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MICRORNA EXPRESSION PROFILE AND DNA DAMAGE RESPONSE IN CULTURED HUMAN FIBROBLASTS IN SPACE

Abstract

Microgravity, or an altered gravity environment from the static 1g, has been shown to influence global gene expression patterns and protein levels in living organisms. Our recent flight experiment on the International Space Station (ISS) was aimed at understanding of the roles microRNA (miRNA) in the adaptation of human cells to the microgravity environment, and whether cells respond differently to DNA damages in space. The small non-coding microRNA (miRNA) can have a broad effect on gene expression networks by mainly inhibiting the translation process. Previously, we investigated changes in the expression of miRNA and related genes under simulated microgravity conditions on the ground using the NASA invented bioreactor. In comparison to static 1 g, simulated microgravity altered a number of miRNAs in human lymphoblastoid cells. Pathway analysis with the altered miRNAs and RNA expressions revealed differential involvement of cell communication and catalytic activity, as well as immune response signaling and NGF activation of NF-kB pathways under simulated microgravity conditions. The network analysis also identified several projected networks with c-Rel, ETS1 and Ubiquitin C as key factors. In the flight experiment on ISS, we investigated the effects of actual spaceflight on miRNA expressions in non-dividing human fibroblast cells in mostly the G1 phase of the cell cycle. A fibroblast is a type of cell that synthesizes the extracellular matrix and collagen, the structural framework for tissues, and plays a critical role in wound healing and other functions. In addition to miRNA expressions, we also investigated the effects of spaceflight on the cellular response to DNA damages. In the experiment conducted on ISS, human fibroblast cells were treated with bleomycin which is known to induce DNA damage including double strand breaks. The cells were then fixed in space for later analysis of DNA damage markers, as well as changes of RNA/miRNA expression profiles in response to the damage. Results of this ISS experiment will provide insight into the adaptation of non-dividing cells to the microgravity environment and how such an adaptation will affect the repair of DNA damages in space from exposure to environmental stresses such as cosmic radiation.