

Determination of Roles of Microgravity and Ionizing Radiation on the Reactivation of Epstein-Barr Virus *in vitro*

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Astronauts experience symptomatic and asymptomatic herpesvirus reactivation during spaceflight. We have shown increases in reactivation of Epstein-Barr virus (EBV), cytomegalovirus (CMV) and varicella zoster virus (VZV) and shedding in body fluids (saliva and urine) in astronauts during space travel. Alterations in immunity, increased stress hormone levels, microgravity, increased radiation, and other conditions unique to spaceflight may promote reactivation of latent herpes viruses. Unique mechanico-physico forces associated with spaceflight can have profound effects on cellular function, especially immune cells. In space flight analog studies such as Antarctica, bed rest studies, and NASA's undersea habitat (Aquarius), reactivation of these viruses occurred, but to a lesser extent than spaceflight. Spaceflight analogs model some spaceflight factors, but none of the analogs recreates all factors experienced in space. Most notably, microgravity and radiation are not included in many analogs. Stress, processed through the HPA axis and SAM systems, induces viral reactivation. However, the respective roles of microgravity and increased space radiation levels or if any synergy exists are not known. Therefore, we studied the effect of modeled space radiation and/or microgravity, independent of the immune system on the changes in cellular gene expression that results in viral (EBV) reactivation.

The effects of modelled microgravity and low shear on EBV replication and cellular and EBV gene expression were studied in human B-lymphocyte cell cultures. Latently infected B-lymphocytes were propagated in the rotating wall bioreactor and irradiated with the various dosages of gamma irradiation. At specific time intervals following exposure to modelled microgravity, the cells and supernatant were harvested and reactivation of EBV were assessed by measuring EBV and gene expression, DNA methylation, and infectious virus production.

It was observed that viral reactivation decreased in microgravity and increased both after radiation and the combination of microgravity and radiation as compared to EBV infected cells that were not subjected to simulated microgravity conditions and or radiations.