

Fiscal Year:	FY 2021	Task Last Updated:	FY 01/17/2022
PI Name:	Bowles, Dawn Ph.D.		
Project Title:	Awakening Endogenous Retroviruses with the Space Environment		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline-- Element/Subdiscipline:			
Joint Agency Name:	TechPort:	No	
Human Research Program Elements:	(1) HHC: Human Health Countermeasures		
Human Research Program Risks:	(1) Immune: Risk of In Mission Impacts, Adverse Health Events or Long-Term Health Impacts due to Altered Immune Response		
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:	2018 HERO 80JSC018N0001-Crew Health and Performance (FLAGSHIP, OMNIBUS). Appendix A-Flagship, Appendix B-Omnibus
Start Date:	10/01/2019	End Date:	12/31/2022
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No. of PhD Candidates:	No. of Master' Degrees:		
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No. of Bachelor's Candidates:	Monitoring Center: NASA JSC		
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Flight Program:			
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COI Name (Institution):			
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Task Description:	<p>Approximately 8% of the human genome is composed of Endogenous Retrovirus (ERVs). These genetic elements have helped shape humans as they exist today. ERVs are normally maintained in a silenced state but non-specific activation of ERVs can occur through application of exogenous stressors, and may have detrimental consequences to the host. Indeed, within the last 5 years a number of studies have demonstrated ERVs to be associated with autoimmune diseases, cancer, and neurological diseases. Extended space travel will expose astronauts to the space radiation and microgravity environments; both of these stressors may influence genomic modifications that may result in non-specific activation of ERVs. Activation of ERVs may result in alterations to molecular pathways within different cell types that might influence negative pathogenic outcomes during space flight. The key central objective of this proposal is to understand how the physical space environment might influence activation of ERVs. We will accomplish this research objective in two aims. In the first aim we will utilize a bioreactor to grow cells in a microgravity environment and evaluate the cells by molecular and immunofluorescence techniques for evidence of ERV activation under this space stressor. The second aim will utilize an established tissue repository that contains multiple tissues from mice exposed to various types and doses of space radiation. We will examine these tissues molecularly and histologically for evidence of ERV activation. This project is significant in that identification of ERVs that respond to specific space conditions may function as early, surrogate markers of putative genomic change. Furthermore, expression of ERV-encoded proteins may be seen as foreign and elicit autoimmune responses.</p>
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	<p>Overall some progress has been made demonstrating the increase in cells with dsRNA (and possibly endogenous retrovirus reactivation) following both gamma and galactic cosmic radiation (GCR) exposure. This project is significant in that identification of ERVs that respond to specific space conditions may function as early, surrogate markers of putative genomic change. Furthermore, expression of ERV-encoded proteins may be seen as foreign and elicit autoimmune responses.</p>
Task Progress:	<p>A549 (human lung fibroblasts) cells, used for radiation, microgravity, and combined effects (10 Gy Gamma + microgravity) experiments, were cultured 3 days prior to treatment. 500 x 10(3) A549 cells were cultured per T-25 for radiation experiments using standard cell culturing techniques and media (10% FBS containing DMEM with high glucose and pyruvate). For microgravity (n=2) and combined effects (n=2) experiments, 350 x 10(3) A549 cells were cultured per Synthecon cell rotator with Cytodex(3) microcarriers. A459 cells were exposed to Gamma at Duke University using the J. L. Shepherd Mark I Model 68A 137Cs Gamma irradiator (8 Gy (n=12) and 10 Gy (n=8)). Each experimental group was treated at the same time and harvested for 2-day and 5-day post-radiation assessment using flow cytometry A459 cells irradiated at Brookhaven National Laboratory (BNL) and harvested at 1-day post-radiation for flow cytometry (150 cGy GCR5-ion samples (n=4)). For all experiments, untreated controls were cultured and harvested identically to their treated counterparts. Indirect flow cytometry assay was developed using the J2 primary antibody, mouse monoclonal anti-double stranded (ds) RNA antibody from Jena Bioscience GmbH, and secondary antibody, Alexa 488 conjugated anti-mouse IgG polyclonal antibody from BioLegend. All cells were fixed and permeabilized using eBioscience™ Foxp3 / Transcription Factor Staining Buffer Set from Invitrogen. 10,000 events were recorded per sample and FlowJo v10.8 (Becton, Dickinson and Company) was used to gate singlet populations for average median fluorescence intensity (aMFI) of detected dsRNA.</p> <p>For individual effects treated samples at 2-days post-radiation, only 8 Gy Gamma showed a significant elevation in aMFI—a 1.30-fold increase (p=0.0175). Combined 10 Gy Gamma and microgravity effects at the 2-day post-radiation timepoint showed a 1.73-fold increase (p=0.0002) in aMFI compared to normal gravity controls and a 1.94-fold increase (p<0.0001) in aMFI compared to 10 Gy Gamma only treated samples. 5-days post-radiation results, however, showed statistical significance across all experimental treatment groups; 8 Gy Gamma, 10 Gy Gamma, and microgravity treated samples showing a 1.33-fold increase (p=0.0155), 2.13-fold increase (p=0.0004), and 2.41-fold increase (p=0.0004) in aMFI, respectively. Combined effects of 10 Gy Gamma and microgravity at the 5-day post-radiation timepoint showed a 4.72-fold (p<0.0001) increase in aMFI compared to normal gravity controls and a 1.96-fold (p=0.0215) increase in aMFI compared to microgravity only treated samples. 1-day post-radiation samples irradiated with GCR5-ion displayed a 1.21-fold increase in aMFI although it was not statistically significant (p=0.47).</p> <p>This study was significantly affected by Covid 19 shutdown. From another study we have developed an extensive tissue repository of mice that have been exposed to various type of radiation including 5 ion GCR sim. Now that we have developed the indirect immunofluorescence assay with the J2 antibody we plan to evaluate some of the tissue in this repository.</p>
Bibliography Type:	Description: (Last Updated: 03/11/2025)