Immune system dysregulation has been documented during and after spaceflight, but it is not known if these changes increase infection susceptibility or pose a significant health risk to crewmembers. Inherent problems with current in-flight research are small sample sizes and the difficulty to control for the many confounding factors that impact on the immune system. As such, it is not known if changes in immunity are due to the microgravity environment per se, or to the stressors associated with landing and re-adaptation to the 1G environment. The present project proposes a Flight Definition investigation, utilizing a longitudinal repeated measures design to determine the effects of long-term exposure to microgravity on hosts of salivary antimicrobial proteins (AMPs), latent viral reactivation, antibacterial properties of saliva, and blood markers associated with innate host immune defense, whilst also considering the impact of other acute stressors such as Soyuz landing. Saliva, urine and blood samples will be collected from crewmembers selected for ISS mission and ground-based controls pre-flight (L-180-L-60), At “early”, “mid” and “late” phases during the 6-month period on the ISS, and up to R+63 on return to Earth. Saliva sampling was selected as the primary source because it is an excellent biological fluid with which to detect broad-spectrum biomarkers of front-line host immune defense and is suitable for the spaceflight environment. Attempts will also be made to establish relationships between salivary and cellular immune markers, viral reactivation and other stressors associated with spaceflight (i.e. mood state disturbances, circadian desynchronization, sleep loss/disruption, stress biomarkers) using serial data. Blood samples will be used for monocyte, NK-cell and neutrophil phenotype and functional assays. 

### Objective

Objective#1. Longitudinally examine the impact of long-term spaceflight (up to 6 months on the ISS) on salivary and cellular markers of innate immune function and latent viral reactivation.

Objective#2. Determine the impact of acute stressors associated with spaceflight on salivary markers of mucosal and innate immune function.

Objective#3. Examine the relationship between changes in salivary and cellular markers of innate immune function and changes in other stressors associated with the spaceflight environment (i.e. circadian desynchronization, sleep loss/disruption, mood state disturbances, stress, infection incidence).

### Relevance

This project will help to establish if spaceflight alters innate immune function, which is important to determine if altered immunity poses a significant risk of an adverse health event among crewmembers. Moreover, these data will serve as a foundation for future countermeasure developments and technological advances to detect real time changes in immune function during subsequent lunar or Mars missions.

### BDC Summary

L-180 and L-60: Blood draw, Saliva sampling, 24 hour urine collection and Health Assessment

### In-flight Operations Summary

FD 10, FD 90 and R-1: Blood draw, Saliva sampling, 24 hour urine collection and Health Assessment

### Subject Selection/Participation Criteria