

THE IMPACT OF LONG DURATION SPACEFLIGHT ON PLASMA ANTIMICROBIAL PROTEINSG. Spielmann¹, B. E. Crucian², S.K. Mehta², H. Kunz¹, D.L. Pierson² and R.J. Simpson¹¹Laboratory of Integrated Physiology, Department of Health and Human Performance, University of Houston, Houston, TX, 77204, ²NASA-Johnson Space Center, Houston, TX, USA**ABSTRACT**

Introduction: Robust immunity is essential for further human exploration of the solar system beyond Earth's orbit. Spaceflight has been associated with immune perturbations and latent viral reactivation. However, logistical constraints have restricted many of these studies to simple pre- and post-flight measures, which are greatly confounded by the stressors associated with launch, landing and re-adaptation to the 1G environment. More in-flight immune data are required particularly during long-duration (3-6 months) spaceflight missions. This study examined the effects of spaceflight on plasma antimicrobial proteins (AMPs) and reactivation of latent herpesviruses. **Methods:** Plasma, saliva and urine samples were obtained from 20 crewmembers who spent ~6-months on the International Space Station (ISS). Samples were collected 180 and 45-days before launch, in-flight (at 'early', 'mid' and 'late' stages of the mission), immediately upon return to Earth (R+0) and 30 days following return (R+30). Plasma LL-37, HNP 1-3 and lysozyme concentrations were determined by ELISA. Saliva Epstein-Barr virus (EBV), varicella zoster virus (VZV) and urine cytomegalovirus (CMV) DNA levels were quantified by Real-Time PCR. Maximum likelihood linear mixed models (LMM) were used to determine main effects of time (pre-flight, in-flight, R+0 and R+30), and EBV, VZV and CMV viral shedding status (shedding or non-shedding) on the concentration of each AMPs. **Results:** Plasma levels of HNP 1-3 were significantly increased during flight, when compared to pre-flight, R+0 and R+30 (+48%, +43% and +64% respectively; $p < 0.05$). Plasma LL-37 levels appeared elevated during flight (+19%, $p=0.100$), but no statistical differences were observed during the different time points. Plasma levels of lysozyme remained unchanged during and after flight. Astronauts who underwent EBV reactivations had reduced concentrations of HNP 1-3 ($p<0.05$) than the astronauts who did not reactive EBV, independently of spaceflight. On the contrary, Astronauts who had VZV reactivations had increased lysozyme concentrations (+30%, $p<0.05$) at all timepoints. Plasma levels of LL-37 were unaffected by viral shedding. **Conclusion:** Long-duration spaceflight alters plasma HNP 1-3 levels and appear to be linked to the reactivation of latent herpesviruses. The in-flight changes observed for HNP 1-3 indicate that certain immune perturbations may be independent of launch/landing stress. Future studies are required to determine if spaceflight induced immune dysregulation increases the risk of an adverse health event before exploration-class planetary missions (i.e. to Mars) can be considered.