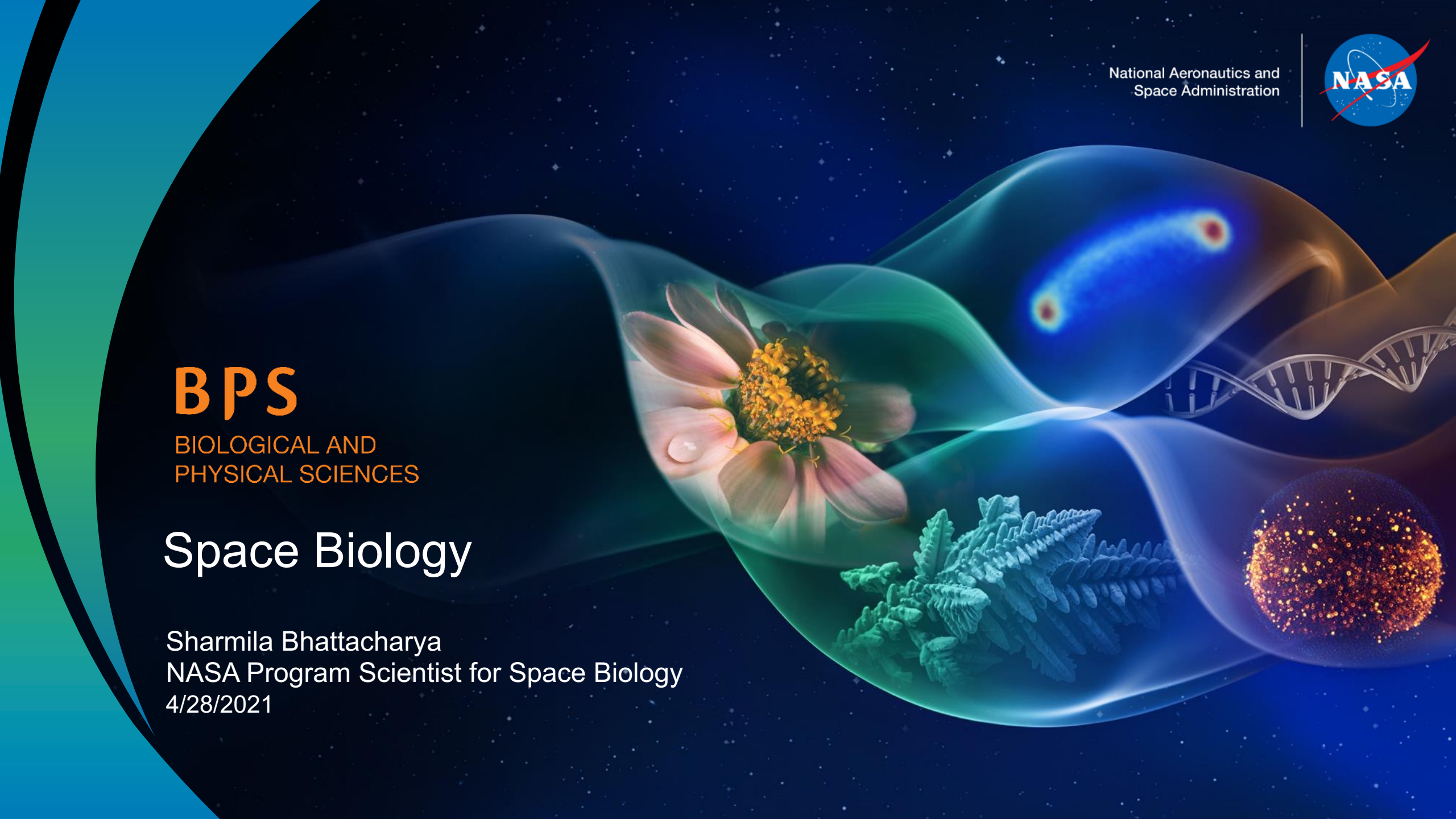
National Aeronautics and Space Administration



BPS

BIOLOGICAL AND PHYSICAL SCIENCES

Space Biology

Sharmila Bhattacharya
NASA Program Scientist for Space Biology
4/28/2021

Early Career

- **Early schooling in Kolkata, India**

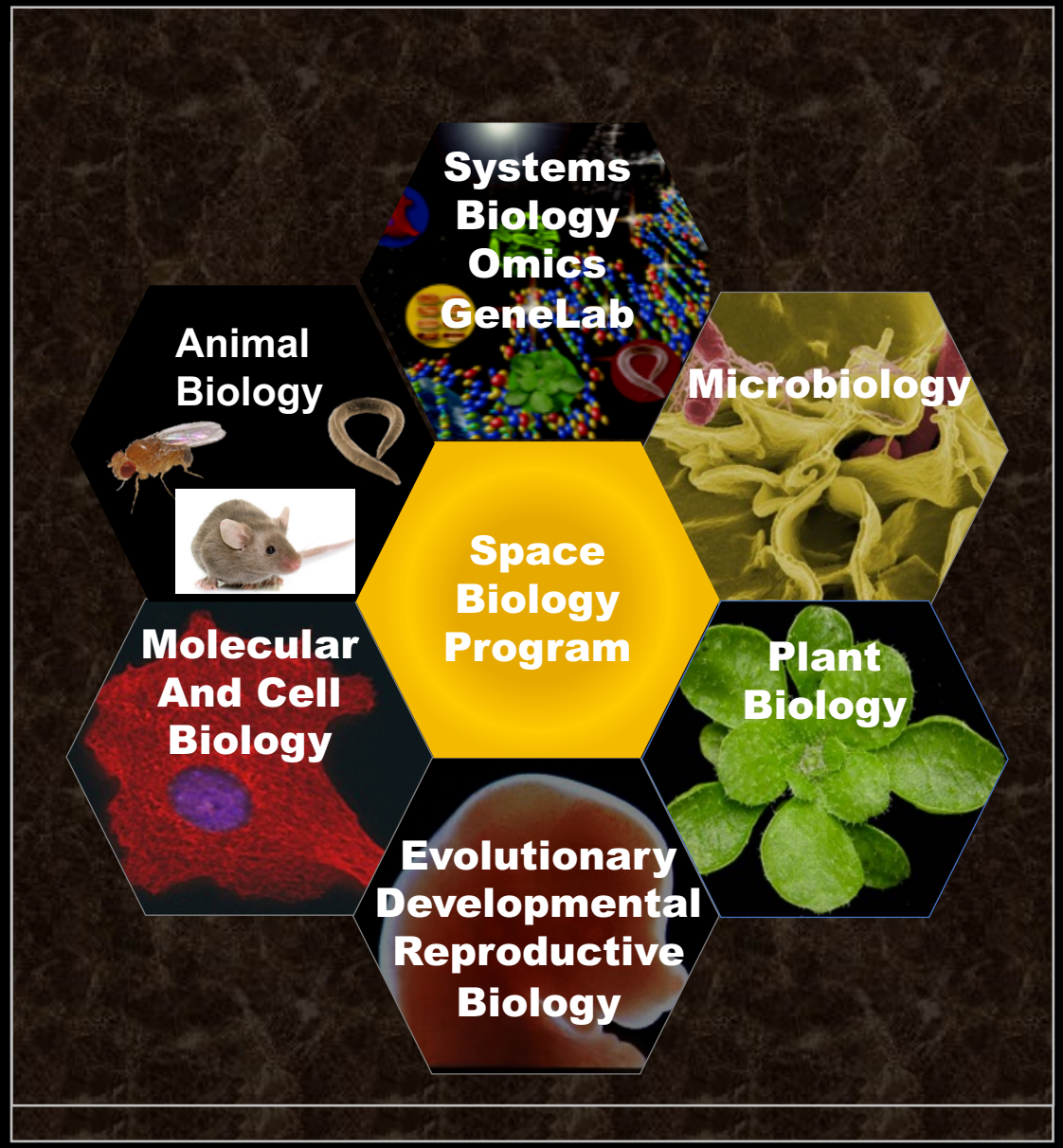
- **Undergraduate Student (BA), Wellesley College, MA** — Biological chemistry (blue-green algae)
- **Graduate Student (MA/PhD), Princeton University, NJ** — Molecular biology (yeast)

- **Post-doctoral researcher, Stanford University** — Neurobiology (fruit flies)
- **Guest lecturer, University of California, Santa Cruz** — Neurobiology (during post-doc)

- **Scientist at NASA** (since 1999) — Effects of gravity and radiation

Science & Science Policy

- **Science:**
  - Scientist and manager at NASA for 22 years
  - Multiple science experiments: on Space Shuttle, SpaceX/commercial rockets, Progress/Soyuz, small autonomous satellites, International Space Station, etc.
- **Space Policy:**
  - Space Policy Advisor
  - The US Senate Committee on Commerce, Science, and Transportation
  - To help with legislative issues behind science and technology
  - Use technical expertise to help inform legislative decisions in the Senate
- **Programmatic Science Management:**
  - Program Scientist for NASA's Space Biology program



Space Biology's overall objectives:

- Discover how biological systems **respond** to the space environment.
- Identify the fundamental **mechanisms** and develop physiological models for biological systems in space.
- Promote **open science** through the GeneLab Data System and Life Science Data Archive.
- Conduct **world-class research** and develop cutting-edge biological **technologies.**
- Provide mechanistic understanding to support human **health in space.**
- Support the transfer of knowledge of space-based research to **benefit life on Earth.**

Databases and Biospecimen Sharing

- *GeneLab (genelab.nasa.gov)*
- *Life Sciences Database Archive (lsda.nasa.gov)*

Space Biology and Altered Gravity

Why study biological effects of microgravity?

- All life on earth have evolved in the Earth's gravitational field. We have little knowledge of what happens to organisms in the apparent absence of this force.
  - Studies in microgravity will tell us how biological systems acclimate and adapt to this new environment
  - Studies in microgravity will also reveal how gravity has driven evolution and continues to influence biological process on Earth.

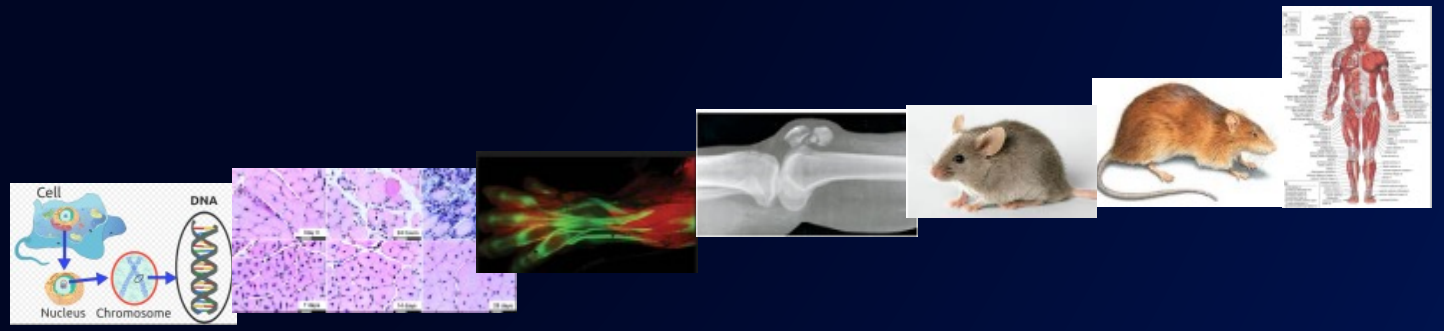
Why study biological effects of hypergravity?

- During space flight, living systems are not only exposed to microgravity, but also experience around 3 g during launch and 3+ g more landing.
- Chronic hypergravity models can be used complement and predict microgravity-associated changes (i.e., the shift from 2 g to 1 g may recapitulate aspects of the shift from 1 g or microgravity.

The Effects of Gravity

The Gravity Dose Response Curve: Threshold or Continuum?

- Gravity induces biological responses at the gene expression, cellular, systems, and whole organism level
- The dose response curve of any of these responses is not fully characterized
- Space Biology has supported multiple ground & flight research projects utilizing a variety of organisms to define dose response curve & adaptation mechanisms from 0 to >2+*g*



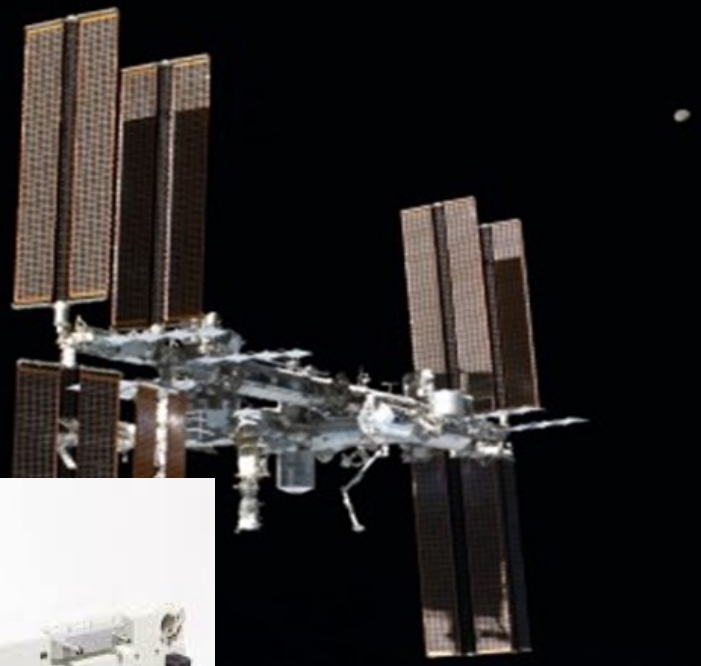
- It is not known if responses are a continuum or are based on reaching thresholds
- It is not known if responses require continuous or intermittent exposures
- It is not known if the sensitivity/dose response changes during development

Research Platforms and Tools

International Space Station (ISS)

Gravity levels encountered:
- Microgravity
- 1g, fractional, and hypergravity (using centrifugation)

Examples of Research Capabilities on the ISS



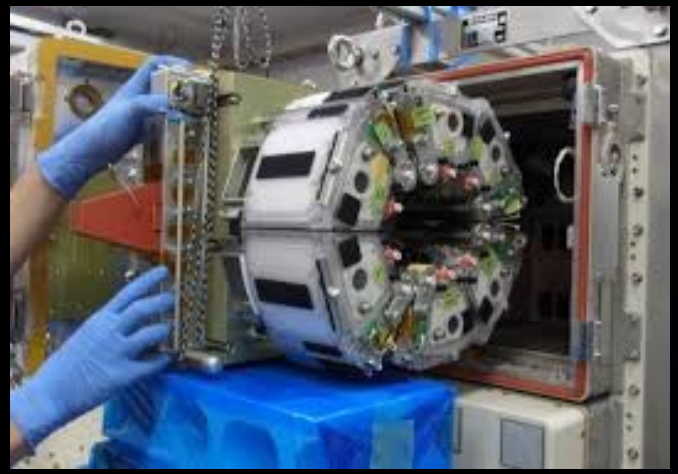
Dedicated Life Sciences Glovebox

Techshot Multi-Use Variable-g Platform (centrifuge systems for Plants, invertebrates, Cells, Microbes)

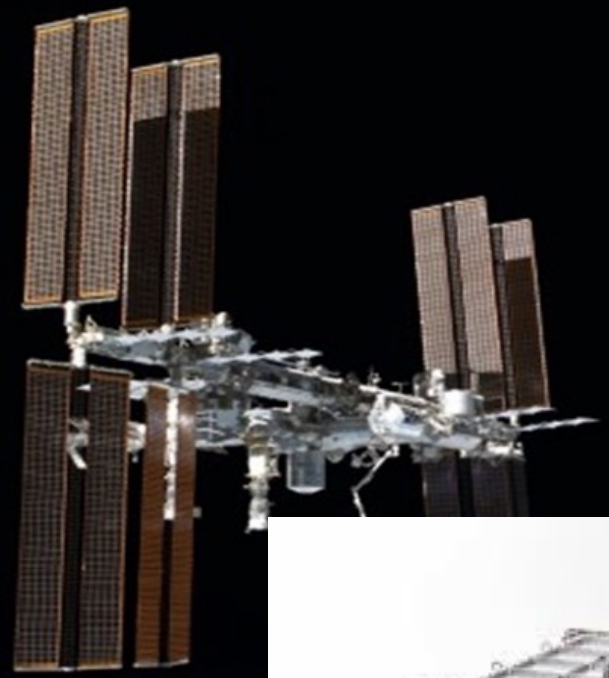
NASA Advanced Plant Habitat

NASA Bioculture System

Rodent Research Capabilities on the ISS



JAXA Mouse Habitat Unit
0xg to 1xg

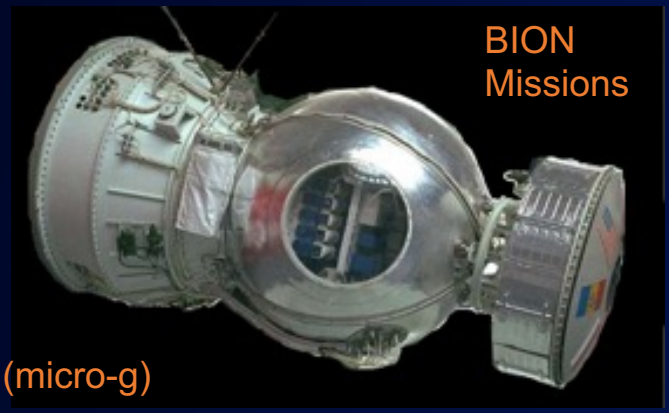


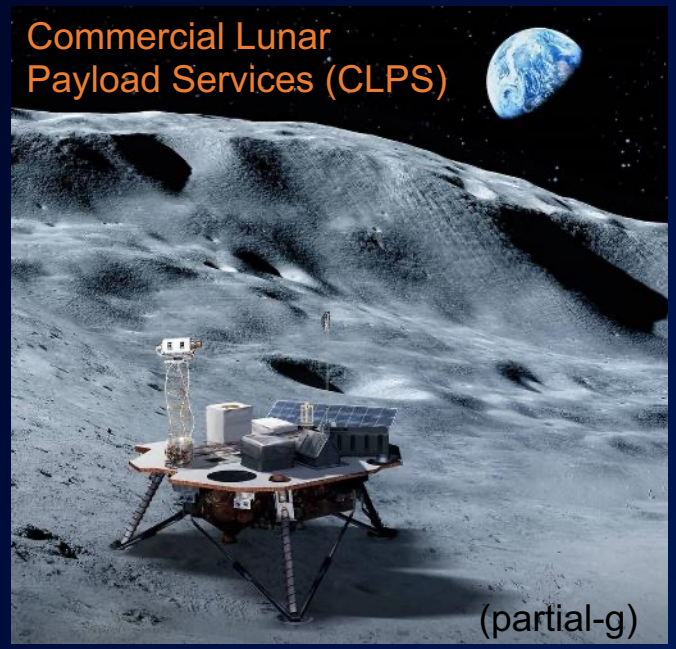
Rodent Habitat

Techshot Dexascan

ISS Rodent Research Handbook: www.nasa.gov/sites/default/files/atoms/files/np-2015-03-016-jsc_rodent-iss-mini-book_detail-508.pdf

Alternative Flight Platforms





Ground-Based Research and Facilities for Space Biology

Ames Research Center (ARC)

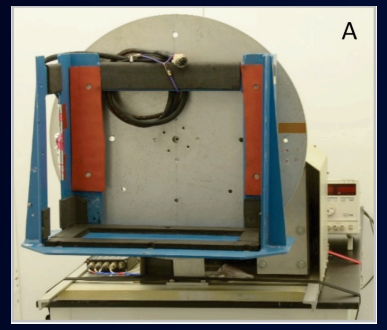
Kennedy Space Center (KSC)

Institutions across the USA

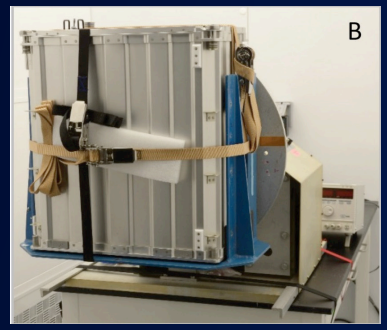
Gravity levels encountered:
- Microgravity, partial gravity (simulated)
- 1g
- Hypergravity (using centrifugation)

Microgravity Simulation Support Facility

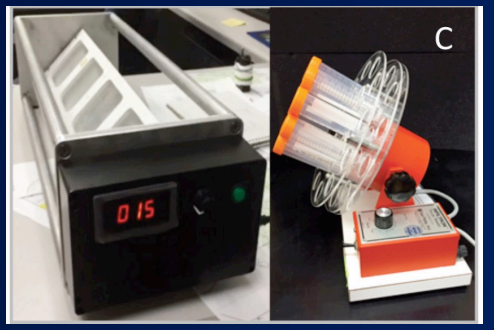
- The Microgravity Simulation Support Facility (MSSF) at Kennedy Space Center (KSC) was established to support visiting scientists for short duration studies utilizing a variety of microgravity simulator devices.
- Some devices negate the directional influence of the "g" vector (providing simulated conditions of micro *or* partial-gravity).
- Simulators can be accommodated within controlled environment chambers allowing investigators to customize and monitor environmental conditions such as temperature, humidity, CO2, and light exposure.
- Supporting facilities: Tissue culture facilities, basic cellular and molecular analysis tools, and advanced confocal fluorescence microscopy are available.



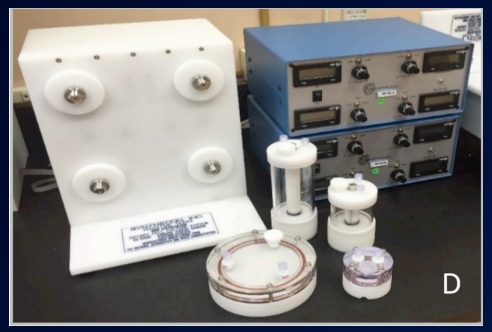
KSC Slow Rotating Clinostat



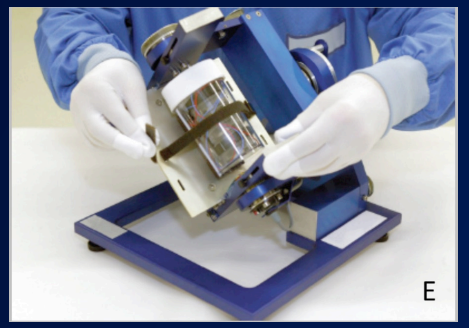
KSC Slow Rotating Clinostat in ISS stowage locker configuration



Additional 2D Clinostats



Synthecon Rotary Cell Culture System w/ autoclavable HARVs and STLVs



Airbus RPM 2.0 configured with experimental vessel

Space Bio-Laboratories, Inc. GRAVITE 3D-clinostat in an incubator

Hypergravity Research Facility for Model Organisms

- Life Science Acceleration Research Facilities at the NASA Ames Research Center to conduct hypergravity studies that cannot be performed in any other NASA facility. The centrifuges offer unique, innovative ways for conducting research and training to cope with the effects of acceleration on human and flight hardware systems.
- Centrifuges can accommodate different types of experimental payloads, such as small animal and plant habitats and experimental hardware and enable researchers to evaluate the effects of hypergravity on various biological specimens.
- The 1.22-Meter Radius Centrifuge supports four specimen cabs, each adaptable to accommodate different types of experiments. Each of the specimen cabs can accommodate a variety of model organisms at various acceleration levels during a single experiment. Powered habitat enclosures include continuous data, video, and temperature monitoring.
- The 1-Meter Radius Centrifuge supports one to four specimen cabs, configured with one or two rotating arms to accommodate different types of experiments. Powered habitat enclosures include continuous data, video, and temperature monitoring.

1.22-Meter Radius Centrifuge (1-4g (with entension)

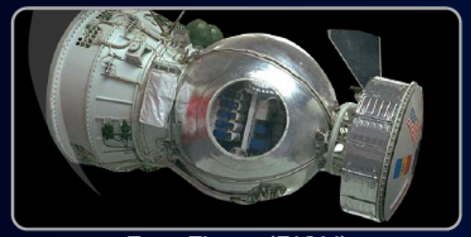
1-Meter Radius Centrifuge (1-3g)

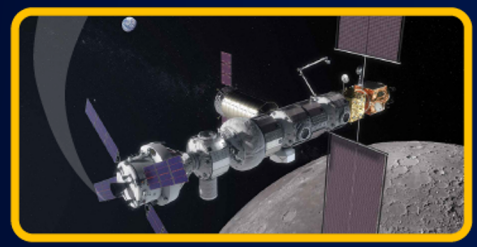
BPS Platforms for Research

*Future Platforms


CubeSat


International Space Station


Free Flyers (BION)

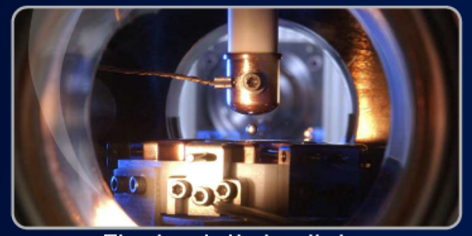

*Lunar Gateway


*Commercial Lunar Lander Services


Drop Tower

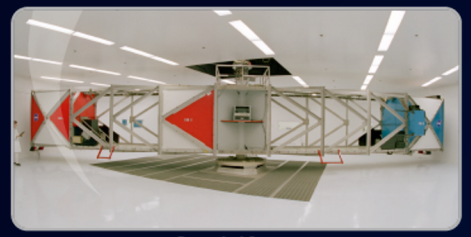

Parabolic Flight


Sounding Rocket
Sub-orbital Vehicle


Electrostatic Levitator


*Human Landing System


Rodent Unloading

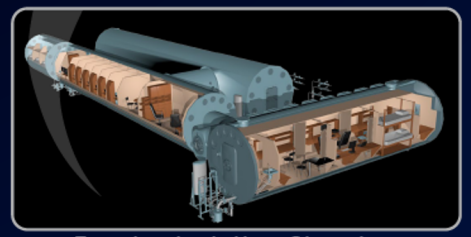

Centrifuge


Balloon Flight


NASA Space Radiation Lab


NASA Isolation Chamber


NSF Polar Station


Russian Isolation Chamber


Gravity Vector Averaging


Physical Sciences
Informatics

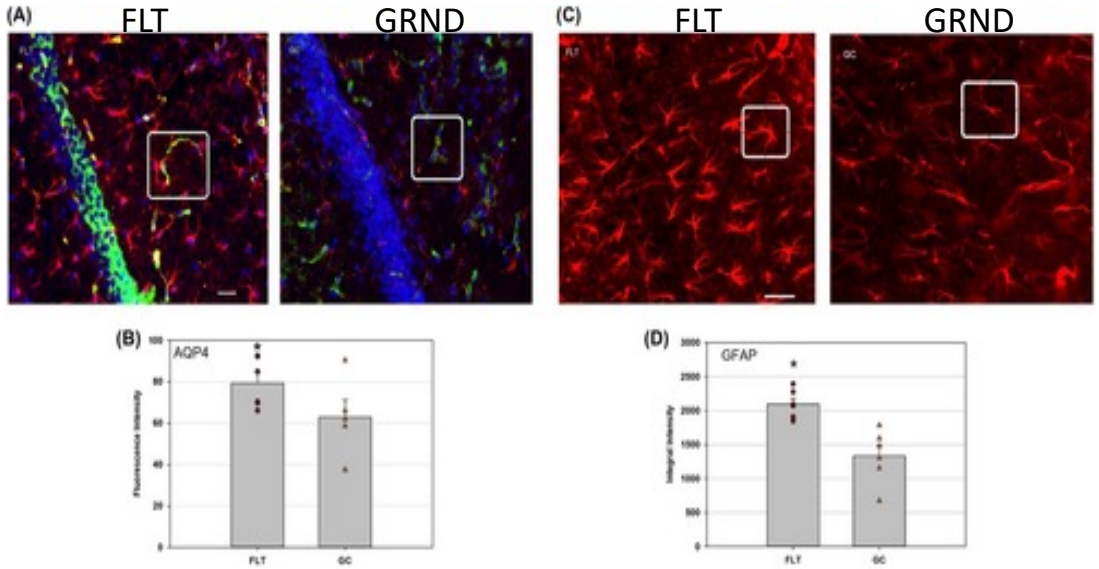

GeneLab

Research Examples

Spaceflight induces oxidative damage to blood-brain barrier integrity in a mouse model.

Mao, Nishiyama, Byrum, Stanbouly, Jones, Holley, Sridharan, Boerma, Tackett, Willey, Pecaut, and Delp. **FASEB J**, September 2020: doi: 10.1096/fj.202001754R

- Spaceflight-induced neuronal damage and potential adverse neurovascular effects constitute a significant health risk for astronauts
- Dr. Mao and her team studied spaceflight's effects on oxidative damage in the mouse brain and its impact on the blood-brain barrier (BBB) integrity.
  - Samples were collected from Rodent Research-9 male mice launched on SpaceX-12 and maintained onboard the ISS for 35 days.
- **The results showed increased oxidative damage and disruption in BBB integrity**, as evidenced by changes in the expression of BBB-related proteins, **changes in proteomic profiles and pathways, cell cycle progression, apoptosis, mitochondrial function, metabolism, and behavior**



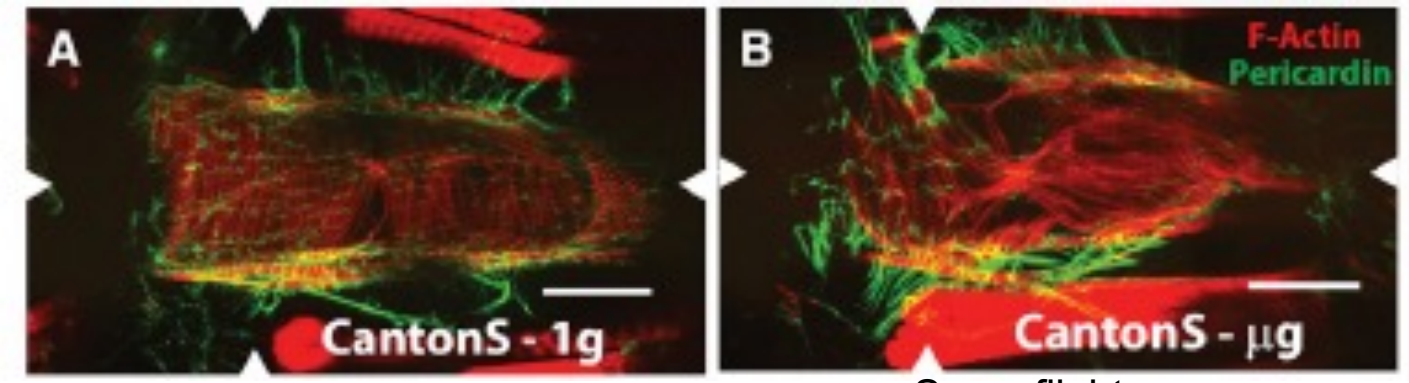
Representative micrographs of brain sections after immunostaining with anti-GFAP and AQP4 antibodies on flight (FLT) and ground control (GC) samples.

Prolonged Exposure to Microgravity Reduces Cardiac Contractility and Initiates Remodeling in *Drosophila*

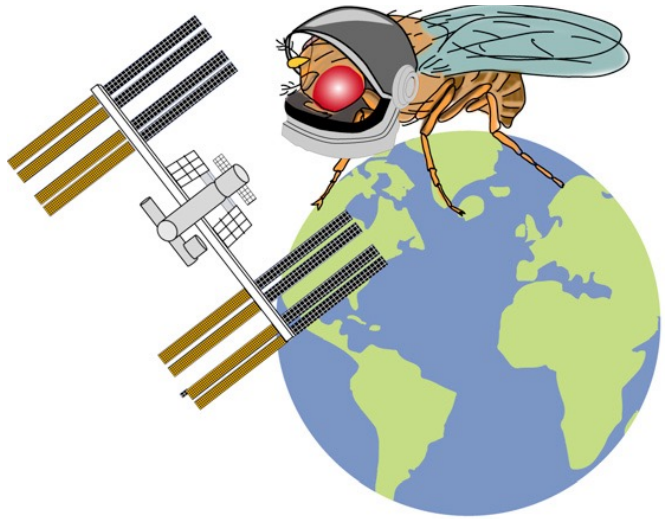
Stanley Walls, Soda Diop, Ryan Birse, Lisa Elmen, Zhuohui Gan, Sreehari Kalvakuri, Santiago Pineda, Curran Reddy, Erika Taylor, Bosco Trinh, Georg Vogler, Rachel Zarndt, Andrew McCulloch, Peter Lee, S. Bhattacharya, Rolf Bodmer, and Karen Ocorr

Cell Reports (2020). https://doi.org/10.1016/j.celrep.2020.108445

Cross section of one chamber of *Drosophila* heart



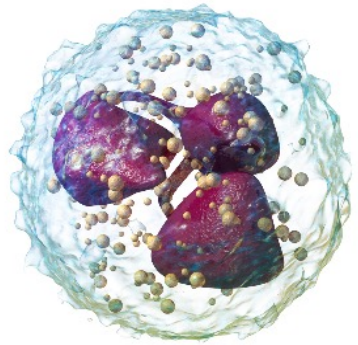
Ground control Spaceflight



- Wall et al. find that exposure to microgravity aboard the **ISS causes heart dysfunction** in fly cardiac model – 2 spaceflight missions, F1 generation bred entirely in space
- Hearts are smaller, **less contractile,** and exhibit changes in genes and proteins that maintain heart structure and function
- **Myofibrillar and extracellular matrix (ECM) disorganization** seen from spaceflight
- Heart defects correlate with reduced sarcomeric and extracellular matrix gene expression
- Increase in proteasome gene expression and increase proteasome aggregates in females in response to spaceflight
- **Tissue remodeling and proteostatic stress may be a fundamental response of heart muscles to microgravity**

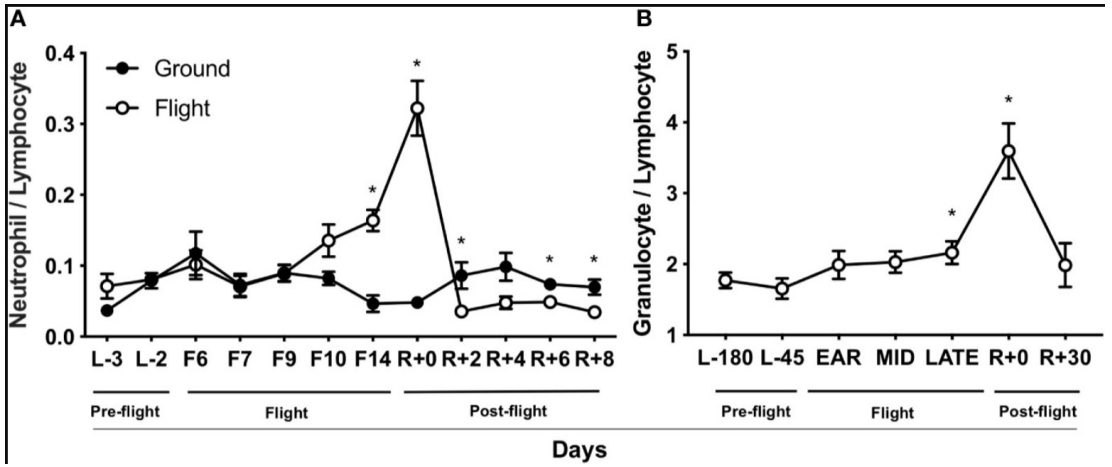
Neutrophil to Lymphocyte Ratio (NLR): A Biomarker to Monitor the Immune Status of Astronauts

Paul, A., Mhatre, S., Cekanaviciute, E., Schreurs, A., Tahimic, C., Globus, R., Anand, S., Crucian, B. & Bhattacharya, S. (Nov 2020). ***Frontiers in immunology***, vol *11*.



- Research has shown that **leukocyte differentials are altered in rodents and humans during spaceflight**
- Simulated microgravity conditions; **cultured human whole blood-leukocytes** were grown in a high-aspect rotating wall vessels (HARV-RWV), plus **hindlimb unloaded (HU) mice**
- Both HARV-RWV simulation of leukocytes and HU-exposed mice **showed elevated NLR profiles comparable to spaceflight exposed samples**

Results indicate an imbalance of redox processes and activation of inflammatory mechanisms, while treatment with an antioxidant treatment *reversed* these effects. These findings suggest that simulated microgravity induces oxidative stress responses that triggered inflammation and are an indicator that **an elevated neutrophil-to-lymphocyte ratio (NLR) is a potential biomarker candidate**.

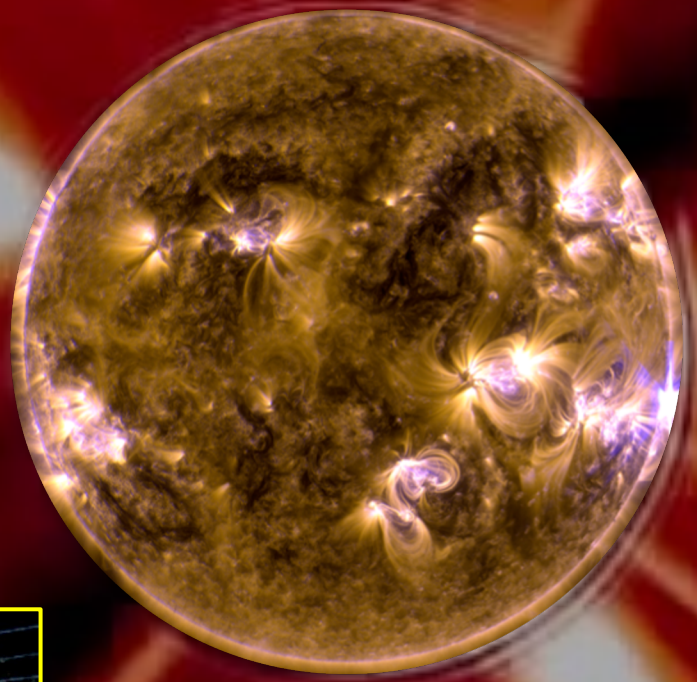


Spaceflight elevates NLR and GLR. **(A)** Rodent NLR from Space Life Sciences (SLS)-2 mission (n = 5–15). **(B)** Human GLR from published data (n = 23). L, launch; F, flight; R, return on Earth denoted in days. “Early”, day 14 in-flight; “mid,” days 60–120 in-flight; and “late,” day 180.

DOI: 10.3389/fimmu.2020.564950

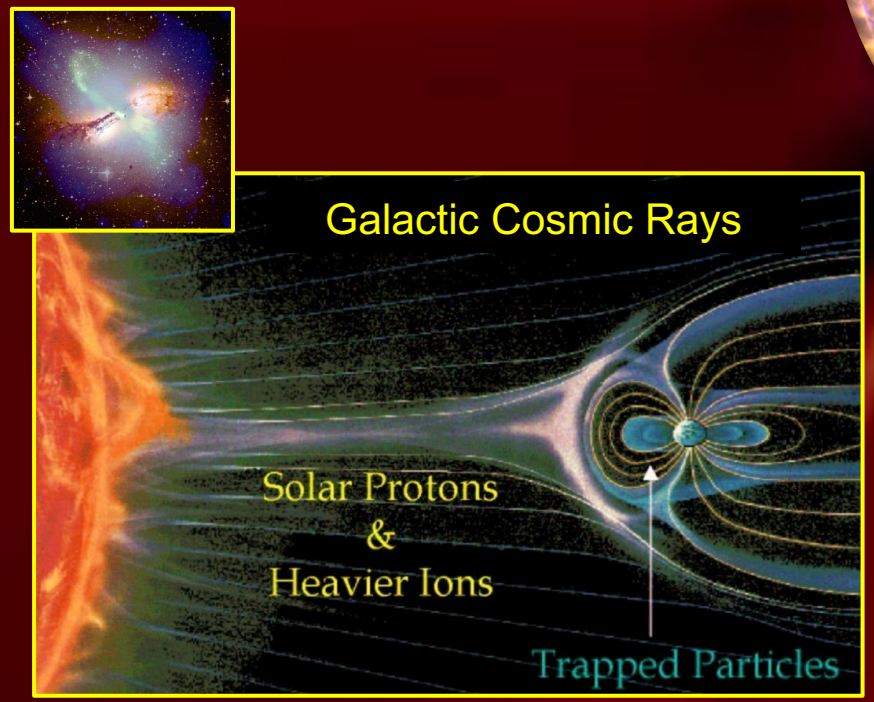
Interplanetary space radiation

What are we going to encounter beyond Low Earth Orbit (LEO)?



Ionizing radiation that will affect biology:

- ❖ Galactic Cosmic Radiation (GCR)
- ❖ Solar Particle Events (SPEs)



Limits of life in space, as studied to date:

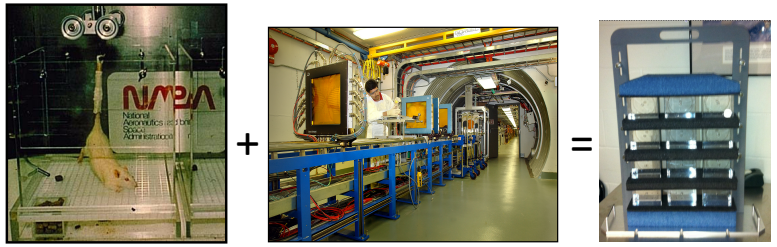
- ✧ 12.5 days on a lunar round trip
- ✧ 1.5 years in low Earth orbit on ISS

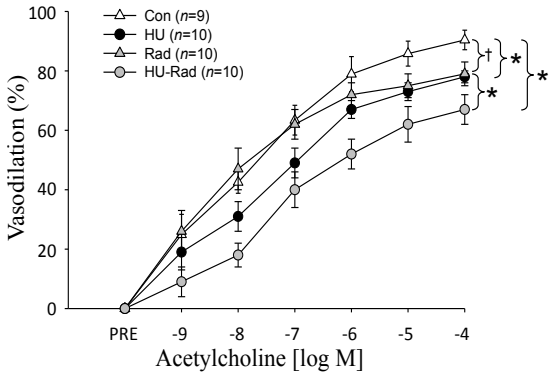
Nitric oxide and oxidative damage-related pathways implicated in some murine responses to simulated microgravity and radiation

A ground-based rodent model of hindlimb unloading (HU) can be used to determine effects of simulated microgravity, alone or combined with radiation, in vascular, immune, CNS and musculoskeletal systems.

1. Vascular dysfunction: Heavy ion radiation and simulated weightlessness impairs vascular reactivity in hindlimb blood vessel to greatest extent when combined via a nitric oxide-dependent mechanism.

Ghosh P, Behnke BJ, Stabley JN, Kilar CR, Park Y, Narayanan A, Alwood JS, Shirazi-Fard Y, Schreurs AS, Globus RK, Delp MD. Radiat Res. 2016;185(3):257-66

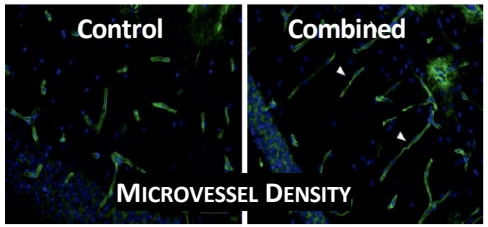




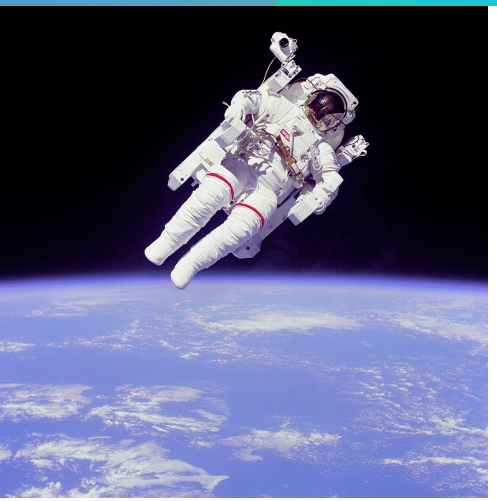
- ^{56}Fe (1 Gy) and simulated microgravity over 2wk each impair peak endothelium-mediated vasodilation in microvessel (PNA), and effect is greatest when combined.
- NO inhibitor abolishes all functional effects of radiation and simulated microgravity.
- Radiation and simulated microgravity differentially regulate oxidative enzyme expression (eNOS, SOD1, XO oxidase).
- Results suggest that the combined challenges of radiation and microgravity during spaceflight impair vasodilator function of resistance arteries mediated by a deficit in NOS signaling.

2. CNS: Simulated microgravity and low-dose/low-dose-rate radiation induce oxidative damage in the mouse brain.

Mao XW, Nishiyama NC, Pecaut MJ, Campbell-Beachler M, Gifford P, Haynes KE, Becronis C, Gridley DS Radiat Res 2016 Jun;185(6):647-57



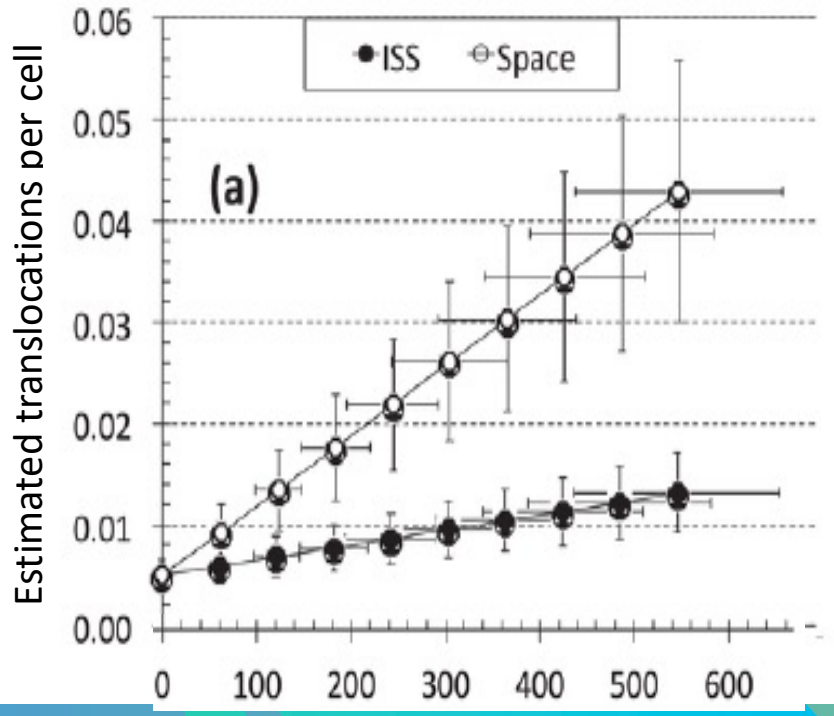
- ^{57}Co (0.04 Gy at 0.01 cGy/h) combined with simulated weightlessness over 3wk appeared to reduce microvessel length density in cerebral cortex 9 mo. later.
- Greatest effects of ^{57}Co on oxidative damage marker in cortex and hippocampus if radiation and simulated microgravity are combined compared to controls.



Increased Chromosomal Aberrations Previously Seen in Blood Lymphocytes in Astronauts (in-vivo) after Spaceflight

- **Increase in chromosomal aberrations previously seen in astronauts even at low Earth orbits during ISS, Mir and STS (shuttle) missions.**
- **80% or more of organ dose equivalents on the ISS are from galactic cosmic rays (GCR) which are difficult to shield, and will be more abundant as astronauts go to the Moon and Mars beyond the Van Allen Belt**

T. Straume, T.C. Slaba, S. Bhattacharya, L.A. Braby. Life Sci Space Res (2017)



F.A. Cucinotta, M.Y.Kim, V. Willingham, and K.George. (2008) *Rad Res*. 170:127. (Studies in ISS, Mir and STS astronauts)

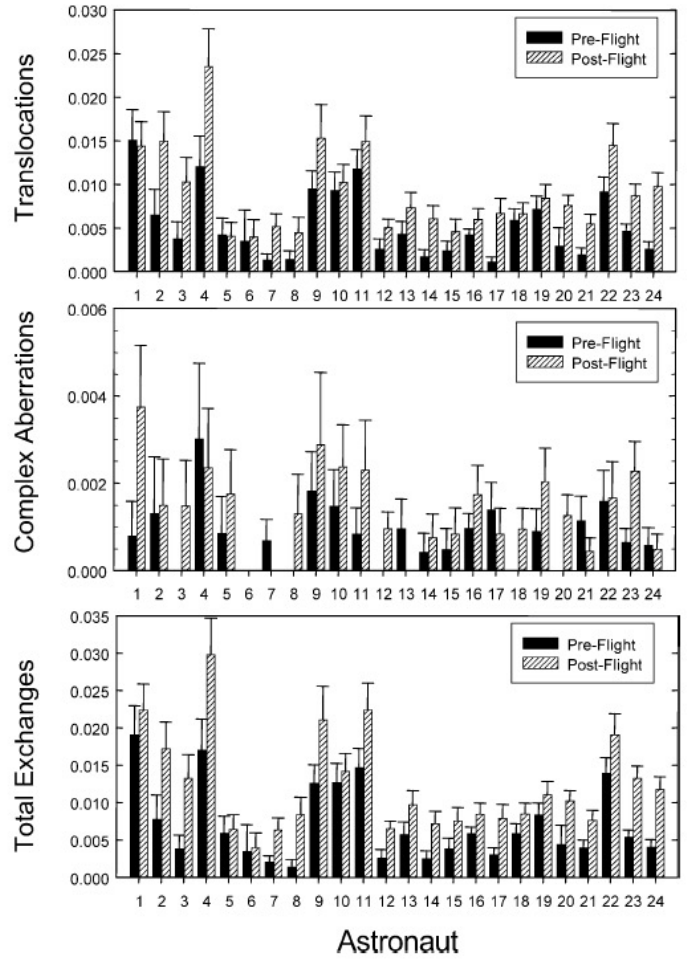
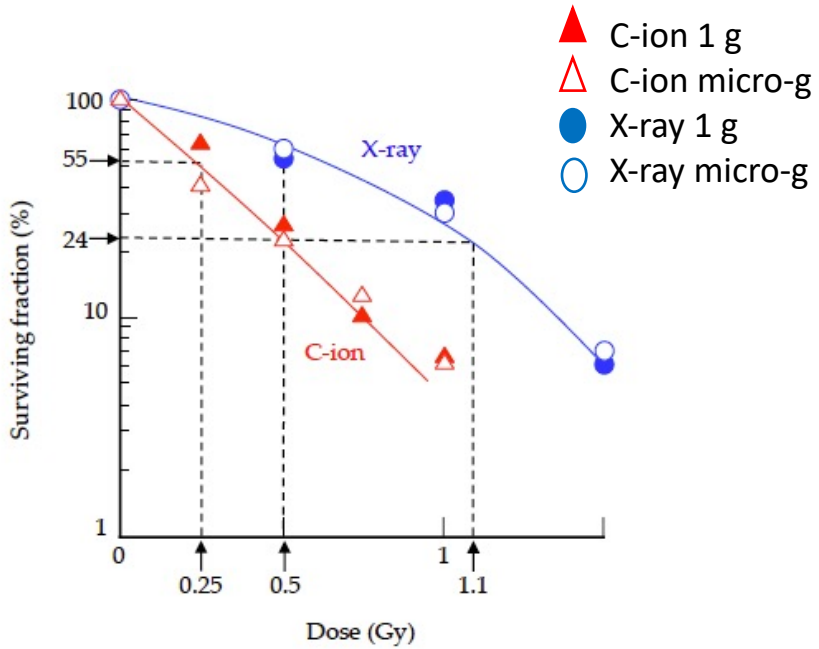
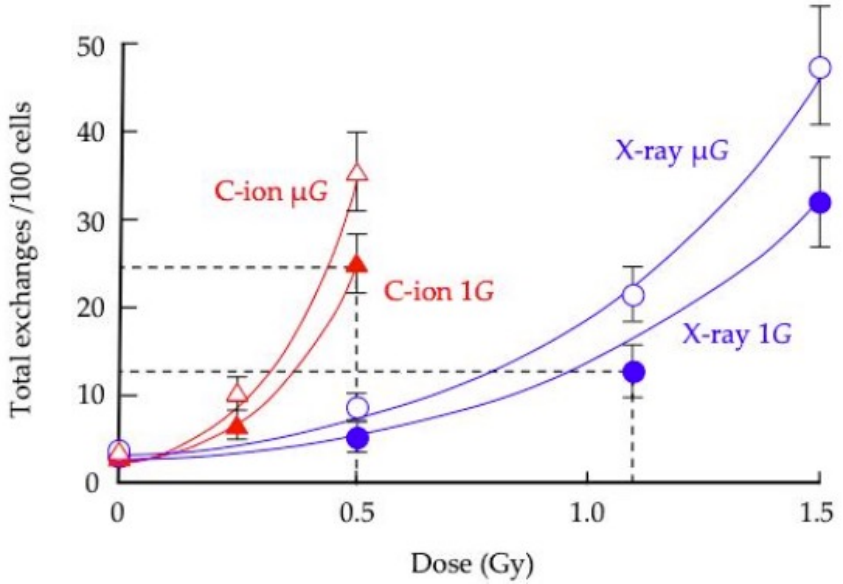


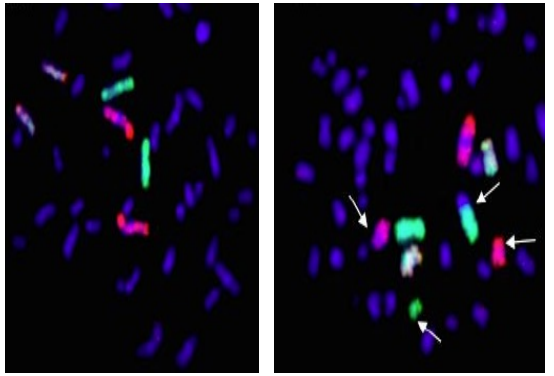
FIG. 4. Frequency of translocations, complex aberrations or total chromosome exchanges measured in each astronaut's blood lymphocytes before and after his or her respective space mission on ISS, Mir or STS. Increases in total exchanges were observed for all astronauts. Translocations (22 of 24) and complex aberrations (17 of 24) were increased in the majority of astronauts.

Radiation and simulated microgravity together causes the largest effect on chromosomal aberrations in human blood lymphocytes "in-vitro"

Sakuya Yamanouchi 1, Jordan Rhone 2, Jian-Hua Mao 3 , Keigi Fujiwara 4, Premkumar B. Saganti 2, Akihisa Takahashi 1,* and Megumi Hada.
Life 2020, 10, 0187 ; doi:10.3390/life10090187







- Radiation exposure decreases cell viability
- Carbon ions are more lethal than x-rays
- **Simulated microgravity has no effect on cell viability**

- **Radiation exposure increases chromosomal aberrations**
- Carbon ions are more injurious than x-rays
- **Simulated microgravity further increases the number of chromosomal aberrations**
  - Some chromosomal aberrations may result in disease (e.g., cancer)

Summary

- Space Biology contributes to basic research (expansion of knowledge) and the fundamental (or mechanistic) arms of research to understand the biological responses to space.

- To do this, Space Biology uses multiple model organisms spanning from the simplest unicellular systems to complex multicellular plant and animal (vertebrate and invertebrate) systems for ground and spaceflight research.

- In spaceflight, organisms can experience microgravity, partial gravity, or hypergravity as well as elevated radiation, and other environmental stressors.

- It will be important for us to determine the biological effects of these space-relevant stressors so that we understand them and develop effective countermeasures to prepare us for long duration human exploration of the Moon and Mars.

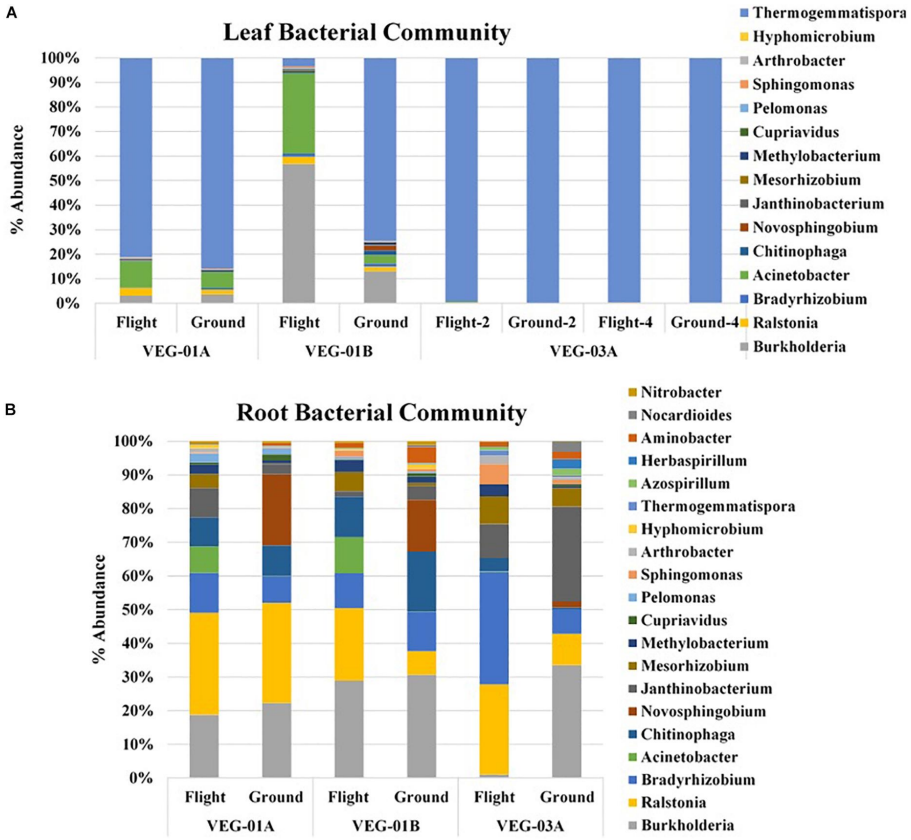
Acknowledgment: Dr. Anthony Hickey – Senior Support Scientist for Space Biology

Thank you!

Microbiological and Nutritional Analysis of Lettuce Crops Grown on the International Space Station

Khodadad, Hummerick, Spencer, Dixit, Richards, Romeyn, Smith, Wheeler, and Massa. **Frontiers in Plant Science**, March 2020: https://doi.org/10.3389/fpls.2020.00199

- Characterization of food safety, microbial communities, and nutritional content of three lettuce crops grown over three years.
- **Indicated that leafy vegetable crops can produce safe, edible, fresh food to supplement to the astronauts' diet,** and provide baseline data for continual operation of the Veggie plant growth units on ISS.



The Influence of Spaceflight on the Astronaut Salivary Microbiome and the Search for a Microbiome Biomarker for Viral Reactivation

Urbaniak, Lorenzi, Thissen, Jaing, Crucian, Sams, Pierson, Venkateswaran, and Mehta. **Microbiome,** April 2020: 8(1):56. doi: 10.1186/s40168-020-00830-z.

(Study sponsored by NASA's Human Research Program with postdoctoral support from Space Biology for environmental sample analyses)

- An investigation into whether and how the human salivary microbiome is affected pre-flight, in- flight (ISS), and post-flight (upon return to Earth).
- **Microbiome (alpha) diversity and richness was significantly increased during exposure to spaceflight, as compared to pre-flight and post-flight data.**
- Beta diversity of the salivary microbiome showed no distinct clustering, suggesting no microbiome differences between subjects and flight status.
- *Streptococcus* was the most abundant organism in the saliva.