Fiscal Year:	FY 2020	**Task Last Updated:**	FY 01/04/2021
PI Name:	Vunjak-Novakovic, Gordana Ph.D.		
Project Title:	Organs on a Chip Platform for Assessing Cosmic Radiation Damage		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:	TRISH--TRISH		
Joint Agency Name:		**TechPort:**	Yes
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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Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	TRISH--Focused Investigations
Start Date:	06/01/2019	**End Date:**	09/30/2020
No. of Post Docs:	2	**No. of PhD Degrees:**	0
No. of PhD Candidates:	1	**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:**	TRISH
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date changed to 9/30/2020 (originally 5/31/2020) per TRISH (Ed., 6/5/2020)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Garty, Guy Ph.D. (Columbia University) Brenner, David Ph.D. (Columbia University) de Nooij, Joriene Ph.D. (Columbia University)		
Grant/Contract No.:	NNX16AO69A-FIP0014		
Performance Goal No.:			
Performance Goal Text:			
Task Description:	Focused Investigation Project This project will implement a novel “organs on a chip” platform to investigate the effects, mechanisms, and protective measures related to cosmic radiation. Human tissues will be bioengineered from induced pluripotent stem cells (iPS cells), matured, physiologically connected by vascular perfusion containing immune cells, and subjected to space radiation and simulated microgravity, separately or simultaneously.		

Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	The significance of our project is that we have made advances in: (1) developing a predictive organs-on-a chip human multi-organ platform for studying effects of radiation damage, (2) tissue engineered organ models for the bone marrow, cardiac muscle, and sensory neurons, and (3) preliminary data on the effects of radioprotective agents on irradiated tissues. Radiation exposure poses significant risks to human health and is associated with a host of both acute and chronic sequelae. Most notorious of the short-term effects of radiation exposure is acute radiation sickness (ARS), which is caused by acute exposures to >1 Gy of radiation and can be broken down into three subtypes: hematopoietic, gastrointestinal, and cerebrovascular. Chronic effects of low-dose, protracted radiation exposure include cataracts, cardiovascular disease, cognitive impairment, reproductive issues, and, most notably, cancer. The types of radiation exposure can be broken down into two categories: low-linear energy transfer (LET) radiation and high-LET radiation. Low-LET radiation consists of x-rays and gamma radiation (from 60-Co or 37-Cs sources, for example). Generally speaking, low-LET radiation causes damage within the cell indirectly through the formation of free radicals. High-LET radiation consists of protons, alpha particles, neutrons, and various high-charge and energy ions called HZE particles. HZE particles are small (<1%) but highly damaging components of galactic cosmic radiation (GCR). They include carbon, silicon, iron, oxygen, neon, magnesium, and calcium ions. High-LET radiation causes direct damage to the cell, including complex DNA damage and alterations to DNA repair pathways. Space radiation consists primarily of protons, followed by alpha particles, and then HZE particles. Neutron radiation is a secondary type of radiation produced when primary components of Galactic Cosmic Rays (GCR) interact with target material, such as spacecraft or human tissue. While HZE particles are a small fraction of GCR, they are the most damaging components to human tissues, forming wide tracks of damage when passing through cells and are of greatest risk for potential deep-space missions. Studies on the effects of high-LET radiation, including those in space and as a result of nuclear warfare, have largely been limited due to the complex logistics and high costs associated with conducting experiments in space. NASA's Brookhaven National Laboratory has developed a terrestrial galactic cosmic ray simulator (GCRSim) comprising of seven different ion types at several energies for a series of 33 separate beams over the course of a single exposure. Simpler radiation source systems, comprising of one or two high-LET radiation types (i.e., mixed neutron, Fe-ion, etc.), are more commonly used by researchers to simulate space radiation given accessibility and experimental constraints. Nevertheless, most of these studies are limited to small animal and 2D human cell culture models. Since human tissue often responds differently to radiation damage than animal tissue, especially in response to injury and repair, experimental data in mice and other small animals have had limited translational use. Human tissue platforms for in vitro studies of integrated human physiology in health and disease are becoming increasingly predictive of clinical data. However, there are no human tissue-based models of the effects of high-LET, mixed neutron radiation exposure that enable predictive studies of the risks associated with spaceflight and the mitigation of these risks. This project was conducted to address this critical gap, through a highly innovative design and validation of a human organs on a chip model of radiation exposure and the use of this model for assessing radiation damage and radiation protective medicines.
Task Progress:	The exact effects of cosmic radiation, the most serious risk encountered during long missions to Moon and Mars (red risk), are still uncertain. There is a compelling need to better understand the safety thresholds and mechanisms of various types of tissue/cell/DNA damage, in order to develop safe and effective measures for radiation protection during extended space travel. The development of human cell based experimental models that are predictive of human physiology would be transformative for understanding and countering the damage caused by cosmic radiation. This proposal is to implement our organs on a chip platform to investigate the effects, mechanisms and protective measures related to cosmic radiation. A combination of human tissues (among heart, liver, bone, bone marrow, skin, sensory neurons, innervated muscle) can be bioengineered from induced pluripotent stem (iPS) cells, matured and physiologically connected by vascular perfusion containing immune cells. We demonstrated the predictive power of this platform for modeling injury and disease. With the addition of strong expertise in radiation biology, we now propose to investigate radiation damage and prevention. Three specific aims will be pursued in an integrated fashion. In Aim 1, we will irradiate the individual tissues with ions that are found in space, and determine the effects of radiation and safety thresholds for each tissue. By using the compact microgravity simulator we have designed and built, we will allow the effects of space radiation exposure and microgravity to be assessed both separately and interactively. In Aim 2, parallel studies will be conducted using multi-tissue platforms with vascular perfusion and circulating immune cells, again with and without exposure to simulated microgravity. In Aim 3, we will investigate the use of radiation-protective agents. The project will be driven by milestones and deliverables and is expected to result in significant new data and a radically new, enabling approach to studies of radiation damage and protection in support of long space missions.
Bibliography Type:	Description: (Last Updated: 04/24/2024)
Articles in Peer-reviewed Journals	Zhuang RZ, Lock R, Liu B, Vunjak-Novakovic G. Review. "Opportunities and challenges in cardiac tissue engineering from an analysis of two decades of advances." Nat Biomed Eng. 2022 Apr 27;6(4):327-38. Review. https://doi.org/10.1038/s41551-022-00885-3 ; PMID: 35478227 , Apr-2022