Hindlimb unloading-induced muscle atrophy and phenotype transition is attenuated in Smad3+/- mice

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Currently, it has been well defined that the microgravity-induced muscle disuse characterized by atrophy and slow-to-fast phenotype transition of the postural muscles, such as soleus muscle, but the basic mechanism underlying the atrophy and phenotype transition of soleus muscle is still unclear. To investigate the developmental mechanisms of muscle atrophy and its phenotype transition under microgravity, the soleus muscle of Smad3+/+ and Smad3+/- mice after 14 days hindlimb unloading was examined. Using histology and immunohistochemistry assay we found that the soleus muscle volume and fiber number appeared a remarkable increases in Smad3+/- mice compared to those in Smad3+/+ control. In addition, Western blot analysis showed that the expression level of myosin heavy chain (MHC)-slow myofiber specific protein in soleus muscle was visibly higher in Smad3+/- mice than in Smad3+/+ mice. In contrast, the expression level of MHC-fast myofiber specific protein in soleus muscle was visibly lower in Smad3+/- mice than in Smad3+/+ mice. Furthermore, RT-PCR revealed that the expression of Smad3 and myogenic regulatory factor (MRF) mRNA was inversely regulated. Finally, we determined that either Smad3 mRNA or Smad3 protein were selectively distributed in quiescent satellite cells in vivo and in reserve cells in vitro. Therefore, our findings suggested that Smad3 might be a key transcriptional factor for soleus muscle atrophy and slow-to-fast phenotype transition of the slow muscle under microgravity. In the future, an agent that regulates Smad3 expression may be used to prevent muscle atrophy during spaceflight.