Fiscal Year:	FY 2011	**Task Last Updated:**	FY 09/15/2011
PI Name:	Goldstein, Lee M.D., Ph.D.		
Project Title:	Effects of Space Radiation on Hippocampal-Dependent Learning and Neuropathology in Wild-Type and Alzheimer's Disease Transgenic Mice		
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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Zip Code:	02118	**Congressional District:**	8
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2011 Space Radiobiology NNJ11ZSA001N
Start Date:	09/01/2011	**End Date:**	08/31/2014
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
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Blakely, Eleanor (Lawrence Berkeley National Laboratory) Moncaster, Juliet (Boston University) Stanton, Patric (New York Medical College)		
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Task Description:	The hippocampus and dentate gyrus are critically important brain regions required for long-term memory formation. Damage to these critical brain regions contributes to memory deficits in patients with Alzheimer's disease. The hippocampus and dentate gyrus are also notable as sites where brain stem cells differentiate into new neurons throughout life, a process called neurogenesis. Exposure to space radiation can result in impairments in learning and long-term reduction in hippocampal neurogenesis. It is unknown how radiation causes these impairments and whether and by what mechanism(s) radiation exposure might predispose individuals to develop Alzheimer's disease. This proposal will utilize a well-characterized and widely used Alzheimer's disease transgenic mouse model (Tg2576) to address the following research objectives: (1) examine the long-term impact of space radiation (SR) on hippocampal-dependent spatial learning and memory, (2) evaluate the potential of SR to accelerate Alzheimer's disease pathogenesis and neuropathology, (3) evaluate a novel non-invasive laser-based eye scanner to detect and monitor molecular changes in the lens of the eye induced by radiation exposure and Alzheimer's disease pathology (Goldstein, et al., Lancet, 2003). A complementary companion study will utilize the same cohort of animal subjects to: (1) evaluate electrical communication between neurons, and changes in function and fine structure of neurons, including dendritic spines where synaptic contacts enable neuronal communication, (2) determine whether SR, in reducing neurogenesis, also alters the functionality of newly-born neurons, and (3) assess whether SR differentially affects electrical or physical function of neurons, and/or accelerates the Alzheimer's disease process. Our proposed studies directly address key objectives of the NASA Human Space Flight Program, including determination of potential space-related SR dependencies related to late CNS risks such as early-onset dementia or Alzheimer's disease, assessment of SR effects on molecular, cellular and tissue environment changes in hippocampus indicative of increased risk of dementia or Alzheimer's disease, and evaluation of biological models of Alzheimer's disease or other forms of dementia that occur in humans. The existing knowledge gap is immense and presents a major obstacle to rational assessment of short- and long-term risk to the central nervous system posed by SR exposure expected during extended human space travel. Our experiments will examine, for the first time, the mechanisms by which SR impairs synaptic function in normal brain, assess whether SR does, in fact, enhance long-term risk of Alzheimer's disease, and provide an experimental system to identify and evaluate new radiation countermeasures. The proposed interdisciplinary research program will provide an integrated scientific foundation to assess and reduce SR-induced risk to the brain, thus enabling a safe path forward for extended human space exploration.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2011.
Bibliography Type:	Description: (Last Updated: 03/10/2021)