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Genetic Markers Associated with Predisposition to Development of Endurance in Athletes

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Abstract This review considers polymorphisms of some genetic markers associated with a predisposition to the development of endurance. Candidate genes for the manifestation of endurance in sports activities are described.

Keywords GWAS, Athletes, Endurance, Genotype, Polymorphism

1. Introduction

It is recognized that individual variability in aerobic performance and the ability to become an elite endurance athlete have a direct genetic predisposition. A large amount of evidence suggests that genetic markers can explain, in particular, the variability in aerobic performance in response to endurance training [2,3]. With the availability of research on genotyping by scientists, a large number of works have been published in which variants of candidate genes have been evaluated, mainly with hypotheses confirming the connection with the status of an elite athlete [1,4,5].

The aim of this systematic review is to evaluate some of the genetic variations and polymorphisms in endurance, muscle strength, and injury susceptibility in competitive sports. This review summarizes the understanding of the relationship between DNA polymorphisms and athletic performance of candidate genes for athletic performance endurance. The search for suitable studies was carried out in the electronic databases PubMed and Web of science.

Endurance or aerobic performance is a person's ability to perform prolonged physical activity of moderate intensity with energy supply, due mainly to oxidative phosphorylation reactions. The lower the level of endurance, which is most often determined by the level of the maximum rate of oxygen consumption by the body (MOC), the more significant the risk factors for mortality, regardless of gender, ethnicity and the presence of diseases [55,56]. In people leading a sedentary lifestyle, aerobic performance is significantly reduced, while in highly qualified athletes training endurance (stayers and intermediates of the MSMK and ZMS qualifications), it is at an extremely high level [57]. The level of human aerobic performance is most determined by the ability of the cardiovascular system to deliver oxygen to working muscles (stroke volume of the heart, hemoglobin mass and volume of circulating blood, capillary density of skeletal muscles and myocardium) and the ability of working muscles to utilize the delivered oxygen (oxidative capacity of muscles / mitochondrial density) [58].

Although increased physical activity is the main reason for improving endurance, there is growing evidence that the initial level of aerobic performance, as well as the response to regular aerobic exercise, varies significantly in different people and is genetically determined [59]. A high initial level of aerobic performance indicates a great giftedness of both a professional and a novice athlete in endurance sports.

Genome -wide association research (GWAS) is a novel approach that involves rapidly scanning several hundred thousand (up to 5 million) markers in complete sets of DNA from many individuals in order to look for genetic variations associated with a particular trait. One of the advantages of the GWAS approach is that it is unbiased with respect to genome structure and prior knowledge of a trait (no hypotheses), unlike candidate gene studies where knowledge of a trait is used to identify candidate loci that contribute to the identification of a sport of interest. [2,6].

Understanding the genetic determinism of sports results brings clarity to the development of approaches to identifying sports talents. Studies related to molecular predictors have identified a number of potentially important DNA polymorphisms that contribute to a predisposition to success in certain sports. A literature search (period: 1999-2021) showed that at least 120 genetic markers are associated with elite athlete status (77 endurance-related genetic markers and 43 power/strength-related genetic markers). Notably, 11 (9%) of these genetic markers (endurance markers: ACE I, ACTN3 577X, PPARA rs4253778 G, PPARGC1A Gly482; power/strength markers: ACE D, ACTN3 Arg577, AMPD1 Gln12, HIF1A 582Ser, MTHFR rs1801131 C, NOS3 rs2070744 T, PPARG 12Ala) showed a positive association with athlete status in three or more studies and six markers (CREM rs1531550 A, DMD rs939787 T, GALNT13 rs10196189 G, NFIA-AS1

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rs1572RBFOX1 C, NFIA-AS1 rs1572RBFOX1 rs719172) were identified after conducting genome-wide association studies (GWAS) of athletes from different countries [1,7]. On the other hand, the significance of 29 (24%) markers has not been replicated in at least one study. Throughout this period, scientists have been aware of the need for further research, including multicenter GWAS, whole genome sequencing, epigenetic, transcriptomic, proteomic and metabolic profiling, as well as meta-analyses on large cohorts of athletes, before these results can be disseminated in sports practice [6,7].

The available literature describes at least 48 genetic markers associated with the development and expression of endurance. These markers are localized in genes, mtDNA and Y-chromosome and were found as a result of case-control studies (athletes-control group). Some of them have been studied in the scientific and practical center of sports medicine of Uzbekistan [8]. A brief description of some of the gene markers recognized in the context of human physical performance endurance is presented below:

ACE localization 17 q 23.3 Alu polymorphism I / D endurance marker I. To date, a lot of data has been accumulated on the association of *ACE gene polymorphism* (D allele) [9]. The gene encoding angiotensin -converting enzyme is the most studied as a "performance gene", associated with endurance, sprinting, as well as other morpho and phenotypes of strength and high performance. The circulating ACE gene has a tonic regulatory function in circulatory homeostasis. A polymorphism (rs1799752) of the gene was identified Human ACE (17q22-q24), in which the presence (insert, allele I), and not the absence (deletion, allele D) of the insert fragment of the Alu - sequence 287 bp long. with lower ACE activity in serum and tissues. Akhmetov in his work showed that an excess of the I allele was associated with some aspects of endurance [1,10]. Similarly, several studies have shown that the ACE D allele is associated with greater strength and muscle size at baseline, as well as an increased percentage of fast twitch muscle fibers. In addition, the allele ACE D has been associated with elite strength athlete status [11,12]. It is associated with the risk of developing: myocardial infarction, arterial hypertension, LVH, hypertrophic cardiomyopathy, obesity, kidney disease and vascular complications of type 2 diabetes, including in athletes [11,13].

ACE is the most studied gene in the genetics of physical activity (more than 60 publications). *The* ACE *I* allele is associated with predisposition to types of physical activity associated with endurance and resistance to hypoxia in various conditions. Thus, the predominance of the ACE I allele (or ACE II genotype) compared to the control group (or sprinters) was found in stayers (running 5000 m or more) and described by S. Myerson et al. back in 1999 [14]. This allele is also associated with high mechanical efficiency of skeletal muscles [11].

ADRB2 16Arg gene allele in 10q24-q26 localization of β-2 adrenergic receptor, 6.7/6.3 kb polymorphism, 6.7-kb endurance marker. β-2 adrenergic receptors as members of G-protein receptors are involved in the expression and regulation of complex functions of the endocrine, cardiovascular, pulmonary, and central nervous systems. [15-16] Being localized in adipose tissue, the β-2 adrenergic receptor is forced to stimulate the breakdown of glycerol and free fatty acid triglycerides, which affect energy expenditure and lipolysis processes. [sixteen]. The Gly16Arg polymorphism (rs1042713 G/A) associated with decreased bronchodilation, resting cardiac output, decreased systolic blood pressure, and reduced risk of obesity [17,18] is located in the 1st exon of the ADRB2 gene. Researchers working in the framework of the project " Genathlete Study » found a prevalence of frequency compared to the control group in elite athletes in the endurance group. Thus, the 16Arg allele can be associated with a predisposition to the development and manifestation of endurance [1,15,17,18].

AMPD1 - Gln12 allele of the AMP deaminase gene in the 1p13 localization of the Gln12Ter polymorphism (rs17602729 C/T), Gln12 endurance marker. During intense physical exercise, the ATP content in muscle fibers decreases to ~50%, and AMP accumulates in them. Akhmetov [1] described the myokinase mechanism of anaerobic ATP resynthesis in skeletal muscles, where the activation of the AMP deaminase enzyme catalyzes the process of AMP deamination (2), resulting in the formation of IMF and ammonia, a biochemical indicator of the intensity of physical exercise. The irreversible reaction catalyzed by AMP deaminase shifts the balance of the myokinase reaction towards the formation of ATP due to the provision of ATP resynthesis during cell muscle fatigue. Due to the accumulation of AMP, AMP- protein kinase is activated, which causes increased fat oxidation, thereby accelerating the intensity of glucose transport in muscle cells. Adenosine monophosphate deaminase (AMPD1) is the most powerful and important regulator of muscle energy metabolism during physical activity. AMPD1, also known as myoadenylate deaminase, is predominant in all skeletal muscle fibers. The gene encoding this skeletal muscle-specific isoform (AMPD1) is located on chromosome 1 (1p13). AMPD1, which mainly expressed in fast-twitch (type II) muscle fibers. Differential expression of the AMPD1 gene may contribute to quantitative variations in enzyme activity in muscle groups with different fiber types. The so-called c34 C>T nonsense mutation (C to T transition at nucleotide 34, p.Gln12X, rs17602729) in exon 2 of the AMPD1 gene turns the glutamine codon (CAA) into a premature stop codon (TAA), which leads to the cessation of protein synthesis, being the main cause of AMPD deficiency [19]. As described *by R. Grealy* and co-authors [18], this polymorphism (rs17602729) in the AMPD1 gene is a common polymorphism among representatives of the Caucasian race, which can impair exercise tolerance. The AMPD1 *C* allele may help athletes achieve elite status in strength sports [1,18,19]. Thus, energy metabolism in the work of skeletal muscles is regulated by AMP deaminase [19].

BDKRB2 9th allele of the bradykinin receptor β2 gene

localization 14q32.1-q32.2. Bradykinin - a polypeptide belonging to the group of kinins, formed during the activation of the kallikrein-kinin system of the blood. Angiotensin-I-converting enzyme (ACE) converts angiotensin - I to angiotensin - II and breaks down bradykinin into inactive enzymes. Inhibition of this enzyme attenuates the degradation of kinins and enhances the action of kinins in many pharmacological studies. Kinins are very potent vasodilating peptides that lower blood pressure by lowering vascular resistance. Under experimental conditions in vitro kinins mediated many metabolic and hemodynamic effects of ACE inhibitors that affect the vascular system [20]. The genes for the kinin -inducible B1 receptor (B(1)R) and the constitutive B2 receptor (B(2)R) contain functional variants: B(1)R-699C (rather than G) and B(2)R. Alleles (-9) (rather than +9) are associated with greater expression of mRNA, and allele B(2)R(-9) with a reduced hypertrophic response of the left ventricle [1,21]. Bradykinin helps to reduce vascular tone and blood pressure. Further, the permeability of capillaries increases, it contributes to the contraction of the smooth muscles of the bronchi and other organs. Bradykinin, by increasing the stroke volume of the ventricles, helps protect myocardial cells from ischemia. Also, having an insulin-like effect, it stimulates the transfer of glucose by peripheral tissues, the same mechanism is observed in the transmission of nerve impulses to the CNS and the peripheral nervous system [22].

bradykinin receptor is expressed in the endothelium and other tissues and is encoded by the *BDKRB2 gene* (localization: 14q32.1-q32.2). In the research of Akhmetov I. in 2008, it was described that the presence of the *BDKRB2* –9/–9 genotype showed an advantage in elite rowers in a 1000 m race compared to carriers of the +9/+9 genotype [22]. In the work of A.G. Williams et al (2004) showed that the *BDKRB2-9* allele is associated with increased muscle contraction efficiency. In the same study, on the example of British athletes, an increase in the frequency of the *BDKRB2* –9 allele was observed with an increase in the length of the profile distance of athletes [26]. The BDKRB2 +9 allele is associated with the risk of developing myocardial hypertrophy in athletes in response to prolonged physical activity [23,26]. Thus, the BDKRB2 –9 allele is associated with high physical performance and endurance.

HIF 1A _ hypoxia-induced factor 1 gene in localization 14 q 21 - q 24 polymorphism Pro 582 Ser (rs 11549465 C / T), endurance marker Pro 582 is a transcriptional regulator of gene expression that ensures cell adaptation to hypoxia. The HIF-1 heterodimer consists of subunits HIF-1 and HIF-1. The expression *of HIF-1 A* and the level of this protein is related to the concentration and partial pressure of oxygen in the blood; what is the reason that the activity of HIF- 1 increases in the state of hypoxia [24]. The gene expression is highest in fast glycolytic muscle fibers compared to slow fibers [25]. *HIF 1 A* is involved in glycolysis (genes for phosphofructokinase, phosphoglycerate kinase, aldolase, actate dehydrogenase, pyruvate kinase), vascular endothelial growth factor *(VEGF),* glucose transport (glucose transporter genes of the GLUT family), and angiogenesis (erythropoietin genes *(EPO),* type 1 VEGF receptor 120 [5,16]. In the *HIF1A gene* encoding subunit 1 of the hypoxia factor, a Pro582Ser polymorphism was found, which is a replacement of cytosine for thymine in the 12th exon in the localization: 14q21-q24), (rs11549465 C/T), which leads to an increase in the transcription activity of the gene allele, increases cell resistance to hypoxia, promotes anaerobic provision of muscle activity, which reduces the aerobic capacity of the body. Other researchers have described data on the association of the *HIF1A* 582Ser allele with a low increase in BMD as a result of physical activity in an untrained group and a predominance of fast muscle fibers in rowers [3,24].

PPARA Rs 4253778 G allele of the gene, activated by proliferators peroxisomes (PPAR) family of nuclear receptors. *PPARA* Rs regulates transcription and encodes promoter proteins of carbohydrate and fat metabolism genes that specifically bind to PPAR-responsive elements. In humans, these proteins do not cause peroxisome proliferation, but in all vertebrate organisms they are referred to as PPARs [27]. Transcription factors that control the expression of several dozen genes are included in the metabolism of carbohydrates and fats. The mechanism of regulation consists in increasing the activity of some genes and suppressing the activity of others. The *PPARA, PPARG,* and *PPARD genes* encoding human PPAR proteins are located on different chromosomes, although they have a similar structure. They consist of 6–8 coding exons, one of which carries information about the N-terminal A/B domain, the other two about the zinc components of the DNA-binding domain, the fourth about the core region, and two about the ligand - binding domain [27,28]. Gene *PPARGC1A* (*PGC1A*; localization: 4p15.1) Gly 482 allele. During prolonged physical exertion, the intensity of metabolic processes in the myocardium and skeletal muscles increases due to an increase in the number of mitochondria in cells and FA oxidation. Long-term aerobic training (eg marathon or 10,000 m) is dependent on circulating free fatty acids and glucose. In contrast, short-distance sprinting and power competitions rely on anaerobic pathways that are particularly mediated with intramuscular creatine phosphate, ATP, and glucose stores. PPARD and *PPARGC1A modulate* the expression of several genes that are involved in the metabolism of free fatty acids and carbohydrates and play an important role in the regulation of energy supply to the skeletal muscles of athletes in the aerobic pathway [28].

PPARGC1A encoding PGC-1 PPAR coactivator. It makes a significant contribution to the occurrence of metabolic changes, the level of expression of which depends on the increasing demands of tissues in the oxidative phosphorylation of substrates. D. _ Krämer *conducted* surveys of elite cyclists in 2006 and showed that the expression of the PPARGC1A gene in skeletal muscles over long distances is significantly higher relative to the control group [29]. The intensity of metabolic processes in myocardial cells and skeletal muscles during prolonged

physical exertion increases significantly due to increased oxidation of fatty acids and an increase in mitochondria in cells. Impact on transcription factors triggers the activation of thermogenesis processes. increases insulin secretion and catabolic effect on fat mass, stimulates the formation of mitochondria, enhances oxidative processes by inducing *UCP2* and *TFAM;* regulation of the composition of muscle fibers regulation of glucose transport, gluconeogenesis, lipo- and chondrogenesis [29,30]. As a result of treatment with unsaturated fatty acids, the expression of the *PPARGC1A* gene increases, while saturated fatty acids do not have such properties. PPARGC1A along with *PPARA* exhibits activation in the myocardium, with a switch of metabolism from carbohydrate to fat. Fasting also contributes to the increase in PPARGC1A expression [1,31,32]. Putative connection of the *PPARGC1A* genotype Gly / Gly + *PPARD* CC on endurance is supported by the fact that the PPARGC1A protein controls muscle plasticity, suppresses inflammatory responses, suggesting that higher expression of *PPARGC1A* and *PPARD* contribute to increased endurance athletes due to significant oxidative stress and inflammatory response caused by intense exercise on endurance, which leads to a significant decrease in the ability to recover during the training process [32].

UCP2 gene 55Val allele of the gene for uncoupling protein 2. Uncoupling proteins UCP1, UCP2, UCP3, UCP4 belong to the family of mitochondrial transporters and are proteins of the inner membrane in organelles. UCP2 is involved in the regulation of fat metabolism and energy expenditure, in the processes of thermogenesis, protection against reactive oxygen species, insulin secretion, and neuroprotection [33]. Expression of the *UCP2 gene* at 11q13 is observed in the heart, lungs, adipose tissues, kidneys and liver, pancreatic cells, and to a lesser extent in skeletal muscles and nervous tissue. In response to aerobic training in human skeletal muscles, the expression of the *UCP2* gene increases. It was found that the most studied gene polymorphism in *UCP2* is the Ala55Val (rs660339C/T) variation. The *UCP2* 55Val allele is associated with high metabolic efficiency of muscle activity and physical activity. In this case, the *UCP2* 55Val allele can be considered as an allele that favors the manifestation of endurance. Since carriers of the Val / Val genotype are at risk of developing metabolic disorders, they are recommended to be highly physically active throughout their lives [34].

UCP3 Rs1800849 T allele of the uncoupling protein 3 gene. Thermogenins are proteins involved in the function of uncoupling oxidation and phosphorylation in the myocardium, mitochondria of skeletal muscles, brown adipose tissue. Oxidation of the respiration substrate occurs. bypassing the phosphorylation reaction, and energy is released in the form of heat [33]. UCP3 at localization 11q13 is encoded by the *UCP3 gene.* It takes part in the transport of fatty acids, thermoregulation, maintenance of glucose homeostasis, neutralization of lipid-induced oxidative stress of reactive oxygen species that damage mitochondria. The polymorphism (rs1800849 C/T) found in humans in the promoter of the UCP3 gene *–55C* /T is the most functionally significant and affects the level of *UCP3 expression.* It has been shown that the carriage of the rarer *UCP3* T allele is associated with high gene activity, low body mass index, reduced fat deposition, and increased levels of high-density lipoproteins. *The UCP3* T allele is also associated with high aerobic capacity in rowing athletes [35,36]. Studies were conducted in rowers, where the determination of aerobic performance indicators in men (academic rowers) showed that carriers of the *UCP3* T allele, on average, show the results of the BMD by 1 l/min more than athletes with the *UCP3* CC genotype [36]. The relationship of the *UCP3* T allele was shown in the same group of athletes in relation to the thickness of the interventricular septum during a one-year training cycle [37,38].

The increase in maximum oxygen consumption (MOC) due to strength training is due to maximum blood flow and a higher density of muscle capillaries in active tissues. In the muscles of the legs of athletes involved in cyclic sports, the number of capillaries can be 5–30% more, and the ratio of the number of capillaries to the number of muscle fibers is 50% higher than in sedentary individuals. Individual differences in the degree of adaptive changes in the form of growth of blood vessels in skeletal muscles and myocardium are largely due to genetic factors that determine hereditary predisposition to perform physical activity of varying intensity and duration [38].

HFE H 63 D. The *HFE gene* is a homeostatic regulator of iron, which is a protein encoding a gene located on chromosome 6. The protein regulates iron absorption and the interaction of the transferrin receptor with transferrin itself. TFRC, the transferrin receptor, is coupled to the HFE protein, so its main mechanism of action is to regulate the iron-storing hormone hepcidin. Individuals with one (C/G or H63D genotype) or two (G/G or D63D genotype) missense mutations of the H63D polymorphism (also known as His63Asp or rs1799945 C/G) show higher circulating iron concentrations than individuals without the mutations. In the group of H63D carriers, there was a positive correlation between iron and hemoglobin [39]. Given the importance of iron and hemoglobin for athletic performance, it can be hypothesized that the HFE H63D gene could confer a real advantage in endurance sports. As shown in a study [40], the HFE allele rs1799945 G (63D), which increases iron levels, is favorable for endurance. In a functional study of Russian athletes, it was confirmed that the G allele was associated with increased VO 2max in men involved in endurance sports. It was found that the favorable effect of the HFE A allele G on aerobic capacity and the ability to become an endurance athlete is mediated through its effect on hematological parameters such as hematocrit, mean concentration of corpuscular hemoglobin, hemoglobin amount, and reticulocyte count [42]. Previous studies in athletes have also shown that variations in genes regulating hematological traits are associated with the athlete's aerobic capacity and endurance [41,42].

MYBPC 3 (rs1052373). A more recent 2020 study by Al -

Khelaifi et al reported the first significant GWAS SNP (rs1052373) in MYBPC3 in relation to endurance athlete status related to cardiac hypertrophy. SNP is also associated with elevated levels of the testosterone precursor androstenediol (3beta, 17beta) disulfate, with elevated VO_{2max}. Both phenotypes have been shown to be associated in promoting superior performance in endurance athletes [43]. Significant identified SNP GWAS (rs 1052373) is located in the gene *MYBPC 3*. *MYBPC3* encodes a myosin-associated protein that is expressed in the cross-bridge region (region C) of the A bands in striated muscle. Phosphorylation of the MYBPC3 protein modulates cardiac contraction [41,44]. Mutations in *MYBPC3* have previously been associated with a lower hyperrelaxation state in patients with hypertrophic cardiomyopathy (HCM) [45]. Intense exercise promotes the remodeling process of the heart by compensating for increases in blood pressure or volume by increasing muscle mass. Therefore, the sports heart is characterized by its specificity. Endurance athletes typically exhibit eccentric cardiac hypertrophy with increased cavity size and wall thickness [46]. There is a correlation dependence on the type of sport performed. As a result, it can be observed that an endurance-trained athlete's heart can provide maximum systolic volume (35% more than an untrained heart) to provide a large cardiac output. Since carriers of the GG allele exhibit a benign HCM phenotype according to the ClinVar NIH database [47], the mild phenotype may enhance exercise-induced physiological adaptation. The dominant effect of rs1052373 GG on increasing VO_{2max} and endurance may support this additional benefit. However, it should be noted that these adaptations may be associated with an increased risk of cardiovascular disease. A group of scientists led by L. Carrier described that in more endurance athletes with high demands on the cardiovascular system (high blood pressure and stroke volume), metabolic signs correspond to a higher risk of cardiovascular disease [48].

NR1H3 rs7120118, TT endurance marker. Rs7120118, located in the *NR1H3 gene*, which codes for the nuclear receptor. Responsible for the regulation of lipid homeostasis, macrophage function, inflammatory foci. C. _ Cummins et al found a significant association between rs7120118 TT carriers and high endurance. NR1H3, also known as X receptor alpha (LXRA) in the liver. Responsible for the regulation of cholesterol homeostasis, including the formation of adrenal steroidogenesis [49]. In 2011, Handa et al found that the high endurance association of rs7120118 could reveal a linkage disequilibrium ($r2$ =0.89, P <0.0001) between rs7120118 TT and functional rs1052373 GG. Since NR1H3 is involved in the regulation of pituitary-hypothalamic-adrenal steroidogenesis, it has been suggested that this may be due to increased synthesis of the testosterone precursor 5alpha-androstane-3alpha, 17alpha-diol disulfate [50]. The reason for the increase in the levels of several steroidal sex hormones involved in testosterone synthesis, including 5alpha-androstane-3alpha, 17alpha-diol disulfate [51] in high-endurance athletes, as indicated in numerous previous studies, is an increase in physical performance through protein synthesis in muscles and accelerate glucose metabolism [51,52].

NFIA gene - AS 2 NFIA genotype - AS 2 rs 1572312 encodes RNA (lnc - RNA) - a long non-coding part. NFIA, being a transcription factor, induces erythropoiesis, while its suppression triggers the process of granulopoiesis [53]. Akhmetov and other researchers have shown that the C allele of NFIA-AS2 rs1572312 is associated with an increase in hemoglobin levels, an increase in the number of reticulocytes and erythrocytes, and activation of erythropoiesis, while the A allele is associated with a high number of neutrophils and an increased ratio of leukocytes to erythrocytes. Thus, these results indicate an allele association WITH *NFIA-AS2* rs1572312 with erythropoiesis activation, and the A allele with activated granulopoiesis. Thus, erythropoiesis, a factor affecting aerobic capacity, contributes to the function of the ability of the rs1572312 polymorphism of the NFIA-AS2 gene to work at a high level in endurance sports [41,53].

The progress made to date in understanding the molecular basis of athletic performance represents only the beginning. The next decade will be an exciting period for sports genomics as research is carried out based on the application of new DNA technologies (whole genome sequencing, GWAS, epigenomic, transcriptomic and proteomic profiling, etc.) and bioinformatics to further analyze and analyze genetic effects on human physical abilities [5].

Elite athletic performance is a multifactorial characteristic influenced by both genetic and environmental factors. The high performance of elite athletes has historically been seen as the result of special talent shaped by intense training. Talent is now thought to be the product of additive genetic components that predispose an athlete to endurance, speed, strength, flexibility, and co-ordination trainability under the control of strong environmental cues, including exercise and nutrition. In this model, genetic predisposition, together with the ability to respond to training, is the key to the superior physical performance of elite athletes [54].

Efforts are currently being made to perform GWAS internationally among athletes from different countries, which will give a more complete picture of the progress made in sports genetics.

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