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Author: Mr. Jian He
State Key Laboratory of Space Medicine Fundamentals and Application, China Astronaut Research and Training Center, China, hejian41@163.com

Dr. Fei Wang
National Key Laboratory of Human Factors Engineering, China Astronaut Research and Training Center, China, wangfei19861226@163.com
Mrs. Hongju Liu
State Key Laboratory of Space Medicine Fundamentals and Application, China Astronaut Research and Training Center, China, 13691535755@163.com
Mr. Wenjiong Li
State Key Laboratory of Space Medicine Fundamentals and Application, China Astronaut Research and Training Center, China, muzijiong2007@163.com
Prof. Xiaoping Chen
National Key Laboratory of Human Factors Engineering, China Astronaut Research and Training Center&State Key Laboratory of Space Medicine Fundamentals and Application, China Astronaut Research and Training Center, China, xpchen2009@163.com

MIR-491 INHIBITS SKELETAL MUSCLE DIFFERENTIATION THROUGH TARGETING MYOMAKER

Abstract

So far, the mechanisms of weightlessness-induced muscle atrophy remain unclear, which will hinder the development of effective protective measures for skeletal muscle atrophy in space. It has been well known that the potential of myogenesis plays an important role in skeletal muscle atrophy. The myogenesis of skeletal muscle has several stages, including satellite cell proliferation, determination, differentiation, fusion and specific muscle formation. MicroRNAs are involved in these stages via regulating the myogenic regulation factors. Recent studies discovered a muscle-specific transmembrane protein, myomaker, is critical for myoblasts fusion. However, the regulatory mechanism of its expression and effects on myogenesis remain elusive. Here, we have performed TargetScan to predict the functional microRNAs which target to myomaker, and then the expression pattern of functional microRNAs and myomaker were explored. Furthermore, we regulated the microRNAs expression to investigate the effects on myogenesis and luciferase reporter assay was constructed to verify its mechanism.

In our present study, we demonstrated that the expression of myomaker was affected by miR-491 during myogenesis both in vivo and in vitro. miR-491 expression gradually increased during the myoblasts differentiation and muscle regeneration, while myomaker displayed an inverse tendency; Down-regulation of miR-491 contributes to increasing myomaker expression, which leads to enhanced fusion capability; Overexpressed miR-491 suppressed myomaker translation and myoblasts fusion. Moreover, the luciferase activity was inhibited by the seed matched region of miR-491 through binding to myomaker 3'-UTR. Taken together, we have confirmed the important role of miR-491 during myogenesis in skeletal muscle and myomaker as an essential mediator, which revealed a novel mechanism of muscle cell fusion. Therefore, miR-491 may be as a useful intervention target for the muscle atrophy protection in space.

key words: miR-491, myomaker, myogenesis