Fiscal Year:	FY 2020	**Task Last Updated:**	FY 10/22/2020
PI Name:	Buettmann, Evan Ph.D.		
Project Title:	Investigating the Effects of Simulated Microgravity Duration and Connexin 43 Deficiency on Bone Fracture Healing		
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:	23284-9097	**Congressional District:**	4
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2020 TRISH-RFA-2001-PD: Translational Research Institute for Space Health (TRISH) Postdoctoral Fellowships
Start Date:	09/01/2020	**End Date:**	08/31/2022
No. of Post Docs:	1	**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:**	TRISH
Contact Monitor:		**Contact Phone:**	
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Key Personnel Changes/Previous PI:			
COI Name (Institution):	Donahue, Henry Ph.D. (MENTOR: Virginia Commonwealth University)		
Grant/Contract No.:	NNX16AO69A-P0501		
Performance Goal No.:			
Performance Goal Text:			
	POSTDOCTORAL FELLOWSHIP Astronauts exposed to long periods of unloading due to extended spaceflight experience on average a decrease in bone strength at 2.0 – 2.5% per month. This sharp decline in bone strength can predispose astronauts to fragility fractures, especially when re-entering a gravity-based loading environment due to extra-vehicular activities, extraterrestrial exploration, off-nominal spacecraft landings, and or upon return to Earth. While emerging evidence suggests that unloading, as would occur in microgravity during spaceflight, impairs fracture healing, the cellular and molecular mechanisms by which this occurs largely remains unknown due to a lack of ground based rodent analog models mimicking spaceflight conditions. Understanding the mechanisms underlying the microgravity induced impairment in bone regeneration following fracture will lead to the development of new countermeasure targets. One potential		

Task Description:	countermeasure target is Connexin 43 (Cx43), the primary gap junction protein in bone. Gap junctions facilitate intercellular communication between neighboring bone cells such as osteoblasts and osteocytes and have been strongly implicated in bone fracture healing and bone adaptation to the mechanical environment. In order to study how the duration of microgravity and Cx43 affect fracture healing outcomes, a novel murine healing model undergoing different periods of unloading before and during fracture healing will be developed and characterized. This model will be created by combining the ground-based microgravity analog, hindlimb unloading, in conjunction with an established mouse endochondral bone healing model, the stabilized open surgical femoral fracture model. Bone healing outcomes via molecular, histological, mechanical, and cellular techniques will be evaluated in wildtype and Cx43 transgenic mice. Furthermore, biomarker characterization of healing progression will be evaluated. The outcomes of this research will provide better mechanistic insight into how microgravity and gravitational reloading such as that found during spaceflight and terrestrial exploration, respectively, affects bone healing. Furthermore, this proposal will identify whether possible treatment strategies targeting Cx43 and or other biological targets is an efficacious approach to augment bone healing during microgravity.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	
Task Progress:	New project FY2020.
Bibliography Type:	Description: (Last Updated: 01/11/2023)