Fiscal Year:	FY 2020	**Task Last Updated:**	FY 08/19/2019
PI Name:	Hada, Megumi Ph.D.		
Project Title:	Combined Effects of Simulated Microgravity and Space Radiation on Human Cells		
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:	(1) Cell Culture (2) Translational (Countermeasure) Potential		
PI Email:	mehada@pvamu.edu	**Fax:**	FY
PI Organization Type:	UNIVERSITY	**Phone:**	936-261-3155
Organization Name:	Prairie View A&M University		
PI Address 1:	College of Arts and Sciences, PO BOX 519, MS-2230, New Science Bldg		
PI Address 2:			
PI Web Page:			
City:	Prairie View	**State:**	TX
Zip Code:	77446	**Congressional District:**	10
Comments:			
Project Type:	GROUND	**Solicitation / Funding Source:**	2016-17 Space Biology (ROSBio) NNH16ZTT001N-FG. App G: Flight and Ground Space Biology Research
Start Date:	10/26/2018	**End Date:**	10/25/2021
No. of Post Docs:	2	**No. of PhD Degrees:**	0
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	1	**No. of Bachelor's Degrees:**	0
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NASA KSC
Contact Monitor:	Zhang, Ye	**Contact Phone:**	321-861-3253
Contact Email:	Ye.Zhang-1@nasa.gov		
Flight Program:			
Flight Assignment:			
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Wang, Jing Ph.D. (University of Texas MD Anderson Cancer Center) Takahashi, Akihisa Ph.D. (Gunma University Heavy Ion Medical Center, Japan) Fujiwara, Keigi Ph.D. (University of Texas MD Anderson Cancer Center)		
Grant/Contract No.:	80NSSC19K0133		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	Space radiation and microgravity are two major environmental stressors for human in space travel. One of the fundamental questions in space biology research is whether the combined effects of microgravity and exposure to cosmic radiation are synergistic. While studies addressing this question have been carried out for half a century in space or using simulated microgravity on the ground, the reported results are conflicting. Although the reason for the variation in results is not known, it is possible that it may be due to the diversity of biological systems used but more importantly to the experimental designs and hardware used in these studies. For the assessment and management of human health risks in future Moon and Mars Missions, it is necessary to obtain more basic data on the molecular and cellular responses to combined effects of radiation and microgravity. To establish a firm baseline database, we propose to undertake a systematic study on cultured mammalian cells' responses to the simultaneous insult of radiation and microgravity (both immediate and long term) to elucidate the molecular signaling pathways that lead to these biological effects. The results of the study will provide cellular and molecular biological bases for the assessment and management of human health risks in space. Recently Dr. Takahashi, co-investigator of this proposal, has developed microgravity-irradiation systems consisting of a 3D clinostat synchronized to the carbon-ion or X-ray irradiation systems. Our new experimental setup allows us to avoid stopping clinostat rotation during irradiation, which was required in all other previous experiments. Gunma University Heavy Ion Medical Center is the only facility in the world where we can expose samples to high-linear energy transfer (LET) irradiation as well as low-LET irradiation under the simulated microgravity condition (i.e., without interrupting clinostat rotation). Our preliminary data obtained from the use of this new device on gene expression in human fibroblasts show that splicing cycle-related genes and cell cycle related genes are significantly up-regulated and S-phase DNA replication and DNA repair-related genes were down-regulated with C-ion irradiation under simulated microgravity. In this proposal we will investigate 3 different endpoints from early to late responses in 2 human cell lines using our new devices to study combined effects of microgravity and space radiation. Human fibroblasts and epithelial cells will be exposed to X-rays and C-ions under the simulated microgravity condition (rotated with 3-D clinostat). Control cells will be irradiated in 1G environment (with the static stage). We will investigate the extent of expression of specific proteins and of the post-translational modification states of signaling proteins (Aim 1), gene expressions and the pathways involved (Aim 2), and the extent of chromosome aberrations (Aim 3) caused by the combined effects of simulated microgravity and radiation. To investigate from the early to late endpoints in the same cell types will provide cellular and molecular biological data that are needed to understand the impact of combined effects of simulated microgravity and space radiation on human health. One of the selected endpoints is chromosome aberration, which is a well-established biomarker for cancer risk and has been used by NASA for the risk assessment of astronauts. Studying this endpoint allows us to compare our results to the astronauts' data after their International Space Station missions. Completion of this proposal will allow us to determine how the combination of microgravity and radiation will affect the transcriptomic, metabolomic, and proteomic states of cells as well as heritable changes in DNA. These finding will allow us to help develop the countermeasures for the future space missions.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Completion of this proposal will allow us to determine how the combination of microgravity and radiation will affect the transcriptomic, metabolomic, and proteomic states of cells as well as heritable changes in DNA. These findings will allow us to help develop the countermeasure for the future space missions.
Task Progress:	Post-translational modification of proteins: Human fibroblasts (1BR-hTERT) were exposed to simulated μG for 0, 15, 30, 60, 120, 240, 480, and 1440 min at Gunma University and total 37 protein samples were collected (4-5 samples for each time points). All samples were shipped to MD Anderson Cancer Center. Currently reverse-phase protein arrays analysis is ongoing for these samples using a panel of 100 antibodies, most of which are targeted to posttranslational modification (PTM) of signaling molecules. Gene expressions: Human fibroblasts (1BR-hTERT) were maintained under standing or rotating conditions for 3 or 24 h after synchronized C-ion or X-ray irradiation at 1 Gy as part of a total culture time of 2 days. Among 57,773 genes analyzed with RNA sequencing, we focused particularly on the expression of 82 cell cycle-related genes after exposure to the radiation and simulated μG. The expression of cell cycle-suppressing genes (ABL1 and CDKN1A) decreased and that of cell cycle-promoting genes (MKI67, KPNA2, CCNB1, STMN1, and MCM4) increased after C-ion irradiation under μG. The cell cycle may pass through the G1/S and G2 checkpoints with DNA damage due to the combined effects of C-ions and μG, suggesting that increased genomic instability might occur in space. Manuscript has been prepared for these results and submitted to Int J Mol Sci. Chromosome aberrations: Using μG-irradiation system, human fibroblasts were exposed to X-rays (0.5 Gy, 1.5 Gy) and carbon ions (0.5 Gy) under the simulated μG condition, and chromosomes were collected with the premature chromosome condensation method in the first mitosis. Chromosome aberrations (CA) were quantified by the 3-color fluorescent in situ hybridization method. Cells exposed to irradiation under the simulated μG condition showed a higher frequency of both simple and complex type of CA compared to cells irradiated under the static condition by either X-rays or carbon-ions. Manuscript has been prepared for these results and published on Int J Mol Sci (see Bibliography section).
Bibliography Type:	Description: (Last Updated: 02/07/2024)
Abstracts for Journals and Proceedings	Rhone JR, Beitman A, Ikeda H, Plante I, Souda H, Yoshida Y, Held KD, Fujiwara K, Takahashi A, Saganti PB, Hada M. "Increased chromosome aberrations in cells exposed simultaneously to simulated microgravity and radiation." 2019 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2019. Abstract book. 2019 NASA Human Research Program Investigators' Workshop, Galveston, TX, January 22-25, 2019. , Jan-2019

Abstracts for Journals and Proceedings	Takahashi A. "Future space experiments for “cancer risk assessment” in the ISS and the Gateway." International Symposium on Space Medicine & Medical Engineering 2019, Kiryu, Japan, March 20, 2019. Abstract book. International Symposium on Space Medicine & Medical Engineering 2019, Kiryu, Japan, March 20, 2019. , Mar-2019
Abstracts for Journals and Proceedings	Hada M. "Collaborative Research – Combined effects of simulated microgravity and space radiation on human cells." International Symposium on Living in Space 2019, Kyoto, Japan, March 15, 2019. Abstract book. International Symposium on Living in Space 2019, Kyoto, Japan, March 15, 2019. , Mar-2019
Abstracts for Journals and Proceedings	Takahashi A. "Gunma University Heavy Ion Medical Center (GHMC): Therapy and space research." International Conference on Technology and Social Science 2019, Kiryu, Japan, May 8, 2019. Abstract book. International Conference on Technology and Social Science 2019, Kiryu, Japan, May 8, 2019. , May-2019
Abstracts for Journals and Proceedings	Chiu Y-J, Thomas TN, Choe LH, Lee KH, Fujiwara K. "The early response of cultured mammalian cells to changes in gravity: Increased actin dynamics." 2nd Mechanobiology Meeting in Vietnam, Quy Nhon, Vietnam, July 7-14, 2019. Abstract book. 2nd Mechanobiology Meeting in Vietnam, Quy Nhon, Vietnam, July 7-14, 2019. , Jul-2019
Articles in Other Journals or Periodicals	Takahashi A, Fujiwara K, Hada M. "Increased chromosome aberrations in cells exposed to simulated space environment with microgravity and radiation." The Cell. 2019 Feb;51(2):76-9. (in Japanese) , Feb-2019
Articles in Peer-reviewed Journals	Ikeda H, Muratani M, Hidema J, Hada M, Fujiwara K, Souda H, Yoshida Y, Takahashi A. "Expression profile of cell cycle-related genes in human fibroblasts exposed simultaneously to radiation and simulated microgravity." Int J Mol Sci. 2019 Sep 26;20(19):E4791. https://doi.org/10.3390/ijms20194791 ; PubMed PMID: 31561588; PubMed Central PMCID: PMC6801845 , Sep-2019
Articles in Peer-reviewed Journals	Hada M, Ikeda H, Rhone JR, Beitman AJ, Plante I, Souda H, Yoshida Y, Held KD, Fujiwara K, Saganti PB, Takahashi A. "Increased chromosome aberrations in cells exposed simultaneously to simulated microgravity and radiation." Int J Mol Sci. 2018 Dec 22;20(1):E43. https://doi.org/10.3390/ijms20010043 ; PubMed PMID: 30583489; PubMed Central PMCID: PMC6337712 , Dec-2018