# A multi targeted dietary supplement as a potential countermeasure for prolonged, deep space exploration

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Deep space exploration, particularly to the Moon and Mars, are currently major goals of NASA and other international space agencies. Long-term space flight presents unique challenges to the human physiology from microgravity, social isolation, altered circadian rhythm and radiation. Oxidative stress has been implicated as a crucial factor in space environment induced injury. Elucidating these detrimental effects on the central nervous system and brain is a primary objective, as they may result in adverse changes in astronaut behavior, mood and performance of critical tasks. We were recently funded by HRP Human Factors Behavioral Performance (HFBP) Element to test the hypothesis that Galactic Cosmic Ray Simulation (GCRsim) 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. 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. Countermeasures to offset neurological damaged and cognitive deficits are paramount for protecting astronauts during deep space transits, but many countermeasures have been found to be unsuitable in ground-based model studies. We have developed a multi targeted dietary supplement (MTDS) designed to simultaneously ameliorate oxidative stress, inflammatory processes, energetic shortfalls, and membrane and mitochondrial deterioration. Administration of this MTDS has improved cognition and longevity in age accelerated and normal aging mice. Specifically, the MTDS was found to prevent a decline in mitochondrial complex III activity and cell loss, as well as prevent an increase in protein carbonyls and mitochondrial 3-nitrotyrosine in the brain of these mice. Further, administration of the MTDS was also found to reduce bone marrow chromosomal aberrations, DNA damage, lymphocyte apoptosis after whole body exposure of 2 Gy γ radiation. Mice exposed to a high dose cranially (10 Gy) had decreased cognitive responses (seen as increased latency time to uncover buried food and decreased novel object recognition), increased plasma 8-OHdG levels, increased markers of cell stress in the brain, decreased hippocampal brain-derived neurotrophic factor (BDNF) protein and decreased plasma levels of cytokines, all of which were ameliorated with treatment of the MTDS. As we have shown the supplement is protective in models of cognitive damage similar space environment stressors, particularly increased oxidative stress, we propose it may be a suitable countermeasure for upcoming deep space exploration.