SPACEFLIGHT-INDUCED CHANGES IN MICROBIAL VIRULENCE AND THE IMPACT TO THE HOST IMMUNE RESPONSE

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Many microbial pathogens have repeatedly exhibited unexpected responses relevant to infectious disease when grown in microgravity and microgravity analogue environments, including changes in final cell concentration, biofilm production, stress resistance, antibiotic sensitivity, gene expression, host-pathogen interactions, and virulence. Notably, the classic foodborne pathogen *Salmonella enterica* serovar Typhimurium displayed increased virulence in animals when cultured in either the spaceflight analogue or true spaceflight environment. Recently, *Serratia marcescens* also was shown to increase virulence when cultured in the spaceflight environment. In parallel, astronaut studies have characterized a persistent spaceflight-induced dysregulation of the human immune system at multiple levels, which suggests an increased risk of infectious diseases. Moreover, astronauts have some degree of clinical infectious disease incidence. However, the contribution of the microgravity environment on host-pathogen interactions and potential for clinical disease remains understudied and poorly characterized.

The goal of this study is to gain insight into the breadth of other medically significant microbial pathogens that may exhibit altered virulence and pathogenesis-related responses when cultured in spaceflight analogue conditions. Specifically, we are characterizing the effect of spaceflight analogue culture (Low Shear Modeled Microgravity/LSMMG) on microbial pathogenesis-related stress responses, *in vitro* host-pathogen interactions, gene expression, and virulence potential in animals using five important model bacterial pathogens, *Salmonella enterica* Enteritidis, *Pseudomonas aeruginosa*, *Burkholderia cepacia*, *Streptococcus pneumoniae*, and enterohemorrhagic *Escherichia coli*.

Herein, we present data from one of these pathogens, the foodborne bacterium, *S. enterica* Enteritidis, which is closely related to *S. enterica* Typhimurium. Phenotypes evaluated included growth profiles, environmental stress responses (acid, oxidative, bile, and thermal stresses), and *in vitro* colonization of 3-D biomimetic cultures of human intestinal tissue containing immune cells. Transcriptomic profiling and virulence studies are ongoing. We show that *S.* Enteritidis exhibited key alterations in pathogenic responses to LSMMG culture that suggest increased infection risk, including several responses which were different from those observed in the closely related pathovar *S.* Typhimurium. This information will provide critical mechanistic insight into the potential impact of microgravity on alterations in microbial virulence and associated infectious disease risk to crew health during spaceflight missions.