Influence of Microgravity on Bacterial Pathogen Virulence and Immune Cell Function—Relevance for Infectious Disease Risk During Spaceflight

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Spaceflight has measurable impacts on astronaut immune profiles as well as the virulence patterns of bacterial pathogens. Data with respect to human immunity indicate diminished T and NK cell function, altered cytokine profiles, persistent inflammation, and latent herpesvirus reactivation. Furthermore, evaluation of International Space Station (ISS) crewmembers gives evidence of compromised immunity, including atypical allergy, infectious disease, and dermatitis. Data with respect to certain human bacterial pathogens suggest modified virulence that may be enhanced. It is therefore critical to examine this interaction of immune dysregulation and increased microbial virulence and whether it might synergistically increase the risk of infectious disease to crew members.

The goal of this study is to use modeled microgravity to study the impact of medically significant ISS bacteria that may have altered virulence on the immune response of the host. This study consists of two primary aims to assess this relationship. First, immune cells will be collected from healthy test subjects and cultured in static or in modeled microgravity conditions together with either control pathogens or with microgravity conditioned pathogens that were grown in bioreactors. Second, immune cells will be collected from astronauts before, during, and after flight and co-cultured with the control or the microgravity conditioned bacteria. Three pathogens were selected for this investigation: *Pseudomonas aeruginosa, Salmonella enterica* serovar Enteritidis and *Burkholderia cepacia*. Previously, the optimal cell to bacteria ratios that produce the greatest immune cell responses have been derived for these three bacteria. Cellular activation, as determined by the induction of cell surface activation markers and cytokine profiles, will be measured. Interactions between cells and bacteria will be assessed using fluorescent and electron microscopy techniques. This study will provide critical information to help understand how microgravity alters microbial virulence and the associated infectious disease risk to crewmembers during spaceflight missions.

Over the past year, the Immunology and Microbiology laboratories at NASA Johnson Space Center have collaborated to process the astronaut subject samples to complete the last year of the flight portion of this study. This included the completion of four astronaut subjects full mission sampling sets. Sample processing included innate and adaptive cell flow cytometry as well as analysis of cytokine concentrations in the supernatant. The ground control segment of the study will take place during FY25 which involves parallel infections run under static and clinostat conditions. The acquired data sets over this 3-year study are now being analyzed to provide a comprehensive set of results and conclusions that will contribute to a more effective risk assessment for astronauts during spaceflight regarding this host-pathogen context.