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| **Fiscal Year:** | FY 2023 | **Task Last Updated:** | FY 06/16/2023 |
| **PI Name:** | Nielsen, Sheila Ph.D. | | |
| **Project Title:** | Characterizing the Effects of Spaceflight on the Candida albicans Adaptation Response | | |
| **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<br>(2) Microbiology | | |
| **Space Biology Cross-Element Discipline:** | (1) Reproductive Biology<br>(2) Immunology | | |
| **Space Biology Special Category:** | (1) Translational (Countermeasure) Potential | | |
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| **Zip Code:** | 59717 | **Congressional District:** | 1 |
| **Comments:** | PI name change to Sheila Nielsen in 2014 (formerly Sheila Nielsen-Preiss)--Ed., 1/12/2015 | | |
| **Project Type:** | FLIGHT | **Solicitation / Funding Source:** | 2014 Space Biology Flight NNH14ZTT001N |
| **Start Date:** | 11/01/2014 | **End Date:** | 12/30/2022 |
| **No. of Post Docs:** | 0 | **No. of PhD Degrees:** | 0 |
| **No. of PhD Candidates:** | 0 | **No. of Master' Degrees:** | 1 |
| **No. of Master's Candidates:** | 1 | **No. of Bachelor's Degrees:** | 5 |
| **No. of Bachelor's Candidates:** | 6 | **Monitoring Center:** | NASA ARC |
| **Contact Monitor:** | Griko, Yuri | **Contact Phone:** | 650-604-0519 |
| **Contact Email:** | Yuri.V.Griko@nasa.gov | | |
| **Flight Program:** | ISS | | |
| **Flight Assignment:** | NOTE: End date changed to 12/30/2022 per NSSC information (Ed., 5/12/22)<br>NOTE: Extended to 4/30/2022 per F. Hernandez/ARC (Ed., 7/27/21)<br>NOTE: Extended to 4/30/2021 per NSSC information (Ed., 7/22/2020)<br>NOTE: Extended to 4/30/2020 per NSSC information (Ed., 4/21/2020)<br>NOTE: Extended to 3/31/2020 per F. Hernandez/ARC and NSSC information (Ed., 6/11/19)<br>NOTE: Extended to 4/30/2019 per F. Hernandez/ARC (Ed., 11/2/17)<br>NOTE: End date changed to 10/31/2017 per NSSC information (Ed., 11/29/16) | | |
| **Key Personnel Changes/Previous PI:** | | | |
| **COI Name (Institution):** | | | |
| **Grant/Contract No.:** | NNX15AB37G | | |
| **Performance Goal No.:** | | | |

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| **Performance Goal Text:** | |
| **Task Description:** | The common yeast pathogen, Candida albicans, can cause a range of diseases from superficial skin infections to systemic and life threatening infections in immunocompromised individuals. Most members of the population are carriers of this yeast at some point in their lifetime. This point becomes more concerning for astronauts who experience diminished immune responsiveness during spaceflight. In addition, many bacteria have been shown to become more virulent when grown in space. The combination of increased virulence and diminished immunity can jeopardize the health and wellbeing of flight crew. The goal of these studies is to characterize the mechanisms underlying the adaptation responses we have observed in yeast grown in modeled microgravity and in spaceflight. In addition, we will focus on determining whether yeast also become more virulent when grown in space, as our observed cellular alterations might predict. Furthermore, we will define the environmental stressors that exist during spaceflight that influence yeast growth. Our overriding research goals are to characterize the virulence of Candida albicans in the space environment, to understand which aspects of the environment contribute to adaptive changes within the yeast, and to identify targets that might be exploited to control yeast infection in space and on Earth. |
| **Rationale for HRP Directed Research:** | |
| **Research Impact/Earth Benefits:** | There are low fluid shear environments within the human host so we hope to exploit the low fluid shear environment of microgravity to better understand the yeast adaptation to this physical force and the microenvironment created by it. Any understanding as to the mechanisms related to antifungal resistance can be generally applied to therapeutic approaches. |
| **Task Progress:** | Cells respond to mechanical or physical changes in the environment as well as to their chemical surroundings. As we explore the eukaryotic cell responses to environmental changes encountered during spaceflight, it is important to identify the source(s) of the environmental stress in order to fully define mechanisms of adaptation. Whether Candida albicans (C. albicans) is responding directly to physical signals generated by fluid shear, or to changes in the microenvironment due to a lack of shear-based mass transfer, remains to be elucidated. During prolonged growth in ground-based simulation, we observed changes in yeast cell morphology (increase in filamentation) and colony morphology (increase in hyper irregular wrinkle) that were reproducible by growth in a high carbon dioxide (5%) environment. To determine whether the cells were responding to chemical changes in the microenvironment, we analyzed genes previously characterized as differentially expressed in response to carbon dioxide levels. OPT1 expression was found to be modestly increased in C. albicans grown in conditions of elevated (5%) CO2, in yeast cultured in simulation bioreactors for up to 12 days, and in yeast cultured on the International Space Station or the Shuttle as part of the Micro-6 and STS-115 payloads, respectively. Studies are being conducted to define whether the direct influence of fluid shear, as well as the secondary effects of accumulated metabolic waste products (CO2) and/or diminished nutrients (including sugars and O2) in the microenvironment, are impacting the yeast response.<br>The overriding hypothesis for this project is that exposure of the yeast, C. albicans to microgravity will alter gene expression and morphology, consistent with a potential increase in virulence. More specifically, diminished fluid shear may result in alterations to the physical environment that contribute, directly or indirectly, to adaptations in the yeast cell surface resulting in increased virulence. Notably, these studies will further explore and document the genotypic and phenotypic parameters of C. albicans associated with pathogenicity, identify specific environmental influences on the physiological adaptation processes, and provide insight into mechanisms used by higher eukaryotes when adapting to spaceflight conditions.<br><br>To assess yeast responses to microgravity, the following flight experiments have been conducted in flight hardware provided by BioServe Space Technologies, Boulder, CO.<br><br>SpX CRS-16 • Fluid Processing Apparatus (FPA) in Group Activation Packs (GAP) with 10 GAPs (5 ea flight and ground) containing 80 FPAs (40 ea flight and ground) to assess the gas microenvironment. SpX CRS-17 • Fluorinated ethylene propylene (FEP) bags were used for serial cultivation and antifungal testing of yeast. • Human monocytes (THP-1) were cultured in 12-well BioCells and challenged with UV-killed C. albicans or sham inoculation. SpX CRS-21 (partial reflight) • FEP bags for serial cultivation of yeast • THP-1 cells cultured in 6 wells of a 12-well BioCell (no yeast challenge condition).<br><br>Temperature for flight samples was controlled through the use of an on-orbit incubator, SABL, at 4C, 30C, and 37C. Frozen samples were stored in an on-orbit freezer, GLACIER or equivalent, and transferred to Cold Stowage for return (< -32C). Temperature for ground controls was controlled by standard incubators/refrigerators set at 4C, 30C, and 37C. Freezing was achieved in a standard -80C freezer.<br><br>In preparation for these flight experiments, a full scale experiment verification test (EVT) was conducted in the Principal Investigator (PI) laboratory with BioServe personnel onsite. The science team consisted of the PI and teams of two (SpX CRS-16) or four (SpX CRS-17) students (one graduate student and 5 undergraduate students). SpX CRS-21 was conducted by the PI alone due to its smaller size and COVID-related precautions.<br><br>All ground controls were conducted near synchronously, with a time offset predetermined for each payload based on timing and complexity of operations, and established by real-time communication with BioServe. For SpX CRS-16, ground GAPs were stored on the horizontal and rotated 180° daily. When at 30C, the ground GAPs were laid on the horizontal and very slowly rocked lengthwise. For SpX CRS-17 and -21, FEP bags were maintained in a horizontal ‘flat’ orientation and flipped once during the incubation period. BioCell units were maintained in a habitat with the plate laying flat.<br><br>The main goal of the most recent payload, Micro-14A, was to serially culture C. albicans over a period of several days to establish whether exposure to microgravity over many generations had an impact on the yeast adaptation responses. Yeast Extract–Peptone–Dextrose (YPD) medium was launched preloaded in FEP bags and the yeast was launched in water-induced stasis. Once on orbit, the yeast was inoculated into the first-in-series FEP bag and cultured at 30C. The following day, an aliquot from the culture was diluted and used to inoculate the second-in-series FEP bag. This cycle continued through 5 days of growth (approx. 70 generations). Cells were frozen each day for analyses upon sample return. Cell density, viability, metabolic gas production, and antifungal resistance were each evaluated.<br><br>In aggregate, these studies have provided the rare opportunity to repeat experiments in different flight hardware and incrementally extend the studies. |

| Bibliography Type: | Description: (Last Updated: 06/23/2023) |
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| Abstracts for Journals and Proceedings | White K, Nielsen S. "Ergosterol levels and antifungal resistance in Candida albicans in microgravity." NCUR 2021, National Conference on Undergraduate Research, Virtual, April 12-14, 2021.<br>Abstracts. NCUR 2021, National Conference on Undergraduate Research, Virtual, April 12-14, 2021. , Apr-2021 |
| Abstracts for Journals and Proceedings | Nielsen S. "Contributions of the gas environment to Candida albicans adaptation to spaceflight." Committee on Space Research (COSPAR) 2021-Hybrid, 43rd Scientific Assembly, Sydney, Australia, January 28-February 4, 2021.<br>Abstracts. Committee on Space Research (COSPAR) 2021-Hybrid, 43rd Scientific Assembly, Sydney, Australia, January 28-February 4, 2021. , Jan-2021 |
| Abstracts for Journals and Proceedings | Nielsen S. "Micro-14A." ISS Increment 64 Science Symposium, Virtual, November, 2020.<br>ISS Increment 64 Science Symposium, Virtual, November, 2020. , Nov-2020 |
| Abstracts for Journals and Proceedings | Baranek L, Nielsen S. "Long term viability of stored dried Candida albicans." Montana State University Research Forum<br>Montana State University Research Forum. , May-2022 |