Fiscal Year:	FY 2023	**Task Last Updated:**	FY 05/30/2023
PI Name:	Mehta, Satish Ph.D.		
Project Title:	Varicella Zoster Virus Shedding After Antiviral Drug (Valacyclovir) Treatment in Antarctic Expeditioners		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Biomedical countermeasures		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	(1) **Immune**:Risk of Adverse Health Event Due to Altered Immune Response		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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PI Organization Type:	NASA CENTER	**Phone:**	281-483-5459
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City:	Houston	**State:**	TX
Zip Code:	77058-2720	**Congressional District:**	36
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2017 HERO 80JSC017N0001-Crew Health and Performance (FLAGSHIP1, OMNIBUS). Appendix A-Flagship1, Appendix B-Omnibus
Start Date:	07/10/2018	**End Date:**	10/01/2023
No. of Post Docs:	0	**No. of PhD Degrees:**	1
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:	Stenger, Michael	**Contact Phone:**	281-483-1311
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Flight Program:			
Flight Assignment:	NOTE: End date changed to 10/1/2023 per T. Sirmons/HRP JSC (Ed., 2/23/23) NOTE: End date changed to 10/1/2022 per L. Singh/HRP JSC (Ed., 4/8/21)		
Key Personnel Changes/Previous PI:	February 23, 2023 One Ph.D. student completed her degree during this period.		
COI Name (Institution):	Crucian, Brian Ph.D. (NASA Johnson Space Center) Locke, James M.D. (NASA Johnson Space Center) Pierson, Duane Ph.D. (NASA Johnson Space Center)		
Grant/Contract No.:	Internal Project		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Previous spaceflight studies indicate that reactivation of varicella zoster virus (VZV), particularly during longer duration spaceflights, can potentially lead to clinical disease including zoster, chronic neuropathic pain, vision loss, stroke, and cognitive impairment. Furthermore, continued viral shedding after spaceflight may cause clinical disease in crew contacts including uninfected or immunocompromised individuals, as well as newborn infants. Thus, it is essential to develop spaceflight countermeasures to prevent VZV reactivation and ensure the health of the crew, as well as the health of their contacts upon return. One such countermeasure is prophylactic administration of an antiviral drug (valacyclovir) against VZV. In order to determine the effectiveness of this countermeasure using a large population, we propose to study VZV shedding in Antarctic expeditioners who have similar patterns of VZV DNA shedding in saliva as astronauts. Countermeasure efficacy of the antiviral drug will be determined by measuring VZV reactivation and shedding in saliva as well as measuring the physiological stress biomarkers (cortisol, DHEA, and salivary amylase) and immune markers (inflammatory cytokines) before, during, and after the winter-over period. The proposed research team has extensive experience in ground-based studies including studies conducted in Antarctica, Aquarius undersea habitat, and artificial gravity, as well as the coordination and conduct of complex multi-laboratory studies. In addition, the research team has proven expertise and experience in immunology, virology, and medical expertise working with infectious diseases and spaceflight subjects. This proposal addresses the need for developing and validating countermeasures as identified in the new NASA Research Announcement (NRA) 80JSC017N0001-OMNIBUS NASA HERO Omnibus Opportunity.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Our studies have demonstrated that reactivation of VZV, particularly during longer duration spaceflight, can potentially lead to clinical disease including zoster, chronic neuropathic pain, vision loss and cognitive impairment. Furthermore, continued viral shedding post-spaceflight may cause clinical disease in crew contacts including uninfected or immunocompromised individuals, as well as newborn infants. Thus, it is essential to develop spaceflight countermeasures to prevent VZV reactivation and ensure the health of the crew, as well as the health of their contacts upon return. One such countermeasure is prophylactic administration of an antiviral drug (valacyclovir) against VZV. In order to determine the effectiveness of this countermeasure with a relatively large population, we propose to study VZV shedding in Antarctic expeditioners who have had similar patterns of VZV DNA shedding in saliva as astronauts. These findings will indicate if valacyclovir treatment will reduce or stop viral reactivation and its shedding in saliva. This will enhance the selection and vetting of potential countermeasures to address clinical risks associated with reduced immune function. This will improve crew health care on International Space Station (ISS) missions, and will further enable exploration-class missions.
Task Progress:	The content of the Task Progress section below is from the Abstract of an article entitled, "Antiviral Treatment With Valacyclovir Reduces Virus Shedding In Saliva Of Antarctic Expeditioners". The article was accepted by the open-source journal, Frontiers in Virology, in May 2023. A science presentation from the PI team was also delivered at the NASA Human Research Program (HRP) Investigators' Workshop (IWS) in February 2023. The citations for both resources can be found in the Bibliography of this report (Ed., 5/30/23) Reactivation and shedding of herpes viruses such as Epstein-Barr virus (EBV), herpes simplex virus 1 (HSV1), varicella zoster virus (VZV), and cytomegalovirus (CMV) increase in astronauts during spaceflight as compared to their preflight and postflight levels. These potential reactivation events increase the risk of associated clinical conditions like herpes zoster, chronic neuropathic pain, vision loss, stroke, cognitive impairment, and cold sores. Furthermore, continued viral shedding for a longer period after space travel may increase the risk of transmitting the virus to crew contacts who are uninfected with the virus – including, but not limited to, the immunocompromised or to newborn infants. Thus, it is essential to develop spaceflight countermeasures to prevent reactivation of these herpes viruses, ensuring the health of the crewmembers and their contacts upon return. One such countermeasure is prophylactic administration of an antiviral drug (valacyclovir) against the alpha herpesviruses (VZV, HSV-1). To determine the effectiveness of this countermeasure using a large population, we studied shedding of EBV, VZV and HSV-1 in Antarctic expeditioners (who have been reported to have similar viral shedding patterns in their saliva during winter-over as astronauts during long spaceflights). Countermeasure efficacy of this antiviral drug was determined by 3 major parameters, including viral load, physiological stress biomarkers (cortisol, DHEA, and amylase) and immune markers (inflammatory cytokines) during the winter-over in the saliva of expeditioners with and without administration of this drug. Thirty-two volunteers from two Antarctic stations (McMurdo and South Pole) participated in this study. Subjects were randomly assigned to either treatment group (valacyclovir HCl: 1 g/day), or placebo group (oyster Calcium 500mg/day). EBV and HSV-1 viral shedding was significantly reduced in the treatment group versus the placebo group by >24 fold (EBV) and >5 fold (HSV1) over the course of winter-over period. No VZV shedding was seen in any of the subjects. 50% of the placebo saliva samples had measurable viral DNA (either EBV, HSV1, or both) compared to 19% of the treatment group. There was no significant change in the Cortisol to DHEA ratio or alpha amylase, indicating physiological stress was similar between the groups. No difference was detected in salivary cytokines except IL-10, which was significantly lower in the treatment group than the placebo group. These data indicate that valacyclovir (1g/day) is a safe and successful intervention to reduce herpes virus reactivations and shedding in individuals subjected to extreme environments and stressors.
Bibliography Type:	Description: (Last Updated: 11/10/2023)
Abstracts for Journals and Proceedings	Diak DM, Mehta SK, Rooney BV, Krieger SS, Nelman-Gonzalez M, Locke JP, Nagel MA, Crucian BE. "Herpes viral shedding decreases in Antarctic expeditioners when given prophylactic antiviral drug (Valacyclovir) treatment." 2023 NASA Human Research Program Investigators' Workshop, "To the Moon: The Next Golden Age of Human Spaceflight", Galveston, TX, February 7-9, 2023. Abstracts. 2023 NASA Human Research Program Investigators' Workshop, "To the Moon: The Next Golden Age of Human Spaceflight", Galveston, TX, February 7-9, 2023. https://web.cvent.com/event/08d8f955-514e-4e10-b860-bd009811ec13/regProcessStep1 , Feb-2023
Articles in Peer-reviewed Journals	Mehta S, Diak DM, Rooney BV, Krieger SS, Nelman-Gonzalez M, Locke JP, Nagel MA, Young M,Crucian BE. "Antiviral treatment with valacyclovir reduces virus shedding in saliva of Antarctic expeditioners." Front Virol. 2023 Jun 2;3:1157659. https://doi.org/10.3389/fviro.2023.1157659 , Jun-2023

Articles in Peer-reviewed Journals	Mehta SK, Szpara ML, Rooney BV, Diak DM, Shipley MM, Renner DW, Krieger SS, Nelman-Gonzalez MA, Zwart SR, Smith SM, Crucian BE. "Dermatitis during spaceflight associated with HSV-1 reactivation." Viruses. 2022 Apr 11;14(4):789. http://dx.doi.org/10.3390/v14040789 ; PMCID: PMC9028032; PMID: 35458519 , Apr-2022