Fiscal Year:	FY 2012	**Task Last Updated:**	FY 08/24/2011
PI Name:	O'Banion, Kerry M.D., Ph.D.		
Project Title:	Local CNS and Systemic Inflammatory Effects Following Proton and Mixed Particle Exposure		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:	HUMAN RESEARCH--Radiation health		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **SR**:Space Radiation		
Human Research Program Risks:	(1) **BMed**:Risk of Adverse Cognitive or Behavioral Conditions and Psychiatric Disorders		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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City:	Rochester	**State:**	NY
Zip Code:	14642-0001	**Congressional District:**	25
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2008 Space Radiobiology NNJ08ZSA001N
Start Date:	11/01/2008	**End Date:**	10/31/2012
No. of Post Docs:	1	**No. of PhD Degrees:**	0
No. of PhD Candidates:	1	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA JSC
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Finkelstein, Jacob (University of Rochester School of Medicine) Williams, Jacqueline (University of Rochester) Olschowka, John (University of Rochester School of Medicine)		
Grant/Contract No.:	NNX08BA09G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	This proposal continues our investigation of inflammatory responses following exposure to space radiation. In particular, we will explore the effects of protons and mixed particle radiation, at doses and fluences expected during space travel, in the brain and lung as well as the systemic circulation of mice. Dose and time dependent alteration in inflammatory indices will be correlated with brain and lung degenerative changes, including failure of hippocampal neurogenesis and alterations in hippocampal dependent learning. We will also explore whether space radiation influences Alzheimer's disease pathogenesis using a unique transgenic mouse model and lung inflammation following challenge with inhaled lipopolysaccharide. Together these studies will address specific gaps in our current knowledge about the acute and late effects of space radiation on vulnerable tissues.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	In this third year of the grant we completed nearly all of the behavioral, late neuroinflammatory, and neurogenesis analyses for data arising from our first set of irradiations that were conducted in May of 2009. This experiment essentially represents Experiment 1.1 of Specific Aim 1 and Experiment 2.1 of Specific Aim 2. The experiment comprises early (6 and 48 h) time points for histological and mRNA measures as well as later time points (1, 6 and 12 months) for neurogenesis and behavioral studies. We completed behavioral analyses for all time points and did not find any effect of radiation in our fear-conditioning paradigm. However, we did find radiation effects on weight gain with doses of 200 cGy that started 2-3 months after irradiation and persisted to 10 months post-irradiation. There were no adverse out to these late time points. We carried out immunohistochemical studies for neuroinflammatory markers (iba-1 and MHC-II, GFAP, and ICAM-1). Despite our original hypothesis that neuroinflammation would occur in mice exposed to protons, we have not found evidence for this idea. As reported last year, we find modest evidence that proton irradiation has lasting effects on hippocampal neurogenesis. These studies are based on staining for doublecortin, a marker for newly generated neurons. Importantly, we demonstrated an immediate effect of proton irradiation on incorporation of BrdU into hippocampal neural precursor cells, with a dose dependent effect starting at 50 cGy. A second series of exposures, involving nearly 750 mice was conducted as part of NSRL Run 09C. These studies essentially comprised experiments 1.2 and 2.2 (Sex Differences) as well as 1.3 and 2.3 (Mixed particle exposure). We have processed tissues collected in this study and find that BrdU positive cells are reduced in the iron + proton condition relative to control and iron alone conditions, 1 month after irradiation. Importantly, we did not detect any differences between male and female mice with regard to radiation effects on neurogenesis. Behavioral analyses at 6 and 12 months post-irradiation showed no difference between irradiated males and females (100 cGy protons). However we did observe a unique behavioral phenotype in male mice subjected to sequential irradiation with iron and protons: there was no decrease in freezing behavior with irradiation in the contextual task; however, mice irradiated with iron and protons showed a dramatic increase in freezing behavior in the novel context. Although we are not sure what this means, one interpretation is that the mice are hyper-vigilant, perhaps due to increased anxiety. A third run at NSRL was conducted in May 2010, and involved 150 mice being irradiated with protons followed by delayed exposure to inhaled LPS (Aim 4). Mice were tested at 3 and 12 months post irradiation. Behavioral analyses reveal an effect of LPS, but no effect of radiation and no synergy between radiation and LPS exposure as anticipated. Histological evaluation of tissues for markers of neuroinflammation as well as effects on neurogenesis is currently underway. Additional analyses of blood and lung tissue from these mice as well as selected groups of mice irradiated in the first two runs is planned for the upcoming grant period. Seventy-five AD transgenic mice (APPswe/PS-1d9; mixed male and female) were irradiated at 3 months of age using 100 cGy of 56Fe (1 GeV/n) particles during NSRL Run 11A. These mice will be behaviorally tested and sacrificed for tissue analysis at 9 months of age to determine the effects of space radiation on Alzheimer’s plaque pathology. During NSRL 11A we were also able to expose 75 male wild-type mice to a modeled solar flare event using a range of proton energies and a total estimated dose of 200 cGy. These mice and 75 sham-exposed mice will be behaviorally tested and sacrificed at 3, 6 and 12 months post-irradiation.
Bibliography Type:	Description: (Last Updated: 03/11/2025)
Abstracts for Journals and Proceedings	O’Banion MK, Hein A, Sweet T, Hurley SD, Wu M, Trojanczyk L, Olschowka JA, Williams JP. "Hippocampal Neurogenesis and Contextual Fear Response in C57BL/6 Mice Exposed to 2 Gy Whole Body Protons." Oral Presentation during the Space Research Session at the 14th International Congress of Radiation Research, Warsaw, Poland, August 28-September 1, 2011. Meeting Program and Abstracts, 14th International Congress of Radiation Research, Warsaw, Poland, August 28-September 1, 2011. Abstract S03-05. p. 22. , Aug-2011
Abstracts for Journals and Proceedings	O’Banion MK, Hein A, Sweet T, Hurley SD, Wu M, Trojanczyk L, Olschowka JA, Williams JP. "Hippocampal Neurogenesis and Contextual Fear Response in C57BL/6 Mice Exposed to 2 Gy Whole Body Protons." Poster Presentation during the 22nd Annual NASA Space Radiation Investigators' Workshop, League City, Texas, September 18-21, 2011. Program and Abstracts. 22nd Annual NASA Space Radiation Investigators' Workshop, League City, Texas, September 18-21, 2011. , Sep-2011