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# The ACTN3 p.Arg577Ter Genetic Variants Biomarker of the Fitness Performance, in Oaxaca Amerindian Population

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**Abstract**

Background. ACTN3 is primarily expressed in fast skeletal muscle fibres. A common nonsense polymorphism in this gene is *ACTN3* R577X (rs1815739:C>T) results in replacement of an arginine (R) with a premature stop codon (X) at amino acid 577 in the fast muscle protein α-actinin-3, which causes an absolute deficiency of α-actinin-3 protein and alterations in muscle metabolism. A common null polymorphism in the ACTN3 gene The ACTN3 p.Arg577Ter allele (p.R577* or R577X) has undergone positive selection, with an increase in the X allele frequency as modern humans migrated out of Africa into the colder, less species-rich Eurasian climates Aim. Analized the frequency of allele or genotypes from ACTN3 p.Arg577Ter genetic variants biomarker of the fitness performance, in Oaxaca Amerindian population. Methods. From people of different ethnic groups the State of Oaxaca, DNA was extracted from peripheral blood to extract DNA using the geneKatcher kit (invitrogene), to amplify the polymorphism p.Arg577Ter was realized by qRT_PCR, using tqman probes by determined by allelic discrimination. Results. The more frequency allele is wild type R in all populations, more tan 50%. The Genotype more prevalent is heterocygote RX. In afromexican population Genotype XX o ter-X/ter-X is a allelic variant. Distribution allelic and genotype is verry heterogenus in the populations. In conclusión the ACTN3 R577X gene variant can be used as a clinical marker for the selection of sports talents in the state of Oaxaca, considering that it has already been validated at the population level, with the R allele being more frequent in the state, which is the one associated with a greater selective advantage in sports that require muscular strength and greater physical performance.

**Keywords:** Actinine-3, Amerindian, Long-Distance Athletes, Sports Talents, Sprint/Power Performance

## Introduction

ACTN3 is gene length has16,940, encodes a member of the alpha-actin binding protein gene family, wich is primarily expressed in fast skeletal muscle fibres and functions as a structural component of sarcomeric Z line. These gene has a locus in 11q13.2, with locus in g.66546-66563, NC_000011.10, position 66,554-907. The protein encodes is involved in crosslinking actin containing thin filaments. An allelic polymorphism in this gene results in both coding and non-coding variants; the reference genome represents the coding allele. The non-functional allele of this gene is associated with elite athlete status. Present two isoforms NP_001095.2 alpha-actinin-3-1, NP_001245300.2 alpha-actinin-3-2, wich present the following domains (Table 1) [1].

**Table 1:** ACTN3 domains structural

| Conserved motifs | NP_001095.2 901aa Location | NP_001245300.2 944aa Location |
|---|---|---|
| FRQ1; Ca2+-binding protein, EF-hand superfamily [Signal transduction mechanisms] | 757-861 | 874 → 940 |
| SPEC; Spectrin repeats, found in several proteins involved in cytoskeletal structure | 409-636 | 452 → 679 |
| Spectrin; Spectrin repeat | 644-747 | 331-340 |
| EFhand_Ca_insen; Ca2+ insensitive EF hand | 831-897 | 807 → 869 |
| CH_ACTN_rpt1; first calponin homology (CH) domain found in the alpha-actinin family | 42 → 146 | 90 → 187 |
| CH_ACTN_rpt2; second calponin homology (CH) domain found in the alpha-actinin family | 150 → 264 | 202-307 |
| EF-hand_7; EF-hand domain pair | No reported | 809 → 868 |

ACTN3 is primarily expressed in fast skeletal muscle fibres. A common nonsense polymorphism in this gene is *ACTN3* R577X (rs1815739:C>T) results in replacement of an arginine (R) with a premature stop codon (X) at amino acid 577 in the fast muscle protein α-actinin-3, which causes an absolute deficiency of α-actinin-3 protein and alterations in muscle metabolism. A common null polymorphism in the ACTN3 gene The ACTN3 p.Arg577Ter allele (p.R577* or R577X) has undergone positive selection, with an increase in the X allele frequency as modern humans migrated out of Africa into the colder, less species-rich Eurasian climates suggesting that the absence of α-actinin-3 may be beneficial in these conditions. Approximately 1.5 billion people worldwide are completely deficient in α-actinin-3. While the absence of α-actinin-3 influences skeletal muscle function and metabolism this does not result in overt muscle disease. α-Actinin-3 deficiency (ACTN3 XX genotype) is constantly underrepresented in sprint/power performance athletes. However, recent findings from our group and others suggest that the ACTN3 R577X genotype plays a role beyond athletic performance with effects observed in ageing, bone health, and inherited muscle disorders such as McArdle disease and Duchenne muscle dystrophy, for then the ACTN3 577XX genotype was associated with high glucose, triglyceride and very low density lipoprotein-cholesterol levels and a higher frequency of hypertriglyceridaemia and insulin resistance in women. In males, the genetic variant showed a trend towards significance for insulin resistance in mexicans population [1-2].

The ACTN3 577X allele appeared to increase the risk of developing IIM; 70% of IIM patients were deficient in α-actinin-3. By contrast, ACTN3 577XX patients seemed to have less severe disease as reflected in lower muscle enzyme levels, from the total of 36% of healthy subjects had the ACTN3 577XX polymorphism (α-actinin-3 deficiency), 18% had the 577RR (homozygous wild type) genotype, and 46% 577RX (heterozygous). In DM/PM, 70% had the ACTN3 577XX polymorphism, 6% RR, and 24% RX [odds ratio (OR) 4.12, 95% confidence interval (CI) 1.67-10.33, $p < 0.001$]. In healthy subjects, the R allele was present in 41% and the X allele in 59% compared to 18% and 82%, respectively, in the IIM group (OR 3.21, 95% CI 1.57-6.66, $p < 0.001$) [3].

In Asian chinese population distribution the SNV rs1815739 from ACTN3 gene, show the genotype frequency was significantly different between the athletes (XX 0 %, XR 53.3 %, RR 46.7 %) and the controls no athletes (XX 16 %, XR 44 %, RR 40 %). Heterozygote or homozygote D ACE Ins/del polymorphism and ACTN3 RR(II/ID/DD + RR/XR) haplogenotype combination was associated with higher VO2max values among defenders than among other players. According to VO2max values. The ACE and ACTN3 genotype combinations significantly differed between the athletes and the controls ($p < 0.05$), these results suggested that the Chinese elite female soccer athletes were more likely to harbor the I allele and the R allele and that the combination of ACE II/ID and ACTN3 RR/XR was a synergetic determinant of the athletic performance of females in soccer [4].

In Spain populoation running Using a cross-sectional experiment, the epidemiology of running-related injuries was recorded for one season in a group of 89 Spanish elite endurance runners, *ACTN3* R577X genotype was obtained in a total of 96 injuries were recorded in 57 athletes. Injury incidence was higher in RR runners (3.2 injuries/1000 h of running) than in RX (2.0 injuries/1000 h) and XX (2.2 injuries/1000 h; $p = 0.030$) runners. RR runners had a higher proportion of injuries located in the Achilles tendon, RX runners had a higher proportion of injuries located in the knee, and XX runners had a higher proportion of injuries located in the groin ($p = 0.025$) [5]. It must be considered that the selection of sports talents is in relation to genetic capacity, which would vary between different ethnic groups, the selection of people for different sports disciplines, then it has to be considered, as we see it in different ethnic groups, including In Mexican mestizos, the actinin-3 marker has differences in its allelic and genotypic frequencies. In the state of Oaxaca, it is a challenge, there are few studies of genetics in sports performance and genetics is little used as a tool for the selection of sports talents. Considering the genetic diversity of the different ethnic groups of the State of Oaxaca, the objective of the study was to determine the frequency of alleles and genotypes of the variant p.Arg577Ter (R>X) (rs1815739) in the Amaerindian populations of the State of Oaxaca.

## Materials and methods

From people of different ethnic groups (Table 1) from the State of Oaxaca, DNA was extracted from peripheral blood to extract DNA using the geneKatcher kit (invitrogene), to amplify the polymorphism p.Arg577Ter was realized by qRT_PCR, using tqman probes by determined by allelic discrimination. with conditions previously published [3, 5]. The participants signed the informed consent. The work was approved by the research and bioethics committees of the Translational Medicine and Precision Medicine Research Center, from Miahuatlán de Porfirio Díaz, Oaxaca.

## Results

The more frequency allele is wild type R in all populations, more tan 50%. The Genotype more prevalent is heterocygote RX. In afromexican population Genotype XX o ter/ter is a allelic variant. Distribution allelic and genotype is verry heterogenus in the populations.

**Table 2**

| Population | Genotype RR | Genotype RX | Genotype XX | Allele R | Alelle X | Total N=subjects |
|---|---|---|---|---|---|---|
| Zapotecas, Central Valleys | 40<br>0.40 | 55<br>0.55 | 5<br>0.05 | 135<br>0.675 | 65<br>0.325 | 100 |
| Zapotecas, Southern Sierra | 35<br>0.12 | 245<br>0.83 | 16<br>0.05 | 315<br>0.53 | 277<br>0.47 | 296 |
| Afromexican, National Pinotepa | 312<br>0.87 | 45<br>0.125 | 3<br>0.005 | 669<br>0.93 | 51<br>0.07 | 360 |
| Chinantecas, Tuxtepec | 205<br>0.67 | 97<br>0.31 | 2<br>0.01 | 507<br>0.83 | 101<br>0.17 | 304 |
| Chontales, Istmo Tehuantepec | 105<br>0.625 | 49<br>0.29 | 14<br>0.08 | 259<br>0.67 | 126<br>0.33 | 168 |
| Huaves, Istmo Tehuantepec | 49<br>0.43 | 45<br>0.39 | 19<br>0.171 | 143<br>0.53 | 128<br>0.47 | 113 |
| Mestizo Central Valleys | 172<br>0.56 | 96<br>0.31 | 38<br>0.126 | 440<br>0.72 | 172<br>0.28 | 306 |

## References


1. Barrón-Cabrera E, Torres-Castillo N, González-Becerra K, Zepeda-Carrillo EA, Torres-Valadez R, Hernández-Cañaveral I, *et al*. The ACTN3 R577X polymorphism is associated with metabolic alterations in a sex-dependent manner in subjects from western Mexico. J Hum Nutr Diet. 2022; 35(4):713-721. Doi: 10.1111/jhn.12948. Epub 2021 Nov 9.
2. Houweling PJ, Papadimitriou ID, Seto JT, Pérez LM, Coso JD, North KN, *et al*. Is evolutionary loss our gain? The role of ACTN3 p.Arg577Ter (R577X) genotype in athletic performance, ageing, and disease. Hum Mutat. 2018; 39(12):1774-1787. Doi: 10.1002/humu.23663
3. Sandoval-García F, Petri MH, Saavedra MA, Cruz-Reyes CV, Jara-Quezada LJ, Dávalos-Rodríguez IP, *et al*. The ACTN3 R577X polymorphism is associated with inflammatory myopathies in a Mexican population. Scand J Rheumatol. 2012; 41(5):396-400. Doi: 10.3109/03009742.2012.669495. Epub 2012 May 29.PMID: 2263989
4. Wei Q. The ACE and ACTN3 polymorphisms in female soccer athletes. Genes Environ. 2021; 43(1):5. Doi: 10.1186/s41021-021-00177-3.
5. Gutiérrez-Hellín J, Baltazar-Martins G, Aguilar-Navarro M, Ruiz-Moreno C, Oliván J, Del Coso J. Effect of ACTN3 R577X Genotype on Injury Epidemiology in Elite Endurance Runners. Genes (Basel). 2021; 12(1):76. Doi: 10.3390/genes12010076.
6. Houweling PJ, Papadimitriou ID, Seto JT, Pérez LM, Coso JD, North KN, *et al*. Is evolutionary loss our gain? The role of ACTN3 p.Arg577Ter (R577X) genotype in athletic performance, ageing, and disease. Hum Mutat. 2018; 39(12):1774-1787. Doi: 10.1002/humu.23663
7. Guilherme JPLF, Oliveira EM. Increased prevalence of the null allele of the p.Arg577Ter variant in the ACTN3 gene in Brazilian long-distance athletes: A retrospective study. Ann Hum Genet. 2024 Jul 1. doi: 10.1111/ahg.12571. Online ahead of print.
8. Akazawa N, Ohiwa N, Shimizu K, Suzuki N, Kumagai H, Fuku N, Suzuki Y. The association of ACTN3 R577X polymorphism with sports specificity in Japanese elite athletes. Biol Sport. 2022; 39(4):905-911. Doi: 10.5114/biolsport.2022.108704
9. Abián-Vicén J, Abián P, Bravo-Sánchez A, Piñas-Bonilla I, Lara B, Del Coso J. Genotype Distribution of the ACTN3 p.R577X Polymorphism in Elite Badminton Players: A Preliminary Study. Genes (Basel). 2022; 14(1):50. Doi: 10.3390/genes14010050
10. Garton FC, North KN. The Effect of Heterozygosity for the ACTN3 Null Allele on Human Muscle Performance. Med Sci Sports Exerc. 2016; 48(3):509-520. Doi: 10.1249/MSS.0000000000000784.
11. Abián-Vicén J, Abián P, Bravo-Sánchez A, Piñas-Bonilla I, Lara B, Del Coso J. Genotype Distribution of the ACTN3 p.R577X Polymorphism in Elite Badminton Players: A Preliminary Study. Genes (Basel). 2022; 14(1):50. Doi: 10.3390/genes14010050.
12. Del Coso J, Rodas G, Soler-Aguinaga A, López-Del Campo R, Resta R, González-Rodenas J, Ferrandis J, *et al*. ACTN3 XX Genotype Negatively Affects Running Performance and Increases Muscle Injury Incidence in LaLiga Football Players. Genes (Basel). 2024; 15(3):386. Doi: 10.3390/genes15030386.
13. Balberova OV, Shnayder NA, Bykov EV, Zakaryukin YE, Petrova MM, Soloveva IA, *et al*. Association of the ACTN3 Gene's Single-Nucleotide Variant Rs1815739 (R577X) with Sports Qualification and Competitive Distance in Caucasian Athletes of the Southern Urals. Genes (Basel). 2023; 14(8):1512. Doi: 10.3390/genes14081512.