SPACE LIFE SCIENCES SYMPOSIUM (A1)
Biology in Space (7)

Author: Prof.Dr. Yingxian Li
China Astronaut Research and Training Cednter, Cocos (Keeling) Islands, yingxianli@aliyun.com

Mr. Yuheng Li
China Astronaut Research and Training Center, China, heng109@126.com
Mr. Guohui Zhong
China, guohuiacc@163.com
Mr. Pengfei Zhang
China, Zhangpengfeili@sina.com
Mrs. Chenyang Zhao
China, zhaochnegyang1990@126.com
Mrs. Weijia Sun
China, sunweijia1026@163.com
Mrs. Zi Xu
China, number1xuzi@163.com

# THE CHANGES OF CD44 EXPRESSION AND ITS EFFECTS ON THE FUNCTION OF OSTEOCLAST UNDER SIMULATED MICROGRAVITY

**Abstract**

Microgravity induced bone loss is one of the key limit factors during human long term space flight. Under microgravity, the changes of extracellular matrix composition, adhesion molecules and cytoskeleton induced the alteration of intracellular signals, which are important to the migration, proliferation, differentiation and apoptosis of osteoblast, osteoclast and osteocyte. *CD44* acts as an cellular surface adhesion molecule, which plays an important role in the signal communication between cells and cells or cells and the surroundings. However, the regulation of *CD44* on bone formation, especially on osteoclast, remains unclear. The effect of *CD44* on bone loss under microgravity has not been reported.

In this study, by inducing Raw 264.7 macrophage into osteoclast with receptor activator of NF-$\kappa$B ligand (RANKL) and macrophage colony stimulating factor (M-CSF), we found that *CD44* mRNA levels significantly increased in this process, and the mRNA levels of osteoclast function-related genes, *CLC7*, *Cathepsin K*, *MMP9*, *Integrinbeta3*, were also obviously up-regulated. Interestingly, the up-regulation of the mRNA levels of *CD44* and osteoclast function-related genes were enhanced under the condition of clinostation simulated microgravity. Besides, tartrate-resistant acidic phosphatase (TRAP) positive cell number increased. However, this effect was significantly attenuated when *CD44* was knocked down with siRNA. During osteoclast differentiation, the levels of phosphorylated Src (Tyr416), Akt (Ser473) and mTOR (Ser2448) increased, and the levels of phosphorylated Akt (Ser473) and mTOR (Ser2448) also increased under clinostation condition, while their levels decreased when *CD44* was knocked down. Furthermore, bone marrow-derived monocyte (BMM) from *CD44* knockout mice showed a reduction in osteoclast differentiation.

These results demonstrated that *CD44* played an important role in the course of differentiation and function of osteoclast. Clinostation simulated microgravity could promote osteoclast differentiation through up-regulation of *CD44* expression, and Src/Akt/mTOR pathway was involved in the regulation of *CD44* on the function of osteoclast.