

# PGE2 Ameliorates Aging-Aggravated Rotator Cuff Muscle Atrophy is Effective in Preventing Massive Rotator Cuff Tear in the Elderly

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## INTRODUCTION:

The aging-related escalation of muscle degeneration impacts the structure and function of rotator cuff muscles, contributing to spontaneous and tear-induced muscle atrophy. This study investigated how prostaglandin E2 (PGE2), a regulator of muscle regeneration, influences muscular structure and mitochondrial function in aged mice by using SW033291 to inhibit PGE2 degradation, revealing potential therapeutic pathways for mitigating rotator cuff muscle deterioration.

## METHODS:

A total of 20 young (5 to 6-month-old) and 100 aged (18 to 20-month-old) female C57BL/6J mice were divided into 2 groups: the first group included young, aged, and aged+SW033291 subgroups and was used to study sarcopenia, and the second group consisted of tear, tear+repair, and tear+repair+SW033291 subgroups and was used to examine the outcomes following an RCT. Tissue staining, muscle mass assessments, functional assays, and mitochondrial function tests were performed.

## RESULTS:

Rotator cuff muscle degeneration was observed in the setting of natural aging and in the setting of a rotator cuff tear (RCT). These conditions together worsened muscle atrophy and fatty infiltration into the muscle, with the aged tear group demonstrating a decrease in muscle mass from a mean and standard deviation of  $45.45 \pm 4.04$  to  $25.18 \pm 1.82$  mg ( $p < 0.001$ ) and a reduction in fiber cross-sectional area (CSA) from  $1,697.3 \pm 108.4$  to  $1,263.0 \pm 56.8 \mu\text{m}^2$  ( $p < 0.001$ ). This was linked to increased 15-prostaglandin dehydrogenase (15-PGDH) activity and a reduction in PGE2 levels in the aged tear group (from  $2.897 \pm 0.177$  to  $1.873 \pm 0.179$  ng/g muscle;  $p < 0.001$ ). SW033291 treatment increased the level of PGE2, reversing muscle atrophy by mitigating mitochondrial dysfunction in both models, as demonstrated by a muscle mass of  $33.50 \pm 3.05$  mg and a CSA of  $1,423.6 \pm 81.3 \mu\text{m}^2$  in the presence of both conditions.

## DISCUSSION AND CONCLUSION:

These findings support the hypothesis that elevated PGE2 levels can improve muscle health by reversing mitochondrial dysfunction, offering a strategy to combat sarcopenia and to enhance rotator cuff repair.

