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| Fiscal Year: | FY 2023 | Task Last Updated: | FY 11/07/2022 |
| 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 | | |
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| 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: | 10/27/2022 |
| No. of Post Docs: | 0 | No. of PhD Degrees: | 0 |
| No. of PhD Candidates: | 2 | 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 KSC |
| Contact Monitor: | Zhang, Ye | Contact Phone: | 321-861-3253 |
| Contact Email: | Ye.Zhang-1@nasa.gov | | |
| Flight Program: | | | |
| Flight Assignment: | NOTE: End date changed to 10/27/2022 per NSSC information (Ed., 9/15/21) | | |
| 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) | | |
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| | <p>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.</p> <p>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.</p> <p>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).</p> <p>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.</p> <p>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.</p> <p>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.</p> |
| Rationale for HRP Directed Research: | |
| Research Impact/Earth Benefits: | <p>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.</p> |
| Task Progress: | <p>Post-translational modification of proteins To identify post-translational modification (PTM), as well as changes in protein expression levels, we used a high throughput method called reverse-phase protein array (RPPA), which is available at the University of Texas MD Anderson Cancer Center. This method uses an array of close to 500 well-characterized antibodies, to which proteins in cell lysates will bind, and the amount of bound proteins to each antibody is quantified. Needless to say, many of the antibodies are against post-translationally modified proteins. Before exposing cells to both radiation and μG, we first analyzed how cells respond to altered gravitational environments. In this year, we have completed the manuscript of the changes in expression and modification of protein after gravity changes with actin dynamics.</p> <p>Gene expressions On the basis of our RNA sequencing (RNA-seq) results, we are proceeding data analysis focusing on human aging-related genes. Specifically, 84 genes encoding key molecules involved in human aging were selected with information from the RT2 Profiler PCR Array panel (QIAGEN polymerase chain reaction/PCR array panel), including several functions (e.g., genomic instability, inflammatory response, cellular senescence, cytoskeleton regulator, oxidative stress, transcriptional regulation, and epigenetics alterations). After combined treatment with C-ion irradiation and simulated μG, the expressions of collagen, type I, alpha 1 (COL1A1) and collagen, type III, alpha 1 (COL3A1), known as cytoskeleton regulators, were decreased (3 h, 24 h); and transcriptional regulation related genes (PHF3 and SMAD2) and DNA binding/RNA binding related gene ZFR (Zinc Finger RNA Binding Protein) were increased. A manuscript is under preparation.</p> <p>Chromosome aberrations We have reported our newly established "Simulator of the environments on the Moon and Mars with Neutron-irradiation and Gravity change" (SwiNG), for in vitro experiments (Takahashi et al., 2020) in last year's report. Samples can be exposed to neutrons at a low-dose-rate (0.5 mGy/day) using Californium-252 in the center of the centrifuge. In this year, using this new device, human fibroblasts 1BR-hTERT were exposed to low dose neutrons for 5 days under simulated space (μG), Moon (1/6G), and Mars (3/8G) conditions for 5 days, and chromosomes were collected by using the premature chromosome condensation methods. Chromosome aberration (CA) analysis with 3-color whole-chromosome Fluorescence In Situ Hybridization (FISH) staining is in progress.</p> |
| Bibliography Type: | Description: (Last Updated: 02/07/2024) |

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| Abstracts for Journals and Proceedings | Takahashi A, Ikeda H, Hada M. "Chromosome aberration induction by simultaneous exposure of partial gravity and low dose-rate neutrons using SwiNG." The 36th Annual Meeting of the Japanese Biology Space Science Society, Gifu, Japan, September 16-18, 2022. Abstracts. The 36th Annual Meeting of the Japanese Biology Space Science Society, Gifu, Japan, September 16-18, 2022. , Sep-2022 |
| Abstracts for Journals and Proceedings | Takahashi A, Ikeda H, Hada M. "Chromosome aberration induction by simultaneous exposure of partial gravity and low dose-rate neutrons simulating outer space, the Moon, and Mars." The 65th Annual Meeting of the Japanese Radiation Research Society, Osaka, Japan, September 15-17, 2022. Abstracts. The 65th Annual Meeting of the Japanese Radiation Research Society, Osaka, Japan, September 15-17, 2022. , Sep-2022 |
| Abstracts for Journals and Proceedings | Ikeda H, Hada M, Takahashi A. "The synergistic effects of radiation and simulated microgravity to expression profile changes of cell cycle / aging-related genes in human fibroblasts." The 65th Annual Meeting of the Japanese Radiation Research Society, Osaka, Japan, September 15-17, 2022. Abstracts. The 65th Annual Meeting of the Japanese Radiation Research Society, Osaka, Japan, September 15-17, 2022. , Sep-2022 |
| Abstracts for Journals and Proceedings | Takahashi A, Ikeda H, Guiruiis FNL, Yoshida Y, Hada M. "Simulator of the environments on the Moon and Mars with neutron-irradiation and gravity-change (SwiNG)." 44th COSPAR Scientific Assembly 2022, Athens, Greece, July 16-24, 2022. Abstracts. 44th COSPAR Scientific Assembly 2022, Athens, Greece, July 16-24, 2022. , Jul-2022 |
| Abstracts for Journals and Proceedings | Hada M, Ikeda H, Plante I, Mao JH, Saganti P, Takahashi A. "Increased chromosome aberrations in human cells exposed to simulated microgravity and radiation simultaneously." 44th COSPAR Scientific Assembly 2022, Athens, Greece, July 16-24, 2022. Abstracts. 44th COSPAR Scientific Assembly 2022, Athens, Greece, July 16-24, 2022. , Jul-2022 |
| Abstracts for Journals and Proceedings | Ikeda H, Hada M, Takahashi A. "Expression profile of cell cycle or aging-related genes in human fibroblasts exposed simultaneously to radiation and simulated microgravity." 44th COSPAR Scientific Assembly 2022, Athens, Greece, July 16-24, 2022. Abstracts. 44th COSPAR Scientific Assembly 2022, Athens, Greece, July 16-24, 2022. , Jul-2022 |
| Abstracts for Journals and Proceedings | Takahashi A. "My future dream through 'Living in Space'." The 11th Annual Meeting of the International Society of Radiation Neurobiology, Virtual, March 19, 2022. Abstracts. The 11th Annual Meeting of the International Society of Radiation Neurobiology, Virtual, March 19, 2022. , Mar-2022 |
| Abstracts for Journals and Proceedings | Guirguis FNL, Yamanouchi S, Takeuchi K, Takahashi S, Tashiro M, Hidema J, Higashitani A, Adachi T, Zhang S, Yoshida Y, Nagamatsu A, Hada M, Takeuchi K, Takahashi T, Sekitomi Y, Takahashi A. "Development of the Simulator of the environments on the Moon and Mars with Neutron-irradiation and Gravity-change (SwiNG)." The 11th Annual Meeting of the International Society of Radiation Neurobiology, Virtual, March 19, 2022. Abstracts. The 11th Annual Meeting of the International Society of Radiation Neurobiology, Virtual, March 19, 2022. , Mar-2022 |
| Abstracts for Journals and Proceedings | Ikeda H, Hada M, Takahashi A. "Comprehensive gene expression analysis of human fibroblasts using 3D clinostat synchronized irradiation systems." 2022 NASA Human Research Program Investigators' Workshop, Virtual, February 7-10, 2022. Abstracts. 2022 NASA Human Research Program Investigators' Workshop, Virtual, February 7-10, 2022. , Feb-2022 |
| Abstracts for Journals and Proceedings | Takahashi A, Yamanouchi S, Takeuchi K, Takahashi S, Tashiro M, Hidema J, Higashitani A, Adachi T, Zhang S, Guirguis FNL, Yoshida Y, Nagamatsu A, Hada M, Takeuchi K, Takahashi T, Sekitomi Y. "SwiNG: Combined-environment simulator of Moon and Mars." 2022 NASA Human Research Program Investigators' Workshop, Virtual, February 7-10, 2022. Abstracts. 2022 NASA Human Research Program Investigators' Workshop, Virtual, February 7-10, 2022. , Feb-2022 |
| Abstracts for Journals and Proceedings | Ju Z, Chiu Y-J, Thomas TN, Yamanouchi S, Yoshida Y, Abe J, Takahashi A, Wang J, Fujiwara K, Hada M. "Early responses of cultured mammalian cells to altered gravitational vector: Adaptation to microgravity and changes in cell motility." 2022 NASA Human Research Program Investigators' Workshop, Virtual, February 7-10, 2022. Abstracts. 2022 NASA Human Research Program Investigators' Workshop, Virtual, February 7-10, 2022. , Feb-2022 |
| Abstracts for Journals and Proceedings | Takahashi A, Suzuki K, Tsuruoka C, Morioka T, Takeshima T, Yoshida Y, Nakamura A, Ikeda H, Hada M, Nagamatsu A, Ohira Y, Inatomi Y, Kakinuma S. "Research on combined effects of space radiation and variable gravity - 2021 Annual Report." The 36th Annual Meeting of the Space Environment Utilization Symposium, Virtual, January 18-19, 2022. Abstracts. The 36th Annual Meeting of the Space Environment Utilization Symposium, Virtual, January 18-19, 2022. , Jan-2022 |
| Abstracts for Journals and Proceedings | Ikeda H, Hada M, Takahashi A. "Combined effects of HZE particle and simulated μ G on gene expression in human fibroblasts." Japanese Society for Quantum Medical Science, Virtual, December 10-11, 2021. Abstracts. Japanese Society for Quantum Medical Science, Virtual, December 10-11, 2021. , Dec-2021 |
| Abstracts for Journals and Proceedings | Hada M, Yamanouchi S, Mao J-H, Ikeda H, Plante I, Saganti PB, Takahashi A. "Increases of chromosome aberrations in human cells exposed simultaneously to simulated microgravity and radiation." 37th Annual Meeting of the American Society for Gravitational and Space Research, Baltimore, MD, November 3-6, 2021. Abstracts. 37th Annual Meeting of the American Society for Gravitational and Space Research, Baltimore, MD, November 3-6, 2021. , Nov-2021 |
| Abstracts for Journals and Proceedings | Yamanouchi S, Adachi T, Yoshida Y, Rhone J, Mao J-H, Fujiwara K, Saganti PB, Takahashi A, Hada M. "The increases of chromosome aberration in human peripheral blood lymphocytes exposed to simulated microgravity and radiation simultaneously." Kitakanto Medical Society Annual Meeting, Maebashi, Japan, September 30-Oct 1, 2021. Abstracts. Kitakanto Medical Society Annual Meeting, Maebashi, Japan, September 30-Oct 1, 2021. , Sep-2021 |

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| Abstracts for Journals and Proceedings | Yamanouchi S, Adachi T, Yoshida Y, Rhone J, Mao J-H, Fujiwara K, Saganti PB, Takahashi A, Hada M. "Chromosome aberrations in human peripheral blood lymphocytes exposed simultaneously to radiation and simulated microgravity." The 64th Annual Meeting of the Japanese Radiation Research Society, Mito, Japan, September 22-24, 2021. Abstracts. The 64th Annual Meeting of the Japanese Radiation Research Society, Mito, Japan, September 22-24, 2021. , Sep-2021 |
| Abstracts for Journals and Proceedings | Yamanouchi S, Adachi T, Yoshida Y, Rhone J, Mao J-H, Fujiwara K, Saganti PB, Takahashi A, Hada M. "Combined exposure to radiation and simulated microgravity increases chromosome aberration in human peripheral blood lymphocytes." The 35th Annual Meeting of Japanese Society for Biological Science in Space, Kanazawa, Japan, September 24-26, 2021. Abstracts. The 35th Annual Meeting of Japanese Society for Biological Science in Space, Kanazawa, Japan, September 24-26, 2021. , Sep-2021 |
| Articles in Peer-reviewed Journals | Beheshti A, McDonald JT, Hada M, Takahashi A, Mason CE, Mognato M. "Genomic changes driven by radiation-induced DNA damage and microgravity in human cells." Int J Mol Sci. 2021 Oct;22(19):10507. Review. https://doi.org/10.3390/ijms221910507 ; PMID: 34638848 PMID: PMC8508777 , Oct-2021 |
| Articles in Peer-reviewed Journals | Ju Z, Thomas TN, Chiu YJ, Yamanouchi S, Yoshida Y, Abe JI, Takahashi A, Wang J, Fujiwara K, Hada M. "Adaptation and changes in actin dynamics and cell motility as early responses of cultured mammalian cells to altered gravitational vector." Int J Mol Sci. 2022 May 30;23(11):6127. https://doi.org/10.3390/ijms23116127 ; PMID: 35682810; PMID: PMC9181735 , May-2022 |
| Awards | Yamanouchi S, Adachi T, Yoshida Y, Rhone J, Mao J-H, Fujiwara K, Saganti PB, Takahashi A, Hada M. "Kitakanto Medical Society Annual Meeting. Best Poster Presentation Award, September 2021. " Sep-2021 |
| Awards | Yamanouchi S, Adachi T, Yoshida Y, Rhone J, Mao J-H, Fujiwara K, Saganti PB, Takahashi A, Hada M. "The 35th Annual Meeting of Japanese Society for Biological Science in Space, Best Presentation Award, September 2021." Sep-2021 |
| Awards | Guirguis FNL. "President's Award for Outstanding Research, Gunma University Graduate School of Medicine, March 2022." Mar-2022 |