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RESEARCH ARTICLE

# WHICH POLYMORPHISM IS THE DISTINGUISHING FACTOR FOR FITNESS ATHLETES: THE ACE INDEL OR ACTN3 RS1815739?

**Onur Eroğlu[1,2], Raif Zileli[2,3], M. Ali Nalbant[1], Tolga Polat [4], Özlem Özge Yılmaz[4], Beste Tacal Aslan[5], Korkut Ulucan [4,5]**

[1] Bilecik Seyh Edebali University, Faculty of Science and Letters, Department of Molecular Biology and Genetics, Bilecik, Turkey
[2] Bilecik Seyh Edebali University, Biotechnology Application and Research Center, Bilecik, Turkey
[3] Bilecik Seyh Edebali University, Faculty of Health Science, Bilecik, Turkey.
[4] Marmara University, Health Sciences Institute, Department of Basic Medical Sciences, Istanbul, Turkey
[5] Marmara University, Faculty of Dentistry, Department of Basic Medical Sciences, Istanbul, Turkey

ORCID: O.E. 0000-0002-3451-8540; R.Z. 0000-0003-4178-5468; M.A.N. 0000-0002-4713-1492; T.P. 0000-0002-1257-5384; O.O.Y. 0000-0002-4085-6159; B.T.A. 0000-0001-5271-7917; K.U. 0000-0002-1304-9386

**Corresponding author:** Korkut Ulucan, **E-mail:** korkutulucan@hotmail.com
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**ABSTRACT**

**Purpose:** The purpose of this research was to investigate the occurrence of ACE InDel and ACTN3 rs1815739 in sub-elite fitness athletes and to determine which gene is distinctive by comparing genotype and allele frequencies with sedentary individuals.

**Material and Methods:** Forty-one sub-elite fitness athletes and the same number of the sedentary volunteers participated in the study. Genetic analyzes of the athletes were determined using molecular-based methods such as DNA isolation from peripheral blood samples by using a commercial kit and genotyping with real-time polymerase chain reaction (Real-Time PCR), and conventional polymerase chain reaction (PCR). The Chi-Square test was used to compare the genotype distribution and I, D, C, and T allele frequencies of ACE InDel and ACTN3 rs1815739 polymorphisms for statistical significance.

**Results:** No statistical difference was found for ACE I/D polymorphism in terms of both genotype distribution (p=0.4438). A comparison of sub-elite fitness athletes and control groups showed that the ACTN3 rs1815739 polymorphism had a statistically significant difference in terms of genotype distribution (p=0.0313).

**Conclusion:** In conclusion, we suggest that the ACTN3 rs1815739 polymorphism is more effective than the ACE InDel polymorphism in fitness athletes.

**Keywords:** ACE, ACTN3, fitness, gene, polymorphism, power

## INTRODUCTION

Since the completion of the Human Genome Project, there has been research examining the relationship between athletic performance and genetics; and those led sports scientists to consider many factors that affect athletic performance, including physiological and environmental factors (1). In addition, the effects of genetic factors that determine

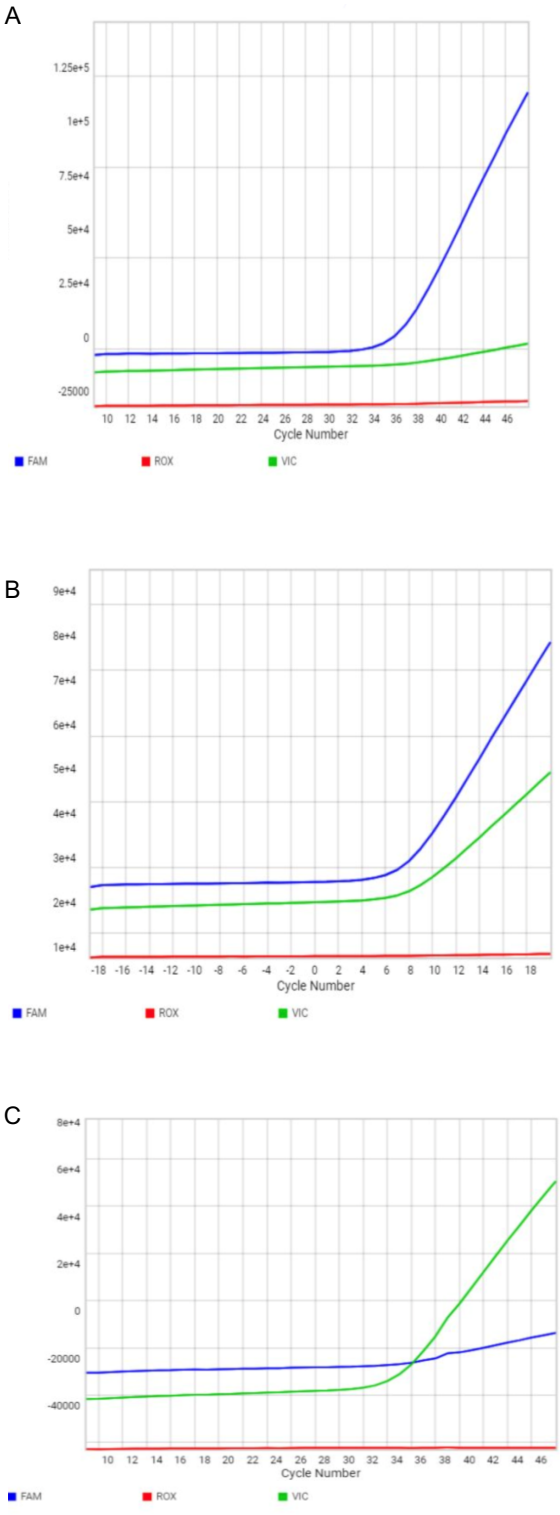


**Figure 1.** Quantitative PCR amplification of the ACTN3 rs1815739 polymorphism. FAM indicates the C allele (blue curve), whereas VIC (green curve) indicates the T allele). (A) The single blue curve indicates the homozygous genotype of RR (CC), whereas (B) the blue and green curves indicate the heterozygous genotype of RX (CT); (C) the green curve for homozygous genotype of TT (XX).

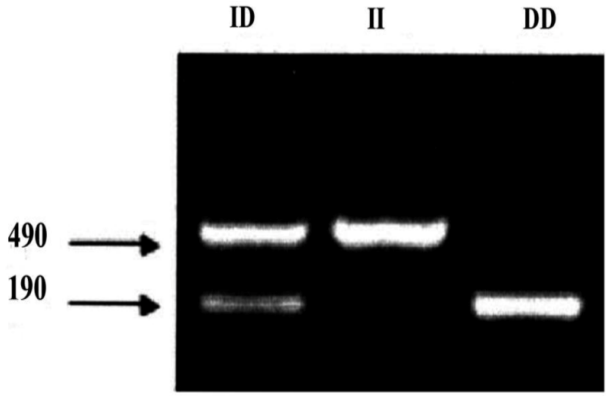


**Figure 2.** Representative image amplification products of the ACE InDel polymorphisms on agarose gel. The band 490 bp in length is the I allele, with a 287 bp insert. The 190 bp band is the D allele.

oxygen consumption, glucose/lipid metabolism, and fast and slow twitch fibers on athletic performance have been reported in studies. These studies formed the basis of sports genetics. The aim of sports genetics studies is the determination of the candidate genes affecting athletic performance, comparing the determined gene regions in successful athletes and sedentary individuals to assess the genetic effects. To have those, it is usually aimed to develop athletes or sedentary individuals in their optimal form by establishing an association between athletic performance and genetic endowments (2, 3).

Environmental and genetic factors influence muscle function and reveal large differences in physical performance phenotypes between individuals. It is known that only a small part of the effect of genetic variants (polymorphism) affecting athletic performance on phenotype can be explained. Various methodological techniques were used to identify correlations between genetic variations and the performance of athletes. Case-control association studies are based on the assumption that candidate gene alleles are more or less common in a group of elite athletes (cases) than in the general population (controls). Cross-sectional association studies examine whether athletes with specific genotypes/alleles exhibit different levels of phenotypic traits compared to other athletes (4, 5).

Along with genetic and environmental factors involved in muscle function and performance metabolism, phenotypic differences arise between individuals. These phenotypic differences reveal the predisposition of individuals regarding athletic performance. To better explain these predispositions,

**Table 1.** Genotype distribution and allele frequency of ACE InDel polymorphism in sub-elite fitness athletes.

| | Genotype | | | *p* Value | Allelic Frequency | | *p* Value |
|---|---|---|---|---|---|---|---|
| | II | ID | DD | | I | D | |
| **Athletes (n=41)** | 11 | 16 | 14 | 0,4438 | 38 | 44 | 0,1596 |
| **Percentage** | 26,8% | 39,0% | 34,2% | | 46,3% | 53,7% | |
| **Control Group (n=41)** | 16 | 15 | 10 | | 47 | 35 | |
| **Percentage** | 39,0% | 36,6% | 24,4% | | 57,3% | 42,7% | |

* The results were considered statistically significant if the $p<0.05$. The $\chi 2$ test was utilized to compare the results with the control group.

case-control studies were conducted between candidate genes and athletic performance. These studies are based on the assumption that the distribution of the candidate gene's allele in the athlete group and control group is correlated and statistically significant (6).

Angiotensin-converting enzyme gene insertion/deletion (ACE InDel) and alpha-actinin-3 (ACTN3) rs1815739 polymorphisms are two of the most widely analyzed genes to explain the relationship between superior athletic performance and the genetics of strength training (7, 8, 9, 10, 11). Therefore, we focused on the two most studied genes, ACE and ACTN3, to explain the relationship between sportive performance and genes in athletes. The ACE gene is situated on chromosome 17q23 and its encoded protein forms a major part of the renin-angiotensin system (RAS) (11). The RAS is responsible for controlling physiological blood pressure. Renin, an enzyme, is released into the bloodstream by particular cells which line the arterioles at the glomerulus, the filtering unit in the kidney. It facilitates the transformation of angiotensinogen, a plasma protein, into angiotensin I, a decapeptide. Following the action of the angiotensin-converting enzyme (ACE) in the blood, angiotensin Ⅰ is converted to an octapeptide, leading to the formation of angiotensin II (9). The hormone Angiotensin II interacts with receptors in the adrenal gland to cause the release of aldosterone, which prompts the kidneys to take up salt and water, narrows the arterioles, and raises blood pressure (13). Effects of ACE InDel polymorphisms are reported in various studies and populations (11, 14, 15). The ACE I allele leads to low ACE enzyme levels and is thought to be linked to better endurance performance. Research has demonstrated that people with the ACE D allele tend to exhibit greater amounts of strength and muscle mass, as well as a higher proportion of fast-twitch fibers. The ACE D allele has also been linked to athletes who are elite-strength (14).

The ACTN3 gene is located at 11q13.1 and is responsible for producing the α-actinin-3 protein. This protein, which is expressed in fast-twitch and type II fibers, is a sarcomere protein and is essential for producing forceful and intense muscle contractions. ACTN3 rs1815739 polymorphism is the result of cytosine-to-thymine exchange in exon 16 of the gene. A stop (X) codon is created in place of the arginine (R) codon, which was previously encoding amino acid 577 of the protein (16). This polymorphism causes ACTN3 deficiency in an individual. ACTN3 rs1815739 polymorphism is a strong candidate for impacting the performance of elite athletes performance (11, 17). The severity of α-actinin-3 deficiency (TT genotype) decreases muscle mass and diameter of fast-twitch fibers and increases the proportion of slow-twitch fibers (15).

In literature, there are some information about the effect of the given polymorphisms on different sports types; most of which have controversial results (19). In addition, the genomic profiles of the fitness athletes are restricted in this term. This report will be the first to have an association with the given polymorphisms and Turkish-based fitness athletes. We hypothesized the link between the given polymorphisms and the power/strength ability of the fitness athletes. Therefore the current study aimed to identify the distribution of ACE InDel and ACTN3 rs1815739 polymorphisms among sub-elite fitness athletes' and compare the results with sedentary people's genetic polymorphisms.

## MATERIAL AND METHODS

### Study Group and Ethical Consideration

Forty-one sub-elite male fitness athletes and the same number of sedentary males (as controls) were included in the study. The main inclusion criteria were the average training sessions of 4-5 days/week and

**Table 2.** Genotype distribution and allele frequency of ACTN3 rs1815739 polymorphism in sub-elite fitness athletes

| | Genotype | | | *p* Value | Allelic Frequency | | *p* Value |
|---|---|---|---|---|---|---|---|
| | **CC** | **CT** | **TT** | | **C** | **T** | |
| **Athletes (n=41)** | 14 | 24 | 3 | **0,0313** | 52 | 30 | **0,0187** |
| **Percentage** | 34,2% | 58,5% | 7,3% | | 63,4% | 36,6% | |
| **Control Group (n=41)** | 7 | 23 | 11 | | 37 | 45 | |
| **Percentage** | 17,1% | 56,1% | 26,8% | | 45,1% | 54,9% | |

* The results were considered statistically significant if the p<0.05. The χ2 test was utilized to compare the results with the control group.

the ones who regularly train within the past 2 years. Eskişehir Osmangazi University, Clinical Research Ethics Committee approved the study protocol (Decision Date: 08.02.2016, No: 01) and the research was performed in line with the Declaration of Helsinki II. All participants signed a written consent form detailing the objectives and procedures of the study. This work was supported by the Scientific Research Organization of Bilecik Şeyh Edebali University (2015-02.BSEÜ.13-01).

### Genotyping

DNA samples were isolated from peripheral blood samples using a commercial DNA isolation kit (Invitrogen, Van Allen Way, Carlsbad, CA, USA). Conventional A260/A280 ratio spectrophotometer values were used to determine the purity of the isolated DNAs. All the isolates had the results between 1.6- 2.0 and all were accepted to have the required purity for the genotyping process. DNA samples have been saved at −20 °C till used for genotyping. The ACTN3 rs1815739 polymorphism was determined using a Real-time PCR (Applied Biosystems StepOne™ Real-Time PCR, Foster City, CA, USA) method using isolated DNA material and the Taqman genotyping assays genotyping kit (Thermo Fisher Scientific Inc., Waltham, Massachusetts, USA). The commercially available primers for the amplification were as previously described (8). Genotyping was performed using 5 µL master mix, 3.50 µL H2O, 0.50 µL assay, and 1 µL (10 ng) DNA for a total of 10. The T (X) allele was determined with FAM primers and the C (R) allele was determined with VIC primers (Figure 1).

The polymerase chain reaction (PCR) was used to genotype the ACE InDel polymorphism from the isolated DNA sample. Briefly, the genotyping reaction was performed in a total volume of 50µL using dNTP concentration 0.5 mM, primer concentration 10 pmol, total DNA amount 100ng, 2U Taq DNA polymerase (Fermentas, Vilnius, Lithuania). The PCR process requires a preliminary denaturation at 95°C for 3 minutes, followed by 35 cycles that consist of 30 seconds at 95°C, 45 seconds at 53°, 1 minute at 72°C, and 10 minutes at 72°C after the last cycle applied as final elongation. The primers for the amplification were as previously described (20). Amplicons were examined using agarose gel electrophoresis with ethidium bromide (0.2g/mL) staining and then visualized under Ultraviolet (UV) light. A genotyping procedure was carried out involving a 490-bp band (representing the II genotype), a 190-bp band (indicative of the DD genotype), or a combination of both bands (indicative of the I/D genotype) (Figure 2).

### Statistical Analysis

The SPSS software package 22 (SPSS Inc., Chicago, IL, USA) was used in the data analysis. The statistical significance of ACE and ACTN3 genes genotype distribution and I, D, C, and T allele frequencies were compared with the Chi-Square test, and the significance was tested at the p<0.05 level at 95% confidence interval.

## RESULTS

In sub-elite fitness athletes (n=41), the numbers and percentages of ACE Indel polymorphism II, ID, and DD genotypes were 11 (26.8%), 16 (39.0%,) and 14 (34.2%), respectively. The D allele (53.7%) was counted with a higher percentage than the I allele (46.3%). The number and percentages of II, ID, and DD genotypes for the control group (n=41) were 16 (39.0%), 15 (36.6%,) and 10 (24.4%), respectively. In the control group, the I allele (57.3%) was counted with a higher percentage than the D allele (42.7%). In the statistical analysis between sub-elite fitness athletes and control groups, no statistical difference was found for ACE I/D polymorphism in terms of both genotype distribution (p=0.4438) and allelic

**Table 3.** Combined distribution of ACE InDel and ACTN3 rs1815739 polymorphisms in sub-elite fitness athletes.

| ***ACE* I/D** | ***ACTN3* rs1815739** | | |
|---|---|---|---|
| **Polymorphisms, n (%)** | **CC** | **CT** | **TT** |
| **DD** | 6 (14,63%) | 8 (19,51%) | - |
| **ID** | 5 (12,20%) | 9 (21,95%) | 2 (4,88%) |
| **II** | 3 (7,32%) | 7 (17,07%) | 1 (2,44%) |

frequency (p=0.1596). ACE InDel polymorphism results are listed in Table 1.

In sub-elite fitness athletes (n=41), the numbers and percentages of ACTN3 rs1815739 polymorphism CC, CT, and TT genotypes were 14 (34.2%), 24 (58.5%), and 3 (7.3%), respectively. The C allele (63.4%) was counted with a higher percentage than the T allele (36.6%). The number and percentages of CC, CT, and TT genotypes for the control group (n=41) were 7 (17.1%), 23 (56.1%), and 11 (26.8%), respectively. In the control group, the T allele (54.9%) was counted with a higher percentage than the C allele (45.1%). A comparison of sub-elite fitness athletes and control groups showed that the ACTN3 rs1815739 polymorphism had a statistically significant difference in terms of genotype distribution (p=0.0313) and allelic frequency (p=0.0187). The outcomes of the ACTN3 rs1815739 variation are shown in Table 2.

## DISCUSSION

Human strength and power are multifactorial concepts that are influenced by both multiple genes and environmental factors (9, 10). Resistance exercise is an effective way to build up skeletal muscle mass because it stimulates muscle protein synthesis (21). The link between individual genome on athletic ability is currently a subject of worldwide investigation. The amount of research on how the ACE and ACTN3 genes associate with the success of power athletes is still limited (4). The current research is a genetic case-control study conducted on Turkish fitness athletes. The novelty of the present study was the evaluation of the ACE InDel and ACTN3 rs1815739 polymorphisms on sub-elite fitness athletes.

ACE InDel polymorphism ID genotype and the ACTN3 rs1815739 CT genotypes are probably the preferred genotypes for Turkish fitness athletes (39.0%; 58.6%, respectively). To date, ACE and ACTN3 polymorphisms had been associated with power, strength, and endurance in determining athletic performance. Those findings suggest that the ACE I allele was linked to endurance, while the D allele was associated with sprinting and power/strength performance. Additionally, ACTN3 CC and CT genotypes were found to be connected to elite power/strength athletes (22, 23). In the present study, we detected no statistically significant difference in the ACE InDel polymorphism (Table 1) between sub-elite fitness athletes and sedentary people (p=0.4438). However, we detected a statistically significant difference in the ACTN3 rs1815739 polymorphism (p=0.0313). Therefore, our results do not support the hypothesis that the ACE InDel polymorphism is related to power/strength ability. However, when the literature is examined, it was that the relationship between ACE and ACTN3 genes and sportive performance is not clear and more studies are needed.

Polat et al. (24) analyzed the same polymorphisms in 11 Turkish bodybuilders. They reported that CT (54%) genotype was higher than the CC (45%) genotype in ACTN3 polymorphism, and the TT genotype was not detected in their cohort. For the ACE I/D polymorphism, 73% of bodybuilders had ID, 18% had II, and 9% had DD genotypes. They highlighted the significance of ACE and ACTN3 polymorphisms associated with stamina in bodybuilders. These findings were in agreement with our findings in the terms of genotype percentage, suggesting the importance of ethnicity in selected polymorphisms.

Muhan et al. (25) investigated the determination of ACTN3 rs1815739 polymorphism in football players and the relationship between the genotypes of football players and their positions. The TT genotype (55.0%) and T allele (72.5%) were found to be higher in football players, while the CT genotype (53.9%) and T allele (53.3%) was higher in the control group. It was determined that midfielders who require endurance are mostly in the TT genotype, while the sprinter strikers are in the CC genotype. Due to the

same ethnicity, nonsimilar results of ACE InDel polymorphism with the current findings may indicate the advantageous the genetic variations in different sports.

Kim et al. (26), reported that they found more DD genotype and D allele in ACE I/D polymorphism in elite strength athletes compared to the control group. Papadimitriou et al., (27), 200 and 400 m. in their study with elite male sprinters compared the sprint times of the athletes with their genotypes. It was revealed that athletes who had the ACE DD genotype in 200 m events had shorter individual running times than those who had the ACE II genotype. Unlike our results, which showed the superiority of the ID genotype, the results of the study supported most of the previous findings.

In another cohort, Scott et al. (11) found that the ACE I/D polymorphism does not have a significant effect on the performance of 114 Jamaican and 113 American sprinter athletes in their study. In a study of 32 female non-elite Turkish athletes, Çam et al. (28) examined the relationship between athletes sprinting and middle-distance running and ACE I/D polymorphism. They found that there were no major variations between genotypes of the ACE I/D polymorphisms in connection to either sprint or middle-distance performance. Similar findings Shahmoradi et al. (29) and Wang et al., (30) both reported that short-distance swimmers have a greater abundance of ACE I alleles compared to the control group.

Studies have revealed the relationship between athletic performance and factors such as ability selection and training response between the ACTN3 gene (31, 32). Some research has indicated that strength athletes have a higher prevalence of the ACTN3 gene CC genotype and a lower prevalence of the ACTN3 TT genotype than the control group (17, 22, 23). Elite wrestlers and competitive bodybuilders had more CC genotypes compared to the control group (33). Yang et al. (23) reported that sprinters had more CC (50%, 30%) and less CT (45%, 52%) and TT (6%, 18%) genotypes than controls. Elite athletes who focused on power-based sports had a higher frequency of the C allele than the control group (34). Some studies did not support the relationship between ACTN3 rs1815739 polymorphism TT genotype and endurance performance in elite strength athletes (29, 30). On the other hand, there are also studies reporting a relationship between ACTN3 rs1815739 polymorphism and power performance in athletes (31,32). Our findings showed the high frequency of CT genotype in fitness athletes, which does not support the previous studies.

There are some previous studies that suggest the unsufficient role of ACTN3 rs1815739 polymorphism on exercise performance. Norman and colleagues (2009) reported that there was no relationship between the ACTN3 gene and power output, fatigue, or power features. They contended that alpha actors have little to no influence on deciding muscle fiber type (31). Contrary to studies reporting that ACTN3 is the "speed gene" in the literature, Lucia et al. (39), discovered that a Spanish long jumper who had participated in the Olympics twice had the TT genotype for the ACTN3 rs1815739 polymorphism. In a similar finding, Druzhevskaya and his friends reported that the world-recorded Russian hammer shooter had TT genotype in ACTN3 rs1815739 polymorphism in a study in 2008.

### Strengths and Limitations

The previous studies were mostly conducted on athletes like sprinters- marathons, and football players; there is not enough information about fitness athletes in terms of genetic research. In the present study, ACE ID and ACTN3 CT genotypes were associated with an advantage for fitness. But our cohort did not reveal any explanation in terms of alleles. The low athletes' number and the lack of biochemical or physical parameters are the main limitations of the present study.

## CONCLUSION

In conclusion, to have a more predictable evaluation of the effect of the given polymorphisms and athletic performance, more studies are needed. In addition, we believe that this first report will help to further investigate the relationship between ACE and ACTN3 genes and physical fitness in athletes.

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**Author contribution:** All authors contributed equally to the process.

**Conflict of interests:** No conflict of interest was declared by the authors.

**Ethical approval**: Eskişehir Osmangazi University, Clinical Research Ethics Committee approved the study protocol (Decision Date: 08.02.2016, No: 01)

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## REFERENCES


1. Corak A, Kapıcı S, Sercan C, Akkoç O, Ulucan K.. A pilot study for determination of anxiety related SLC6A4 promoter "S" and "L" alleles in healthy Turkish athletes. Cellular and Molecular Biology 2017; 63(5): 29-31.
2. Melián Ortiz A, Laguarta-Val S, Varillas-Delgado D. Muscle work and its relationship with ACE and ACTN3 polymorphisms are associated with the improvement of explosive strength. Genes 2021;12(8): 1177.
3. Ulucan K, Topal ES, Aksulu BK, Yaman B, Çiftci İC, Bıyıklı T. Atletic Performance, Genetics and Gene Doping. IKSST J 2015;7(2):58-62.
4. Gineviciene V, Jakaitiene A, Aksenov MO, Aksenova AV, Druzhevskaya AM, Astratenkova IV, Utkus A. Association analysis of ACE, ACTN3 and PPARGC1A gene polymorphisms in two cohorts of European strength and power athletes. Biology of Sport 2016;33(3):199-206.
5. Bulgay C, Kasakolu A, Kazan HH, Mijaica R, Zorba E, Akman O, Bayraktar I, Ekmekci R, Koncagul S, Ulucan K, et al. Exome-Wide Association Study of Competitive Performance in Elite Athletes. Genes 2023; 14(3):660.
6. 6.Semenova EA, Hall ECR, Ahmetov II. Genes and Athletic Performance: The 2023 Update. Genes 2023;14(6):1235.
7. Dogan M, Aslan BT, Ulucan K. Comparison of potential biomarker, ACTN3 rs1815739 polymorphism, for athletic performance of Turkish athletes. Cellular and Molecular Biology 2022;68(5):54-59.
8. Eroğlu O, Zileli R, Ali Nalbant M, Ulucan K. Prevalence of alpha actinin-3 gene (ACTN3) R577X and angiotensin converting enzyme (ACE) insertion/deletion gene polymorphisms in national and amateur Turkish athletes. Cellular and Molecular Biology 2018;64(5):24-28.Ahmetov II, Fedotovskaya ON. Current progress in sports genomics. Advances in Clinical Chemistry 2015;70:247-314.
9. Hughes DC, Day SH, Ahmetov II, Williams AG. Genetics of muscle strength and power: polygenic profile similarity limits skeletal muscle performance. Journal of Sports Sciences 2011;29(13):1425-1434.
10. Scott RA, Irving R, Irwin L, Morrison E, Charlton V, Austin K, Pitsiladis YP. ACTN3 and ACE genotypes in elite Jamaican and US sprinters. Medicine & Science in Sports & Exercise 2011;42(1):107-112.
11. Woods DR, Humphries SE, Montgomery HE. The ACE I/D polymorphism and human physical performance. Trends in Endocrinology & Metabolism 2000;11(10):416-420.
12. Goessler KF, Cornelissen VA, de Oliveira EM, de F Mota G, Polito MD. ACE polymorphisms and the acute response of blood pressure to a walk in medicated hypertensive patients. Journal of the Renin-Angiotensin-Aldosterone System 2015;16(4):720-729.
13. Pescatello LS, Kostek MA, Gordish-Dressman H, Thompson PD, Seip RL, Price TB, Hoffman EP. ACE ID genotype and the muscle strength and size response to unilateral resistance training. Medicine & Science in Sports & Exercise 2006;38(6):1074-1081.
14. Drozdovska SB, Dosenko VE, Ahmetov II, Ilyin VN. The association of gene polymorphisms with athlete status in Ukrainians. Biology of Sport 2013;30(3):163-167.
15. Ulucan K, Bayyurt GM, Konuk M, Güney AI. Effect of alpha-actinin-3 gene on trained and untrained Turkish middle-school children's sprinting performance: a pilot study. Biological Rhythm Research 2014;45(4):509-514.
16. Eynon N, Ruiz JR, Femia P, Pushkarev VP, Cieszczyk P, Maciejewska-Karlowska A, Lucia A. The ACTN3 R577X polymorphism across three groups of elite male European athletes. PLoS ONE 2012;7(8):e43132.
17. 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. Physiological Genomics 2007;32(1):58-63.
18. Ulucan K. Literature review of Turkish sportsmen in terms of ACTN3 R577X polymorphism. Clinical and Experimental Health Sciences 2016; 6(1), 144-147.
19. Guney AI, Ergec D, Kirac D, Ozturhan H, Caner M, Koc G, Kaspar K, Ulucan K, Agirbasli M. Effects of ACE polymorphisms and other risk factors on the severity of coronary artery disease. Genet Mol Res 2013;12:6895–6906.
20. Damas F, Phillips S, Vechin FC, Ugrinowitsch C. A review of resistance training-induced changes in skeletal muscle protein synthesis and their contribution to hypertrophy. Sports Medicine 2015;45:801-807.

21. Cieszczyk P, Sawczuk M, Maciejewska-Karlowska A, Ficek K. ACTN3 R577X polymorphism in top-level Polish rowers. Journal of Exercise Science & Fitness 2012;10(1):12-15.
22. Yang N, MacArthur DG, Gulbin JP, Hahn AG, Beggs AH, Easteal S, North K. ACTN3 genotype is associated with human elite athletic performance. The American Journal of Human Genetics 2003;73(3): 627-631.
23. Polat T, Dogan CS, Dogan M, Akcay T, Ulucan K. Distribution of α-actinin-3 rs1815739 and angiotensin-1 converting enzyme InDel polymorphisms in Turkish bodybuilders. Biomedical Reports 2020;13(6):1-1.
24. Muhan A, Polat T, Yılmaz ÖÖ, Tacal Aslan B, Ulucan K. Investigation of ACTN3 rs1815739 polymorphism, physical characteristics, and position—relation in football players: A team sample. Research in Sport Education and Sciences. 2023;25(1):14-18.
25. Kim CH, Cho JY, Jeon JY, Koh YG, Kim YM, Kim HJ, Kim C. ACE DD genotype is unfavorable to Korean short-term muscle power athletes. International Journal of Sports Medicine 2010;31(01):65-71.
26. Papadimitriou ID, Lucia A, Pitsiladis YP, Pushkarev VP, Dyatlov DA, Orekhov EF, Eynon N. ACTN3 R577X and ACE I/D gene variants influence performance in elite sprinters: a multi-cohort study. BMC Genomics 2016;17(1):1-8.
27. Cam S, Colakoğlu M, Colakoğlu S, Berdeli A. The ACE I/D gene polymorphism and physical performance in a non-elite female cohort. Turkish Journal of Sports Medicine 2005;40(1):1-8.
28. Shahmoradi S, Ahmadalipour A, Salehi M. Evaluation of ACE gene I/D polymorphism in Iranian elite athletes. Advanced Biomedical Research 2014;3:207.
29. Wang G, Mikami E, Chiu LL, De Perini A, Deason M, Fuku N, Galloway SD. Association analysis of ACE and ACTN3 in elite Caucasian and East Asian swimmers. Medicine and Science in Sports and Exercise 2013;45(5):892-900.
30. Norman B, Esbjornsson M, Rundqvist H, Osterlund T, Von Walden F, Tesch P. A. Strength, power, fiber types, and mRNA expression in trained men and women with different ACTN3 R577X genotypes. Journal of Applied Physiology 2009;106(3):959-965.
31. Gómez-Gallego F, Santiago C, González-Freire M, Muniesa CA, Del Valle MF, Perez M, Lucia A. Endurance performance: genes or gene combinations?. International Journal of Sports Medicine 2009;30(01):66-72.
32. Djarova T, Watson G, Basson A, Grace J, Cloete J, Ramakoaba A. ACTN3 and TNF gene polymorphism association with C-reactive protein, uric acid, lactate and physical characteristics in young African cricket players. Afr J Biochem Res 2011;5(1):22-27.
33. Papadimitriou ID, Papadopoulos C, Kouvatsi A, Triantaphyllidis C. The ACTN3 gene in elite Greek track and field athletes. International Journal of Sports Medicine 2008;29(04):352-355.
34. Yang N, Macarthur D, Wolde B, Onywera VO, Boit MK, Wilson RH, North K. ACTN3 genotype ıs not associated with elite endurance athlete status in Ethiopians and Kenyans. Medicine & Science in Sports & Exercise. 2005;37(5):472.
35. Schneider AJ, Rupert JL. Constructing winners: The science and ethics of genetically manipulating athletes. Journal of the Philosophy of Sport 2009;36(2):182-206.
36. Druzhevskaya AM, Ahmetov II, Astratenkova IV, Rogozkin VA. Association of the ACTN3 R577X polymorphism with power athlete status in Russians. European Journal of Applied Physiology 2008;103(6):631-634.
37. Fiuza-Luces C, Ruiz JR, Rodríguez-Romo G, Santiago C, Gómez-Gallego F, Yvert T, Lucia A. Are 'endurance'alleles 'survival'alleles? Insights from the ACTN3 R577X polymorphism. PloS One 2011;6(3):e17558.
38. Lucia A, Oliván J, Gómez-Gallego F, Santiago C, Montil M, Foster C. Citius and longius (faster and longer) with no α-actinin-3 in skeletal muscles?. British Journal of Sports Medicine 2007;41(9):616-617.