Final Technical Report—NASA NAG2-942

Title: Neural-Thyroid Interaction on Skeletal Isomyosin Expression in Zero Gravity

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Project Goals:

The primary goal of the project was to develop a ground based model to first study the role of the nerve and of thyroid hormone (T3) in the regulation of body growth and skeletal muscle growth and differentiation in rodents. A primary objective was to test the hypothesis that normal weight bearing activity is essential for the development of antigravity, slow twitch skeletal muscle and the corresponding slow myosin heavy chain (MHC) gene; whereas, T3 was obligatory for general body and muscle growth and the establishment of fast MHC phenotype in typically fast locomoter muscles. These ground based experiments would provide both the efficacy and background for a spaceflight experiment (referred to as the Neurolab Mission) jointly sponsored by the NIH and NASA. Note that this project was jointly funded by NIH (NS 33483) and NASA NAG2-942.

Summary Key Findings:

Collectively the results of these studies provided the following insights.

1) Both and intact nerve and thyroid hormone is essential for the normal growth and differentiation of skeletal muscle into its fast- and slow-contractile phenotype.

2) T3 is essential for maintaining a normal growth-hormone/ insulin Like Factor-1 (IGF-1) axis to insure normal somatic growth. Further T3 is obligatory for the transition in MHC phenotype form the neonatal state to the adult state via the regulation chiefly on the neonatal and adult fast type IIb MHC genes.

3) Normal weight bearing activity is essential during the first three weeks of development for both the growth of antigravity skeletal muscles such as the sole3us and vastus intermedius, and its normal expression of the slow MHC gene.

4) The importance of weight bearing activity in the normal growth of skeletal muscle appear to be mediated via the local of expression of IGF-1, which acts in an autocrine-paracrine fashion to stimulate proliferation, differentiation, and anabolic processes in the muscle.

5) Weight bearing activity is not obligatory for the expression of the fast MHC isoforms, but T3 appears to be necessary for the normal induction of the fast type IIb MHC gene in a developing animal.

Publications.

1) Adams, G., F., S. A. McCue, M. Zeng, and **K. M. Baldwin**. Time course of myosin heavy chain transitions in neonatal rats: importance of innervation and thyroid state. Am. J. Physiol. 276: R954-R961, 1999.

2) Adams, G. R., S. A. McCue, P. W. Bodell, M. Zeng, and **K. M. Baldwin**. The effects of spaceflight on rat hindlimb development I: muscle mass and IGF-1 expression. J. Appl. Physiol. 88: 894-903, 2000.

3) Adams, G. F. Haddad, S. A. McCue, P. W. Bodell, M. Zeng, L Qin, A. X. Qin, and **K. M. Baldwin.** The effects of spacflight on rat hindlimb development II: expression of myosin heavy chain isoforms. J. Appl. Physiol. 88:904-916, 2000.

4) Adams, G. R., F. Haddad, and **K. M. Baldwin**. Interaction of spaceflight and thyroid state on somatic and skeletal muscle growth and myosin heavy chain expression in neonatal rats. J. Gravitational Physiology (In Press)

5) Adams, G. R., F. Haddad, and **K. M. Baldwin**. The interaction of space flight and thyroid state on somatic and skeletal muscle growth and myosin heavy chain expression in neonatal rats. (In press: text book on NASA Neurolab Spaceflight Mission).