

### **Cellular and Molecular Biology**

#### Review

# The role of genetic and hormonal factors in shaping exercise responses and performance in children: a comprehensive review



CMB

### Gholamreza Zourmand<sup>1</sup>, Morteza Taheri<sup>2</sup>, Ebrahim Shaabani Ezdini<sup>3</sup>, Khadijeh Irandoust<sup>3,4\*</sup>

<sup>1</sup> Department of Physical Education and Sport Science, Huanggang Normal University, Huanggang, China <sup>2</sup> Department of Behavioral and Cognitive Sciences in Sport, Faculty of Sport Sciences and Health, University of Tehran, Tehran ,Iran

<sup>3</sup> Department of Sports Sciences, Faculty of Social Sciences, Imam Khomeini International University, Qazvin, Iran <sup>4</sup> BITA Department for Scientific Sports Studies, Qazvin, Iran

### **Article Info**

### Abstract



Article history:

**Received:** January 18, 2025 **Accepted:** April 14, 2025 **Published:** May 31, 2025

Use your device to scan and read the article online



This review aims to explore the role of genetic and hormonal factors in shaping exercise responses and performance in children, providing insights into their implications for training and talent identification. A comprehensive narrative review of the literature was conducted, analyzing studies published between 2014 and 2024. The review focused on genetic predispositions, key hormones regulating exercise performance, and their combined influence on physical development in children. Data were collected from peer-reviewed journals and analyzed using a descriptive approach to identify patterns and practical applications in pediatric exercise science. The review highlights that genetic factors play a foundational role in determining physical attributes such as muscle composition, aerobic capacity, and metabolic efficiency. Key genes, including ACTN3 and ACE, have been linked to variations in strength, endurance, and recovery potential. Hormonal factors, particularly growth hormone, insulin-like growth factor-1, testosterone, and cortisol, dynamically influence exercise adaptation, with significant changes occurring during developmental stages. The interaction between genetic and hormonal influences suggests that personalized training approaches can optimize performance while considering developmental stages and environmental factors. Ethical considerations surrounding genetic testing for talent identification remain a critical concern, emphasizing the need for responsible and evidence-based application in pediatric sports programs. Therefore, it is crucial to understand the relationship between genetic and hormonal factors for designing individualized exercise programs that enhance athletic potential while ensuring long-term health and well-being. Future research should focus on integrating genetic and hormonal insights with environmental and behavioral factors to develop holistic training strategies for children.

**Keywords:** Genetics, Hormones, Exercise performance, Children, Talent identification, Personalized training, Physical development.

### 1. Introduction

Understanding the factors that influence exercise responses and performance in children is a topic of increasing interest in both sports science and pediatric health [1]. Children exhibit significant variability in their physical capabilities, and this variability is often attributed to a combination of genetic and hormonal factors. Genetic predisposition plays a crucial role in determining an individual's response to physical activity, influencing attributes such as muscle composition, endurance, and strength [2, 3]. Additionally, hormonal changes during growth and development significantly impact physical performance, regulating processes such as muscle growth, energy metabolism, and recovery [4]. Investigating the interplay between genetic and hormonal influences is essential for developing tailored exercise interventions that optimize children's health and athletic potential [5].

Genetics contribute to physical performance by af-

fecting key physiological traits such as aerobic capacity, muscle fiber type distribution, and metabolic efficiency [6]. Studies have identified specific genetic markers that are associated with enhanced athletic potential in children, including variations in genes related to muscle function, oxygen utilization, and recovery [7]. These genetic variations can explain why some children respond more favorably to training programs than others [8]. The identification of genetic predispositions has led to discussions on personalized training regimens that cater to an individual's unique genetic profile, offering opportunities for early talent identification and targeted training strategies [9]. However, the ethical considerations surrounding genetic testing in children remain a significant concern, emphasizing the importance of balanced approaches that consider both potential benefits and risks [10-12].

Hormonal regulation is another critical factor influencing exercise performance in children. Hormones such as

<sup>\*</sup> Corresponding author.

E-mail address: irandoust@soc.ikiu.ac.ir (K. Irandoust).

Doi: http://dx.doi.org/10.14715/cmb/2025.71.5.10

growth hormone, insulin-like growth factor-1, cortisol, and sex hormones play a pivotal role in muscle development, energy balance, and recovery [13-15]. During childhood and adolescence, hormonal fluctuations can significantly impact physical performance, with puberty serving as a key period of change [16]. Differences in hormonal responses between boys and girls further highlight the complex interplay of biological factors that shape exercise adaptations [17]. Growth hormone, for instance, is known to influence muscle hypertrophy and bone development [18], while cortisol levels can affect energy metabolism and stress responses during exercise [19]. Understanding these hormonal influences is essential for designing ageappropriate training programs that align with developmental stages and physiological capacities [20].

The growing prevalence of physical inactivity and associated health concerns underscores the importance of examining genetic and hormonal factors in children's exercise performance [21]. Childhood obesity, metabolic disorders, and sedentary lifestyles pose significant challenges to public health, making it imperative to identify the biological underpinnings of physical fitness and develop effective intervention strategies [14]. Genetic and hormonal insights can contribute to personalized exercise programs that cater to individual needs, promoting physical activity from an early age and fostering lifelong healthy habits [22]. By leveraging advancements in genetic research and endocrinology, it is possible to create targeted interventions that enhance physical fitness outcomes and reduce the risk of lifestyle-related diseases [23].

Despite the potential benefits of genetic and hormonal insights, challenges remain in translating research findings into practical applications. The complexity of geneenvironment interactions presents significant hurdles in applying genetic findings to exercise training [24]. Ethical considerations surrounding genetic testing, particularly in minors, require careful assessment to ensure that such information is used responsibly [25]. Additionally, socioenvironmental factors such as nutrition, access to sports facilities, and parental support play crucial roles in shaping exercise responses, highlighting the multifaceted nature of physical performance in children [26]. Future research should focus on integrating genetic and hormonal data with environmental and behavioral factors to develop holistic approaches that support children's physical development [27].

The primary objective of this comprehensive review is to analyze and synthesize existing literature on the role of genetic and hormonal factors in shaping exercise responses and performance in children. By examining recent studies and theoretical frameworks, this review aims to provide a deeper understanding of how genetic predispositions and hormonal fluctuations contribute to physical fitness outcomes. Furthermore, the review seeks to highlight practical implications for pediatric exercise programs, informing coaches, parents, and healthcare professionals on evidence-based strategies to optimize children's athletic potential.

### 2. Methods

### 2.1. Literature search strategy

This narrative review was conducted using a comprehensive literature search to gather relevant scientific studies published between 2014 and 2024. A systematic approach was applied to identify research articles, review papers, and meta-analyses related to genetic and hormonal factors influencing exercise responses and performance in children. The primary databases used for this search included PubMed, Scopus, Web of Science, and Google Scholar, ensuring broad coverage of the topic across various disciplines, including sports science, genetics, endocrinology, and pediatrics. Search terms were carefully selected based on the study's objectives and included keywords such as "genetic factors in exercise performance," "hormonal regulation of physical activity," "children and exercise adaptation," "genetics and sports performance," and "pediatric endocrinology and physical fitness." Boolean operators such as AND and OR were used to refine searches and identify studies that met the inclusion criteria.

### 2.2. Inclusion and exclusion criteria

Studies were selected based on predefined inclusion and exclusion criteria to ensure the relevance and quality of the reviewed literature. Inclusion criteria consisted of studies focusing on children and adolescents up to 18 years of age, articles published in peer-reviewed journals, and studies investigating the role of genetic and hormonal factors in physical activity and performance. Only studies published in English and within the specified timeframe were considered. Exclusion criteria included studies that focused solely on adults, animal studies, articles without a clear methodological framework, and papers with inconclusive or contradictory findings without supporting evidence. Additionally, studies that did not provide a direct link between genetic or hormonal factors and exercise responses were omitted from the review.

### 2.2.1. Data extraction and analysis

A structured data extraction process was implemented to systematically collect and analyze relevant information from the selected studies. The extracted data included details such as study design, population characteristics, sample size, genetic markers or hormones investigated, outcome measures related to exercise performance, and key findings. Particular attention was given to studies that employed advanced molecular techniques, such as genome-wide association studies (GWAS) and hormonal profiling, to ensure a thorough understanding of the interplay between genetic and hormonal influences on exercise responses in children. The findings were categorized based on themes such as genetic predisposition to endurance and strength training, the influence of pubertal hormonal changes, and gene-environment interactions.

### 2.2.2. Quality assessment

To ensure the credibility and reliability of the included studies, a quality assessment was performed using established criteria such as study design, sample representativeness, methodological rigor, and statistical analysis. Studies employing randomized controlled trials (RCTs), cohort studies, and longitudinal designs were given preference, while cross-sectional studies were critically evaluated for their limitations in establishing causal relationships. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were used as a reference to enhance transparency and reproducibility in the

# 3. Genetic factors influencing exercise responses in children

Genetic factors are pivotal in influencing exercise responses and physical performance in children, contributing to significant inter-individual variability [28, 29]. Studies have demonstrated that genetic predisposition accounts for a substantial proportion of the differences observed in aerobic capacity, muscle strength, and metabolic efficiency among children engaged in physical activities [30]. Various genetic markers have been identified that correlate with exercise performance, suggesting that inherited traits influence the way children respond to different types of training regimens. This genetic influence extends to traits such as muscle fiber composition, oxygen uptake efficiency, and recovery time following exercise [31, 32]. Children with specific genetic profiles may exhibit superior endurance capabilities, while others may demonstrate enhanced strength and power attributes, underlining the complexity of genetic contributions to physical performance [2]. Inter-individual variability in exercise performance can be attributed to polymorphisms in genes related to muscle contraction, cardiovascular function, and metabolic pathways. These genetic variations not only affect baseline physical capabilities but also determine the extent to which an individual can improve with training interventions. Research has shown that children with favorable genetic predispositions tend to experience greater gains in fitness levels compared to their peers, emphasizing the role of genetics in shaping athletic potential [4, 33].

Among the various genetic markers associated with exercise performance, specific genes have been widely studied for their contribution to different physical attributes. The ACTN3 gene, which encodes alpha-actinin-3, is one of the most extensively researched genetic factors linked to athletic performance [34, 35]. This gene is particularly associated with fast-twitch muscle fibers, which are crucial for power and speed-related activities. Individuals with the RR genotype of the ACTN3 gene are often found to have a higher proportion of these muscle fibers, making them better suited for activities requiring explosive power, such as sprinting and weightlifting [36]. Conversely, the XX genotype is linked to endurance-oriented traits, favoring slow-twitch muscle fibers that support prolonged aerobic activity [6, 37]. The ACE gene, encoding the angiotensin-converting enzyme, has also been identified as a key determinant of exercise performance [38]. The presence of the I allele in the ACE gene is associated with enhanced endurance performance, as it contributes to greater efficiency in oxygen utilization and cardiovascular function. In contrast, the D allele has been linked to increased strength and power capabilities, providing a genetic advantage for activities requiring short bursts of intense effort [7, 31, 39]. Another important gene, PPA-RA, plays a role in lipid metabolism and energy utilization during exercise. Variants of this gene have been shown to influence the body's ability to utilize fat as a fuel source, impacting endurance performance and overall exercise efficiency. These genetic insights provide a foundation for understanding how inherited factors influence physical capabilities in children, shaping their responses to various types of physical activities [8, 40].

Different genetic profiles contribute to variations in

exercise modalities, with distinct genetic influences observed in endurance and strength-related performance [37, 41]. Endurance-based activities, such as long-distance running and cycling, require efficient oxygen delivery, sustained energy production, and muscle fatigue resistance. Genetic factors that enhance aerobic capacity, mitochondrial function, and cardiovascular efficiency play a critical role in optimizing endurance performance. Studies have found that children with favorable genetic profiles related to aerobic metabolism exhibit superior endurance capabilities and are better able to sustain prolonged physical exertion [5, 42]. Strength-related exercise modalities, on the other hand, depend on factors such as muscle fiber composition, neuromuscular coordination, and anaerobic energy production. Genetic variants that enhance muscle hypertrophy, contractile force, and power output provide a distinct advantage in strength-oriented sports such as weightlifting, gymnastics, and sprinting. The interplay between genetic predisposition and environmental factors, such as training and nutrition, further modulates an individual's potential in these exercise modalities, highlighting the complex interactions between inherited traits and lifestyle choices [20]. Genetic testing has been increasingly utilized to identify children's potential in different exercise domains, allowing for the customization of training programs based on their genetic predispositions. However, ethical considerations surrounding genetic testing in minors remain a concern, emphasizing the need for responsible application of genetic insights in sports and fitness settings [43, 44].

The emerging field of epigenetics has provided new perspectives on how environmental factors interact with genetic predispositions to influence exercise adaptation in children. Epigenetic modifications, such as DNA methylation and histone acetylation, play a crucial role in regulating gene expression without altering the underlying genetic code. These modifications are influenced by factors such as physical activity, nutrition, and lifestyle choices, demonstrating that gene-environment interactions can significantly impact exercise responses and performance [13-15]. Studies have shown that regular physical activity can induce beneficial epigenetic changes that enhance metabolic efficiency, muscle adaptation, and overall fitness. For instance, exercise-induced DNA methylation changes have been observed in genes related to energy metabolism and muscle growth, suggesting that training can modify gene expression patterns to optimize physical performance [45]. Childhood represents a critical period for epigenetic programming, where lifestyle interventions can have long-lasting effects on health and fitness outcomes. Encouraging regular physical activity and healthy nutritional habits during early developmental stages can promote favorable epigenetic modifications that support long-term exercise adaptations and overall well-being [9]. Additionally, emerging evidence suggests that epigenetic factors may partially explain the inter-individual variability in exercise responses, highlighting the need for personalized approaches that consider both genetic and environmental influences [23].

Despite the significant progress in understanding genetic and epigenetic contributions to exercise performance in children, several challenges remain in translating these insights into practical applications. The complexity of gene-environment interactions, ethical concerns related to genetic testing, and the potential for misinterpretation of genetic data pose challenges for integrating genetic insights into youth sports programs. Moreover, the dynamic nature of growth and development in children further complicates the assessment of genetic influences, necessitating longitudinal studies to better understand how genetic predispositions evolve over time [22]. Future research should focus on exploring the combined effects of genetic and environmental factors, identifying potential intervention strategies that leverage genetic insights while promoting holistic approaches to physical development [18]. By integrating genetic and epigenetic data with environmental and behavioral factors, it is possible to develop comprehensive strategies that optimize exercise responses and performance in children [19]. This integrated approach can help create individualized training programs that maximize children's athletic potential while ensuring their long-term health and well-being [14].

In conclusion, genetic factors play a crucial role in shaping exercise responses and performance in children, influencing attributes such as endurance, strength, and metabolic efficiency. Key genes such as ACTN3, ACE, and PPARA have been identified as significant contributors to physical performance, with distinct effects on endurance and strength-related modalities. Future research should continue to explore the interplay between genetic predispositions and environmental influences, providing a deeper understanding of how to optimize exercise responses and promote lifelong health in children. A summary of the gene descriptions is provided in Table 1.

# 4. Hormonal regulation of exercise responses in children

Hormonal regulation plays a crucial role in influencing exercise responses and performance in children, as hormones act as primary mediators of physiological development and adaptation to physical activity. Throughout childhood and adolescence, hormones regulate growth, energy metabolism, and tissue development, making them essential determinants of physical fitness. Hormonal influence on physiological development is particularly evident in the musculoskeletal system, cardiovascular function, and metabolic processes, where hormones such as growth hormone, insulin-like growth factor-1, testosterone, and cortisol work in synergy to support the body's response to exercise [46, 47]. These hormones not only facilitate the growth and repair of tissues but also contribute to energy regulation, muscle adaptation, and recovery following physical exertion. The intricate balance of these hormones ensures optimal development and performance in response to varying physical demands, making them critical factors in designing effective exercise programs for children and adolescents. Variations in hormonal levels during different growth stages significantly influence physical capabilities, emphasizing the need for age-specific training strategies that align with hormonal fluctuations to optimize growth and exercise performance [13-15].

Several key hormones play a vital role in children's exercise performance, with growth hormone being one of the most critical. Growth hormone is essential for promoting longitudinal bone growth, stimulating protein synthesis, and enhancing muscle hypertrophy. It also facilitates the mobilization of fat stores for energy production, thereby supporting endurance activities and overall energy efficiency during exercise. The secretion of growth hormone increases in response to physical activity, particularly during high-intensity exercises, contributing to muscle recovery and adaptation over time. Insulin-like growth factor-1, closely associated with growth hormone, mediates many of its anabolic effects, promoting cell growth and differ-

Category	Key Factor/Gene	Explanation
Inter-individual Variability	Genetic Predisposition	Accounts for substantial differences in aerobic capacity, muscle strength, and metabolic efficiency among children engaged in physical activities.
Specific Genes	ACTN3 Gene	- RR genotype: Associated with fast-twitch muscle fibers (power activities) XX genotype: Favors endurance-oriented traits (slow-twitch muscle fibers).
	ACE Gene	- I allele: Associated with enhanced endurance performance and oxygen utilization - D allele: Linked to increased strength and power capabilities.
	PPARA Gene	Plays a role in lipid metabolism and energy utilization during exercise. Variants influence the body's ability to utilize fat as a fuel source, impacting endurance performance and exercise efficiency.
Exercise Performance	Exercise Modality Influences	- Different genetic profiles contribute to variations in endurance versus strength- related performance Genetic factors enhance aerobic capacity for endurance activities- Others favor muscle hypertrophy and power output for strength activities.
Epigenetics	Epigenetic Modifications	- Environmental factors interact with genetic predispositions through DNA methylation and histone acetylation, regulating gene expression without altering the genetic code Regular physical activity can induce beneficial epigenetic changes.
Developmental Impact	Critical Development Period	Childhood represents a crucial period for epigenetic programming, where lifestyle interventions can have long-lasting effects on health and fitness outcomes.
Research & Ethical Considerations	Research Challenges	- Complexity of gene-environment interactions Ethical concerns related to genetic testing in minors- Potential misinterpretation of genetic data Challenges for integrating genetic insights into youth sports programs.

 Table 1. Summary of gene descriptions.

entiation in various tissues. This hormone plays a pivotal role in muscle development and repair, enabling children to build strength and endurance in response to training. Studies have shown that regular physical activity enhances the secretion and effectiveness of insulin-like growth factor-1, highlighting its importance in exercise-induced muscle adaptation [23]. Testosterone, another critical hormone in exercise performance, is primarily known for its anabolic effects on muscle growth and strength. Although its levels are relatively low in prepubescent children, they increase significantly during puberty, leading to marked improvements in muscle mass and strength. Testosterone influences protein synthesis and neuromuscular coordination, making it particularly relevant for strength-based exercises and athletic performance during adolescence. Cortisol, often referred to as the stress hormone, plays a dual role in exercise performance. While it aids in the mobilization of energy stores and supports metabolic function during physical activity, prolonged elevated levels can lead to muscle breakdown and impaired recovery. Managing cortisol levels through appropriate training and recovery strategies is essential to prevent overtraining and ensure optimal physical development in children [18].

Sex differences in hormonal responses to exercise become increasingly evident as children progress through puberty, with significant variations in hormone levels between boys and girls. Puberty marks a critical period of hormonal changes that influence physical development and exercise performance, with boys experiencing a surge in testosterone levels that facilitates greater muscle growth and strength development. This hormonal shift contributes to the observed differences in physical capabilities between boys and girls, with boys generally exhibiting higher muscle mass, strength, and power output. In contrast, estrogen, the primary female sex hormone, plays a significant role in modulating fat distribution, bone density, and endurance capacity in girls. Estrogen enhances collagen synthesis and promotes the maintenance of bone health, making it particularly important for activities that require flexibility and endurance. These hormonal differences influence training responses, with boys typically benefiting more from resistance training and girls demonstrating superior endurance adaptations. Understanding these gender-related differences is essential for designing exercise programs that cater to the unique physiological needs of boys and girls, ensuring balanced development and injury prevention [14]. The influence of puberty on exercise performance is further complicated by individual variability in the timing and progression of hormonal changes, highlighting the need for personalized training approaches that consider each child's developmental stage [22].

Endocrine adaptations to different types of exercise vary depending on the nature and intensity of the physical activity, with resistance training and aerobic exercise eliciting distinct hormonal responses. Resistance training, which involves high-intensity, short-duration exercises, primarily stimulates the production of anabolic hormones such as growth hormone and testosterone. These hormones promote muscle hypertrophy, increase strength, and enhance neuromuscular coordination, making resistance training particularly beneficial for developing muscular strength and power in children. Regular engagement in resistance training has been shown to improve hormonal profiles, leading to greater muscle mass and strength gains over time. However, appropriate load management and progression are crucial to prevent excessive stress on the developing musculoskeletal system and avoid potential negative effects on growth and development [4]. In contrast, aerobic exercise, which involves sustained, moderate-intensity activities such as running, cycling, and swimming, primarily stimulates the release of hormones involved in energy metabolism and cardiovascular adaptation. Growth hormone and insulin-like growth factor-1 play a central role in enhancing aerobic capacity by promoting efficient energy utilization and supporting endurance adaptations. Aerobic exercise also influences cortisol levels, with moderate-intensity activities helping to regulate cortisol secretion and prevent excessive stress responses. However, prolonged endurance training without adequate recovery can lead to chronically elevated cortisol levels, which may impair muscle recovery and overall performance [19]. Balancing resistance and aerobic training is essential for promoting comprehensive physical development in children, allowing for the optimal regulation of hormonal responses and minimizing the risk of overtraining or hormonal imbalances [45].

The interaction between exercise and hormonal regulation underscores the importance of adopting a holistic approach to training that considers the dynamic physiological changes occurring throughout childhood and adolescence. Integrating appropriate nutrition, sleep, and recovery strategies is essential for supporting hormonal balance and maximizing exercise adaptations. Nutritional factors such as adequate protein intake, micronutrient sufficiency, and hydration play a significant role in optimizing hormonal responses to exercise, ensuring that children receive the necessary nutrients to support growth and physical performance. Sleep is another critical factor that influences hormonal regulation, with inadequate sleep leading to disruptions in growth hormone secretion and impaired recovery processes. Ensuring sufficient rest and recovery is essential for maintaining hormonal balance and promoting long-term physical development [20]. Psychological factors, including stress and motivation, also influence hormonal responses to exercise, with chronic stress leading to elevated cortisol levels that can negatively impact performance and growth. Creating a supportive and enjoyable exercise environment can help mitigate stress-related hormonal imbalances and foster positive attitudes toward physical activity [48].

Despite the growing understanding of hormonal regulation in exercise responses, several challenges remain in translating research findings into practical applications. Variability in hormonal responses among children, influenced by factors such as genetics, environment, and individual maturity levels, presents challenges in standardizing training protocols. Additionally, ethical considerations surrounding hormone-related interventions in youth sports require careful attention to ensure that training practices align with developmental needs and long-term health outcomes [26]. Future research should focus on exploring the interactions between genetic and hormonal factors, and identifying personalized approaches that optimize exercise performance while safeguarding health and wellbeing. Longitudinal studies tracking hormonal changes over time can provide valuable insights into the long-term impact of exercise on hormonal regulation and physical development, contributing to evidence-based practices in In conclusion, hormonal regulation is a fundamental aspect of children's exercise responses, influencing growth, energy metabolism, and adaptation to physical activity. Key hormones such as growth hormone, insulin-like growth factor-1, testosterone, and cortisol play significant roles in shaping physical performance, with distinct effects observed in resistance and aerobic training modalities. Pubertal changes introduce sex-specific differences in hormonal responses, necessitating tailored training approaches that consider individual developmental stages. By integrating scientific insights into practice, it is possible to optimize exercise responses and promote lifelong physical well-being in children. A summary of the hormonal regulation of exercise responses in children is presented in Table 2.

### 5. Interaction between genetic and hormonal factors

The interaction between genetic and hormonal factors plays a fundamental role in determining exercise performance in children. Genetics provide the foundational blueprint for physiological attributes such as muscle composition, aerobic capacity, and metabolic efficiency, while hormones act as regulatory agents that modulate these genetic potentials in response to various internal and external stimuli [49]. The complex interplay between these two biological components shapes the development of physical abilities and adaptation to exercise training. For example, genetic predispositions may determine baseline muscle fiber composition, but hormonal fluctuations during growth spurts can enhance or inhibit the expression of these traits, resulting in varied responses to physical activity [50]. Understanding how these factors work together is crucial for developing individualized training strategies that align with a child's unique physiological profile and developmental stage [5].

Gene-hormone interactions significantly impact training adaptations by influencing muscle growth, energy utilization, and recovery mechanisms. Specific genetic variants related to muscle function and cardiovascular efficiency can enhance an individual's response to the anabolic effects of hormones such as growth hormone and testosterone [51]. For instance, variations in the ACTN3 gene, which is associated with fast-twitch muscle fibers, may interact with hormonal surges during puberty to promote strength and power development in children. Individuals with the RR genotype of the ACTN3 gene tend to have a higher percentage of fast-twitch fibers, which can be further enhanced by the increased production of testosterone during adolescence, leading to superior performance in strength-based activities. Similarly, the ACE gene, which influences cardiovascular efficiency, interacts with hormonal regulators such as insulin-like growth factor-1 to optimize endurance performance by improving oxygen uptake and utilization during prolonged exercise. These interactions underscore the importance of considering both genetic and hormonal factors when designing training programs, as they collectively determine the extent and rate of physical development [6].

Developmental stages play a critical role in shaping the interaction between genetic and hormonal factors, with significant variations observed from childhood to adolescence. During early childhood, hormonal levels remain relatively stable, and genetic predispositions primarily

Table 2. Summary of hormonal regulation of exercise responses in children.

Category	Key Hormone/Factor	Explanation
Growth & Development	Growth Hormone	Essential for longitudinal bone growth, protein synthesis, and muscle hypertrophy. Secretion increases in response to physical activity, particularly high-intensity exercises, contributing to muscle recovery and adaptation.
	Insulin-like Growth Factor-1 (IGF-1)	Mediates many growth hormone's anabolic effects, promoting cell growth and differentiation. Plays a pivotal role in muscle development and repair, enabling children to build strength and endurance in response to training.
Muscle & Strength	Testosterone	Known for anabolic effects on muscle growth and strength. Levels increase significantly during puberty, leading to improvements in muscle mass and strength. Influences protein synthesis and neuromuscular coordination.
Stress & Recovery	Cortisol	Plays a dual role in exercise performance, aiding in energy mobilization but potentially causing muscle breakdown if chronically elevated. Managing cortisol levels is essential to prevent overtraining.
Pubertal Differences	Sex Differences	Become increasingly evident during puberty. Boys experience testosterone surges leading to greater muscle growth, while estrogen in girls modulates fat distribution, bone density, and endurance capacity.
Exercise Adaptation	Exercise Type Adaptation	Resistance training primarily stimulates anabolic hormones like growth hormone and testosterone, while aerobic exercise influences hormones involved in energy metabolism and cardiovascular adaptation.
External Factors	Environmental Influences	Nutrition, sleep, and psychological factors significantly impact hormonal balance and exercise adaptation. Adequate protein intake, micronutrient sufficiency, and hydration optimize hormonal responses.
Research & Ethical Considerations	Research Challenges	Variability in hormonal responses among children poses challenges in standardizing training protocols. Ethical considerations surrounding hormone- related interventions in youth sports require careful attention.

dictate physical attributes such as muscle composition and aerobic capacity. However, as children approach puberty, hormonal changes become more pronounced, exerting a greater influence on genetic expression and modifying the body's response to exercise [52]. The onset of puberty triggers the release of key hormones such as growth hormone and testosterone, which interact with genetic predispositions to enhance muscle growth, bone density, and overall physical performance. Boys typically experience a more significant increase in testosterone levels, which amplifies their genetic potential for strength and power development, while girls benefit from increased estrogen levels that support endurance and flexibility. These developmental differences highlight the need for gender-specific training interventions that consider both genetic and hormonal

influences to optimize performance outcomes [14]. The dynamic interaction between genetic and hormonal factors is further influenced by environmental conditions such as nutrition, training load, and lifestyle habits [53]. Nutritional intake plays a crucial role in supporting hormonal balance and optimizing the expression of genetic potential. Adequate protein intake, for example, is essential for maximizing the anabolic effects of growth hormone and insulin-like growth factor-1, promoting muscle hypertrophy and recovery. Conversely, poor nutrition can suppress hormonal responses and limit the realization of genetic potential, leading to suboptimal performance outcomes [54]. Training load and intensity also influence the gene-hormone interaction, with appropriately structured exercise regimens enhancing hormonal responses and facilitating greater adaptations. High-intensity resistance training, for instance, can stimulate the production of testosterone and growth hormones, further amplifying the genetic predisposition for strength development in children with favorable genetic profiles. On the other hand, excessive training without adequate recovery can lead to hormonal imbalances, such as elevated cortisol levels, which may negatively impact genetic expression and hinder performance progress [18].

Gene-hormone interactions extend beyond physical performance to include factors such as injury susceptibility and recovery. Certain genetic variants have been associated with an increased risk of musculoskeletal injuries, and hormonal fluctuations can further influence this predisposition. For example, variations in the COL5A1 gene, which affects collagen synthesis and tendon integrity, may interact with hormonal changes during growth spurts, increasing the likelihood of injuries such as tendinopathies and ligament tears. Understanding these interactions allows for the implementation of preventive measures, such as targeted strength training and flexibility programs, to mitigate injury risks and support long-term athletic development. Recovery processes are also influenced by genetic and hormonal factors, with growth hormone and insulin-like growth factor-1 playing critical roles in tissue repair and regeneration. Genetic predispositions related to inflammatory responses and muscle repair can influence the effectiveness of these hormonal mechanisms, determining the speed and quality of recovery following exercise or injury [19].

Despite the significant influence of genetic and hormonal interactions on exercise performance, challenges remain in translating these findings into practical applications. One of the primary challenges is the variability in individual responses, as the same genetic profile may elicit different outcomes depending on hormonal status and environmental factors. Additionally, ethical considerations regarding genetic testing in children must be carefully addressed to ensure that such information is used responsibly and does not lead to undue pressure or unrealistic expectations. Educating parents, coaches, and healthcare professionals about the complex interplay between genetics and hormones is essential for fostering a supportive and informed approach to youth sports and physical development [26].

The growing field of personalized medicine and sports science offers promising avenues for leveraging genetic and hormonal insights to enhance training outcomes in children. Advances in genetic screening and hormonal profiling provide opportunities for early identification of strengths and weaknesses, allowing for the customization of training programs that align with individual physiological profiles. Personalized approaches can help optimize performance, reduce the risk of overtraining and injuries, and promote long-term engagement in physical activity. However, it is essential to balance scientific advancements with practical considerations, ensuring that training interventions remain evidence-based and tailored to the unique needs of each child [10-12].

In conclusion, the interaction between genetic and hormonal factors is a key determinant of exercise performance in children, influencing physical development, training adaptations, and recovery processes. Genetics provide the underlying framework for physical capabilities, while hormones act as modulators that enhance or inhibit these genetic potentials in response to various stimuli. The influence of developmental stages, environmental factors, and training regimens further complicates this relationship, highlighting the need for a comprehensive and individualized approach to exercise programming. By understanding and leveraging the interplay between genetics and hormones, it is possible to optimize training outcomes and support healthy physical development in children, paving the way for lifelong engagement in physical activity and sports [22]. A summary of Interaction Between Genetic and Hormonal Factors in Table 3.

### 6. Practical implications for training and talent identification

The application of genetic and hormonal insights in sports science and pediatric exercise programs has the potential to revolutionize the way young athletes are trained and developed. Understanding the genetic predisposition of children allows for the identification of inherent strengths and weaknesses, enabling the design of exercise programs that maximize their potential while minimizing the risk of injury and burnout. Hormonal regulation, on the other hand, provides valuable information on the timing and intensity of training that aligns with developmental stages, ensuring that interventions are both safe and effective. In pediatric exercise programs, integrating genetic and hormonal assessments can aid in structuring training regimens that cater to individual physiological needs, optimizing both performance outcomes and overall health. By identifying children with a genetic predisposition for endurance, strength, or speed, coaches and sports scientists can tailor training programs to enhance these innate abilities while also addressing potential deficiencies

Genetics and hormones in child exercise.

 Table 3. Summary of interaction between genetic and hormonal factor.

Category	Key Interaction/Factor	Explanation
Fundamental Mechanisms	Foundational Interplay	Genetics provide the blueprint for physiological attributes, while hormones act as regulatory agents that modulate these genetic potentials in response to stimuli. This interaction shapes the development of physical abilities and adaptation to exercise.
Specific Gene/ Hormone Links	Gene-Hormone Training Impact	- Specific genetic variants related to muscle function can enhance an individual's response to anabolic hormones ACTN3 gene variants interact with pubertal testosterone to promote strength development ACE gene interacts with insulin-like growth factor-1 to optimize endurance performance.
Developmental Stages	Developmental Stage Influence	- During early childhood, genetic predispositions primarily dictate physical attributes As children approach puberty, hormonal changes become more pronounced, exerting greater influence on genetic expression and modifying exercise response.
Modulating Factors	Environmental Modulation	<ul> <li>Nutrition, training load, and lifestyle habits influence gene-hormone interactions.</li> <li>Adequate protein intake maximizes anabolic effects of growth hormone Appropriate training intensity enhances hormonal responses and facilitates greater adaptations.</li> </ul>
Injury & Recovery	Injury and Recovery Factors	- Gene-hormone interactions affect injury susceptibility and recovery Variations in genes like COL5A1 may interact with hormonal changes during growth spurts, influencing injury risk Recovery processes are influenced by growth hormone and genetic factors related to inflammatory responses.
Implementation Challenges	Implementation Challenges	- Individual variability in responses presents challenges, as the same genetic profile may elicit different outcomes depending on hormonal status- Ethical considerations regarding genetic testing in children must be carefully addressed.
Personalization Potential	Personalized Approach Potential	- Advances in genetic screening and hormonal profiling provide opportunities for customizing training programs that align with individual physiological profiles This can optimize performance, reduce overtraining risks, and promote long-term engagement in physical activity.
Holistic Approach	Comprehensive Framework	- The relationship between genes and hormones is influenced by developmental stages, environmental factors, and training regimens, highlighting the need for an individualized approach to exercise programming for children.

through targeted interventions. This approach allows for a more efficient allocation of training resources and helps in nurturing young talent based on scientifically validated criteria rather than subjective observations alone [4].

Personalized training approaches based on genetic and hormonal profiles have gained increasing attention in the field of pediatric sports science. Individualized training regimens take into account the unique physiological responses of children to different types of exercise, thereby enhancing their ability to improve performance while avoiding the negative effects of overtraining. For instance, children with genetic markers associated with fasttwitch muscle fibers and higher testosterone levels may benefit more from strength and power training, whereas those with genetic predispositions for aerobic efficiency and endurance-related hormonal responses may excel in long-distance running or endurance sports. Personalized exercise prescriptions can also be beneficial in addressing specific training adaptations, such as muscle recovery and injury prevention, by understanding how hormonal fluctuations affect tissue repair and energy metabolism. Tailoring exercise programs to align with the natural hormonal cycles of growing children can help optimize peak performance periods and ensure proper recovery during times of hormonal fluctuations, such as puberty. Moreover, understanding genetic markers related to metabolism can assist in designing nutrition plans that complement training efforts, ensuring that young athletes receive adequate fuel for their physiological demands. Personalized training strategies not only enhance performance but also contribute to long-term athlete development by promoting sustainable training loads and fostering healthy lifestyle habits from an early age [14].

Despite the potential benefits, the use of genetic testing for talent identification in sports raises several ethical considerations and limitations that must be carefully addressed. One of the primary ethical concerns revolves around the potential misuse of genetic information to categorize or limit children's opportunities in sports based on their genetic predisposition. There is a risk that genetic testing could create undue pressure on children to pursue specific sports or training regimens based solely on their genetic profiles, potentially leading to psychological stress and limiting their ability to explore diverse athletic interests. The commercialization of genetic testing in youth sports also raises concerns regarding data privacy and the potential for discrimination based on genetic predispositions. Ensuring informed consent and safeguarding genetic data are essential aspects of ethical practice when utilizing genetic information in talent identification programs. Additionally, the accuracy and predictive value of genetic testing in determining athletic potential remain areas of debate within the scientific community. While genetic markers provide valuable insights into certain physiological traits, they do not account for environmental influences, motivation, or the dynamic nature of human development. Relying too heavily on genetic testing without considering the multifactorial nature of athletic performance could result in an overly deterministic approach that overlooks the potential for improvement through training and experience [10-12].

Another limitation of genetic testing in sports talent identification is the variability in gene expression influenced by environmental factors such as training, nutrition, and lifestyle choices. Even children with a favorable genetic predisposition may not achieve optimal performance without the appropriate training and support systems in place. Conversely, children without specific advantageous genetic markers may still achieve high levels of performance through dedicated training and adaptive responses to exercise. This highlights the importance of adopting a holistic approach that combines genetic insights with comprehensive training methodologies that consider individual goals, developmental stages, and psychosocial factors. The dynamic nature of hormonal regulation also adds complexity to talent identification processes, as hormonal responses to exercise can vary widely based on factors such as stress, sleep, and overall health. Therefore, while genetic and hormonal testing can provide valuable supplementary information, they should be used as part of a broader athlete development framework rather than as standalone predictors of success [22].

Implementing genetic and hormonal assessments in pediatric sports programs requires collaboration between coaches, healthcare professionals, and sports scientists to ensure that the data is interpreted and applied responsibly. Educating all stakeholders on the appropriate use and limitations of genetic and hormonal information is crucial to prevent unrealistic expectations and promote ethical decision-making. Parents also play a vital role in ensuring that genetic insights are used to support their child's development positively and encouragingly rather than imposing undue pressure or expectations. Ethical guidelines and regulatory frameworks should be established to govern the use of genetic testing in youth sports, ensuring that it is used primarily to enhance athlete well-being and development rather than for exclusionary or exploitative purposes. The development of standardized protocols for genetic and hormonal assessments can help ensure consistency and reliability in their application, allowing for evidence-based decision-making in talent identification and training design [26].

Looking forward, the integration of genetic and hormonal insights into sports training holds great promise for advancing the field of personalized exercise science, but it must be approached with caution and a focus on ethical responsibility. Future research should continue to explore the interaction between genetic and environmental factors, with an emphasis on understanding how training interventions can modulate genetic expression and hormonal responses over time [55]. Longitudinal studies tracking young athletes' development from childhood to adolescence can provide valuable insights into the longterm effects of genetic and hormonal influences on performance outcomes. Advances in technology, such as wearable devices and real-time biomonitoring, may also offer new opportunities for tracking physiological responses to exercise and optimizing training strategies based on individual needs. However, it is essential to balance scientific advancements with a commitment to ethical integrity and the overall well-being of young athletes to ensure that genetic insights are used as tools for empowerment rather than limitation [18].

In conclusion, the application of genetic and hormonal insights in pediatric sports programs offers exciting possibilities for optimizing training and talent identification. Personalized training approaches based on individual genetic and hormonal profiles have the potential to enhance performance while minimizing the risk of injury and overtraining. However, the ethical considerations and limitations associated with genetic testing must be carefully navigated to ensure that these tools are used responsibly and in the best interest of the child. By adopting a balanced and evidence-based approach, sports scientists, coaches, and healthcare professionals can harness the power of genetic and hormonal data to support the holistic development of young athletes, fostering a positive and sustainable engagement with physical activity and sports.

### 7. Conclusion

The review of genetic and hormonal factors influencing exercise responses and performance in children highlights the intricate interplay between inherited traits and biological regulatory mechanisms. Genetic predisposition plays a foundational role in determining key physical attributes such as muscle composition, endurance capacity, and metabolic efficiency, while hormonal fluctuations act as modulators that dynamically influence these traits throughout childhood and adolescence. Together, these factors shape an individual's ability to respond to training stimuli, adapt to physical challenges, and achieve optimal performance levels. The interaction between genetic and hormonal influences underscores the importance of adopting personalized approaches to exercise programming that cater to the unique physiological profiles of children, ensuring both safety and effectiveness in their athletic development.

Practical recommendations emerging from this review emphasize the need for individualized training strategies that align with genetic predispositions and hormonal profiles. Tailoring exercise programs based on a child's specific genetic and hormonal characteristics can help maximize their potential while minimizing the risk of injury or overtraining. Personalized approaches should incorporate considerations for developmental stages, ensuring that training interventions are appropriately timed to align with critical periods of growth and maturation. Additionally, a holistic approach that integrates nutritional support, adequate rest, and psychological well-being is essential to optimize performance outcomes and promote overall health. Educating coaches, parents, and healthcare professionals about the implications of genetic and hormonal factors can further enhance the effectiveness of training programs and foster a supportive environment for young athletes.

Despite the potential benefits of leveraging genetic and hormonal insights, several challenges remain in translating these findings into practical applications. One of the primary challenges is the complexity of gene-environment interactions, as factors such as training load, nutrition, and psychosocial influences play a significant role in shaping physical performance. The ethical considerations associated with genetic testing, particularly in minors, also present obstacles that must be carefully managed to avoid undue pressure, unrealistic expectations, or privacy concerns. Additionally, the dynamic nature of hormonal fluctuations requires continuous monitoring and adaptation of training protocols, which can be resource-intensive and logistically challenging. Addressing these challenges will require a collaborative effort among researchers, practitioners, and policymakers to develop evidence-based guidelines that prioritize the well-being and development of young athletes.

Looking ahead, future research should focus on advancing the understanding of how genetic and hormonal factors interact with lifestyle and environmental influences to shape exercise responses over time. Longitudinal studies tracking the physical development of children through various stages of growth will provide valuable insights into the long-term impact of genetic predispositions and hormonal adaptations on performance outcomes. Advances in technology, such as wearable devices and biomonitoring tools, offer promising opportunities for real-time tracking of physiological responses and personalized training adjustments. Furthermore, the integration of genetic and hormonal insights into broader public health initiatives can help promote lifelong engagement in physical activity and support efforts to combat sedentary lifestyles and related health conditions in children.

In conclusion, the interplay between genetic and hormonal factors represents a critical determinant of exercise performance and adaptation in children. A nuanced understanding of these influences can inform the development of tailored training programs that maximize potential while ensuring the holistic well-being of young athletes. While challenges exist in the practical implementation of genetic and hormonal insights, ongoing research and technological advancements hold promise for refining and expanding their applications in pediatric exercise science. By adopting a balanced approach that prioritizes ethical considerations, scientific evidence, and individualized support, stakeholders can contribute to the development of healthier, more active generations of children equipped to achieve their physical potential.

### **Authors' contributions**

Authors contributed equally to this article.

### Declaration

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

### **Transparency statement**

Data are available for research purposes upon reasonable request to the corresponding author.

### Acknowledgments

We would like to express our gratitude to all individuals helped us to do the project.

### **Declaration of interest**

The authors report no conflict of interest.

### Funding

According to the authors, this article has no financial support.

### **Ethics considerations**

As a review of existing literature, this study did not involve direct interaction with human participants or the collection of primary data. Ethical approval was therefore not required. However, care was taken to appropriately credit all sources and adhere to principles of academic integrity. The review also prioritized the inclusion of studies that had undergone ethical scrutiny, ensuring that the findings presented are based on ethically conducted research.

### References

- Estevan I, De Meester A, Barnett LM (2023) Advancing the understanding in the association between actual/perceived motor competence and health-related factors among children and adolescents. Psychol Sport Exerc 67:102420. doi: 10.1016/j.psychsport.2023.102420
- Eynon N, Voisin S, Lucía A, Wang G, Pitsiladis Y (2017) Preface: Genomics and Biology of Exercise Is Undergoing a Paradigm Shift. BMC Genomics 18 (S8). doi: 10.1186/s12864-017-4184-6
- Eynon N, Birk R (2011) Using Genetic Tests for Talent Identification in Sports: Too Soon to Be True. J Pediatr Endocrinol Metab 24 (7-8). doi: 10.1515/jpem.2011.283
- Kitazawa H, Hasegawa K, Aruga D, Tanaka M (2021) Potential Genetic Contributions of the Central Nervous System to a Predisposition to Elite Athletic Traits: State-of-the-Art and Future Perspectives. Genes 12 (3):371. doi: 10.3390/genes12030371
- Lin W-Y, Chan C-C, Liu YL, Yang AC, Tsai SJ, Kuo P-H (2019) Performing Different Kinds of Physical Exercise Differentially Attenuates the Genetic Effects on Obesity Measures: Evidence From 18,424 Taiwan Biobank Participants. Plos Genet 15 (8):e1008277. doi: 10.1371/journal.pgen.1008277
- He L, Roie EV, Bogaerts A, Morse CI, Delecluse C, Verschueren S, et al. (2018) Genetic Predisposition Score Predicts the Increases of Knee Strength and Muscle Mass After One-Year Exercise in Healthy Elderly. Exp Gerontol 111:17-26. doi: 10.1016/j. exger.2018.06.030
- Bunc V, Skalská M (2014) Are the Children's Predispositions for Physical Exercise Influenced by Their Body Mass? Am J Sports Sci Med 2 (5):177-80. doi: 10.12691/ajssm-2-5-1
- Loland S (2015) Against Genetic Tests for Athletic Talent: The Primacy of the Phenotype. Sports Med 45 (9):1229-33. doi: 10.1007/s40279-015-0352-5
- Goncharov S, VI G, Do S, Ti Dk, Sp K, Ea N, et al. (2014) Genetic Predisposition to Essential Hypertension in Children: Analysis of 17 Single Nucleotide Polymorphisms. Fiziol Zh 59 (6):12-24. doi: 10.15407/fz59.06.012
- Kuliev A (2021) Preimplantation Genetic Testing for Inherited Cancer Predisposition. Adv Cancer Res Clin Imaging 3 (2). doi: 10.33552/acrci.2021.03.000557
- Kuliev A, Rechitsky S (2018) Preimplantation Genetic Testing (PGT) for Cardiac Disease. Invasive Cardiol 01 (02). doi: 10.35841/invasive-cardiology.1.2.1-4
- 12. Kuliev A, Tatiana P, Prokhorovich M, Svetlana R (2021) Preimplantation Genetic Testing for Inherited Predisposition to Cardiac Disease. Ann Heart 5 (1). doi: 10.36959/652/399
- Wu Y, Zhong L, Li G, Han L, Fu J, Yu L, et al. (2021) Puberty Status Modifies the Effects of Genetic Variants, Lifestyle Factors and Their Interactions on Adiponectin: BCAMS Study Front Endocrinol 12. doi: 10.3389/fendo.2021.737459
- Wu YP, Aspinwall LG, Parsons BG, Stump TK, Nottingham K, Kohlmann W, et al. (2020) Parent and Child Perspectives on Family Interactions Related to Melanoma Risk and Prevention After CDKN2A/p16 Testing of Minor Children. J Community Genet 11

(3):321-9. doi: 10.1007/s12687-020-00453-9

- Wu YP, Mays D, Kohlmann W, Tercyak KP (2017) Pediatric Predispositional Genetic Risk Communication: Potential Utility for Prevention and Control of Melanoma Risk as an Exemplar. J Genet Couns 26 (5):887-93. doi: 10.1007/s10897-017-0105-8
- 16. Klain A (2024) Exercise-Induced Bronchoconstriction, Allergy and Sports in Children. Ital J Pediatr 50 (1). doi: 10.1186/s13052-024-01594-0
- Buczkowska EO (2014) Metabolic Syndrome Is the Problem in Young Diabetics? Fam Med Med Sci Res 03 (04). doi: 10.4172/2327-4972.1000148
- Schwarzer M, Molis A, Schenkl C, Schrepper A, Britton SL, Koch LG, et al. (2021) Genetically Determined Exercise Capacity Affects Systemic Glucose Response to Insulin in Rats. Physiol Genomics 53 (9):395-405. doi: 10.1152/physiolgenomics.00014.2021
- Nakano Y, Rabinowicz R, Malkin D (2022) Genetic Predisposition to Cancers in Children and Adolescents. Curr Opin Pediatr 35 (1):55-62. doi: 10.1097/mop.00000000001197
- Elam KK, Chassin L, Lemery-Chalfant K, Pandika D, Wang FL, Bountress K, et al. (2017) Affiliation with Substance-using Peers: Examining Gene-environment Correlations Among Parent Monitoring, Polygenic Risk, and Children's Impulsivity. Dev Psychobiol 59 (5):561-73. doi: 10.1002/dev.21529
- Aaltonen S, Latvala A, Jelenkovic A, Rose RJ, Kujala UM, Kaprio J, et al. (2020) Physical Activity and Academic Performance: Genetic and Environmental Associations. Med Sci Sports Exerc 52 (2):381-90. doi: 10.1249/MSS.00000000002124
- Reschke M, Biewald E, Bronstein L, Brecht IB, Dittner-Moormann S, Driever F, et al. (2021) Eye Tumors in Childhood as First Sign of Tumor Predisposition Syndromes: Insights from an Observational Study Conducted in Germany and Austria. Cancers 13 (8):1876. doi: 10.3390/cancers13081876
- 23. Friedrich U, Bienias M, Zinke C, Prazenicova M, Lohse J, Jahn A, et al. (2022) Clinical Criteria for Genetic Testing in Pediatric Oncology Show a Low Specificity and Miss Every 4<sup>th</sup> child Carrying a Cancer Predisposition. MedRxiv doi: 10.1101/2022.10.22.22281392
- Holden LR, Haughbrook R, Hart SA (2022) Developmental Behavioral Genetics Research on School Achievement Is Missing Vulnerable Children, to Our Detriment. New Dir Child Adolesc Dev 2022 (183-184):47-55. doi: 10.1002/cad.20485
- Zelley K (2024) Update on Genetic Counselor Practice and Recommendations for Pediatric Cancer Predisposition Evaluation and Surveillance. Clin Cancer Res 30 (18):3983-9. doi: 10.1158/1078-0432.ccr-24-1165
- 26. Pienar C, Pop L, Lazarescu M, Costachescu R, Mogoi M, Mare R, et al. (2023) Genetic Predisposition to Primary Lactose Intolerance Does Not Influence Dairy Intake and Health-Related Quality of Life in Romanian Children: A Hospital-Based Cross-Sectional Study. Children 10 (6):1075. doi: 10.3390/children10061075
- Li H, Sisoudiya SD, Martin-Giacalone BA, Khayat MM, Dugan-Perez S, Marquez-Do DA, et al. (2020) Germline Cancer Predisposition Variants In Pediatric Rhabdomyosarcoma: A Report From the Children's Oncology Group. Jnci Natl Cancer Inst. doi: 10.1093/jnci/djaa204
- De Geus EJC (2021) A genetic perspective on the association between exercise and mental health in the era of genome-wide association studies. Mental Health Phys Act 20:100378. doi: 10.1016/j.mhpa.2020.100378
- 29. Posthumus M, Collins M (2016) Genetics and Sports. Basel: Karger
- Leońska-Duniec A, Ahmetov II, Zmijewski P (2016) Genetic variants influencing effectiveness of exercise training programmes in obesity - an overview of human studies. Biol Sport 33 (3):207-

14. doi: 10.5604/20831862.1201052

- Bıçakçı B, Cięszczyk P, Humińska-Lisowska K (2024) Genetic Determinants of Endurance: A Narrative Review on Elite Athlete Status and Performance. Int J Mol Sci 25 (23):13041. doi: 10.3390/ijms252313041
- 32. Klevjer M, Nordeidet ADAN, Hansen AF, Madssen E, Wisløff U, Brumpton BM, et al. (2022) Genome-Wide Association Study Identifies New Genetic Determinants of Cardiorespiratory Fitness: The Trøndelag Health Study. Med Sci Sports Exerc 54:1534-45
- Al-Khelaifi F, Diboun I, Donati F, Botrè F, Abraham D, Hingorani A, et al. (2019) Metabolic GWAS of elite athletes reveals novel genetically-influenced metabolites associated with athletic performance. Sci Rep 9 (1):19889. doi: 10.1038/s41598-019-56496-7
- 34. Bulgay C, Cepicka L, Dalip M, Yıldırım S, Ceylan HI, Yılmaz ÖÖ, et al. (2023) The relationships between ACTN3 rs1815739 and PPARA-α rs4253778 gene polymorphisms and athletic performance characteristics in professional soccer players. BMC Sports Sci Med Rehabil 15 (1):121. doi: 10.1186/s13102-023-00733-0
- Meckel Y, Eliakim A, Nemet D, Levin N, Ben-Zaken S (2020) PPARD CC and ACTN3 RR genotype prevalence among elite soccer players. Sci Med Footb 4:156-61
- Aslam MA, Ma EB, Huh JY (2023) Pathophysiology of sarcopenia: Genetic factors and their interplay with environmental factors. Metabolism. 149:155711. doi: 10.1016/j.metabol.2023.155711
- Thomaes T, Thomis M, Onkelinx S, Goetschalckx K, Fagard R, Lambrechts D, et al. (2013) Genetic predisposition scores associate with muscular strength, size, and trainability. Med Sci Sports Exerc 45 (8):1451-9. doi: 10.1249/MSS.0b013e31828983f7
- Akbari M, Eghtedarian R, Hussen BM (2022) Angiotensin I converting enzyme gene polymorphisms and risk of psychiatric disorders. BMC Psychiatry 22:351. doi: 10.1186/s12888-022-04007-w
- Mohammadi D, Hakimian M, Moradzadegan A (2023) Investigating a Variant in the ACE Gene in Ahvaz Male and Female Athletes Compared to the Control Group with Normal Body Mass. Gene Cell Tissue 10 (2):e133946. doi: 10.5812/gct-133946
- Zi Y, Bartels M, Dolan C (2024) Genetic confounding in the association of early motor development with childhood and adolescent exercise behavior. Int J Behav Nutr Phys Act 21:33. doi: 10.1186/s12966-024-01583-w
- Bouchard C, Rankinen T, Timmons JA (2011) Genomics and genetics in the biology of adaptation to exercise. Compr Physiol 1 (3):1603-48. doi: 10.1002/cphy.c100059
- 42. Huls A, Ickstadt K, Schikowski T, Kramer U (2017) Detection of gene-environment interactions in the presence of linkage disequilibrium and noise by using genetic risk scores with internal weights from elastic net regression. BMC Genet 18 (1):55. doi: 10.1186/s12863-017-0519-1
- Kennedy AL, Shimamura A (2019) Genetic Predisposition to MDS: Clinical Features and Clonal Evolution. Blood 133 (10):1071-85. doi: 10.1182/blood-2018-10-844662
- Bojarczuk A (2024) Ethical Aspects of Human Genome Research in Sports-A Narrative Review. Genes 15 (9):1216. doi: 10.3390/ genes15091216
- Furutani E, Shimamura A (2019) Genetic Predisposition to MDS: Diagnosis and Management. Hematology 2019 (1):110-9. doi: 10.1182/hematology.2019000021
- Mennitti C, Farina G, Imperatore A, De Fonzo G, Gentile A, La Civita E, et al. (2024) How Does Physical Activity Modulate Hormone Responses? Biomolecules 14 (11):1418. doi: 10.3390/ biom14111418
- 47. Athanasiou N, Bogdanis GC, Mastorakos G (2023) Endocrine responses of the stress system to different types of exercise. Rev

Endocr Metab Disord 24 (2):251-66. doi: 10.1007/s11154-022-09758-1

- Lawankar R (2024) A Systematic Study on the Elevated Risk of Ankylosing Spondylitis in Adolescents Engaged in Intense Physical Exercise. Int J Res Orthop 10 (6):1347-53. doi: 10.18203/ issn.2455-4510.intjresorthop20243133
- Guth LM, Roth SM (2013) Genetic influence on athletic performance. Curr Opin Pediatr 25 (6):653-8. doi: 10.1097/ MOP.0b013e3283659087
- Millward DJ (2021) Interactions between Growth of Muscle and Stature: Mechanisms Involved and Their Nutritional Sensitivity to Dietary Protein: The Protein-Stat Revisited Nutrients 13 (3):729. doi: 10.3390/nu13030729
- 51. Farr JN, Laddu DR, Blew RM, Lee VR, Going SB (2013) Effects of physical activity and muscle quality on bone develop-

ment in girls. Med Sci Sports Exerc 45:2332-40. doi: 10.1249/ MSS.0b013e31829c32fe

- 52. Viner RM, Allen NB, Patton GC (2017) Puberty, Developmental Processes, and Health Interventions. Washington (DC): The International Bank for Reconstruction and Development / The World Bank
- 53. Alegría-Torres JA, Baccarelli A, Bollati V (2011) Epigenetics and lifestyle. Epigenomics 3 (3):267-77. doi: 10.2217/epi.11.22
- Mazza E, Troiano E, Ferro Y, Lisso F, Tosi M, Turco E, et al. (2024) Obesity, Dietary Patterns, and Hormonal Balance Modulation: Gender-Specific Impacts. Nutrients 16 (11):1629. doi: 10.3390/nu16111629
- Nasb M, Wei M, Lin B, Chen N (2024) Unraveling precision exercise: A journey from efficacy to molecular insights. Adv Exerc Health Sci 1 (1):3-15. doi: 10.1016/j.aehs.2024.01.004