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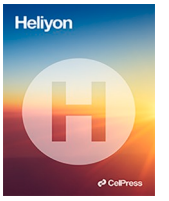

Review article

Myogenic differentiation markers in muscle tissue after aerobic training

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ABSTRACT

Aerobic training induces a myriad of adaptations in muscle tissue, encompassing alterations in muscle fiber type composition, hypertrophy, and metabolic capacity. Understanding the potential role of myogenic differentiation markers (MDFs), such as Pax7, MyoD, Myogenin, and myosin heavy chain (MHC) isoforms, in mediating these adaptations is of paramount importance. The review delves into the intricate molecular mechanisms underlying the regulation of MDFs following aerobic training, elucidating the role of key signaling pathways including the MAPK/ERK, PI3K/Akt, and AMPK pathways, among others. These pathways play pivotal roles in orchestrating the expression and activity of MDFs, ultimately influencing muscle adaptation and regeneration. The comprehension of MDFs in the context of aerobic training is far-reaching, offering the potential for targeted interventions to optimize muscle adaptation and regeneration. This review identifies the need for further research to unveil the precise molecular mechanisms of the activation and interaction of myogenic differentiation markers with other signaling pathways, as well as to explore their potential as therapeutic targets for muscle-related conditions. This review article also provides a thorough analysis of MDFs in muscle tissue after aerobic training, highlighting their potential clinical implications and outlining future research directions in this area.

1. Introduction

Regular physical exercise, particularly aerobic training, is known to induce numerous adaptations in skeletal muscle tissue. These adaptations contribute to improved muscle function, endurance, and overall health [1]. One key aspect of these adaptations is the regulation of myogenic differentiation, which involves the activation and differentiation of muscle stem cells (satellite cells) into mature muscle fiber [2]. Understanding the changes in myogenic differentiation markers (MDFs) following aerobic training is of great scientific and clinical importance. Identifying these markers provides insights into the molecular mechanisms that underlie muscle adaptation and regeneration, ultimately leading to the development of targeted interventions for muscle-related pathologies. Numerous studies have investigated the effects of aerobic training on MDFs in both human and animal models [3,4]. The expression levels of key markers such as Pax7, MyoD, Myogenin, and myosin heavy chain (MHC) isoforms have been extensively studied to elucidate the cellular and molecular events associated with muscle adaptation and regeneration [5,6]. Aerobic training has been

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shown to increase the expression and activation of MDFs in skeletal muscle tissue. The upregulation of Pax7 indicates an enhanced regenerative capacity and potential for muscle growth [7]. MyoD, a key transcription factor involved in myogenic differentiation, is also upregulated following aerobic training, promoting the transition of satellite cells into myoblasts. Furthermore, the expression of Myogenin, a marker of terminal differentiation, is increased, leading to the formation of mature muscle fibers [6,8,9]. In addition to the expression of these markers, aerobic training induces shifts in MHC isoforms, indicating changes in muscle fiber type composition. These shifts have been observed toward a greater proportion of slow-twitch oxidative fibers, which are more fatigue-resistant and exhibit enhanced metabolic capacity [10]. Aerobic training elicits substantial alterations in the myosin heavy chain (MHC) isoform distribution, particularly influencing the composition of skeletal muscle fibers, which is characterized by a transition from fast-twitch to slow-twitch muscle fibers, critical for enhancing endurance capacity. Specifically, aerobic exercise increases the proportion of MHC I isoforms, which are associated with slow-twitch fibers that exhibit greater oxidative capacity and fatigue resistance. For instance, a study demonstrated that after a 12-week aerobic training regimen, older women exhibited a significant increase in MHC I protein levels, accompanied by a downregulation of MHC IIa and IIx isoforms, indicating a shift towards a more oxidative muscle phenotype beneficial for metabolic health. Furthermore, during sustained aerobic activities, there is notable recruitment of fast-twitch fibers, particularly type IIA, which adapt to enhance endurance capabilities; this is evidenced by a decrease in MyHC IIb isoforms and an increase in MyHC IIa isoforms, reflecting the muscle's plasticity in response to prolonged aerobic exercise. Additionally, aging muscles display similar plasticity; research indicates that older adults can achieve a shift towards an oxidative MHC phenotype through regular aerobic training, suggesting that aerobic exercise can foster advantageous adaptations in muscle fiber composition even in aging populations. It is suggested that various signaling pathways, including the MAPK/ERK, PI3K/Akt, and AMPK pathways, play crucial roles in mediating the adaptive responses of satellite cells to exercise stimuli [11,12]. The MAPK/ERK, PI3K/Akt, and AMPK signaling pathways are integral to the adaptive responses of satellite cells to exercise stimuli, facilitating muscle regeneration and growth. Activation of the MAPK/ERK pathway is crucial for regulating satellite cell proliferation and differentiation, promoting myogenic processes essential for muscle repair post-exercise. Concurrently, the PI3K/Akt pathway plays a pivotal role in mediating anabolic responses and enhancing protein synthesis and muscle hypertrophy by promoting mTOR activity, which is vital for muscle fiber growth. Furthermore, AMPK functions as a key energy sensor that responds to increased AMP levels during exercise, orchestrating metabolic adaptations by regulating glucose uptake, fatty acid oxidation, and mitochondrial biogenesis. This pathway not only

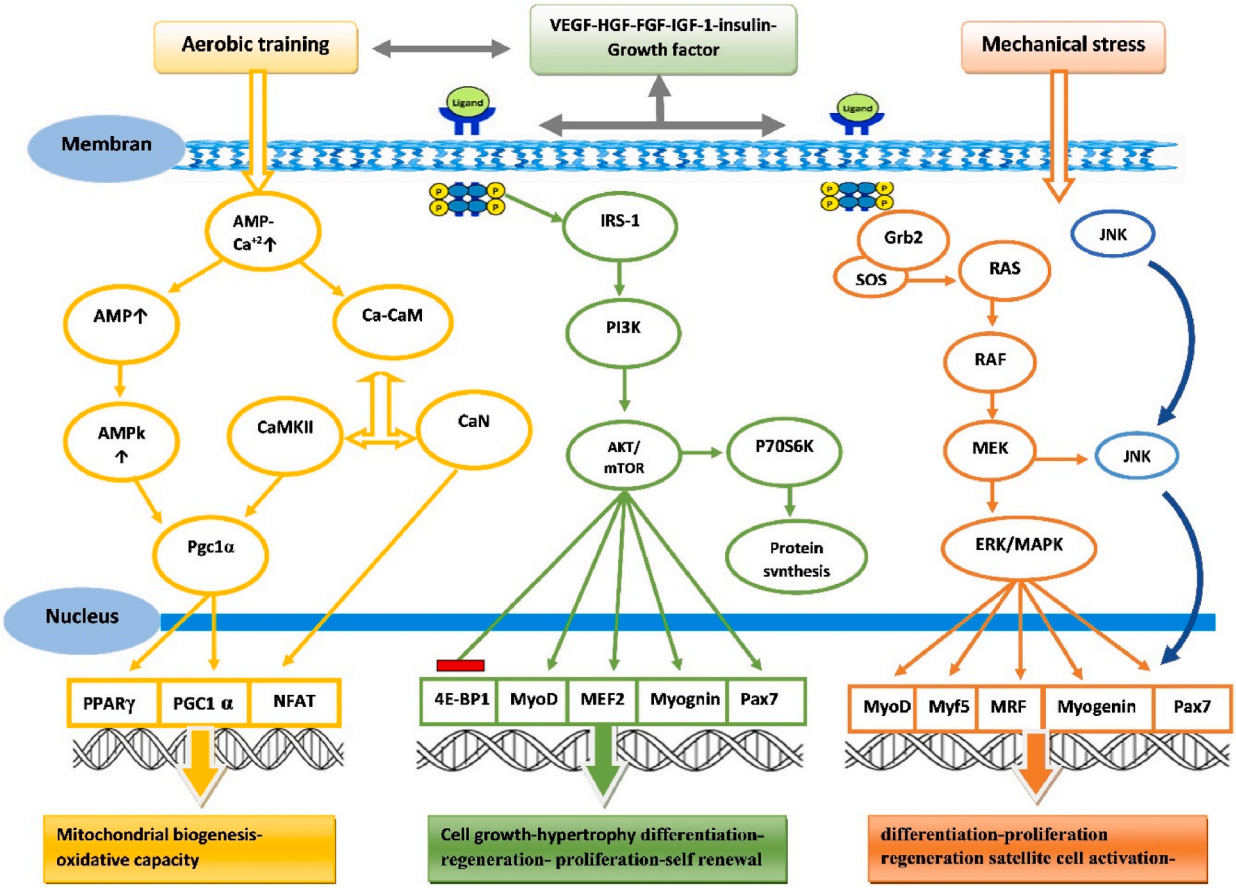

Fig. 1. The graphic abstract highlights the adaptations of muscle tissue due to aerobic training, emphasizing the role of myogenic differentiation markers and associated signaling pathways.

supports energy homeostasis but also influences satellite cell function by modulating their metabolic state and promoting oxidative muscle phenotypes. These pathways interact to ensure that satellite cells effectively respond to the metabolic demands imposed by exercise, thereby enhancing muscle plasticity and functional capacity. While significant progress has been made in understanding the effects of aerobic training on MDFs, there are still gaps in knowledge that warrant further investigation. These include the identification of specific exercise parameters (e.g., intensity, duration, frequency) that optimize MDFs, the influence of age and sex on these markers, and the potential interactions between aerobic training and other interventions such as nutritional supplementation [13,14]. This review article seeks to explore the alteration of MDFs in muscle tissue following aerobic training. The intricate molecular events and signaling pathways that govern the regulation of these vital markers will also be illuminated. Understanding these mechanisms is crucial, as it not only enriches our comprehension of the physiological and biochemical changes that skeletal muscle undergoes in response to exercise stimuli, but also paves the way for developing targeted interventions aimed at enhancing muscle health (see Fig. 1).

2. Methods

2.1. Literature search strategy

A comprehensive literature search was conducted to identify relevant studies investigating MDFs in muscle tissue after aerobic training. The following electronic databases were searched: PubMed, Web of Science, and Scopus. The search terms included combinations of keywords such as "MDFs," "muscle tissue," "aerobic training," and related terms. The search was limited to articles published in English.

2.2. Study selection criteria

The retrieved articles were screened based on predetermined inclusion and exclusion criteria. Inclusion criteria consisted of studies that examined MDFs in muscle tissue following aerobic training in both human and animal models. Studies focusing on other forms of exercise or interventions such as resistance training, high-intensity interval training, voluntary wheel running, etc. were excluded. Additionally, only studies published in peer-reviewed journals were considered for inclusion.

2.3. Data extraction

Data from the selected studies were extracted using a standardized form. The following information was recorded: study characteristics (e.g., author, year of publication), study design, sample size, participant characteristics (if applicable), aerobic training protocol, assessment methods for MDFs, and key findings related to MDFs in muscle tissue.

2.4. Data synthesis and analysis

The extracted data were synthesized to provide a comprehensive overview of the effects of aerobic training on MDFs in muscle tissue. Key findings were summarized, including changes in the expression levels of specific MDFs. Furthermore, any reported shifts in muscle fiber type composition were analyzed.

The methodological quality and risk of bias of the included studies were assessed using appropriate tools. To evaluate the methodological quality and risk of bias of the included studies, we employed established assessment tools tailored to the specific study designs under review. For randomized controlled trials, we utilized the "RoB 2 tool", which focuses on multiple domains of bias, including selection, performance, detection, attrition, and reporting biases. Each domain is assessed through a series of signaling questions that help determine whether there is a low, high, or some concerns regarding bias. This structured approach allows for a systematic evaluation of the trial's design, conduct, and reporting practices. For randomized controlled trials, the Cochrane Collaboration's tool for assessing the risk of bias was utilized which is crucial for evaluating the methodological quality of randomized controlled trials (RCTs) in systematic reviews. Introduced in 2008 and updated in 2019 as RoB 2, it enhances transparency and reliability in healthcare research. The tool identifies potential biases in RCT design, conduct, analysis, and reporting, helping researchers assess the validity of study findings. The original version included key domains such as selection bias, performance bias, and attrition bias, with reviewers assigning risk judgments of "low," "high," or "unclear." RoB 2 streamlines the assessment process with signaling questions and an algorithm that categorizes risks. Despite its strengths, challenges remain regarding inter-rater agreement and consistent application across studies. Feedback from focus groups has led to improvements in guidance and training resources. The assessment criteria included study design, sample size, participant characteristics, blinding, control groups, outcome measures, and statistical analysis methods. Studies with high methodological quality and low risk of bias were given greater weight in the final analysis.

2.5. Limitations

The limitations identified in the studies may significantly affect the validity and generalizability of the findings. Small sample sizes can lead to insufficient statistical power, increasing the risk of Type I and Type II errors, which may result in erroneous conclusions regarding intervention effectiveness. Variations in study designs and protocols across included studies introduce inconsistencies in

intervention implementation and measurement, complicating comparisons and potentially obscuring true effects. Additionally, heterogeneity in participant characteristics, such as age, sex, health status, and fitness levels, can further complicate result interpretation and may lead to variability in exercise intervention responses, making broad conclusions difficult. Furthermore, potential publication bias poses a risk, as studies with positive results are more likely to be published than those with negative or inconclusive findings, skewing the evidence base and overrepresenting successful outcomes.

4. Conclusion

In conclusion, this review article aims to provide a comprehensive understanding of the expression patterns, regulation, and signaling pathways associated with myogenic differentiation factors (MDFs) in response to aerobic training. Our analysis identifies key markers involved in muscle adaptation and regeneration, highlighting their modulation through targeted interventions. The specific findings indicate that manipulating the expression and activity of MDFs can significantly enhance muscle performance, endurance, and metabolic health in individuals engaged in aerobic training. This knowledge has important implications for developing novel therapeutic strategies aimed at improving muscle-related conditions and optimizing exercise training outcomes.

Furthermore, understanding the temporal patterns of MDF expression and their correlations with muscle adaptation offers valuable insights into the dynamics of muscle regeneration and remodeling. Targeted interventions focused on MDF modulation may open new avenues for optimizing muscle adaptation and recovery.

Future research should prioritize elucidating the molecular mechanisms underlying MDF regulation, exploring the temporal patterns of their expression, and identifying effective strategies for their modulation. These efforts will not only advance our understanding of muscle biology but also enhance therapeutic interventions for muscle-related disorders.

CRediT authorship contribution statement

Rastegar Hoseini: Writing – review & editing, Writing – original draft, Conceptualization. **Zahra Hoseini:** Writing – review & editing, Writing – original draft, Resources. **Ayob Kamangar:** Resources, Methodology.

3. Ethical considerations

As this review article is based on a synthesis of existing literature, no ethical approval was required. The study selection and data extraction processes were carried out following ethical guidelines and the principles of scientific rigor.

3.1. Aerobic training and muscle adaptation

Aerobic training-induced adaptations are known to induce a range of in muscle tissue, leading to improved performance, endurance, and metabolic health [1]. In recent years, there has been growing interest in understanding the potential role of MDFs in mediating aerobic training-induced adaptations, as well as the cellular and molecular signaling pathways involved. One of the key adaptations to aerobic training is the alteration of muscle fiber type composition [15]. Human skeletal muscles comprise different types of fibers, broadly categorized as slow-twitch (Type I) and fast-twitch (Type II) fibers [16]. Slow-twitch fibers are characterized by high fatigue resistance, rich capillarization, and oxidative metabolism, while fast-twitch fibers are associated with high force production and glycolytic metabolism [17]. Aerobic training has been shown to promote a shift towards a greater proportion of slow-twitch fibers [18]. This shift is thought to occur due to the activation of MDFs, such as Pax7, MyoD, and Myogenin [5,6] which play critical roles in satellite cell activation, proliferation, and differentiation [19]. Increased expression of PAX7 is indeed associated with the expansion of the satellite cell pool, which can lead to differentiation into various muscle fiber types, including slow-twitch fibers [20].

MyoD and Myogenin, transcription factors involved in myogenic differentiation, are upregulated following aerobic training, promoting the transition of satellite cells into myoblasts and facilitating the formation of slow-twitch fibers [5,6,8]. Aerobic training can also lead to muscle hypertrophy, characterized by an increase in muscle fiber size. While hypertrophy is often associated with resistance training, it has been observed in response to aerobic exercise as well [21]. The mechanisms underlying aerobic-induced hypertrophy are complex and multifactorial; MDFs are thought to play a role in aerobic-induced hypertrophy [13]. Increased expression of Pax7, MyoD, and Myogenin following aerobic training may facilitate satellite cell activation, proliferation, and fusion with existing muscle fibers, contributing to the hypertrophic response [6,13,22]. Furthermore, the activation of signaling pathways such as the MAPK/ERK, PI3K/Akt, and AMPK pathways may also be involved in mediating hypertrophic adaptations [23]. Aerobic training is well-known for its positive effects on metabolic capacity, including improvements in glucose homeostasis, lipid metabolism, and mitochondrial function [24,25]. These metabolic adaptations allow for enhanced energy production and utilization during prolonged exercise [24]. MDFs may influence metabolic capacity through their impact on muscle fiber type composition [15]. Slow-twitch fibers, which are more prevalent following aerobic training, have a higher oxidative capacity and greater capacity for lipid oxidation [26]. This shift in fiber-type composition, mediated by MDFs, may contribute to the improved metabolic profile observed after aerobic training.

Several cellular and molecular signaling pathways have been implicated in mediating the effects of aerobic training on muscle tissue. The MAPK/ERK pathway, activated by exercise-induced mechanical stress and growth factors, has been shown to influence satellite cell activation and differentiation [27,28]. The PI3K/Akt pathway, activated by insulin and exercise-induced muscle

contractions, plays a crucial role in protein synthesis, cell growth, and hypertrophy [29,30]. Additionally, the AMPK pathway, activated by changes in intracellular energy status, regulates energy metabolism and mitochondrial biogenesis [31].

These signaling pathways are interconnected and can converge on the activation of MDFs, ultimately leading to the observed adaptations in muscle tissue following aerobic training. The precise interplay and cross-talk between these pathways are complex and require further investigation [32].

3.2. Expression and regulation of MDFs

The expression patterns and regulation of MDFs, including Pax7, MyoD, Myogenin, and MHC isoforms, play critical roles in muscle development, regeneration, and adaptation [5,8]. Understanding these patterns and regulatory mechanisms provides insights into the molecular events underlying myogenic differentiation and its interactions with other signaling pathways. Satellite cells are resident muscle stem cells responsible for muscle regeneration [33,34]. In quiescent muscle, Pax7 is highly expressed in the satellite cell population. Upon activation, Pax7 is downregulated as satellite cells undergo proliferation and differentiation. The regulation of Pax7 expression involves various factors and signaling pathways [35]. Pax7 expression is positively regulated by transcription factors such as MyoD and Myf5, which are involved in myogenic determination and differentiation [35]. Additionally, growth factors such as FGF, HGF, and IGF-1 can stimulate Pax7 expression and satellite cell activation [36–38]. Conversely, negative regulators like Notch signaling pathway components can downregulate Pax7 expression, promoting satellite cell differentiation [39]. MyoD plays a central role in myogenic determination and differentiation [40,41]. It is involved in the activation of quiescent satellite cells and their commitment to the myogenic lineage [42]. MyoD expression is tightly regulated during muscle development and regeneration [41]. The regulation of MyoD expression involves multiple signaling pathways and molecular mechanisms. MyoD expression is positively regulated by factors like Pax7, Myf5, and MRF4, which are involved in myogenic lineage determination [43]. Activation of the MAPK/ERK pathway, triggered by growth factors and exercise-induced mechanical stress, can promote MyoD expression [44]. The PI3K/Akt signaling pathway enhances MyoD expression, thereby promoting myogenic differentiation [30,45]. Myogenin, a crucial transcription factor, plays a significant role in the terminal differentiation of myoblasts into mature muscle fibers. It is highly expressed during the later stages of myogenic differentiation and is essential for the formation of contractile proteins and the maturation of muscle fibers [9,46]. The expression of Myogenin is regulated by several factors and signaling pathways. Notably, MyoD positively regulates Myogenin expression by binding to the regulatory regions of the Myogenin gene and activating its transcription. Other transcription factors, such as MEF2, also contribute to this regulation [47]. Furthermore, the activation of the MAPK/ERK pathway and calcium-dependent signaling pathways can enhance Myogenin expression and promote myogenic differentiation [48]. Myosin heavy chain (MHC) isoforms are structural proteins that determine the contractile properties and functional characteristics of muscle fibers. Different isoforms are expressed in various muscle fiber types, including slow-twitch oxidative (Type I) and fast-twitch glycolytic (Type II) fibers [49]. The regulation of MHC isoform expression involves a combination of intrinsic factors, such as transcription factors like MyoD and Myogenin, and extrinsic factors influenced by various signaling pathways. Notably, the calcineurin/NFAT pathway and the PGC-1α/PPARγ pathway can modulate MHC isoform expression [50,51]. These pathways are activated by calcium signaling, metabolic stress induced by exercise, and endurance training [6,48]. The expression and regulation of myogenic differentiation factors (MDFs) are closely interconnected with other signaling pathways involved in muscle development, regeneration, and adaptation. For instance, the MAPK/ERK pathway—activated by growth factors and mechanical stress from exercise—stimulates the expression of MyoD and Myogenin, thereby promoting satellite cell activation and myogenic differentiation [44,48,52]. Additionally, the calcineurin/NFAT pathway influences MHC isoform expression and muscle fiber type composition through calcium signaling [53]. Additionally, the PGC-1α/PPARγ pathway, activated by metabolic stress and endurance exercise training, can modulate MHC isoform expression and mitochondrial biogenesis [6,48]. The interaction between these signaling pathways and MDFs is complex and dynamic, allowing for coordinated and integrated responses to various stimuli and environmental cues. The expression patterns and regulation of MDFs. These markers are intricately involved in satellite cell activation, myogenic determination, differentiation, and fiber type specification. The regulation of their expression involves the interplay of various intrinsic and extrinsic factors, as well as the interaction with other signaling pathways [5,6,52].

3.3. Effects of aerobic training on myogenic differentiation markers

The effects of aerobic training on MDFs have been extensively investigated in both human and animal models. Numerous studies have examined the expression levels of MDFs following aerobic training. These markers play crucial roles in satellite cell activation, proliferation, and differentiation, thereby influencing muscle regeneration and adaptation [5,6,8]. The literature consistently demonstrates that aerobic training can lead to alterations in the expression levels of MDFs [13].

For instance, increased expression of Pax7, a marker of satellite cell activation and self-renewal, has been observed following aerobic training This upregulation suggests an enhanced regenerative capacity and potential for muscle growth [7,33]. Similarly, the expression of MyoD is upregulated following aerobic training [6,41]. During aerobic exercise, physiological stress signals activate satellite cells, leading to their proliferation and differentiation into myoblasts, a process that is mediated by MyoD. Increased levels of MyoD facilitate the transition of these myoblasts into mature muscle fibers, including slow-twitch fibers, which are crucial for endurance activities. Studies indicate that aerobic training enhances the expression of MyoD alongside other myogenic markers, thereby promoting muscle hypertrophy and improving functional capacity. This response is part of the adaptive mechanisms that allow skeletal muscle to better withstand the demands of prolonged physical activity, ultimately contributing to improved muscle performance and recovery following exercise.

MyoD promotes the transition of satellite cells into myoblasts, which are precursor cells for muscle fiber formation [54]. Increased MyoD expression indicates an active process of muscle regeneration and adaptation [40,41]. Myogenin has also been shown to exhibit increased expression following aerobic training [8,9,46]. This suggests that the formation of mature muscle fibers is enhanced, contributing to muscle adaptation and improved performance [5]. Moreover, aerobic training has been associated with shifts in MHC isoforms, which are characteristic of different muscle fiber types. These shifts indicate changes in fiber type composition, with a potential increase in slow-twitch oxidative fibers. Such changes in MHC isoform expression are related to improved endurance and metabolic capacity [10,18]. The literature reveals that the temporal patterns of myogenic differentiation marker expression following aerobic training are dynamic and can vary depending on several factors. The duration and intensity of the training regimen, as well as individual characteristics, may influence the time course of marker expression changes [4,7]. In the early stages of aerobic training, an acute upregulation of MDFs is often observed This acute response reflects the initial activation and mobilization of satellite cells, priming them for subsequent regeneration and adaptation [7]. As training continues, marker expression levels may stabilize or exhibit a gradual decrease, indicating a transition from an acute response to a more sustained, adaptive state [7,55]. Correlations between changes in myogenic differentiation marker expression levels and muscle adaptation following aerobic training have been reported in several studies [7,10,21,34]. Increases in marker expression have been associated with muscle hypertrophy, improved muscle strength, and enhanced endurance performance. These correlations suggest that changes in MDFs play a role in mediating muscle adaptation to aerobic training by promoting satellite cell activation, proliferation, and differentiation, these markers contribute to muscle regeneration, fiber formation, and remodeling, ultimately leading to improved muscle function and performance [56]. The effects of aerobic training on MDFs are mediated by various cellular and molecular signaling pathways. The MAPK/ERK, PI3K/Akt, and AMPK pathways, among others, have been implicated in regulating the activation and expression of MDFs [8,45,57]. The existing literature provides strong evidence for the effects of aerobic training on MDFs in both human and animal models [6,11,27,35].

Increased expression levels of Pax7, MyoD, and Myogenin, as well as shifts in MHC isoforms, have been consistently observed following aerobic training [5,6,10]. These changes indicate enhanced satellite cell activation, proliferation, and differentiation, leading to muscle regeneration, fiber formation, and remodeling [6,56]. The temporal patterns of marker expression and their correlations with muscle adaptation highlight the dynamic nature of these processes. Furthermore, cellular and molecular signaling pathways, including the MAPK/ERK, PI3K/Akt, and AMPK pathways, play crucial roles in mediating the effects of aerobic training on MDFs [8,45,57].

3.4. Mechanisms and signaling pathways

The regulation of MDFs following aerobic training involves a complex interplay of signaling pathways and molecular mechanisms [44]. Several key pathways, including the MAPK/ERK, PI3K/Akt, and AMPK pathways, among others, play crucial roles in mediating the effects of aerobic training on MDFs [8,45,57]. In response to aerobic training, the MAPK/ERK pathway is stimulated, leading to the activation of downstream transcription factors such as MyoD and Myogenin [44,45,57]. Activation of the MAPK/ERK pathway can enhance the expression of MyoD [41,44]. MyoD promotes the activation and commitment of satellite cells to the myogenic lineage, facilitating muscle regeneration and adaptation [40,43]. Similarly, the expression of Myogenin can be upregulated by the MAPK/ERK pathway, contributing to the formation of mature muscle fibers [9].

Overall, the MAPK/ERK pathway acts as a critical mediator of myogenic differentiation marker expression following aerobic training [57]. The PI3K/Akt pathway is another important signaling pathway involved in the regulation of MDFs following aerobic training It is activated by insulin and exercise-induced muscle contractions, contributing to protein synthesis, cell growth, and hypertrophy [30,45]. In response to aerobic training, the activation of the PI3K/Akt pathway can enhance the expression of MyoD and promote myogenic differentiation [45,58,59]. Increased MyoD expression stimulates satellite cell activation and commitment to the myogenic lineage, facilitating muscle regeneration and adaptation [40,43]. The PI3K/Akt pathway also plays a role in the regulation of muscle hypertrophy, which is associated with changes in myogenic differentiation marker expression [45]. The AMP-activated protein kinase (AMPK) pathway is an energy-sensing pathway that is activated by changes in intracellular energy status, such as exercise-induced metabolic stress The AMPK pathway regulates energy metabolism and mitochondrial biogenesis, which are critical for muscle adaptation following aerobic training [57,60]. Activation of the AMPK pathway can influence the expression and activity of MDFs [45]. AMPK activation promotes the expression of Pax7 which might contribute to the expansion of the satellite cell pool and subsequent myogenic differentiation [7,33,61]. Furthermore, the AMPK pathway can enhance the expression of MHC isoforms [62].

In addition to the MAPK/ERK, PI3K/Akt, and AMPK pathways, other signaling pathways and molecular mechanisms are involved in the regulation of MDFs following aerobic training [8,45,57]. These include the calcineurin/NFAT pathway, the PGC-1α/PPARγ pathway, and various growth factors and cytokines [48,53]. The calcineurin/NFAT pathway, activated by calcium signaling, plays a role in MHC isoform expression and muscle fiber type specification [53]. The PGC-1α/PPARγ pathway, activated by metabolic stress and endurance exercise training, can modulate MHC isoform expression and mitochondrial biogenesis [6,48]. Growth factors and cytokines, such as IGF-1, FGF, and HGF, are also involved in the regulation of MDFs. These factors can stimulate satellite cell activation, proliferation, and differentiation, contributing to muscle regeneration and adaptation [63,64]. The regulation of MDFs following aerobic training involves a network of signaling pathways and molecular mechanisms. The MAPK/ERK, PI3K/Akt, and AMPK pathways, among others, play crucial roles in mediating the effects of aerobic training on MDFs. Activation of these pathways leads to the upregulation of key transcription factors, including MyoD and Myogenin, promoting satellite cell activation, proliferation, and differentiation [8,45,52,57]. The intricate interplay and cross-talk between these signaling pathways and molecular mechanisms needs to be elucidated which will deepen our understanding of muscle adaptation to aerobic training and potentially inform therapeutic interventions for muscle-related conditions.

Aerobic training leads to significant adaptations in muscle tissue, primarily through changes in muscle fiber composition, hypertrophy, and metabolic capacity. It promotes a shift toward a higher proportion of slow-twitch (Type I) fibers, enhancing endurance and fatigue resistance, mediated by myogenic differentiation markers like Pax7, MyoD, and Myogenin. These markers play crucial roles in satellite cell activation and muscle fiber maturation. Additionally, aerobic exercise can induce muscle hypertrophy by activating satellite cells and facilitating their fusion with existing fibers. Key signaling pathways, including MAPK/ERK, PI3K/Akt, and AMPK, regulate these processes by influencing the expression of myogenic markers and contributing to improved metabolic functions such as glucose homeostasis. Understanding these mechanisms is essential for optimizing training interventions aimed at enhancing muscle health and performance.

Consent for publication

All authors provided input into the manuscript, reviewed the final draft, and provided consent for publication.

Ethics approval

Not applicable.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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