

Fiscal Year:	FY 2023	Task Last Updated:	FY 08/03/2023
PI Name:	Ronca, April Elizabeth Ph.D.		
Project Title:	VNSCOR: Oxidative Stress and the Neuroconsequences of Spaceflight Environment		
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 Cognitive or Behavioral Conditions and Psychiatric Disorders (2) Sensorimotor : Risk of Altered Sensorimotor/Vestibular Function Impacting Critical Mission Tasks		
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:	650.400.6019
Organization Name:	NASA Ames Research Center		
PI Address 1:	Space Biosciences Research Branch		
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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:	2	No. of Bachelor's Degrees:	2
No. of Bachelor's Candidates:	8	Monitoring Center:	NASA JSC
Contact Monitor:	Whitmire, Alexandra	Contact Phone:	
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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:	Stephanie Puukila, PhD added as Ames Co-I with expertise in space radiation, animal cognition and behavior, and countermeasures.		
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) Puukila, Stephanie Ph.D. (Blue Marble Space Institute of Science)		
Grant/Contract No.:	Internal Project		
Performance Goal No.:			

Performance Goal Text:	
Task Description:	<p>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 identified and developed strategies to characterize and mitigate the potential risks via countermeasures.</p>
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	<p>Extensive progress was made during this reporting period on the first two project aims with two publications and multiple abstracts focussed on acute GCRsim dose-response and combinatorial effects of spaceflight stressors (isolation, simulated microgravity, and simulated galactic cosmic rays/GCRsim) on crew-aged mice. Data were collected on neural, behavioral, and immune outcomes at varying timepoints in relation to spaceflight stressor exposure.</p> <p>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.</p> <p>Predictive modeling efforts are underway integrating multiple measures derived from the current project with planned expansions across VNSCOR Teams.</p>
Bibliography Type:	Description: (Last Updated: 09/08/2023)
Abstracts for Journals and Proceedings	<p>Tahimic CGT, Dubose M, Korostenskij I, Semel M, Mhatre SD, Alwood JS, Yasaman Shirazi-Fard Y, Lowe M, Iyer JS, Puukila SA, Paul AM, Rubinstein L, Delp M, Goukassian D, Ronca AE. "Defining the molecular signatures of cardiovascular responses to simulated space radiation." Committee on Space Research (COSPAR) 2022 44th Scientific Assembly, Athens, Greece, July 16-24, 2022.</p> <p>Abstracts. Committee on Space Research (COSPAR) 2022 44th Scientific Assembly, Athens, Greece, July 16-24, 2022. , Jul-2022</p>
Abstracts for Journals and Proceedings	<p>Puukila SA, Siu O, Mhatre SD, Lowe M, Tabares Ruiz SN, Tahimic CGT, Rubinstein L, Alwood JS, Ronca AE. "Neurobehavioral effects of five-ion GCRsim exposure in male and female mice." 68th Annual Meeting, Radiation Research Society, Waikoloa Village, Hawaii, October 16-19, 2022.</p> <p>Abstracts. 68th Annual Meeting, Radiation Research Society, Waikoloa Village, Hawaii, October 16-19, 2022. , Oct-2022</p>

Abstracts for Journals and Proceedings	Ronca AE, Iyer JS, Mhatre SDS, Puukila SA, Tabares Ruiz SN, Hayes J, Dubose M, Siu O, Burke M, Semel M, Lowe M, Shirazi-Fard Y, Rubinstein L, Sowa MB, Paul AM, Tahimic CGT, Alwood JS. "Sex differences and deep space stressors: effects of 5-ion GCRsim, simulated microgravity and social isolation on immune function, brain and behavior in mice." 68th Annual Meeting, Radiation Research Society, Waikoloa Village, Hawaii, October 16-19, 2022. Abstracts. 68th Annual Meeting, Radiation Research Society, Waikoloa Village, Hawaii, October 16-19, 2022. , Oct-2022
Abstracts for Journals and Proceedings	Mitchell C, Burke M, Christenson LK, Ronca AE, Paul M. "Assessment of Dose-dependent Endocrine and Immune Responses to Simulated Ionizing Radiation." American Astronautical Society, Von Braun Symposium, Huntsville, Alabama, October 26-28, 2022. Abstracts. American Astronautical Society, Von Braun Symposium, Huntsville, Alabama, October 26-28, 2022. , Oct-2022
Abstracts for Journals and Proceedings	Juarez K, Burke M, Larsen E, Wong K, Talyansky Y, Tahimi CGT, DuBose M, Semel M, Christenson LK, Iyer JS, Mhatre SD, Puukila SA, Tabares Ruiz SN, Rubinstein L, Lowe M, Shirazi-Fard Y, Alwood JS, Ronca AE, Paul AM. "Investigating the relationship between immune function and adrenal hormones following simulated ionizing radiation." American Society for Gravitational and Space Biology, Houston, Texas, November 9-12, 2022. Abstracts. American Society for Gravitational and Space Biology, Houston, Texas, November 9-12, 2022. , Nov-2022
Abstracts for Journals and Proceedings	Rubinstein L, Paul AM, Mhatre SD, Iyer JS, Puukila SA, Siu O, Lowe M, Houseman C, Abegaz M, Tabares Ruiz SN, O'Neil N, Allen AR, Alwood JS, Globus RK, Tahimic CGT, Ronca AE. "Neuro-behavioral consequences of low dose radiation social isolation and sex differences in the longevity MCAT mouse model." American Society for Gravitational and Space Biology, Houston, Texas, November 9-12, 2022. Abstracts. American Society for Gravitational and Space Biology, Houston, Texas, November 9-12, 2022. , Nov-2022
Abstracts for Journals and Proceedings	Siu O, Puukila SA, Rubinstein L, Tahimic CGT, Lowe M, Korosteskij I, Semel M, Iyer JS, Mhatre SD, Shirazi-Fard Y, J. S. Alwood JS, Paul AM, Ronca AE. "The effects to exposure of simulated spaceflight radiation on behavioral health of male and female mice." American Society for Gravitational and Space Biology, Houston, Texas, November 9-12, 2022. Abstracts. American Society for Gravitational and Space Biology, Houston, Texas, November 9-12, 2022. , Nov-2022
Abstracts for Journals and Proceedings	Puukila SA, Siu O, Mhatre SD, Lowe M, Tabares Ruiz SN, Tahimic CGT, Rubinstein L, Alwood JS, Ronca AE. "Early and late neurobehavioral effects of male and female mice exposed to five-ion GCRsim." American Society for Gravitational and Space Biology, Houston, Texas, November 9-12, 2022. American Society for Gravitational and Space Biology, Houston, Texas, November 9-12, 2022. , Nov-2022
Abstracts for Journals and Proceedings	Taylor SC, Nies P, Stoltz A, Olson M, Burke M, Paul, Tahimic C, Ronca A, Christenson L. "Impact of simulated galactic cosmic radiation and hindlimb unloading on the mouse adrenal gland morphology and histology." American Society for Gravitational and Space Biology, Houston, Texas, November 9-12, 2022. Abstracts. American Society for Gravitational and Space Biology, Houston, Texas, November 9-12, 2022. , Nov-2022
Abstracts for Journals and Proceedings	Paul AM, Mitchell C, Burke M, Olson M, Juran C, Christenson LK, Puukila SA, Tabares Ruiz SN, Iyer, JS, Mhatre SD, DuBose, M, Lowe M, Rubinstein L, Sowa M, Shirazi-Fard Y, Alwood JS, Tahimic CGT, Ronca AE. "Integrative endocrine and immune responses to simulated ionizing radiation in mice." 2023 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 7-9, 2023. Abstracts. 2023 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 7-9, 2023. , Feb-2023
Abstracts for Journals and Proceedings	Tahimic CGT, DuBose Mollie, Semel M, Korostenskij I, Santos J, Krikourian O, Palatsidis I, Puukila SA, Mhatre SD, Iyer JS, Paul A, Alwood JS, Shirazi-Fard Y, Rubinstein L, Tabares Ruiz SN, Lowe M, Delp M, Goukassian D, Ronca AE. "Cardiovascular responses to simulated spaceflight: molecular signatures and surrogate outputs to measure CVD risk." 2023 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 7-9, 2023. Abstracts. 2023 NASA Human Research Program Investigators' Workshop, Galveston, Texas, February 7-9, 2023. , Feb-2023
Abstracts for Journals and Proceedings	Ronca AE, Puukila, SA, Tabares Ruiz SN, Iyer JS, Mhatre SD, Dubose M, Hayes J, Siu O, Burke M, Semel M, Lowe M, Rubinstein L, Sowa M, Shirazi-Fard Y, Alwood JS, Paul AM, Tahimic CGT. "Sex-specific effects of simulated spaceflight on immune, neural and behavioral responses in crew age-matched mice." 2022 NASA Human Research Program Investigators' Workshop. Abstracts. 2022 NASA Human Research Program Investigators' Workshop. , Nov-2022
Articles in Peer-reviewed Journals	Burke M, Wong K, Talyansky Y, Mhatre S, Mitchell C, Juran C, Olsen M, Iyer J, Puukila S, Tahimic C, Christenson, L, Lowe M, Rubinstein L, Shirazi-Fard Y, Sowa M, Alwood JS. Ronca A#, Paul A# (#Corresponding Authors) "Sexual dimorphism during integrative endocrine and immune responses to ionizing radiation in mice." Nature Scientific Reports. , Sep-2023
Articles in Peer-reviewed Journals	Puukila S, Siu O, Rubinstein L, Tahimic C, Lowe M, Tabares Ruiz Steffy, Korostenskij I, Semel M, Iyer J, Mhatre S, Shirazi-Fard Y, Alwood J, Paul A, Ronca A. "Galactic cosmic radiation alters acute and delayed species typical behavior in male and female mice." Life, Special Issue on Spaceflight Challenges , Mar-2023
Articles in Peer-reviewed Journals	Mhatre SD, Iyer J, Puukila S, Paul AM, Tahimic CGT, Rubinstein L, Lowe M, Alwood JS, Sowa MB, Bhattacharya S, Globus RK, Ronca AE. "Neuro-consequences of the spaceflight environment." Neurosci Biobehav Rev. 2022 Jan;132:908-35. https://doi.org/10.1016/j.neubiorev.2021.09.055 ; PubMed PMID: 34767877 , Jan-2022