Fiscal Year:	FY 2020	**Task Last Updated:**	FY 09/17/2020
PI Name:	O'Banion, Kerry M.D., Ph.D.		
Project Title:	Impact of Space-Radiation Induced Alterations on Toxic Protein Accumulation Associated with Neurodegenerative Disease		
Division Name:	Human Research		
Program/Discipline:			
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 Behavioral Conditions and Psychiatric Disorders		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	kerry_obanion@urmc.rochester.edu	**Fax:**	FY 585-756-5334
PI Organization Type:	UNIVERSITY	**Phone:**	585-275-5185
Organization Name:	University of Rochester		
PI Address 1:	Box 603		
PI Address 2:	601 Elmwood Ave		
PI Web Page:			
City:	Rochester	**State:**	NY
Zip Code:	14642-0001	**Congressional District:**	25
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2014-15 HERO NNJ14ZSA001N-RADIATION. Appendix D: Ground-Based Studies in Space Radiobiology
Start Date:	01/29/2016	**End Date:**	11/28/2020
No. of Post Docs:	0	**No. of PhD Degrees:**	3
No. of PhD Candidates:	3	**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:	Elgart, Robin	**Contact Phone:**	281-244-0596 (o)/832-221-4576 (m)
Contact Email:	shona.elgart@nasa.gov		
Flight Program:			
Flight Assignment:	NOTE: End date changed to 11/28/2020 per NSSC information (Ed., 8/25/20)		
Key Personnel Changes/Previous PI:	November 2016: There have been no changes to key personnel.		
COI Name (Institution):	Deane, Rashid Ph.D. (University of Rochester) Majewska, Anna Ph.D. (University of Rochester) Williams, Jacqueline Ph.D. (University of Rochester)		
Grant/Contract No.:	NNX16AE07G		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	In addition to the risk of cancer, there is concern that prolonged exposure of astronauts to deep space radiation will lead to degenerative changes in different organ systems, including the brain. Indeed we previously demonstrated that space radiation impaired cognitive performance and exacerbated Alzheimer's disease (AD) pathology in a widely used mouse model of AD. Accumulation of the toxic peptide amyloid-ß occurs in AD and has been clearly established as an inherited cause of the disease. Space radiation at relatively modest doses elicits chronic inflammation and oxidative stress responses that alter normal brain function and may contribute to amyloid-ß accumulation by inhibiting normal clearance mechanisms. Recent data from our laboratory shows reduced clearance of amyloid-ß in mouse brain many months after exposure to space radiation. Thus, we hypothesize that radiation exacerbates Alzheimer's disease pathology by altering the ability of the brain to remove amyloid-ß. To address this hypothesis we propose experiments that explore three possible cellular mechanisms linking radiation-induced neuroinflammation to reduced amyloid-ß clearance. We also propose to determine whether a drug that reduces brain inflammation and enhances amyloid-ß clearance can mitigate radiation-induced changes in Alzheimer's pathology and cognitive decline in a mouse model of the disease. Taken together, these studies will lead to a better understanding of the biological mechanisms underlying risks for neurodegenerative disease after space radiation exposure.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Our research explores mechanisms by which toxic proteins involved in neurodegenerative diseases might accumulate in brain tissue following radiation exposure. Our results in mice using space-relevant radiation types and doses may inform about possible risks to individuals exposed to radiation on Earth whether during medical procedures or unplanned accidental exposures.
Task Progress:	Reporting period: January 29, 2019 – January 28, 2020. In this fourth year of the grant we carried out irradiations at NASA Space Radiation Laboratory (NSRL) for 2 of our proposed experiments and a new supplemental experiment. More specifically, during NSRL Run 19B, we irradiated 80, 6-month old C57BL/6 female mice with 50 cGy 600 MeV/µ iron, 50 cGy 300 MeV/µ silicon, or 100 cGy protons mimicking an solar particle event (SPE) as a supplement to Experiment 3.1. We also ran 47 additional male and female APP/PS1 mice with iron (50 cGy, 600 MeV/µ) for Experiment 4.1. Finally, as part of a graduate student supplement to this award, we irradiated a total of 80 Thy1-eYGP transgenic mice with or without CR3, male and female with 50 cGy SimGCRSim (n = 10 per group). In all cases appropriate numbers of sham-irradiated mice were similarly processed at the NSRL (e.g., placed in holders for similar times), but not exposed to radiation. All mice were shipped back to Rochester for further experiments. We carried out all behavioral and tissue collections with these animals during the grant period or during a period in 2020 when our laboratory was effectively shutdown due to COVID-19 based on special permission to complete ongoing "irreplaceable" animal based studies. This shutdown slowed our progress with carrying out tissue analyses of mice from experiments 3.1 and 4.1, which are now underway and will be completed in the current and final grant period. We presented three sets of results from this work at the NASA Human Research Program Investigators' Workshop in 2020 and have published 3 CNS (central nervous system) radiation papers (one in 2019, two in 2020) that were partially supported by this grant.
Bibliography Type:	Description: (Last Updated: 03/09/2021)
Abstracts for Journals and Proceedings	O'Banion MK, Deane R, Belcher E, Hinkle J, Dionisio-Santos D, Williams JP, Olschowka JA. "Impact of space-radiation induced alterations on toxic protein accumulation associated with neurodegenerative disease." Presented at 2020 NASA Human Research Program Investigators' Workshop and 30th Annual Space Radiation Investigator's Workshop, Galveston, TX, January 27-30, 2020. Conference Program. 2020 NASA Human Research Program Investigators' Workshop and 30th Annual Space Radiation Investigator's Workshop, Galveston, TX, January 27-30, 2020. , Jan-2020
Abstracts for Journals and Proceedings	Hinkle J, O'Banion MK, Olschowka J. "Does microglial CR3 expression modulate space radiation dependent CNS damage?" Presented at 2020 NASA Human Research Program Investigators' Workshop and 30th Annual Space Radiation Investigator's Workshop, Galveston, TX, January 27-30, 2020. Conference Program. 2020 NASA Human Research Program Investigators' Workshop and 30th Annual Space Radiation Investigator's Workshop, Galveston, TX, January 27-30, 2020. , Jan-2020
Articles in Peer-reviewed Journals	Hinkle JJ, Olschowka JA, Love TM, Williams JP, O'Banion MK. "Cranial irradiation mediated spine loss is sex-specific and complement receptor-3 dependent in male mice." Sci Rep. 2019 Dec 11;9(1):18899. https:// ; PubMed PMID: 31827187; PubMed Central PMCID: PMC6906384 , Dec-2019
Articles in Peer-reviewed Journals	Dionisio-Santos DA, Olschowka JA, O'Banion MK. "Exploiting microglial and peripheral immune cell crosstalk to treat Alzheimer's disease." J Neuroinflammation. 2019 Apr 5;16(1):74. Review. https:// ; PMID: 30953557; PMCID: PMC6449993 , Apr-2019