that there was no statistically significant difference between all three genotypes in terms of the right foot variable (CC genotype t (1,624) = p > 0.05, CT genotype t (-0,465) = p > 0.05, TT genotype t(0,323) = p > 0.05).

Table 1. An investigation of specific athletic performance factors based on the *ACTN3* rs1815739 polymorphism

Variables	Genotype	n	Pre-test M±S.s.	Post-test M±S.s	t	p
Right foot	CC (RR)	17	9,47±,53	9,49±,52	-,303	,766
	CT (RX)	22	9,58±,79	9,66±,72	-,779	,445
	TT (XX)	11	9,95±,63	10,01±,68	-,691	,505
Left foot	CC (RR)	17	9,48±,48	9,37±,51	1,624	,124
	CT (RX)	22	9,56±,87	9,62±,76	-,465	,647
	TT (XX)	11	9,98±,67	9,96±,73	,323	,753

*p <0,05.

The distribution frequencies of the *ACTN3* R577X gene polymorphisms were determined as follows: RR 34%, RX 44%, and XX 22%. The allele counts and percentages for C and T were calculated as 39 (54.16%) and 33 (45.84%), respectively.

In the past two decades, there has been a growing number of research examining the correlation between genetics and athletic ability. Athletic talents are determined by a combination of environmental and genetic influences, with heredity playing a crucial role in physical adaptation and, consequently, athletic performance. Although numerous research have investigated this correlation, the results in this domain remain constrained, and the challenges of accessing a substantial number of exceptional athletes from other fields are well recognized.

In the research conducted by Ahmetov et al. (2016), it was reported that at least 155 genetic markers were associated with elite athlete status (Ahmetov et al., 2016; Bray et al., 2009). Research on gene polymorphism in elite athletes yields useful insights. The topic at hand is whether genetic tests can accurately identify inherent advantages in terms of skill and psychomotor performance (Beunen et al., 2010; Cerit, 2018). Several research have investigated the correlation between the *ACTN3* R577X polymorphism and athletic performance in various sports and athlete populations (Zilberman-Schapira et al., 2012; Ulucan, 2016). A study on Finnish sprinters found that α-actinin-3, which is present in individuals with the R-allele, has a significant impact on high-level sports activities that require dominant anaerobic performance. It is important to note that none of the athletes included in the study had the XX genotype (Niemi and Majamaa, 2005). According to a report, football players with the *ACTN3* gene XX genotype have higher levels of VO2max in comparison to individuals with different genetic variants. Moreover, individuals with the RR genotype have demonstrated superior performance in sprint and jump tests measuring distances of 10, 20, and 30 meters (Pimenta et al., 2013). In addition, researchers discovered that athletes with the RR genotype had greater explosive leg muscular strength (Orysiak et al., 2014), improved sprint speeds, and a higher proportion of type II muscle fibers compared to athletes with the XX genotype in jump tests (Ahmetov et al., 2016). In their study, Vincent et al. (2007) found that athletes with the RR genotype had a greater proportion and number of type IIx fibers compared to athletes with the XX genotype. Additionally, they observed that the α-actinin-3 protein content was higher in type IIx fibers than in type IIa fibers (Vincent et al., 2007). In the study conducted by Ulucan et al. (2009), it was revealed that the RR genotype was present in the majority of the 112 athletes (77.68%), with the remaining 20.54% having the RX genotype and 1.79% having the XX genotype. The athletes were divided into three groups: 24 in swimming, 40 in wrestling, and 48 in basketball. During the genotype distribution investigation, specifically among the wrestlers, it was found that 77.5% had the RR genotype, 22.5% had the RX genotype, and none had the XX genotype. Within the population of basketball players, the RR genotype accounted for 77.08%, the RX genotype accounted for 20.83%, and the XX genotype accounted for a mere 2.08%. Within the group of short distance swimming athletes, the RR genotype was present in 79.17% of individuals, the RX genotype was present in 16.67% of individuals, and the XX genotype was detected at a rate of 4.17%. According to Ulucan et al. (2009), the preponderance of the R allele indicates a natural inclination in the specific sports disciplines being studied (Ulucan et al., 2009). In a comparable study carried out by Kasimay et al. (2009), the study focused on examining the links between genotype and phenotype in 37 football players. Specifically, the study compared their *ACTN3* genotypes with their maximum oxygen consumption (VO2max). The researchers found that 59% of football players had the RR genotype, 30% had the RX genotype, and 11% had the XX

genotype. They also observed that football players with the XX genotype had significantly higher VO2max values compared to those with other genotypes. In a separate study involving elite athletes, the analysis of the *ACTN3* R577X gene revealed a statistically significant difference between athletes and sedentary individuals in terms of the RR and RX genotypes. The study included a total of 105 athletes from various sports such as athletics, basketball, judo, taekwondo, wrestling, cycling, football, and tennis. Reported to exhibit variations. There were notable disparities in the distribution of R and X alleles between sports and inactive persons (Kasimay et al. 2009). In the meta-analysis study conducted by El Ouali et al. (2024), it was observed that power athletes had greater frequencies of the RX genotype compared to the other two genotypes. Additionally, the R allele was found to be more prevalent than the others. The study also identified a consistent trend in these findings (El Ouali et al. 2024). The distribution frequencies of *ACTN3* R577X gene genotypes were determined as follows: RX 44%, RR 34%, and XX 22%, as shown in Table 1 of our study. The allele counts and percentages for C and T were calculated as 39 (54.16%) and 33 (45.84%), respectively. The genotype and allele distribution results presented in Table 1 match with the data reported by Ulucan et al. (2009), Sanlisoy et al. (2011), and Ulucan et al. (2014) (Ulucan et al., 2009; Sanlisoy et al., 2011; Ulucan et al., 2014). According to a study conducted by Yang and his colleagues, the *ACTN3* 577R allele was found to potentially offer an advantage in power and speed-based sports among a group of 429 elite athletes from several sports disciplines. This study showed significant disparities in the prevalence of this genetic variant, particularly among highly skilled sprinters. The sprinters had a lower occurrence of the 577X allele and 577XX genotype in comparison to the control group. Curiously, none of the 35 female elite sprinters analyzed exhibited the 577XX gene. (Yang et al., 2003). A further study examined the correlation between the *ACTN3* rs1815739 polymorphism and running performance during matches in highly skilled professional football players. The study sample consisted of 116 individuals (36.8%) with the RR genotype, 156 individuals (49.5%) with the RX genotype, and 43 individuals (13.7%) with the XX genotype (Del Coso et al., 2024). These findings highlight that the presence of the 577R allele confers a clear advantage in sports that need both power and speed. As a result, the high occurrence of the 577XX genotype is observed in the general population. In another study, the impact of the *ACTN3* R577X genotype on the athletic performance of young sprinters (n=20) and inactive students (n=30) was investigated. The study aimed to assess the correlation between genotypes and 50-meter running timings. Within this particular framework, researchers have noted that individuals with RR and RX genotypes display significantly faster 50-meter running times compared to sedentary persons with the same genotypes. This suggests that these athletes demonstrate exceptional performance (Ulucan et al., 2014). In contrast to the previously mentioned studies, our study (Table 1) found no significant difference between all three genotypes when evaluating the pre-test and post-test measurements of the sample group using the Arrowhead Agility Ability Test. A separate research study discovered a direct relationship between *ACTN3* R577X genotypes and grip strength in young males. Individuals possessing the XX genotype exhibited markedly diminished hand grip strength in comparison to those with the RR genotype. Nevertheless, there were no notable disparities in grip strength among persons with the XX and RX genotypes, or among individuals with the RR and RX genotypes.

The researchers reported that there was no significant correlation found between genotypes and either sprint phenotype- or endurance characteristics (Shang et al., 2012). In González-Estrada et al. (2023) study, *ACTN3* was seen to

differ between elite athletes (n = 225) and a control group (n = 225) consisting of individuals who engaged in regular physical activity but were not high-level competitors and participated in recreational exercise three times a week. No statistically significant difference was observed in terms of genotypes (González-Estrada et al., 2023). Nevertheless, certain discoveries contradict the assertion that *ACTN3* R577X genotypes are linked to strength and power in weightlifting, powerlifting, and throwing events. Ginevieene et al. (2016) found no changes in the distribution of *ACTN3* R577X alleles/genotypes among athletes, weightlifters, and throwers in their research (Gineviciene et al., 2016). Garatachea et al (2014), Bell et al. (2012), and Ruiz et al. (2011) all found that the *ACTN3* R577X polymorphism does not offer any advantages in terms of muscle strength or other strength-related characteristics (Garatachea, 2014; Bell et al., 2012; Ruiz et al., 2011). The study compared the frequencies of the *ACTN3* R577X allele and genotype between elite athletes and non-elite athletes. Significant differences were found between the two groups, with elite athletes (n = 168) specializing in different sports and non-elite controls (n = 148) in terms of the *ACTN3* R577X variant. Although the *ACTN3* RR and XX genotypes were more prevalent in the control group compared to athletes, it was noted that the RX genotype was more common among athletes than controls (Canikli et al., 2022).

Conclusion

Based on the current research, the RR genotype of the *ACTN3* gene, also known as the "speed gene", is more common among athletes involved in physical activities that prioritize strength and speed. This genotype is believed to be advantageous for elite athletes in sports that demand power, speed, and strength. It is generally accepted that the gene variants being discussed are highly improbable to manifest the same outcomes observed in top athletes, namely in terms of strength, power, and speed, among persons who are not elite or have inactive lifestyles.

A primary constraint that limits the quality of results derived from genetics-related research is the limited number of samples. Individual factors frequently demonstrate modest impact sizes, as qualities like athletic performance are influenced by numerous genes and circumstances. Given the small sample size and the inability to control independent variables like individual differences in focus and motivation during the pre-test and post-test applications, it is crucial for the predictability of approaches to *ACTN3* gene variants to be improved. It is thought that more research is necessary to reveal the relationship between these gene polymorphisms and athletic ability. Nevertheless it is thought that the findings obtained from our study have the potential to improve future research in the same subject.

Author's contributions

I. Çatalo:
Investigation; Resources; Writing- original draft and Writing.

M. Cerit:
Conceptualization; Data curation; Formal analysis; Self-Funded; Investigation; Methodology; Project administration; Resources; Software; Validation; Visualization; Writing original draft; and Writing - review & editing.

M. Anılır:
Resources; Supervision; Validation; Visualization; Writing -original draft; and Writing -review & editing.

K. Ulucan:
Resources; Supervision; Validation; Visualization; Writing -original draft; and Writing -review & editing.

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Conflict of interest

No conflict of interest was declared by the authors.

References

Ahmetov II, Egorova ES, Gabdrakhmanova LJ, Fedotovskaya ON (2016) Genes and athletic performance: an update. Genetics and Sports 61:41-54.

Ahmetov II, Fedotovskaya ON (2015) Current progress in sports genomics. Advances in Clinical Chemistry 70:247-314.

Ahmetov II, Hall EC, Semenova EA, Pranckevičienė E, Ginevičienė V (2022) Advances in sports genomics. In Advances in Clinical Chemistry 107:215-263.

Akhmetov II, Astranenkova IV, Rogozkin VA (2007) Association of PPARD gene polymorphism with human physical performance. Molekuliarnaia Biologiia 41(5):852-857.

Bell W, Colley JP, Evans WD, Darlington SE, Cooper SM (2012) *ACTN3* genotypes of Rugby Union players: distribution, power output and body composition. Annals of Human Biology 39(1):19-27.

Beunen GP, AI Thomis M, Peeters MW (2010) Genetic variation in physical performance. The Open Sports Sciences Journal 3(1).

Bray MS, Hagberg JM, Perusse L, Rankinen T, Roth SM, Wolfarth B, Bouchard C (2009) The human gene map for performance and health-related fitness phenotypes: the 2006-2007 update. Medicine Science in Sports Exercise 41(1):34-72.

Bulgay C, Cetin E, Orhan O, Ergun MA (2020) The effects of the *ACTN3* and *ACE* genes on the sportive performance of athletes. Inonu Univ J Phys Educ Sport Sci 7:1-12.

Canikli A, Nursal A. F, Unver S, Yigit S (2022) *ACTN3* R577X variant: could it be a determinant of sports performance in elite athletes in a Turkish population? Journal of Genetics 101(1): 22.

Cerit M (2018) Hypothetical approach to the location of genotypes (*ACE* & *ACTN3*) associated with energy systems for the athletic performance. Journal of Sports Sciences Research 3(1):97-105.

Cingi H (1994) Sampling theory. HU Faculty of Science Publications.

Del Coso J, Rodas G, Soler-Aguinaga A, López-Del Campo R, Resta R, González-Rodenas J, et al (2024) *ACTN3* XX Genotype Negatively Affects Running Performance and increases muscle injury incidence in laliga football players. Genes 15(3):386.

El Ouali EM, Barthelemy B, Del Coso J, Hackney AC, Laher I, Govindasamy K, et al (2024) A systematic review and meta-analysis of the association between *ACTN3* R577X genotypes and performance in endurance versus power athletes and non-athletes. Sports Medicine Open 10(1):37.

Garatachea N (2014) *ACTN3* R577X polymorphism and explosive leg-muscle. IJSPP 0331.

George D (2011) SPSS for windows step by step: a simple study guide and reference, 17.0 update, 10/e. Pearson Education India.

Gineviciene V, Jakaitiene A, Aksenov MO, Aksenova AV, Druzhevskaya AM, Astratenkova IV, et al (2016) Association analysis of *ACE*, *ACTN3* and *PPARGC1A* gene polymorphisms in two cohorts of European strength and power athletes. Biology of Sport 33(3):199-206.

González-Estrada GD, Berrio GB, Gómez-Ríos D (2023) Association between *ACE*, *ACTN3*, *AGT*, *BDKRB2*, and *IL-6* gene polymorphisms and elite status in Colombian athletes. Journal of Physical Education and Sport 23(4):1036-1043.

Guilherme JPLF, Semenova EA, Zempo H, Martins GL, Junior AHL, Miyamoto-Mikami E, et al (2020) Are genome-wide association study identified single-nucleotide polymorphisms

associated with sprint athletic status? A replication study with 3 different cohorts. International Journal of Sports Physiology and Performance 16(4):489-495.

He C, Holme J, Anthony J (2014) SNP genotyping: the KASP assay. Crop breeding: methods and protocols 75-86

Kasimay O, Sevinc D, Iseri O, Ulucan K, Unal M, Guney AI (2009) Skeletal muscle gene *ACTN3* and physicalperformance: genotype-phenotype corelation. Journal of Sports Science and Medicine Suppl 11:121.

Lockie RG, Jalilvand F (2017) Reliability and criterion validity of the Arrowhead change-of-direction speed test for soccer. Facta Universitatis, Series: Physical Education and Sport 15(1):139-151.

Ma F, Yang Y, Li X, Zhou F, Gao C, Li M, Gao L (2013) The association of sport performance with *ACE* and *ACTN3* genetic polymorphisms: a systematic review and meta-analysis. PloS One 8(1):e54685.

Niemi AK, Majamaa K (2005) Mitochondrial DNA and *ACTN3* genotypes in Finnish elite endurance and sprint athletes. European Journal of Human Genetics 13(8):965-969.

Orysiak J, Busko K, Michalski R, Mazur-Różycka J, Gajewski J, Malczewska-Lenczowska J, et al (2014) Relationship between *ACTN3* R577X polymorphism and maximal power output in elite Polish athletes. Medicina 50(5):303-308.

Pimenta EM, Coelho DB, Veneroso CE, Coelho EJB, Cruz IR, Morandi RF, et al (2013) Effect of *ACTN3* gene on strength and endurance in soccer players. The Journal of Strength and Conditioning Research 27(12):3286-3292.

Pitsiladis Y, Wang G, Wolfarth B, Scott R, Fuku N, Mikami E, et al (2013) Genomics of elite sporting performance: what little we know and necessary advances. British Journal Of Sports Medicine 47(9):550-555.

Ruiz JR, Fernández del Valle M, Verde Z, Díez-Vega I, Santiago C, Yvert T, et al (2011) *ACTN3* R577X polymorphism does not influence explosive leg muscle power in elite volleyball players. Scandinavian Journal of Medicine and Science in Sports 21(6):e34-e41.

Sanlisoy F, Altintas N, Buyukyazi G, Candan N (2011) Investigation of *ACTN3* R577X genotype distribution of elite athletes in the Aegean region. Cumhuriyet Medical Journal 33(2):153-159.

Shang X, Zhang F, Zhang L, Huang C (2012) *ACTN3* R577X polymorphism and performance phenotypes in young Chinese male soldiers. Journal of Sports Sciences 30(3):255-260.

Ulucan K (2016) Literature review of Turkish sportsmen in terms of *ACTN3* R577X polymorphism. Clinical and Experimental Health Sciences 6(1).

Ulucan K, Ciloglu F, Sesal C, Ergec D, Kirac D, Sahin İ, et al (2009) *ACTN3* gene R577X polymorphism in Turkish sprint power athletes. Medimedgen Abstract Book 33.

Ulucan K, Gole S (2014) *ACE* I/D polymorphism determination in Turkish elite wind-surfers. Sport Science Review 23(1-2):79.

Ulucan K, Gole S, Altindas N, Guney AI (2013) Preliminary findings of α-actinin-3 gene distribution in elite Turkish wind surfers. Balkan Journal of Medical Genetics 16(1):69-72.

Varillas-Delgado D, Del Coso J, Gutiérrez-Hellín J, Aguilar-Navarro M, Muñoz A, Maestro A, Morencos E (2022) Genetics and sports performance: the present and future in the identification of talent for sports based on DNA testing. European Journal of Applied Physiology 122(8):1811-1830.

Vincent B, De Bock K, Ramaekers M, Van den Eede E, Van Leemputte M, Hespe P, Thomis MA (2007) *ACTN3* (R577X) genotype is associated with fiber type distribution. Physiological Genomics 32(1):58-63.

Yang N, MacArthur DG, Gulbin JP, Hahn AG, Beggs AH, Easteal S, North K (2003) *ACTN3* genotype is associated with human elite athletic performance. The American Journal of Human Genetics 73(3):627-631.

Zilberman-Schapira G, Chen J, Gerstein M (2012) On sports and genes. Recent Patents on DNA & Gene Sequences (Discontinued) 6(3):180-188.

1000 Genomes Project Consortium (2015) A global reference for human genetic variation. Nature 526(7571):68.