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MiR-103 Inhibits Osteoblast Proliferation Mainly through Suppressing Cav 1.2 Expression in Simulated Microgravity

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Abstract : Emerging evidence indicates that microRNAs (miRNAs) play important roles in modulating osteoblast function and bone formation. However, the influence of miRNA on osteoblast proliferation and the possible mechanisms underlying remain to be defined. In this study, we aimed to investigate whether miR-103 regulates osteoblast proliferation under simulated microgravity condition through regulating Cav1.2, the primary subunit of L-type voltage sensitive calcium channels (LTCCs). We first investigated the effect of simulated microgravity on osteoblast proliferation and the outcomes clearly demonstrated that the mechanical unloading inhibits MC3T3-E1 osteoblast-like cells proliferation. Using quantitative Real-Time PCR (qRT-PCR), we provided data showing that miR-103 was up-regulated in response to simulated microgravity. In addition, we observed that up-regulation of miR-103 inhibited and down-regulation of miR-103 promoted osteoblast proliferation under simulated microgravity condition. Furthermore, knocking-down or over-expressing miR-103, respectively, up- or down-regulated the level of Cav1.2 expression and LTCCs currents, suggesting that miR-103 acts as an endogenous attenuator of Cav1.2 in osteoblasts under the condition of simulated microgravity. More importantly, we showed that the effect of miR-103 on osteoblast proliferation was diminished in simulated microgravity, when co-transfecting miR-103 mimic or inhibitor with Cav1.2 siRNA. Taken together, our data suggest that miR-103 inhibits osteoblast proliferation mainly through suppression of Cav1.2 expression under simulated microgravity condition. This work may provide a novel mechanism of microgravity-induced detrimental effects on osteoblast, identifying miR-103 as a novel possible therapeutic target in bone remodeling disorders in this mechanical unloading.

Keywords : microRNA, osteoblasts, cell proliferation, Cav1.2, simulated microgravity
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