

ORIGINAL ARTICLE

Ji Won Kim · Oh Yun Kwon · Myoung Hee Kim

Differentially expressed genes and morphological changes during lengthened immobilization in rat soleus muscle

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Abstract To examine the effect of lengthened immobilization on the expression of genes and concomitant morphological changes in soleus muscle, rat hindlimbs were immobilized at the ankle in full dorsiflexion by plaster cast. After removing the muscle (after 1 hr, 1, 4, and 7 days of immobilization), morphology and differential gene expression were analyzed through electron microscopy and differential display reverse transcription-polymerase chain reaction (DDRT-PCR), respectively. At the myotendinous junction (MTJ), a large cytoplasmic space appeared after 1 hr of immobilization and became enlarged over time, together with damaged Z lines. Interfibrillar space was detected after 1 day of immobilization, but diminished after 7 days. At the muscle belly, Z-line streaming and widening were observed following 1 hr of immobilization. Disorganization of myofilaments (misalignment of adjacent sarcomeres, distortion, or absence of Z lines) was

detected after 4 days. Furthermore, mitochondrial swelling and cristae disruption were observed after 1 day of stretching. A set of 15 differentially expressed candidate genes was identified through DDRT-PCR. Of 11 known genes, seven (*Atp5g3*, *TOM22*, *INrf2*, *Slc25a4*, *Hdac6*, *Tpm1*, and *Sv2b*) were up and three (*Podxl*, *Myh1*, and *Surf1*) were down-regulated following immobilization. In the case of *Acyp2*, 1-day stretching-specific expression was observed. *Atp5g3*, *Slc25a4*, *TOM22*, and *Surf1* are mitochondrial proteins related to energy metabolism, except *TOM22*, which has a chaperone-like activity located in the mitochondrial outer membrane. Together with these, *INrf2*, *Hdac6*, *Podxl*, and *Acyp2* are related more or less to stress-induced apoptosis, indicating the responses to apoptotic changes in mitochondria caused by stretching. The expression of both *Tpm1* and *Myh1*, fast twitch isoforms, suggests adaption to the immobilization. These results altogether indicate that lengthened immobilization regulates the expression of several stress/apoptosis-related and muscle-specific genes responsible for the slow-to-fast transition in soleus muscle despite profound muscle atrophy.

Key words skeletal muscle · lengthened immobilization · differentially expressed genes · morphological changes

Ji Won Kim
Department of Physical Therapy
College of Health Science
Baekseok University
Cheonan, Korea

Oh Yun Kwon
Department of Physical Therapy
College of Health Science
Yonsei University
Wonju, Korea

Myoung Hee Kim (✉)¹
Department of Anatomy, Embryology Lab., Brain Korea 21
Project for Medical Science, Yonsei University College of
Medicine, Seoul 120-752, Korea
Tel: +82 2 2228 1647
Fax: 82 2 365 0700
E-mail: mhkim1@yumc.yonsei.ac.kr

¹Present address: Department of Anatomy, Embryology Lab,
Yonsei University College of Medicine, 134 Schinchondong,
Sodaemoongu, Seoul, Korea.

Introduction

Muscle stretch is a general therapeutic maneuver used to increase range of motion (ROM) by elongating structures that have adaptively shortened and become hypomobile for a long time. Several studies have examined the effects of muscle stretch in a lengthened position (Tabary et al., 1972; Williams and Goldspink, 1973; Dix and Eisenberg, 1990; Williams, 1990), and suggested that the stretched muscle fibers increase the number of sarcomeres to maintain a normal passive