Biochemical adaptation/responses to inactivity.

Booth FW and Roberts MD. Department of Biomedical Sciences. University of Missouri, USA

The wheel-lock (WL) model for depressed ambulatory activity in rats exhibit metabolic maladies within 53-173 hours after WL begins. We sought to identify very early changes in gene expression during WL for the purpose to discover intrinsic skeletal muscle mechanisms sensing the decline in contractile activity. WL began after 21-23 days of voluntary running in growing female Wistar rats. No changes in mRNA occupancy on skeletal muscle polyribosomes were observed at WL29h and only eight mRNAs from 27,342 tested mRNA sequences were altered on Affymetrix Rat Gene 1.0 ST Arrays at WL53h in the polyribosomal fraction compared to WL5h. Two of the eight changed mRNAs were Ankrd2 and Csrp3 mRNAs in the polyribosomal fraction (genes putatively encoding mechanical stretch sensors). The changes were verified with RT-PCR. Relative to WL5h controls, Ankrd2 and Csrp3 mRNA in the whole-tissue fraction was downregulated at WL53h and WL173h. Relative to WL5h animals, Ankrd2 protein expression was significantly decreased in WL23d rats, and Csrp3 protein decreased in WL173h and WL23d rats. Thus, early declines in Ankrd2 and Csrp3 mRNAs, genes with putative mechanical stretch-sensing functions, were found after ending voluntary running, which were subsequently followed by declines in their protein levels. Current studies are pursuing causes of the Ankrd2 and Csrp3 mRNA changes with the intent of identifying mechanosensing pathways in skeletal muscle that become dysregulated with physical inactivity.