Fiscal Year:	FY 2021	**Task Last Updated:**	FY 12/02/2020
PI Name:	Maletic-Savatic, Mirjana M.D., Ph.D.		
Project Title:	Counteracting Space Radiation by Targeting Neurogenesis in a Human Brain Organoid Model		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	TRISH--TRISH		
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	77030-3411	**Congressional District:**	9
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2020 TRISH Space Radiation Solicitation TSRAD-2020. Translational Research Institute for Space Health (TRISH) Human-Based Models to Study Effects of Space Radiation and Countermeasures
Start Date:	10/01/2020	**End Date:**	09/30/2022
No. of Post Docs:		**No. of PhD Degrees:**	
No. of PhD Candidates:		**No. of Master' Degrees:**	
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No. of Bachelor's Candidates:		**Monitoring Center:**	TRISH
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Grosshans, David M.D., Ph.D. (The University of Texas M.D. Anderson Cancer Center) Gaber, Mostafa Ph.D. (Baylor College of Medicine) Young, Damian Ph.D. (Baylor College of Medicine) Liu, Zhandong Ph.D. (Baylor College of Medicine)		
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Task Description:	Neurogenesis, the generation of new neurons throughout life, is essential for formation of new spatial memory and mood control in the hippocampus. New neurons are formed from neural stem cells, which are very sensitive to all forms of radiation. If exposed, they die and therefore, neurogenesis declines leading to decline in learning and memory as well as depression. Therefore, understanding this phenomenon in the context of space radiation is of utmost importance if we are to avoid at least some of the cognitive and mental health pathologies during space flight. Herein, we propose to examine neurogenesis in the human brain organoid models exposed to Linear Energy Transfer (LET) proton beam to mimic Galactic Cosmic Rays (GCR). These models are ideal not only to examine the effects of radiation on neural stem cells but also the effects of drug compounds, because they provide a high-throughput system with multiple neurogenic sites (rosettes) and diverse cell types including both neurons and astrocytes. We will use two complementary cerebral organoid models and will expose them to the proton beam at the MD Anderson Proton Center at different time points and different frequency of exposure and will examine molecular, metabolic, cellular, and physiological properties of the variety of cell types that are part of the neurogenic niche. Furthermore, we will take advantage of our new small molecules that promote neural stem cell self-renewal and neurogenesis in animal models in vivo. Based on their mechanism of action, they may also decrease microglial inflammation, thus targeting multiple elements of the neurogenic niche. In addition, we will use transient bursts of electrical stimulation as a non-pharmacological countermeasure to GCR-radiation, as increased neuronal activity promotes neurogenesis. Overall, our proposal is responsive to all requirements of this solicitation and stands to deliver new data relevant to the effects of space radiation on multiple human cell types that are part of the neurogenic niche and the efficacy of countermeasures on molecular, metabolic, cellular, and physiological properties of these cells. Our work focuses on neurogenesis as this is the only natural mechanism to regenerate lost brain tissue in vivo in the center for learning and memory and mood control. Thus, the relevance to this solicitation and NASA objective in general is high.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project for FY2021.
Bibliography Type:	Description: (Last Updated: 10/20/2022)