Fiscal Year:	FY 2024	**Task Last Updated:**	FY 09/21/2023
PI Name:	Ott, C. Mark Ph.D.		
Project Title:	Spaceflight-Induced Changes in Microbial Virulence and Impact to the Host Immune Response		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Microhost**:Risk of Adverse Health Effects Due to Host-Microorganism Interactions		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	77058	**Congressional District:**	36
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	Directed Research
Start Date:	10/01/2019	**End Date:**	09/30/2025
No. of Post Docs:		**No. of PhD Degrees:**	
No. of PhD Candidates:	1	**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	1
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA JSC
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:	Note: During this reporting period, Phillip Stafford, Ph.D. (Arizona State University) was added to the project (Ed., 1/12/23).		
COI Name (Institution):	Nickerson, Cheryl Ph.D. (CoPI-- Arizona State University grant 80NSSC20K0016) Barrila, Jennifer Ph.D. (Arizona State University) Oubre, Cherie Ph.D. (NASA Johnson Space Center) Crucian, Brian Ph.D. (NASA Johnson Space Center) Stafford, Phillip (Arizona State University)		
Grant/Contract No.:	Directed Research		
Performance Goal No.:			
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Task Description:	One of the critical factors to ensure crew health, safety, and performance is anticipating the risk for infectious disease during human deep space exploration and habitation. In 2006 and 2007, our spaceflight experiments aboard the Space Shuttle and International Space Station (ISS) demonstrated that the foodborne pathogen, Salmonella enterica serovar Typhimurium (S. Typhimurium), increased its virulence in response to culture in the spaceflight environment. These findings were in agreement with our initial studies using spaceflight analogue conditions for this same organism. Since those experiments, unexpected alterations in other microbial pathogen characteristics that may or may not be related to disease have also been documented in response to both spaceflight and spaceflight analogue culture. However, the range of bacteria whose true virulence in animals is altered in response to spaceflight (and spaceflight analogue) culture and the degree to which their virulence may be altered remains poorly understood. In parallel to the observations regarding microgravity exposure and bacterial virulence, multiple studies onboard ISS have documented and characterized the dysregulation of the human immune system associated with spaceflight. The phenomenon is generally characterized by altered leukocyte reductions in T and Natural Killer (NK) cell function, altered plasma cytokine profiles, and the reactivation of latent herpesviruses. Most of these studies were generally performed by returning astronaut biosamples for evaluation. Akin to microbial studies, spaceflight analogue cell culture is also well established as a terrestrial analogue that mimics key aspects of microgravity on immune cell activation. For example, both T and NK cells exhibit inhibited activation during spaceflight analogue cell culture. Unknown, and almost completely uninvestigated, is the possible synergistic effect between increased microbial virulence and reductions in immune cell function during microgravity/spaceflight conditions. Should virulence increase for multiple pathogens during crewed deep space missions, synergy with diminished immunity could increase crew health risk for infectious diseases during pending missions of exploration. The NASA Human Research Program created a specific ‘Knowledge Gap’ in their Integrated Research Plan regarding this issue, but to date, no study has provided an integrated systematic approach to address this Gap. Using spaceflight analogue technology, the proposed studies are incorporating microbial and mammalian cell culture, animal studies, and ISS crew immune cell studies in an integrated systematic approach to better understand how these systems shape the dynamics of the host-pathogen interaction that lead to infectious disease in microgravity conditions. Our hypothesis is that the incidence of higher virulence observed in both spaceflight and spaceflight analogue culture for the foodborne pathogen S. Typhimurium is not limited to this organism, and that multiple bacteria will exhibit similar increases in virulence when cultured under spaceflight analogue conditions. We further hypothesize that spaceflight-induced alterations in crew immune cell function will lead to compromised defenses against pathogen infection, which when combined with alterations in microbial virulence, will lead to a synergistic response that will reflect greater risk to crew health. Accordingly, the goal of this study is to gain an understanding of medically important microorganisms relevant to crew health that exhibit altered virulence and pathogenesis-related properties and the impact of those changes on the crew immune cell response using spaceflight analogue culture conditions. This study is incorporating relevant ISS bacterial pathogens that have either been identified from operational microbial monitoring activities or that have a clear route of infection for the crew, including potential foodborne pathogens applicable to future development of bioregenerative food systems.
Rationale for HRP Directed Research:	The MicroHost research plan aims to determine which microorganisms develop altered virulence when exposed to spaceflight conditions and understand the synergistic effect of altered microbial virulence and dysregulated immunity on crew health risks for deep space missions. Insufficient time for solicitation: Continued delays in initiating the proposed study will continue to impact the schedule and decrease our likelihood of gaining the knowledge needed to close the risk. Note that the delay in this work may impact the Path to Risk Reduction (PRR) color change from yellow to green and put the studies outside of the window for use of the International Space Station (ISS). Two prior solicitations have been released (in 2009 and 2014) for ground-based proposals to understand microbial responses to simulated microgravity. Even though the prior solicitations were written clearly, the selected studies did not focus on identifying the microbial alterations that would gain the understanding needed to inform the risk, and they did not produce the needed ground-based investigations on mechanisms. The 2009 selection addresses collective changes of organisms within the human microbiome, and the 2014 selection addresses viral reactivation. The selected studies will provide information applicable to the gaps Micro-101 to better understand the potential impact of microgravity on microbial virulence and Micro-201 to better understand the contribution of these changes on adverse health events. Completion of the proposed work will provide clear evidence as to the operational applicability of these original microbial virulence data to a variety of microorganisms and will include measurements of host immune responses to microbial challenge. Access to Previous Crew Data: This proposed study will leverage previous microbiology operational and research data as well as previously published immunology research data to provide a better understanding of impacts of microbial changes to the host and to determine the need for countermeasure evaluation as outlined in our PRR.
Research Impact/Earth Benefits:	This research will enrich life on Earth through the use of space technology and the application of biomedical knowledge. Specifically, this study will utilize the microgravity spaceflight platform to 1) to broaden our knowledge of the host-pathogen interaction that leads to infectious disease, and 2) for the development of new therapeutic strategies to combat infectious disease for the general public.
Task Progress:	Updated progress on the five test microorganisms to support this project are listed below and have included extensive interactions via routine video telecons and emails with the Principal Investigator and external Consultants. Our Institutional Animal Care and Use Committee (IACUC) proposal was accepted by the Johnson Space Center (JSC) IACUC. Progress on this study includes: Salmonella Enteritidis: • Growth kinetics, stress responses, infection of 2-D monolayers and 3-D tissue culture models have been completed. One virulence trial in mice has been completed, with a second trial planned in October 2023. Transcriptomic studies are ongoing. Manuscript in preparation. Pseudomonas aeruginosa: • Growth kinetics and stress responses have been completed. 3-D tissue culture infections and transcriptomic studies are ongoing.

	Burkholderia cepacia: • Growth kinetics and several stress responses have been completed. 3-D tissue culture infections and transcriptomic studies are ongoing. Streptococcus pneumoniae: • Obtained a new S. pneumoniae strain due to limited survival characteristics of the original strain. Growth conditions and media requirements are being optimized. Enterohemorrhagic E. coli: • Growth kinetics completed. Stress responses have been completed. Two trials of 2-D macrophages infections and 3-D tissue culture infections have been completed with triplicate trials to be completed shortly. Transcriptomic studies are ongoing. One virulence trial in mice has been completed, with a second trial planned in October 2023.
Bibliography Type:	Description: (Last Updated: 10/14/2024)
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