

³¹P MAGNETIC RESONANCE SPECTROSCOPY OF CALPAIN 3 KNOCKOUT MOUSE SKELETAL MUSCLE

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Introduction

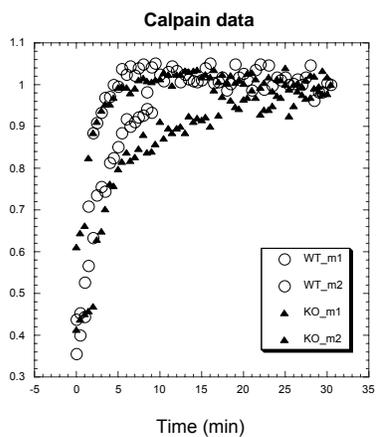
Calpain 3 is a non-lysosomal cysteine protease which is known to be a cause of limb-girdle muscular dystrophy type 2A (LGMD2A). Calpain 3 has been shown to have a role in sarcomere formation and remodeling. During sarcomere remodeling, the rate of atrophy and growth are significantly lower in muscles deficient in Calpain 3 (C3KO). The purpose of this study is to determine the difference in the *in-vivo* oxidative capacity of calpain 3 knockout mice hindlimb muscles using ³¹P MRS compared to wild-type.

Methods

³¹P MR data were acquired in a Bruker 11T spectrometer using a 6-mm x 12-mm oblong ³¹P surface coil, placed over the belly of the gastrocnemius muscles. A 3-cm ¹H surface coil was placed underneath the hindlimb to adjust magnetic field homogeneity. An inflatable blood pressure cuff was positioned around the animal's thigh in order to induce ischemia in the gastrocnemius following a baseline measurement. Spectra were collected with a 50 μ s square pulse, a TR of 2 seconds, sweep width of 10,000 Hz and 8,000 complex data points in 60 point bins starting at rest (10 min), during ischemia (30 min), and throughout recovery (30 min). Areas of the resting γ -ATP, Pi, and PCr peaks were determined using area integration following saturation correction. Dynamic changes in PCr levels were determined using complex principal component analysis. The pseudo-first-order rate constant for PCr recovery (kPCr) was determined and used to calculate the *in vivo* oxidative capacity.

Results and Discussion

During 30 minutes of ischemia, the PCr levels decreased by 45 to 55% while Pi levels increased approximately five-fold over baseline. The rate of recovery following ischemia appears to be higher for the wild-type animals compared to the knockout indicating a decrease in the *in vivo* oxidative capacity of skeletal muscle.



	WT (wild type) n = 2	KO (knockout) n = 2
1	0.6	0.36
2	0.50	0.52

Acknowledgements

This research was supported by NIH-RO1HD37645, NIH-RO1HD40850. NMR data were obtained at the Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS) facility in the Evelyn F. and William L. McKnight Brain Institute of the University of Florida.