TAK1 Signaling Regulates the Secretory Capacity of Skeletal Muscle Fibroblasts in Response to Inflammatory Cytokines

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Skeletal muscle cells regulate and provide many bodily functions. Skeletal muscle cells support movement, posture, and temperature regulation. In addition, skeletal muscle triggers an immune response, releasing inflammatory stimuli under exercise-induced tension. Skeletal muscle is held together by a significant spindle-shaped cell dubbed the skeletal muscle fibroblast (SMF). Research in Cell Metabolism (Wei W. et al.) found that SMFs were the most responsive cell type to exercise in mice, secreting proteins vital for muscle growth and healing. This suggests that the skeletal muscle's immune response may trigger SMF secretion, regulating their synthetic capacity. TAK1 kinase plays a key role in controlling skeletal muscle mass, immune adaptation, and protein synthesis in SMFs. This research aims to explore the role of inflammatory stimuli in SMF secretion, alongside the extent to which TAK1 regulates translation and secretion through tissue-specific knockdown methods. By analyzing protein secretion in SMFs exposed to exercise-induced cytokines (IL-6, IL-10, TGFA, IL1B), this study seeks to provide insights into skeletal muscle function. It is hypothesized that TAK1 signaling in SMFs regulates translation and secretion that may be important to responses of skeletal muscle to exercise.TGFA and IL1B significantly increased SMF secretion, nearly doubling protein output compared to the mean and other cytokines. Further, knocking down the TAK1 gene with iCre in SMF media treated with IL1B and TNFA led to a significant reduction in protein secretion, indicating that TAK1 kinase is a critical regulator of protein synthesis and adaptation in skeletal muscle after exercise.

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