Fiscal Year:	FY 2010	**Task Last Updated:**	FY 07/29/2009
PI Name:	Wang, Huichen		
Project Title:	Molecular Basis of DNA Repair and Protection from Apoptosis in Neuronal Progenitors Exposed to Space Radiation		
Division Name:	Human Research		
Program/Discipline:	HUMAN RESEARCH		
Program/Discipline--Element/Subdiscipline:			
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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Zip Code:	77446	**Congressional District:**	10
Comments:	Formerly at Emory University, relocated in September 2014 (Ed., 7/7/15)		
Project Type:	Ground	**Solicitation / Funding Source:**	2008 Space Radiobiology NNJ08ZSA001N
Start Date:	10/01/2008	**End Date:**	09/30/2012
No. of Post Docs:	2	**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
No. of Master's Candidates:	1	**No. of Bachelor's Degrees:**	
No. of Bachelor's Candidates:		**Monitoring Center:**	NASA JSC
Contact Monitor:	Cucinott1a, Francis	**Contact Phone:**	281-483-0968
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Reiss, Krzysztof (Temple University)		
Grant/Contract No.:	NNX08BA08G		
Performance Goal No.:			
Performance Goal Text:			
Task Description:	The health risks to astronauts exposed to space radiation include cognitive deficits and possibly accelerated aging. While the pathogenesis of radiation-induced cognitive dysfunction remains largely uncharacterized, it is thought to include loss of neural progenitors from the brain. Understanding of the molecular and cellular bases underlying neuronal loss and/or dysfunction is absolutely required for the development of counter measures before, during and possibly after space missions. Since experiments in humans are not possible, studies in this direction will benefit from appropriate biological model systems. The neurodegenerative effects of space radiation are likely to derive from DNA damage in the central nervous system (CNS). Therefore, research involving repair of this type of DNA lesions is critical for the development of new neuroprotective countermeasures. In the present proposal, we introduce an in vitro model of neural progenitors (neurospheres), which is derive from the brain of mouse embryo from neurodegenerative transgenic mice to study the detrimental effects of space radiation at the mechanistic level. Using this biological model, we will study DNA		

	damage repair and apoptosis of proliferating and differentiated neural progenitor exposed to low dose of high charge and energy nuclei and protons. The proposed studies will provide novel insights into the molecular and cellular mechanisms underlying CNS risks from space radiation and will help to predict and countermeasure health risks from space radiation particularly with regard to effects on the CNS.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	This proposal will study the mechanism of DNA damage and oxidative stress in neuronal cells induced by high energy particle, iron, and protons, compared to X-ray. This study will provide possible ways to develop accurate quantitative estimates to the risk of the central nervous system (CNS) from galactic cosmic ray (GCR) and solar particles events following long-term space travel.
Task Progress:	This is the first year term of NASA funded grant NNX08BA08G. During this period, we run one beam time (1.2 hour of 56Fe 1000 MeV and 2 hours od Proton 1000 MeV) in NASA Space Radiation Laboratory. The PI and two postdoctoral fellow presented the results at the 20th Annual NASA Space Radiation Health Investigators' Workshop, 2009, and Radiation Research Society's 55th Annual Meeting, 2009. One paper had been published in peer reviewed journal. The PI, two postdoctoral fellows, and one master student candidate worked on this project. A Summary of the results: The health risks to astronauts exposed to space radiation include cognitive deficits and possibly accelerated aging. However, the pathogenesis of radiation-induced cognitive dysfunction remains largely uncharacterized. The neurodegenerative effects of space radiation are likely to derive from DNA damage in the central nervous system (CNS). PARP-1 catalyzes poly(ADP-ribosyl)ation on DNA and proteins as immediate response to DNA damage induced by ionizing radiation or following oxidative stress. . In this study, we used an in vitro system based on cultures of mouse embryo neuronal progenitor cells (neurospheres) to study the function of PARP-1 in the induction of clustered DNA damage after low LET an high LET radiation as well as molecular basis of DNA repair. Space radiation induced clustered DNA damage including oxidized base damage, DNA single-strand breaks and double-strand breaks were detected by a modified single cell electrophoresis, and immunodetection of 8-oxo-dG, in neurospheres and PARP-1 proficient and deficient cells. We found that Poly(ADP-ribose) Polymerase 1 (PARP-1) inhibitor induce more DNA damage in neuronal progenitor cells following 56Fe particle and proton irradiation. PARP-1 inhibition also delayed the decay of gamma-H2AX foci and the residual foci associated with new replicated DNA. The level of ATM (Ataxia Telangiectasia Mutated) phosphorylations was increased in neurospheres after treatment with PARP-1 inhibitor and following irradiation. Mutation of PARP-1 in MEF cells dramatically decrease DNA damage repair. These suggest that PARP-1 may play a role in protecting neuronal cells following space radiation. The detail of mechanism and biological effectiveness are under study.
Bibliography Type:	Description: (Last Updated: 11/13/2019)
Articles in Peer-reviewed Journals	Wang H, Liu S, Zhang P, Zhang S, Naidu M, Wang H, Wang Y. "S-phase cells are more sensitive to high-linear energy transfer radiation." Int J Radiat Oncol Biol Phys. 2009 Jul 15;74(4):1236-41. PubMed PMID: 19545789 , Jul-2009