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Author: Dr. Chongzhen WANG
Guilin Medical University, China, 022101043@fudan.edu.cn

AN EPIGENETIC MECHANISM FOR DECREASED MHC EXPRESSION IN MACROPHAGES UNDER SIMULATED MICROGRAVITY

Abstract

Purpose: To study the effects of microgravity upon the expression of CD80, CD86, and MHC on macrophage cells and the underlying mechanisms. Methodology: Primary mouse macrophages were cultured under normal gravity condition and simulated microgravity condition in a rotary cell culture system. The expression of CD80, CD86, and MHC under the two conditions were compared by flow cytometry. The relevant transcriptional factor(s) and histone acetylation were assayed by western blot. Trichostatin A, an inhibitor of histone deacetylases, was used to study the role of histone deacetylation in the regulation of MHC expression by microgravity. Results: The expression of I-Ab (an MHC class molecule), but not of CD80 or CD86, on non-stimulated murine macrophages was decreased by simulated microgravity. Furthermore, the induction of CD86 expression by LPS and the induction of I-Ab expression by IL-4 on macrophages were inhibited by simulated microgravity. Decreased expression of the master regulatory factor of MHC (the class transactivator) and decreased histone acetylation were found in macrophages under simulated microgravity. Increasing histone acetylation through inhibition of histone deacetylases was able to increase the expression of I-Ab in macrophages under simulated microgravity. Conclusions: Simulated microgravity may decrease the expression of MHC in macrophages. Histone deacetylation plays a role in the down-regulation of MHC expression in macrophages by simulated microgravity. This is the first study showing that histone deacetylation plays a role in the regulation of gene expression by microgravity.