TACSM Abstract

Micronized Biocompatible Ceramic Promotes Muscle Derived IL-6 Release in Disuse

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Category: Doctoral

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ABSTRACT

Skeletal muscle is remarkably plastic and undergoes significant muscle wasting in response to mechanical unloading. Chronic bedrest and microgravity conditions promote disuse-induced muscle atrophy and dysfunctional myogenesis. While these pathological effects have been well documented, there are currently no effective therapies to remedy this muscle loss. Time-release ion matrices (TRIM) are amorphous non-crystalline biomaterials that promote regenerative gene transcription when injected in soft tissue. However, the detailed pathways involved in TRIM activated regeneration of skeletal muscle are unexplored. Degenerative and regenerative inflammation are key processes in regeneration. **PURPOSE:** The purpose of this study was to investigate muscle inflammation in response to TRIM treatment in a model of disuse muscle atrophy. **HYPOTHESIS:** We hypothesized that TRIM would not promote degenerative inflammation in rat tibialis anterior (TA) muscles after 10 days of hindlimb unloading (HU). **METHODS:** 5-month-old F344 rats were assigned to three groups (n=6): ambulatory control (CON), hindlimb unloaded (HU), and hindlimb unloaded with TRIM (HUT). 1.4 mg of TRIM particles suspended in 280 μL of sterile saline were administered via intramuscular injection into the right TA of HUT rats 24 hours prior to starting the 10-day unloading protocol. At the end of the experiment, right TA muscles were snap frozen and serum collected for biochemical analyses. Nine inflammatory biomarkers (IFN-γ, IL-1β, IL-4, IL-5, IL-6, IL-10, IL-13, KC/GRO, TNF-α) were measured by sandwich immunoassay methods in TA muscle homogenate and serum using a commercially available kit and detection system (V-PLEX Proinflammatroy Panel 2 (rat), Meso Scale Discovery). **RESULTS:** Muscle-derived IL-6 secretion was significantly increased in TRIM treated TA's compared to CON (CON, 6.92 ± .71 pg/ml; TRIM, 14.82 ± 3.2 pg/ml; P=0.03). HU TA's had a significant increase in IL-1β expression compared to CON, while TRIM TA's blunted this response (CON, 21.38 ± 1.99 pg/ml; HU, 29.38 ± 1.45 [P=0.02]; TRIM, 27.60 ± 2.28 pg/ml). No significant differences were found between groups in serum-derived IL-6 secretion (CON, 149.2 ± 12.1 pg/ml; HU, 170.3 ± 15.8; TRIM, 159.9 ± 12.8 pg/ml; P=0.56), as well as no differences in serum IL-1β (CON, 270.4 ± 19 pg/ml; HU, 265.4 ± 34; TRIM, 235.3 ± 35 pg/ml; P=0.68). **CONCLUSION:** Results support the hypothesis that TRIM would not promote degenerative inflammation in muscle. Importantly, TRIM increased muscle-derived IL-6 expression known to stimulate myogenesis, while mediating increased IL-1β secretion seen in HU. We suggest TRIM promotes localized regenerative inflammation in treated skeletal muscle.