OXIDATIVE STRESS AND THE NEUROCONSEQUENCES OF SPACEFLIGHT ENVIRONMENT - IMMUNE DYSREGULATION AND ANTIOXIDANT DIETARY COUNTERMEASURE EFFICACY

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In this project, we 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 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 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. The project will address NASA's efforts to rapidly advance the characterization of risks and identify 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 female astronauts, the two most recent NASA Astronaut Corps class selections, comprised of ~50% women as compared to men, signal the need to understand how sex differences affect physiological adaptation and health in the space environment. Here, we will determine how key features of the deep space environment may interact to increase risk to crewmembers by negatively impacting health and performance, and identify and develop strategies to characterize and mitigate the potential risks via countermeasures.

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