Fiscal Year:	FY 2021	**Task Last Updated:**	FY 05/26/2022
PI Name:	Ronca, April Elizabeth Ph.D.		
Project Title:	VNSCOR: Oxidative Stress and the Neuroconsequences of Spaceflight Environment -- Immune Dysregulation and Antioxidant Dietary Countermeasure Efficacy		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **HFBP**:Human Factors & Behavioral Performance (IRP Rev H)		
Human Research Program Risks:	(1) **Bmed**:Risk of Adverse Behavioral Conditions and Psychiatric Disorders (2) **CNS**:Risk of Acute (In-flight) and Late Central Nervous System Effects from Radiation Exposure (IRP Rev G) (3) **Sensorimotor**:Risk of Altered Sensorimotor/Vestibular Function Impacting Critical Mission Tasks (Revised as of IRP Rev M)		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	april.e.ronca-1@nasa.gov	**Fax:**	FY
PI Organization Type:	NASA CENTER	**Phone:**	650.604.3595
Organization Name:	NASA Ames Research Center		
PI Address 1:	Space Biosciences Research Branch, NASA Human Research Program (HRP)/Human Health Countermeasures (HHC)		
PI Address 2:	MS 236-7		
PI Web Page:			
City:	Moffett Field	**State:**	CA
Zip Code:	94035	**Congressional District:**	18
Comments:	November 2019: PI is located at NASA Ames Research Center and remains affiliated with Wake Forest University School of Medicine		
Project Type:	GROUND	**Solicitation / Funding Source:**	2018 HERO 80JSC018N0001-Crew Health and Performance (FLAGSHIP, OMNIBUS). Appendix A-Flagship, Appendix B-Omnibus
Start Date:	10/01/2019	**End Date:**	09/30/2025
No. of Post Docs:	2	**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:		**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA JSC
Contact Monitor:	Whitmire, Alexandra	**Contact Phone:**	
Contact Email:	alexandra.m.whitmire@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: End date changed to 09/30/2025 per L. Juliette/JSC (Ed., 5/7/22)		
Key Personnel Changes/Previous PI:	Joshua Alwood, Ph.D. was added as a CoInvestigator due to his expertise in bone physiology. Linda Guttmann, Ph.D. left the project in December, 2020. Amber Paul, Ph.D. is now at Embry–Riddle Aeronautical University. Candice Tahimic, Ph.D. is now at the University of North Florida.		
COI Name (Institution):	Tahimic, Candice Ph.D. (University of North Florida) Paul, Amber Ph.D. (Embry-Riddle Aeronautical University) Mhatre, Siddhita Ph.D. (NASA Ames Research Center) Iyer, Janani Ph.D. (NASA Ames Research Center) Alwood, Joshua (NASA Ames Research Center)		

Grant/Contract No.:	Internal Project
Performance Goal No.:	
Performance Goal Text:	
Task Description:	The proposed project will test the hypothesis that Ionizing Radiation (IR), microgravity, and social isolation combine synergistically to trigger an oxidative stress response that alters immune homeostasis, brain structure and function, and neurobehavioral and cognitive performance. Specific Aims for this project are: (1) Determine dose-response curves for acute 'Five-Ion GCR (galactic cosmic ray) Simulation' exposure for immune, brain, and performance responses in crew age-matched adult male and female mice; (2) Determine effects of acute 'Five-Ion GCR Simulation' exposure singly and in combination with simulated microgravity and social isolation, on immune, brain, and performance responses in crew age-matched male and female mice mimicking deep space missions; and (3) Determine efficacy of the dietary antioxidant, Nicotinamide Mononucleotide (NMN), a key intermediate in nicotinamide adenine dinucleotide (NAD+) biosynthesis. The project relies on established and highly translatable ground-based mouse models and assays with IR exposures to be performed at the NASA Space Radiation Laboratory (NSRL). The experimental approach will provide definitive data on the timing and mechanisms involved in the oxidative stress response, immune, and brain changes, and ensuing functional (behavioral/cognitive) impairments expected during human transit to Mars. This project will identify potential immune biomarkers for, and mechanisms underlying, structural and functional changes in the immune and nervous systems leading to behavioral/cognitive performance deficits, and its potential application to develop effective countermeasures to mitigate negative health effects of long duration space habitation. This proposal addresses NASA's efforts to rapidly advance the characterization of risks and identifying appropriate countermeasures in anticipation of future deep space missions. Ensuring crew health and performance during extended transits necessitates that sensorimotor and cognitive abilities remain strong to avoid potentially catastrophic health and safety outcomes. Further, despite historically low numbers of females astronauts, recent NASA Astronaut Corps class selections, comprised of 50% and 40% women as compared to men, signal the need to understand how sex and gender differences affect physiological adaptation and health in the space environment. This integrative project, developed by a cross-disciplinary team highly experienced in spaceflight and radiation research, utilizes established space biosciences research protocols and variables, and time-honored, as well as modern, research methodologies. We will address major risks and associated gaps: (1) Risk of Acute (In-flight) and Late Central Nervous System Effects from Radiation (CNS), (2) Risk of Altered Sensorimotor/Vestibular Function Impacting Critical Mission Tasks (SM), and Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders that have been combined into the NASA CNS, BMed, and SM (CBS) Integrated Research Plan. Here we have adhered to primary goals set forth in Human Exploration Research Opportunities (HERO) Appendix A to determine how key features of the deep space environment may interact to increase risk to a crew by negatively impacting health and performance, and we have identifed and developed strategies to characterize and mitigate the potential risks via countermeasures.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	The study is underway. Extensive progress was made during this reporting period on the Virtual NASA Specialized Center of Research (VNSCOR). The VNSCOR Team met extensively to discuss touch points across the project and hone our experimental designs. The VNSCOR includes two species, mouse and rat, with mature male and female subjects approximating crew ages, and six standardization protocols across three laboratories. The timeline for the combined space stress model remains identical across groups with all animals experiencing each stressor for identical lengths of time and at the same timepoints – this will allow a standard model at the NASA Space Radiation Laboratory (NSRL) to be developed for future studies. According to this timeline, all Principal Investigator (PI) teams will perform hindlimb unloading as the microgravity model, and irradiate all animals with the 5-ion GCRsim at both a low (15 cGy) and high dose (50 cGy) that most closely mimics the mission travel time to Mars. A slightly lower protein diet, containing no estradiol, will be used to closely mimic the diet of astronauts and limit the effects of circulating estrogen. Additionally, efforts are being made to create similar animal care and handling conditions. To maintain all original grant aims, each group will return to their respective institutions and perform a minimum of two identical behavioral assays to measure changes in sensorimotor (adhesive removal) and memory (novel object recognition) functions. Using three Luminex based arrays each group will evaluate peripheral blood markers to elucidate potential predictive biomarkers of behavioral performance. These data together, will be combined into a predictive statistical model to identify potential biomarkers that may predict behavior decrements and neuroinflammation across three institutions and two species. In February 2021, our team customized and shipped 100 hindlimb unloadin (HU) cages to Brookhaven National Laboratory (BNL) for the Rosi team, and worked onsite at University of California San Francisco (UCSF) training the Rosi Team in this procedure. Despite the COVID-19 pandemic, my own Team was able to travel to NSRL during this reporting period, complete 5-ion GCRsim exposure, perform acute behavioral (sensorimotor) and immune measures at 72 post-IR, and dissect the Intermediate group. Delayed group mice were shipped to NASA Ames Resarch Center (ARC) to undergo cognitive and behavioral testing, which will be followed by dissection. After dissection, data analysis will begin.
Bibliography Type:	Description: (Last Updated: 05/24/2022)
Abstracts for Journals and Proceedings	Paul AM, Rubinstein L, Mhatre SD Iyer J, Wong K, Lowe M, Abegaz M, O'Neil N, Tahimic C, Alwood JS, Globus RK, Ronca AE. "Altered immune differentials between male and female mice independent of ionizing radiation." 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. Abstracts. 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. , Feb-2021
Abstracts for Journals and Proceedings	Puukila S, Lemon JA, Ronca AE, Jones JA, Montesinos CA, Boreham DR. "A multi targeted dietary supplement as a potential countermeasure for prolonged, deep space exploration." 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. Abstracts. 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. , Feb-2021

Abstracts for Journals and Proceedings	Ronca AE, Rubinstein L, Paul A, Mhatre SD, Iyer JS, Puukila SA, Lowe M, Sowa M, Globus R, Alwood JS, Tahimic C. "Oxidative stress and the neuroconsequences of spaceflight environment - immune dysregulation and antioxidant dietary countermeasure efficacy." 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. Abstracts. 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. , Feb-2021
Abstracts for Journals and Proceedings	Rosi S, Sanford L, Ronca A. "The combined space stress model– social isolation, altered gravity, and GCR- effects on memory, sensorimotor function, and neuroinflammatory response as to predict astronaut performance." 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. Abstracts. 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. , Feb-2021
Abstracts for Journals and Proceedings	Rubinstein L, Paul A, Mhatre SD, Iyer JS, Puukila SA, Lowe M, Houseman C, Abegaz M, Tabares Ruiz, O'Neil N, Sowa M, Alwood JS, Globus RK, Tahimic C, Ronca AE. "The combined space stress model – social isolation, altered gravity, and GCR – effects on memory, sensorimotor function, and neuroinflammatory response as to predict astronaut performance. " 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. Abstracts. 2021 NASA Human Research Program Investigators' Workshop, Virtual, February 1-4, 2021. , Feb-2021