骨格筋の損傷・再生に反応して筋核は移動するか？

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Do Myonuclei Translocate in Response to Damage and Regeneration of Skeletal Muscle Fibers?

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Dystrophin-deficient (*mdx*) mouse is a well known animal model for Duchenne muscular dystrophy. The muscles of *mdx* mice are characterized by cycles of muscle fiber necrosis followed by regeneration[2]. Further, the regenerating fibers can be easily identified, because they contain conspicuous internal (central) myonuclei[1]. Williams et al.[3] reported that fibers with either a predominantly centrally located string of myonuclei, or a combination of central nuclei and peripheral pattern of nuclei appeared in soleus muscle fibers of *mdx* mice. However, it is unclear how the change of localization of myonuclei within a fiber is induced. It is not known whether the total number of myonuclei in a whole single muscle fiber response to necrosis/regeneration cycle, either. Therefore, the current study was performed to test the hypotheses that myonuclei translocate cross-sectionally from central to peripheral region, or that central myonuclei are lost due to apoptosis and new myonuclei are accreted at the peripheral region when the regeneration of fiber is advanced. The total number and location of myonuclei in single soleus muscle fibers, sampled from tendon-to-tendon, were measured in *mdx* and wild type (WT) mice. Apoptotic myonuclei were checked by using the terminal deoxynucleotidyl transferase dUTP-mediated nick-end labeling method. Further, the existence of any evidence, which may help the translocation of myonuclei, was also investigated by analyses using electron microscopy.

Three types of muscle fibers of *mdx* mice with myonuclear distribution at either central, peripheral, or both central and peripheral region were observed. All of the myonuclei were located at the peripheral region in WT mice. The total number of myonuclei in whole fiber was identical between *mdx* and WT mice and between fibers with different distribution of myonuclei in *mdx* mice and peripheral nucleus was noted where the central nucleus was missing. Fiber size, sarcomere number, myonuclear size, myosin heavy chain expression, satellite cell number, and neuromuscular junction were identical between each type of fiber. Apoptosis was not detected in any myonuclei located either central or peripheral region of fibers. Thus, it was suggested that apoptosis-related loss of central myonuclei and regeneration-related new accretion at the peripheral region is not the cause of the different distribution of myonuclei seen in muscle fibers in *mdx* mice. But it was speculated that cross-sectional translocation of myonuclei may be induced in response to regeneration from central to peripheral region, although microscopic evidence of any structures were not observed around myonuclei.

This study was supported by the Grantin-Aid for Scientific Research S (19100009, Y.O.) from Japan Society for the Promotion of Science and the Grantin-Aid for the Academic Frontier Project (Waseda University: 2005-2010) of the Ministry of Education, Culture, Sports, Science and Technology (K.I.).

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