BPS Advisory Committee Meeting April 25-26, 2024

Space Biology Program Update

Sharmila Bhattacharya Space Biology Program Scientist Lynn Harrison Deputy Space Biology Program Scientist Anthony Hickey Space Biology Senior Support Scientist John Howard Space Biology Program Executive

Biological & Physical Sciences

National Aeronautics and Space Administration







Recent Spaceflight Missions



Recent Activities and Achievements



Accomplishments in Open Science



Space Biology Funding Opportunities



Science Highlights

Recent Missions

Ó

Biological Experiment 1 (Bio-Expt 1) carrying plant, fungi, and algae launched on Artemis I

- Experiments were launched on 11/16/2022 and returned on 12/11/2022
- Bio-Expt 1 seeks to uncover the genetic and biochemical pathways in model organisms that confer the best survival advantage under combined spaceflight stressors
- Won the NASA 2023 Agency Honor Award for Group Achievement !



Timothy Hammond



Frederica Brandizzi



Chlamydomonas reinhardtii



Arabidopsis thaliana



Bio-Expt 1 launch





Zheng Wang

Aspergillus niger



Saccharomyces cerevisiae



Luis Zea

Rodent Research-20

- This experiment was designed to study the effects of spaceflight on the fertility of adult female mice:
- Forty female mice were launched to the ISS on SpX-29 on Nov. 9th, 2023.
- After 60 days, tissues were preserved on the ISS from half the cohort for subsequent analysis.
- Remainder of the cohort returned to Earth alive on SpX-29 (12/22/23) and were mated with male mice.
- Mating was successful and F1 pups were born and delivered to the PI for further analysis (02/28/24).
- Multigenerational studies are ongoing with some potentially interesting epigenetic phenotypes.





Dr. Lane Christenson, KUMC





MVP-Cell-02A

Experimental Evolution of *Bacillus subtilis* Populations in Space: Mutation, Selection, and Population Dynamics



PI: Dr. Craig Everroad, NASA Ames Research Center

- MVP-Cell-02A launched on NG-19 in August 2023 and ran successfully on the ISS.
- Different strains of Bacillus subtilis were 'raced' along solid surfaces to allow continuous selection. Imaging captured adaptive changes in fitness.
- Upon return on SpX-29, deep sequencing of winners will identify mutation rates, mechanisms, and targets of selection.
- This investigation advances our understanding of the evolutionary processes and challenges facing biological systems during long-term space exploration and habitation.

MABL-A: Role of Mesenchymal Stem Cells in Microgravity Induced Bone Loss

- MABL-A assesses the effects of microgravity on bone marrow mesenchymal stem cells (MSCs), specifically their capacity to secrete bone forming and bone dissolving cytokines (small secreted proteins that affect other cells).
- MABL-A launched on NG-20 on January 30th, and flight samples will return on SpX-30 in April 2024.
- MCSs from 12 human bone marrow donors (6 males and 6 females, 3 young and 3 old in each group) were used.
- MSCs produce bone-forming cells and are known to play a role in making and repairing skeletal tissues.
- Results aim to provide a better understanding of the basic molecular mechanisms of bone loss caused by spaceflight and normal aging on Earth.



PI: Abba Zubair, M.D., Ph.D. Mayo Clinic, Jacksonville, FL



Half of samples were differentiated into Osteoblasts/Osteocytes, while half were not.

Mouse Habitat Unit-8 (MHU-8) Mission

- The NASA-JAXA Joint Partial-gravity Rodent Research Mouse Habitat Unit-8 (JPG-RR MHU-8) mission is the first rodent mission to test partial gravity using centrifugation on ISS (0, 0.33, 0.66, 1 g).
- Multi-disciplinary study involving principal and coinvestigators from Space Biology, HRP and JAXA.
- PI team will investigate multiple biological systems (bone, muscle, cardiovascular system, neuro-performance, circadian rhythms, and microbiome).





Vitaterna Fuller Space Biology

Bouxsein

HRP



Takahashi JAXA



Launch and Return of More Space Biology Experiments

- Several BPS-funded space biology flight experiments were launched and returned on SpaceX-26, 27, 28, 29, NG-18, and -20, CREW-5 and -7; and Axiom-3.
- The experiments supported included Plant Habitat (PH)-03A and B, PH-06, Veggie (VEG)-05, DynaMoS, APEX-10, BRIC-25, and BRIC-26.
- Principal Investigators supported were Drs. Paul (University of Florida), Massa (KSC), Jansson (PNNL), Gilroy (University of Wisconsin), Iyer-Pascuzzi (Purdue University), and Rice (University of Florida).
- Experiments asked a range of biological questions, encompassing plant-microbe interactions, plant epigenetics, crop production, bacterial quorum sensing, and microbiome dynamics.
- Organisms studied included Arabidopsis thaliana, Solanum lycopersicum (tomato), Bacillus subtilis, Staphylococcus aureus and a consortium of soil microbes.



VEG-05



PH-03A



BRIC-25



Plant Experiments Anticipated on NG-21 & SpX-31

- Plant Habitat (PH)-07: PI Dr Massa
 - Will investigate how controlled water stress affects plant health and the microbiome in 'Outredgeous' red romaine lettuce, grown under ISS conditions.
- Advanced Plant Experiments (APEX) in Space-09: PI: Dr. Handakumbura
 - Will investigate the impact of spaceflight on C3 and C4 metabolism using the model grasses, *Brachypodium distachyon* and *Setaria viridis*.
- VEG-06: PI: Dr. Lewis
 - Will determine how microgravity affects interaction between alfalfa plants and symbiotic Nitrogen-fixing (N-fixing) bacteria.
- ARTEMOSS: PI: Dr. Zupanska
 - Will determine how the combined effect of cosmic ionizing radiation and microgravity affects the biology of the Antarctic moss *Ceratodon purpureus*.
- Biological Research in Canisters (BRIC)-Light Emitting Diode (LED)-002: PI: Dr. Gilroy
 - Will investigate plant microbial pathogenicity during spaceflight using Arabidopsis thaliana.





Recent Activities & Achievements

NASA Senior Scientist and BPSfunded PI receive prestigious awards



Dr. Raymond Wheeler was selected as a **Fellow of the American Society for Gravitational and Space Research** (ASGSR) in recognition of distinguished contributions to the advancement of gravitational and space research.



Dr. Anna-Lisa Paul, Director of the Interdisciplinary Center for Biotechnology Research (ICBR) at the University of Florida was honored as Lifetime Fellow by the American Association for the Advancement of Science (AAAS).

A Researcher's Guide to Plant Science (2023) is Published

The guide contains the following information:

- A broad overview of what has been learned from plant/crop research on the ISS.
- A description of plant growth hardware on the ISS and associated support facilities.
- What it takes to develop and launch plant experiments on the ISS.



www.nasa.gov/connect/ebooks/researchers_guide_plant_science_detail.html

NASA Space Life Sciences Library (NSLSL) is released for public use

- NSLSL database development initiated by the Microgravity Simulation Support Facility (MSSF) was completed on 07/25/2023.
- The NSLSL is a public-access database that houses peer-reviewed publications, dissertations, NASA technical publications, white papers, and patents related to space life sciences.
- The NSLSL will provide a valuable resource for the space life science community.



Homepage of the NSLSL https://public.ksc.nasa.gov/nslsl/ NASA Kennedy Space Center establishes partnerships with an Australian Research Council (ARC) center that seeks to enable human deep space exploration through plant and food redesign.



Plant Space Biology takes center stage at the largest gathering of plant scientists in North America

- The American Society of Plant Biologists (ASPB) : 2023 annual meeting in Savannah, Georgia Aug 5-9.
- A plenary symposium titled, Thriving in Deep Space: Plant Biology for the Moon, Mars, and Beyond: more than 1000 attendees from 50 countries got to know about the field of plant space biology.



NASA Plant Space Biology exhibit booth at the Savannah Convention Center





Space Biology-funded PI Dr. Janet Jansson giving an ASPB plenary talk on microbial dynamics in space



Plants in Space educational booth at the Forsyth Farmer's Market

International Collaborative Workshop

- Space agencies from the International Life Sciences Working Group (ISLSWG) and the European Low Gravity Research Association (ELGRA) are organizing a workshop titled "Plant Science for Space Exploration and Earth Applications"
- The workshop will be held at the Spine in Liverpool, United Kingdom from September 3-6, 2024
- Four scientific sessions:
 - Plant Adaptation and Response to Space Environmental Stress
 - Plants for Environmental Control and Life Support Systems in Space
 - Advances in Plant Gravitational Biology and Space Genomics
 - Enabling Technologies for Crop Production in Space and Applications for Earth Agriculture



More Collaborations

• With ISSNL (ISS National Lab):

- Biospecimen sharing collaboration for RR-28 experiment (PI: Ramkumar).
- "Preclinical Validation of a Modifier Gene Therapy to Prevent Spaceflight-Associated Oxidative Stress and Apoptosis in Microgravity Model of Dry Macular Degeneration".
- Procured an OCT (Optical Coherence Tomography) machine to enable science analysis & tissues will be archived in Space Biology's open science sample repository (NBISC: https://osdr.nasa.gov/bio/)

• With ESA & JAXA (The European and Japanese Space Agencies):

- Open science data collaboration for "omics" data between ESA and NASA for Genelab (in work).
- JAXA and NASA have cross-referenced each other's open science databases to facilitate searches.
- With Partners from the International Life Sciences Working Group (ISLSWG):
 - Organizing an international Plant Workshop titled "Plant Science for Space Exploration and Earth Applications" at the ELGRA meeting in 2024 (POC: Elison Blancaflor)
- With ARES (NASA's Astromaterials Research and Exploration Science) division:
 - Partnered on Lunar Regolith ROSES solicitation (highlighted in the last section of this talk)
- With HRP (Human Research Program):
 - Partnered on HRP's Flagship Solicitation 2024 (highlighted in the last section of this talk)
 - "Space Tomatoes" collaboration with HRP to vet procedures for crew consumption with FDA, USDA, EPA etc.

Accomplishments in Open Science

 Open Science Data Repository (OSDR)

6

Open Science Data Repository Released

Physiological/Phenotypic/Imaging/ Environmental Telemetry Data



Molecular/Omics Data



Biospecimens



NASA Open Science Data Repository (OSDR) osdr.nasa.gov/bio

- Single Submission Portal (BDME)
- User Interface/Website Tool for RDSAs (Research Data Submission Agreements)
- Maximally Open Access with Necessary Controls for Sensitive Data
- Data Maximally FAIR



OSDR Database (GeneLab and ALSDA)



Reuse of Data and Enabling New Discoveries



The **Space Omics and Medical Atlas (SOMA) across orbits** package of manuscripts to be published in **Nature Portfolio**.

• Upcoming • •

International collaboration of papers related to space biology and aerospace medicine featuring data from the first **all-civilian crewed mission**, *Inspiration4 (I4)*.

- Over 100 institutions from more than 25 countries
- Featuring collaborative metaanalysis manuscripts from the AWGs
- Data submitted to OSDR
- Led by Christopher Mason and Afshin Beheshti

• To be published in April/May 2024

Expanded OSDR: Controlled Access Data



New app: Multi-Study Viz

Expanding GeneLab visualization app to now compare data across RNA-seq studies. Users can now discover how gene expression changes within one study or across multiple studies. https://visualization.genelab.nasa.gov/data/

PC2



				10.1	nuro p-value:
ne k					
o cano				Maximum adjus	.ted p-value:
plot Group 1	Copy CSV Excel PC	DF Print			Search:
r plot Group 2	ENSEMBL	Symbol	LOG2FC	PVAL	ADJP
итар) Е					
A	Search ENS	Search Symbol	Search LOG2FC	Search PVAL	Seerch ADJP
DS-4786LDS-	ENSMU500000031543	Ank1	-1.8700695226	5e-10	0.0000069515
GLDS-1376GLDS-	EN5MU5G0000044309	Apol7c	0.956731259	1.42e-8	0.0000561777 0.0001143909 0.0003180109
GLDS-1736GLDS- 8GLDS-245	ENSM//500000020108	Ddit4	-1.2769254691	3.85e-8	
S-478GLDS-488GLDS-	ENSWU500000032080	Appel	-1.2372393607	134e-7	
738GL05-7688GL05-245	ENSMUS00000030302	Atp2b2	-1.1445791174	1.528e-7	0.0003293267
ANSV(S):	ENSWUS00000029188	Sic34a2	-1.5189323708	2.281e-7	0.0004512668
TOPS:	ENSMU500000030244	Oys2	0.5579928642	0.0000010983	0.0017383056
wight	ENSMUS00000021579	Lric14b	-0.9323304158	0.0000012277	0.0017388094
F SAMPLES 112	ENSMUS00000048521	Cxor6	0.6073468945	0.0000012451	0.0017388094
W GENES 10617	ENSMJ500000006574	Slo4a1	-1.4885038062	0.0000015841	0.0020765442
Selection	ENSEMBL	Symbol	LOG2FC	PVAL	ADJP
s 1: Ground Control	Showing 1 to 10 of 10,514 entries	STR 2010 100	1000000000	Previous 1 2 3	4 5 _ 1.052 Next





Environmental Data App and RadLab



The Environmental Data App (EDA) is a portal where users can visualize and compare ISS (International Space Station) cabin environmental telemetry data and radiation data gathered from spaceflight missions.

https://visualization.osdr.nasa.gov/eda

cecraft. In RadLab ISS, Lidal Data overvi ecraft I ISS, REM Total dose rat O Total flux Data compari asuremen Time series Total dose ra O Linear O Log) Total flux $R^2 = 0.4$ Data access / A Time period Pair plot ecal Start: 01/01/2023, 12:00 AM ISS Lidal uGy/hor otal dose rate (both as

- GCR

- SAA

RadLab is a portal that aims to provide a single point of access to radiation telemetry data from multiple databases maintained by multiple space agencies.

https://visualization.osdr.nasa.gov/radlab

ESA Omics Data

In the next 5 years, ESA estimates they will collect 300 TB of omics data.

- Majority of the omics projects are transcriptomics across several platforms using various organisms.
- To utilize the current infrastructure, ESA SciSpacE team has requested all omics data be submitted and hosted on GeneLab (via OSDR).
- Formal agreement for collaboration is currently in progress.



This initiative aims to centralize space omics data for the scientific community, facilitating cross-analysis and interoperability (FAIR), and leading to cost savings by avoiding infrastructure duplication.

Cross linking HREDA and OSDR

HREDA - Human and Robotic Exploration Data Archive (ESA)

HRE Data Archive Qe to HREDA Home Page			Advanced Search	HREDA Help		SIGN IN	eesa		
×	× + Investigations Search History platform is ISS -								
Investigation		Investigation Name	Missions 🔺	Team Coordinator(s) Name(s)	Start 🔺	End 🔺	Description *	Platform 🔺	
Name or description Platforms	Lad	3DC	Inc08, Inc09, Inc19, Inc20	Massimo Sabbatini	2003-10-21	2009-10-11	A 3D-Camera was flow to the ISS for taking stereoscopic images of the interiorof the ISS, and in particular of its experiment facilities. The photos wereconsidered as a novel concept to visualise the interior of the ISS for diversepurposes.	ISS	
x ISS × •		Airway Monitoring	Inc41, Inc42, Inc45, Inc46, Inc47, Inc48, Inc49, Inc50, Inc53, Inc54, Inc55, Inc56, Inc57, Inc58, Inc59, Inc60	Lars Karlsson	2014-09-11	2019-10-03	The main goal was to determine the lung diffusion capacity for nitric oxide (NO).	ISS	
MISSIONS		ANALOG-1	Inc61, Inc62	Kjetil Wormnes	2019-10-04	2020-04-17	The METERON ANALOG-1 experiment was a technology demonstration and teleoperations concept experiment, assessing the efficiency and effectiveness of an robotic control interface for performaning geological tasks.	ISS	
Category Select categories		ANITA-1	Inc15, Inc16, Inc17	Gijsbert Tan	2007-04-10	2008-10-14	The project was a technology demonstrator flight experiment for continuous air quality monitoring inside the crewed cabin of the ISS.	ISS	
Research Keywords		ANITA-2	Inc66, Inc67, Inc68	Atle Honne, Johannes Witt	2021-10-18	2023-03-28	ANITA-2 is a compact gas analyser which can analyse and quantify 33 trace contaminants in the atmosphere aboard the ISS automatically.	ISS	
Select keywords 👻	<u>lad</u>	Antioxidant Protection - PROMETEO	Inc67, Inc68	Gianni Ciofani, Giada Graziana Genchi	2022-03-31	2023-03-28	This project investigated polydopamine nanoparticles-based (NP-based) countermeasures to microgravity- and cosmic radiation-induced oxidative stress.	ISS	
Team Participant Name of member(s)	<u>[.11</u>	AquaMembrane	Inc43, Inc47, Inc49	Maja Tommerup	2015-03-12	2016-10-30	This research investigated the ability of the Aquaporin membrane to removeresiduals of Dimethylsilanediol (DMSD) in the ISS Water recycling system. Inaddition, NASA was evaluating the use of the Aquaporin membrane forreplacement of the ISS Water Processor	ISS	
Start/end dates dd/MM/yyyy = dd/MM/yyyy in Investigations with data		ASIM	Inc55, Inc56, Inc57, Inc58, Inc59, Inc60, Inc61, Inc62, Inc63, Inc64, Inc65, Inc66, Inc67, Inc68	Torsten Neubert	2018-02-28	2023-03-28	ASIM is an Earth observation facility for the study of severe thunderstorms and their role in the Earth's atmosphere and climate.	ISS	
CLEAR	Lad	Astro Pi	Inc51, Inc52, Inc53, Inc58, Inc59, Inc60, Inc61, Inc64, Inc65, Inc66, Inc67, Inc68, Inc69	David Honess	2017-04-11	2023-09-20	Astro PI is a competition scheme for school students, asking for thedevelopment of codes for the AstroPI/ Raspberry PI computer on board the ISS. The resulting data are retransmitted to the school teams.	ISS	

OSDR – Open Science Data Repository (NASA)

		NASA Open S	icience for Life in Space	Home About ় Data & Tr	ools 🗸 Working Grou	ps v Help v
General Search Filters	Open Sci	ence Data Repos	sitory Search			
Data Source	Search Datase	rts.		۹		Sort By: Release Date *
GeneLab ALSDA NIH GEO EB PRIDE ANLMG-RAST		Characterization of B blofilms)	liofilm Formation, Growth, a	and Gene Expression on Diff	erent Materials and E	ttemin per page 25 ▼ 1-25 of 454 I < < > >I nvironmental Conditions in Microgravity (Morphology of Penicilium rubens
-	-	Organisms	Factors	Assay Types	Release Date	Description
Data Type Study Experiment	Study OSD-628	Penicillium rubens	Spaceflight Growth Environment Time	Molecular Cellular Imaging	12-Sep-2023	Microorganisms' natural ability to live as organized multicellular communities – also known as biotims – provides them with unique survival advantages. For instance, biotims are protected against en
Biospecimen Payload		Highlights: Image File Din a/sda	nensions Platform And Sample Lat	eling Information Labeling Protocol /	4LSDA with a reusable te	mplate, which was created through feedback provided by subject matter experts in the ALSDA
Show more 🖌		Combined space stre	essors induce independent	behavioral deficits predicted	by early peripheral bl	ood monocytes (Behavioral Assays)
Study Search Filters		Organisms	Factors	Assay Types	Release Date	Description
Project Type Ground Spaceflight	Study OSD-618	Mus musculus	Hindlimb Unloading Ionizing Radiation Sex Housing Condition	Behavior Behavior Behavior Behavior Behavior Behavior	29-Aug-2023	interplanetary space travel poses many hazards to the human body. To protect astronaut health and performance on critical missions, there is first a need to understand the effects of deep space hazard
High Altitude		Highlights: And Objects B ALSDA alsda	alance Beam - Assay Characterist	cs Balance Beam - Analysis Charact	eristics ALSDA with a reu	sable template, which was created through feedback provided by subject matter experts in the
Assay Type		Characterization of B aeruginosa biofilms)	iofilm Formation, Growth, a	and Gene Expression on Diff	erent Materials and E	nvironmental Conditions in Microgravity (Morphology of Pseudomonas
Amplicon Sequencing Assay Bisulfite Sequencing Behavior Behavior (Gait)		Organisms	Factors	Assay Types	Reliesse Date	Description

To enhance discoverability, HREDA and OSDR will cross link experiment pages and data from common missions.

Formal agreement with ESA for collaboration is currently in progress

Cross linking with JAXA ibSLS



Welcome to NASA GeneLab - the first comprehensive space-related omics database; users can upload, download, share, store, and analyze spaceflight and spaceflight-relevant data from experiments using model organisms.

Integrated Biobank for Space Life Sciences (ibSLS)



Perform large-scale analysis of biological omics data



0

Recent & Anticipated Future Funding Opportunities

Space Biology Solicitation for Lunar Regolith (Simulant) Studies

Research Studies Released as ROSES Program Element E.9:

- Selections Announced: Jan 2024
 - Released in collaboration with NASA's Astromaterials Research and Exploration Science (ARES) Division
 - ARES will supply lunar regolith simulant that is formulated to resemble regolith present within the Lunar Highlands of the lunar south pole, (near the candidate landing sites proposed for the Artemis III Mission).
 - The curation office will supply lunar regolith collected from Apollo missions to a subset of awardees with demonstrated progress with simulant to conduct a final set of validation studies using genuine material.
 - In grants selected for a total of \$ 2.3 million over 3 years.

Space Biology Solicitation to Study How Organisms can Thrive in Space

ROSES-2022 Program Element E.11: "Research Pathfinder for Beyond Low Earth Orbit Space Biology Investigations":

- Selections Announced: ~Sept 2023
 - Initially intended for launch on Artemis II but could not be accommodated on that mission.
 - Selected 1 proposal for flight on ISS and 1 as a ground study.
 - 2 grants selected for a total of 1.5M over 3 years

HRP's Recent Call in Collaboration with Space Biology

2024 HERO Appendix A, Topic 2: NASA Human Research Program Flagship Opportunity:

- Released: Oct 2, 2023;
- Step-1 Proposals (mandatory) Due: Nov 1, 2023
- Final Step-2 Proposals Due: Jan 30, 2024
 - The NASA Human Factors and Behavioral Performance (HFBP) Element within HRP
 - Appendix A, Topic 2, "Biomarker exploration system for measuring operationally meaningful performance in future exploration missions".
 - Animal ground studies with radiation in conjunction with other relevant stressors such as sleep loss, circadian misalignment etc.
 - Funding over 3 years for a total of \$1.2M (inclusive of directs and indirects).

Consortium in Biological Sciences:

Space Biology will release a solicitation for space-relevant research investigations in response to the Commerce, Justice, Science, and Related Agencies Fiscal Year 2024 Appropriations Bill.

- This program element is established in response to the <u>Explanatory</u> <u>Statement</u> (page 67) of the Commerce, Justice, Science, and Related Agencies Fiscal Year 2024 Appropriations Bill. That language directs that NASA shall "establish a consortium including academic institutions with demonstrated expertise within the human health, animal, and plant sciences."
 - \$2.5M total for up to 5 years period of performance.
 - To be Released under ROSES-2024:
 - Anticipated Release: ~Summer 2024

Space Biology's Upcoming Annual ROSES Solicitation:

 The plan is for Space Biology to release solicitations for animal, cellular, and plant biology that is responsive to the National Academies' Decadal Recommendations as part of the ROSES 2024 announcements.



Science Highlights

(Can only cover a small number of items from a much larger number.)

Evidence of Spaceflight-Induced Adverse Effects on Photoreceptors and Retinal Function in the Mouse Eye.

Citation: Mao, X.; Stanbouly, S.; Holley, J.; Pecaut, M.; Crapo, J. Int. J. Mol. Sci. 2023, 24, 7362.

- Spaceflight induces neuro-ocular changes in astronauts during and after space flight.
- The RR-18 mission (PI Dr. Vivien Mao, Loma Linda U.) characterized acute oxidative damage in ocular structure and retinal function of mice and evaluated the efficacy of an antioxidant in reducing spaceflight-induced changes in the retina.
- Postflight evaluations showed increases in retinal oxidative stress and apoptotic cell death after spaceflight and decreases in the amplitudes of alpha and beta waves.
- Treatment with the antioxidant, BuOE (superoxide dismutase mimic), significantly reduced levels of oxidative stress, but levels of apoptotic cell death, and ERG metrics remained unchanged.



Peggy Whitson performing an eye check aboard the International Space Station. Credit NASA.





Flight induced oxidative stress in cones (yellow signal) which was mitigated by treatment with the antioxidant, BuOE.s

Genetic diversity modulates the physical and transcriptomic response of skeletal muscle to simulated microgravity in male mice

Citation: Zeineddine, Y., Friedman, M.A., Buettmann, E.G. et al. npj Microgravity 9, 86 (2023)..

- Astronaut data shows considerable variation in muscle loss in response to microgravity1.
- Strength losses vary from 0–55% for missions between 30-380 days2,3,4.
- Study compared response of muscle in 8 mouse strains to 3 weeks of hind limb unloading.
- Saw substantial differences in muscle loss between strains.
- Differences are reflected in the magnitude and pattern of changes within muscles from each strain.





Red is unloaded. Blue is control. Adapted from Figure 3 of Zeineddine et al. 2023.

A/J mouse



NOD/ShiLtJ mouse



Sex Differences in Muscle Health in Simulated Micro- and Partial-gravity Environments in Rats.

Rosa-Caldwell ME, Mortreux M, Wadhwa A, Kaiser UB, Sung DM, Bouxsein ML, Rutkove SB. Sports Med Health Sci. 2023 Sep 12;5(4):319-328. doi: 10.1016/j.smhs.2023.0

- Male and female Fisher rats underwent either castration/ovariectomy (CAST/OVX) or sham surgeries.
- After recovery, animals were exposed to either simulated microgravity (0g), partialgravity (40% of weight bearing, 0.4g), or full weight bearing (1g) interventions for 28 days.
- Measurements of muscle size and strength were evaluated prior to and after interventions.
- Females had greater musculoskeletal aberrations during exposure to both microgravity and partial-gravity environments; these differences are not dependent on the presence of sex steroid hormones.



Histology of soleus muscles. Purple shows type 2 fibers, green type 1.



SHAM = sham surgery animals with intact gonads, CAST = castrated males, OVX = ovariectomized females.

Space Biology grants 80NSSC21K0311 and 80NSSC19K1598 to Dr. Megan Rosa-Caldwell and Dr. Seward Rutkove, respectively.

Open Science Enabled. Toward countering muscle and bone loss with spaceflight: GSK3 as a potential target.

Baranowski RW, Braun JL, Hockey BL, Yumol JL, Geromella MS, Watson CJF, Kurgan N, Messner HN, Whitley KC, MacNeil AJ, Gauquelin-Koch G, Bertile F, Gittings W, Vandenboom R, Ward WE, Fajardo VA. iScience. 2023 Jul 21;26(7):107047. <u>https://pubmed.ncbi.nlm.nih.gov/37360691</u>

- In the musculoskeletal system, GSK3 is a negative regulator of muscle and bone mass. Possible target to mitigate spaceflight impacts.
- Study measured the level of GSK3 muscles from mice flown on BION-M1, RR-1, RR-9, and RR-18 obtained from BSP and NBISC.
- Reduced GSK3β in soleus muscles from all missions, correlated with a change from slow to fast twitch muscle fiber types.
- GSK3 knock-down mice showed increased soleus muscle mass, myogenic signaling, and preserved muscle strength after 7 days of hindlimb suspension.
- These results point to GSK3 inhibitors like lithium and tideglusib as being interesting candidates for future investigations.



The authors used **tissue from NBISC and BSP** to show that **GSK3** β content was reduced (-36%) in murine soleus muscles after ~30 days of spaceflight. *Gsk3* muscle knockdown (GSK3^{mKD}) preserved muscle strength after hindlimb suspension. Spaceflight reduced bone mineral density in mice. GSK3^{mKD} increased FNDC5 expression and tibia bone mineral density.

Spaceflight reveals new insights into telomere function that may help plants survive harsh environments

Barcenilla BB, Meyers AD, Castillo-González C, Young P, Min JH, Song J, Phadke C, Land E, Canaday E, Perera IY, Bailey SM, Aquilano R, Wyatt SE, Shippen DE (2023) *Nature Communications*. 14(1):7854. doi: 10.1038/s41467-023-41510-4.

- Repetitive DNA sequences called telomeres are protective structures at the end of chromosomes that serve as biomarkers of the health of an organism.
- An enzyme called telomerase maintains the length of telomeres.
- Telomere length in roots of *Arabidopsis thaliana* plants grown on the ISS remained unchanged despite exhibiting enhanced telomerase activity.
- Results indicate a novel protective function of telomerase in plants that is independent of telomere length.



Telomeres (yellow) in Arabidopsis chromosomes (blue)



Spaceflight



Plant telomerase activity is higher in spaceflight than that on Earth

Ground Control

Plant response to flooding is facilitated through cytosolic calcium signaling

Bakshi A, Choi WG, Kim SH, Gilroy S (2023) New Phytologist 240(5):1830-1847. doi: 10.1111/nph.19274

- Excess water (flooding) is harmful to some plant species because it depletes oxygen in the root zone.
- The manner, by which water behaves in microgravity could cause excessive water accumulation in crop roots.
- Calcium functions as signaling molecules in cells of living organisms.
- This paper shows that signaling pathways that dictate how plants respond to flooding is mediated by calcium through a protein called Cation Exchanger 2 (CAX2).
- CAX2 could present a genetic target to increase plant survival under flooding stress.





4 weeks flooding

Arabidopsis thaliana mutants lacking the CAX2 protein tolerate excess water.

Modeled microgravity affects innate immunity in a beneficial animal-microbe symbiosis that has implications for astronaut health in space

Duscher AA, Vroom MM, Foster JS (2024) Scientific Reports 14(1):2912 doi: 10.1038/s41598-024-53477-3

- The innate immune system is the animal's first line of defense against invading microbes and toxins.
- Microgravity could lead to a dysregulation of innate immunity and pose a health issue for astronauts.
- The Hawaiian bobtail squid Euprymna scolopes and the beneficial bacterium Vibrio fischeri was used as a model to study how simulated microgravity affect the NFkB signaling pathway, a component of the innate immune response pathway.
- Results showed that low-sheared modeled microgravity (LSMMG) accelerated the expression of genes associated with the NFkB pathway, reinforcing previous findings that spaceflight could negatively impact innate immunity.



Hatchling of bobtail squid with the location of the symbiotic light organ depicted (white arrow).



Example of a high aspect-ratio vessel used to simulate LSMMG.

Plenty of Exciting Results and Interesting Trends,

- Study of mitochondrial dysregulation and metabolism changes from space (from model organisms to Twin Study).
- Epigenetics animals, plants, and microbes.
- Understanding the effects of genetic diversity, sex-specific changes, multigenerational effects.
- Crops for the future; fundamental research of plant physiology, omics, cellular, and metabolic responses.
- Look to the future with research on CLDs (commercial LEO platforms) and Beyond LEO (Artemis, CLPS, Orion, and Gateway) –
 - Tissue chips & organoids
 - Model organisms
 - Plants
- Will continue to look at decadal recommended science and more ahead!

but....

CHALLENGE: making things fit in a flat or declining budget environment!



National Aeronautics and Space Administration

0

Thank You!

Biological & Physical Sciences