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School of Health Promotion and Kinesiology

Formoterol Treatment In Vitro Preserves Expression of Genes Related to Mitochondrial Biogenesis, Metabolism, and Cell Survival During Skeletal Muscle Myogenesis

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Introduction

- Skeletal muscle (SKM) is an important tissue influencing total metabolism and regulator of metabolic homeostasis.
- Muscle loss can contribute to mitochondrial dysregulation leading to a decline in muscle function and metabolism.
- Exercise training increases the mitochondrial capacity of SKM leading to an increase in metabolism.
- Previous studies in our lab observed that In Vitro SKM cell treatment with Formoterol (FORM), a beta-adrenergic receptor agonist, maintained baseline expression of factors associated with the regulation of metabolism and functional capacity of mitochondria:
  - ❖β2-adrenergic receptor
  - ❖Peroxisome proliferator-activated receptor gamma coactivator-1 alpha (PGC-1α)
  - ❖Peroxisome proliferator-activated receptor gamma coactivator-1 beta (PGC-1β)

Purpose

- To explore the effect of In Vitro FORM on the expression of genes associated with metabolism in human SKM cells.

Methods

- Commercially obtained, human, SKM myoblasts (n = 4) were cultured in growth media and proliferated until 70% confluency.
- The growth media was then replaced with differentiation media and cells were differentiated for three days before initiation of daily treatment of 30 nM FORM or Control (CON). Treatment continued until terminal differentiation (day 6).
- Total RNA was extracted at day 1 of differentiation (D1), 24 hours post-treatment (D4), and 72 hours post-treatment (D6).
- Gene expression was analyzed by qPCR for TFAM, ERRα, NRF-1, Nrf2, and ATG5.

Results

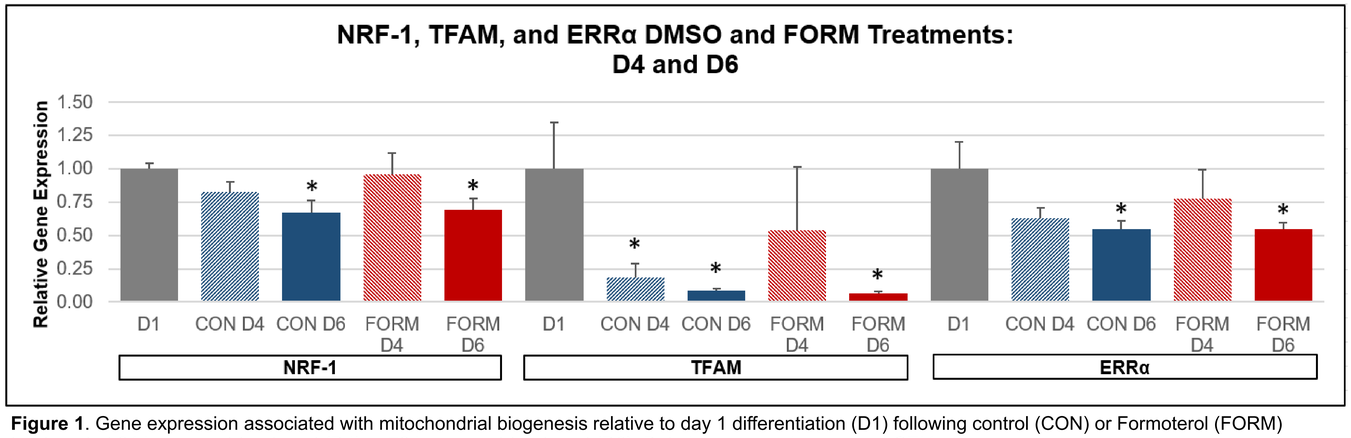

Figure 1. Gene expression associated with mitochondrial biogenesis relative to day 1 differentiation (D1) following control (CON) or Formoterol (FORM) treatment at 24 hours post-treatment (D4) or 72 hours post-treatment (D6). Data is expressed as mean ± SEM.
* indicates significance

Results (Cont.)

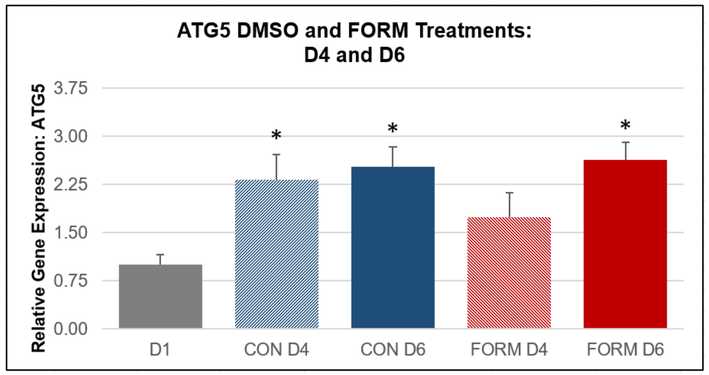

Figure 2. ATG5 gene expression relative to day 1 differentiation (D1) following control (CON) or Formoterol (FORM) treatment at 24 hours post-treatment (D4) or 72 hours post-treatment (D6). Data is expressed as mean ± SEM.
* indicates significance

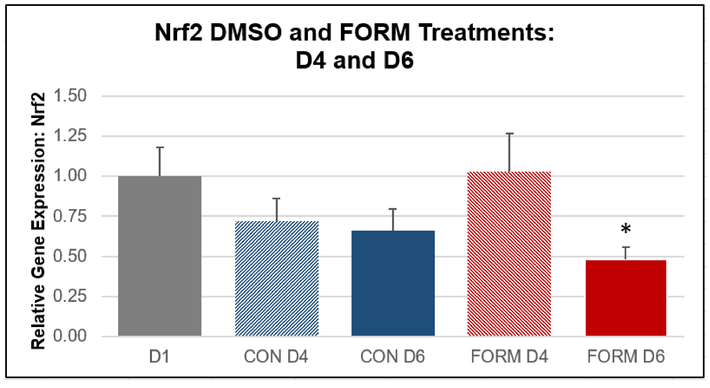

Figure 3. Nrf2 gene expression relative to day 1 differentiation (D1) following control (CON) or Formoterol (FORM) treatment at 24 hours post-treatment (D4) or 72 hours post-treatment (D6). Data is expressed as mean ± SEM.
* indicates significance

Conclusion

- These results indicate that Formoterol treatment prevented the D4 decrease in expression of TFAM and ERRα, indicating a preservation of mitochondrial biogenesis and beta oxidation potential during mid-myogenesis.
- Additionally, Formoterol treatment prevented the D4 increase in expression of ATG5, suggesting a reduction in the signaling of autophagy.