Adaptation of Muscle Size and Force by Mechanical Stimuli

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Background
In vivo, mechanical loading of muscle by immobilization at extended length causes hypertrophy and an increase in the number of sarcomeres in series [1]. Mechanical loading may affect muscle protein turnover directly or indirectly by stimulating the expression of insulin-like growth factor 1 (IGF-1) [2], which is an autocrine anabolic factor in muscle. However, the mechanical stimulus for adaptation and induction of IGF-1 expression is not well known. Skeletal muscle finite element models have shown that strain distributions are likely to occur in vivo due to epimuscular myofascial force transmission [3]. The aim of this study was to investigate effects of high muscle fiber strain per se on hypertrophy, adaptation of the number of sarcomeres in series and IGF-1 expression and to compare sarcomere strain distributions in isolated muscle fibers in vitro with those in vivo.

Methods
To test the effects of high muscle fiber strain, single muscle fibers (with basal lamina and endomysium) were dissected from m. iliofibularis of Xenopus laevis and attached to a force transducer in a culture chamber (20 ºC). Isolated fibers were cultured in a serum-free medium either at passive slack length (mean sarcomere length 2.3 µm) or at extended lengths (12% over slack “high strain”) for 10 to 24 days. Before and after culture, fiber cross-sectional area (CSA) and the number of sarcomeres remained constant. IGF-1 mRNA expression in the muscle fibers was determined using in situ hybridization. Serial sarcomere strain distributions within the isolated muscle fibers were analyzed using laser diffraction. Sarcomere strain distributions within a muscle in its natural context of connective tissue were investigated using a 3D Finite element model of a rat EDL with epimuscular connections to surrounding tissues [3].

Results
During culture, tetanic force of fibers cultured at passive slack length (n=5) remained unchanged. For fibers cultured at high strain, tetanic force decreased by 1.4±0.2% (mean±SEM, n=5) per day. For both conditions, CSA and number of sarcomeres remained constant. IGF-1 mRNA expression levels in fibers cultured at high strain did not differ from those cultured at slack length. These results are in contrast to the effects of immobilization of muscle in vivo at an extended length. The coefficient of variation of sarcomere lengths within extended isolated muscle fibers was <5%. At extended muscle lengths, the finite element model predicts a higher coefficient of variation of sarcomere lengths within the muscle fibers.

Conclusions
We conclude that the lack of adaptation in isolated muscle fibers is accompanied by a smaller variation of sarcomere length along the cultured muscle fiber. The possibility exists that in vivo adaptation of muscle fiber size is regulated by local mechanical stimuli that vary along the muscle fiber length.

References