Fiscal Year:	FY 2014	**Task Last Updated:**	FY 12/07/2014
PI Name:	Barrila, Jennifer Ph.D.		
Project Title:	Evaluating the Spaceflight Infectious Disease Risk Potential of Pathogenic and Commensal microorganisms using Caenorhabditis elegans as a Human Surrogate Model for Infection		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Environmental health		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **SHFH**:Space Human Factors & Habitability (archival in 2017)		
Human Research Program Risks:	(1) **Medical Conditions**:Risk of Adverse Health Outcomes and Decrements in Performance Due to Medical Conditions that occur in Mission, as well as Long Term Health Outcomes Due to Mission Exposures (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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Zip Code:	85287-0001	**Congressional District:**	9
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2012 Crew Health NNJ12ZSA002N
Start Date:	09/09/2013	**End Date:**	09/08/2014
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
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Castro, Sarah (NASA Johnson Space Center)		
Grant/Contract No.:	NNX13AR16G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Understanding the impact of the spaceflight environment on the disease-causing potential of a wide variety of pathogenic and commensal microbes is critical for ensuring crew health, safety, and performance. Changes that occur to both the immune system of astronauts and pathogenesis of microbes during spaceflight could represent a formidable challenge to the successful transition from short-to-long duration missions. This is a critical issue to address since a) the crew's immune system is dysfunctional during flight, and b) results from our collaborative team and others have demonstrated that spaceflight and/or spaceflight-analogue culture globally alters the virulence, gene expression, and/or pathogenesis-related phenotypes of several microbial pathogens. This proposal aims to further improve infectious disease risk assessment for astronauts by investigating the likelihood that a variety of microorganisms may exhibit alterations in virulence in response to the microgravity environment. We will accomplish this by profiling changes in virulence, persistence in the host, and targeted changes in gene expression of a select panel of pathogenic and commensal microorganisms exposed to spaceflight-analogue culture using the Rotating Wall Vessel (RWV) bioreactor. Microbes proposed for this study include 1) Salmonella Typhimurium, 2) Staphylococcus aureus, 3) a Space Shuttle environmental isolate of Burkholderia cepacia, and 4) Lactobacillus acidophilus, a commensal microorganism. The nematode Caenorhabditis elegans (C. elegans) will be used as a human surrogate model of infection to evaluate changes in microbial virulence in response to RWV culture and will also be profiled for targeted changes in the expression of genes important for host immunity. Moreover, as astronauts have dysfunctional immune systems during spaceflight, the susceptibility of an immunocomprised C. elegans mutant to infection with these same microbes will also be evaluated. Results from this work hold potential to provide deeper insight into the likelihood, consequence, and respective uncertainties of this HRP risk.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This research will broaden our knowledge of the host-pathogen interaction that leads to infectious disease, and will provide fundamental new insight into mechanisms important for the development of new therapeutic strategies to combat infectious disease for the general public.
Task Progress:	Understanding the impact of the spaceflight environment on the virulence potential of a wide variety of microorganisms is critical for ensuring crew health, safety, and performance. Changes that occur to both the immune system of astronauts and pathogenesis of microbes during spaceflight could represent a formidable challenge to the successful transition from short-to-long duration missions. The goal of this work was to assess the feasibility of using the roundworm Caenorhabditis elegans (C. elegans) as a model host organism for investigating transient changes in virulence of microbes cultured under spaceflight analogue conditions in the Rotating Wall Vessel (RWV) bioreactor. The design of this study was such that only the bacteria were cultured in the RWV, while the C. elegans hosts (wild type and an immunocompromised mutant) were grown prior to infection on standard nematode growth media (NGM) agar plates on their normal laboratory diet of Escherichia coli OP50. The infections then took place in liquid medium using a variety of exposure times (1-18 hours) in order to minimize any reversion of the low-shear modeled microgravity (LSMMG)-associated phenotypes (i.e., changes in virulence and pathogenesis-related stress resistance) during the infection. Microorganisms profiled in this work included: 1) Salmonella enterica serovar Typhimurium, 2) Staphylococcus aureus, and 3) an ISS potable water isolate of Burkholderia cepacia. Under the conditions of this study, we found that transient exposure of the RWV-cultured microbes to C. elegans in a static dish was not sufficient for establishing a lethal infection in the nematode relative to the uninfected control nematodes fed on OP50. The outcomes of the infection process in liquid were quite different from what was previously reported for these pathogens using a solid agar medium. This indicates the need for further study design optimization. Persistence studies with S. Typhimurium did however indicate an early difference in the bacterial colonization numbers within the nematode intestine infected with LSMMG versus control cultures. We also observed an interesting phenotype following S. aureus infection, in which the bacterium appeared to form a biofilm-like structure around the anterior of the worm in liquid. Studies are ongoing to further investigate these findings.
Bibliography Type:	Description: (Last Updated: 12/08/2014)
Abstracts for Journals and Proceedings	Castro SL, Nickerson CA, Ott CM, Forsyth RJ, Rideout A, Alverdy JC, Barrila J. "Evaluating the Spaceflight Infectious Disease Risk Potential of Pathogenic and Commensal microorganisms using Caenorhabditis elegans as a Human Surrogate Model for Infection." Presented at the 2014 Human Research Program Investigators' Workshop, Galveston, TX, February 12-13, 2014. 2014 Human Research Program Investigators' Workshop, Galveston, TX, February 12-13, 2014. Immunology and Microbiology Posters, http://www.hou.usra.edu/meetings/hrp2014/pdf/3267.pdf , Feb-2014
Abstracts for Journals and Proceedings	Barrila J, Ott CM, Forsyth RJ, Davis R, Wilson JW, Nickerson CA. "Experimental Considerations for the Proper Assessment of Spaceflight-induced alterations in Microbial Virulence " 30th Annual Meeting of the American Society for Gravitational and Space Research, Pasadena, CA, October 22-26, 2014. 30th Annual Meeting of the American Society for Gravitational and Space Research, Pasadena, CA, October 22-26, 2014. Abstract number IP.32. , Oct-2014
Awards	Barrila J. "2014 Thora W. Halstead Young Investigator's Award, American Society for Gravitational and Space Research, October 2014." Oct-2014