31. SWACSM Abstract

Macrophage Response to Damage in Old and Young Skeletal Muscle

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ABSTRACT

PURPOSE: In skeletal muscle, macrophages migrate to damaged fibers, influencing the inflammatory response during muscle regeneration. Macrophages experience polarization, exhibiting different phenotypes described as M1 (pro-inflammatory) and M2 (anti-inflammatory.) Failure to properly transition between phenotypes inhibits fiber regeneration. Previous animal literature suggests that dysregulated macrophage polarization may contribute to the decreased regenerative capacity of aging muscle. The purpose of this study is to quantify macrophage response and polarization in a model of muscle damage and regeneration in older humans. We hypothesized that older people would have a higher percentage of M2 macrophages relative to the young. METHODS: Seven young $(25 \pm 3 \text{ y})$ and nineteen elderly $(67 \pm 4 \text{ y})$ male subjects were recruited for participation in the study. Muscle damage and regeneration events were initiated in one leg by electrically induced maximal eccentric contractions. Muscle biopsies were collected from the electrically stimulated leg pre and 9 days post stimulation. Biopsy samples were prepared for histological analysis and stained by immunohistochemistry to visualize macrophage content. Anti-CD68 antibodies were used as a panmacrophage marker, while an anti-CD206 antibody was used to identify M2 macrophage. **RESULTS:** Both groups (young and elderly) demonstrated an increase in the number of damaged fibers following the protocol (p=.0006), but no significant effect of age was observed(add P). The total number of CD68+ cells increased post intervention (p<.0001), and was higher in the young age group (p=.045). Additionally, there was a significant age x time interaction with total CD68+ increasing more in the young group post damage (p=.048). CD206+ cells were quantified as a percentage of total macrophage content. Overall there was a higher proportion of CD206+ macrophages in the elderly group both pre and post damage (p<.0001). There was no significant age x time interaction (add P). CONCLUSION: These data demonstrate that the protocol was successful in eliciting similar muscular damage in both age groups. Damage in young muscle elicits a greater macrophage response post damage. A higher proportion of macrophages present in older muscle tissue exhibit an M2 phenotype.