Fiscal Year:	FY 2022	**Task Last Updated:**	FY 01/12/2023
PI Name:	Didier, Kaylin Ph.D.		
Project Title:	Ionizing Radiation and Immune Responses: Exploring Sex Differences		
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		
PI Email:	didier2@wisc.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	580-623-1941
Organization Name:	University of Wisconsin, Madison		
PI Address 1:	Department of Kinesiology		
PI Address 2:	200 Observatory Dr		
PI Web Page:			
City:	Madison	**State:**	WI
Zip Code:	53715	**Congressional District:**	2
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2021 TRISH-RFA-2101-PD: Translational Research Institute for Space Health (TRISH) Postdoctoral Fellowships
Start Date:	09/01/2021	**End Date:**	12/31/2023
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:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: End date changed to 12/31/2023 per TRISH (Ed., 8/5/23) NOTE: End date changed to 08/31/2023 per TRISH (Ed., 2/23/23)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Schrage, William Ph.D. (MENTOR: University of Wisconsin, Madison)		
Grant/Contract No.:	NNX16AO69A-P0603		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	POSTDOCTORAL FELLOWSHIP Astronauts will soon be deploying on deep space missions to Mars, and will be exposed to continuous low dose, high energy ionizing radiation (IR). This IR is different from Earth orbit radiation; therefore, this kind of space radiation may lead to undefined acute and chronic health problems from continuous radiation exposure. Previous research on the effects of space radiation have predominantly studied male astronauts. Data from cancer patients receiving radiation, or animal research, suggest women might show an exaggerated inflammation response, making them more likely to develop diseases of the heart or blood vessels (vascular cells). These unknown sex differences remain as unexplored as deep space. The purpose of this fellowship proposal is to investigate how men and women differ in their immune and vascular response to IR, as radiation may increase or accelerate disease burden in astronauts who traveled into deep space. The first study goal is to test increasing levels of IR to see if the inflammation response is more sensitive in one sex versus the other. Immune cells from healthy adults will be exposed to IR and followed for 24 hours. Measurements include signals the cells produce, signals inside and on the surface of immune cells that change their function. In the second study, immune and vascular cells are placed together after IR, to see if crosstalk between cells is different between the sexes. Methods from study one will be repeated in both cell types, plus measuring adhesion molecules on the surface of vascular cells that allow immune cells to bind and amplify inflammation. Crosstalk is expected to magnify the inflammation response. The findings are expected to help develop sex-specific interventions to minimize risk from IR, so astronaut health and mission success are maximized.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	To address several of the noted limitations from both clinical, animal, and cellular studies, and to make a substantial inroad into human pathophysiology of IR, our approach includes the following: 1) tightly controlling repeatable radiation type and dose rate relevant to space environment, 2) well-characterized healthy adult population, with robust sex hormone profiling, 3) quantifying numerous circulating biomarkers which focus on a key control points in vascular inflammation (S100A8/9, DAMPs, cytokines), and 4) immune-vascular interactions to interrogate a complex network of radiation damage and immunologic response. Moreover, our research team expertise encompasses immunology and cardiovascular physiology to maximize interpretation of data. In summary, our innovative research design and study team are poised to make a substantial leap forward into understanding sex-specific mechanisms of ionizing radiation damage.
Task Progress:	Astronauts will soon be deploying on deep space missions to Mars, and will be exposed to continuous low dose, high energy ionizing radiation (IR). This IR is different from Earth orbit radiation; therefore this kind of space radiation may lead to undefined acute and chronic health problems from continuous radiation exposure. Previous research on the effects of space radiation have predominantly studied male astronauts. Data from cancer patients receiving radiation, or animal research, suggest women might show an exaggerated inflammation response, making them more likely to develop diseases of the heart or blood vessels (vascular cells). These unknown sex differences remain as unexplored as deep space. The purpose of this fellowship proposal is to investigate how men and women differ in their immune and vascular response to IR, as radiation may increase or accelerate disease burden in astronauts who travel into deep space. The first study goal is to test increasing levels of IR to see if the inflammation response is more sensitive in one sex versus the other. Immune cells from health adults will be exposed to IR and followed for 24 hours. Measurements include signals the cells produce, signals inside and on the surface of immune cells that change their function. In the second study, immune and vascular cells are placed together after IR, to see if crosstalk between cells is different between the sexes. Methods from study one will be repeated in both cell types, plus measuring adhesion molecules on the surface of vascular cells that allow immune cells to bind and amplify inflammation. Crosstalk is expected to magnify the inflammation response. The findings are expected to help develop sex-specific interventions to minimize risk from IR, so astronaut health and mission success are maximized. The only remaining steps from year 1 to complete are actual radiation exposure of cells (1 week) with follow-up immunology assays and analysis (2 weeks); thus, we feel confident we are largely on track for this fellowship. We have increased recruitment for the biospecimen samples during the second half of the year and are currently at 100% of male and 73% of female samples collected. Looking forward toward Year 2, we aim to: • Submit at least 2 manuscripts from Aim 1 data. • Learn laboratory culture practices to grow endothelial cells and study the interactions between endothelial cells and immune cells-the goal for Aim 2. • Complete the second round of irradiation (Year 2) allowing flexibility for follow-up or confirmation experiments based on Aim 1 findings. • Repeat radiation studies on other immune cell types for preliminary data for future grants.
Bibliography Type:	Description: (Last Updated:)