Fiscal Year:	FY 2014	**Task Last Updated:**	FY 07/26/2013
PI Name:	Mao, Xiao Wen M.D.		
Project Title:	Role of Oxidative Stress in Mediating the Effects of Combined Exposure to Simulated Microgravity and Radiation on Neurovascular Remodeling in Mouse		
Division Name:	Space Biology		
Program/Discipline:	SPACE BIOLOGY		
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	(1) Animal Biology: Vertebrate		
Space Biology Cross-Element Discipline:	(1) Neurobiology		
Space Biology Special Category:	(1) Translational (Countermeasure) Potential		
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Zip Code:	92350-0001	**Congressional District:**	31
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2012 Space Biology NNH12ZTT001N
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No. of Bachelor's Candidates:		**Monitoring Center:**	NASA ARC
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Gridley, Daila Ph.D. (Loma Linda University) Hartman, Richard Ph.D. (Loma Linda University) Pecaut, Michael Ph.D. (Loma Linda University)		
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Task Description:	One of the main concerns for long-term deep manned space missions are health risk associated with altered gravitational environment and prolonged exposure to low-dose radiation above levels normally found on Earth. Microgravity and radiation exposure has known to produce a number of neurological disturbances and neurodegeneration by space flight condition. However, the pathophysiological process from adaptive response to irreversible oxidative damage in the brain vasculature and the underlying mechanism(s) of these disturbances are less studied and remain unclear. Our proposal seeks to fill in gap by testing the hypothesis that NADPH oxidase is a critical source of the neurovascular oxidative stress following space flight condition that mediates vascular remodeling in the brain, thus disrupting communication between endothelial cells and astrocytes and altering production of extracellular matrix (ECM) proteins. It is further proposed that these changes will contribute to increased vascular permeability and blood-brain barrier (BBB) disturbance, thus resulting in neurological deficit. Our specific aims are 1) Define the causal relationships between space flight condition induced NADPH oxidase expression, vascular damage, and BBB function following microgravity and/or low-dose irradiation in mature mice using neuropathology, stereological, and automated image analysis, and neurobehavioral outcomes. 2) Determine if space flight condition-induced oxidative stress is mediated through NADPH oxidase in brain microvasculature. Nox2, (a subunit of NADPH oxidase) gene knockout (Nox2(-/-)) mice and wild-type (Nox2(+/+)) C57BL/6 mice will be used in this ground-based animal study. Hindlimb suspension will be used to model the unloading, fluid shift, and physiological stress aspects of the microgravity component. Low-dose/low-dose-rate (LDR) gamma-irradiation (0.5Gy at 0.01cGy/h) will be delivered to the whole-body of mature adult mice to simulate the radiation component for over 21 days while the animals are tailed-suspended in cages for microgravity simulation. We will evaluate the radiation- and microgravity-induced brain vascular and tissue remodeling at multiple time points (1day to 12 months post-irradiation). Together, our unique, integrative, and quantitative activities with advanced imaging techniques, stereological analysis, and behavioral tests will provide insight into the molecular mechanisms of space flight condition-induced oxidative damage on brain tissue and vascular remodeling. Understanding how factors and environmental stress impact on vasculature, tissue remodeling, and function will increase our knowledge and focus toward more effective countermeasures during human space flight and planetary exploration. Our study will also lend new insights into the causes and possible treatments of debilitating neurovascular-related disease and neurodegeneration by targeting NADPH oxidase activation.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2014.
Bibliography Type:	Description: (Last Updated: 10/12/2024)