Fiscal Year:	FY 2021	**Task Last Updated:**	FY 09/14/2021
PI Name:	Cromer, Walter Ph.D.		
Project Title:	The Effect of Simulated Space Radiation on the Interaction of the Metabolome, Immune System, and Lymphatic Anatomy of the Gastrointestinal Tract		
Division Name:	Human Research		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	(1) **SR**:Space Radiation		
Human Research Program Risks:	(1) **Cancer**:Risk of Radiation Carcinogenesis (2) **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:			
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No. of Post Docs:	0	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**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:**	NASA JSC
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:	September 2021 report: No changes		
COI Name (Institution):	Endsley, Mark Ph.D. (University of Texas, Galveston)		
Grant/Contract No.:	80NSSC20K1436		
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Task Description:	We will examine the changes that space relevant radiation have on the immune system, vascular architecture, and metabolome (bacterial products of metabolism) of the gastrointestinal (GI) tract. We know that each of these factors interact with each other to create a balanced system that ensures normal function of the digestive tract (digestion, nutrient absorption, protection from pathogens, tolerance of commensal bacteria) and promote the health of the whole organism. We believe that space radiation is the primary driving factor in imbalances between these factors which leads to system dysfunction. We will assess each of these factors (metabolome, immune, and vascular) in a manner that allows us to make conclusions about not only the state of each component individually but how it could impact the other systems. We will use standard metabolomic analysis of cecal contents (mass spectroscopy) accompanied by RNA deep sequencing to examine the pathways associated with those changes. This will allow us to determine if there are changes in metabolites that impact immune and GI function (indole, butyrate, etc.) and why. We will use immunofluorescent staining of sections of the bowel wall, Peyer's patches, and mesenteric lymph node to determine changes in the number and distribution of immune cells in the tissue. We will pair this with RNA sequencing of those tissues to determine the activation status of the cells and in the cases of the Peyer's patches and mesenteric nodes the production of factors (IL-7, CCL19, CCL21, etc.) by the stromovascular fraction that maintain a normal environment for the immune cells within. Finally, we will stain the aforementioned tissues for vascular markers (CD31, Lyve-1, etc.) to determine if there are changes in the vascular structures of the tissue. We will deliver a number of products from this proposal including the data listed as well as broad genomic and metabolomic data that will be archived for use by other investigators. More specifically we will provide data pertaining to degenerative effects of simulated space radiation on the interlocking systems of the metabolome, immune, and vascular system of the GI tract. The significance of this proposal is that it will be the first proposal to address the 3 listed components, metabolome, immune, and vasculature as a single system. We will also determine mechanistically how simulated space radiation interferes with each component individually and how that impacts the other linked systems.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	In addition to providing information on the effects of galactic cosmic radiation (GCR) simulated radiation this work will provide the first in depth analysis of the effect of radiation on lymphatic vessels. While there has been some work on radiation and lymph node and lymphatic endothelium there is no work on the effects on the conduit vessels. This will provide important information on the secondary effects of radiation therapy in association with lymphedema.
Task Progress:	Currently we have completed the initial phase of RNA deep sequencing of 2 tissues associated with the GI tract, the large bowel wall, and the mesenteric lymph node. These tissues along with mesenteric lymphatic vessels, small bowel wall, Peyer's patches, and cecum were isolated in later January 2021 and submitted to the Texas A&M University (TAMU) RNA sequencing core. As of September 14th 2021, we have only received the data from the large bowel and mesenteric lymph node. This data represents only a partial picture but there is a pattern emerging in part of the data. Bearing in mind this data only comes from males (female samples were scheduled for year 2 to confirm no issues existed with the tissue), which are more susceptible to form colorectal cancer (CRC), there is a distinct genomic pattern emerging that matches the fingerprints associated with azoxymethane + dextran sodium sulfate (AOM+DSS) model of CRC in gamma irradiated animals. Interestingly, the GCR irradiated animals had a randomly dispersed pattern of expression that did not match CRC or other cancers that have been described. We are using a drug matching AI driven analysis to interpret what pathology this most closely resembles. In addition to the general CRC finding there are a number of general cancers related micro RNAs that are altered by both gamma and GCR. The genes we had identified as critical to maintaining normal immune homeostasis within the lymph node were also changed but not in the manner we suspected. We presumed that the genes that maintain homeostasis would be decreased by radiation as injury to the cells of the stromovascular fraction reduced their viability. This does not seem to be the case. There were in fact changes but they almost universally were in the positive direction. This would suggest either an active immune response is occurring (which may be due to tissue injury) or a compensation to potential loss of homeostasis. These changes are also being mapped by AI and will hopefully yield a more precise picture of what is occurring. Currently, we are preparing tissues from the female animals for sequencing and will submit tissues for metabolomics as a batch (male and female) as they are more sensitive to batch variation. This will complete in the next 3-6 months depending on core backlogs. We have encountered one major issue with the completion of the grant. Due to COVID restrictions we were not able to participate in the final campaign from our collaborators' experiment and were unable to fix those tissues for microscopy. They did provide the tissue frozen which was already a monumental undertaking for the group due to limited workforce (and which we are very grateful for). We will substitute a number of biochemical assays to replace some of the data that microscopy would provide.
Bibliography Type:	Description: (Last Updated: 10/23/2024)