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# The Investigation of Relationship Between Sporting Performance and Mitochondria and Genes

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## Abstract

The aim of this study was to investigate the relationship between sports performance and mitochondria and gene. The study included the summarization of the studies registered in Pubmed-Central, Pubmed and Google Scholar internet databases. Sporting performance is a multifactorial phenomenon that is affected by most factors. Genetics, which are candidate to be one of these factors, may have a significant power on sports performance. So far, many genetic markers have been identified for the relationship between sport and genetics. These can be localized in the autosome, gonosome chromosomes and mitochondria. Mitochondria are a double-layered cell organelle with its own DNA, RNA, and ribosome. mtDNA has both fewer nucleotides and a smaller amount of genes compared to DNA in the nucleus. However, genes in mtDNA may be critical to athletic performance. At the end of the study, it was determined that haplogroups and some polymorphisms in mtDNA may be important regulators on sports performance. This can significantly determine the low, medium and high intensity performance characteristics of athletes. As a result, genes in mtDNA may have significant effects on athletes' endurance capacities by influencing mitochondrial biogenesis. Conducting clinical studies based on robust methodologies in this field may make valuable contributions to sports sciences.

***Keywords:*** *DNA, Gene, Mitochondria, mtDNA, Sport*

## Sportif Performans ile Mitokondri ve Gen İlişkisinin İncelenmesi


### Özet

Bu çalışmanın amacı, sportif performans ile mitokondri ve gen arasındaki ilişkinin incelenmesidir. Çalışma; Pubmed-Central, Pubmed ve Google Akademik internet veri tabanlarında yer alan kayıtlı çalışmaların özetlerini içermektedir. Sportif performans çoğu faktörden etkilenen multifaktöriyel bir fenomendir. Bu faktörlerden biri olmaya aday genetik, spor performansı üzerinde önemli bir güce sahip olabilir. Şimdiye kadar, spor ve genetik arasındaki ilişkiye yönelik birçok genetik belirteç tanımlanmıştır. Bunlar otozom, gonozom kromozomlarda ve mitokondride lokalize olabilir. Mitokondri kendi DNA'sı, RNA'sı ve ribozomu olan çift katmanlı bir hücre organelidir. mtDNA, çekirdekte bulunan DNA'ya kıyasla hem daha az nükleotitli hem de daha az gene sahiptir. Buna rağmen mtDNA'daki genler sportif performans üzerinde kritik öneme sahip olabilir. Çalışma sonunda mtDNA'daki haplogrupların ve bazı polimorfizmlerin sportif performans üzerinde önemli regülatörler olabileceği sonucu tespit edilmiştir. Bu durum, sporcuların düşük, orta ve yüksek şiddetteki performans karakteristiklerini önemli ölçüde belirleyebilir. Sonuç olarak, mtDNA'daki genler mitokondriyal biyogenezi etkileyerek, sporcuların dayanıklılık kapasiteleri üzerinde önemli etkilere sahip olabilir. Bu alanda sağlam metodolojilere dayalı klinik çalışmaların yapılması spor bilimlerine değerli katkılar sağlayabilir.



***Anahtar Kelimeler:*** *DNA, Gen, Mitokondri, mtDNA, Spor*

## Introduction

Sporting performance is a concept that expresses genetic, proper nutrition, training, adaptation, physiological, biomotor, physical, and mental efficiency (Kararkuş and Kılınç, 2006; Banfi et al., 2012). Sports are a phenomenon with multifactorial characteristics that is affected by many internal and external factors. Internal factors which have the power to affect sporting performance can be listed as age, gender, intelligence, anthropometry, anatomy, metabolic activities, autonomic nervous system, psychological balance and heredity. External factors can be listed as nutrition, ergogenic supports, training environment, clothing, sports fans, heat, light, climate, materials, social environment, injury history, coaches, spectators, etc. (Bayraktar and Kurtoğlu, 2004; Bayraktar and Kurtoğlu, 2009). Metabolic activities within these factors, which are subject to the physiological efficiency of the athlete, may have a critical importance for the success of the athlete. For this purpose, the function of mitochondria in the cell in relation to the physiological capacity of the athlete may be an important issue to be focused on. As the power source of the organism, mitochondria have a critical role in the supply of oxygen needed by cells, tissues and muscles for metabolism, especially aerobic endurance. Mitochondria play a key role in skeletal muscle bioenergy and cell function (Distefano and Goodpaster, 2018, Daussin et al., 2021; Flockhart et al., 2021).

Many studies have been conducted to improve performance in sports sciences (Aktop and Seferoğlu, 2014). Some of these research results have revealed that sportive performance limits may be related to genetic that has a considerable effect on endurance performance (Doğgün, 2022). In contrast to most of the factors that affect the endurance ability of the athlete for the relevant sport, some events of genetic origin occurring in the cell mitochondria can significantly differentiate the course of sporting performance. Accordingly, factors such as genetic factors, cardiovascular endurance, elite athlete status, muscle strength, genetic phenotypes of physical performance, and varying grades of exercise intolerance are highly effective on different skill conditions of athletes (Rankinen et al., 2001; Ahmetov et al., 2016).

To this end, the aim of current study was to investigate the relationship between sports performance and mitochondria and genes. We believe that the results obtained from this study will guide scientists working in this field.

## Methods

In this review, studies on the relationship between sports performance and mitochondria and genes were used. Pubmed-Central and Pubmed registered in the NCBI (National Center for Biotechnology Information) search engine, and Google Scholar database were scanned. In the review, 54 studies that can be accessed on the subject were used. Regarding sports performance, 40 of these studies are related to mitochondria, ROS (reactive oxygen species) and mitochondrial biogenesis. 14 studies focused on the effect of mtDNA genes on sports performance. The study was designed in the form of a traditional review. The study included experimental, meta-analysis, and review type research articles conducted in the relevant subject. Articles that were not original were excluded from the evaluation. The distributions of the documents obtained regarding the data used in the study are shown in Figure 1.

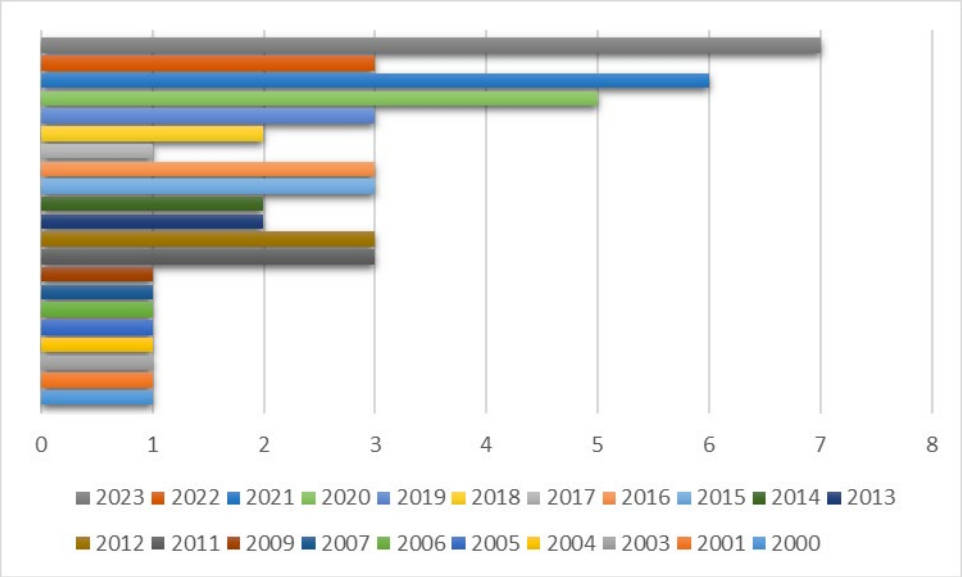


Figure 1 Distributions of the data used in the study for the years

As can be seen in Figure 1, there has been a significant increase in the studies on this field in recent years. In the review, the data obtained by typing the keywords mitochondria, mitochondrial biogenesis and sport, reactive oxygen species and sport, sport and genetic, mtDNA genes and sporting performance were evaluated.

## Mitochondria and Their Function in The Cell

Mitochondria are an important cell organelle that regulates many physiological functions such as cell signaling, ROS, calcium homeostasis, apoptosis, steroid hormone, iron mineral synthesis, oxidative phosphorylation, TCA (tricarboxylic acid) cycle, cell division, beta

oxidation of fatty acids, etc. (Kenney et al., 2013; Pérez-Treviño et al., 2020; Picca et al., 2021). Mitochondria, which are considered as the power plant of the eukaryotic cell, also have a key role in the production of ATP (adenosine triphosphate) which is the main source of chemical energy (Metin et al., 2020; Koma, et al., 2021). Mitochondria, which are a combination of the Greek words mitos (thread) and khondrial (grain), are a special cell structure with its own DNA, RNA, and ribosome with a double-layered membrane unlike other organelles (Eken et al., 2018). Mitochondria, which have their own unique ring-shaped DNA, encode 37 genes corresponding to 16,569 base pairs. Mitochondria, which have a lesser number of nucleotides than the DNA in the nucleus, functionally have a higher level of metabolic activity in terms of the genes they encode. This is especially important for energy production through oxidative phosphorylation, thermoregulation, calcium homeostasis, and the elimination of ROS (Thurairajah et al., 2018). Mitochondria are very important regulator in maintaining the physiological order of the cell. In this perspective, mitochondria have a key role in compensating for ATP in the peripheral blood circulation (Baykara et al., 2016). The fact that mitochondria have such an effect may make more vulnerable to mutation than DNA in the nucleus. Furthermore, mitochondria have the ability to carry information across the cell membrane by producing and releasing a variety of small molecules (Trumpff et al., 2021). Additionally, mitochondria have important roles in food physiology and biochemistry. For this purpose, mitochondria convert carbohydrates and fats into CO2 and H2O, which are metabolic wastes, through the electron transport chain in their inner membrane (Akın et al., 2021).

Mitochondria, which play a key role in many physiological processes, are a cell organelle inherited from generation to generation. For this reason, mitochondria are a maternally inherited cell organelle and the majority of their proteins are nuclear encoded (Allemailem et al., 2021). The number of maternal mitochondria is influenced by a number of biological processes that take place during the moment of sexual reproduction. For example, sperm from the father contains between 100 and 1.000 mitochondria, whereas the egg cell of the mother contains between 100.000 and 1.000.000 mitochondria. In addition, during the fertilization of theegg by the sperm, only the DNA belonging to the nucleus is transferred into the egg and the organelles of the sperm cannot reach the zygote, which causes some losses in the total number of mitochondria (Koç and Sarıca, 2003). As a result, the number of maternal mitochondria remains unchanged. For this reason, the quality and number of mother's mitochondria may have a great importance on mitochondrial endurance capacity due to aerobic respiration. For this purpose, the low number of mitochondria in male individuals compared to

female individuals may suggest that males may have a more sensitive metabolism against gender-related mitochondrial disorders.

**Mitochondria and Reactive Oxygen Species and Their Interaction with Exercise**

Free radicals are structures with unpaired electrons in their orbitals. ROS, which are the type of these radicals, have a dual role in cell physiology, especially in redox reactions, reduction-oxidation. The ROS that constitute free radicals consist of hydroxyl, superoxide, lipid peroxyl, peroxyl, and alkoxyl. Excessive secretion of ROS in metabolism can cause a number of diseases by exerting pathogenic effects in some cases. In contrast, adequate ROS release is critical for the healthy maintenance of certain biological processes, including gene expression (Karabulut and Gülay, 2016; Giorgi et al., 2018). The radical and nonradical types of ROS realized in the ETS (electron transport system) at the end of the TCA (Tricarboxylic acid cycle) process of metabolism are shown in Figure 2 (Büyükuslu and Yiğitbaşı, 2015).

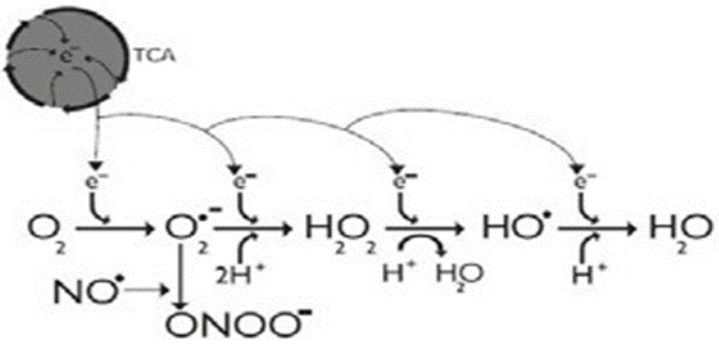


Figure 2 Differentiated radical and nonradical species of ROS at the end of TCA

In Figure 2, the changes that oxygen changes in the process of pairing with electron molecules are shown from left to right as superoxide, nitric oxide, peroxynitrite, hydrogen peroxide, hydroxyl, and water.

The main purpose of physical activity is to improve personal health and physical capacity (Malm et al., 2019). During these activities, the oxygen consumption and the release of ROS increase importantly as simultaneously (Yamada et al., 2020; Clemente-Suárez et al., 2023). The increase in ROS levels with exercise significantly impairs the physiological functioning of mitochondria. The increase in oxidative stress levels in mitochondria in parallel with rising exercise load activates a number of mechanisms in the regeneration of mitochondria. Nuclear genomes, one of these regulatory mechanisms, are very important in the development of mitochondria. If this need cannot be met, oxidative stress, which increases due to the release of ROS, can reach critical levels (Doğan and Çoban, 2023). In the end of this process, some

functional impairments can be seen in mitochondria. Disruptions in mitochondria due to ROS release may also negatively affect the function of mitochondria in the aerobic energy system over time and may cause serious losses in sportive performance. On the contrary, low and moderate ROS production will positively affect sports performance and improve adaptation to muscle endurance (Lewis et al., 2016). Increased release of ROS at the mitochondrial level causes disruptions in the functions of the basic macromolecules used by metabolism in aerobic energy production. The release of ROS significantly disrupts the chemical structures of lipids, proteins, and nucleic acids (Güleç, 2017). This can affect metabolic processes, and it causes the formation of free radicals (Gönenç, 1997).

**Mitochondrial Biogenesis and Reflects on Sport**

Throughout exercise, ATP is a crucial chemical compound for sustainable performance. Oxidative phosphorylation has an important role during ATP production. ATP synthesis through oxidative phosphorylation is essential for prolonged exercise (Niemi and Majamaa, 2005). This makes mitochondria important in exercises. As a result, mitochondria enzyme activity increases aerobic capacity in sports (Yıldız, 2012). This effect of mitochondria on the aerobic system has a key role in the synthesis of ATP, which has an important function in muscle contraction mechanisms. Increased load with exercise results in significant decreases in ATP stores. Decreases in ATP stores at the end of sporting performance cause the activation of some mitochondrial mechanisms, especially the stimulation of mitochondrial biogenesis. NRF1 (nuclear respiratory factor 1), PGC-α (peroxisome proliferator-activated receptor gamma coactivator-1α), and TFAM (mitochondrial transcription factor A) proteins are important agents on this mechanism (Şahin and Alver, 2022).

Mitochondrial biogenesis is a process in which 13 proteins encoded by mtDNA and more than 1000 nuclear-encoded mitochondrial proteins are regulated at the transcriptional level (Morrish and Hockenbery, 2014). Mitochondrial biogenesis plays a key role in the formation of new mitochondria in cells (Purhonen et al., 2023). In particular, regular exercise positively affects the efficiency of mitochondrial biogenesis in metabolism by increasing the level of mitochondria in muscle cells and the ability to synthesize ATP (Ohlsson et al., 2020). Exercise is a series of movements that have positive effects on mitochondrial function (Taivassalo and Haller, 2004). The effects of exercise on cell mitochondria may also increase the mechanical work capacity of muscles. Additionally, this may have positive effects on muscle diseases. It may be particularly critical in the treatment of myopathy, which has a

devastating effect on muscle. A study by Taivassalo et al. (2006) found that exercise has many potential benefits in patients with mitochondrial myopathy. In another study, Safdar et al. (2011) concluded in their study that endurance exercise may be an effective method to reduce mitochondrial disorders.

**Relationship between Sporting Performance and Genetics**

Physiological limits have made it necessary to investigate in depth some of the factors that affect sports performance. Genetics, which is a candidate to be one of them, may be a factor that determines the biological and physiological limits of human beings. Genetics explains many physiological and biological factors of human beings (Karayılan et al., 2013). The effect of genetic factors in the development of sporting performance has been confirmed by some studies in this field (Dinç and Gökmen, 2019). For this reason, many gene variants that may be effective on sportive performance have been defined. So far, many genetic markers have been identified for the relationship between sport and genetics. Some of them are automosal and others are mitochondrial and on the X chromosome (Eroğlu and Zileli, 2015). Additionally, studies have shown that there are also gene polymorphisms localized on the Y chromosome (Koku, 2015). Some of the genes polymorphisms that are assumed to have an effect on sporting performance are associated with strength, power, flexibility and soft tissue injuries, while others are associated with endurance and increased VO2 max capacity. Genetics is a direct influence on physical performance in many sports branches and is associated with phenotypes such as aerobic capacity, muscle strength and power (Baltazar-Martins et al., 2020). Some genes that may be associated with sporting performance are shown in Table 1 (Ahmetov et al., 2022; Varillas-Delgado et al, 2022; Kahya, 2023; Semenova et al., 2023).

Table 1

Characteristics of some genes studied associated with sporting performance

| Gene | Full name | Location | Polymorphism |
|---|---|---|---|
| *ACE* | Angiotensin Converting Enzyme | 17q23.3 | rs4646994 |
| *ACTN3* | Actinin Alpha 3 | 11q13.1 | rs1815739 |
| *AGT* | Angiotensinogen | 1q42.2 | rs699 |
| *AMPD1* | Adenosine Monophosphate Deaminase 1 | 1p13 | rs17602729 |
| *COL5A1* | Collagen V Alpha I | 9q34.3 | rs12722 |

| | | | |
|---|---|---|---|
| *IGF2* | Insulin-Like Growth Factor II | 11p15.5 | rs680 |
| *MYBPC3* | Myosin-Binding Protein C 3 | 11p11.2 | rs1052373 |
| *NOS3* | Nitric Oxide Synthase 3 | 7q36.1 | rs1799983 |
| *PPARA* | Peroxisome Proliferator-Activated Receptor Alpha | 22q13.31 | rs4253778 |
| *PPARGC1A* | Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1-Alpha | 4p15.2 | rs8192678 |
| *UCP2* | Uncoupling protein 2 (Mitochondrial, Proton Carrier) | 11q13.4 | rs660339 |
| *UCP3* | Uncoupling protein 3 (Mitochondrial, Proton Carrier) | 11q13.4 | rs1800849 |

## Effects of mtDNA Genes on Sporting Performance

There has been a significant increase in studies on the relationship between exercise and mtDNA, recently (Zanini et al., 2021). Although mitochondria have many factors that may affect the balance of energy production, some subproteins of mtDNA, 13 mRNA, may have a key role in sporting performance. For this reason, mitochondria may have a positive effect on endurance performance in sport and may significantly improve the athlete's sporting performance and efficiency capacity. To this end, aerobic and athletic capacity may be a condition in the control of genes in mtDNA. Studies have shown that some mtDNA genes affect the body's energy balance through physical activity and this may be especially important in obesity. It is known that MOTS-c peptide in mtDNA is stimulated by exercise and SMORF (small open reading frames) activated from mitochondrial 12S rRNA has an important effect on this peptide (Kumagai et al., 2023; Wan et al., 2023). (Figure 3-4).

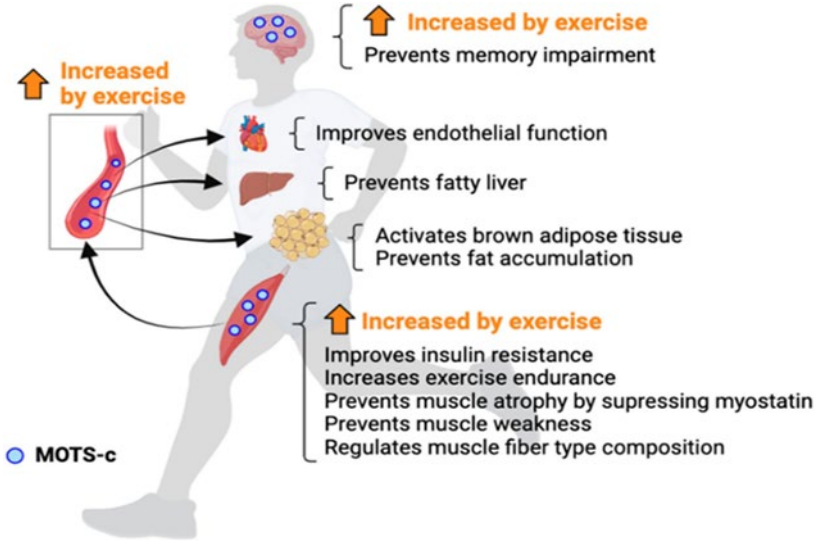

Figure 3 Effects of MOTS-c on exercise association and metabolism

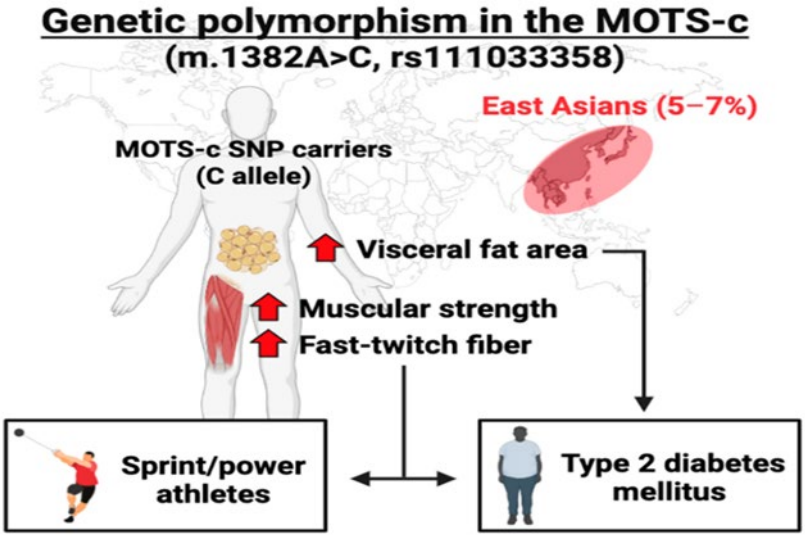


Figure 4 Some features of MOTS-c rs111033358 polymorphism

Regarding the relationship between sporting performance and mtDNA, Maruszak et al. (2014) concluded in their study that mtDNA haplogroups and some polymorphisms localized in the control region of mtDNA may be associated with endurance performance. Mikami et al. (2012) concluded in their study that m.152T>C, m.514 (CA) repeat and m.568-573 polymorphisms in the mtDNA control region of endurance and intermediate strength athletes showed statistically significant differences compared to the control group. In the same study, it was observed that m. 204 T>C polymorphism was found with a higher frequency in mtDNA control areas in athletes with sprint performance. In another study by Castro et al. (2007) it was concluded that mitochondrial haplogroups may be associated with elite level endurance performance in sports. Additionally, they found that the rs13368A allele may be associated with low-level endurance. Fritzen et al. (2019) concluded in their study that endurance training and mitochondrial genomes may be interrelated structures. Kiiskilä et al. (2019) reported that mtDNA genes were different the in terms of endurance and strenght/power performance. In another study by Nogales-Gadea et al. (2011) it was found that mitochondrial V haplogroup may be associated with elite level endurance performance. To this end, it is thought that gene regions of mtDNA are generally associated with endurance performance. This happens when mitochondria provide the energy necessary for endurance. Genes, however, in mtDNA may not only determine performance characteristics for long-term endurance in sport. Mitochondria and the gene variants within them may meet the urgent energy needs of the athlete, during moderate-intensity sporting activities. For this purpose, Kim et al. (2012) concluded in their study that

mtDNA specific haplogroups, M and N9, may be gene variants associated with moderate intensity power sports.

The haplogroups in mtDNA related to sporting performance may significantly influence the level of performance by creating antagonistic effect. Scott et al. (2009) concluded in their study that the mtDNA haplogroup distribution of international athletes belonging to the Kenyan population was relatively different and this was expressed as low L3 haplogroup and high L0 haplogroup.

Regarding the influence of genes in mtDNA on endurance performance in sports, the athlete's VO2 max capacity may play a critical role. Although VO2 max capacity is significantly affected by mitochondrial biogenesis, gene expressions of mtDNAs may have an important effect on mitochondrial biogenesis. Some studies have shown that mtDNA genes with sedentary individuals may affect on aerobic performance. For this purpose, Eynon et al. (2011) concluded in their study that mtDNA genes, which have non-athletes, contributed positively to aerobic performance depending on their VO2 max consumption status. In contrast to this study, Murakami et al. (2001) did not find any statistical relationship between mtDNA polymorphism and endurance capacity in young sedentary people.

Mitochondria, which have very important effects on sporting performance, are nowadays closely associated with the concept of elite level. To this end, Chen et al. (2000) concluded in their study that sequence variants (D-loop) in the start region of mtDNA may be associated with elite level sporting performance.

**Conclusion**

In the current study, it was found that haplogroups and some polymorphisms in mtDNA may be important regulators on sports performance. This can significantly determine the low, medium and high intensity performance characteristics of athletes. As a result, genes in mtDNA may have significant effects on athletes' endurance capacities by influencing mitochondrial biogenesis. It was considered that the results obtained from the study may present significant contributions to the athletes and coachs. Conducting clinical studies based on robust methodologies in this field will make valuable contributions to sports sciences.

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