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REVIEW

Nutrigenetic Markers Related to Nutrient Metabolism, Recovery, and Performance in Athletes: a Review of Current Evidence

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Abstract

Purpose of Review This review aimed to evaluate current evidence regarding genetic markers associated with athletic performance, recovery, injury susceptibility, nutrient metabolism, responsiveness to ergogenic aids, and dietary behaviour in athletes.

Recent Findings Classical candidate-gene studies and contemporary genome-wide investigations have identified numerous genetic variants associated with power and endurance performance, skeletal muscle capillarization, cardiac adaptation, energy metabolism, and injury susceptibility. Variants related to carbohydrate, fat, and branched-chain amino acid metabolism may contribute to inter-individual differences in substrate utilization and exercise responses. Genetic markers associated with iron, folate, and vitamin D metabolism, as well as variants influencing caffeine metabolism and sensitivity, are also relevant to sports nutrigenetics. However, differences in sample characteristics, ancestry, sport discipline, and exercise protocols limit the consistency and generalizability of the available findings.

Summary Athletic performance and nutritional responses are polygenic and multifactorial traits. Therefore, no single genetic variant should be considered an independent determinant of performance capacity or nutritional requirements. Genetic information should be interpreted together with dietary intake, biochemical indicators, training characteristics, clinical status, and individual tolerance. Current evidence remains insufficient to support the routine use of nutritional or supplementation strategies based solely on genotype.

Keywords Sports genomics · Nutrigenetics · Athletes · Performance · Personalized nutrition

Abbreviations

HGP	Human Genome Project
DNA	Deoxyribonucleic Acid
SNP	Single Nucleotide Polymorphism
VO_2max	Maximal Oxygen Uptake
ACTN3	Alpha-Actinin-3
AGT	Angiotensinogen
ACE	Angiotensin-Converting Enzyme
ADRB2	Adrenergic Beta-2 Receptor
βAR	Beta-Adrenergic Receptor
β1AR	Beta-1 Adrenergic Receptor
β2AR	Beta-2 Adrenergic Receptor
β3AR	Beta-3 Adrenergic Receptor
NOS3	Nitric Oxide Synthase 3
eNOS	Endothelial Nitric Oxide Synthase
NO	Nitric Oxide
RAB3GAP2	RAB3 GTPase-Activating Non-Catalytic Protein Subunit 2
GALNT13	Polypeptide N-Acetylgalactosaminyltransferase 13
MYBPC3	Myosin-Binding Protein C3
AMPD1	Adenosine Monophosphate Deaminase 1
AMP	Adenosine Monophosphate
IMP	Inosine Monophosphate
NH_3	Ammonia
ADP	Adenosine Diphosphate
ATP	Adenosine Triphosphate
CK	Creatine Kinase
CKM	Muscle-Specific Creatine Kinase
CrP	Creatine Phosphate

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COL5A1	Collagen Type V Alpha-1 Chain
MMP	Matrix Metalloproteinase
MMP3	Matrix Metalloproteinase 3
SLC2A4	Solute Carrier Family 2 Member 4
GLUT4	Glucose Transporter Type 4
PPARGC1A	Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1-Alpha
PGC-1α	Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1-Alpha
PPARA	Peroxisome Proliferator-Activated Receptor Alpha
CD36	Cluster of Differentiation 36
BCAA	Branched-Chain Amino Acid
mTOR	Mechanistic Target of Rapamycin
p70S6K	70-kDa Ribosomal Protein S6 Kinase
PPM1K	Protein Phosphatase, Mg^{2+}/Mn^{2+} Dependent 1 K
MCT1	Monocarboxylate Transporter 1
SLC16A1	Solute Carrier Family 16 Member 1
VDR	Vitamin D Receptor
MTHFR	Methylenetetrahydrofolate Reductase
HFE	Homeostatic Iron Regulator
VO_2peak	Peak Oxygen Uptake
CNS	Central Nervous System
CYP1A2	Cytochrome P450 Family 1 Subfamily A Member 2
ADORA2A	Adenosine A2A Receptor

Introduction

Completion of the Human Genome Project enabled a more detailed characterization of the human genome and inter-individual genetic differences. Genetic variants may influence gene expression or alter the structure and function of encoded proteins, thereby contributing to variability in health, disease susceptibility, nutrient metabolism, and physiological responses. However, these outcomes generally arise from complex interactions among multiple genetic and environmental factors rather than from a single genetic variant [1–3]. Athletic performance is a complex phenotype influenced by training, nutrition, recovery, psychological characteristics, environmental conditions, and genetic predisposition. Numerous genetic variants have been associated with power, endurance, aerobic capacity, exercise-induced muscle damage, recovery, and injury susceptibility. Nevertheless, only a limited proportion of the 251 polymorphisms associated with athlete status have been consistently replicated across independent studies [4–6]. Power performance primarily depends on fast-twitch muscle fibre recruitment, neuromuscular activation, muscle cross-sectional area, and glycolytic capacity, whereas endurance performance is influenced by mitochondrial density, oxidative capacity, skeletal muscle capillarization, haemoglobin concentration, and maximal oxygen uptake [7]. Genetic findings should therefore be evaluated together with sport-specific physiological demands, training, nutrition, and environmental exposures.

Nutrition is a major determinant of athletic performance and recovery, although athletes may differ in macronutrient metabolism, micronutrient status, substrate utilization, dietary behaviour, and responses to ergogenic aids. Nutrigenetics examines how genetic differences modify responses to nutrients and dietary components, whereas nutrigenomics investigates how nutrients influence gene expression and cellular pathways [8, 9]. Although these disciplines may contribute to personalized sports nutrition, the validity of genotype-based recommendations depends on the functional relevance of the variant, independent replication, and intervention studies directly investigating nutrition-gene interactions. Because nutritional and exercise-related traits are largely polygenic and context dependent, recommendations based on isolated genetic variants should be interpreted cautiously [6, 10].

This review evaluates genetic markers associated with athletic performance, recovery, injury susceptibility, macro and micronutrient metabolism, responses to ergogenic aids, and dietary behaviour. It integrates evidence from candidate-gene and genome-wide studies and discusses the potential application of genetic information in sports nutrition within current scientific and translational limitations. The thematic domains examined and their associated genetic markers are presented in Table 1.

Classical Candidate Genes in Athletic Performance

Alpha-Actinin-3 (ACTN3) Gene

Alpha-actinin-3, encoded by the ACTN3 gene, is a sarcomeric protein predominantly expressed in fast type II muscle fibers involved in explosive movements [11]. The ACTN3 rs1815739 (c.1729 C > T) polymorphism influences muscle fiber characteristics, and the TT genotype causes α-actinin-3 deficiency in approximately 18% of the global population, potentially affecting athletic performance and susceptibility to eccentric exercise-induced muscle damage [12, 13]. The C allele and CC genotype are generally more frequent in power and elite athletes, whereas the T allele and TT

Table 1 Study design

Headings and References	Genes
Classical Candidate Genes in Athletic Performance	1. Alpha-Actinin-3 (ACTN3) 2. Angiotensinogen (AGT) 3. Angiotensin-Converting Enzyme (ACE) 4. Adrenergic Beta-2 Receptor (ADRB2) 5. Nitric Oxide Synthase 3 (NOS3)
Contemporary Genome-Wide Markers in Athletic Performance	1. RAB3 GTPase Activating Non-Catalytic Protein Subunit 2 (RAB3GAP2) 2. Polypeptide N-Acetylgalactosaminyl-transferase 13 (GALNT13) 3. Myosin Binding Protein C3 (MYBPC3)
Genetic Markers Associated with Adverse Exercise Responses, Recovery, and Injury Susceptibility	1. Alpha-Actinin-3 (ACTN3) 2. Adenosine Monophosphate Deaminase 1 (AMPD1) 3. Muscle-Specific Creatine Kinase (CKM) 4. Collagen Type V Alpha 1 Chain (COL5A1) 5. Matrix Metalloproteinase 3 (MMP3)
Genetic markers associated with macronutrient metabolism that affect athletic performance and recovery	1. Solute Carrier Family 2 Member 4 (SLC2A4) 2. Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1-Alpha (PPARGC1A) 3. Peroxisome Proliferator-Activated Receptor Alpha (PPARA) 4. Cluster of Differentiation 36 (CD36) 5. Protein Phosphatase, Mg^{2+}/Mn^{2+} Dependent 1 K (PPM1K) 6. Monocarboxylate Transporter 1 (MCT1)/ Solute Carrier Family 16 Member 1 (SLC16A1)
Genetic markers associated with micronutrient metabolism that affect athletic performance and recovery	1. Vitamin D Receptor (VDR) 2. Methylenetetrahydrofolate Reductase (MTHFR) 3. Homeostatic Iron Regulator (HFE)
Ergogenic Aid Responsiveness	1. Cytochrome P450 1A2 (CYP1A2) 2. Adenosine A2A Receptor (ADORA2A)
Behavioural Nutrigenetics and Dietary Adherence	1. Cytochrome P450 Family 1 Subfamily A Member 2 (CYP1A2) 2. Adenosine A2A Receptor (ADORA2A)

genotype are more commonly associated with endurance traits [14, 15]. Sex-specific findings similarly indicated higher frequencies of power-related C alleles and CC/CT genotypes in male athletes and endurance-related T alleles and TT genotypes in female athletes [16]. Overall, the C allele appears to favor power-oriented performance, while the T allele is more closely related to endurance capacity.

Angiotensinogen (AGT) Gene

The angiotensinogen (AGT) gene encodes a protein known as angiotensinogen, which plays an essential role in the production of angiotensin II and represents a key component in the regulation of blood pressure. In athletes, variants of the AGT gene may influence physical performance and endurance by modifying physiological characteristics such as blood pressure, cardiac function, and muscular endurance. A well-characterized polymorphism of the angiotensinogen gene is Met235Thr (rs699) [17]. This study reported a higher frequency of the AGT Met235Thr (rs699) CC genotype in power athletes than in sedentary controls and endurance athletes, suggesting that the C allele may be associated with power performance through angiotensin II mediated support of skeletal muscle development [18]. In another study, Japanese sprinters and wrestlers were found to carry the CC/CT genotypes at a higher frequency than the control group [19]. Similarly, a study involving Turkish long-distance and short-distance runners showed that the C allele of the AGT rs699 polymorphism can enhance performance in power-focused sports such as sprinting [20]. Overall, based on the findings of these studies, the AGT C allele may be associated with power-oriented performance in some athletic populations.

Angiotensin-Converting Enzyme (ACE) Gene

Angiotensin-converting enzyme (ACE), a key component of the renin–angiotensin system, regulates blood pressure through fluid balance and the conversion of angiotensin I to angiotensin II. It also contributes to bradykinin degradation, erythropoiesis, tissue oxygen delivery, vascular tone, respiratory activity, inflammatory responses, and skeletal muscle function [21–23]. The ACE rs1799752 polymorphism comprises insertion (I) and deletion (D) alleles, generally associated with endurance and power performance, respectively [24]. The DD genotype has been linked to speed, power, anaerobic capacity, endurance, and soccer-specific performance in young female soccer players, as well as power-related traits in swimmers [25–27]. However, a Lithuanian study associated the II genotype and I allele with greater speed and power performance [28]. Overall, although findings vary across populations, the D allele is more commonly related to power-oriented performance, whereas the I allele is generally associated with endurance.

Adrenergic Beta-2 Receptor (ADRB2) Gene

β-adrenergic receptors (βARs) are a subset of G protein-coupled receptors activated by endogenous catecholamines. In humans, three subtypes of β-adrenergic receptors have been identified: β1-adrenergic receptor, β2-adrenergic receptor, and β3-adrenergic receptor, and their genes have

been related to metabolic and cardiovascular phenotypes, which might influence exercise capacity [29]. The ADRB2 gene encodes the β2-adrenergic receptor, which mediates the effects of catecholamines such as adrenaline and noradrenaline. By influencing respiratory, cardiovascular, and metabolic functions, β2-adrenergic receptors contribute to exercise performance through bronchodilation, increased heart rate, oxygen delivery, and fatty acid mobilization [30, 31]. The ADRB2 rs1042713 (Gly16Arg) polymorphism may influence receptor sensitivity and activity, with certain variants associated with aerobic capacity and energy-use efficiency [32, 33]. The G allele has been reported to be more frequent in power athletes than in controls and linked to improved pulmonary fluid clearance and bronchodilation after short-term exercise [34, 35].

Nitric Oxide Synthase 3 (NOS3) Gene

Endothelial nitric oxide synthase (eNOS), encoded by the NOS3 gene, produces nitric oxide through the conversion of L-arginine to L-citrulline and contributes to vascular regulation, metabolism, muscle fiber characteristics, and oxygen–nutrient delivery to skeletal muscle [36, 37]. The NOS3 rs2070744 (− 786T/C) polymorphism has been associated with athletic performance; the T allele has been reported more frequently in long-distance swimmers and endurance athletes, while some Ukrainian and Italian studies also observed higher T-allele frequencies in power-oriented athletes [37–39]. Nevertheless, pooled evidence and subsequent research indicate that the T allele and particularly the T/T genotype may be more strongly associated with endurance performance [40, 41]. The classical candidate genes associated with athletic performance, their corresponding polymorphisms, and the main findings reported in the literature are summarized in Table 2.

Contemporary Genome-Wide Markers in Athletic Performance

RAB3 GTPase Activating Non-Catalytic Protein Subunit 2 (RAB3GAP2) Gene

The RAB3 GTPase-activating non-catalytic protein subunit 2 (RAB3GAP2) gene is involved in vesicular transport, endothelial function, and microvascular regulation. Because skeletal muscle capillarization supports oxygen and nutrient delivery, metabolite exchange, oxidative metabolism, and exercise adaptation, greater capillary density may contribute to endurance performance and metabolic efficiency during prolonged exercise [42–44].

The RAB3GAP2 rs115660502 variant has been identified as a genome-wide marker associated with skeletal muscle capillary-to-fibre ratio and endurance-athlete status. Its G allele was associated with a higher capillary-to-fibre ratio and was more frequent in elite endurance athletes but less frequent in power athletes than in controls [45]. From a sports nutrigenetics perspective, rs115660502 does not directly indicate specific nutrient requirements but may serve as an indirect marker of microvascular adaptations affecting oxygen transport, substrate utilization, nutrient delivery, and recovery [4, 6].

Table 2 Classical candidate genes in athletic performance

Gene	Effect on Performance	Polymorphism	Findings from the Literature
ACTN3	May influence fast-twitch muscle fibre function and performance requiring rapid contraction and explosive power	rs1815739	The C allele and CC genotype have been associated with power-oriented performance, whereas the T allele and TT genotype have been more frequently associated with endurance-related traits
AGT	May influence muscular and cardiovascular responses through regulation of the renin-angiotensin system.	rs699	The C allele and CC/CT genotypes have been reported more frequently in power-oriented athletes than in endurance athletes or controls in some populations.
ACE	Regulates vascular tone, fluid balance, tissue oxygen delivery, and skeletal muscle function, which may influence power and endurance performance	rs1799752	The D allele and DD genotype have generally been associated with speed- and power-oriented performance, whereas the I allele and II genotype have more frequently been associated with endurance performance.
ADRB2	May influence respiratory, cardiovascular, and metabolic responses through bronchodilation, oxygen delivery, and substrate mobilization	rs1042713	The G allele has been reported more frequently among power athletes and has been associated with selected respiratory and exercise-related responses.
NOS3	Regulates nitric oxide production, vascular function, skeletal muscle blood flow, and oxygen and nutrient delivery during exercise	rs2070744	The T allele and TT genotype have been associated with endurance performance in several studies, although higher T-allele frequencies have also been reported in some power-oriented athlete populations. Further studies are required.

Polypeptide N-Acetylgalactosaminyltransferase 13 (GALNT13) Gene

The polypeptide N-acetylgalactosaminyltransferase 13 (GALNT13) gene encodes an enzyme involved in the initiation of O-linked glycosylation, a post-translational modification process that may influence cellular signalling, tissue-specific protein function, and neuromuscular pathways. The GALNT13 rs10196189 variant has recently been associated with sprint and power performance. Genome-wide and replication studies reported that the G allele was more frequent in elite sprint–power athletes than in controls and endurance athletes [46, 47]. GALNT13 is highly expressed in brain tissue, and its associated gene networks may involve synaptic signalling and glycosylation pathways. These findings suggest that the rs10196189 G allele may contribute to sprint–power performance through neuromuscular and synaptic mechanisms; however, confirmation in diverse populations and functional studies is required.

Myosin-Binding Protein C3 (MYBPC3) Gene

The Myosin-Binding Protein C3 (MYBPC3) gene encodes myosin-binding protein C in cardiac muscle tissue. It plays a significant role in sarcomere structure, contraction regulation, and cardiac function. This gene is of particular interest in sports genomics due to its association with cardiac hypertrophy and exercise-induced cardiac remodeling processes. The MYBPC3 rs1052373 variant has been reported in recent genome-wide association studies as one of the markers potentially associated with elite endurance athlete status. In a GWAS study by Al-Khelaifi and colleagues, it was demonstrated that the rs1052373 GG genotype may be associated with elite endurance athlete status, and this association was supported across different athlete cohorts [48]. Riguene et al. (2023), also noted that MYBPC3 polymorphisms may be associated with exercise-induced cardiac remodeling in athletes; however, they emphasized that these findings should be interpreted with caution due to the gene's association with hypertrophic cardiomyopathy [49]. Overall, the current findings suggest that the MYBPC3 rs1052373 variant may be associated with endurance-focused athletic performance and exercise-induced cardiac adaptation processes. However, to directly interpret this association in terms of performance capacity, cardiac remodeling, or athlete nutrition, further studies are needed that involve larger sample sizes, are conducted across different populations, and evaluate multiple genetic markers in conjunction. Contemporary genome-wide markers associated with athletic performance and the related findings from the literature are presented in Table 3.

Genetic Markers Associated with Adverse Exercise Responses, Recovery, and Injury Susceptibility

Alpha-Actinin-3 (ACTN3) Gene

The ACTN3 rs1815739 polymorphism, widely recognized for its association with power-related athletic performance, has also been investigated in relation to recovery capacity and injury susceptibility. Evidence summarized in a systematic review indicates that variation in the ACTN3 genotype is linked not only to injury occurrence but also to injury severity. Individuals carrying the TT genotype appear to be more vulnerable to non-contact injuries, including muscle strains, ankle sprains, and elevated levels of exercise-induced muscle damage [50]. A study supporting these observations showed that the ACTN3 TT genotype is associated with injury susceptibility in professional soccer players. Specifically, the TT genotype, associated with α-actinin-3 deficiency, was reported to increase both general and serious injury risk compared to the CC genotype; the CT genotype was similarly associated with a higher probability of injury [12]. In contrast to these findings, research

Table 3 Contemporary genome-wide markers in athletic performance

Gene	Effect on Performance	Polymorphism	Findings from the Literature
RAB3GAP2	It may contribute to endurance performance by supporting skeletal muscle capillarization and the transport of oxygen and nutrients.	rs115660502	The G allele has been associated with a higher capillary-to-fiber ratio and elite endurance athlete status. It is thought that this variant may contribute to microvascular adaptations in endurance-focused performance.
GALNT13	Neuromuscular function may be associated with sprint and power performance through synaptic signaling and glycosylation processes.	rs10196189	The G allele has been reported at a higher frequency in elite sprinters and power athletes. It has been suggested that this variant may be associated with power-focused athletic performance.
MYBPC3	It may influence endurance performance through cardiac contractile regulation and exercise-induced cardiac adaptation.	rs1052373	The GG genotype has been associated with elite endurance athlete status. This variant may be related to aerobic capacity and exercise-induced cardiac remodeling.

involving female soccer players reported no meaningful differences in football-specific performance metrics or injury incidence between carriers of the C allele and those carrying the T allele, suggesting that the relationship between ACTN3 polymorphism and injury risk may vary according to sex and population characteristics [32].

Adenosine Monophosphate Deaminase 1 (AMPD1) Gene

Adenosine monophosphate deaminase 1 (AMPD1) contributes to skeletal muscle energy metabolism by converting AMP into IMP and ammonia, thereby supporting ATP production during intense exercise. AMPD1 deficiency may cause excessive AMP accumulation, early fatigue, reduced exercise capacity, cramps, and myalgia [33, 51]. The AMPD1 rs17602729 (C34T) polymorphism affects enzyme activity, and T-allele carriers may require longer recovery periods between resistance-training sessions and experience greater post-exercise soreness [52, 53].

Athletes with the CC genotype have been reported to sustain fewer ankle, knee, and overall injuries and participate in more matches than T-allele carriers (McCabe and Collins, 2018). Similarly, the CC genotype was more frequent among injury-free elite endurance athletes, whereas the T allele has generally been observed less frequently in athletic populations [33, 52, 54]. Overall, the T allele may be associated with slower recovery and greater susceptibility to exercise-related symptoms and injuries, while the CC genotype may confer a more favourable recovery and injury profile.

Muscle-Specific Creatine Kinase (CKM) Gene

The muscles obtain energy through the hydrolysis of the energy-storing form of adenosine triphosphate, which stores free energy. The production of ATP from ADP through the enzyme action of creatine kinase is given by the following chemical equation: . Energetically, muscle energy production depends on the enzyme creatine kinase [55]. Creatine kinase comes in two subforms, known as M and B for muscle and brain, respectively. The two subforms combine to make three different dimers: two homodimers, CK-M and CK-B, and the heterodimer CK-MB. In muscles, the homodimer CK-M predominates over the other subforms [56]. This enzyme is encoded by the CKM gene. The CKM rs8111989 gene polymorphism (c.*800A > G) has been shown to participate in the regulation of energy balance in muscle cells and the production of adenosine triphosphate (ATP) in muscle tissue during vigorous contraction of the muscles [57].

In professional football players, the GA genotype was associated with a higher incidence and severity of muscle injuries than the AA and GG genotypes [58]. Similarly, severe injuries and muscle tears occurred more frequently among GA carriers, whereas mild injuries were more common in players with the GG genotype. A-allele carriers also experienced severe injuries more frequently than GG homozygotes [59]. Overall, the CKM rs8111989 GA genotype may be associated with increased susceptibility to muscle injury.

Collagen Type V Alpha 1 Chain (COL5A1) Gene

The COL5A1 gene encodes the α1(V) chain of type V collagen, which contributes to collagen fibril organization and the mechanical properties of connective tissues. The COL5A1 rs12722 C > T polymorphism has been associated with reduced type V collagen content, potentially altering fibril structure, tensile strength, and tissue stiffness and thereby increasing susceptibility to musculoskeletal injuries [60]. The TT genotype has been associated with greater injury severity than the TC and CC genotypes [61].

Among elite Australian football players, TT carriers experienced more contact-related bone injuries per match and more moderate-severity injuries than non-TT players [62]. The rs12722 variant has also been associated with ligament injury susceptibility in individuals of European ancestry [63]. However, research in Japanese populations found no association with sports-related muscle injury or passive muscle stiffness [64]. Overall, the T allele may increase injury susceptibility in some populations, although ethnic and population-specific differences limit definitive conclusions.

Matrix Metalloproteinase 3 (MMP3) Gene

Matrix metalloproteinases regulate extracellular matrix remodelling and contribute to tendon structure and mechanical integrity. Repetitive loading may disrupt this balance, promoting chronic tendinopathy and, in severe cases, tendon rupture [65]. The MMP3 rs650108 GG and rs679620 AA genotypes were more frequent among elite athletes with tendinopathy than among asymptomatic controls, suggesting increased injury susceptibility [65]. These genotypes were also more prevalent in professional athletes with anterior cruciate ligament rupture than in uninjured controls [66]. Overall, the rs650108 G and rs679620 A alleles may be associated with greater susceptibility to tendon and ligament injuries.

Although general nutritional strategies may support recovery and tissue health, direct evidence demonstrating genotype-specific benefit remains limited. Genetic markers related to adverse exercise responses, recovery, and injury risk are summarized in Table 4.

Table 4 Genetic markers associated with adverse exercise responses, recovery, and injury susceptibility

Gene	Effect on Performance	Polymorphism	Findings from the Literature
ACTN3	May increase susceptibility to injuries such as muscle damage and ankle sprains	rs1815739	Possession of the TT genotype increases susceptibility to muscle-related injuries in athletes.
AMPD1	Plays a role in regulating skeletal muscle energy metabolism during physical activity; affects exercise capacity and may cause early fatigue, cramps, and/or myalgia	rs17602729	Individuals carrying the T allele require longer rest periods between training sessions.
CKM	Involved in the efficiency of ATP production	rs8111989	A-allele carriers exhibit a higher frequency of severe injuries compared with GG genotype carriers.
COL5A1	Involved in collagen structure; may influence injury susceptibility	rs12722	The T allele may increase susceptibility to injury.
MMP3	Plays a role in tendon integrity and is associated with tendinopathy risk	rs650108 rs679620	Individuals carrying rs650108 GG and rs679620 AA genotypes may have an increased risk of tendinopathy.

Genetic Markers Associated with Macronutrient Metabolism that Affect Athletic Performance and Recovery

Carbohydrate Metabolism and Exercise Performance

Carbohydrates are a major fuel source during moderate- and high-intensity exercise, and adequate muscle glycogen and blood glucose availability help maintain exercise intensity and delay fatigue [67, 68]. Genetic variants affecting glucose transport and carbohydrate oxidation may therefore contribute to individual differences in exercise performance.

The Solute Carrier Family 2 Member 4 (SLC2A4) gene encodes GLUT4 (Glucose Transporter Type 4), the principal glucose transporter in skeletal muscle and adipose tissue. Exercise and insulin stimulate GLUT4 translocation, increasing muscle glucose uptake and supporting post-exercise glycogen synthesis [69]. Among elite long-distance runners, the SLC2A4 rs5418 A allele and AA genotype were more frequent than in controls, while the A allele showed greater promoter activity, suggesting a possible association with GLUT4 expression, glucose uptake, and endurance performance [70].

The Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1-Alpha (PPARGC1A) gene encodes PGC-1α, which regulates mitochondrial biogenesis, substrate oxidation, and aerobic metabolism. Although PPARGC1A rs8192678 genotype frequencies did not differ between elite runners and controls, Ser-allele carriers achieved faster running performance than Gly/Gly homozygotes [71, 72]. Overall, SLC2A4 rs5418 and PPARGC1A rs8192678 may influence carbohydrate metabolism and aerobic performance, but current evidence is insufficient to support genotype-specific carbohydrate recommendations.

Fat Metabolism and Substrate Utilization

Fatty acids are an important fuel source during prolonged low- to moderate-intensity exercise. Their transport into skeletal muscle and oxidation within mitochondria may support endurance and preserve muscle glycogen, making maximal fat oxidation relevant to metabolic flexibility and endurance performance [73].

The Peroxisome Proliferator-Activated Receptor Alpha (PPARA) gene encodes peroxisome proliferator-activated receptor alpha, a transcription factor that regulates genes involved in fatty acid transport, mitochondrial β-oxidation, and lipid metabolism. Peroxisome Proliferator-Activated Receptor Alpha rs4253778 is a G > C variant located in intron 7 of the gene. Among Polish rowers, the GG genotype and G allele were more frequent in elite athletes than in sedentary controls, and the G allele was identified as an endurance-related variant [74]. Similarly, in a study of elite athletes from different sporting disciplines, the G allele was associated with endurance athlete status, whereas the C allele was associated with soccer and other sports involving greater power and speed demands [75].

The Cluster of Differentiation 36 (CD36) gene encodes a fatty acid translocase involved in long-chain fatty acid uptake and oxidation in skeletal muscle [76]. Although CD36 rs1761667 did not differ significantly between elite Moroccan athletes and controls, the G allele was more frequent and the AA genotype less frequent among cyclists than field hockey players [14]. Overall, PPARA rs4253778 and CD36 rs1761667 may contribute to differences in fat oxidation and substrate utilization, but current evidence is insufficient to support genotype-specific dietary fat recommendations.

Protein and BCAA (Branched-Chain Amino Acids) Metabolism

Protein and branched-chain amino acids are important for muscle protein synthesis, post-exercise recovery, and training adaptation. Branched-Chain Amino Acids (BCAAs), comprising leucine, isoleucine, and valine, may stimulate muscle protein synthesis after exercise, particularly through leucine-mediated activation of the mTOR and p70S6K signalling pathways [77].

The Protein Phosphatase, Mg^{2+}/Mn^{2+} Dependent 1 K (PPM1K) gene encodes a mitochondrial phosphatase that regulates BCAAs catabolism by activating the branched-chain α-ketoacid dehydrogenase complex. The PPM1K rs1440581 and rs7678928 variants have been associated with circulating BCAAs concentrations. Hu and colleagues reported that the rs1440581 C allele and CC genotype were associated with higher serum valine and total BCAAs levels, while rs7678928 may also contribute to variability in BCAAs metabolism [78]. The PPM1K rs1440581 may also influence metabolic responses to dietary composition. In individuals following energy-restricted diets, this variant interacted with dietary fat and carbohydrate intake in relation to changes in glucose, insulin, and β-cell function [79]. These findings suggest that PPM1K variation may contribute to the relationship between BCAAs metabolism and individual responses to macronutrient intake. Collectively, PPM1K rs1440581 and rs7678928 may contribute to inter-individual differences in BCAAs catabolism and circulating amino acid concentrations. However, current evidence is insufficient to support genotype-specific protein or BCAAs intake recommendations for athletes.

Lactate Transport and High-Intensity Exercise: MCT1 rs1049434

Lactate is produced through glycolytic metabolism during high-intensity exercise and may be utilized as an energy substrate by oxidative tissues. Its transport between cells is important for acid–base regulation and the maintenance of intense exercise performance [80].

The Monocarboxylate Transporter 1 (MCT1) gene, also known as SLC16A1 (Solute Carrier Family 16 Member 1), encodes monocarboxylate transporter 1, which cotransports lactate and hydrogen ions across the cell membrane. MCT1 rs1049434 is an A > T variant resulting in a Glu490Asp substitution and has been associated with lactate transport capacity [81]. In Brazilian and European athletes, the A allele and AA genotype were more frequent among endurance athletes and were associated with higher VO_2max and lower blood lactate accumulation [82]. In Japanese long-distance runners, the AA genotype was also associated with athlete status and aerobic capacity indicators [83]. Among elite football players, A allele carriers performed better than TT homozygotes during the final stages of a repeated-sprint test. However, genotype-related lactate responses may vary according to exercise type and sex [81, 84]. Overall, MCT1 rs1049434 may contribute to inter-individual differences in lactate transport, aerobic capacity, and high-intensity exercise performance. However, this variant should not be used alone to guide nutritional or recovery strategies [82, 83]. Genetic markers associated with macronutrient metabolism, substrate utilization, and exercise performance, together with the main findings from the literature, are presented in Table 5.

Genetic Markers Associated with Micronutrient Metabolism That Affect Athletic Performance and Recovery

Vitamin D Receptor (VDR) Gene

Vitamin D contributes to calcium–phosphorus homeostasis, bone health, skeletal muscle function, and exercise performance, partly through VDR-mediated regulation of muscle cell proliferation and differentiation [85]. Accordingly, common Vitamin D Receptor (VDR) polymorphisms, including FokI (rs2228570), BsmI (rs1544410), ApaI (rs7975232), and TaqI (rs731236), have been investigated in relation to muscle power, injury susceptibility, and athletic performance [86–88]. However, findings remain inconsistent. Although certain FokI and BsmI genotypes were prevalent among Turkish athletes, other studies found no significant association between FokI and athletic performance [87, 89]. ApaI has been associated with injury severity in professional soccer players, while specific FokI and BsmI variants may increase stress-fracture susceptibility; nevertheless, no associations with physical performance or fat-free mass development were observed in young soccer players [61, 90, 91]. The BsmI rs1544410 variant has also been linked to hamstring, but not quadriceps, muscle power in Swedish women [92]. Thus, the effects of individual VDR variants should be interpreted cautiously because muscle power, recovery, injury risk, and vitamin D status are polygenic and environmentally influenced traits.

Vitamin D deficiency is common among athletes and may impair musculoskeletal health and performance [93, 94]. Although maintaining adequate vitamin D levels may support muscle function and recovery, supplementation responses vary between individuals [95]. Athletes with low serum vitamin D levels may therefore benefit from individualized assessment and clinically monitored

Table 5 Genetic markers associated with macronutrient metabolism that affect athletic performance and recovery

Gene	Effect on Performance	Polymorphism	Findings from the Literature
SLC2A4	May influence skeletal muscle glucose uptake, glycogen replenishment, and carbohydrate utilization during endurance exercise.	rs5418	The A allele and AA genotype were more frequent in top-level long-distance runners and were associated with greater promoter activity.
PPARGC1A	May influence carbohydrate oxidation, mitochondrial biogenesis, aerobic capacity, and skeletal muscle adaptation.	rs8192678	The G allele has been associated with aerobic capacity and endurance status in some studies, whereas the Ser allele was associated with faster performance in elite long-distance runners.
PPARA	May influence fatty acid oxidation, lipid metabolism, and energy production during endurance exercise.	rs4253778	The G allele and GG genotype have been associated with elite endurance athlete status, whereas the C allele has been linked to some power and speed-oriented sports.
CD36	May influence long-chain fatty acid transport into skeletal muscle and fat oxidation during exercise.	rs1761667	The G allele was more frequent in elite cyclists than in field hockey players, whereas the AA genotype was less frequent among cyclists.
PPM1K	May influence BCAA catabolism, circulating amino acid concentrations, and metabolic responses to macronutrient intake.	rs1440581, rs7678928	The rs1440581 C allele and CC genotype have been associated with higher valine and total BCAA concentrations. rs1440581 may also modify metabolic responses to dietary fat and carbohydrate intake.
MCT1/SLC16A1	May influence lactate transport, aerobic capacity, and repeated high-intensity exercise performance.	rs1049434	The A allele and AA genotype have been associated with endurance athlete status, higher VO_2max, and lower lactate accumulation. Better repeated-sprint performance has also been reported in A allele carriers.

supplementation; however, current evidence is insufficient to support genotype-specific vitamin D recommendations.

Methylenetetrahydrofolate Reductase (MTHFR) Gene

The methylenetetrahydrofolate reductase (MTHFR) gene is central to folate metabolism and homocysteine regulation. The C677T polymorphism reduces enzyme activity and may increase homocysteine concentrations, potentially impairing cardiovascular health and physical performance [96]. In Turkish elite athletes, the CC genotype and C allele were more frequent than in sedentary controls [97]. Conversely, the TT genotype has been associated with higher homocysteine and lower folate and vitamin B12 concentrations, accompanied by reduced aerobic and anaerobic power [98]. Athletes carrying the TT genotype may warrant closer biochemical assessment of homocysteine, folate, and vitamin B12 status. Dietary or supplementation strategies should be guided by biochemical findings rather than genotype alone.

Iron-Related Genetic Markers

The Homeostatic Iron Regulator (HFE) gene encodes a protein involved in hepcidin regulation, intestinal iron absorption, and systemic iron homeostasis. Because iron is essential for haemoglobin and myoglobin synthesis, oxygen transport, mitochondrial energy production, and muscle metabolism, HFE variation may influence aerobic capacity and endurance performance [99].

The HFE rs1799945 (H63D) polymorphism is a C > G substitution, and its G allele has been associated with higher serum iron and transferrin saturation. The CG and GG genotypes were more frequent among elite endurance athletes than controls, while male G-allele carriers exhibited higher VO_2max values than individuals with the CC genotype [99]. Genotypes associated with moderate or high iron loading have also been linked to greater VO_2peak and endurance performance in competitive male athletes [100]. Similarly, among Korean distance runners, throwing athletes, and controls, rs1799945 was the only investigated candidate variant significantly associated with endurance performance [101].

Table 6 Genetic markers associated with micronutrient metabolism that affect athletic performance and recovery

Gene	Effect on Performance	Polymorphism	Findings from the Literature
VDR	Influences bone health, muscle function, and physical performance; different polymorphisms may exert variable effects	FokI (rs2228570) BsmI (rs1544410) ApaI (rs7975232) TaqI (rs731236)	Certain polymorphisms have been associated with muscle performance or injury risk, although findings remain inconsistent.
MTHFR	Regulates folate metabolism and homocysteine levels; polymorphisms may affect performance and health	rs1801133	The TT genotype has been associated with higher homocysteine and lower folate and vitamin B12 status; closer biochemical monitoring may therefore be warranted.
HFE	May influence iron homeostasis, oxygen transport, mitochondrial energy production, and aerobic capacity.	rs1799945	The G allele and CG/GG genotypes have been associated with elite endurance athlete status, higher VO_2max/VO_2peak, and better endurance performance. A significant association with endurance performance has also been reported in Korean athletes.

However, increased iron status is not invariably beneficial because HFE variants may increase susceptibility to iron overload. Genetic findings should therefore be evaluated alongside ferritin, hemoglobin, transferrin saturation, serum iron, inflammatory markers, and dietary history. Overall, the rs1799945 G allele may be associated with iron metabolism and endurance capacity, but it should be considered a complementary marker rather than an independent basis for iron supplementation. Related genetic markers are summarized in Table 6.

Ergogenic Aid Responsiveness

Cytochrome P450 1A2 (CYP1A2) Gene

Caffeine enhances performance primarily by antagonizing adenosine receptors in the central nervous system. The CYP1A2 gene encodes the principal enzyme responsible for caffeine metabolism, and its rs762551 polymorphism may partly explain inter-individual differences in caffeine response [102]. Individuals with the AA genotype are generally classified as fast metabolizers, whereas AC and CC carriers are considered slow metabolizers. Evidence suggests that AA carriers may experience greater caffeine-induced improvements in aerobic endurance performance than C-allele carriers [103, 104]. However, findings remain inconsistent across exercise types. Caffeine intake at 3 mg/kg improved resistance exercise, sprint, and vertical-jump performance in resistance-trained men, but no significant differences were observed between AA and AC/CC carriers [105]. Similarly, caffeine mouth rinsing did not improve 10-km running or vertical-jump performance in AC or CC carriers, while combined caffeine and blackcurrant supplementation produced no performance benefit in male cyclists [106, 107]. Conversely, during a 10-km cycling trial, caffeine at 2 and 4 mg/kg improved performance in AA carriers, had no benefit in AC carriers, and impaired performance at 4 mg/kg in CC carriers [103]. Thus, CYP1A2 may influence caffeine's ergogenic effects, although study heterogeneity and inter-individual variability prevent definitive genotype-specific recommendations [102].

Adenosine A2A Receptor Gene (ADORA2A)

The adenosine A2A receptor, encoded by the ADORA2A gene, is a G protein-coupled receptor involved in central nervous system, cardiovascular, and immune functions. Caffeine antagonizes this receptor, potentially reducing perceived fatigue, increasing alertness, and modifying exercise and recovery responses. Therefore, ADORA2A variants may partly explain inter-individual differences in caffeine responsiveness [108, 109].

The ADORA2A rs5751876 polymorphism comprises C and T alleles. Women with the TT genotype showed increased cycling work after consuming 5 mg/kg caffeine, whereas this response was not observed in C-allele carriers; TT carriers also exhibited a lower exercise-induced inflammatory response following caffeine intake [108, 110]. However, caffeine at 3 mg/kg improved power, sprint, jump, and muscular endurance outcomes in resistance-trained C-allele carriers, while a 6 mg/kg dose improved selected performance measures in adolescent athletes independently of genotype [109, 111]. Thus, although the TT genotype may be associated with ergogenic and anti-inflammatory responses in some individuals, inconsistent findings prevent genotype-specific supplementation recommendations. ADORA2A rs5751876 should therefore be considered a complementary rather than an independent marker for guiding caffeine use. Genetic markers related to individual responses to caffeine and the corresponding literature findings are summarized in Table 7.

Table 7 Ergogenic aid responsiveness

Gene	Effect on Performance	Polymorphism	Findings from the Literature
CYP1A2	Plays a role in caffeine metabolism; fast and slow metabolizer genotypes may influence performance	rs762551	The AA genotype has been associated with greater ergogenic responses to caffeine in some studies, although findings remain inconsistent.
ADORA2A	May influence performance, perceived fatigue, and exercise-induced inflammatory responses to caffeine.	rs5751876	The TT genotype has been associated with greater exercise work output and a lower inflammatory response following caffeine intake in some studies. However, ergogenic effects have also been reported in C allele carriers, and findings remain inconsistent.

Behavioural Nutrigenetics and Dietary Adherence

Behavioural nutrigenetics examines the potential influence of genetic differences on food preferences, consumption patterns, individual responses to nutrients and bioactive compounds, and adherence to nutritional plans. However, dietary behaviour in athletes is shaped by interactions among genetic predisposition, cultural habits, nutrition knowledge, psychosocial characteristics, economic conditions, training schedules, and food accessibility. Genetic findings should therefore not be interpreted as independent determinants of dietary behaviour, but rather as complementary information that may support the assessment of inter-individual variability [112, 113].

Caffeine metabolism and sensitivity represent one of the most extensively investigated examples of behavioural nutrigenetics in athletes. Variations in CYP1A2 have been associated with inter-individual differences in caffeine metabolism, whereas ADORA2A variants have been linked to central nervous system responses, anxiety sensitivity, and sleep-related effects. These characteristics may influence the frequency, dose, timing, and tolerance of caffeine consumption. Nevertheless, findings regarding the effects of CYP1A2 and ADORA2A variants on the ergogenic response to caffeine remain inconsistent. Caffeine use should therefore be evaluated by considering genotype together with habitual intake, sleep quality, adverse effects, and individual performance responses [114, 115].

Genetic differences related to macro- and micronutrient metabolism may influence athletes' metabolic responses to nutrients and their individual monitoring requirements. Variability in carbohydrate, fat, and amino acid metabolism, as well as iron, folate, and vitamin D status, may be associated with energy utilization, recovery, and responses to nutritional plans. However, the clinical relevance of genetic information should be evaluated together with dietary intake, biochemical indicators, body composition, training load, and athlete-reported tolerance [112, 113].

Genetic information should not be used as an independent criterion for food or supplement selection. To promote long-term dietary adherence, nutritional plans should be aligned with the athlete's energy and nutrient requirements, sport discipline, training schedule, daily routine, preferences, and tolerance. Behavioural nutrigenetics should therefore be regarded not as an independent decision-making tool, but as a complementary approach supporting individualized assessment and regular monitoring in the development of practical and sustainable nutritional strategies [112, 116].

Conclusions and Recommendations

In this review, current evidence on genetic factors associated with athletic performance, recovery, injury susceptibility, nutrient metabolism, and responses to ergogenic aids was evaluated within the frameworks of sports genomics and nutrigenetics. The available findings indicate that genetic variation may contribute to inter-individual differences in power- and endurance-related performance, substrate utilization, micronutrient metabolism, and recovery responses. However, these outcomes are complex and multifactorial and cannot be adequately explained by individual genetic variants alone. The integration of genetic information with dietary assessment, biochemical indicators, training characteristics, and sport-specific requirements may contribute to a more comprehensive understanding of individual responses in athletes. Nevertheless, current evidence remains insufficient to support nutritional or supplementation strategies based solely on genotype. Further controlled studies involving larger and more diverse athletic populations are required to clarify the practical relevance of nutrition–gene interactions. In conclusion, the genetic markers discussed in this review provide a framework for understanding the biological variability underlying exercise performance and nutritional responses. Future research integrating genetic, metabolic, phenotypic, and dietary data may strengthen the scientific basis of personalized sports nutrition and support the development of more reliable applications in athletic practice.

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