Formoterol Stimulation In Vitro Influences Myogenic Regulatory Factors During Myogenesis in Human Skeletal Muscle Cells

CHASE M. WHITE[1], GENA D. GUERIN[2], EMILY L. ZUMBRO[1], RYAN A. GORDON[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

The process of myogenesis within skeletal muscle (SKM) is essential for growth and repair and is coordinated via the expression of myogenic regulatory genes. Previous animal studies have reported that formoterol, a beta-adrenergic receptor agonist, has stimulating effects on genes related to SKM mitochondrial function and biogenesis, similar to effects found for exercise. Lesser known is the potential "exercise mimetic" influence that formoterol stimulation may have during the stages of myogenesis, especially in human SKM cells. **PURPOSE**: To investigate the effects of formoterol stimulation on expression of myogenic regulatory genes during myogenesis in human SKM cells. **METHODS**: Human SKM myoblasts (n = 6 per group) were cultured and differentiated until mature myotube formation (Day 6). Groups included control cells (CON) and cells stimulated by 30nM formoterol for 3h prior to RNA extraction points (FORM). Total RNA was extracted during mid-myogenesis (Day 4) and at terminal differentiation (Day 6) (a cell culture model of investigating myogenesis). Gene expression for Myogenic factor 5 (Myf5), Myogenic differentiation 1(MyoD), and Myogenin (MyoG) was determined by qPCR. Data was analyzed using repeated measures ANOVA. **RESULTS**: Myf5: There was no change for either condition for D4. D6 CON was lower than D4 CON (-0.25). D6 FORM was greater than D4 FORM (0.65) and D6 CON (0.75). MyoD: D4 FORM was lower than D4 CON (-0.57). D6 FORM was greater than D4 FORM (0.85) and lower than D6 CON (-0.16). D6 CON was lower than D4 CON (-0.33). MyoG: D4 FORM was lower than D4 CON (-0.72). D6 CON was lower than D4 CON (-0.44). D6 FORM was lower than D6 CON (-0.24). All reported differences are significant ($p < 0.05$). Data are expressed as fold changes. **CONCLUSION**: As expected, for the CON group, Myf5, MyoD, and MyoG expression all decreased from D4 mid-myogenesis to D6 terminal myogenesis, indicating finalization of the myogenic gene program. For the FORM group, Myf5 expression was elevated at D6 compared to CON while MyoG and MyoD expression was lower than CON for D4 and D6. The interpretation is that FORM stimulation increased stimulus of D4 myoblast proliferation and, thus, delayed initiation of differentiation. These results, coupled with other preliminary data from our lab showing increased mitochondrial biogenesis with this model of investigation, suggests that this exercise mimetic stimulation may cause shift in the cell towards bioenergetic preference rather than fusion of myotubes.