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The Immunometabolic Post-exercise Response in Adipose and Muscle Tissue: The Role of the Complement System

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Introduction

Exercise is a powerful modulator of metabolic and immune health, influencing processes in multiple tissues, including adipose and muscle. The immediate and prolonged effects of physical activity are mediated through complex interactions between metabolic and immune signaling pathways. One emerging area of research in this context is the role of the complement system, a key component of innate immunity, in modulating the post-exercise responses in adipose and muscle tissues. The complement system, traditionally known for its role in pathogen defense, has recently been recognized as a critical player in metabolic regulation and tissue homeostasis. This dual role positions it as a central mediator of the immunometabolic response to exercise. Adipose tissue and skeletal muscle, both critical for energy storage and expenditure, undergo significant physiological changes during and after exercise. The complement system appears to contribute to these adaptations by modulating inflammatory responses, tissue remodeling, and substrate utilization. This article delves into the intricate interplay between the complement system and the post-exercise responses in adipose and muscle tissues. It examines the metabolic and immune dynamics elicited by exercise, the role of the complement system in these processes, and the implications for metabolic health and exercise performance.

Description

Adipose tissue, traditionally viewed as an energy storage depot, is now recognized as an active endocrine organ that regulates metabolism and immune responses. Exercise-induced adaptations in adipose tissue are mediated, in part, by the complement system. Complement proteins, particularly ASP, enhance lipolysis and fatty acid re-esterification during exercise. Complement activation modulates adipocyte signaling pathways involved in energy metabolism, such as AMP-activated protein kinase and peroxisome proliferator-activated receptor pathways. Exercise induces a transient influx of macrophages into adipose tissue, which is regulated by complement-derived chemotactic factors. Complement activation promotes a shift from pro-inflammatory (M1) to anti-inflammatory (M2) macrophage polarization, facilitating tissue repair and recovery. Complement proteins contribute to extracellular matrix remodeling, a key process in adapting to exercise-induced mechanical stress. Exercise stimulates the conversion of white adipose tissue to metabolically active brown-like (beige) adipocytes, a process influenced by complement signaling.

Skeletal muscle is the primary site of glucose uptake and a major contributor to systemic energy metabolism during exercise. The complement system plays a pivotal role in muscle repair, inflammation resolution, and metabolic adaptations. Exercise-induced muscle damage activates the complement system, leading to the recruitment of neutrophils and macrophages to the site of injury. Complement proteins, such as C3a and C5a, promote the clearance of cellular debris and the transition to anti-inflammatory signaling. Complement activation enhances the proliferation and differentiation of satellite cells, critical for muscle repair. Complement signaling influences mitochondrial biogenesis and oxidative phosphorylation, key adaptations to endurance exercise. Complement activation modulates insulin signaling and glucose transporter (GLUT4) translocation in skeletal muscle. Complement proteins regulate intramuscular lipid turnover, ensuring an adequate energy supply during prolonged exercise. Complement-derived signals regulate macrophage function in skeletal muscle, balancing inflammatory and regenerative processes. Exercise-induced cytokines, such as interleukin-6 (IL-6), interact with complement pathways to coordinate systemic energy metabolism [1,2].

Conclusion

The complement system plays a central role in mediating the immunometabolic responses to exercise in adipose and muscle tissues. By regulating inflammatory signaling, substrate metabolism, and tissue remodeling, complement activation contributes to the beneficial adaptations associated with physical activity. Understanding these processes offers valuable insights into the mechanisms underlying exercise-induced health benefits and provides a foundation for developing targeted interventions to enhance recovery, performance, and metabolic health. As research continues to uncover the intricate interplay between immunity and metabolism, the complement system is poised to remain at the forefront of exercise physiology and immunometabolism.

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