

Myogenic Regulatory Factor Expression is Downregulated Following Formoterol Stimulation in Thyroid Hormone Depleted Skeletal Muscle

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ABSTRACT

In skeletal muscle (SKM), gene expression of transcription factors regulating myogenesis are dependent on Thyroid Hormone (TH) signal transduction. Expression of myogenic regulatory factors may be altered due to dysregulated TH metabolism, which may result in SKM dysfunction and intolerance to exercise in individuals with hypothyroidism. **PURPOSE:** Implement an in vitro model of hypothyroidism in SKM and determine the response of myogenic regulatory factor expression during several stages of myogenesis following TH depletion. Formoterol, an exercise mimetic, was also used to examine the effects of exercise signaling on myogenesis in TH depleted cells. **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 myogenic regulatory factors (Myf5, MyoD, MyoG) was determined by qPCR.

RESULTS: ThD decreased Myf5 at both Day 4 and Day 6 compared to control ($P < 0.001$). Myf5 was increased following ThD + F compared to ThD at Day 4 ($P < 0.05$). MyoD decreased following ThD at both Day 4 and Day 6 ($P < 0.001$). Further, MyoD was decreased following ThD + F at both Day 4 and Day 6 compared to ThD ($P < 0.001$). ThD had no effect on MyoG at Day 4 and Day 6; however, MyoG was decreased following ThD + F compared to ThD and control at both time points ($P < 0.001$). Data are expressed as mean \pm SEM. **CONCLUSION:** TH depletion had no effect on MyoG but did reduce the expression of both Myf5 and MyoD at both Day 4 and Day 6. Additionally, ThD+F resulted in the lowest expression of MyoG and MyoD for both time points. These results indicate TH depletion and formoterol stimulation may inhibit myotube maturation.