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LETTER TO THE EDITOR

A Hypothetical Dual Pathway Therapeutic Strategy for Managing Rheumatoid Arthritis Associated Sarcopenia

Dear Editor,

Rheumatoid arthritis is a chronic autoimmune disease that affects many tissues in the body. The disease mainly targets the joints, but its systemic effects are often ignored (Babaahmadi et al., 2023). One overlooked complication is rheumatoid arthritis associated sarcopenia. Sarcopenia in these patients begins early and progresses steadily. It reduces muscle mass and limits physical activity. Many patients describe this weakness as more disabling than joint pain. This condition deserves more attention in clinical practice (Bennett et al., 2023). Sarcopenia in rheumatoid arthritis is driven by chronic inflammation. Cytokines such as TNF-α, IL-6, and IL-1β remain elevated in most patients. These cytokines activate muscle catabolic pathways. NF-κB and JAK-STAT signaling increase protein degradation (Ding et al., 2025; Lozada-Mellado et al., 2024). Muscle repair becomes slow and inefficient. Reduced physical activity worsens this imbalance. Pain, fatigue, and stiffness prevent regular movement. This cycle accelerates muscle loss. Current rheumatoid arthritis therapies mainly target joint inflammation. Disease-Modifying Antirheumatic Drugs and biologics reduce inflammatory signals. They help control pain and joint swelling. However, they do not fully protect muscle tissue. Muscle wasting continues even when joint disease improves. Many patients show persistent functional impairment. This gap in therapy highlights an unmet need.

A hypothetical therapeutic approach may help address this problem. The concept involves two main strategies. The first strategy focuses on myostatin modulation. Myostatin is a negative regulator of muscle growth. High inflammation in rheumatoid arthritis increases myostatin levels. This elevation accelerates muscle atrophy. Blocking myostatin may preserve muscle mass. Several studies in other diseases support this idea. Complete myostatin blockade can cause side effects. These include cardiac strain and muscle fibrosis. A partial and controlled approach may be safer. Partial modulation may allow balanced muscle regeneration. It may prevent sudden stress on the cardiovascular system. The second strategy targets mitochondrial dysfunction. Mitochondria in skeletal muscle become damaged during chronic inflammation. Oxidative stress reduces ATP production. Muscle cells tire easily. Mitochondrial dysfunction also triggers apoptosis in muscle fibers. These changes worsen sarcopenia. A potential solution involves mitochondria-targeted treatment. These targeted treatment improve electron transport efficiency. They reduce oxidative injury in the mitochondria. Early experimental studies show encouraging outcomes. Both strategies may work better when combined. Myostatin modulation promotes muscle growth. Mitochondrial therapy improves energy supply. Together, they may create a supportive environment for muscle recovery (Figure 1). A cyclic method of delivery may enhance safety. Patients may receive a short phase of myostatin modulation. This can be followed by a phase of mitochondrial support. The cycle may continue based on clinical response. This approach avoids prolonged suppression of normal pathways. It also gives time for muscle tissue to adapt. Rehabilitation must play a role in this model. Controlled exercise can activate muscle regeneration pathways. Low-intensity resistance training improves strength. Aerobic exercises enhance mitochondrial function. Physiotherapists can design personalized routines. These routines must match disease activity and patient tolerance. Combining the hypothetical therapy with guided rehabilitation may improve outcomes. It provides both biological and mechanical support for the muscle.

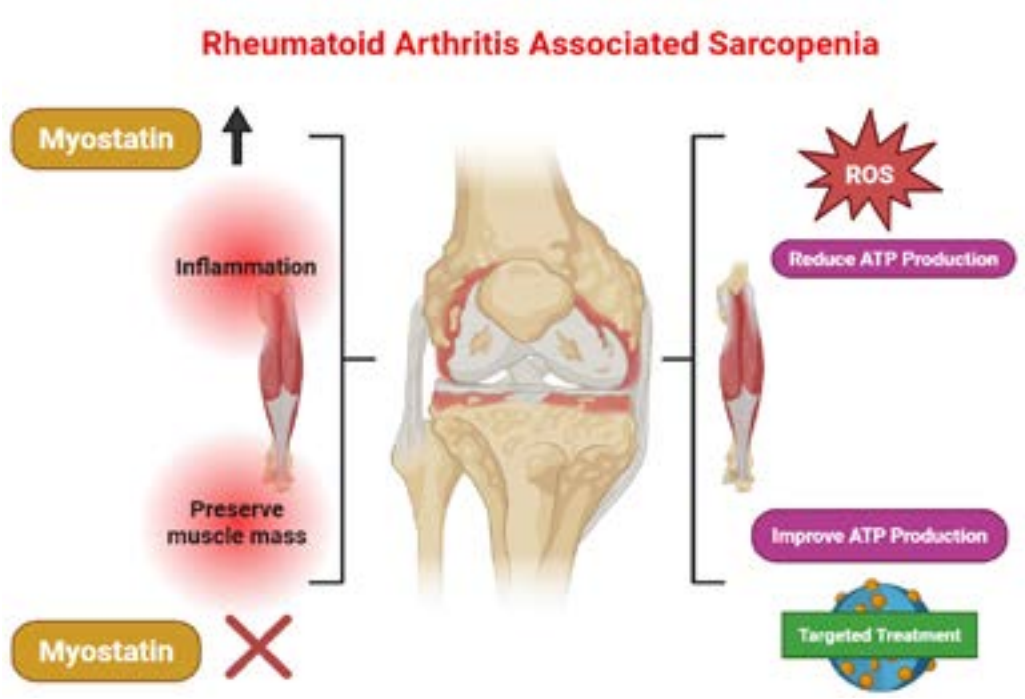

Figure 1: Conceptual overview of rheumatoid arthritis–associated sarcopenia and the proposed dual-pathway therapeutic strategy. Chronic inflammation in rheumatoid arthritis increases myostatin levels, which accelerates muscle loss and weakens muscle mass. Elevated reactive oxygen species (ROS) further impair mitochondrial function and reduce ATP production, contributing to progressive sarcopenia. The hypothetical therapeutic model involves partial myostatin inhibition to preserve muscle tissue and mitochondria-targeted treatments to restore ATP production.

Declarations

Ethics approval statement

Not Applicable

Consent to participate

Not applicable

Consent to publish

Not applicable

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Competing Interests

The authors declare that they have no conflict of interest

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Reference

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