Fiscal Year:	FY 2005	**Task Last Updated:**	FY 02/08/2006
PI Name:	Raber, Jacob Ph.D.		
Project Title:	Neurogenesis and cognition in human apoE transgenic mice following 56Fe radiation		
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:	Portland	**State:**	OR
Zip Code:	97239-3011	**Congressional District:**	1
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2004 Radiation Biology NNH04ZUU005N
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No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**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:			
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Key Personnel Changes/Previous PI:	0		
COI Name (Institution):			
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Of the major human isoforms of apolipoprotein E (E), E4 is associated with age-related cognitive decline and increased risk to develop Alzheimer's disease (AD). The space radiation environment contains 56Fe. 56Fe radiation exposure causes cognitive injury and might predispose E4 subjects to cognitive injury and an earlier onset or more severe extent of AD. The pathogenesis of this injury may involve loss or injury to neural precursor cells in the dentate subgranular zone (SGZ) of the hippocampus, which is involved in complex learning requiring the ability to learn about multiple relationships among stimuli. Disturbances in hippocampal functioning reduce spatial learning and memory. The granule cells of the dentate gyrus are involved in spatial memory and their radiation-induced depletion implicated in cognitive deficits. Our data show reduced numbers of proliferating cells and immature neurons and spatial learning and memory impairments in wild type mice x-irradiated at 2 months and behaviorally tested 3 months later. Treatments that damage neuronal precursor cells or their progeny might reduce neurogenesis and impair hippocampus-dependent cognitive

Task Description:	functions in an E isoform-dependent fashion. Our data indicate that neuronal expression of E3 protects immature neurons against radiation injury and that E3 is more potent than E4 in supporting neuronal proliferation. After irradiation, SGZ precursor cells undergo rapid apoptotic cell death, which might involve oxidative stress. Oxidative stress might also play a critical role in later reductions in hippocampal neurogenesis. E isoforms differ in their ability to protect against neurotoxicity and apoptosis and oxidative stress. Isoform-specific effects of E on 56Fe radiation-induced oxidative stress, apoptosis, and loss of proliferating SGZ cells rapidly after 56Fe-irradiation or oxidative stress later after irradiation might contribute to their effects on cognitive injury later in life. We hypothesize that human E isoforms are associated with different levels of 56Fe-induced loss of neural precursor cells and hippocampus-dependent cognitive injury, and that these effects can be ameliorated by antioxidants. The Specific Aims are: 1A. Determine if E isoform is associated with radiation-induced apoptosis of neural precursor cells in the dentate SGZ; 1B. Determine the role of E isoform in the development of radiation-induced cognitive deficits and whether the severity of these deficits are associated with apoptosis of neural precursor cells in the dentate SGZ. Mice will be tested 3 months following radiation; 1C. Determine how E isoform affects neurogenesis following 56Fe- irradiation, and determine if this effect is related to the severity of radiation-induced cognitive deficits; 2A. Determine if the presence of a specific E isoform is associated with markers of oxidative stress following radiation injury; and 2B. Determine if the antioxidant a-lipoic acid enhances cognitive function and reduces radiation-induced cognitive impairments and whether this ability is E isoform-dependent. Mice will be irradiated with 56Fe ions (0 to 3 Gy). We will assess cognitive impairments using behavioral tests that require hippocampal functioning and quantify of radiation-induced changes using immunohistochemistry.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	Please note that this is a new grant for the FY 2005 year. The investigator will provide a task progress at the time of the one year anniversary of the grant. If you need more information, please contact the Task Book Help Desk at taskbook@nasaprs.com.
Bibliography Type:	Description: (Last Updated: 10/30/2023)