Fiscal Year:	FY 2018	**Task Last Updated:**	FY 01/30/2019
PI Name:	Nelson, Gregory A. Ph.D.		
Project Title:	VNSCOR: Responses of the Nervous System to Chronic, Low Dose Charged Particle Irradiation		
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) **Immune**:Risk of Adverse Health Event Due to Altered Immune Response (3) **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:	grnelson@llu.edu	**Fax:**	FY 909-558-4035
PI Organization Type:	UNIVERSITY	**Phone:**	909-558-8364
Organization Name:	Loma Linda University		
PI Address 1:	Basic Sciences, Div. Radiation Research 11175 Campus Street		
PI Address 2:	Chan Shun Pavilion, Room A-1024		
PI Web Page:			
City:	Loma Linda	**State:**	CA
Zip Code:	92350-1700	**Congressional District:**	31
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2016-2017 HERO NNJ16ZSA001N-SRHHC. Appendix E: Space Radiobiology and Human Health Countermeasures Topics
Start Date:	04/15/2018	**End Date:**	11/02/2022
No. of Post Docs:		**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:	Williams, Thomas	**Contact Phone:**	281-483-8773
Contact Email:	thomas.j.will1@nasa.gov		
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Hartman, Richard Ph.D. (Loma Linda University) Mao, Xiao Wen M.D. (Loma Linda University) Rosi, Susanna Ph.D. (University of California San Francisco) Vlkolinsky, Roman Ph.D. (Loma Linda University) Wroe, Andrew Ph.D. (Loma Linda University)		
Grant/Contract No.:	80NSSC18K0785		
Performance Goal No.:			
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Task Description:	[Ed. note Jan 2019: See also project, "VNSCOR: Mechanisms of Radiation-Induced Changes in Sustained Attention and Social Processing" (PI: Catherine Davis)] NELSON/DAVIS VIRTUAL NASA Specialized Center of Research (NSCOR): The project is an combined experimental campaign combined with "Mechanisms of Radiation-Induced Neurobehavioral Defictis (PI: Davis) (see above for official project title) to quantify responses for an interrelated set of central nervous system (CNS) outcome measures in mice to acute and protracted exposures to protons at a dose of 0.5 Gy and sham controls; acute and protracted exposures to 0.25 and 0.5 Gy of charged particles; and acute and protracted exposures to 0.5 and 1.5 Gy of gamma rays. All proposed work will use wild type mice and will be performed under Institutional Animal Care and Use Committee (IACUC) approved protocols in Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC)-certified facilities at Loma Linda University (LLU), the University of California (UCSF), and Brookhaven National Laboratory (BNL). For all three specific aims the species is Mus musculus, strain C57Bl/6J. Ages are 5 - 6 months at acquisition and the beginning of 42 day irradiation procedures. Sexes are males and females. Scheduled sacrifices are at 1 week, 30 days, 90 days, 6 months, and 12 months post-irradiation. Behavioral testing will occur prior to the use of the same animals for terminal assays. All outcome measures will be quantified in males (N=960) and a subset of measures less prone to sex-dependent variability will be quantifies in females (N=220) for a total of N = 1180. ORIGINAL PROPOSAL DESCRIPTION: Evidence has accumulated from animal studies that the central nervous system (CNS) undergoes deleterious changes after exposure to charged particle radiation such as protons and high atomic number atomic nuclei that are found in space as galactic cosmic rays and solar particle events. Observed changes include inflammation, oxidative stress, loss of neuron (dendrite) branches and connections (synapses), altered signaling molecules, altered electrical properties, loss of blood vessels, and impaired behavioral performance. If humans respond to charged particles in the same way as animals, then it is possible that deleterious changes may be sufficient to cause cognitive and other behavioral impairments that could compromise spaceflight missions and astronaut health. The current evidence is based primarily on short exposures to single radiation types. However, space radiation is a complex mixture of these particles and exposures accumulate gradually over the course of missions. It is well established in radiation biology that reduction of the dose rate can have a profound effect on the outcome. Therefore, to better simulate the space environment, we propose to expose adult mice to either 0.5 Gy protons or 0.25 and 0.5 Gy mixtures of helium, oxygen, and silicon particles in 2:1:1 ratios as they are found in space. Then we will deliver the exposures over long time periods (up to 6 weeks) in multiple short exposures (fractions) compatible with particle accelerator operations. These results would be compared to results from acute exposures to establish the Dose Rate Effectiveness Factors (DREFs) which are needed for risk estimation for astronaut health. We predict that the high numbers (fluence) of protons will result in multiple traversals of cells within short times that may elicit interacting biological responses, whereas the lower fluence of higher charged ions will result in rare independent events. DREFs > 1 are predicted for protons and DREFs ~1 are predicted for high Z particles. We will also compare the "protracted" exposures of charged particle mixtures to gamma rays to determine whether they have equivalent dose effects or are more effective. The relative biological effectiveness factor (RBEs) will be derived. These RBEs are utilized in predicting densely ionizing radiation effects in humans for whom only gamma ray and X-ray data are available with the assumption that the ratios obtained in animal models are realistic surrogates for humans. We will test both male and female animals as their responses are not identical and the astronaut population is of mixed gender. For each of the exposure regimens we will conduct a battery of behavior tests, measure electrophysiological properties in tissue slices, and quantify changes in the structure and composition of the tissue using state of the art biochemical, histochemical, and microscopy methods. This will allow us to identify the underlying physiological changes most sensitive to dose rate and radiation quality and how they combine to produce behaviors that are adaptive or maladaptive. Together the data generated by the project will enhance NASA's ability to translate animal assessments of CNS structure and function to humans, and to update risk estimates based on single radiation species, high dose rate irradiation protocols, to higher fidelity space-like exposures of charged particle mixtures delivered at dose rates approaching those observed in space.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2018.
Bibliography Type:	Description: (Last Updated: 03/13/2024)