The American Journal of Applied sciences
(ISSN – 2689-0992)
Published: December 24, 2021 | **Pages:** 1-11
Doi: https://doi.org/10.37547/tajas/Volume03Issue12-01

IMPACT FACTOR
2021: 5. 634

OCLC - 1121105553

Journal Website: https://theamericanjournals.com/index.php/tajas

Distribution Of PPARG Gene Pro12Ala Polymorphism

Yakubov Mirakbar Daniyarovich
Center Of Advanced Technologies, Tashkent, Uzbekistan

Dalimova Dilbar Akbarovna
Center Of Advanced Technologies, Tashkent, Uzbekistan

ABSTRACT

The present study reports for the first time the genotypic distribution of PPARG Pro12Ala polymorphism in group of Uzbek athletes. The human peroxisome proliferator-activated receptor gamma (PPARγ) is involved in lipid storage, glucose homeostasis and adipocyte differentiation. Pro-allele contributes to the development of high physical performance in sports where you need extra physical stamina, and Ala-allele - in sports based on the strength and speed. An analysis of the distribution frequency of genotypes of the PPARG gene, based on the general model of inheritance, in the group of athletes involved in football, was statistically significant compare to control (p =0.004). These results suggest that the presence of PPARG Ala allele, which increases the sensitivity of muscle tissue to insulin, and thus enhancing its anabolic effect on skeletal muscle, predisposes the development and display of speed-power qualities. In addition, we are studied frequencies of Pro/Ala genotypes in Uzbek population in comparison with Russian, Ukrainian, Italian, Bosnian and Herzegovinian, and Ethiopian samples. In conclusion, the present data seem to suggest that some selective factors such as climate could have influenced the present distribution of the Ala allele.

KEYWORDS

Peroxisome Proliferator-Activated Receptor Gamma (PPARG), Polymorphism, Human Genetics, Genetic Predisposition To Sport.

INTRODUCTION

Physical performance phenotypes are characterized as quantitative and multifactorial because they are influenced by both multiple genes (polygenic) and

environmental factors. Physical activity and specific training are environmental factors that contribute or add to the observed differences in physical performance between individuals. Analyses of the genetic determinants of endurance performance as well as strength abilities provide information concerning the contribution of genes. Interaction effects between genes and the environment (dependence of training response on genes) and the identification of genes or coding variants in relation to athletes' characteristics are particularly interesting [1]. It is also worth noticing that information about the phenotypic modulation by genetic variation important for metabolic regulation could be used to understand the metabolic function of the gene of interest [2]. For these reasons, the number of genetic studies on the role of inheritance in fitness and performance traits and the impact of genetic variation on health and prevention of diseases has been systematically expanding in the last years.

Many genes have been investigated for their potential contributions to human variation in fitness, performance or trainability [3]. Among genetic loci and markers shown to be related to physical performance or health related fitness phenotypes, the Peroxisome Proliferator activated Receptors genes (PPAR) are especially interesting for exercise scientists and physicians due to the multiple physiological roles of Proteins encoded by them. PPAR proteins are lipid-activated nuclear receptors, which belong to the nuclear hormone receptor superfamily [4]. The transcriptional activity of PPARs is mediated by PPAR retinoid X receptor (RXR) heterodimers that bind to specific DNA sequence elements termed PPREs (PPAR response elements) in the regulatory region of their target genes. The predominant role of PPARs is the transcriptional regulation of enzymes and other proteins involved in energy homeostasis (lipid and carbohydrate metabolism). PPARs also control expression of genes active in vascular biology, tissue repair, cell Proliferation and differentiation, and even sexual dimorphism [5, 6, 7]. Because physical fitness largely depends on the balance between lipid-carbohydrate metabolism and precise substrate usage, the PPAR transcriptional factors and their co-activators constitute an area of interest to sport scientists.

Three PPAR isotypes: PPARα (alias NR1C1), PPARδ (also called PPARβ or NR1C2 or NUC-1 or FAAR) and PPARγ (alias NR1C3), have been identified so far in vertebrates and mammals [8]. These receptors exhibit a different tissue distribution and functions and, to some extent, different ligand specificities [6]. In humans, a separate gene encodes each PPAR isoform: PPARα is encoded by the PPARA gene located on chromosome 22, PPARγ by the PPARG gene on chromosome 3, and PPARδ by the PPARD gene on chromosome 6 [9].

Peroxisome Proliferator-activated receptor γ (PPARγ) is a transcriptional regulator involved in energy control and lipid/glucose homeostasis. PPARγ is highly expressed in adipocytes, serves as a critical regulator of fat cell differentiation and promotes the formation of mature triglyceride-rich adipocytes. It also appears to be a key regulator of abiogenesis, fatty acid storage and energy balance [10]. Due to PPARγ's role in controlling lipid/glucose metabolism, it is regarded as a physiological factor associated with predispositions to hyperlipidemia, insulin resistance, type 2 diabetes mellitus, obesity and cardiovascular diseases [11].

The American Journal of Applied sciences
(ISSN – 2689-0992)
Published: December 24, 2021 | **Pages:** 1-11
Doi: https://doi.org/10.37547/tajas/Volume03Issue12-01

IMPACT FACTOR
2021: 5. 634
OCLC - 1121105553

Differential PPARG promoter usage and alternative splicing produce different mRNAs, including at least four transcripts (PPARγ1, PPARγ2, PPARγ3 and PPARγ4) that differ at their 5-prime ends [12]. However, the Protein sequences of PPARγ1, γ3 and γ4 are identical (this Proteins are encoded by exons 1 to 6 of the PPARG gene) while the PPARγ2 Protein contains 28 additional amino acids at the N-terminus that are encoded by the exon B fragment of the PPARG gene. The shorter PPARγ1 has a relatively broad expression pattern including the gut, brain, vascular cells, and immune and inflammatory cells, whereas PPARγ2 is found at high levels mainly in adipose tissues [5].

The C34G substitution (rs1801282) is located within the exon B sequence of the PPARG gene, resulting in the Pro12Ala polymorphism described in the PPARγ2 Protein [13]. The 12Ala allele shows a decreased binding affinity of the PPARγ2 Protein to the PPRE sequences in responsive Promoter regions, resulting in low activation of target genes [14, 15]. The functional relevance of the Pro12Ala amino acid change in the PPARγ2 Protein results from its localization within the PPARγ molecule. This SNP was first identified in 1997 [13] within the AF-1 domain of the amino terminus of the PPARγ2 Protein, that controls ligand-independent transcriptional activity. Presumably, the Pro12Ala change in the AF-1 domain may indirectly facilitate the chemical modification of some amino acids residues (phosphorylation and/or simulation) responsible for decreasing the PPARγ2 activity. The association between the Pro12Ala polymorphism and the divergent transcriptional activity of PPARγ was confirmed during in vitro experiments. The estimation of the transcriptional activity of the 12Ala PPARG2 variant, compared to the Pro12 variant, indicated that the PPARG 12Ala allele is associated with a less active form of PPARγ2 Protein characterized by decreased abilities to activate the transcription of prepared constructs containing PPRE [15] or specific genes [14]. These results were confirmed in vivo in association studies demonstrating changes in the expression of PPARG target genes depending on the Pro12Ala genotypes [16, 17, 18].

PPARγ2 is a transcriptional factor required for the proper expression of hundreds of genes engaged in cellular metabolism. The alterations in the activity of the PPARγ2 12Ala variant may be responsible for different physiological effects observed not only in adipocytes (where PPARγ2 is primarily expressed) but also in other tissues of the human body, for example, in muscle cells. At first glance, this may seem surprising because PPARγ2 is minimally expressed in the skeletal muscles, but there are some physiological explanations for this fact. PPARγ2 acts as a molecular sensor that controls the metabolism and transport of fatty acids in different tissues and is known as a modulator of insulin-signaling pathways sensitizing skeletal muscle and the liver to the actions of insulin. The positive association between the PPARG 12Ala allele and improved insulin sensitivity was confirmed by a number of studies [14, 19, 20]. Enhanced insulin sensitivity suppresses lipolysis, which in consequence causes a decreased release of FFAs (Free Fatty Acids) [21]. Such an insulin-induced inhibition of lipolysis in adipocytes resulting in reduced plasma FFA availability may favor using glucose in muscle cells. This specific shift of energy balance towards glucose utilization rather than FFA mobilization upon insulin stimulation seems to be more

efficient in PPARG 12Ala carriers due to the improved insulin sensitivity observed in such individuals. This assumption was confirmed in a study in which the effect of decreasing the lipid oxidation with an accompanying increase of the rates of muscle glucose uptake and its cellular metabolism after insulin stimulation was mainly observed in lean subjects carrying the 12Ala allele, while the Pro12Pro12 homozygotes revealed significantly lower substrate flexibility [22]. The physiological needs of an athlete's body require very subtle energy substrate regulation and mediation of the balance between fatty acid and glucose metabolism, especially in terms of metabolic stress for prolonged exertion or short-term, very intense exercises. As presented above, PPARγ2 influences the energy substrate selection. For athletes who perform sports that involve lifting, jumping, throwing and short sprints, the anaerobic system is regarded as a fundamental mechanism of energy production. In anaerobic metabolism, glucose is the most important fuel, as it is needed for glycolysis to provide the amount of energy required for very short (approximately 20-30 s) and very intense physical efforts. Increased glucose utilization in working skeletal muscles promoted by the presence of the PPARG 12Ala allele in individual's genotype may be one of the key elements crucial for athletes performing short-term exercises [23].

The aforementioned flexibility of energy substrate usage is an element that is unquestionably crucial for performing the physical exercises characteristic of athletes. However, body mass and composition can be considered equally important factors in athletic performance. Because PPARγ regulates adipocyte differentiation and controls body fat storage, the relevance of the PPARG polymorphism in the context of susceptibility to obesity is of major interest. The different consequences of carrying the PPARG 12Ala allele on BMI were observed in overweight/obese and lean subjects [24, 25]. A meta-analysis of 40 datasets from 30 independent studies revealed that the PPARG Pro12Ala polymorphism had an effect on BMI in individuals with marked obesity (12Ala carriers had a higher BMI than Pro12 homozygotes), while this effect was not observed in lean subjects [26]. These findings indicate that the Pro12Ala polymorphism modulates body weight, but its impact is modified by other genetic components and environmental factors such as dietary habits or physical activity levels. A study on non-diabetic subjects indicated that the beneficial additive effects of physical exercise and healthy (i.e., rich in polyunsaturated fatty acids) diet are restricted to PPARG Pro12Pro12 homozygotes. In 12Ala allele carriers, the relationships between diet, activity level and body weight are more complicated: the beneficial effects are only observed when the polyunsaturated to saturated fatty acid ratio and physical activity are simultaneously elevated [27]. These data may suggest that the PPARG 12Ala allele is positively associated with a susceptibility to obesity; however, the observed effects of its presence in an individual's genotype strongly depend on that individual's lifestyle behaviors. Taking these findings into consideration, one main conclusion for athletes seems to be particularly important: to develop a favorable weight-to-strength ratio in professional athletes who are PPARG 12Ala allele carriers, strict dietary discipline should be maintained. This is likely to be especially important for athletes competing in sports that involve lifting, jumping, throwing and short sprints, for whom strength abilities are essential. For

physically active 12Ala allele carriers, strict diet seems to be a crucial environmental factor that favorably modulates the influence of their genetic components, and most likely enables them to achieve a high performance level. It is suggested that the proper combination of genotype, training and diet is most likely responsible for developing the appropriate relations between body mass and strength in athletes [23].

The role of PPARG in athletic performance is multifarious because PPARγ also regulates bone mass, which is a phenotype trait that creates a structural scaffold crucial for effective load transfer in athletes. There is evidence for an antiosteogenic action of PPARγ. The study of PPARG-deficient mice as well as in vitro experiments revealed that PPARγ haplo insufficiency promotes osteoblast genesis [28] and enhances bone development. The reduced transcriptional activity of PPARγ results in a decreased expression of PPARγ target genes coding for antiosteogenic-signalling factors [29]. Based on data obtained in mouse models, the reduction of PPARG activity associated with the Pro12Ala polymorphism could enhance osteoblastogenesis, resulting in increased bone mass in humans. Thus, athletes carrying the PPARG 12Ala allele might benefit from having stronger bones that are better adjusted to withstand extreme forces and transfer loads that are over the normal loading conditions. This aspect is especially important for athletes performing strength sports such as powerlifting or weightlifting, for which tremendous weight loads are transferred throughout the whole training program and during competition [23]. Taking into account the physiological role of the PPARγ protein, it was suggested that the PPARG Pro12Ala polymorphism can be a genetic factor that contributes to the polygenic profile of athletic performance. The hypothesis that the PPARG 12Ala allele is associated with strength athlete status was verified in Polish athletes and, after analysis of the genotyping results, it was demonstrated that a significantly higher frequency of the PPARG 12Ala allele in the subgroup of the Polish athletes designated "strength athletes" compared to the frequency observed in the control group [23]. These results are in accordance with a previous study [30] showing that the 12Ala allele was more prevalent in the similar group of strength athletes (sprinters, throwers and weightlifters). Ahmetov et al. [30] also detected a hypertrophic effect of the PPARG 12Ala allele on muscle fibers, suggesting that the 12Ala allele is associated with the development and manifestation of the speed and force qualities. Moreover, the PPARG 12Ala allele was also overrepresented in a large cohort of Russian rowers [31], indicating the importance of the strength component in the overall performance of this strength-endurance discipline.

Considering all facts presented above, the PPARG 12Ala allele may be recognized as a relevant genetic factor favoring strength abilities in professional athletes, especially in terms of insulin-dependent metabolism, a shift of the energy balance towards glucose utilization and the development of a favorable weight-to-strength ratio.

It is well known that the genetic association may vary depending on the population that is why it so important to carry out these studies in different populations. Until now, the studies of polymorphisms of PPARG gene not carried out for Uzbek athletes.

The American Journal of Applied sciences
(ISSN – 2689-0992)
Published: December 24, 2021 | **Pages:** 1-11
Doi: https://doi.org/10.37547/tajas/Volume03Issue12-01

IMPACT FACTOR
2021: 5. 634
OCLC - 1121105553

The aim of our study was to determine the frequency of genotypes PPARG gene Pro12Ala polymorphism in Uzbek athletes and frequencies of Pro/Ala genotypes in Uzbek population in comparison with Russian, Ukrainian, Italian, Bosnian and Herzegovinian, and Ethiopian samples.

MATERIALS AND METHODS

Blood samples for molecular genetic analysis of PPARG gene polymorphism were taken from 100 Uzbek athletes involved in different sports and 101 nonathletic individuals for control group. Genomic DNA was extracted from the whole blood using Miller's protocol [32]. Genotyping PPARG gene polymorphism by using Polymerase chain reaction -restriction fragment length polymorphism protocol (PCR-RFLP) with TaqI enzyme. Pro12Ala was genotyped using forward primer: forward 5'-TCTCTCCGTAATGGAAGACC-3', and a mismatch reverse primer R: 5'-GCATTATGAGACATCCCCAC-3', generating a fragment of 154 bp digested by TaqI to 133 bp. The amplified PCR product containing Pro12Ala SNPs was digested with HpaI restriction enzymes, respectively, at 37 °C overnight.

Restriction fragments was analyzed by 3% agarose gel electrophoresis. Genotyping was repeated for fifty percent of all samples (including all mutant homozygous and al heterozygous samples for Pro12Ala SNPs and randomly selected other samples) with 100% reproducibility. Statistical analyses were performed using on-line open program "Gen-expert" (http://gen-expert.ru). Statistical significance was set as $p<0.05$. The differences in genotype frequencies between cases and controls were assessed by chi-square (x2) test.

RESULTS AND DISCUSSION

PPARG gene encodes peroxisome proliferator activated receptor gamma, gamma-nuclear receptor, which involved in cell differentiation, muscle tissue, fat and carbohydrate metabolism. Ala allele carriers are more likely to preserve physical activity, as far as their muscles are capable to utilize glucose in greater extent. It was found that the PPARG Pro12 Ala polymorphism has association with the susceptibility to sports. Pro-allele contributes to the development of high physical performance in sports where you need extra physical stamina, and Ala-allele - in sports based on the strength and speed.

The genotyping results of the control group allowed us to determine the frequency of allelic variants of PPARG Pro12Ala polymorphism, which was as follows: 75.4% Pro/Pro, 24.8% Pro/Ala and 0% Ala/Ala. PPARG genotype distribution amongst athletes and controls were consistent with Hardy-Weinberg equilibrium ($p>0.05$). In the control group, the frequency of rare Ala allele was 12.4 %. This parameter was higher on 3.2 % for cyclists, on 5.6 % for academic rowing and on 14.9 % for football players (Table 1).

Table 1. Allele distribution for *PPARG* in cases and controls

Sports	Frequency distribution of alleles, %		x^2	p
	Pro	*Ala*		

The American Journal of Applied sciences
(ISSN – 2689-0992)
Published: December 24, 2021 | **Pages:** 1-11
Doi: https://doi.org/10.37547/tajas/Volume03Issue12-01

IMPACT FACTOR
2021: 5. 634
OCLC - 1121105553

	Cases	Controls	OR (95% CI)	Cases	Controls	OR (95% CI)		
Cycle racing (N=16)	84.4	87.6	0.76(0.27-2.16)	15.6	12.4	1.31(0.46-3.72)	0.26	0.61
Boxing (N=12)	100	87.6	7.04(0.42-119.36)	0	12.4	0.14(0.01-2.41)	3.34	0.07
Rugby (N=14)	89.3	87.6	1.18(0.33-4.19)	10.7	12.4	0.85(0.24-3.02)	0.06	0.8
Football (N=33)	72.7	87.6	0.38(0.19-0.75)	27.3	12.4	2.66(1.34-5.27)	8.19	0.004
Academic roving (N=25)	82.0	87.6	0.64(0.28-1.48)	18.0	12.4	1.55(0.67-3.58)	1.09	0.3

Table 2. Genotype frequencies of the *PPARG Pro12Ala* polymorphism comparing with Uzbek population

№	Population	N	Genotypes, %			p
			Pro/Pro	*Pro/Ala*	*Ala/Ala*	
1	Uzbek	101	75.2	24.8	0	0.16
2	Russian	100	68.7	28.1	3.2	0.13
3	Ukrainian	82	70.7	28	1.2	0.46
4	Italian	111	81.5	18.5	0	0.44
5	Bosnian and Herzegovinian	43	72.1	20.9	7	0.03
6	Ethiopian (Africa)	79	91.1	8.9	0	0.02

An analysis of the distribution frequency of genotypes of the PPARG gene, based on the general model of inheritance, in the group of athletes involved in football, was statistically significant compare to control (p =0.004).

These results suggest that the presence of PPARG Ala allele, which increases the sensitivity of muscle tissue to insulin, and thus enhancing its anabolic effect on skeletal muscle, predisposes the development and display of speed-power qualities. Thus, it seems reasonable to include genotyping of

PPARG Pro12Ala polymorphism in the complex of genetic testing of athletes, and young people who are planning to engage with football sport activities.

The frequencies of the PPARG Pro/Ala genotypes Uzbek population observed in comparison with literature dates Russian, Ukrainian, Italian, Bosnian and Herzegovinian and Ethiopian samples. In each group the genotype frequencies were consistent with Hardy - Weinberg equilibrium ($p>0.05$) (Table 2). No significant differences in Uzbek population with Russian ($p=0.13$), Ukrainian ($p=0.46$) and Italian ($p=0.44$) populations were found. In comparison with Bosnian and Herzegovinian significantly different by high level Ala/Ala genotype 7% ($p=0.03$), reliable difference was discovered, while comparing with Ethiopian population (Africa) due to dominating Pro/Pro genotype and rather law frequency of Pro/Ala genotype in this population ($p=0.02$) [33, 34, 35, 36].

CONCLUSION

In conclusion, the present data seem to suggest that some selective factors such as climate could have influenced the present distribution of the Ala allele. There is an increasing need to study the genetic structure of peoples now living in pre-industrial societies where future changes in environmental factors, mainly dietary habits, could interferes with their genes and endanger their health.

REFERENCES

1. Beunen G., Thomis M. //Gene driven power athletes? Genetic variation in muscular strength and power / BrJSportsMed. 2006. 40 (10): P.822-823.
2. Karpe F., Ehrenborg E.E. // PPARδ in humans: genetic and pharmacological evidence for a significant metabolic function / CurrOpinLipidol. 2009. 20(4): P.333-336.
3. Bray M.S., Hagberg J.M., Pérusse L., et al. // The human gene map for performance and health-related fitness phenotypes: the 2006-2007 update / Med Sci Sports Exerc. 2009. 41(1): P.35-73.
4. Desvergne B., Wahli W. // Peroxisome proliferator activated receptors: nuclear control of metabolism / Endocr Rev. 1999. 20: P.649-688.
5. Michalik L., Auwerx J., Berger J.P., et al. // International union of pharmacology. LXI. Peroxisome proliferator activated receptors / Pharmacol Rev. 2006. 58: P.726-741.
6. Yessoufou A., Wahli W. // Multifaceted roles of peroxisome proliferator-activated receptors (PPARs) at the cellular and whole organism levels / Swiss Med Wkly. 2010; w13071; P.140.
7. Nuclear Receptors Nomenclature Committee. A unified nomenclature system for the nuclear receptor superfamily. Cell. 1999. 97: P.1-3.
8. www.ncbi.nlm.nih.gov/gene
9. Eynon N., Meckel Y., Alves A.J., et al. // Is there an interaction between PPARD T294C and PPARG C1A Gly482Ser polymorphisms and human endurance performance? / ExpPhysiol. 2009a. 94 (11): P.1147-1152.
10. Meirhaeghe A., Amouyel P. // Impact of genetic variation of PPARG in humans / Mol Genet Metab. 2004. 83(1-2): P.93-102.
11. Fajas L., Auboeuf D., Raspe E., et al. // The organization, promoter analysis,

and expression of the human PPARG gene / J Biol Chem. 1997. 272: P.18779-18789.

12. Yen C.J., Beamer B.A., Negri C., et al. // Molecular scanning of the human peroxisome proliferator activated receptor γ (hPPARG) gene in diabetic Caucasians: identification of a Pro12Ala PPARG2 missense mutation / BiochemBiophys Res Commun. 1997. 241: P.270-274.
13. Deeb S.S., Fajas L., Nemoto M., Pihlajamäki J., Mykkänen L., et al. // A Pro12Ala substitution in PPARG2 associated with decreased receptor activity, lower body mass index and improved insulin sensitivity / Nat Genet. 1998. 20: P.284-287.
14. Masugi J., Tamori Y., Mori H., Koike T., Kasuga M. // Inhibitory effect of a Proline-to-Alanine substitution at codon 12 of peroxisome proliferator-activated receptor-γ 2 on thiazolidinedione-induced adipogenesis / BiochemBiophys Res Commun. 2000. 268(1): P.178-182.
15. Yamamoto Y., Hirose H., Miyashita K., Nishikai K., Saito I., et al. // PPARG2 gene Pro12Ala polymorphism may influence serum level of an adipocyte-derived protein, adiponectin, in the Japanese population / Metabolism. 2002. 51: P.1407-1409.
16. Schneider J., Kreuzer J., Hamann A., Nawroth P.P., Dugi K.A. // The Proline 12 Alanine substitution in the peroxisome Proliferator-activated receptor-γ2 gene is associated with lower lipoprotein lipase activity in vivo / Diabetes. 2002. 51: P.867-870.
17. Simon I., Vendrell J., Gutierrez C., Fernández-Real J.M., Vendrell I., et al. // Pro12Ala substitution in the peroxisome proliferator-activated receptor-γ is associated with increased leptin levels in women with type-2 diabetes mellitus / Horm Res. 2002. 58: P.143-149.
18. Ek J., Andersen G., Urhammer S.A., Hansen L., Carstensen B., et al. // Studies of the Pro12Ala polymorphism of the peroxisome proliferator-activated receptor-γ2 (PPAR-G2) gene in relation to insulin sensitivity among glucose tolerant Caucasians / Diabetologia. 2001. 44(9): P.1170-1176.
19. Koch M., Rett K., Maerker E., et al. // The PPARγ2 amino acid polymorphism Pro 12 Ala is prevalent in offspring of type II diabetic patients and is associated to increased insulin sensitivity in a subgroup of obese subjects / Diabetologia. 1999. 42: P.758-762.
20. Stumvoll M., Wahl H.G., Löblein K., et al. // The Pro12Ala polymorphism in the peroxisome proliferator-activated receptor-γ2 gene is associated with increased antilipolytic insulin sensitivity / Diabetes. 2001. 50: P.876-881.
21. Vänttinen M., Nuutila P., Pihlajamäki J., et al. // The effect of the Ala12 allele of the peroxisome proliferator-activated receptor-γ2 gene on skeletal muscle glucose uptake depends on obesity: a positron emission tomography study / ClinEndocrinolMetab. 2005. 90(7): P.4249-4254.
22. Thamer C., Haap M., Volk A., et al. // Evidence for greater oxidative substrate flexibility in male carriers of the Pro12Ala polymorphism in PPARG2. HormMetab Res. 2002. 34: P.132-136.

23. Beamer B.A., Yen C.J., Andersen R.E., et al. // Association of the Pro12Ala variant in the peroxisome proliferator activated receptor-γ2 gene with obesity in two Caucasian populations / Diabetes. 1998. 47: P.1806-1808.

24. Doney A., Fischer B., Frew D., et al. // Haplotype analysis of the PPARG Pro12Ala and C1431T variants reveals opposing associations with body weight / BMC Genet. 2002. 3: P.21.

25. Ek J., Urhammer S.A., Sørensen T.I., et al. // Homozygosity of the Pro12Ala variant of the peroxisome proliferation activated receptor-γ2 (PPAR-γ2): divergent modulating effects on body mass index in obese and lean Caucasian men / Diabetologia. 1999. 42(7): P.892-895.

26. Franks P.W., Luan J., Browne P.O., et al. // Does peroxisome proliferator-activated receptor γ genotype (Pro12Ala) modify the association of physical activity and dietary fat with fasting insulin level? / Metabolism. 2004. 53 (1): P.11-16.

27. Kawaguchi H., Akune T., Yamaguchi M., et al. // Distinct effects of PPARγ insufficiency on bone marrow cells, osteoblasts, and osteoclastic cells / J Bone Miner Metab. 2005. 23: P.275-279.

28. Cock T.A., Back J., Elefteriou F., et al. // Enhanced bone formation in lipodystrophic PPARG (hyp/hyp) mice relocates haematopoiesis to the spleen. EMBO Rep. 2004. 5: P.1007-1012.

29. Ahmetov I.I., Mozhayskaya I.A., Lyubaeva E.V., et al. // PPARG gene polymorphism and locomotor activity in humans / Bull ExpBiol Med. 2008. 146 (5): P.630-632.

30. Akhmetov I.I., Popov D.V., Mozhayskaya I.A., et al. // Association of regulatory genes polymorphisms with aerobic and anaerobic performance of athletes / Ross FiziolZhIm. 2007. 93 (8): P.837-843.

31. Ahmetov I.I., Mozhayskaya I.A., Lyubaeva E.V., Vinogradova O.L., Rogozkin V.A. // Association of polymorphism PPARG with a predisposition to the development of power-speed / Biomedical technologies improve efficiency in the conditions of intense physical exertion. – 2007. 3, P.22-28.

32. Miller S.A., Dykes D.D., Polesky H.F. // A simple salting out procedure for extracting DNA from human nucleated cells / Nucleic Acids Res 1988. 16: P.1215.

33. Bondar I.A., Filipenko M.L., Shabelnikova O.Yu., Sokolova E.A.. // Association of polymorphism PPARG pro12ala rs1801282 marker with diabetes type 2 in Novosibirsk region and other population / Siberian medical journal, 2014. 29 (2), P.75-78.

34. Zyablitsev S.V., Mokriy V.Ya. Association of polymorphism 12Pro with diabetes type 2 / Clinical endocrinology and endocrine surgery. 2016. 3 (55), P.33-37.

35. Dujic T., Bego T., Mlinar B., Semiz S., Malenica V., Prnjavorac B., Ostanek B., Marc J., Causević A. // Effects of the PPARG gene polymorphisms on markers of obesity and the metabolic syndrome in bosnian subjects / Journal of Medical Biochemistry. 2014. 33(4), P.323-332.

36. Scacchi R., Pinto A., Rickards O., Pacella A., De Stefano G.F., Cannella C., Corbo R.M.. // An analysis of peroxisome

Published: December 24, 2021 | **Pages:** 1-11
Doi: https://doi.org/10.37547/tajas/Volume03Issue12-01
IMPACT FACTOR
2021: 5. 634
OCLC - 1121105553

proliferator-activated receptor gamma (PPAR-G2) Pro12Ala polymorphism distribution and prevalence of type 2 diabetes mellitus (T2DM) in world populations in relation to dietary habits. Nutrition / Metabolism & Cardiovascular Diseases. 2007. 17, P.632-641.