REVIEW

The Genetic Basis of Endurance and Long-Distance Running Performance in Athletes from the African Region: A Narrative Review

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Abstract

This narrative review examines why African athletes, particularly those from Kenya and Ethiopia, who have consistently dominated international long-distance running, prompting research into the interplay between genetic and environmental determinants of endurance. Although high-altitude living, habitual physical activity, and cultural practices contribute significantly, genetic predispositions are increasingly recognized as central to this phenomenon. Candidate genes such as *ACTN3, ACE, PPARGC1A, VEGFA*, and *ADRB2* have been implicated in muscle fiber composition, mitochondrial biogenesis, oxygen delivery, and energy metabolism, although associations vary across populations. Studies have also highlighted the role of mitochondrial DNA variants, nuclear mitochondrial interactions and epigenetic modifications in regulating endurance adaptations. Inconsistent findings in African cohorts underscore the complexity of genetic diversity and polygenic inheritance. Beyond genetics, physiological traits such as higher VO_2 max fractions, superior fatigue resistance, and more efficient running economy distinguish East African runners from their non-African counterparts. Environmental influences, including hypoxic exposure, habitual childhood running, and strong sociocultural incentives, interact dynamically with genetic factors, supporting the concept of gene culture coevolution. Emerging areas such as the gut microbiome and injury- susceptibility genetics further broaden the scope of endurance research. Practical applications of these findings include the potential use of genetic profiling to personalize training, nutrition, and injury prevention strategies, however ethical concerns and limited predictive accuracy remain barriers. Future directions emphasize the integration of multi-omics combining genomics with transcriptomics, proteomics, and metabolomics to reveal functional pathways underlying endurance beyond simple genetic associations. Overall elite endurance performance in African athletes reflects a multifactorial synergistic effect of genetics, environment, and culture, offering insights for advancing sports genomics and performance optimization.

Key words: Endurance genetics; African athletes; Long-distance-running physiology; Multi-omics; VO_2 max

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Introduction

The dominance of East African athletes, particularly from Kenya and Ethiopia, in long-distance running has drawn significant scientific attention. While high-altitude living, specialized training, and a specific diet contribute to endurance, growing evidence highlights the role of genetic predispositions (3). East African runners consistently excel in events such as the 5,000 m, 10,000 m, and marathon, raising questions about the interplay between environment and genetics in shaping performance (3). Genetic studies have identified markers including *ACTN3, ACE, PPARGC1A*, *VEGFA,* and *ADRB2*, which influence muscle fiber distribution, cardiovascular efficiency, oxygen uptake, and energy metabolism all crucial for endurance performance (1, 2, 3). These genetic traits may enhance physiological efficiency in East African athletes compared to non-athlete populations, suggesting possible population-specific adaptations (4, 5). In addition, it suggests that these populations possess unique genetic variants that optimize aerobic capacity, thereby supporting their sustained dominance in global competitions (4, 5).

Equally important is the interaction between genetic predispositions and environmental influences. High-altitude training environments, characteristic of regions in Kenya and Ethiopia, synergize with genetic advantages to maximize oxygen utilization, mitochondrial efficiency, and endurance capacity (6, 12, 13). This interaction underscores the importance of considering both inherited and environmental factors when evaluating elite athletic success. Despite advances in sports genetics, significant gaps remain. Much of the literature is limited to small cohorts or narrow populations, restricting broader conclusions (7,15). Furthermore, the complexity of gene–environment interactions remain largely unexplored, underscoring the need for more comprehensive studies (15,18). This narrative review therefore seeks to integrate current findings on the genetic and environmental determinants of endurance performance, focusing particularly on East African long-distance runners. By synthesizing recent research, the review aims to clarify how these factors contribute to elite performance and to provide insights for future directions in sports genetics and training optimization.

Methods

The current narrative review was performed on a comprehensive search of the published literature focusing on genetic, physiological, and environmental factors of endurance performance in African long-distance runners. The relevant articles were located with the help of electronic databases, such as PubMed, Scopus, Web of Science, and Google Scholar. The search included the articles published between 1999 and 2025 and was restricted to articles published I English. The search strategy incorporated standardized Medical Subject Headings (MeSH) terms and Boolean operators. Keywords and search combinations included: (“endurance performance” OR “aerobic capacity” OR “VO_2 max”) AND (“African athletes” OR “Kenyan runners” OR “Ethiopian runners”) AND (“genetics” OR “ACTN3” OR “ACE gene “OR “PPARGC1A” OR “VEGFA” OR “ADRB2” OR “endurance genetics”) AND (“long-distance running” OR “elite performance”).

Original research articles and review papers investigating genetic, physiological, and environmental factors influencing endurance performance were included. Studies focusing on non-endurance sports or unrelated clinical populations were excluded. Additionally, the reference lists of selected articles were screened to identify further relevant studies.

Physiological and Biomechanical Basis of Endurance

Sports performance is multifactorial, but in endurance running, physiological factors such as cardiovascular capacity, VO_2 max, lactate threshold, running economy (RE), muscle fiber type, enzyme activity, and genetic background play pivotal roles (4). Elite East African runners, particularly Kenyans, demonstrate exceptional endurance profiles. Studies reveal that their VO_2 max values and velocities at both VO_2 max and lactate threshold are highly predictive of 10-km race performance (4). Although Africans and Caucasians may exhibit similar VO_2 max levels, African runners typically sustain a higher fraction of VO_2 max, contributing to superior fatigue resistance (5, 6).

Muscle biochemistry also distinguishes African athletes. Elevated oxidative enzyme activity, such as citrate synthase, supports efficient aerobic metabolism and reduced lactate accumulation during intense efforts. These runners often exhibit a predominance of Type I (slow twitch) fibers and greater capillary density, which enhances oxygen delivery and endurance performance. Notably, African runners in controlled studies exhibited 21% longer time to fatigue, 38% lower plasma lactate accumulation, and 50% higher citrate synthase activity compared to Caucasian counterparts (6).Training methods further optimize performance. Among elite Kenyan athletes, high-speed training strongly correlated with improved vVO_2 max and 10km outcomes. Biomechanical efficiency also contributes: East African runners, including Eritreans, demonstrate more economical RE at submaximal speeds, facilitated by stride mechanics such as shorter ground-contact times and optimized stride frequency (5).

Genetic Factors in Endurance Performance

Endurance capacity has been linked to multiple genetic determinants; however, their effects vary across populations. The *ACE I/D* polymorphism has been extensively studied and is referred to as one of the common genetic variations in *ACE,* where either the insertion (I allele) or deletion (D allele) of a 287 bp fragment in intron 16 of the gene is observed. The I allele is often associated with reduced *ACE* activity, enhanced cardiovascular efficiency, and improved endurance in Caucasian and mixed-ancestry cohorts. In contrast, no significant association has been observed in elite Kenyan and Ethiopian runners, suggesting that environmental or alternative genetic influences may predominate in these groups (3, 7).The *ACTN3 R577X* polymorphism is one of the genetic variants that may influence the performance of an athlete in term of the muscle function and endurance. Where the X allele favours endurance phenotypes in many non-African studies, its prevalence is exceptionally low among East and West Africans (≈1% in Kenyans/Nigerians, ~11% in Ethiopians), and no enrichment in endurance athletes has been demonstrated (8, 16). Other candidate genes, including *PPARGC1A, ADRB2,* and *VEGF*, have been implicated in mitochondrial biogenesis, oxidative metabolism, vascular adaptation, and substrate utilization, although the strength of these associations remains inconsistent across populations (8,15). Furthermore, mitochondrial DNA (mtDNA) variants and haplogroups influence aerobic performance, with endurance athletes exhibiting unique mutational profiles associated with more efficient oxidative phosphorylation (9). Coordination between nuclear regulators of mitochondrial biogenesis (e.g., *PPARGC1A*) and mtDNA appears essential for optimal aerobic metabolism. Emerging evidence highlights the role of

epigenetic regulation. Endurance training induces widespread DNA methylation changes, particularly at enhancer regions, modulating genes involved in metabolism, mitochondrial function, and inflammation (10). Exercise intensity is correlated with hypomethylation of key metabolic genes, such as *PGC-1α, PDK4*, and *PPARδ*, which enhances gene expression and promotes endurance adaptations (11). Collectively, endurance performance arises from complex interactions between genetic, mitochondrial, and epigenetic mechanisms, with population-specific variation underscoring the importance of integrative, multi-omics approaches.

Female Athletes & Genetics

Sex-specific genetic and epigenetic factors significantly shape endurance performance. Variants in genes such as *ACTN3* and *ACE* influence endurance, but their effects differ between males and females due to hormonal regulation and gene–hormone interactions (7, 14, 29). Estrogen, for instance, enhances mitochondrial function and muscle repair, supporting recovery and endurance in females, while testosterone contributes to muscle mass and oxygen transport, creating sex-dependent physiological advantages (29). Epigenetic mechanisms add another layer of regulation. Endurance training can induce sex-specific modifications such as DNA methylation and histone acetylation, which altering gene activity linked to energy metabolism and adaptation (10, 30). Notably, methylation differences in *FOXO1* and *FOXO3*, genes central to muscle adaptation and mitochondrial biogenesis, have been observed between male and female athletes, highlighting distinct regulatory pathways in endurance responses (30). Despite these findings, most genetic and epigenetic studies disproportionately focus on male athletes, limiting understanding of female-specific determinants of performance (15, 29, 30). This gap is especially evident for African female athletes, who combine unique genetic backgrounds with distinctive cultural and environmental exposures (4, 5, 6, 12, 13). Their underrepresentation restricts the development of evidence-based training and nutrition strategies tailored to their needs, thereby hindering a comprehensive understanding of the factors driving their elite endurance success (30).

Injury Risk & Recovery Genetics

Genetic factors significantly influence an athlete's susceptibility to tendon injuries, particularly through variations in collagen-related genes. The *COL5A1* gene, which encodes type V collagen, has been associated with increased risk of tendon and ligament injuries, especially in Caucasian populations. Specifically, the TT genotype of the rs12722 polymorphism in *COL5A1* has been shown to have a positive association with tendon and ligament injuries (25). Similarly, variants in the *COL1A1* gene, which encodes type I collagen, have been linked to anterior cruciate ligament (ACL) injuries, indicating a genetic predisposition to tendon injuries (26). Beyond collagen genes, other genetic factors also contribute to the risk of tendon injury. For instance, polymorphisms in the matrix metalloproteinase-3 (*MMP3*) gene, which is involved in extracellular matrix remodeling, have been associated with tendon injuries (18). Additionally, variations in the tenascin-C (*TNC*) gene, which plays crucial role in tendon development and repair, have been associated with an increased susceptibility to tendon injury (28).

Population Genetics of African Athletes

East African populations such as the Kalenjin (Kenya) and Oromo (Ethiopia) have been shown to have genetic differentiation in regions of the genome associated with traits relevant to

endurance running things like anthropometry, energy metabolism, circulatory and respiratory systems, and calcium homeostasis (12).

However, the studies do not support the idea that elite endurance runners from Ethiopia or Kenya form genetically isolated groups: their mitochondrial DNA (maternal lineages) and broader genome profiles largely overlap with those of the general populations from which they come (9, 12). In terms of altitude adaptation and signs of natural selection, research among Ethiopian highlanders (e.g. Amhara, Oromo) has found evidence for distinct adaptations to hypoxia. For example, in genome-wide scans of, Ethiopian high-altitude populations have revealed differences in hemoglobin levels compared to lowland populations, and selection signals in genes such as CBARA*1, VAV3, ARNT2*, and *THRB*, some of which are in or related to the HIF-1 pathway (12, 13). These adaptations appear to have evolved independently from those seen in other known high-altitude populations (Tibetans, Andeans), pointing to convergent evolution but with differing genetic loci (13). When comparing African endurance athlete populations with non-African ones, many of the well-known "candidate genes" identified in European or Asian cohorts (e.g. *ACE, ACTN3*) have shown inconsistent or weak association in African samples. The failure to replicate strong effects in Africans partly due to the high genetic diversity in African populations, smaller sample sizes, differences in linkage disequilibrium, and distinct demographic histories (7, 14, 16, 17).

Environmental and Cultural Interactions

Environmental and cultural factors substantially influence endurance performance in East African athletes. High-altitude living in regions such as the Ethiopian Highlands and Kenya's Rift Valley exposes individuals to chronic hypoxia, promoting physiological adaptations including increased erythropoietin production, elevated hemoglobin concentration, and enhanced oxygen transport (12, 13). Training interventions modeled on the "live high–train low" strategies demonstrate additional benefits for sea-level performance through improvements in hemoglobin mass and mitochondrial efficiency (6, 4). Habitual physical activity during childhood is another determinant. Rural populations often engage in high daily activity levels including walking, running, and physical chores, which are associated with superior cardiorespiratory fitness in adulthood (6). Many elite Kenyan runners report running long distances to school, which reinforces their efficient running economy and endurance capacity (15). Cultural and socioeconomic contexts also significantly influence performance. Distance running in East Africa provides opportunities for social mobility and economic advancement, motivating athletes to adopt rigorous training and disciplined lifestyles (13). Moreover, running is often integrated into community identity and daily practice, reducing barriers to participation. Socioeconomic constraints, while limiting resources, may simultaneously foster endurance potential through physically demanding routines that build foundational fitness.

Gut Microbiome & Endurance

Recent research highlights the gut microbiome's influence on endurance performance. Species such as *Veillonella* metabolize exercise-induced lactate into propionate, a short-chain fatty acid that enhances energy availability and endurance. A landmark study demonstrated that colonizing germ-free mice with *Veillonella atypica* from marathon runners improved treadmill performance, suggesting a causal relationship (23). Human studies similarly show endurance athletes possess distinct microbiome profiles

enriched in carbohydrate- and lactate-metabolizing species (23, 24). The microbiome thus acts as a mediator between training, diet, and metabolism, particularly in athletes with high-carbohydrate diets. Integrating microbiome, genomic, and metabolomic data may enable personalized endurance optimization strategies (24).

Gene–Culture Coevolution

Cultural practices in East Africa, especially among the Kalenjin people of Kenya, may have promoted genetic selection for endurance running through gene–culture coevolution. This process suggests that cultural behaviors and genetic evolution influence each other, leading to adaptive traits suited to specific environments (31). From an early age, children in these regions engage in regular long-distance running, such as traveling to school, which may have created selective pressure favoring genes linked to superior aerobic capacity, oxygen efficiency, and optimal muscle composition (4, 6, 12). Over generations, these traits likely became more common within the population (30). Additionally, the high social and economic value placed on running success reinforced this cultural and genetic relationship. Achieving athletic success enhances social prestige and provides financial benefits, encouraging the persistence and propagation of endurance-related genetic variants, ultimately shaping the remarkable long-distance running abilities observed in East African populations (6, 12).

Comparisons with Other Populations

Studies comparing African endurance athletes with non-African populations show that many candidate gene associations identified in European or Asian cohorts often do not replicate in East African runners. For example, the *ACTN3* R577X polymorphism has a very low frequency of the XX genotype in Kenyans (~1%) and Nigerians, whereas in Ethiopians, it is higher (~11%), However, no enrichment of the XX genotype has been found among endurance athletes compared with local controls (14, 15). Similarly, although the *ACE* I allele (insertion) is associated with endurance in some Caucasian groups (e.g. South African Ironman competitors), studies among Ethiopian and Kenyan endurance runners show no significant difference in *ACE* I vs D frequencies between athletes and their non-athlete local populations (7, 16). Moreover, large meta-analyses of endurance genetics have failed to identify a set of common endurance-associated variants that are consistent across multiple ethnic cohorts, underscoring that allele frequencies, linkage disequilibrium patterns, environmental pressures and genetic architecture differ substantially among populations (12, 17). Table 1 shows the implications of several candidate genes in modulating endurance performance.

Practical Applications and Ethical Considerations

Genetic testing offers potential for personalized training by identifying predispositions to endurance, injury risk, and recovery profiles. Studies indicate that athletes and coaches acknowledge the role of genetics in elite performance and express interest in genetic testing for tailored training programs (18, 19). However, the scientific community remains cautious, as current evidence linking specific genetic variants to endurance performance is limited (1, 3, 14, 17). The use of genetic testing in sports raises ethical concerns, including genetic discrimination, privacy issues, and the potential for misuse of genetic information (19, 21). Experts emphasize the need for responsible implementation, ensuring fairness and protecting athlete privacy (18, 19). Additionally, the World Anti-Doping Agency (WADA) prohibits non-therapeutic genetic modifications for performance enhancement, highlighting the importance of maintaining the integrity of sports (20).

Table 01: Comparative Genetic Associations in Endurance Performance

Gene	Role in Endurance	Findings in non-Africans	Findings in Africans
ACE I/D	Cardiovascular efficiency, oxygen uptake	I allele often linked with better endurance in Caucasians & mixed populations	No significant association in Kenyan/Ethiopian elite runners (7, 16)
ACTN3	Muscle fiber composition (power vs endurance)	XX genotype linked with endurance in Europeans & Asians	XX genotype very rare: ~1% Kenyans/Nigerians, ~11% Ethiopians; no enrichment among elite athletes (14, 15)
PPARGC1A	Mitochondrial biogenesis, oxidative metabolism	Positive associations in some cohorts	Inconsistent findings; population-specific effects (8)
ADRB2	Energy metabolism, cardiovascular adaptation	Associated with endurance adaptations in some studies	Associated with endurance adaptations in some studies (3, 6)
VEGFA	Angiogenesis, oxygen delivery	Reported association with endurance phenotypes in European cohorts	No clear enrichment in African athletes (1,12)

Challenges and Limitations

Many studies on the genetic determinants of endurance performance in African athletes suffer from small sample sizes, which undermines statistical power and can lead to false positives or overestimation of effect sizes. For instance, a narrative review by "Genetic Determinants of Endurance" noted that polymorphisms such as *ACE* I/D and *ACTN3* R577X showed inconsistent associations across populations in part because some studies had very few participants or unbalanced ethnic representation; this variability reduces the replicability and the generalizability of findings (7, 14, 15, 16). Another meta-analysis of genetic variants in endurance and power sports observed that the cohorts of athletes are often small, loosely defined, and drawn from heterogeneous populations, which weakens the ability to correlate genotype with phenotype precisely (7, 13). Genetic research in African populations also raises important ethical and sociocultural issues (2, 21). A scoping review of genetics and genomics policies in Africa reveals that existing regulatory frameworks across many countries are incomplete, particularly in areas such as informed consent, benefit-sharing, feedback on individual genetic findings, and community engagement (21). Additionally, concerns have been raised about exploitation when external research centers lead studies without equitable local collaboration or authorship. This issue has been documented in genetic studies using DNA samples from Cameroon, where many publications had minimal involvement from Cameroonian institutions and researchers (2, 21).

Applied/Practical Section

Genetic profiling holds promise for personalizing endurance training by aligning programs with an athlete's genetic makeup (1, 3, 4). Variants in genes such as AC*E, ACTN3,* and *VEGFA* influence cardiovascular efficiency, muscle fiber composition, and angiogenesis, allowing for more targeted training and injury prevention (1, 3, 6, 14). Genetic information can also optimize nutrition, as polymorphisms affecting carbohydrate metabolism influence glycogen storage and utilization, enabling diet plans that sustain endurance performance (10, 24). Athletes genetically predisposed to endurance may benefit from high-volume, low-intensity training, while those with power-oriented profiles respond better to shorter, high-intensity sessions (3, 22). However, relying solely on genetic testing is problematic, as current evidence linking specific polymorphisms to endurance remains limited and inconsistent. Gene–environment interactions including training, nutrition, and altitude exposure play important roles, particularly among East African runners (4, 5, 6, 12, 16). Experts caution that genetics should complement, not replace, conventional training methods and must not be used for talent identification until stronger scientific evidence emerges (18, 19, 20).

Future Directions

Future endurance research should integrate genetics with proteomics and metabolomics to reveal how genetic variants influence molecular and energy pathways. Multi-omics approaches provide a systems-level view by linking DNA variation to protein and metabolite profiles (1, 2, 3, 24). Studies have connected endurance with mitochondrial gene expression, angiogenesis, and biomarkers of energy metabolism and oxidative stress (4, 5, 6, 8, 9, 10, 11). Genome-wide association studies (GWAS) and polygenic risk scores (PRS) are promising approaches to understanding the complex genetic basis of endurance performance. Unlike single-gene studies, GWAS allow the detection of several genomic loci that can be related to elite endurance phenotypes, whereas PRS allows estimating the overall genetic predisposition. The use of these analytical models on large and carefully characterized African cohorts can help to improve the understanding of polygenic contributions and help to create personalized training programs. (2, 12, 13, 22). Integrating molecular, environmental, and training data may improve personalized strategies, though genetic testing's predictive power remains limited without broader molecular context (14, 15, 16, 17, 18, 19, 20, 21, 23). Table 02 summarizes the chronological development of key discoveries in endurance genetics and physiology between 1960 and 2020.

Table 02: Timeline of Key Research Milestones in Endurance Genetics and Physiology (1960–2020)

Period	Key research focus	Examples
1960-1970	Early physiological studies	VO2 max, lactate threshold, cardiovascular efficiency (4, 5, 6)
1980-1990	Biochemical & muscle composition research	Muscle fiber typing, oxidative enzyme activity (4, 6, 7)
2000	Candidate gene era	ACTN3, ACE, PPARA, ADRB2 VEGFA associations (1, 3, 8, 14, 15)
2010	Mitochondrial & epigenetic focus	mtDNA haplogroups, DNA methylation in PGC 1 (9, 10, 11)
2020	Multi-omics & systems biology approaches	GWAS, transcriptomics, proteomics, metabolomics (2, 22, 24, 23)

Conclusion

Elite endurance in African athletes is a result of complex interactions among genetic, physiological, environmental, and cultural factors, rather than a single factor. Genes such as *ACE, ACTN3, PPARGC1A, VEGFA,* and mitochondrial variants have been studied; however, results remain inconsistent due to genetic diversity and polygenic inheritance. Physiological traits such as high VO_2 max, fatigue resistance, and running economy are influenced by altitude, active lifestyles, and cultural motivations, highlighting the synergistic effect between genetic factors and environmental influences. Emerging areas, such as epigenetics, microbiome, and multi-omics, offer valuable insights but also face significant ethical and methodological challenges. Progress requires large African cohorts, fair collaborations, and integrated genomic cultural approaches.

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