Fiscal Year:	FY 2023	**Task Last Updated:**	FY 10/28/2022
PI Name:	Mason, Christopher Ph.D.		
Project Title:	Spatiotemporal Mapping of the Impact of Spaceflight on the Heart and Brain		
Division Name:	Space Biology		
Program/Discipline:			
Program/Discipline--Element/Subdiscipline:			
Joint Agency Name:		**TechPort:**	No
Human Research Program Elements:	None		
Human Research Program Risks:	None		
Space Biology Element:	(1) Cell & Molecular Biology (2) Animal Biology: Vertebrate		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
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Zip Code:	10021-5663	**Congressional District:**	12
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2020 Space Biology NNH20ZDA001N-SB E.12. Flight/Ground Research
Start Date:	12/01/2021	**End Date:**	11/30/2024
No. of Post Docs:	1	**No. of PhD Degrees:**	1
No. of PhD Candidates:	2	**No. of Master' Degrees:**	1
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	1
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA ARC
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Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:	NA		
COI Name (Institution):	Costes, Sylvain Ph.D. (NASA Ames Research Center) Galazka, Jonathan Ph.D. (NASA Ames Research Center) Giacomello, Stefania Ph.D. (Kungliga Tekniska Hogskolan)		
Grant/Contract No.:	80NSSC22K0254		
Performance Goal No.:			
Performance Goal Text:			
Task Description:	To prepare for future human exploration missions far from Earth, NASA's Space Biology Program is seeking to build a better understanding of the effects of spaceflight and zero gravity on the biology of microorganisms, plants, and animals in spacecraft, the International Space Station (ISS), and also in ground-based analog experiments. The National Research Council recommended that NASA undergo studies to elucidate the effects of short and long duration spaceflight on the biology of all three categories of organisms. Technological advances in next-generation sequencing (NGS), spatial transcriptomics, and proteomics (spatial omics), several of which we describe below, create an unprecedented opportunity for in-depth molecular studies applicable to the purposes of NASA's Space Biology Program. This provides scientists, engineers, and clinicians a more comprehensive view of the functional dynamics of organisms as they evolve and respond to unique or highly selective environments including the ISS. Spaceflight causes changes in cell signaling pathways that are better understood only by increasing the analysis resolution level. In this project, we will deploy new technologies, i.e. spatial transcriptomics, single-nucleus RNA-sequencing, multi-omic spatial mapping (human and microbial), and systems biology algorithms to discover new insights relevant to the impact of spaceflight on human health. These data and methods will shed light on the complex biosystem dynamics that spaceflight causes in humans. We will be able to clearly dissect the gene expression changes occurring at the single-cell level, analyze how these changes affect the cell-cell genetic and physical interactions, and begin the first-ever in vivo human-microbial interaction maps from spaceflight. To do so we will conduct rigorous and cutting-edge omics analysis using two complementary platforms (10x Genomics Visium and Nanostring's GeoMx) with six main rodent organs collected		

	throughout several past spaceflight missions and their corresponding ground controls. Our integrated biology approach will allow us to understand physiological, anatomic, and molecular mechanisms of adaptation and response in animals to spaceflight. For our organism-wide study we will leverage the extensive amount of samples collected throughout several Rodent Research (RR) missions which are accessible through the Life Sciences Data Repository (LSDA). Several of these specimens have already been allocated for Dr. Mason through LSDA. Our study will represent the first-of-its-kind in space biology and will provide foundational discoveries that will allow us to understand not only how astronaut conditions can be improved during spaceflight, but also how the changes induced by spaceflight can be translated into modern medicine to improve human health on Earth. Moreover, we will apply several statistical and machine learning techniques in order to predict changes induced by spaceflight at the organism level for future long-term missions.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	We will be able to clearly dissect the gene expression changes occurring at the single-cell level, analyze how these changes affect the cell-cell genetic and physical interactions, and begin the first-ever in vivo human-microbial interaction maps from spaceflight. To do so we will conduct rigorous and cutting-edge omics analysis using two complementary platforms (10x Genomics Visium and Nanostring's GeoMx) with six main rodent organs collected throughout several past spaceflight missions and their corresponding ground controls. Our integrated biology approach will allow us to understand physiological, anatomic, and molecular mechanisms of adaptation and response in animals to spaceflight.
Task Progress:	Overall progress and work to date: In the past year, we have focused efforts on curating and testing banked tissues for processing with spatial and single-cell methods. Specifically, we have focused on the retinal tissues (acquired and tested), liver, brain, femur, heart, and duodenum. We have dissected test samples from donor mice in our laboratory, and processed on Visium, and also we have run one sample through single-nucleus RNA-seq (snRNA-seq) using the 10xGenomics Chromium controller and assay. So far, we have: 1) Completed sample selection and quality control (QC), including the RNA Integrity Number (RIN) and cell count matrices; 2) Ran two Visium tests and continued data processing optimization; 3) Tested single nucleus RNA sequencing (snRNA-seq) on retina tissues, and finished the sequencing; 4) Tested the new SpaTial Enhanced REsolution Omics sequencing (STEREO-seq) spatial biology tool, to use as an orthogonal method if needed. Of note, we have also established a collaboration with NanoString Technologies (NanoString) to optimize the processing of samples for the GeoMx Digital Spatial Profiler system, and we have also placed an order to acquire the latest instrument that has the highest resolution for profiling tissues, call the CosMx, which is slated for delivery in Q4 2022 at Weill Cornell Medicine. We have one paper that used the methods described in our grant for spatial biology profiling in COVID-19 patients: Park J, Foox J, Hether T, Danko DC, Warren S, Kim Y, Reeves J, Butler DJ, Mozsary C, Rosiene J, Shaiber A, Afshin EE, MacKay M, Rendeiro AF, Bram Y, Chandar V, Geiger H, Craney A, Velu P, Melnick AM, Hajirasouliha I, Beheshti A, Taylor D, Saravia-Butler A, Singh U, Wurtele ES, Schisler J, Fennessey S, Corvelo A, Zody MC, Germer S, Salvatore S, Levy S, Wu S, Tatonetti NP, Shapira S, Salvatore M, Westblade LF, Cushing M, Rennert H, Kriegel AJ, Elemento O, Imielinski M, Rice CM, Borczuk AC, Meydan C, Schwartz RE, Mason CE. System-wide transcriptome damage and tissue identity loss in COVID-19 patients. Cell Reports Med. 2022 Feb 15;3(2):100522. https:// We have two other papers in review about the Spatial Tissue analysis algorithms, which we expect to be published in 2023. Also, I have been serving on the National Academies of Science (NAS) Decadal Survery Panel on Research in Space for NASA, where many of the tools and methods described in our grant are being added to the NAS report that will be sent to Congress: https://
Bibliography Type:	Description: (Last Updated: 07/10/2024)
Articles in Peer-reviewed Journals	Park J, Foox J, Hether T, Danko DC, Warren S, Kim Y, Reeves J, Butler DJ, Mozsary C, Rosiene J, Shaiber A, Afshin EE, MacKay M, Rendeiro AF, Bram Y, Chandar V, Geiger H, Craney A, Velu P, Melnick AM, Hajirasouliha I, Beheshti A, Taylor D, Saravia-Butler A, Singh U, Wurtele ES, Schisler J, Fennessey S, Corvelo A, Zody MC, Germer S, Salvatore S, Levy S, Wu S, Tatonetti NP, Shapira S, Salvatore M, Westblade LF, Cushing M, Rennert H, Kriegel AJ, Elemento O, Imielinski M, Rice CM, Borczuk AC, Meydan C, Schwartz RE, Mason CE. "System-wide transcriptome damage and tissue identity loss in COVID-19 patients." Cell Reports Med. 2022 Feb 15;3(2):100522. https://doi.org/10.1016/j.xcrm.2022.100522 , Feb-2022
Articles in Peer-reviewed Journals	Saravia-Butler AM, Schisler JC, Taylor D, Beheshti A, Butler D, Meydan C, Foox J, Hernandez K, Mozsary C, Mason CE, Meller R. "Host transcriptional responses in nasal swabs identifies potential SARS-CoV-2 infection in PCR negative patients. " iScience. 2022 Oct 7;105310. https://doi.org/10.1016/j.isci.2022.105310 ; PMID: 36246576; PMCID: PMC9540688 , Oct-2022
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