Fiscal Year:	FY 2022	**Task Last Updated:**	FY 10/01/2021
PI Name:	Crucian, Brian Ph.D.		
Project Title:	Spaceflight-Induced Immune System Dysregulation and Microgravity-Associated Alterations in Microbial Virulence – Infectious Disease Risk for Astronauts		
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) **Immune**:Risk of In Mission Impacts, Adverse Health Events or Long-Term Health Impacts due to Altered Immune Response (2) **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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City:	Houston	**State:**	TX
Zip Code:	77058-3607	**Congressional District:**	36
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	Directed Research
Start Date:	10/01/2020	**End Date:**	09/30/2024
No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
Contact Monitor:	Brocato, Becky	**Contact Phone:**	
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:	October 2021 report: Audrie Colorado, Ph.D. was added as Co-Investigator because of her expertise in preparation and growth of bacterial microbes. She replaced George Makedonas, Ph.D. on the investigation, who departed NASA service.		
COI Name (Institution):	Ott, Mark Ph.D. (NASA Johnson Space Center) Oubre, Cherie Ph.D. (NASA Johnson Space Center) Krieger, Stephanie M.S. (KBR/NASA Johnson Space Center) Nelman-Gonzalez, Marya B.A. (KBR/NASA Johnson Space Center) Mehta, Satish Ph.D. (KBR/NASA Johnson Space Center) Colorado, Audrie Ph.D. (KBR/NASA Johnson Space Center)		
Grant/Contract No.:	Directed Research		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Over the past 50 years, microorganisms have displayed unexpected responses relevant to infectious disease when grown in microgravity (and microgravity analogues), including changes in final cell concentration, biofilm production, stress resistance, antibiotic sensitivity, gene expression, and virulence. In parallel, astronaut studies have characterized a persistent spaceflight-induced dysregulation of the human immune system, consisting of altered leukocyte distribution, reductions in T and Natural Killer (NK) cell function, altered cytokine profiles, and reactivation of latent herpesviruses. Further, astronauts have some degree of clinical incidence, primarily infectious disease episodes, and atopic dermatitis. The impact of microgravity on host-pathogen interactions and potential for clinical disease remains understudied and poorly characterized. The goal of this study is to use spaceflight analogue conditions to define the relationship between altered virulence of medically-significant microorganisms aboard the International Space Station (ISS) and the immune response of the host, including astronaut immune cells. This information will provide critical understanding into the impact of microgravity on potential alterations of microbial virulence and associated infectious disease risk to crew health during spaceflight missions. Specific Aims: Specific Aim 1: Profile the synergistic relationship between spaceflight analogue-altered bacterial virulence characteristics and spaceflight analogue-altered immune cell function. Alterations in immune cell responses will be evaluated when human primary immune cells are challenged with pathogens in normal and spaceflight analogue growth conditions. Specific Aim 2: Profile antimicrobial efficacy for astronauts participating in spaceflight via challenge with spaceflight analogue cultured bacterial pathogens. Primary immune cells from astronauts will be profiled before, during, and post-flight to identify alterations in host response to pathogens in normal and spaceflight analogue conditions. This will be the first study to apply an integrated systematic approach to understand the relationship between spaceflight, immune cell function, and infectious disease risk for the crew. The results from this study will enhance the current infectious disease risk assessment for the crew, elucidate the relationship to clinical disease, and support future development and application of effective countermeasures for treatment and prevention.
Rationale for HRP Directed Research:	The immune research task aims to determine which microorganisms develop altered virulence when exposed to spaceflight conditions and understanding 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-102 for Microbiome and Micro-201 for the viral reactivation study, but not Micro-202 as requested in the solicitation. 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 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 joint PRR. Via the recent ‘Epstein Barr,’ ‘Integrated Immune,’ ‘Salivary Markers,’ and ‘Functional Immune’ investigations of astronaut immunocompetence during flight, and via collaborations with the Japan Aerospace Exploration Agency (JAXA) ‘Multi Omics’ and European Space Agency (ESA) ‘Immuno,’ ‘Immuno2,’ and ‘MoCISS’ ISS investigations, the Johnson Space Center (JSC) team has access to unique astronaut data. These data will be necessary to select assays that define crew alterations during flight, relevant for the current Host-Pathogen proposal. Also, for Aim 1, comparisons to previous crew findings, especially for repeat flyers, will be relevant to interpret the data in the context of crew health risks.
Research Impact/Earth Benefits:	
Task Progress:	Over the past 50 years, microorganisms have displayed unexpected responses relevant to infectious disease when grown in microgravity (and microgravity analogues), including changes in final cell concentration, biofilm production, stress resistance, antibiotic sensitivity, gene expression, and virulence. In parallel, astronaut studies have characterized a persistent spaceflight-induced dysregulation of the human immune system, consisting of altered leukocyte distribution, reductions in T and Natural Killer (NK) cell function, altered cytokine profiles, and reactivation of latent herpesviruses. Further, astronauts have some degree of clinical incidence, primarily infectious disease episodes and atopic dermatitis. The impact of microgravity on host-pathogen interactions and potential for clinical disease remains understudied and poorly characterized. The goal of this study is to use spaceflight analogue conditions to define the relationship between altered virulence of medically-significant microorganisms aboard the International Space Station (ISS) and the immune response of the host, including astronaut immune cells. This information will provide critical understanding into the impact of microgravity on potential alterations of microbial virulence and associated infectious disease risk to crew health during spaceflight missions. Specific Aims: Aim 1: Profile the synergistic relationship between spaceflight analogue-altered bacterial virulence characteristics and spaceflight analogue-altered immune cell function. Alterations in immune cell responses will be evaluated when human primary immune cells are challenged with pathogens in normal and spaceflight analogue growth conditions. Aim 2: Profile antimicrobial efficacy for astronauts participating in spaceflight via challenge with spaceflight analogue cultured bacterial pathogens. Primary immune cells from astronauts will be profiled before, during, and post-flight to identify alterations in host response to pathogens in normal and spaceflight analogue conditions. This will be the first study to apply an integrated systematic approach to understand the relationship between spaceflight, immune cell function, and infectious disease risk for the crew. The results from this study will enhance the current infectious disease risk assessment for the crew, elucidate the relationship to clinical disease, and support future

development and application of effective countermeasures for treatment and prevention.

In 2021, Immunology and Microbiology laboratory personnel worked diligently to optimize the culture conditions and flow cytometry panels prior to beginning work on crew samples. This included several trial runs testing different microbial growth conditions, cellular surface markers, and preparations for analysis by confocal and fluorescent microscopy. The trial runs included testing of 4 bacteria: Burkholderia cepacia, Salmonella enteritidis, Pseudomonas aeruginosa, and Enterohemorrhagic E. coli. The bacteria were cultured with both whole blood and peripheral blood mononuclear cells.

The IRB (Institutional Review Board) protocol for this study was submitted and approved in March 2020. Informed consent briefings for crew members began in December 2020. To date, five crew members have enrolled in this study and the first two sample collections (L-180 and L-90) have occurred for two of those individuals. Additionally, two crew members are scheduled for their first sample collection (L-180) in early October 2021.

Bibliography Type:	Description: (Last Updated: 05/15/2025)