*TACSM Abstract*

# An In Vitro Investigation Of The Effects Of Formoterol On Thyroid Hormone-Related Gene Expression During Myogenesis

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ABSTRACT

Thyroid hormone (TH) is a primary driver of skeletal muscle (SKM) metabolism as well as myogenesis through stimulation its genetic targets. The conversion and activation of thyroid hormone (T4 to T3) is controlled by local deiodinase 2 and 3 (DIO2, DIO3) activity. This leads to expression of nuclear receptors in promotor regions of specific genes including sarco/endoplasmic reticulum calcium ATPase 1(SERCA1), which is important for homeostasis of calcium regulation during muscle contraction. **PURPOSE**: The purpose of the study was to examine the effects of the exercise mimetic Formoterol (FORM), a beta-adrenergic receptor agonist, on the expression of thyroid hormone-related genes during myogenesis In Vitro. **METHODS**: Commercially obtained, primary, human SKM myoblasts (n = 4) were cultured and differentiated for one day before initiation of daily treatment of 30 nM FORM or vehicle, dimethyl sulfoxide (DMSO) which continued until day 6 of differentiation. Total RNA was extracted on one day (D1), four days (D4), and six days (D6) post differentiation. Gene expression for DIO2, DIO3, SERCA1, SERCA2, thyroid hormone receptor α (THRα), and thyroid hormone receptor β (THRβ) was analyzed by qPCR. **RESULTS**: Expression of DIO2 decreased from D1 to D4 for both DMSO ($P<0.001$) and FORM ($P<0.05$). Similarly, DIO2 decreased from D1 to D6 for both DMSO ($P<0.001$) and FORM ($P<0.001$) treatment. DIO3 expression decreased from D1 to D6 for both DMSO and FORM ($P<0.05$) treatments. THRα expression decreased from D1 to D4 for both DMSO ($P<0.05$) and FORM ($P<0.001$). THRβ expression decreased from D1 to D6 for both DMSO and FORM ($P<0.05$). SERCA1 expression only decreased for DMSO between D1 and D6 ($P<0.05$). No differences were found for SERCA2. **CONCLUSION**: Conversion of TH by DIO2 and DIO3 is an important mechanism regulating proliferation and differentiation during myogenesis. During cell culture, cells do not receive signals for activity as found In Vivo, thus mimicking sedentary behavior and resulting in decreased thyroid hormone related gene expression. In our study, FORM appeared to prevent the decrease found for SERCA1 expression in the DMSO treatment, indicating that "exercise" stimulation can increase or maintain calcium pump activity as compared to "sedentary" muscle conditions. It is possible that exercise stimulates the expression of genes related to TH signaling and metabolism during myogenesis. Future studies with Formoterol treatment will explore additional treatment timelines and genetic targets for analysis.