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The Role of Biomarkers in Elite Sports

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Abstract: Biomarkers have emerged as valuable tools in the realm of elite sports, providing objective measures of athletes' physiological responses and potential for performance optimization. This article review delves into the significance and implications of biomarkers in elite sports, emphasizing their crucial role in supporting athletes' training, recovery, and overall success. The integration of biomarkers offers unprecedented opportunities for evidence-based decisions, personalized strategies, and injury prevention, revolutionizing the landscape of elite sports. Through comprehensive literature review and analysis, this article highlights the tremendous promise of biomarkers in optimizing athletic performance while also addressing the ethical considerations surrounding their implementation. As research continues to advance, biomarkers are poised to reshape the future of elite sports, enhancing performance and paving the way for the next generation of sporting legends.

Keywords: Biomarkers, elite sports, performance optimization, physiological responses, training, recovery, injury prevention, evidence-based decisions, personalized strategies, talent identification, ge-netic biomarkers.

1. Introduction

Sports performance and athlete monitoring have undergone remarkable advancements in recent years, driven by the integration of cutting-edge scientific approaches [1]. Traditionally, coaches and sports scientists relied on subjective measures to assess an athlete's condition, which often led to a lack of precision and limited understanding of the underlying physiological responses. However, with the advent of biomarker research, the landscape of sports science has been revolutionized, offering objective and quantifiable insights into an athlete's biological state [2].

Elite sports represent the pinnacle of athletic performance, where athletes continuously strive for excellence and break barriers in their respective disciplines [3]. In this pursuit of greatness, athletes and their support teams are constantly seeking innovative approaches to optimize performance, prevent injuries, and gain a competitive edge. Biomarker analysis has emerged as a groundbreaking tool in the realm of elite sports, offering objective measures of an athlete's physiological responses and potential for peak performance.

Biomarkers, which encompass a wide range of measurable biological substances and indicators, have the unique ability to provide valuable insights into an athlete's internal physiological state [2]. These biomarkers can be extracted from blood, saliva, urine, and other bodily fluids, allowing coaches and sports scientists to gain a deeper understanding of an athlete's readiness, recovery status, and overall health [4].

This article review aims to explore the significance and implications of biomarkers in elite sports, delving into their crucial role in supporting athletes' training, recovery, and overall success. By providing objective and quantifiable data, biomarker analysis enables evidence-based decisions that go beyond traditional subjective performance assessments.

Through personalized training and recovery strategies, biomarker analysis empowers coaches to tailor individualized plans, considering an athlete's unique responses to training stimuli [5]. This approach maximizes training adaptations, minimizes the risk of overtraining and fatigue, and fosters peak performance.

Moreover, the integration of biomarkers in injury prevention allows for early detection of potential risks, enabling timely interventions and safeguarding athletes' well-being. Additionally, biomarkers play a significant role in injury rehabilitation, aiding in monitoring healing progress and guiding return-to-play decisions [6].

The integration of genetic biomarkers further enriches the understanding of individual athletic potential. Genetic variations have been associated with specific athletic traits, such as sprinting ability and endurance performance. Exploring the use of genetic biomarkers in sports opens new frontiers for talent identification and the development of personalized training approaches, ultimately contributing to improved athletic outcomes [7].

While biomarkers show great promise in elevating elite sports performance, ethical considerations are of utmost importance. Ensuring athletes' informed consent, safeguarding data privacy, and adopting responsible biomarker data use are vital to uphold athlete rights and welfare.

2. Materials and Methods

To compile this comprehensive review, a systematic literature search was conducted across various scientific databases to identify relevant articles related to the role of biomarkers in elite sportws. The search was carried out in databases such as PubMed. The primary focus was on peer-reviewed articles published within the last 10 years (from 2013 to 2023). The selected time frame ensures the inclusion of recent research while still capturing substantial developments in the field.

Keywords: The search strategy was designed using relevant keywords related to the topic of interest. Keywords such as "biomarkers," "elite sports," "performance optimization," "physiological responses," "training," "recovery," "injury prevention," "genetic biomarkers," and "talent identification" were used to identify relevant articles.

3. Blood biomarkers

Blood biomarkers play a pivotal role in elite sports, providing valuable insights into an athlete's physiological state and performance capabilities [8]. These biomarkers, measurable indicators found in the blood, offer objective and real-time information that coaches, sports scientists, and medical professionals can use to optimize training regimens, monitor recovery, and prevent injuries. The use of blood biomarkers in elite sports has transformed how athletes prepare and compete, enhancing their performance and overall well-being.

Some of the key blood biomarkers used in elite sports include:

3.1. Lactate

Lactate, also known as lactic acid, is a molecule that plays a crucial role in energy metabolism, particularly during intense physical activity and anaerobic exercise [9]. It is produced as a byproduct of the breakdown of glucose in the absence of sufficient oxygen. Lactate is commonly associated with the sensation of muscle fatigue and the "burn" experienced during high-intensity exercise [10].

During aerobic exercise, where oxygen is readily available, glucose is broken down in the cells through a process called glycolysis, resulting in the production of pyruvate. Pyruvate then enters the mitochondria and undergoes further breakdown, generating energy for sustained exercise [11]. However, during high-intensity or anaerobic exercise, oxygen supply may not meet the increased energy demand, leading to an accumulation of pyruvate. To prevent an excessive buildup of pyruvate, the body converts it into lactate through a process called lactic acid fermentation [12].

Contrary to the common misconception, lactate itself is not responsible for muscle fatigue and the burning sensation experienced during intense exercise. Instead, it serves as an essential energy source for working muscles and other tissues. Furthermore, lactate is quickly cleared from the bloodstream and used as a fuel by various tissues, including the heart, liver, and skeletal muscles, during recovery and low-intensity exercise [13].

The measurement of blood lactate levels provides valuable insights into an athlete's exercise intensity and training adaptation. The lactate threshold is a critical parameter used in sports science, representing the exercise intensity at which lactate begins to accumulate faster than it can be cleared from the bloodstream [14]. Training at or just below the lactate threshold is often utilized to improve an athlete's endurance capacity and performance.

Lactate testing is commonly performed through a procedure known as lactate threshold testing or lactate profiling [15]. During the test, an athlete exercises at progressively increasing intensities, and blood samples are taken to measure lactate levels. The results help determine an individual's lactate threshold and aid coaches in developing personalized training programs that optimize performance gains while avoiding excessive lactate accumulation [16].

3.2. Glucose

Glucose is a simple sugar and a fundamental source of energy for all cells in the human body [17]. It serves as the primary fuel for the brain, muscles, and various organs. Glucose is a vital component of the body's energy metabolism, and its concentration in the bloodstream is tightly regulated to maintain stable blood sugar levels [18].

After consuming carbohydrates through the diet, the body breaks down these complex carbohydrates into glucose through the process of digestion. Subsequently, glucose is assimilated into the circulatory system and conveyed to cells across the entirety of the organism.

The hormone insulin, produced by the pancreas, plays a crucial role in regulating glucose levels. Insulin facilitates the uptake of glucose into cells, where it is used for energy or stored as glycogen for future energy needs [19].

The balance between glucose production and utilization is critical for maintaining normal blood sugar levels [20]. In healthy individuals, blood glucose levels are typically kept within a narrow range, primarily between 70 to 100 milligrams per deciliter (mg/dL) in the fasting state and rising to around 120 to 140 mg/dL after a meal. This tight regulation is essential for optimal cellular function and energy homeostasis.

In elite sports, glucose plays a central role in fueling exercise and supporting athletic performance. During physical activity, the body's energy demand increases, and glucose becomes a primary energy source for working muscles [21]. Depending on the intensity and duration of exercise, the body may use glucose derived from the bloodstream, muscle glycogen stores, or stored liver glycogen for energy.

For endurance athletes engaged in prolonged exercise, maintaining adequate glucose levels is crucial to sustain performance [22]. To support this, athletes often consume carbohydrate-rich foods or sports drinks during training and competition to replenish glycogen stores and maintain blood glucose levels. Proper carbohydrate intake can delay fatigue and enhance endurance capacity [23].

In addition to its role as a fuel source, glucose is also important for cognitive function. The brain heavily relies on glucose as its primary energy source, and stable blood sugar levels are essential for maintaining mental alertness and focus during training and competition [17].

3.3. Iron

Iron is an essential mineral that plays a vital role in various physiological processes within the human body, including oxygen transport, energy metabolism, and immune function [24]. It is a crucial component of hemoglobin, the protein in red blood cells responsible for carrying oxygen from the lungs to tissues throughout the body. Iron is also a key element in myoglobin, a protein found in muscle cells that facilitates oxygen storage and release during muscle contraction [25].

The primary function of iron is to support the oxygen-carrying capacity of red blood cells. Oxygen binds to iron in hemoglobin, forming oxyhemoglobin, which then travels through the bloodstream, delivering oxygen to tissues and organs [26]. This process is essential for energy production, as oxygen is a critical component of cellular respiration, the process by which cells generate adenosine triphosphate (ATP), the energy currency of the body.

Iron is obtained through the diet and absorbed in the small intestine. Iron deficiency can occur due to inadequate dietary intake, poor iron absorption, or increased iron requirements, such as during periods of growth, pregnancy, or intense physical activity. Iron deficiency leads to a condition called anemia, characterized by a decrease in red blood cell count and a reduced ability to transport oxygen effectively. Anemia can result in fatigue, weakness, reduced exercise tolerance, and impaired athletic performance.

In elite sports, iron status is of particular importance due to the high demands placed on athletes' bodies [27]. Endurance athletes, in particular, are at risk of iron deficiency due to factors such as increased iron losses through sweating and gastrointestinal bleeding, as well as inadequate dietary iron intake to meet elevated demands . Female athletes may also be more susceptible to iron deficiency due to menstrual blood loss [28].

Monitoring iron status is essential for elite athletes to optimize performance and prevent anemia-related complications. Blood tests, such as measurement of hemoglobin, hematocrit, serum iron, ferritin (an iron storage protein), and transferrin saturation, can provide insights into an athlete's iron status [29]. Regular monitoring of iron levels allows coaches and sports scientists to intervene promptly with appropriate dietary adjustments, iron supplementation, or medical management if necessary.

Maintaining adequate iron levels through a balanced diet rich in iron sources, such as lean meats, poultry, fish, legumes, nuts, and fortified cereals, is crucial for optimal athletic performance [30]. Athletes should also be mindful of factors that can enhance or inhibit iron absorption, such as vitamin C, which enhances iron absorption, and certain compounds in tea and coffee, which can inhibit iron absorption.

In conclusion, iron is an essential mineral critical for oxygen transport, energy metabolism, and immune function in the human body. For elite athletes, maintaining proper iron status is crucial for optimizing athletic performance and preventing anemia-related complications. Regular monitoring of iron levels, coupled with a well-balanced diet and proper supplementation when needed, ensures that athletes are equipped to meet the physical demands of training and competition effectively.

4. Salivary biomarkers

Salivary biomarkers have emerged as valuable tools in elite sports, providing non-invasive and real-time insights into an athlete's physiological responses, stress levels, and immune function [31]. Saliva, easily and painlessly collected, contains a wide range of biomolecules that reflect an athlete's health, training adaptation, and readiness to perform. The use of salivary biomarkers in elite sports offers several advantages, including convenience, frequency of sampling, and the ability to monitor an athlete's well-being closely throughout training and competition [32].

Some of the key salivary biomarkers used in elite sports include:

4.1. Alpha-amylase

Alpha-amylase is an enzyme found in various bodily fluids, including saliva and pancreatic secretions, where it plays a crucial role in the digestion of carbohydrates [33]. Its primary function is to break down complex starch molecules into smaller, more easily digestible sugars such as maltose and maltotriose. This process, known as amylolysis or starch hydrolysis, occurs in the mouth during the initial stages of digestion and continues in the small intestine after food reaches the stomach [34].

In the context of sports and exercise, alpha-amylase has garnered attention as a salivary biomarker with potential applications in athlete monitoring and performance assessment [35]. The activity of alpha-amylase in saliva can be affected by various factors, including stress, exercise intensity, and sympathetic nervous system activity. Thus, it has been studied as an indicator of the body's physiological response to exercise and training [36].

During exercise, especially during high-intensity or stressful situations, the sympathetic nervous system is activated, leading to an increase in stress hormones such as adrenaline and noradrenaline [37]. These hormones can stimulate the salivary glands to secrete alpha-amylase into the saliva. Therefore, measuring the activity of salivary alpha-amylase can provide insights into an athlete's stress response and readiness to perform [38].

Studies have shown that the levels of salivary alpha-amylase can vary depending on the type of exercise and the individual's training status. For example, prolonged endurance exercise may lead to increased salivary alpha-amylase activity, reflecting the body's response to prolonged physical stress [39]. In contrast, high-intensity interval training (HIIT) may result in even higher alpha-amylase levels due to the combination of physical and psychological stress.

The measurement of salivary alpha-amylase has been explored as a potential tool to monitor an athlete's training load and recovery status. It may help coaches and sports scientists assess an athlete's physiological adaptation to training, identify signs of overtraining, and tailor training programs accordingly [40]. Additionally, alpha-amylase can be used in conjunction with other biomarkers, such as cortisol, to gain a more comprehensive understanding of an athlete's stress response.

While salivary alpha-amylase shows promise as a salivary biomarker in sports, its interpretation requires careful consideration of various factors that may influence its levels, including exercise type, psychological stress, and individual variations [41]. Standardized protocols and consistent measurement techniques are essential for reliable and meaningful data.

4.2. Immunoglobulin A (IgA)

Immunoglobulin A (IgA) is an essential class of antibodies that plays a crucial role in the immune system's defense against infections. It is the predominant immunoglobulin in mucosal secretions, such as saliva, tears, respiratory secretions, and gastrointestinal fluids [42]. IgA acts as the body's first line of defense against pathogens that attempt to enter the body through these mucosal surfaces [43].

The primary function of IgA is to prevent the attachment and colonization of bacteria, viruses, and other pathogens on the mucosal linings of various organs, including the respiratory tract, digestive system, and urinary tract [44]. By doing so, IgA helps prevent infections and the spread of pathogens from the mucosal surfaces into the bloodstream and deeper tissues.

IgA antibodies are produced by plasma cells, a type of white blood cell, in the mucosal-associated lymphoid tissue (MALT) and other lymphoid tissues [45]. Unlike other classes of antibodies, IgA can exist in different forms: as a monomer in the bloodstream and as a dimer when secreted into mucosal secretions [46]. The secreted IgA is equipped with a specialized component called the secretory component, which protects it from degradation by enzymes in the mucosal environment.

In the context of sports and exercise, IgA has been studied as a salivary biomarker with potential applications in monitoring an athlete's immune status and response to training and competition [47]. The concentration of salivary IgA can fluctuate in response to various factors, including exercise intensity, stress, and immune challenges.

During intense training or competition, athletes may experience temporary suppression of their immune function, commonly known as the "open window" period [48]. This phenomenon occurs due to the redistribution of immune cells and a transient decrease in salivary IgA levels [49]. The open window period is a vulnerable time for athletes as it may increase the risk of infection and illness. Monitoring salivary IgA levels can provide insights into an athlete's immune status and help identify periods of heightened vulnerability, allowing for appropriate adjustments to training loads and recovery strategies [50].

It is important to note that other factors, such as sleep, nutrition, and overall health, can also influence salivary IgA levels. Therefore, interpreting salivary IgA data should be done in conjunction with other relevant physiological and training-related information [51].

4.3. Nitric oxide (NO)

Nitric oxide (NO) is a gas molecule that acts as a signaling molecule in the body, playing a crucial role in various physiological processes [52]. It is produced by a group of enzymes called nitric oxide synthases (NOS) from the amino acid L-arginine. NO has diverse effects on different tissues and organs, and its functions are involved in cardiovascular health, immune responses, and neurotransmission, among other processes [53].

In the context of sports and exercise, NO has garnered considerable attention due to its effects on blood vessels and its potential impact on athletic performance [54]. Here are some key roles of nitric oxide in relation to exercise:

Vasodilation: One of the main functions of NO is to promote the relaxation and dilation of blood vessels, a process known as vasodilation. During exercise, the production of NO increases, leading to vasodilation in the skeletal muscles [55]. This widening of blood vessels allows for improved blood flow, oxygen, and nutrient delivery to the working muscles, enhancing exercise performance.

Oxygen Delivery: By promoting vasodilation, NO helps ensure efficient oxygen delivery to active muscles during exercise. This oxygen supply is essential for aerobic energy production and endurance activities [56].

Exercise Performance: NO's role in enhancing blood flow and oxygen delivery to muscles can improve exercise performance, especially in endurance-based activities like running, cycling, and swimming [57].

Recovery: Nitric oxide may also play a role in post-exercise recovery by aiding in nutrient and waste product clearance from muscles, helping reduce muscle soreness and promote faster recovery [58].

Mitochondrial Function: NO has been shown to influence mitochondrial function, the energy-producing organelles within cells. Improved mitochondrial function can enhance the efficiency of energy production during exercise [59].

To enhance NO production, some athletes use dietary supplements containing precursors to NO, such as L-arginine or L-citrulline. These supplements are thought to increase NO availability and improve exercise performance. However, the effectiveness of NO supplements remains a topic of ongoing research, and the benefits may vary among individuals and different exercise modalities [60].

It is important to note that while NO plays a beneficial role in exercise performance, excessive NO production can lead to oxidative stress and potential adverse effects. Therefore, maintaining a balanced and regulated production of NO is essential for its positive effects on athletic performance and overall health.

5. Urine biomarkers

Urine biomarkers have gained significance in elite sports as non-invasive indicators of an athlete's health, hydration status, and metabolic responses [61]. The analysis of specific molecules and substances in urine provides valuable insights into an athlete's physiological state, helping coaches, sports scientists, and medical professionals optimize training, monitor recovery, and prevent health issues [62]. Urine biomarkers offer several advantages, including ease of collection, frequency of sampling, and the ability to track changes over time.

Some of the key urine biomarkers used in elite sports include:

5.1. Creatinine

Creatinine is a waste product generated from the breakdown of creatine, a compound found in muscles as part of the energy production process [63]. It is produced at a relatively constant rate in the body and is filtered out of the blood by the kidneys, then excreted through urine. Creatinine is a valuable marker for kidney function and is commonly measured in blood and urine tests to assess renal health [64].

In the context of sports and exercise, creatinine is relevant for several reasons:

Muscle Metabolism: Creatine, the precursor of creatinine, plays a vital role in the phosphagen system, a rapid energy system used during short bursts of intense exercise, such as weightlifting, sprinting, and jumping [65]. Creatine stores high-energy phosphate groups that can be rapidly transferred to adenosine diphosphate (ADP) to replenish adenosine triphosphate (ATP), the primary energy source for muscle contraction [66].

Exercise Performance: The availability of creatine and its ability to replenish ATP quickly can impact an athlete's performance in high-intensity, short-duration activities. Some athletes use creatine supplementation to enhance muscle creatine stores and potentially improve their performance in power-based sports [67].

Hydration and Kidney Function: Creatinine is routinely measured in urine tests to assess kidney function and overall health. The creatinine clearance test, which compares the levels of creatinine in blood and urine, provides an estimation of the glomerular filtration rate (GFR), an essential indicator of kidney function [68].

Dehydration: During intense exercise, especially in hot and humid conditions, athletes may experience dehydration, which can lead to increased creatinine levels in the blood. Elevated creatinine levels may be a sign of dehydration and the need for proper rehydration strategies [69].

It's important to note that while creatinine is a useful marker for assessing kidney function and hydration status, it should not be confused with creatine supplements. Creatine supplements are distinct from creatinine and are used to increase muscle creatine stores, potentially benefiting short-duration, high-intensity exercise performance. Athletes interested in using creatine supplements should consult with a healthcare professional or sports nutritionist to determine proper dosing and ensure safety.

5.2. Sodium

Sodium is an essential mineral and electrolyte that plays a critical role in maintaining various physiological processes in the human body [70]. It is one of the major positively charged ions (cations) in the extracellular fluid and is crucial for maintaining fluid balance, nerve function, muscle contractions, and acid-base balance.

The primary source of dietary sodium is table salt, which is composed of sodium chloride. Other sources of sodium in the diet include processed and packaged foods, as sodium is often used as a preservative and flavor enhancer [71].

Here are some key functions of sodium in the body:

Fluid Balance: Sodium plays a vital role in regulating fluid balance within and outside cells. It helps maintain proper hydration levels by controlling the movement of water in and out of cells [72]. Sodium concentration outside cells is essential for controlling the movement of water into and out of cells, preventing cellular swelling or dehydration.

Nerve Function: Sodium is involved in generating electrical impulses necessary for nerve function and communication between nerve cells. It helps transmit nerve signals, allowing the body to respond to various stimuli and control muscle movements [73].

Muscle Contraction: Sodium is essential for muscle contractions, including the muscles involved in voluntary movements (skeletal muscles) and those in the heart (cardiac muscles). The influx of sodium into muscle cells triggers the release of calcium, which initiates the process of muscle contraction [74].

Acid-Base Balance: Sodium, along with other electrolytes like bicarbonate and chloride, helps regulate the body's acid-base balance, ensuring that the blood's pH remains within a narrow range for proper physiological functioning [75].

Sodium levels in the body are tightly regulated by the kidneys, which adjust the amount of sodium excreted in urine based on the body's needs. When sodium intake is high, the kidneys excrete excess sodium to maintain balance [76]. Conversely, when sodium intake is low, the kidneys conserve sodium to prevent deficiency.

In the context of sports and exercise, sodium is particularly important for athletes, as they can lose significant amounts of sodium through sweat during physical activity, especially in hot and humid conditions [77]. Proper hydration and electrolyte replacement are crucial for maintaining optimal performance, preventing dehydration, and avoiding conditions like heat-related illnesses.

Athletes engaged in intense or prolonged exercise may need to replenish lost sodium and other electrolytes through sports drinks, electrolyte supplements, or sodium-containing foods to support their hydration needs and overall performance [78].

As with any dietary component, moderation is key when it comes to sodium intake. While sodium is essential for the body's proper functioning, excessive sodium consumption has been associated with high blood pressure and an increased risk of cardiovascular diseases. Therefore, athletes and the general population should aim for a balanced diet that meets sodium needs without excessive intake.

6. Genetic biomarkers

Genetic biomarkers in elite sports refer to specific variations in an athlete's DNA that can influence their athletic performance, injury risk, and training responsiveness [79]. The study of genetic biomarkers has gained prominence in recent years, offering valuable insights into an athlete's genetic profile and its potential impact on sports performance [80]. Understanding genetic biomarkers can aid in talent identification, personalized training programs, and injury prevention in elite sports.

Some of the key genetic biomarkers used in elite sports include:

6.1. ACTN3 gene

The ACTN3 gene, also known as the alpha-actinin-3 gene, is a gene that encodes the alpha-actinin-3 protein [81]. This gene is primarily expressed in fast-twitch muscle fibers, which are responsible for rapid, forceful movements, such as those involved in sprinting and power-based sports [82].

The alpha-actinin-3 protein is part of the actin-binding protein family and plays a role in muscle function and structure [83]. It is involved in anchoring the actin filaments, which are essential components of the muscle contractile apparatus, to the Z-discs within muscle cells. This anchoring contributes to the structural stability of muscle fibers during muscle contraction.

A particular variation in the ACTN3 gene, known as the R577X polymorphism, results in the absence of the alpha-actinin-3 protein in skeletal muscles. This variation leads to the production of a non-functional form of the protein [84]. Approximately 18-20% of the global population carries two copies of the X allele, resulting in the absence of alpha-actinin-3 in their muscles. These individuals are often referred to as "non-responders" to the ACTN3 gene.

Research has shown that the presence or absence of the alpha-actinin-3 protein may influence athletic performance, particularly in activities requiring high power and sprinting ability [85]. Individuals with the XX genotype (absence of alpha-actinin-3) may have a potential advantage in endurance-based activities due to the higher proportion of slow-twitch muscle fibers in their muscles [86]. On the other hand, those with the RR genotype (presence of alpha-actinin-3) may have an advantage in power-based sports due to the higher proportion of fast-twitch muscle fibers.

It is important to note that athletic performance is influenced by a complex interplay of genetic factors, training, nutrition, and other environmental factors. While the ACTN3 gene variation may have some impact on athletic performance, it is not the sole determinant, and many successful athletes may possess various genetic makeups.

The study of the ACTN3 gene and its role in sports performance is an active area of research, and its practical applications in sports talent identification and development are still evolving.

6.2. ACE gene

The ACE gene, also known as the angiotensin-converting enzyme gene, is another gene that has been extensively studied in the context of sports performance and athletic ability [87]. This gene encodes the angiotensin-converting enzyme (ACE), which plays a role in the renin-angiotensin-aldosterone system (RAAS) and the regulation of blood pressure and cardiovascular function [88].

The ACE enzyme is involved in the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor that raises blood pressure [89]. Additionally, ACE is responsible for breaking down bradykinin, a vasodilator that lowers blood pressure. The balance between these two opposing effects helps regulate blood pressure and cardiovascular homeostasis.

The ACE gene has a well-known insertion/deletion (I/D) polymorphism, where a 287 base-pair segment can be either inserted (I allele) or deleted (D allele) in the gene. As a result, individuals can have three possible genotypes: II, ID, or DD [90].

Studies have shown that the ACE gene polymorphism may be associated with differences in endurance performance and muscle fiber composition. The II genotype has been linked to better endurance performance and a higher proportion of slow-twitch muscle fibers, which are well-suited for activities requiring endurance and aerobic capacity. On the other hand, the DD genotype has been associated with better performance in power-based activities and a higher proportion of fast-twitch muscle fibers, which are involved in explosive movements and power-based sports.

6.3. NRF2 gene

The NRF2 (Nuclear factor erythroid 2-related factor 2) gene is a critical regulatory gene that plays a central role in the body's antioxidant defense system [91]. It is a transcription factor that regulates the expression of numerous genes involved in the antioxidant response, detoxification, and cellular protection against oxidative stress.

When the body is exposed to oxidative stress, such as from environmental pollutants, UV radiation, or intense exercise, reactive oxygen species (ROS) are generated [92]. ROS are highly reactive molecules that can damage cells and tissues if not neutralized. The NRF2 gene is activated in response to oxidative stress and triggers the production of antioxidant enzymes and other protective molecules.

Here's how the NRF2 gene functions:

Activation: Under normal conditions, NRF2 is sequestered in the cytoplasm by a protein called Keap1. When oxidative stress occurs, modifications to Keap1 cause NRF2 to dissociate from Keap1 and translocate into the cell nucleus [93].

Gene Expression: Once in the nucleus, NRF2 binds to specific DNA sequences called antioxidant response elements (AREs) in the promoter regions of target genes. This binding activates the transcription of various antioxidant and cytoprotective genes, such as heme oxygenase-1 (HO-1), NAD(P)H: quinone oxidoreductase (NQO1), glutathione peroxidase (GPx), and superoxide dismutase (SOD) [94].

Antioxidant Response: The proteins encoded by these NRF2-regulated genes act as powerful antioxidants and enzymes involved in detoxification processes. They help neutralize ROS, repair damaged DNA, and maintain cellular integrity during times of oxidative stress [95].

The NRF2 pathway is an essential defense mechanism that protects cells and tissues from oxidative damage, inflammation, and various diseases associated with oxidative stress, such as cardiovascular disease, cancer, neurodegenerative diseases, and aging-related conditions [96].

In the context of sports and exercise, the NRF2 gene and its pathway have gained attention for their potential role in protecting athletes from exercise-induced oxidative stress [97]. Regular and intense physical activity can lead to the generation of ROS, which may contribute to muscle fatigue, inflammation, and muscle damage. The NRF2 pathway helps mitigate these effects by inducing the expression of antioxidant enzymes and other protective molecules [98].

It's important to note that genetic variations (polymorphisms) in the NRF2 gene may exist among individuals, and some variations may influence the efficiency of NRF2 activation and antioxidant response. However, the practical application of NRF2 gene testing for sports performance is still an area of ongoing research, and its use in this context is not common.

7. Inflammatory biomarkers

Inflammatory biomarkers are specific molecules or substances found in the blood or other bodily fluids that indicate the presence or level of inflammation in the body [99]. Inflammation is a natural response of the immune system to injury or infection, but chronic or excessive inflammation can be detrimental to health and athletic performance. Monitoring inflammatory biomarkers in elite sports provides valuable information about an athlete's recovery status, training response, and overall well-being.

Some of the key inflammatory biomarkers used in elite sports include:

7.1. Interleukins

Interleukins are a group of signaling proteins, also known as cytokines, that play a central role in regulating the immune system and promoting communication between various cells in the body [100]. They are produced by a variety of immune cells, including white blood cells (leukocytes) and macrophages, and are involved in coordinating immune responses to infections, inflammation, and tissue repair [101].

Interleukins are numbered sequentially (e.g., IL-1, IL-2, IL-6, etc.), and each member of the interleukin family has specific functions and effects on different immune cells and tissues. Some of the key interleukins and their roles include:

IL-1: IL-1 is a pro-inflammatory cytokine that stimulates immune responses, including the activation of white blood cells and the production of other inflammatory mediators [102]. It plays a critical role in the body's defense against infections and initiating the inflammatory response.

IL-2: IL-2 is involved in the growth and activation of T cells, a type of immune cell responsible for directly attacking infected or cancerous cells. It is essential for the development of a strong immune response [103].

IL-4: IL-4 is an anti-inflammatory cytokine that helps regulate immune responses and promotes the production of antibodies by B cells. It is involved in the immune response against parasites and allergic reactions [104].

IL-6: IL-6 is a multifunctional cytokine that regulates both inflammatory and anti-inflammatory processes. It is involved in the acute-phase response to tissue injury or infection and plays a role in the immune response to exercise and muscle repair [105].

IL-10: IL-10 is an anti-inflammatory cytokine that helps regulate and suppress excessive immune responses, preventing chronic inflammation and tissue damage [106].

IL-17: IL-17 is involved in the recruitment and activation of immune cells during inflammation and is associated with various autoimmune and inflammatory diseases [107].

Interleukins are not only essential for fighting infections and promoting immune responses but also have significant implications in various disease processes, including autoimmune disorders, allergies, and inflammatory conditions [108]. As a result, they are targets of medical research and therapeutic interventions to modulate immune responses and treat immune-related diseases.

In the context of sports and exercise, interleukins have been studied as biomarkers to assess immune system responses to acute and chronic exercise, training stress, and recovery [109]. Understanding the levels and dynamics of specific interleukins in response to exercise can provide insights into an athlete's immune status, recovery capacity, and overall well-being [110].

It is important to note that the regulation and interactions of interleukins within the immune system are complex and can vary based on individual factors, exercise intensity, and other environmental conditions. Researchers and sports scientists continue to explore the roles of interleukins in sports performance, recovery, and overall health to better understand their impact on athletes.

7.2. Myeloperoxidase (MPO)

Myeloperoxidase (MPO) is an enzyme found in the azurophilic granules of certain immune cells, particularly neutrophils and monocytes [111]. It plays a crucial role in the innate immune response and is involved in the body's defense against pathogens, such as bacteria and fungi.

When the immune system detects the presence of pathogens or foreign invaders, neutrophils and monocytes are recruited to the site of infection. Once these immune cells are activated, they release MPO into the extracellular space, where it catalyzes the production of hypochlorous acid (HOCl) from hydrogen peroxide (H2O2) and chloride ions (Cl-) present in the surrounding environment [112].

Hypochlorous acid is a powerful oxidizing agent and a potent antimicrobial agent. It helps neutralize and kill pathogens by damaging their cell membranes and disrupting their cellular processes [113]. MPO-mediated oxidative reactions are an essential component of the innate immune response, contributing to the elimination of invading microorganisms and promoting tissue repair and inflammation resolution.

In addition to its role in the immune response, MPO has also been associated with inflammation and oxidative stress in various disease conditions. Elevated MPO levels have been observed in conditions like atherosclerosis, acute coronary syndromes, inflammatory bowel disease, and chronic obstructive pulmonary disease (COPD) [114]. In these diseases, MPO can contribute to tissue damage and inflammation due to the excessive production of reactive oxygen species and the formation of oxidized molecules.

In the context of sports and exercise, MPO has been studied as a biomarker for monitoring inflammatory and oxidative stress responses to physical activity. Intense or prolonged exercise can lead to temporary increases in MPO levels, reflecting the activation of the immune system and the production of reactive oxygen species during exercise-induced inflammation [115].

Monitoring MPO levels in athletes can provide valuable information about their immune and inflammatory responses to training and competition. It may help identify periods of increased immune system activation and inflammation, which can guide training and recovery strategies to optimize athletic performance and reduce the risk of overtraining or injury.

7.3. C-reactive protein (CRP)

C-reactive protein (CRP) is a biomarker that is synthesized by the liver as a response to inflammatory processes occurring within the organism. It is a part of the acute-phase response, which is the rapid and nonspecific reaction of the immune system to tissue injury, infection, or inflammation [116]. CRP levels rise quickly in the blood in response to these conditions and can serve as an indicator of systemic inflammation.

CRP is a pentameric protein, meaning it is made up of five identical subunits. It plays a crucial role in the immune system by binding to certain molecules on the surface of bacteria, viruses, and damaged cells [117]. This binding activates the complement system, a group of proteins that work together to facilitate immune responses, including the destruction of pathogens and the clearance of cellular debris.

Measurement of CRP levels in the blood is a common clinical test used to assess the presence and severity of inflammation in various conditions, such as infections, autoimmune diseases, and cardiovascular diseases [118]. High levels of CRP may indicate ongoing inflammation and can help healthcare providers monitor disease progression and response to treatment.

In the context of sports and exercise, CRP can also be used as a biomarker to monitor the inflammatory response to physical activity [119]. Intense or prolonged exercise can cause temporary inflammation, muscle damage, and oxidative stress. This acute inflammatory response is a natural part of the body's adaptation to exercise and plays a role in muscle repair and strengthening [120].

After intense exercise, CRP levels in the blood can increase, reflecting the acute inflammatory response to the physical stress of exercise. Monitoring CRP levels in athletes can provide insights into their body's response to training and help identify periods of increased inflammation and potential overtraining [4].

It is essential to note that exercise-induced inflammation is generally a normal and beneficial response to training. However, excessive or chronic inflammation can be detrimental to an athlete's health and performance. Proper training, nutrition, and recovery strategies are important to optimize the inflammatory response to exercise and support overall well-being.

Tabel 1. Comprehensive Overview of Biomarkers in Elite Sports (SD= standard deviation, CRP=C-reactive protein, IgA= Immunoglobuline A)

Study	Study design	Sample size (n)	Age (Mean ± SD)	Gender M/F	Biomarkers	Value	Significance
Francavilla et al. [121]	Investigation	35	25.3 ± 4.9 years	100% male	Cortisol Testosteron IgA	21.8 nmol/L 1.2 nmol/L 131.9 μg/mL	Periods of high intensity training
Pacheco et al. [122]	Case series	6	Over 65 years	83.3% / 16.7%	IL-6 TNF-α IL-8	4800 pg/mg 3800 pg/mg 1300 pg/mg	Higher levels which mean better control of inflammation
Sinnott et al. [123]	Original Investigation	4	19 ± 4 years	20% / 80%	IgA Cortisol	168.69(24.19) μg.ml-1 10.49(1.89) ng.ml	Increases during more intense training
Mariscal et al. [31]	Case study	21	23.0 ± 5.4 years	100% female	Cortisol IgA	Increased with 4.77 ng/ml Decreased with 495.5 μg/ml	Physiologic stress
Anderson et al. [124]	Prospective	20	19.1 ± 1.1 years	100% male	Cortisol IL-6 Testosteron	5.33 nmol/L 5.60 pg/mL 341.1 pmol/L	Overtraining
Borchers et al. [125]	Cohort study	9	48 ± 8.8 years	100% male	Cortisol Testosteron IL-8	1.8 μg/dL 298.3 pg/mL 59.9 pg/mL	Ultraendurance
Tominaga et al. [126]	Controlled trial	10	19.4 ± 1.5 years	100% male	IL-6 IL-4 Uric acid	1.8 pg/mL 100 pg/mL 0.4 mg/mgCr	Increased exercise intensity
Wołyniec et al. [127]	Case series	20	37.2 ± 7.4 years	90% / 10%	Creatinine Uric acid	0.99 mg/dL 5.65 mg/dL	Very long physical activi
Jouffroy et al. [128]	Observational	47	43 ± 7 years	100% male	Creatinine CRP Lactate	119 μmol/L 6.9 mg/L 3.3 mmol/L	Due to ultra-distance exercise-practice
Spada et al. [129]	Cohort study	58	21–28 years	50% / 50%	IL-18	0.06 ng/mg	Due to increased exercise intensity
Atkins et al. [130]	Prospective	63	46 ± 10 years	49% / 51%	Creatinine	366.24 mg/dL	Increase due to Intensity of exercise
Cai et al. [131]	Observational	103	19 years	51% / 49%	Lactate	1.12 mmol/L	Very long physical activity
Artells et al. [132]	Pilot study	60	25.52 ± 2.5 years	100%	Genotype AA Genotype GG	Increase ligament injuries No ligament injuries	Intense training
Li et al. [133]	Prospective	206	20±1 years	65% / 35%	ACTN3 gene	RX+XX genotype	ACTN3 RR genotype performed significantly better in terms of handgrip strength
Schreiber et al. [134]	Controlled trial	30	19-40 years	100% male	IL-6 TNF- α CRP	No changes 443.82 pg/mg No changes	Prolonged and multi-day training session
Ammar et al. [135]	Case series	9	21±0.5 years	100% male	Creatinine CRP	87.33 μmol/l 01.32 mg/L	Improve the weight-lifting performance.

8. Disscusion

Biomarkers have emerged as powerful tools in elite sports, offering valuable insights into athletes' physiological responses and potential performance enhancement [4]. This discussion explores the significance and potential applications of biomarkers in optimizing elite sports performance, emphasizing their crucial role in supporting athletes' training, recovery, and overall success.

Biomarkers provide objective measures of an athlete's physiological state, going beyond traditional subjective performance assessments [2]. Coaches and sports scientists can utilize blood and salivary biomarker analysis to gain precise data on an athlete's readiness and recovery status, making evidence-based decisions to optimize athletic performance [136].

Elite athletes are unique in their responses to training stimuli, necessitating personalized approaches. Biomarker analysis enables coaches to tailor training and recovery strategies based on athletes' specific biomarker profiles, maximizing training adaptations, minimizing injury risks, and fostering peak performance [137].

The intensive training regimens in elite sports can lead to overtraining and fatigue, potentially affecting an athlete's performance and well-being. Biomarker analysis, particularly for markers related to inflammation and muscle damage, allows for early detection of these conditions, prompting appropriate adjustments in training loads and recovery interventions [136].

Nutrition and hydration are critical components of an athlete's performance and recovery. Biomarkers related to hydration status, electrolyte balance, and nutrient metabolism offer valuable insights to sports nutritionists, facilitating the design of personalized nutrition plans that optimize fueling and enhance recovery [138]. Using information from the audio-visual environment to optimize this process, it would be advisable to proceed in a similar way and prevent injuries, which is a priority for elite athletes [139].

Injury prevention is a top priority for elite athletes. Biomarker analysis can identify athletes at higher risk of injury, enabling targeted injury prevention strategies. Additionally, biomarkers aid in injury rehabilitation by monitoring healing progress and guiding return-to-play decisions [2].

Advancements in genetic research have uncovered genetic biomarkers that influence athletic performance. Genetic testing supports talent identification, revealing an athlete's genetic potential and predisposition for specific sports disciplines, assisting sports organizations in talent recruitment and development [79].

Ethical considerations are of paramount importance when incorporating biomarker analysis in elite sports. Ensuring informed consent, protecting athletes' data privacy, and adhering to responsible biomarker data use are essential to uphold athlete rights and well-being.

The future of biomarkers in elite sports holds promising prospects. Ongoing research and technological innovations may uncover novel biomarkers, providing deeper insights into athlete physiology and performance optimization, further elevating the field of elite sports performance.

9. Conclusions

In conclusion, the integration of biomarkers in elite sports holds immense promise for optimizing performance and advancing athlete well-being. Through objective performance assessments, personalized training strategies, and injury prevention, biomarkers offer invaluable insights that traditional methods cannot provide.

Biomarker analysis facilitates evidence-based decisions, enabling coaches and sports scientists to fine-tune training programs to suit individual athlete responses. This tailored approach fosters greater training adaptations and reduces the risk of overtraining and fatigue, ensuring athletes perform at their peak.

Furthermore, biomarkers play a pivotal role in injury prevention by identifying athletes at higher risk, allowing for targeted interventions and timely rehabilitation. By prioritizing athletes' health, the risk of career-threatening injuries can be minimized, prolonging athletes' careers and enhancing their longevity in the sport.

The potential of genetic biomarkers in talent identification opens up new avenues for scouting and recruiting athletes best suited for specific sports disciplines. Identifying innate talents can lead to the cultivation of future champions and the development of diverse athletic talents across various sports.

Ethical considerations remain of utmost importance in biomarker implementation. Respecting athletes' rights, ensuring data privacy, and maintaining transparency are fundamental to building trust and ensuring the responsible use of biomarker data.

As research continues to advance, novel biomarkers may be discovered, providing deeper insights into athlete physiology and performance optimization. The future of biomarkers in elite sports is undoubtedly bright, holding the promise of unlocking new dimensions in human performance and pushing the boundaries of athletic excellence.

In essence, biomarkers have already begun to transform the world of elite sports, and their full potential is yet to be realized. With ethical implementation and ongoing research, biomarkers will undoubtedly play an instrumental role in shaping the future of elite sports, optimizing performance, and paving the way for the next generation of sporting legends.

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