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Author: Prof. Qing Ge  
Peking University Health Science Center, China, geqingq717@163.com

THE INTESTINAL MICROBIOTA CONTRIBUTES TO COLONIC EPITHELIAL CHANGES IN  
SIMULATED MICROGRAVITY MOUSE MODEL

**Abstract**

Exposure to microgravity leads to alterations in multiple systems. But microgravity-related changes in the gastrointestinal tract and its clinical significance have not been well studied. We used hindlimb unloading (HU) mouse model to simulate the microgravity condition and investigated the changes of intestinal microbiota and epithelial cell homeostasis in this mouse model. Compared to ground controls, HU affected fecal microbiota composition with a profile characterized by the expansion of Firmicutes and decrease of Bacteroidetes. The colon epithelium of HU mice showed decreased goblet cells numbers, reduced epithelial cell turnover, and decreased expression of genes involved in defense responses. As a result, increased susceptibility to DSS-induced colitis was observed in HU mice. Co-housing of ground control mice with HU mice resulted in reduced colonic goblet cells in the former group of mice. This reduction of colonic goblet cells in HU mice could be alleviated by transplantation of feces from ground control mice to HU mice. These results indicate that simulated microgravity changes intestinal microbiota, leading to altered colonic epithelial cell homeostasis and increased susceptibility to colitis. The animal results emphasize the necessity for evaluating the astronauts' intestinal homeostasis and susceptibility to inflammatory diseases in distant space travels. It also urges the development of probiotic-based countermeasures to improve the intestinal health of astronauts.