TACSM Abstract

Mitochondrial Biogenesis is Dysregulated in Thyroid Hormone Depleted Muscle Cells Despite Stimulatory Effects of Formoterol

EMILY L. ZUMBRO[1], GENA D. GUERIN[2], RYAN A. GORDON[1], CHASE M. WHITE[1], DREANNA M. MCADAMS[1], MATTHEW L. SOKOLOSKI[1], DAVID L. NICHOLS[1], and ANTHONY A. DUPLANTY[1]

[1]Exercise Physiology Laboratory; Department of Kinesiology; Texas Woman's University; Denton, TX
[2]Human Performance Laboratory; Department of Kinesiology; Texas Wesleyan University; Fort Worth, TX

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Advisor / Mentor: Duplanty, Anthony (ADuplanty@twu.edu)

ABSTRACT

Skeletal muscle (SKM) is an important regulator of metabolism and adaptations from exercise training influences mitochondrial function. Thyroid hormone (TH) is a regulator of SKM processes, including mitochondrial biogenesis. **PURPOSE**: To use an in vitro model of hypothyroidism to test the hypothesis that SKM cells will have dysregulated mitochondrial homeostasis. Additionally, the exercise mimetic, formoterol, was used to determine the effects of exercise signaling on mitochondrial biogenesis. **METHODS**: Human SKM myoblasts (n = 6 per group) were cultured and differentiated until mature myotube formation (Day 6). Groups included control cells (CON), TH depleted cells (ThD), and TH depleted cells plus formoterol stimulation (ThD+F; 30nM for 3h). Total RNA was extracted during mid-myogenesis (Day 4) and at terminal differentiation (Day 6). Gene expression for Peroxisome Proliferator-Activated Receptor Gamma Coactivator-1 Alpha (PGC-1α), Mitochondrial Transcription Factor A (TFAM), and Nuclear Respiratory Factor 1 (NRF1) was determined by qPCR. Data was analyzed by repeated measures ANOVA. **RESULTS**: PGC-1α: D4 ThD was decreased compared to D4 ThD+F (-4.6); D4 ThD+F was increased compared to D4 CON (4.6); D6 CON was decreased compared to D6 ThD+F (-2.9); D6 ThD was decreased compared to D6 ThD+F (-3.7). TFAM: D4 ThD+F was greater than D4 CON (3.6); D4 ThD+F was greater than D6 ThD+F (3.6); D6 ThD was decreased compared to D6 CON (-0.55); D6 ThD+F was decreased compared to D6 CON (-0.63). NRF1: D4 ThD was decreased compared to D4 CON (-0.31); D4 ThD was greater than D4 ThD+F (0.36); D4 ThD was greater than D6 ThD (0.17); D4 ThD+F was decreased compared to D4 CON (-0.67); D6 CON was decreased compared to D4 CON (-0.18); D6 ThD was decreased compared to D6 CON (-0.3); D6 ThD+F was decreased compared to D6 CON (-0.42). All reported differences are significant ($p < 0.05$). Data are expressed as fold changes. **CONCLUSION**: ThD media resulted in reduced NRF1 signaling in both D4 and D6 with a subsequent decrease in D6 only for TFAM. Formoterol resulted in the expected stimulation of PGC-1α at both D4 and D6, but subsequent signaling for genes associated with mitochondrial biogenesis common to PGC-1α stimulation were lost as a result of TH depletion at D6 only for TFAM and both D4 and D6 for NRF1.