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PIEZO1 CHANNEL ACT AS A SPACE ENVIRONMENT MECHANOTRANSDUCER IN BONE METABOLISM

Abstract

The investigation of the osteoblasts' sense and response in space environment aids in the understanding of the molecular mechanism of bone loss. Piezo1, a mechanosensitive ion channel, is sensing mechanical forces and causing changes in cellular biological effects. It's noteworthy that Piezo1 deficiency in osteoblastic cells leads to bone loss, and recent studies have demonstrated that Piezo1 can affect osteoblast-osteoclast crosstalk in response to mechanical forces. Accordingly, we speculated that Piezo1 is involved in space-induced osteogenesis inhibition, especially as an initial sensors of space environmental factors. Here we used primary osteoblast to investigate the effects of the simulated space environment in bone metabolism, and elucidated the function of Piezo1 channel in primary osteoblasts. After simulated microgravity and ionizing radiation, alone or combination, the differentiation, maturation, and mineralization of osteoblasts was reduced, while the cell membrane expression of Piezo1 protein was also significantly decreased compared with control. The decreased Piezo1 expression after simulated microgravity and combined with ionizing radiation was accompanied with decreased calcium influx. To further elucidate whether microgravity and ionizing radiation induced the inhibition of osteogenesis is relied on the Piezo1 pathway activity modulation, we knocked down endogenous Piezo1 using Piezo1 siRNA, the mineralized nodule formation potentiality and the Runx2 protein expression were significantly decreased. These results suggest that Piezo1 participated in osteogenesis in osteoblasts, especially in simulated space environment induced osteogenesis inhibition. Intriguingly, addition of Yoda1, a Piezo1 agonist, rescued osteoblast differentiation and bone formation in simulated microgravity stimuli. Taken together, these data suggest that Piezo1 functions as a key mechanotransducer that sense and respond to space environmental signal to intracellular signaling during osteoblast differentiation. In this study, we have gained further insights that Piezo1 acts in osteoblasts as a regulator of bone metabolism via sensing space environments. More importantly, activation of Piezo1 may serve as a potential therapeutic target for bone loss exposed to the space environment. Key words: space bone loss; Piezo1; microgravity; ionizing radiation