Biological and Physical Sciences

SPACE BIOLOGY PROGRAM: IN DEPTH BRIEFING

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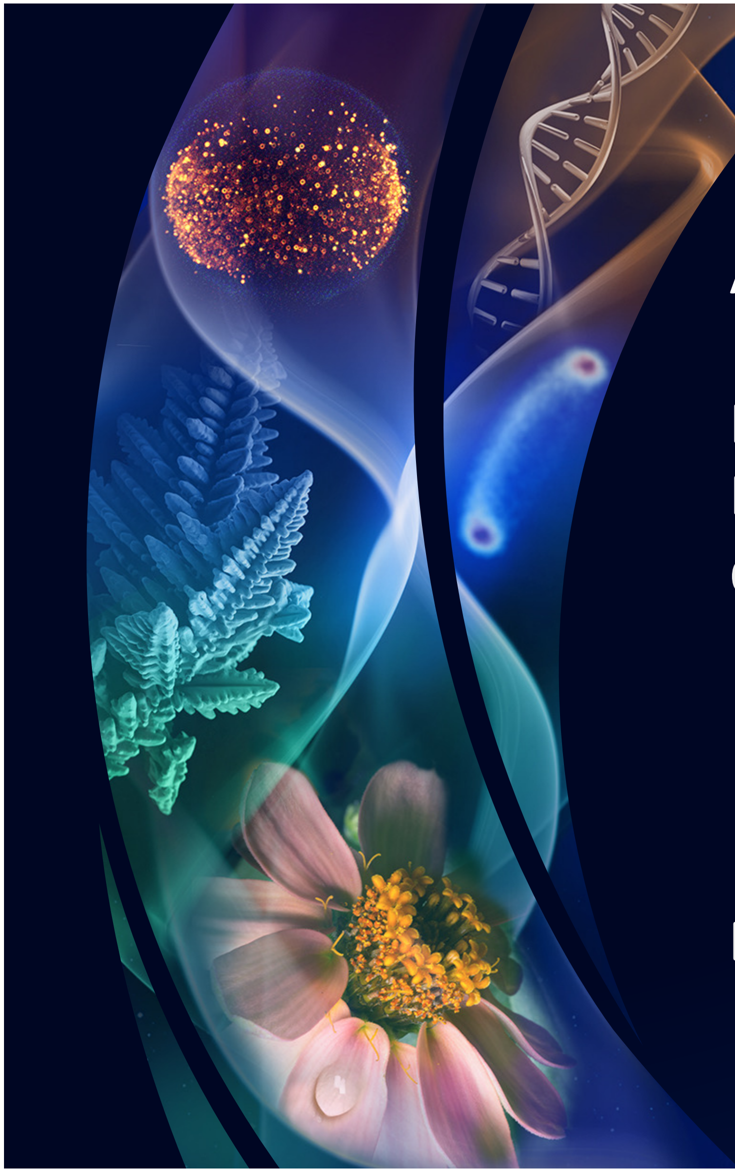
Decadal Survey Committee Meeting
Jan 24, 2022

National Aeronautics and Space Administration



Agenda

A) Thriving in Deep Space (TIDES)
- Challenges of Interest: Spaceflight Stressors

B) Science Topic Areas of Importance to Space Biology

C) Other Transformative science areas

1. Omics/Systems Biology / Quantitative Genomics
2. Genetic Engineering in Plants
3. Plant & Animal Responses to Regolith
4. 3D Tissues and Organ-on-Chip models
5. Artificial Intelligence / Machine Learning (AI/ML)
6. Automation, Miniaturization, and Data Telemetry

D) BACK-UP:

- Platforms for Science for Flight and Ground

Thriving in Deep Space (TIDES)

- Ground studies
- Space studies
- Ground & space studies

Understand Fundamental Mechanisms

Use model organisms to determine how animals/humans respond to deep space environments

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Build the Blocks to Support Human Life

Understand how model plants, crops, & seeds respond to and can thrive in deep space environments

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Build a Foundation for Sustained Life on Mars

Engineer habitats and ecosystems to enable astronauts' independence from Earth

- Stabilize human/animal-plant-microbial ecosystems in the context of multiple deep space stressors

DEEP SPACE STRESSORS

Gravity | Radiation | Temperature/Atmosphere | Day/Night/Circadian Cycle | Regoliths | Isolation

PLATFORM PROGRESSION

Ground → Sub-Orbital → LEO/ISS → Gateway → Lunar Surface → Mars Transit → Martian Surface

MODEL ORGANISM PROGRESSION

Unicellular (e.g., yeast/fungi etc.)

→ Invertebrate (e.g., flies, worms, tardigrades) → Vertebrate (e.g., mice, rats, fish; tissue chips)

→ Simple model plants (e.g., *Arabidopsis*) → Plants for micronutrients, etc.

→ Humans

Thriving in Deep Space (TIDES)

Biological effects of multiple **deep-space stressors**

1. Radiation
2. Gravity
3. Temperature & Atmosphere
4. Day & Night Light Cycles
5. Isolation
6. Regoliths

Cannot accurately replicate on the ground

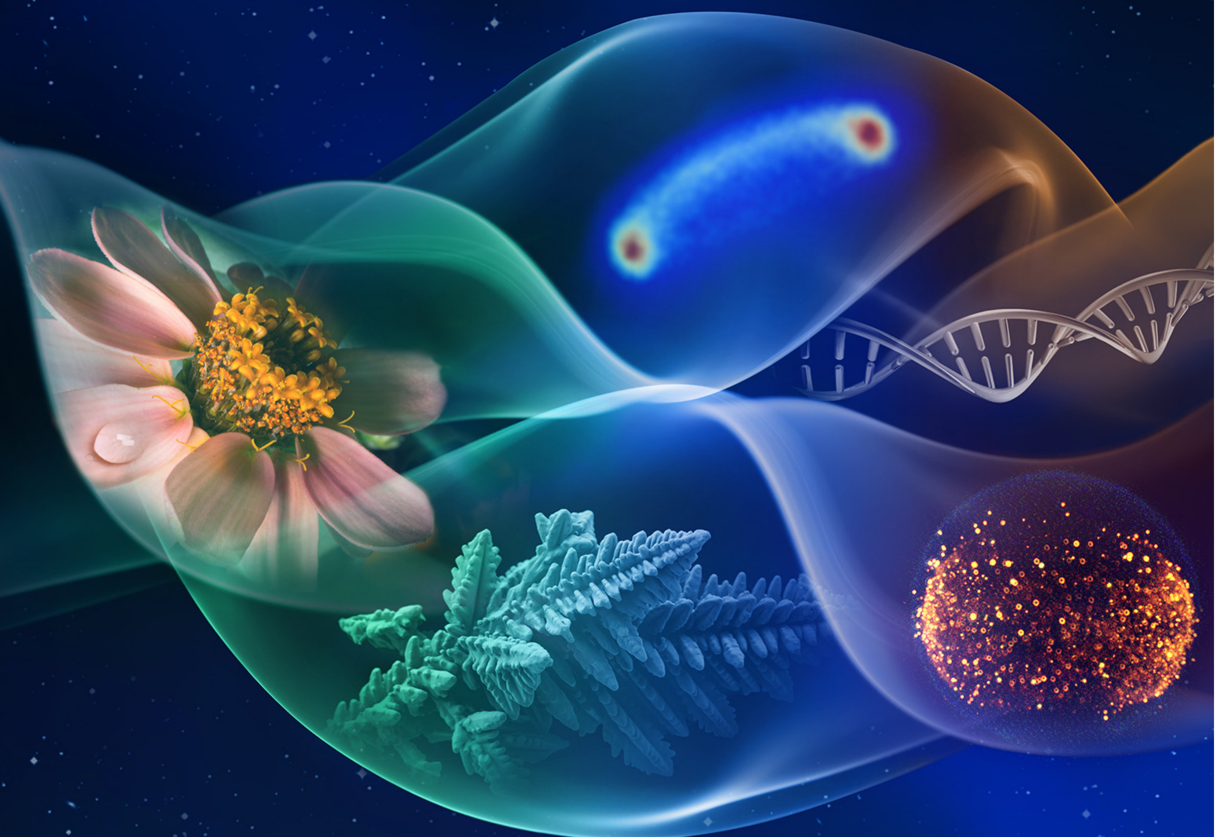
Heavy ions can impact biological systems

Transformative biological science and exploration applications

1. Animal biology — Vertebrate and invertebrate models to probe analogous changes in humans

2. Plant Biology — From plant models to crops to sustain life for long-term human habitation

Microbiology — How it influences animals and plants in space

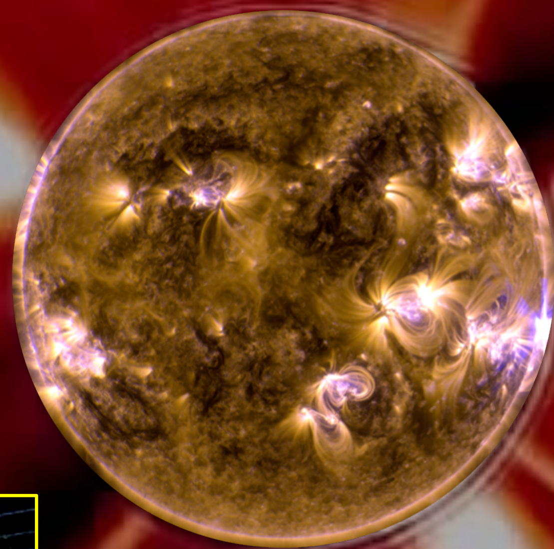


Challenges of Interest:

Spaceflight Stressors - Radiation & Gravity

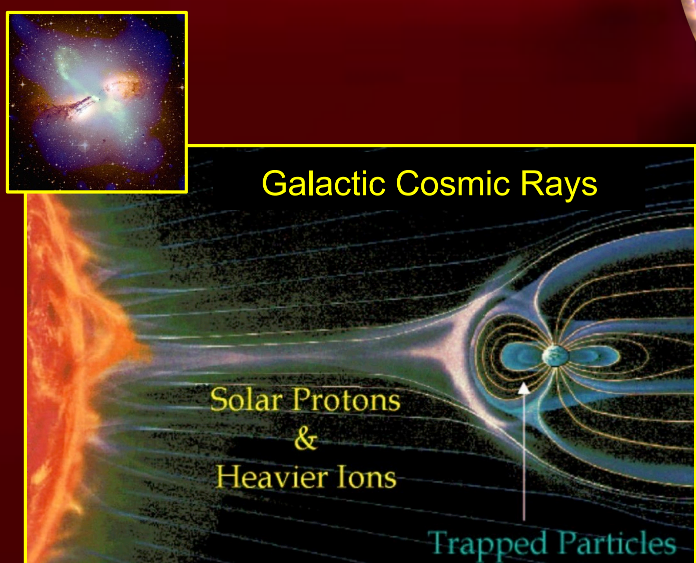
Interplanetary space radiation

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



Ionizing radiation that will affect biology:

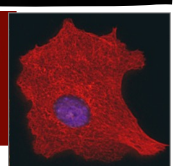
- ❖ **Galactic Cosmic Radiation (GCR)**
- ❖ **Solar Particle Events (SPEs)**



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**



Combined Effects of Spaceflight Stressors

Spaceflight stressors can include:

- Elevated levels of ionizing radiation
- Altered gravity conditions
  - Microgravity, hypergravity, partial gravity on planetary surface
- Elevated CO2 levels; altered PO_2
- Exposure to regoliths/dust
- Altered day/night light cycles
- Social isolation, etc.

Ionizing radiation and altered gravity are two important, spaceflight stressors that show various responses when applied together, depending on the organism, tissue type and assay. When combined, a given response to stressor may be:

- Amplified (additive, synergistic)
- No effect
- Suppressed (data not shown)

Bottom line:

We still have a ***very limited understanding of how living organisms respond to the combinations of the various spaceflight stressors.***

It is ***critical to expand our knowledge base***, enabling us to better prepare for possible risks to astronaut health posed by long-duration spaceflight missions to the Moon and Mars.

Increase in Frequency of Lethal Mutations in *Drosophila* male germ cells during spaceflight

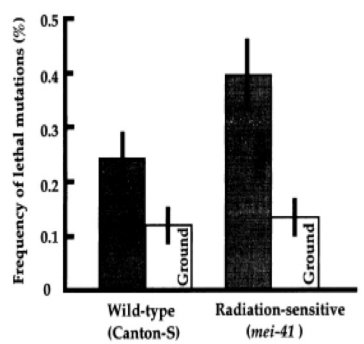
Sex-linked recessive F2 screen

M.Ikenaga, I. Yoshikawa, M.Kojo, T. Ayaki, H.Ryo, K. Ishizaki, T. Kato, H.Yamamoto and R. Hara (1997). *Biological Sciences in Space* 11:346. (Space shuttle Endeavor flight)

Adult males sent into space for 8 days, mated after return. Analyzed F2 offspring for lethality of irradiated X chromosome inherited from grandfather from space.

Strain	Exp. group	No. of X-chromosomes tested	No. of lethal X-chromosomes detected	Frequency of lethal mutations* (% ±SE)
wild type Canton-S	flight	9,176	22	0.24 ±0.051#
	ground control	9,177	11	0.12 ±0.036
radiation-sensitive *mei-41*	flight	9,355	37	0.40 ±0.065§
	ground control	8,975	12	0.13 ±0.037

*Number of lethal X-chromosomes divided by the number of X-chromosomes tested.
#Significantly different at the 5% level from the ground control group.
§Significantly different at the 1% level from the ground control group.



Effects of radiation and spaceflight on *Arabidopsis thaliana* plant seeds

Long Duration Mission (5.8 yr) *Arabidopsis thaliana* seeds with ambient radiation

M.W. Zimmerman, K.E. Gartenbach, and A.R. Kranz (1994). *Adv Space Res* 14:51 (LDEF mission)

- Very long duration mission, at higher than usual orbit (324-479 km compared to 350-390 km for ISS)
- Found significant changes that correlate with radiation hits (Biostack concept)
- Significant **decrease in germination, increased delays in germination**
- **Increased mutation frequencies**

Long duration study with ambient radiation, shows significant spaceflight effects on seed germination and mutation frequencies when seeds hit with radiation in flight.

Arabidopsis thaliana seeds irradiated with particle beams on the ground or exposed to radiation during Antarctic balloon flight

B.Califar, R.Tucker, J. Cromie, N. Sng, R. A. Schmitz, J. A. Callaham, B. Barbazuk, A-L. Paul, and R.J. Ferl (2018)
http://gravitationalandspaceresearch.org/index.php/journal/article/view/824

- Proof-of-concept experiment to assess the genomic impact of space radiation on seeds
- Secondary payload for the December 2016 high-altitude (36-40 km), 30 day south polar balloon flight above Antarctica (ANT).
- Investigation of the biological effects of Galactic Cosmic Radiation (GCR) at Brookhaven National Laboratory (BNL).
- BNL and ANT-treated Seeds showed **significantly reduced germination rates & elevated somatic mutation rates when compared to non-irradiated controls**, with the BNL mutation rate being higher than that of ANT.
- Genomic DNA from plants presenting distinct aberrant phenotypes was evaluated with whole-genome sequencing

Effects also seen on seed germination and mutation frequencies with Antarctic balloon flight and in ground studies with GCR radiation.

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) was used to determine effects of simulated microgravity, alone or combined with radiation, in vascular, immune, CNS and musculoskeletal systems.

Vascular dysfunction: Heavy ion radiation and simulated weightlessness impairs vascular reactivity in hindlimb blood vessel to greatest extent when combined. Effect mediated 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

Hindlimb Unloading (HU) to simulate weightlessness

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Space radiation simulations At BNL/NSRL

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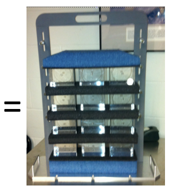
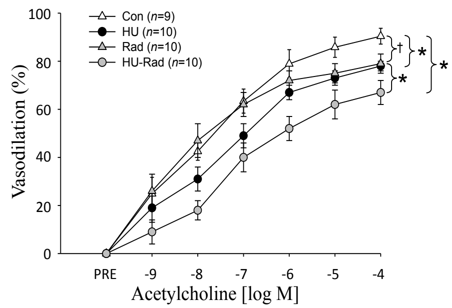


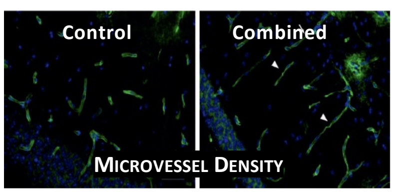
HU during irradiation



- ^{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***.

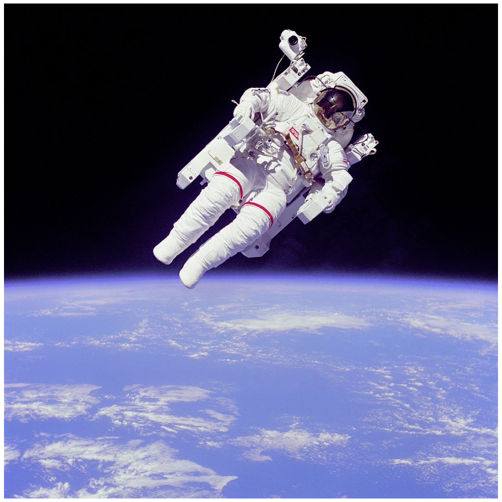
CNS: Simulated microgravity and low-dose/low-dose-rate radiation induce oxidative damage in the mouse brain.

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.
- Additional recent evidence for adverse effects of spaceflight, as well as combined simulated weightlessness and radiation, on markers of Blood Brain Barrier, behavior, and oxidative stress in the eye.

Increased chromosomal aberrations previously observed in lymphocytes of 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 (e.g., charged carbon, iron, silicon ions etc.) which are difficult to shield, and will be more abundant as astronauts go beyond the Van Allen Belt

TABLE 2
Test of Possible Increase in Frequencies of Complex Chromosomal Aberrations or Translocations for Combined Astronaut Samples from ISS Missions or all Mir, STS and ISS Missions using Biodosimetry

Mission(s)	Cells scored pre-flight	Cells scored post-flight	Aberrations (WGE) pre-flight	Aberrations (WGE) post-flight	Relative number and 95% CL	*P* value
Complex aberrations						
ISS	143,505	164,856	113	143	1.58 [1.26, 1.99]	$<10^{-4}$
ISS, Mir and STS	151,591	188,988	189	248	1.51 [1.23, 1.85]	$<10^{-4}$
Translocations						
ISS	143,505	164,856	636	1181	1.76 [1.60, 1.93]	$<10^{-4}$
ISS, Mir and STS	151,591	188,988	823	1654	1.75 [1.61, 1.90]	$<10^{-4}$

Note. The number of complex aberrations or translocations is represented as whole genome equivalents (WGE) to account for variations in painted chromosomes at different missions.

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

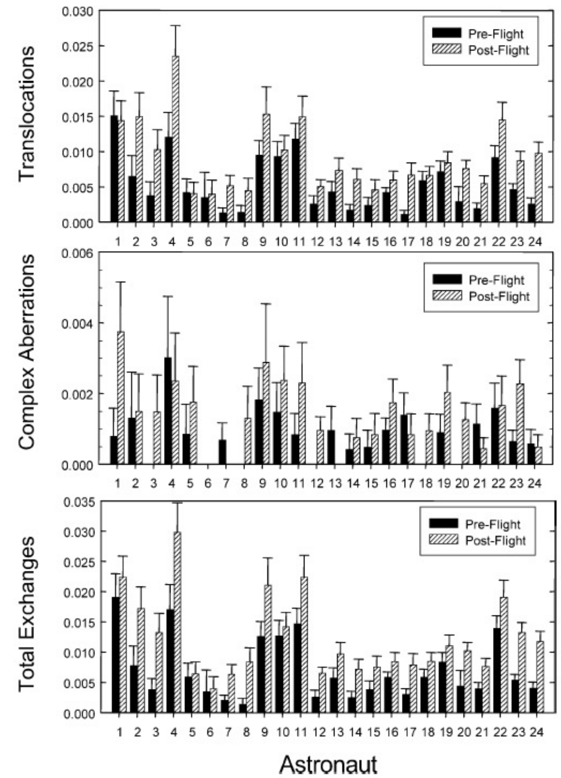
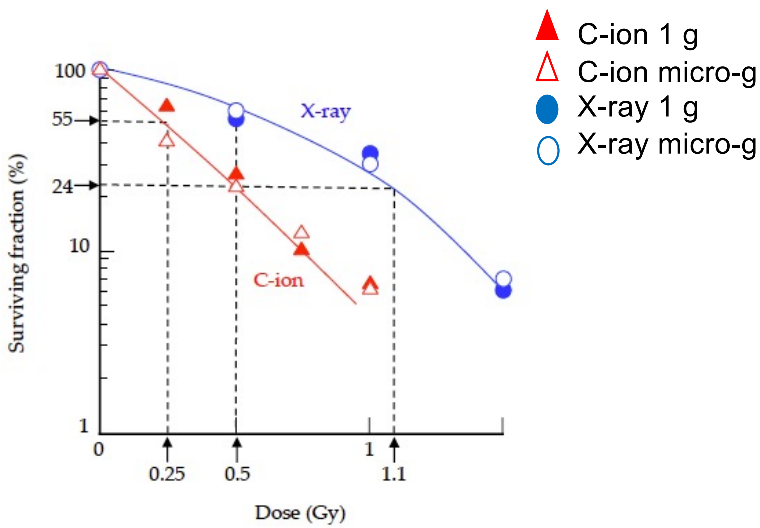
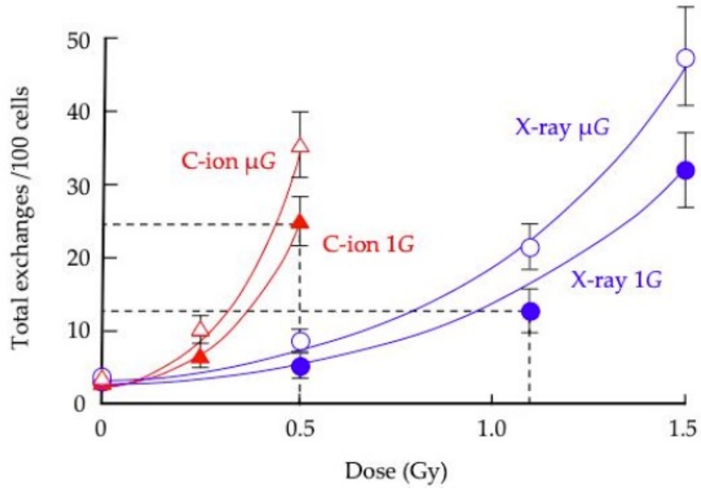


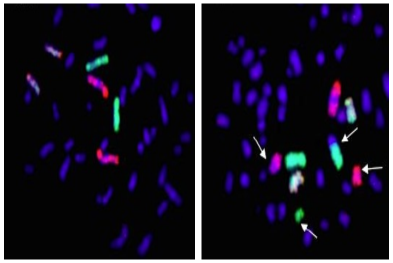
FIG. 4. Frequency of translocations, complex aberrations or total chromosome exchanges measured in each astronaut's blood lymphocytes before and after his or her respective space mission on ISS, Mir or STS. Increases in total exchanges were observed for all astronauts. Translocations (22 of 24) and complex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

Cell culture studies suggest that simulated microgravity treatment can increase the frequency of chromosomal aberrations in irradiated human lymphocytes, resembling results seen previously in astronauts

S. Yamanouchi, J. Rhone , J. Mao, K. Fujiwara, P.B. Saganti , A. Takahashi ,* and M. Hada 2.*. 2020. Life **10**: p. 187.



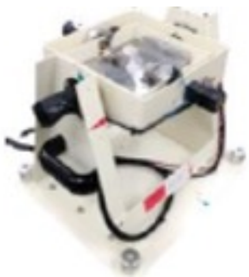




Fluorescence In-situ Hybridization (FISH) visualization of chromosomes in human lymphocytes.

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

- Radiation exposure increases frequency of chromosomal aberrations (CA)
- Carbon ions show more CA than x-rays
- **Simulated microgravity further increases the number of chromosomal aberrations in irradiated samples**



Clinostat for Simulated Microgravity Exposure

Summary of results from the combination of radiation and microgravity in spaceflight

- Significant effects of radiation observed in many multicellular organisms during spaceflight.
  - Assay choice is important since radiation hits are low probability events.

- Multicellular and embryonic systems, including plants, insects, and other invertebrate and vertebrate animals, can be acutely sensitive to combined effects of reduced gravity and radiation
  - Organism and tissue choices are important to generate sufficient sample size, “n”.
  - Use of in-flight centrifuged 1g controls can help distinguish the effects of radiation from altered gravity

- Human lymphocytes from astronauts show significant increases in chromosome damage even on ISS missions (low Earth orbits), with its relatively low radiation exposures. However, GCR effects are significant and responsible for 80% of the damage at these orbits.

- Higher orbits or interplanetary travel introduce greater radiation exposures, including GCR, and likely also greater effects on all organisms, including humans.
  - Ground based accelerators, while important for obtaining preliminary data, do not accurately reproduce space radiation in terms of long-term, low dose rate, variability and combination of radiation species.

- Possible underlying mechanisms responsible for combinatorial effects of microgravity and radiation on multicellular organisms need further study.

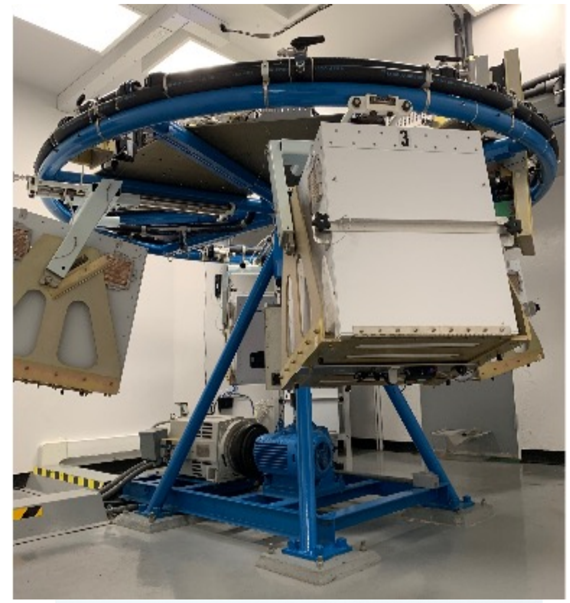
Therefore, we need to use various organisms amenable to spaceflight experimentation to obtain statistically reliable data on the combined effects of space radiation, altered gravity, and other spaceflight stressors.

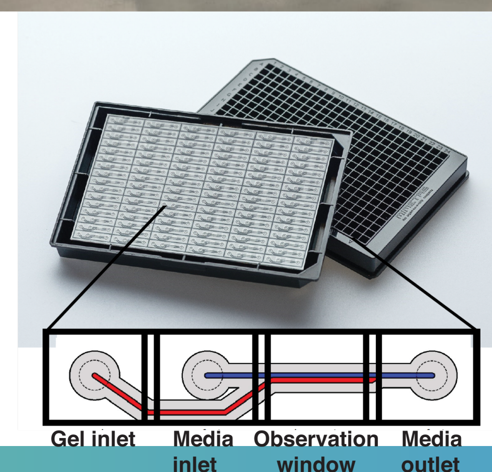

Science Topic Areas of Importance to Space Biology

Animal Biology – Vertebrates & Invertebrates

Continued animal research is critical to support human health for future exploration and habitation missions.

- Utilize eukaryotic animal models of increasing complexity to evaluate the **long-term effects of spaceflight** on physiology, behavior, metabolism, and molecular changes of the nervous system, cardiopulmonary, immune, skeletomuscular, endocrine, and digestive systems in terms of the combined effect of deep space radiation and altered gravity environments, and other relevant spaceflight stressors.
- Characterize changes during long-duration, multigenerational growth off-Earth
- **Use of animals** as translational and accelerated **disease models**.
- Interactions of animals with **microbial environment to assess pathogenesis outcomes** and use the knowledge to enable human exploration.
- Development and testing of biomarkers in animal models for early detection and screening of the **effects of space radiation and microgravity** on human health.
- Development of **novel radiation countermeasures** using animal models.
- Support the development and flight implementation of novel approaches such as **high-throughput 3D tissue chips and human organ-on-chip approaches** and validate against whole organisms.
- Use **genetic and genomic tools** and understand the factors responsible for the **variability of responses to the space environment** between individuals, populations, and species.
- Perform longitudinal studies in animal model systems to parameterize predictive computational modeling.
- Provide leadership in gathering **comprehensive omics & other datasets** and archiving metadata; promote data sharing to ensure the broadest access and support predictive science (e.g., systems biology).

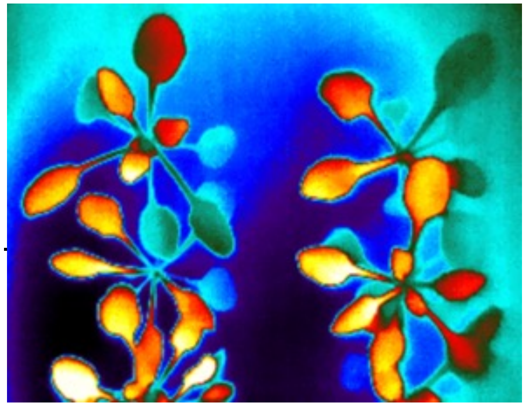




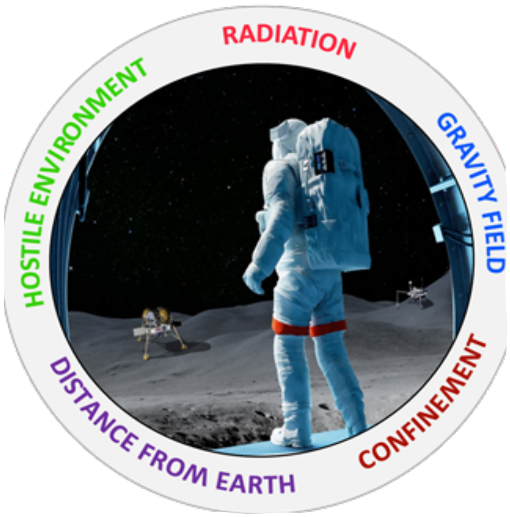
Plant Biology

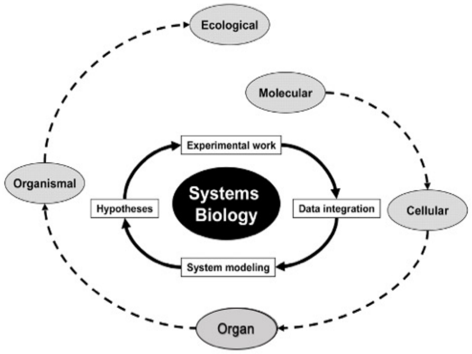
Plant Biology is a critical research area to supplement dietary nutrients and maintain crew behavioral health during long-duration deep space missions.

- Study **plant cellular and molecular responses and adaptations** to spaceflight.
- Evaluate **plant microbial dynamics** in the built space environment.
- Understand plant disease responses under deep space conditions.
- Investigate seed microbial biopriming to promote crop growth in space.
- Maximizing **the use of regoliths as a medium for plant growth** on the Moon and Mars.
- Consider microbes for biomining (regoliths) and waste processing.
- Develop effective, sustainable methods for delivering water and nutrients to plants in micro and partial gravity.
- Develop non-destructive plant health monitoring technologies for spaceflight.
- **Use targeted breeding / genetic engineering approaches** to optimize space crops.
- Improve space crop photosynthesis, including carbon fixation, light interception, and assimilate partitioning.
- **Identify space radiation concerns for plants** and develop countermeasures.
- Understand gravity and atmospheric pressure thresholds related to plant physiological responses and space crop production.
- Characterize plants to provide safe human dietary supplementation in spaceflight.
- **Characterize changes during multigenerational plant growth** off-Earth.



Challenges of Interest for the future





Systems Biology: ***Summing the component parts to create a model for predicting how the system will change over time and under varying environmental conditions. This approach could be applied to multiple biological systems to develop predictive models of the effect of long-duration spaceflight.***

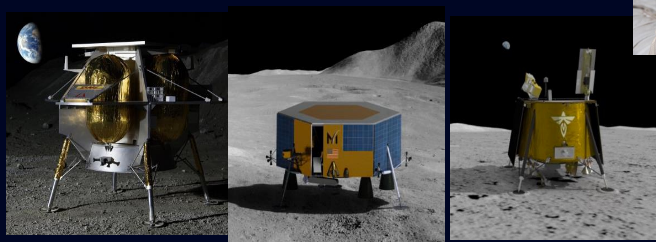
- Effects of combined spaceflight stressors: e.g., deep-space radiation and altered gravity

Research Campaign: ***Are there research campaigns to consider?***

Use well-characterized biological model organisms to understand the complex biological consequences of exposure to deep space's unique environment:

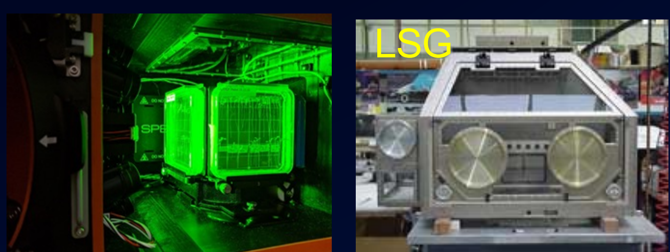
- ***Approach:*** **Conduct a sequence of Earth-based, low Earth orbit (LEO), and lunar/cis-lunar investigations (in the next decade & more),** with transit to and on Mars research as the long-term goal (in the 2030's timeframe). Populations of **biological model organisms of increasing complexity will be used to gather data on changes in the underlying responses to space-unique environmental stressors,** which do not occur in everyday Earth-based systems. The data from whole organisms, cellular, and organ systems will be compared within populations and across organisms to create a database that ultimately enables predicting physiological responses of humans to the deep space environment. **Facilities/equipment/hardware/habitats required for lunar/cis-lunar spaceflight experimentation needs to be developed** for Space Biology.
- **Resources for ground-based studies** could include ionizing radiation facilities (see slide 21), NASA's Space Radiation laboratory at Brookhaven National Laboratories (BNL), hypergravity facilities, and simulated microgravity platforms. Flight studies could compare results between ground (1g, baseline radiation), the ISS (microgravity, low radiation environment), autonomous free flyers (microgravity, high radiation environment), and lunar surface (1/6g, high radiation environment), in long-duration multigenerational studies with biological model organisms. Appropriate radiation sensors and flight hardware would be developed for free flyers and lunar missions.

Capabilities for Animal & Model Organism Studies on the Moon

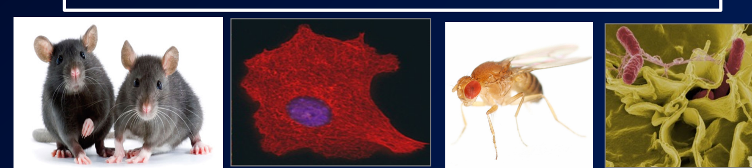


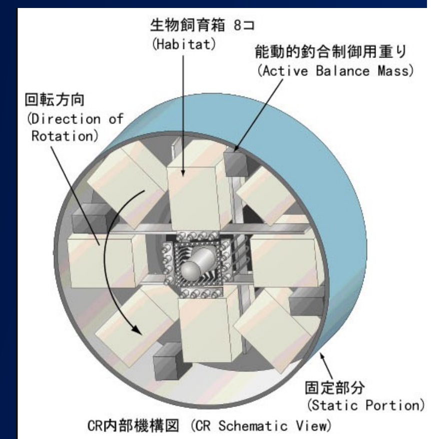
Taking science to the lunar surface

Habitats & analytical tools for research



- Use well-characterized animal model organisms & cellular systems to understand the complex biological consequences of exposure to deep space's unique environment.
- Facilities/equipment/habitats required for lunar surface experimentation with animals and related systems, need to be developed for Space Biology.
- Centrifuges that can simulate 1g or fractional g loads, can be used to differentiate between the biological effects of altered gravity vs other stressors like radiation.





Challenges of Interest for the future *(continued)*

Research Campaign: Are there research campaigns to consider?

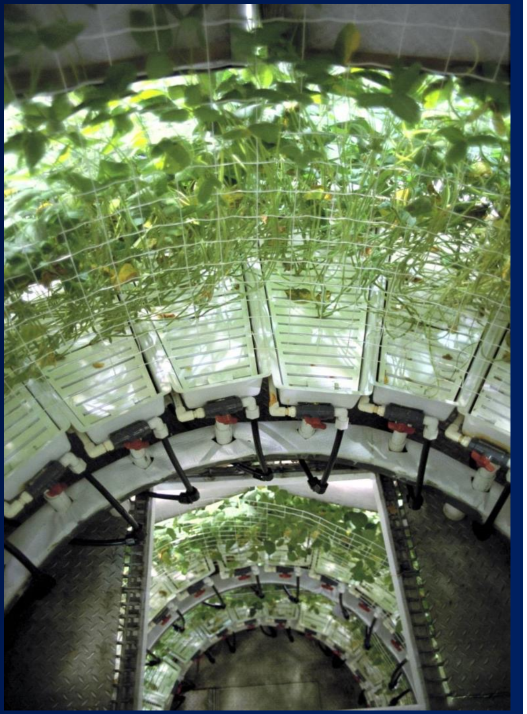
Develop a plant growth facility on the lunar surface to understand the complex biological consequences of exposure to deep space's unique environment and validate the ability to produce supplemental nutrients for future space explorers.

Approach: Develop a pressurized modular facility on the Moon to grow and test plants with automated health monitoring, sensor technologies, water recovery, nutrient and water delivery systems.

- Utilize genetic engineering, quantitative genomics, and other tools to test and optimize different plant types for suitability to the deep space environment.
- Study plant microbial interactions, stability and reliability of the plant growth systems at a larger scale than we currently have on the ISS.
- Assess the use of lunar regoliths as a growth medium.
- Evaluate techniques for biomanufacturing of pharmaceuticals, and other valuable bioproducts for long term human exploration.
- Resources for ground-based studies could include ionizing radiation facilities (see next slide), and NASA's Space Radiation laboratory at Brookhaven National Laboratories (BNL).
- Partnerships with internationals could further help with the infusion of new technologies, capabilities, and resources.

Growing Plants on the Moon

Develop a plant growth facility on the lunar surface to understand the complex biological consequences of exposure to deep space's unique environment and validate the ability to produce supplemental nutrients for future space explorers



Challenges of Interest for the future *(continued)*

Supporting Research Capabilities: Are there large hardware facilities to consider?

Ground Facilities: Gravity Radiation PlanEt Simulator (GRAPES)

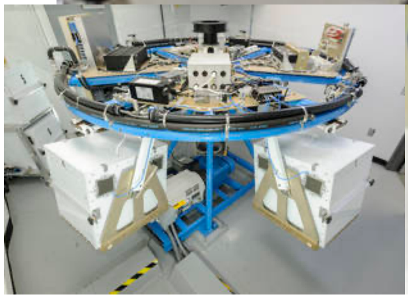
Ground facility that replicates conditions on the Moon and Mars to conduct realistic ground studies mimicking the type of environment that organisms (and supporting hardware) will have to endure under those harsh conditions. Large environmental chambers with chronic low dose-rate radiation capabilities, planetary conditions such as light cycle, simulated partial gravity, exposure to lunar/martian dust simulants, vibration, acoustic, circadian disruption, and altered atmospheric conditions (CO_2, O_2, humidity, temperature) as experimental cofactors.

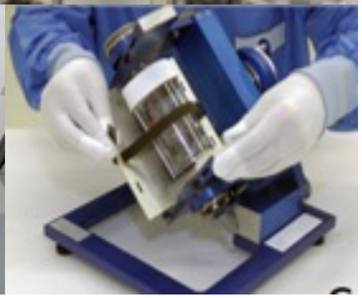
Approach:

The implementation sites could include centrifuges and simulated microgravity capabilities to simulate gravity as a continuum combined with chronic gamma irradiation sources of low-LET low dose-rate ionizing radiation, and opportunities where similar gravity simulators can be used in conjunction with low dose-rate of simulated high-LET radiation. [Note: BNL is unable to provide chronic doses of low dose-rate high LET radiation].

Lunar Science Facilities:

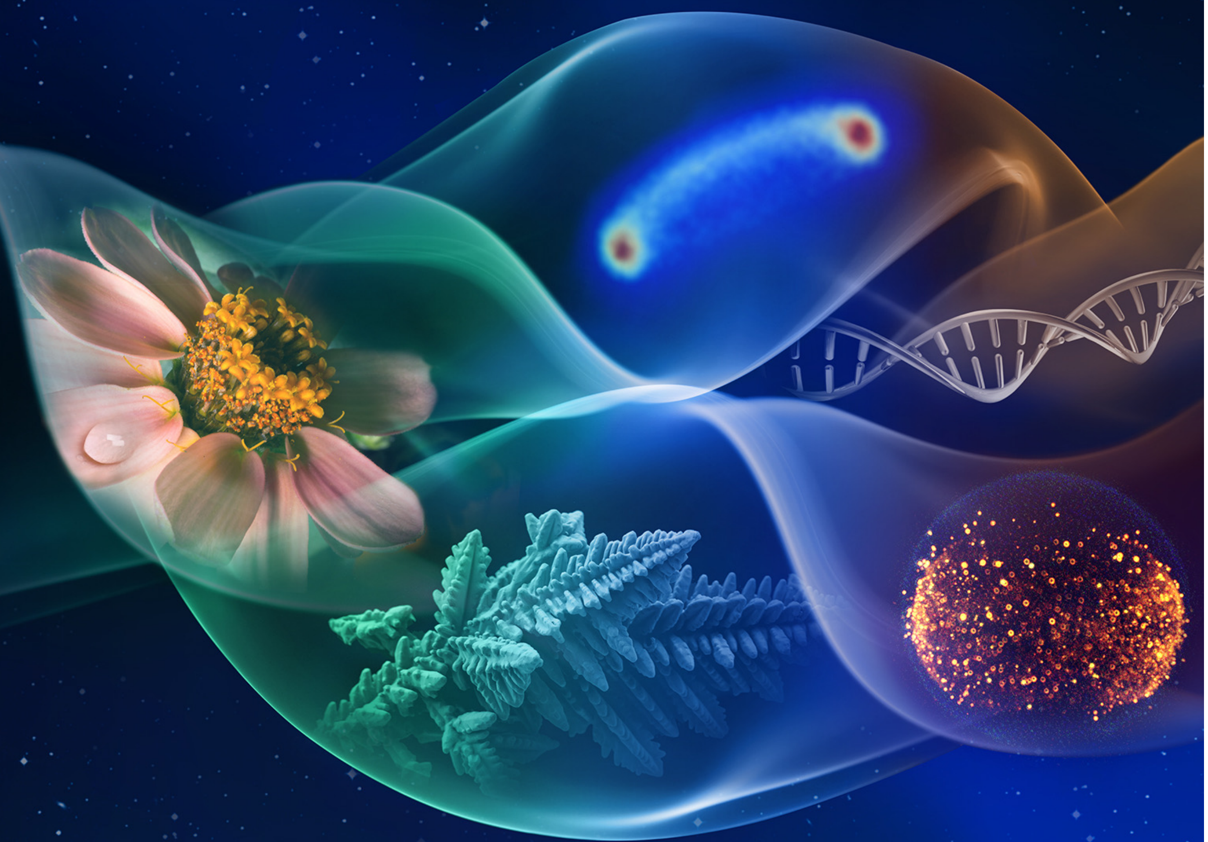
Develop science capabilities for use on the Lunar surface like we currently have for the ISS: Multi-organismal facilities with habitats, automated science capabilities, conditioned environments, video cameras, lighting, radiation and other sensors etc. to test biological systems/organisms and microphysiological systems responses, in the absence or presence of radiation shielding, lunar dust exposure, 1g centrifugation, etc.



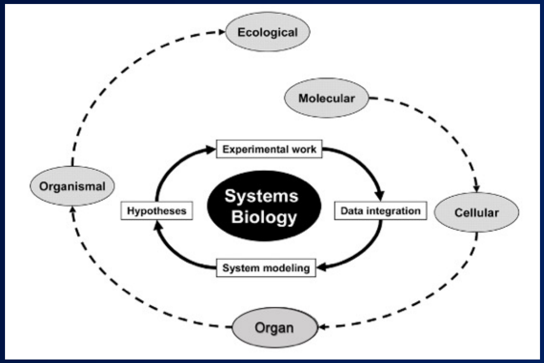


Other Transformative Science Areas

(also recorded at Oct 13, 2021 CBPSS presentation)



1. Transformative area: "Omics" and Systems Biology



- **Changes in the field as a whole**
  - Enhancement/development of methodologies:
    - "Omics"
    - Systems biology
    - Quantitative genomics
- **NASA-funded research for Open Science**
  - Development of the GeneLab database (https://genelab.nasa.gov/)
    - Archive space-relevant omics data and metadata and provides collaborative space to share, analyze, visualize data
  - Update of the NASA Biological Institutional Scientific Collection (NBISC) [also known as Ames Life Sciences Data Archive (ALSDA)] – archive of spaceflight-relevant vertebrate and invertebrate animal tissues, cells, data, etc. (https://www.nasa.gov/ames/research/space-biosciences/alsda)
    - Efforts underway to link GeneLab database closely with the NBISC to facilitate efficient curation of samples along with ancillary data

(desire to include microbiological & plant samples; and irradiated animal tissue in the future)

1a. Transformative Area: Systems Biology

- **Effects of Combined Spaceflight Stressors: e.g., deep-space radiation and altered gravity**
  - Use well-characterized biological model organisms to understand the complex biological consequences of exposure to deep space's unique environment:

Approach:

- Sequence of ground-based and spaceflight experiments in **low-Earth orbit (LEO) and beyond LEO**.
- Populations of **model organisms of increasing complexity** **(e.g., yeast, worms, flies, mice/rodents, etc.)**
- Response to space-unique environmental stressors
- Data from cells, organs, and the whole organism will be compared within populations and across organisms to develop a systems biology model that ultimately enables predicting physiological responses of humans to the deep space environment.

Ground-based Studies

- NASA's Space Radiation laboratory at Brookhaven National Laboratories.
- Other radiation facilities.
- Simulated microgravity platforms.
- Hypergravity facilities.

Flight Studies

- Compare results between ground (1g, baseline radiation) and
  - ISS/LEO (microgravity, low radiation environment)
  - Autonomous free flyers (microgravity, high radiation environment)
  - Lunar surface (1/6g, high radiation environment)
- Utilize long-duration multigenerational studies with biological model organisms
- Flight hardware should be adapted (from those used in LEO) or developed for free flyers and lunar missions.

1b. Transformative Area: Quantitative Genomics

- **Quantitative Genomics: Understand the genetic basis of complex traits using genotype to phenotype mapping.**
  - Use well-characterized quantitative genomics model systems (e.g., flies, mice, plants) to identify genes and pathways that affect the variation of traits relevant to the space environment. Ground-based studies may be needed preliminarily for the larger organisms (e.g., mice and plants) followed by spaceflight of selected lines. Small organisms like flies can be flown in space for genome wide association studies (GWAS) to identify genes and genetic variants that confer better survival and behavior in the space environment.

-Workshop held by NASA Space Biology on May 26, 2021: See link
-White papers submitted from the science community as a result of the Workshop

2. Transformative area: Genetic Engineering in Plants

Changes in the Field as a Whole:

- Can now evaluate all genes in combination with phenomics, proteomics, metabolomics and use as inputs to computational modeling.
- Deep insight and understanding of the gene networks and metabolic pathways allows the plant breeder to put together the best collection of 20,000+ genes using available genomic tool sets.
- This has enabled **Predictive Breeding** that shortens the time to a new crop by understanding what all the genes are doing so they can be combined into the best plant for the conditions.
- Genome editing techniques are currently being used to validate pathway models quickly, and to create predicted “quality” crops (e.g., tailored starch composition in potato or corn).
- Recent changes in plant genetic engineering
    - Sequencing technology developments
    - Genome-wide editing technology developments
    - CRISPR delivery – Nanotechnology
    - CRISPR delivery – Viral engineering
    - Multi-Omics developments
    - Breeding enhancement through AI data integration
- Accomplishments in Genetically Modified (GM) crops
    - Food security
    - Natural products
- Future Perspective: Synthetic Evolution

Credit NASA

Credit NASA

2. Transformative Area: Genetic Engineering of Plants

Plant Growth and Development
- Compact size (low height and volume)
- High yield
- High edible/inedible biomass ratio (harvest index)
- Reliable germination
- Rapid growth to first yield
- Uniform growth and development between individuals
- Propagules with long shelf stability (seeds, cuttings)
- Sustained production capability over long duration
- Low debris formation (leaves, flowers, pollen, seeds, etc., remain attached)
- Custom microbiome of plant protective and growth promoting microorganisms

Produce Nutrition
- High levels of antioxidants
- High levels of beneficial phytonutrients
- High levels of Potassium and Magnesium
- High levels of Vitamins, especially C, B_1, and K
- Low levels of Iron
- Low levels of antinutrients

Produce Organoleptic Acceptability
- Intense flavors
- Good texture
- Good appearance, color, aroma

Plant Physiology
- Stress tolerance (esp. water stress)
- Ability to grow well under conditions of:
  - Elevated CO2
  - Low relative humidity
  - Uniform temperature of 20-23°C
  - Narrow spectrum electric lights
  - Short photoperiods (to save lighting energy) or continuous photoperiods
- Tolerance of broad environment range
- Tolerance of reduced pressure
- No dormancy requirements
- Pleasing aroma
- Low release of volatile organics
- High sodium tolerance (e.g., urine recycling)
- Preference for ammonia nitrogen sources (e.g., urine recycling)

Post Harvest
- Good produce shelf life or storage on the plant
- Reduced processing – e.g., seeds easy to remove from seed coats
- Easy composting/digestion of inedible plant material for nutrient reclamation Use of inedible waste as resources for other food system components
  - (e.g., fish, edible fungus, cellular ag feedstocks)
- Other useful materials produced from inedible waste
  - (e.g., life support, shielding, building, fuel)

3a. Transformative Area: Plant Responses to Lunar Regolith & Simulants

Background:

- **Lunar Regolith/Dust (Apollo):** In the 1970's, **seminal work** was done to show that **plants could be exposed to lunar regolith (Apollo samples) without any major negative effects**. In fact, plants could **uptake nutrients/minerals from lunar regolith** and show changes in lipid and chloroplast content when grown in contact with lunar regolith.
  - However, *limited plant growth experiments* have been conducted *"in contact with" small amounts* of returned moon material
- Given the desire to employ the ***In Situ* Resource Utilization (ISRU) approach to "live off the land"** when habitats are established on the moon and Mars, enabling the growth of plants in lunar regolith would be important.
- **Geomicrobiology investigates the interactions of micro organisms with geological substrates** and has enormous potential in the settlement of space
  - by helping modify regolith to enable plant growth; and serve as an element in Bioregenerative Life Support Systems (BLSS) with the ability to produce oxygen, sink carbon dioxide, and recycle organic and inorganic materials.
- The bulk of NASA research for growing plants in lunar regolith, however, was done back in the Apollo era.

Credit: Getty Images/iStockphoto

3b. Transformative Area: Animal Responses to Lunar Regolith

- In the late 1960s, a study was done that indicated that protists, invertebrates, and fish could be exposed to crushed lunar rock without any apparent negative effects. (Benschoter, et al. Science. 1970).

- Several studies over the next decades, however, provided additional evidence that regolith exposure had potentially negative effects on animal health at the physiological, cellular, and molecular levels.

Studies with Lunar Dust (Apollo 14):

- Rat Inhalation studies with lunar dust showed **concentration-dependent increases in inflammation biomarkers in bronchial alveolar lavage fluid**, as measured by cellular components (total cell, neutrophil/lymphocyte counts), and cytotoxic biomarkers (enzymes [LDH, γGT and AST]). (Lam, et al., *Inhal Toxicol*., 2013).
- Rat benchmarking studies with lunar dust (intratracheal instillation) **determined the safe periodic exposure estimate for humans was between 0.5-1.0 mg/m^3** during long stays in habitats on the lunar surface (James et al., *inhal Toxicol*., 2013).
- Lunar dust is a mild irritant to mammalian eyes (rabbit) (Meyers et al., *BMC Ophthalmol*., 2012).

3b. Animal Responses to Lunar Regolith (continued)

Studies with Lunar Dust/Regolith Simulant (LDS/LRS)

- LDS treatment of isolated rat synaptosomes resulted in **increased glutamate binding to the nerve terminals,** indicating potential neurotoxicity (Krisanova, et al., Astrobiology, 2013).
- Treatment of macrophages with lunar regolith/soil simulant (LRS) resulted in a **concentration-dependent increase of inflammatory markers** with increased Induced Nitric Oxide Synthase (iNOS) (Chatterjee, et al., *J Toxicol and Environ Health A*., 2010), as well as moderate cytotoxicity, alterations of cell morphology, and phagocytosis of simulant as noted in a separate study (Li, et al., *Appl Toxicol.*, 2019).
- Lunar soil simulant treatment of **neuronal and lung cell lines resulted in cytotoxicity and both genomic and mitochondrial DNA damage** (as measured by qPCR – lesions block amplification) (Caston, et al., *Geohealth*, 2018).
- Rodent studies conducted indicate that **the intratracheal instillation of LDS in rats** causes inflammatory damage that affects autonomic function, leading to **inflammatory myocardial fibrosis** (Sun et al., *Toxicol Res.* 2019), and the aggregation and **infiltration of lymphocytes and neutrophils in the lung** which **may lead to inflammatory pulmonary fibrosis** (Sun et al., *Environ Toxicol.* 2018).

> ➢ Will need more data for sustained plant growth on surfaces beyond LEO
> ➢ and the effects of stressors like lunar dust on animals.

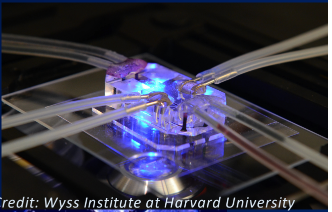
4. Transformative area: **3D Tissues and Organ-on-Chip Models**

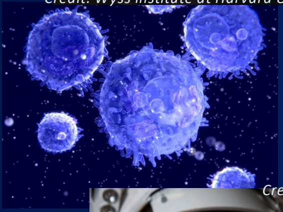
<u>**Background and Advances in Last 10 years**</u>

- **First Human Organ-on-Chip - Lung-on-Chip Reported by Harvard in 2010.**
- **NIH's** National Center for Advancing Translational Sciences **(NCATS),** US Food and Drug Administration **(FDA)** and the Defense Advanced Research Projects Agency **(DARPA)** launched a $70M program in 2012 to expand capability to 10 organs-on-chip.
- **As of 2021: 12 Organs** can be linked for comprehensive systems biology; systems available for purchase.

<u>**Changes in the field as a whole**</u>**:**

- ***Science advances***: Human induced pluripotent stem cell-derived models for personalized healthcare; Disease modeling; Cancer; Infectious Disease; Inflammation; Microbiome; Neuroscience; Drug screening and toxicity.
- ***Program advances***: NCATS Tissue-Chips-in-Space Program initiated in 2017; Tissue Chip Testing Centers for validating MPS began in 2016; Clinical Trials-on-Chip Program launched in 2020; FDA Advancing New Alternative Methods awards for countermeasure development and toxicology; **EPA** SBIR awards using organ-on-chip for predictive toxicology.
- ***Funding advances***: Government & other agencies (**NASA, ISSNL** [ISS National Labs], **TRISH** [Translational Research Institute for Space Health]), **pharmaceutical companies** and small businesses.
- ***Commercialization advances***: global organ on chips market valued at $50.8 million in 2020 – up 60% since 2015; expected to grow to $177.8 million in 2025 and reach $350.8 million in 2030.

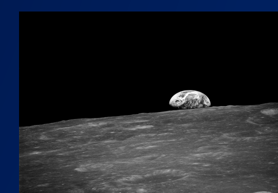

Credit: Wyss Institute at Harvard University

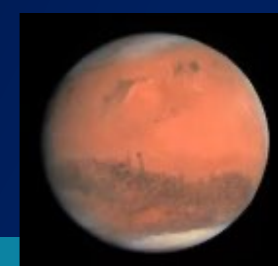



Credit: NASA

4. 3D Tissues & Organ-on-Chip Models (cont.)

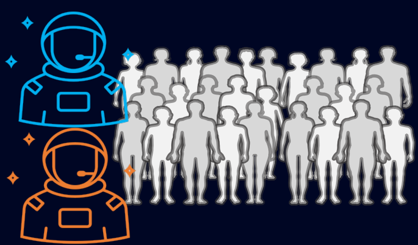
- Utilize robust *in vitro* model systems that are developed and tested first in ground studies
- Then validate *in vitro* model system designs using ISS/LEO (low-Earth orbit) as a testbed
- Conduct long duration spaceflight missions beyond low-Earth orbit with *in vitro* models
- Determine underlying mechanisms of spaceflight response of human-derived tissue/organ systems
- Comparing results between ground, ISS, beyond LEO and Lunar Surface can uncover the contributions of multiple stressors such as altered gravity and radiation on biology



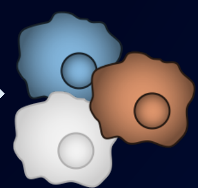


4. 3D Tissues & Organ-on-Chip Models (cont.)

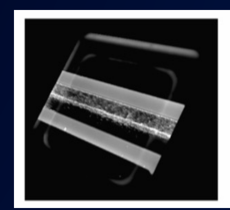
Personalized models:
- Genomic and epigenetic associations→ mechanisms → targets for countermeasures and biomarkers
- Individual astronaut's risk



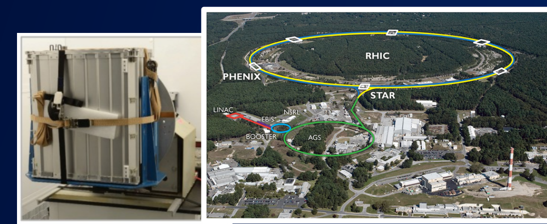
Donors



iPSC-derived cells

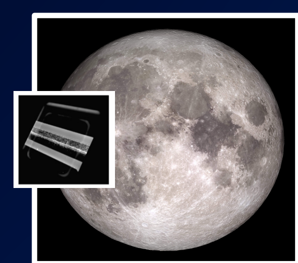


3D Tissue/Organ Models



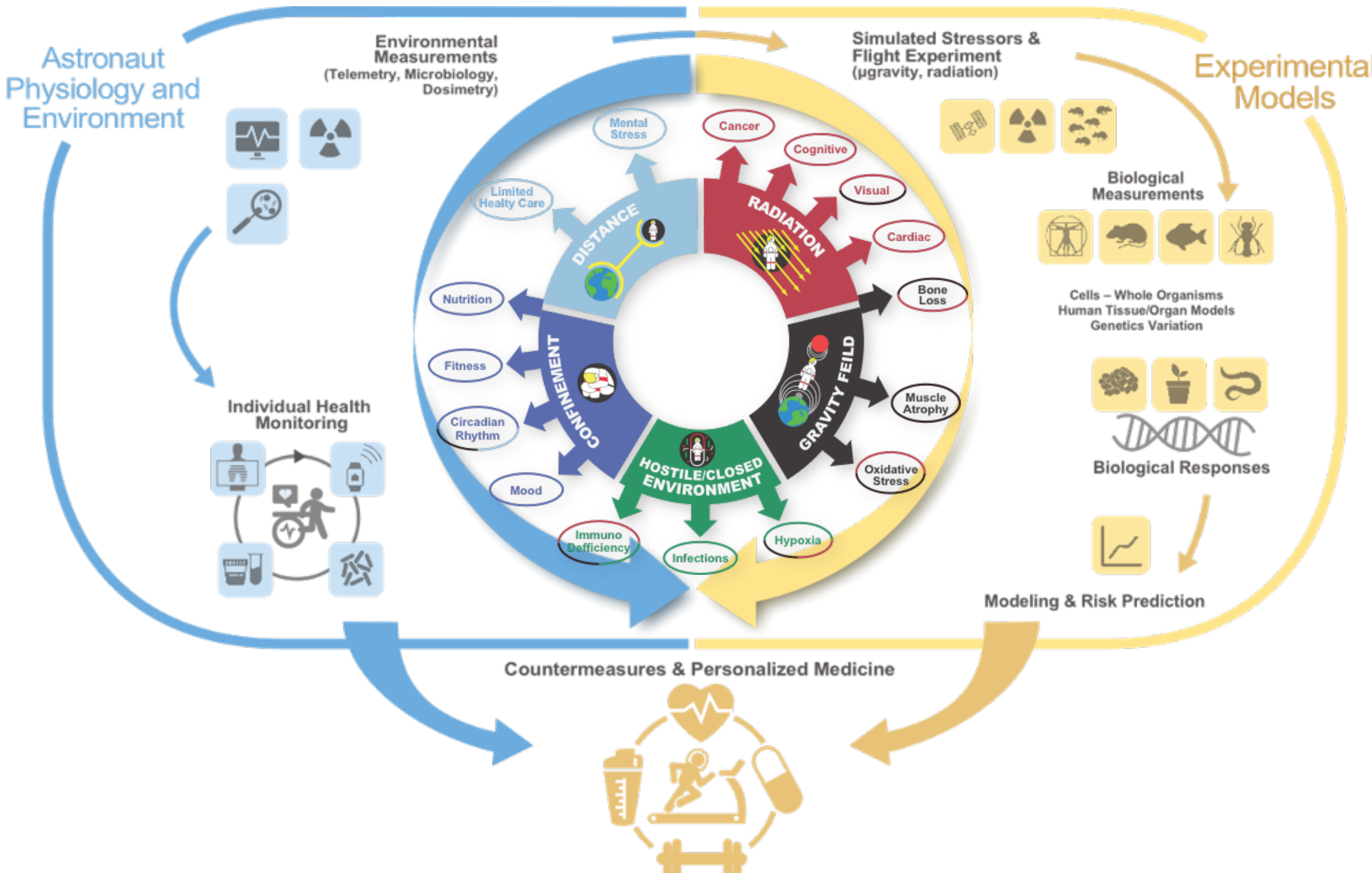
Simulated spaceflight stressors: microgravity, ionizing radiation

LEO / BLEO / Lunar Surface payloads:
- Radiation
- Altered Gravity
- Environmental Conditions



- Fundamental space biology research
- Personalized biomarkers
- Personalized countermeasures

Integration of Research Areas:



5. Transformative Area: **Artificial Intelligence/Machine Learning (AI/ML)**

- **Changes in the field as a whole**
  - Protein folding prediction – game changer for drug development (e.g., AlphaFold).
  - Personalized medicine - AI/ML teams integrated into personalized medicine programs.
  - Disease prediction using omics data (e.g., 23&Me – Cancer Genome Atlas - GeneLab).
  - Wearable health devices (e.g., longitudinal data generation).
  - Diagnostics (e.g., medical imaging, breath analyzer, wearable data interpretation).
  - Image analysis, including biological images (e.g., microscopy data).
  - NLP (Natural Language Processing) which can play an important role in ingesting knowledge from publications.
  - **Market growth from US$ 93B in 2021 forecast to be $ 997B by 2028** *(Grand View Research, Report ID: GVR-1-68038-955-5, June 2021)*
- **Changes in NASA-funded research: Utilizing AI/ML to address topics like the effects of space on physiology**
  - **FDL : Frontier Development Lab** – 2019 to 2021: Life Sciences AI/ML challenges
    - FDL2019 - *Synthetic biosensor data*
    - CRISP - Causal Relation and Inference Search Platform (CRISP)
      - *FDL2020 **(Mayo Clinic)** – AI Colon cancer causal inferencing model from clinical data (NASA interest in testing causal model for cancer in the context of Cancer risk)*
      - *FDL2021 (**Space Biology**, **Human Research Program** [HRP], & **Intel)** - Extension of CRISP in the context of radiation-induced cancer with mixed-data (human and mice) to scale risk from mice to human.*
  - Space Biology – FY21/25: AI/ML pilot CRISP + SPOKE + Modeling portal: *Radiation exposure risk prediction modeling using human & animal data (omics & phenotypic data)*
  - Human Research Program – FY22: AI/ML:
    - *Applying CRISP for risk prediction on at least two targets: bone loss, CNS, behavioral, or cancer. Using at least omics data and possibly physiological/phenotypic data (Ames Life Sciences Data Archive)*
    - *Deployment of federated learning algorithms using intel technology for analysis of private astronaut data without specific access to the data.*
  - AI/ML Workshop held by NASA's Space Biology program: June 24 – 25, 2021.

5. Transformative Area: Artificial Intelligence/Machine Learning (AI/ML) (cont.)

- **Multi-omics data are quantitative and allow for standardization and meta-analysis**
  - AI/ML to extract knowledge from very diverse types of data (e.g., mice vs human, omics vs non-omics, sparse datasets, etc.)
- **Biological data are often qualitative (e.g., imaging, behavior, etc.) and require human scoring.**
  - Increasing role of AI/ML to interpret qualitative data and quantify them
  - AI/ML to automate data transformation, data curation, human interaction for data entry
  - AI/ML to relate back to the quantitative data
- **Biological responses are the result of very complex networks of interacting parts**
  - AI/ML methods allow the testing of such networks and identify the true cause of a given response. Causal inference methods will play a critical role in the following applications:
    - Onboard live diagnostic/prevention/monitoring for Astronauts' health status in remote situation away from Earth
    - Better risk models for mission planning
  - Microbiome is a complex system, critical to plant/animal/human health and its changes could be better interpreted by AI/ML.
- **Use for AI/ML-powered Research Facilities and Analysis Platforms in Space**
- **Other related tools that could help with above uses:**
  - Federated learning is the ability to send AI tools to the data (keeping data private, but letting the tool learn from the data) – game changer to deal with private/sensitive patient data (e.g., for astronaut or flight-relevant human data).
  - xAI (Explainable AI) –a paradigm shift, moving from a "black box action" to "human trustworthy recommendation" by the machine.

6. Transformative area: Automation & Miniaturization

- **Changes in the field as a whole**
  - Drive towards miniaturization for medical equipment, laboratory sampling tools for patients, etc.
  - Increased automation for high-throughput analyses of samples.
  - Increased use of telemedicine tools.

- **Changes in NASA-funded research**
  - Increased utilization of miniaturized, automated equipment for spaceflight.
  - Increased need for data telemetry from science experiments in deep space missions with no sample return.
  - Telemetry-based Biology Workshop to be held on Aug. 18, 2021.

(Registration at: https://docs.google.com/forms/d/e/1FAIpQLSd6uSRJj6etgXP42tyk92HnqpcDyztSeEPX7dpPUwvv-HpW4w/viewform)

6. Transformative Area: Utilizing Automation, Miniaturization & Data Telemetry

- **Science-focused Habitat (SciHab) for Deep Space**
  - **Multi-platform habitat designed to house life science experiments for the lunar surface and perhaps can also be utilized for free-flyer missions, Gateway, etc.:**
    - Modular to accommodate multiple types of organisms
    - Autonomous readouts of biological endpoints and health of the system
    - Data telemetry for near real-time monitoring and report out
    - Conditioned environment
    - Videography / lighting
    - Radiation sensors

Additional Areas of Consideration:

- Current research cadence limited by hardware/habitats availability for spaceflight research in LEO (Veggie/APH; Rodent Habitat, etc.)
- NASA Biological Institutional Science Collection (NBISC)*: need to expand our sample and tissue collection to include microbial and plant samples in addition to animal samples. Also, need to expand animal collection to include radiation-treated samples, etc. *(will allow more researchers to engage with spaceflight data and samples than we can currently afford to enable)*
- Consider opportunities for a series of dedicated Space Biology experiments like the BION series of missions *(would allow testing of larger payloads with larger "n" samples sizes; higher radiation exposure levels; automated experiments; pathogenic or other experiments not allowed on ISS, etc.)*
- Follow-up grant funding for mid-career researchers.
- Supplemental grants for graduate students working in Space Biology-funded PI labs with active grants.

** Note: NBISC is the successor of the ALSDA (Ames Life Sciences Data Archive)*

Importance of the Decadal Survey to Space Biology

Example quote from ROSES-2020 Program Element E.12 Space Biology Call for Flight and/or Ground Research Proposals:
*"To be responsive to this program element...proposals must address an appropriate Focus Area described...
All investigations should also align with the priority recommendations listed in Table 13.1 of the Decadal Survey"*

Mapping of All Active FY2021 Projects to Decadal Recommendations

Reccomendation ID	Reccomendation	Number of Projects*
P1	Establish a microbial observatory program on the ISS to conduct long-term,multigenerational studies of microbial population dynamics.	38
P2	Establish a robust spaceflight program of research analyzing plant and microbial growth and physiological responses to the multiple stimuli encountered in spaceflight environments.	69
P3	Develop a research program aimed at demonstrating the roles of microbial-plant systems in long-term life support systems.	9
AH2	The preservation/reversibility of bone structure/strength should be evaluated when assessing countermeasures	11
AH3	Bone loss studies of genetically altered mice exposed to weightlessness are strongly recommended.	6
AH5	Conduct studies to identify underlying mechanisms regulating net skeletal muscle protein balance and protein turnover during states of unloading and recovery.	12
AH6	Conduct studies to develop and test new prototype exercise devices and to optimize physical activity paradigms/prescriptions targeting multisystem countermeasures.	1
AH8	Determine the basic mechanisms, adaptations, and clinical significance of changes in regional vascular/interstitial pressures (Starling forces) during long-duration space missions.	10
AH9	Investigate the effects of prolonged periods of microgravity and partial gravity (3/8 or 1/6 g) on the determinants of task-specific, enabling levels of work capacity.	5
AH10	Determine the integrative mechanisms of orthostatic intolerance after restoration of gravitational gradients (both 1 g and 3/8 g).	1
AH14	Both to address the mechanism(s) of the changes in the immune system and to develop measures to limit the changes, data from multiple organ/system-based studies need to be integrated.	16
AH15	Perform mouse studies of immunization and challenge on the ISS, using immune samples acquired both prior to and immediately upon re-entry, to establish the biological relevance of the changes observed in the immune system. Parameters examined need to be aligned with those in humans influenced by flight.	1
AH16	Studies should be conducted on transmission across generations of structural and functional changes induced by exposure to space during development. Ground-based studies should be conducted to develop specialized habitats to support reproducing and developing rodents in space.	12
CC2	Determine whether artificial gravity (AG) is needed as a multisystem countermeasure and whether continuous large-radius AG is needed or intermittent exercise within lower-body negative pressure or short-radius AG is sufficient.	3
CC8	Expand the use of animal studies to assess space radiation risks to humans from cancer, cataracts, cardiovascular disease, neurologic dysfunction, degenerative diseases, and acute toxicities such as fever, nausea, bone marrow suppression, and others.	15
CC10	Expand understanding of gender differences in adaptation to the spaceflight environment through flight- and ground-based research, particularly potential differences in bone, muscle, and cardiovascular function and long-term radiation risks.	5

*Note: Each project usually maps to more than one Decadal Recommendation.

Task Book

https://taskbook.nasaprs.com/tbp/welcome.cfm

https://taskbook.nasaprs.com/tbp/index.cfm

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Search Task Book (FY2004 - present)

Maps/Metrics

Search Task Book Archives (FY1995 - 2003)

Search Bibliography (FY2004 - present)

SPACELINE Current Awareness Lists

Space Life & Physical Sciences Research Highlights

Related Links

- GeneLab
- Physical Sciences Information System
- Space Biology Science Plan 2016-2025
- Human Research Program Documents
- Human Research Roadmap
- TechPort
- International Space Station Research Experiments
- Life Sciences Data Archive
- NSPIRES
- Translational Research Institute for Space Health
- NASA Space Radiation Laboratory(NSRL)

Task Book: Biological & Physical Sciences Division and Human Research Program

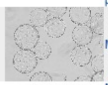
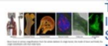
Advanced Search

Search Criteria:
Fiscal Year: All
Division: Space Biology

Total Tasks: 458 | Total PIs: 287 | Total COIs: 570
Total Post Docs: 377 | Total Master Students: 183 | Total PHD Students: 351 | Total Bachelor Students: 574

Start New Search | Show Bibliography | Export Result Set

Pages: First 2 3 4 5 6 7 8 9 10 11 Next10 Last ll Prev Next | Page No.1 of 19 | Items per Page: 25 Go

	PI Name	Institution		Project Title	Division	HRP Element	HRP Risk	HRP Gap	Year	Start Date End Date	Task Last Updated
1.	Alberts, Jeffrey Ph.D.	Indiana University		Individual and Group Behavior of Bion-M1 Rodents	Space Biology				2015	08/01/2009 06/30/2015	08/01/ 2019
2.	Alfano, Robert Ph.D.	City College of City University of New York		Biophotonic Plant (Moss) Stress Detection	Space Biology				2011	06/09/2009 12/08/2010	06/08/ 2011
3.	Allen, Christopher A Ph.D.	University of Texas Medical Branch		The Impact of Microgravity on Streptococcus pneumoniae Gene Expression and Virulence Potential	Space Biology				2007	08/01/2004 07/30/2007	10/29/ 2007
4.	Allen, Josephine Ph.D.	University of Florida		Microgravity Effects on Co-cultured Vascular Cells Types	Space Biology				2020	02/01/2017 01/31/2020	05/31/ 2020
5.	Allen, Josephine Ph.D.	University of Florida		Microgravity Effects on the Function of Vascular Stem Cells	Space Biology				2016	08/16/2013 10/15/2015	01/10/ 2016
6.	Almeida, Eduardo A C Ph.D.	NASA Ames Research Center		Does Gravity Influence Matrix Survival Signaling	Space Biology				2004	10/01/2001 09/30/2004	03/17/ 2006
7.	Almeida, Eduardo A C Ph.D.	NASA Ames Research Center		The Effects of Microgravity on the Tissue Regenerative Potential of Stem Cells--Flight	Space Biology				2010	10/01/2009 05/31/2012	09/24/ 2009
8.	Almeida, Eduardo A C Ph.D.	NASA Ames Research Center		The Role of Artificial Gravity in Promoting Tissue-Regenerative Matrix-Integrin-Kinase Cell Signaling (Ground/Flight)	Space Biology				2013	06/01/2009 11/30/2012	12/05/ 2012
9.	Almeida, Eduardo A C Ph.D.	NASA Ames Research Center		The Role of P21/CDKN1a Pathway in Microgravity-Induced Bone Tissue Regenerative Arrest - A Spaceflight Study of Transgenic P21/CDKN1a Null Mice in Microgravity	Space Biology				2022	11/01/2014 09/30/2022	11/17/ 2021
10.	Almeida, Eduardo A C Ph.D.	NASA Ames Research Center		The Role of the p53 Pathway in Spaceflight-Induced Tissue Degeneration	Space Biology				2013	08/01/2009 09/30/2014	06/14/ 2013
11.	Alwood, Joshua Ph.D.	NASA Ames Research Center		2012 Presidential Early Career Award for Scientist and Engineers (PECASE)--Epigenetic Regulation and Skeletal Sex Hormone Receptors During Simulated Spaceflight	Space Biology				2019	04/01/2015 10/01/2018	02/28/ 2019
12.	Alwood, Joshua Ph.D.	NASA Ames Research Center		Bone Loss During Simulated Weightlessness: The Role of Osteoclasts	Space Biology				2015	11/01/2013 03/31/2015	06/30/ 2015
13.	Angelaki, Dora Ph.D.	Washington University Medical School		Multisensory Interactions to Discriminate Gravity From Translational Acceleration	Space Biology				2007	07/01/2004 06/30/2007	06/28/ 2007
14.	Angelaki, Dora Ph.D.	Washington University Medical School		Multisensory Interactions to Discriminate Gravity from Translational Accelerations	Space Biology				2004	07/01/2001 06/30/2004	06/02/ 2004
15.	Barber, Diane L. Ph.D.	University of California - San Francisco		Mechanosensing and Mechanotransduction by the Na-H exchanger NHE1	Space Biology				2007	05/01/2004 04/30/2007	07/30/ 2007
16.	Barton, Elisabeth Ph.D.	University of Pennsylvania		Identification of mechano-sensors to protect against skeletal muscle atrophy	Space Biology				2011	05/01/2009 04/30/2011	07/29/ 2011

Conclusion

- As NASA plans to…
  - return to the lunar surface,
  - develop sustainable lunar habitation, and
  - prepare to explore Mars

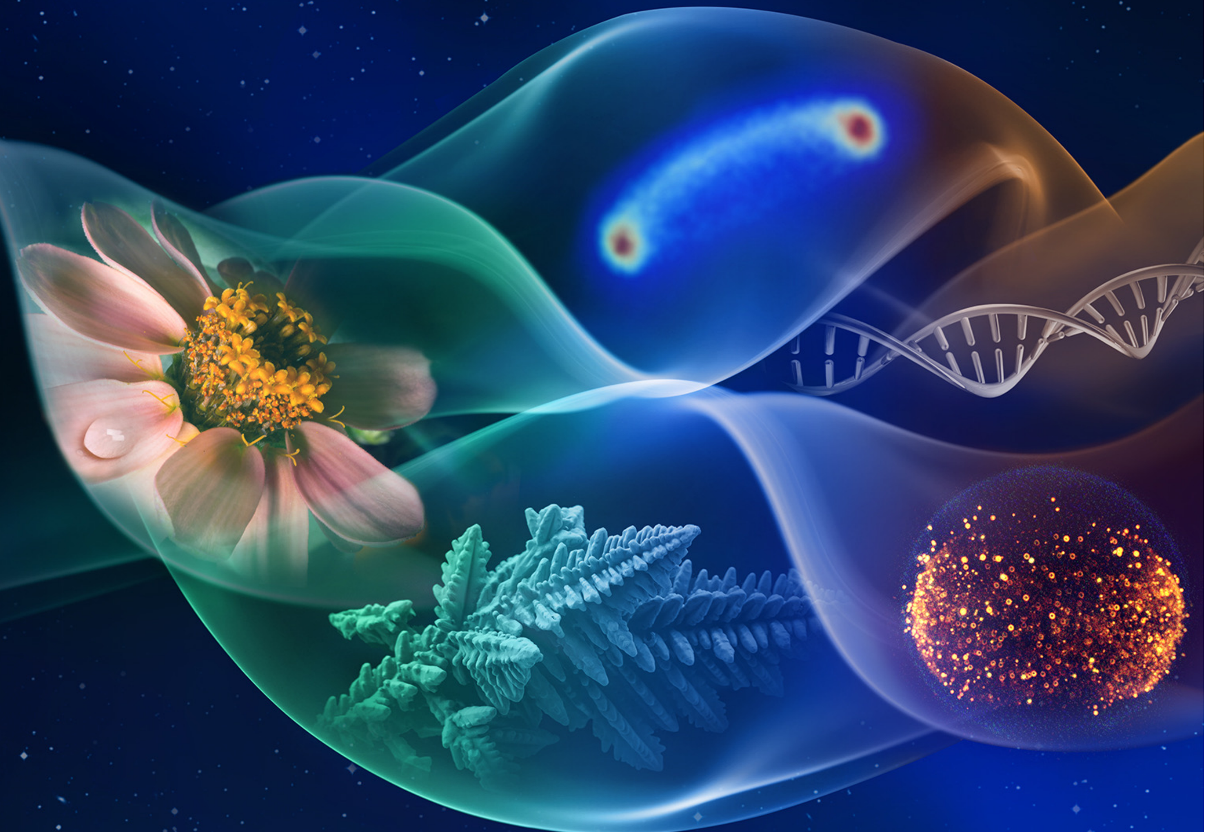
- Space Biology intends to…
  - utilize multiple biological model systems and
  - spaceflight platforms

➢ To understand the mechanisms of change in biological systems in response to long duration exposure to deep space,

➢ Enable exploration,

➢ Benefit Earth: human health & controlled environment agriculture.

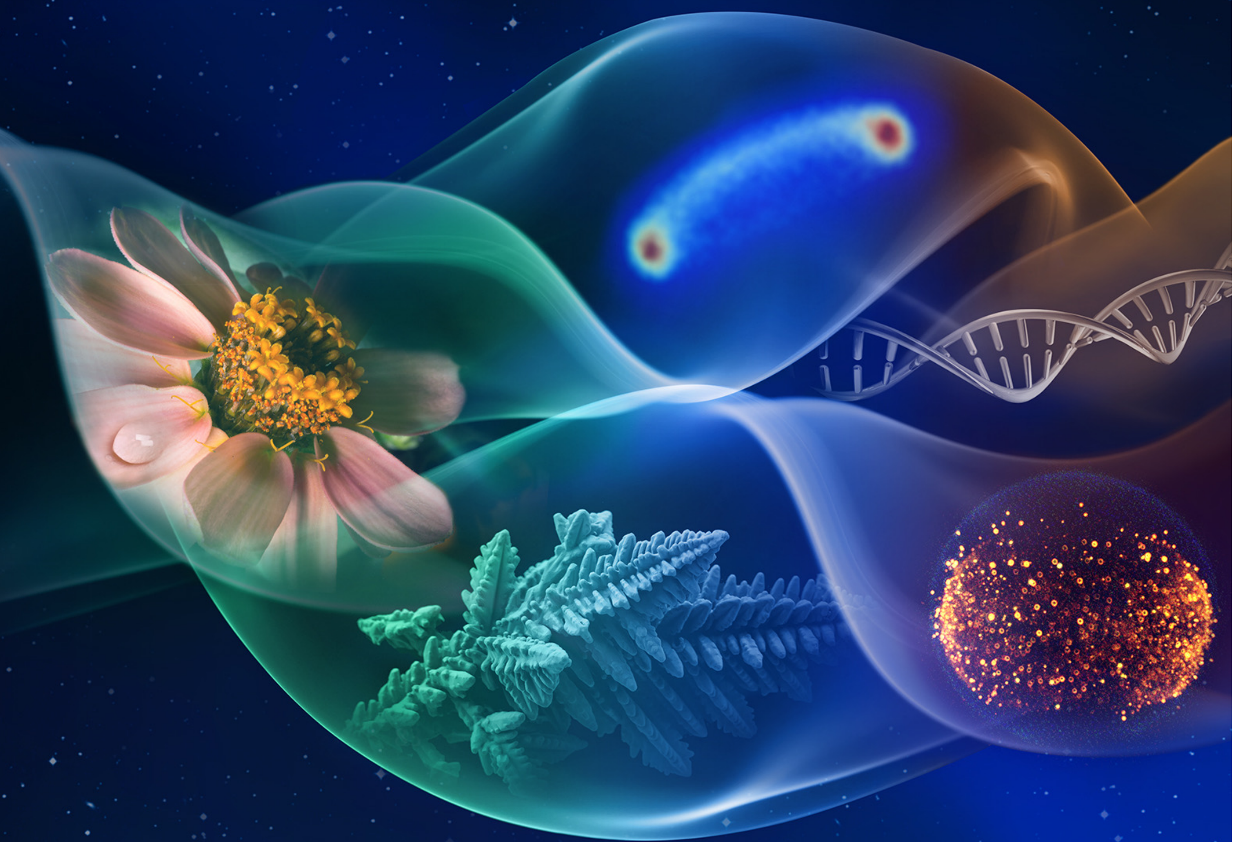
Thank you!



Anthony Hickey, Lisa Carnell, Kevin Sato, Howard Levine, Parag Vaishampayan, Denise Freeland, Elizabeth Keller, Sylvain Costes, Lauren Sanders, Graham Lau, Siddhita Mhatre, Trudy Mackay, Gioia Massa, Ray Wheeler, Ye Zhang, Bruce Link. I am grateful to all of them for their contributions, as well as to those who are unnamed here.

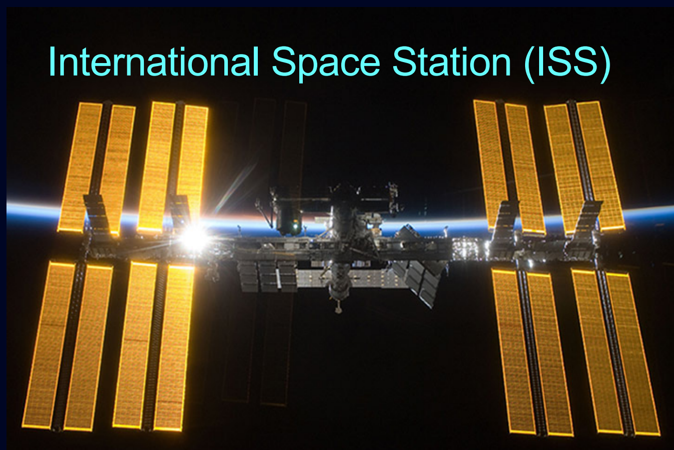
Utilizing Different Platforms in Space

- Lunar surface experiments – partial gravity (1/6g), long-duration experiments (months to years, long-term goal of sustained lunar habitation), automated & miniaturized equipment, data telemetry, high doses of ambient radiation.
- Cis-lunar (e.g., Gateway) – microgravity, long-duration experiments (months to years), automated & miniaturized equipment, data telemetry, high doses of ambient radiation.
- Free flyers/satellites – microgravity, very long-duration experiments (months to years), automated & miniaturized equipment, data telemetry, high doses of ambient radiation for beyond LEO free flyers.
- The ISS and commercial LEO platforms – microgravity, long-duration experiments (months), lower ambient radiation doses than in deep space, utilize available laboratory resources (e.g., freezers, microscopes, gloveboxes/biosafety cabinets, incubators, bone densitometers, PCR machines, etc.).
- Suborbital – short exposure to microgravity (minutes), manual or automated experiments, low ambient radiation exposure due to duration and orbital height.
- Balloon flights – long-duration experiments possible (weeks to months), radiation exposure can be elevated by adjusting altitude and duration of flight.



Current Platforms Utilized in Space and on the Ground

Research in Low Earth Orbit (LEO)

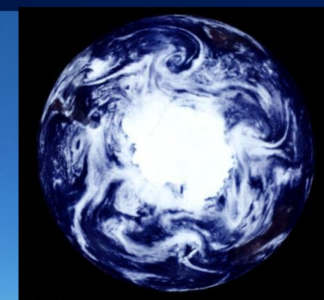


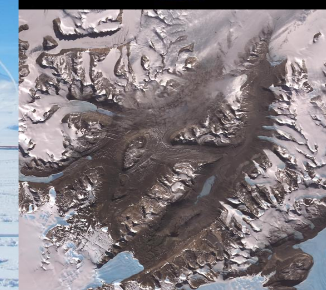
- The majority of Space Biology’s most recent experiments in LEO have been conducted on the ISS
- The ISS involves an international partnership of five space agencies from 15 countries
- It has been continuously occupied since November 2000
- It is 356 feet (109 meters) end-to-end, one yard shy of the full length of an American football field including the end zones
- Through Expedition 60, the microgravity laboratory has hosted nearly 3,000 research investigations from researchers in more than 108 countries.
- For information on resources and hardware available for science experiments on the ISS visit the Space Station Research Explorer at: https://www.nasa.gov/mission_pages/station/research/experiments/explorer/

One example of a Free Flyer Series of Missions: Bion

- In 2019 NASA selected nine Space Biology grant proposals for Space Biology research experiments, the investigators of which will have an opportunity to conduct rodent experiments to be flown on a biosatellite mission, known as Bion-M2, with the Russian space agency Roscosmos.
- This will be this second biosatellite in the Bion-M series launched Roscosmos and the Institute of Biomedical Problems of the Russian Academy of Sciences (IBMP RAS).
- Bion-M2 will carry 75 mice and launch to an altitude of 500-620 miles (800-1000 km) within the inner Van Allen Belt where they will be exposed to radiation levels much greater than those on the International Space Stations which operates at an altitude of about 250 miles (350 km) above Earth.
- The goal of these uncrewed Cosmos/Bion missions, the first of which was launched in 1973, is to investigate how the space environment affects living organisms, with emphasis on animal morphology and physiology, gravitational biology, and radiation biology.
- American investigators have taken part in a great number of experiments flown on nine Cosmos/Bion missions of different durations between 1975 and 1996, the Foton-M1 and Foton-M2 missions completed in 2005 and 2007, as well as a 30-day Bion-M1 mission successfully implemented in 2013.
- **These missions serve as an example of other future free flyer missions that can be dedicated to science experiments for long duration exposure to higher radiation environments, etc. in preparation for future deep space missions.**

Antarctic/Stratospheric Balloon Flights





Balloons are often associated with meteorological studies—gauging weather conditions such as temperature, pressure and humidity in the Earth's atmosphere. But for NASA and other scientists, they also serve as a stepping-stone for critical space research.

Recently, biological sciences researchers have started using balloons as an experimentation platform. In the context of NASA's planned Artemis and Mars missions, access to "near space" can advance scientists' understanding of how biological organisms respond to extreme environments analogous to those found on the Moon and Mars. High-altitude and scientific balloons provide experimental access to various levels of rarefied air, as far up as the stratosphere (above 99% of the atmosphere).

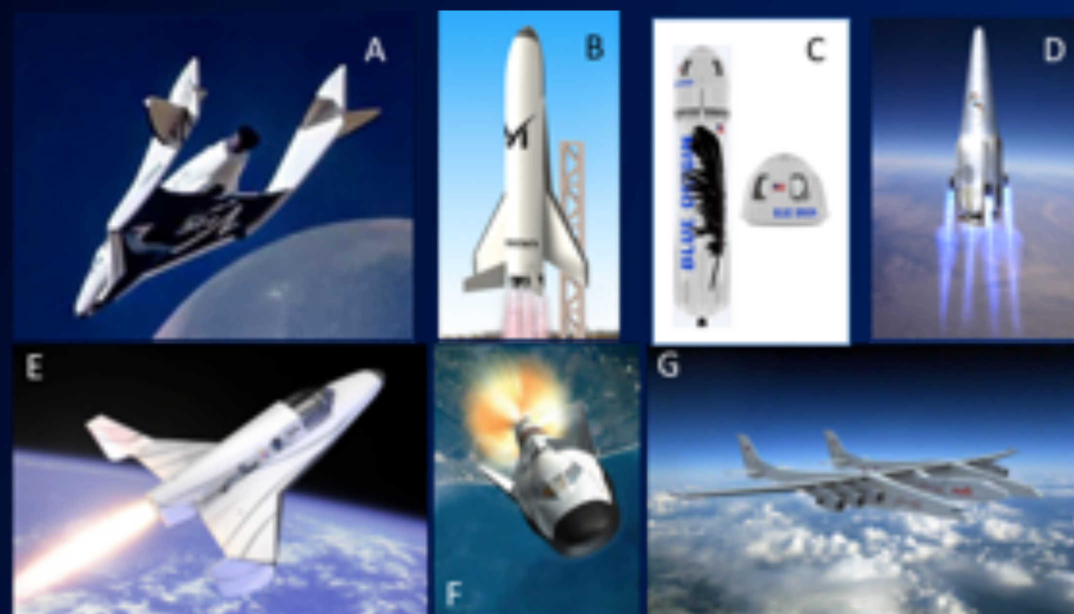
Such work enables researchers to gain initial data about the effects of higher levels of radiation and other factors on biological systems in a more cost-effective and timely manner than if they were to wait for an opportunity to run their experiments on the International Space Station or other orbital platforms.

NASA's facility in Antarctica can offer researchers the most robust balloon research platform for preparing deep-space experiments, as the radiation encountered at the high altitudes at the magnetic pole is analogous to that encountered in deep space. Support for the Antarctic campaign is provided by the National Science Foundation Office of Polar Programs.

Sub-Orbital Flights

Suborbital flights can be used to expose specimens to transient periods of microgravity which can last several minutes (e.g., 2-5 minutes).

They can be used to mature experiment from ground-based research to spaceflight, to demonstrate hardware function, or for scientific research that can be accomplished during short-duration exposures to microgravity.



Ground-Based Research Platforms: Acceleration Facilities

Researchers can use the unique suite of acceleration facilities at NASA Ames 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. The human-rated centrifuge facilities provide a test bed for optimizing human performance, evaluating crew technologies and integrating human systems into the flight environment. The non-human-rated centrifuges 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.

1.22-Meter Radius Centrifuge

Accommodates small animal, plant and hardware payloads

1 Radius Centrifuge

Accommodates small animal, plant and hardware payloads

20-G Centrifuge (8.84-Meter Radius Centrifuge)

Offers unique, innovative ways to conduct research and training to solve real-world problems related to the effects of acceleration on systems.

Human Performance Centrifuge (1.98-Meter Radius Centrifuge)

Accommodates 1-2 supine human subjects.

Ground-Based Research Platforms: Microgravity Simulation Support Facility (MSSF)

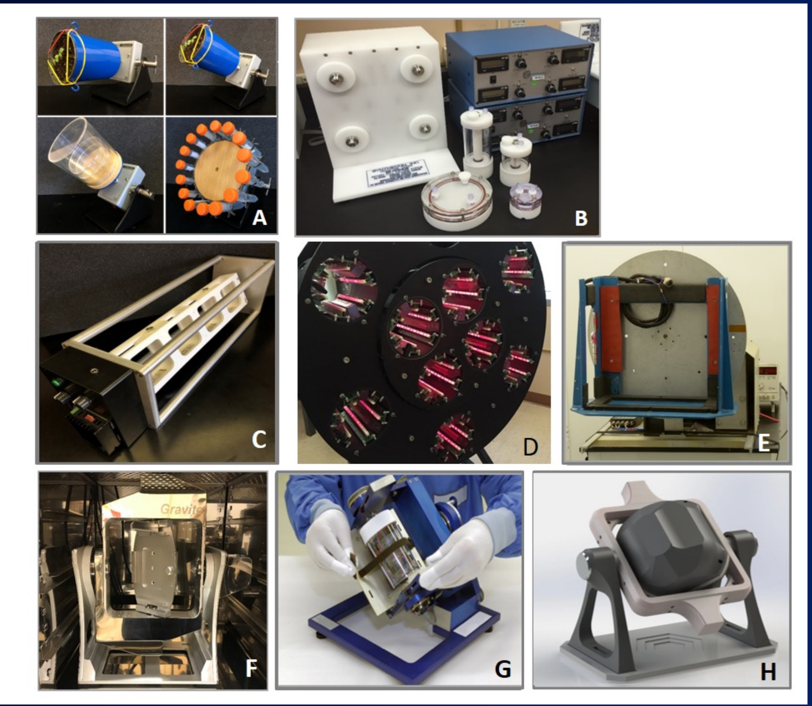
- The Microgravity Simulation Support Laboratory (MSSL) at KSC supports visiting scientists for studies utilizing a variety of specialized microgravity simulator devices to conduct **ground-based microgravity and partial gravity research**. The facility provides controlled environment chambers, a tissue culture facility, and confocal fluorescence microscopy.

Microgravity Simulators Currently Available for Use:

- 2-Dimensional (2-D) Clinostats (A, n=6)
- Rotating Wall Vessel Clinostats (Rotating Bioreactors; B, n=2)
- KSC 2-D Clinostat with LED (C, n=2)
- KSC Heavy Load 2-D Clinostat with middeck locker payload (D, n=1)
- Large 4' Diameter 2D Clinostat with Light Emitting Diodes (LED) (E, n=1)
- Gravite 3-Dimensional (3-D) Clinostat (F, n=2)
- Random Positioning Machine (G, n=4)
- SciSpinner 3-D Clinostat (H, n=2)

Customized Science Carrier Modules Available for Use:

- Dual LED Light Illuminated Stage for 100mm2 Petri Plates
- 60mm^2 Petri Plates Time-Course Removable Module
- Plant Growth Chamber
- 50ml Tube Holders
- Live Cell Imager
- HARV Holders for 3D Clinostat and RPM



Essential Fresh Sample Analytical Capabilities Available for Use:

- Guava EasyCyte 8HT Flow Cytometer System
- BioTek Synergy H1M Plate Reader
- Bio-Rad CFX96 Touch Real-Time PCR System
- NanoDrop One Spectrophotometer
- Nikon A1R Confocal Microscopy System
- Nikon SMZ25 Stereo Dissecting Scope

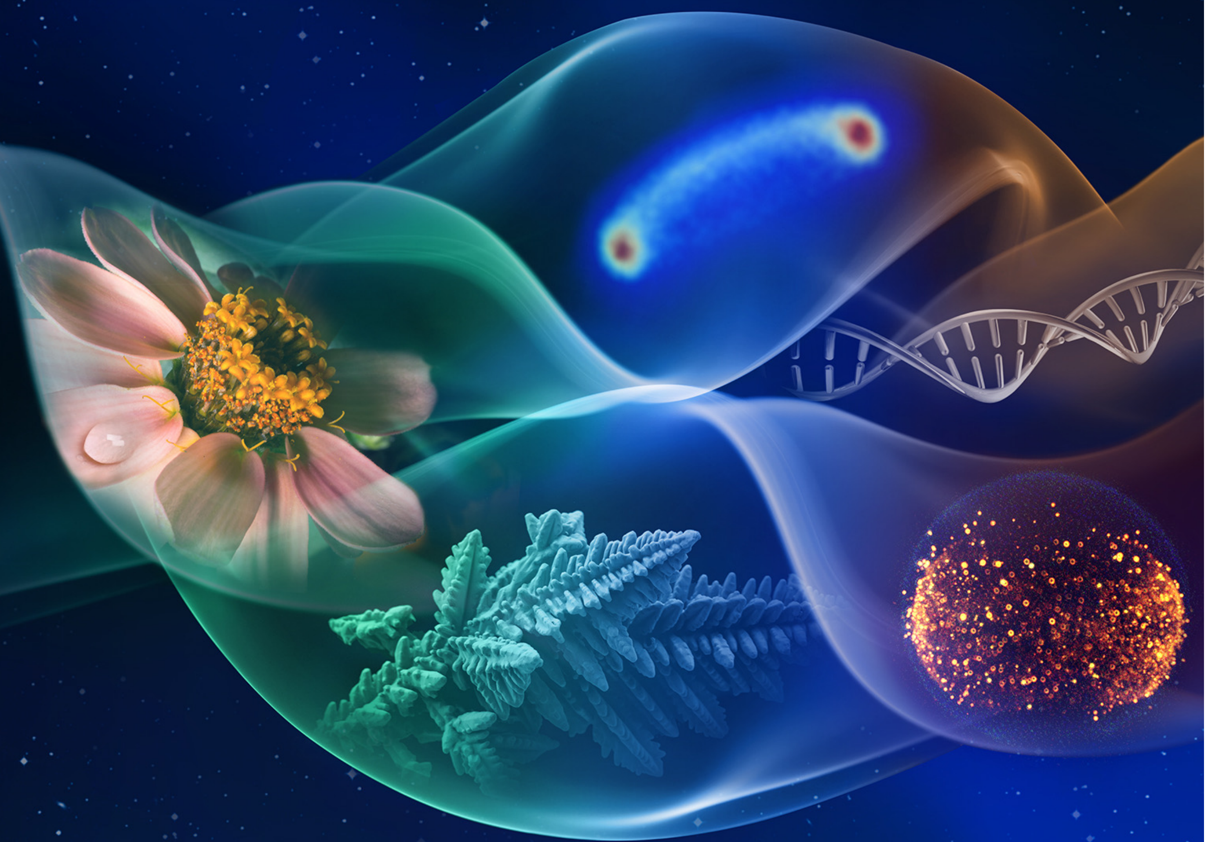
Ground-Based Research Platforms: NASA Space Radiation Lab (NSRL)

Since astronauts now routinely spend six or more months in space, they receive more exposure to ionizing radiation, a stream of particles that, when passing through the body, can ionize atoms and molecules within that substance. The ionization process damages components of living cells, including DNA, that may inhibit cell reproduction and repair.

The research conducted at NSRL increases our understanding of the link between ionizing radiation and cell damage. The work as NSRL seeks to limit the damage to healthy tissue by cosmic radiation, leading to safer space exploration for astronauts.

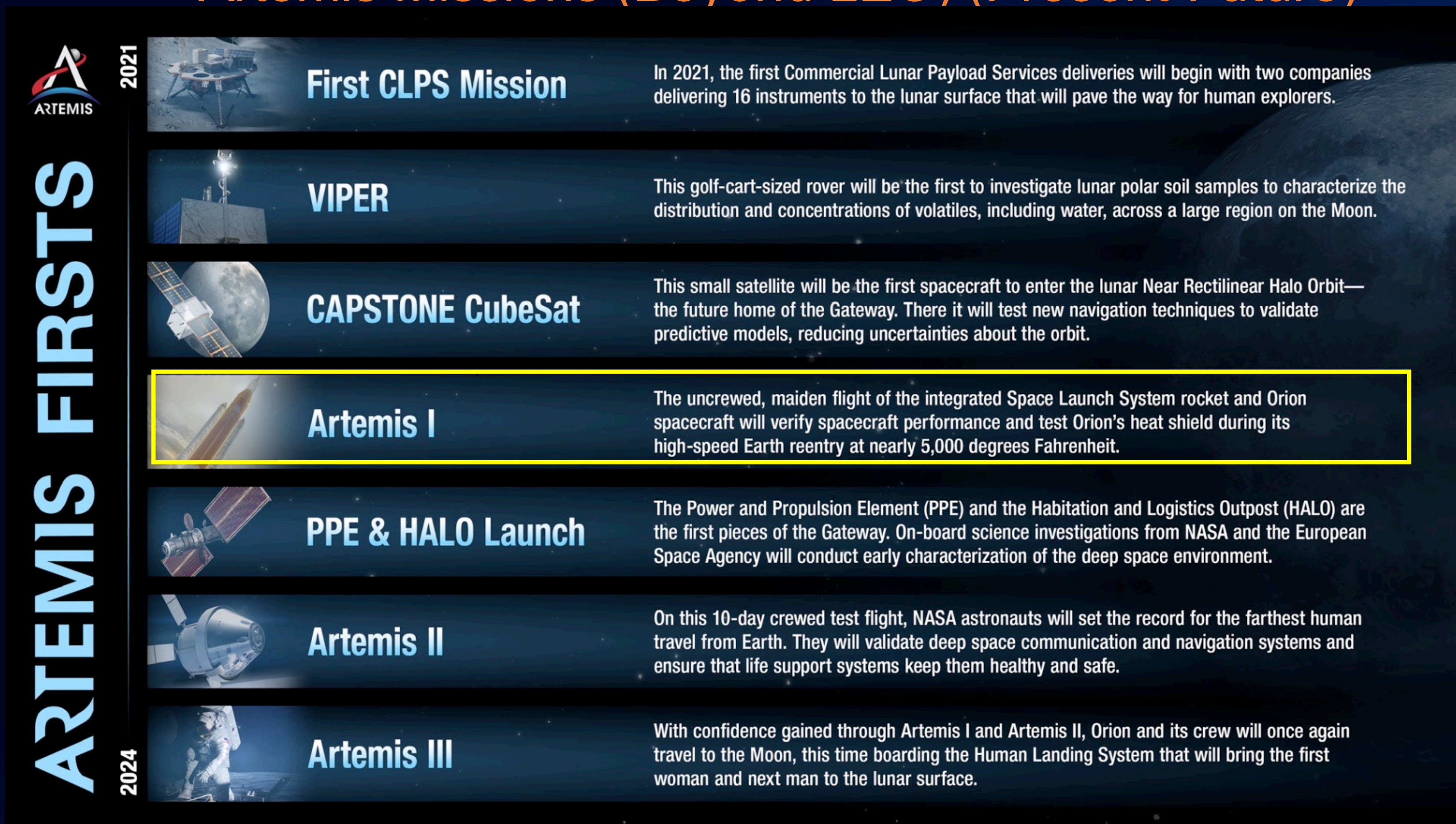
https://www.flickr.com/photos/brookhavenlab/3585684993

The NSRL uses beams of heavy ions extracted from Brookhaven's Booster accelerator, the best in America for radiobiology studies, to simulate the cosmic rays found in space. NSRL features its own beam line dedicated to radiobiology research and state-of-the-art specimen preparation resources. Within NSRL, scientists expose biological specimens---tissues, cells, and whole organisms --to beams of heavy ions. Other experimenters use industrial materials as samples, studying their suitability for space suits and spacecraft shielding.



Current Plans for Platforms to be Utilized in Space

Artemis Missions (Beyond LEO) (Present-Future)



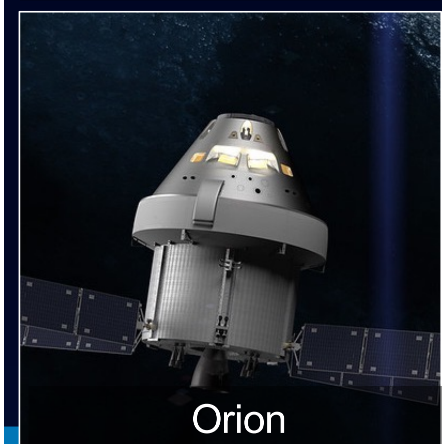
https://www.nasa.gov/sites/default/files/atoms/files/artemis_plan-20200921.pdf

Artemis Missions (Beyond LEO): Artemis Snapshot

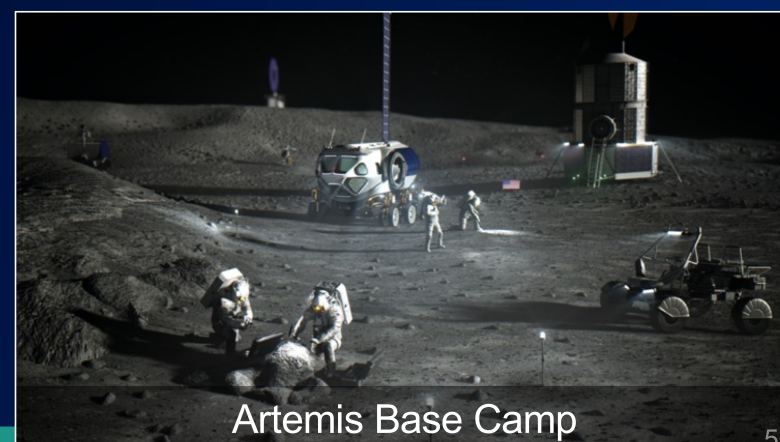

Space Launch System (SLS)


Commercial Lunar Payload Services

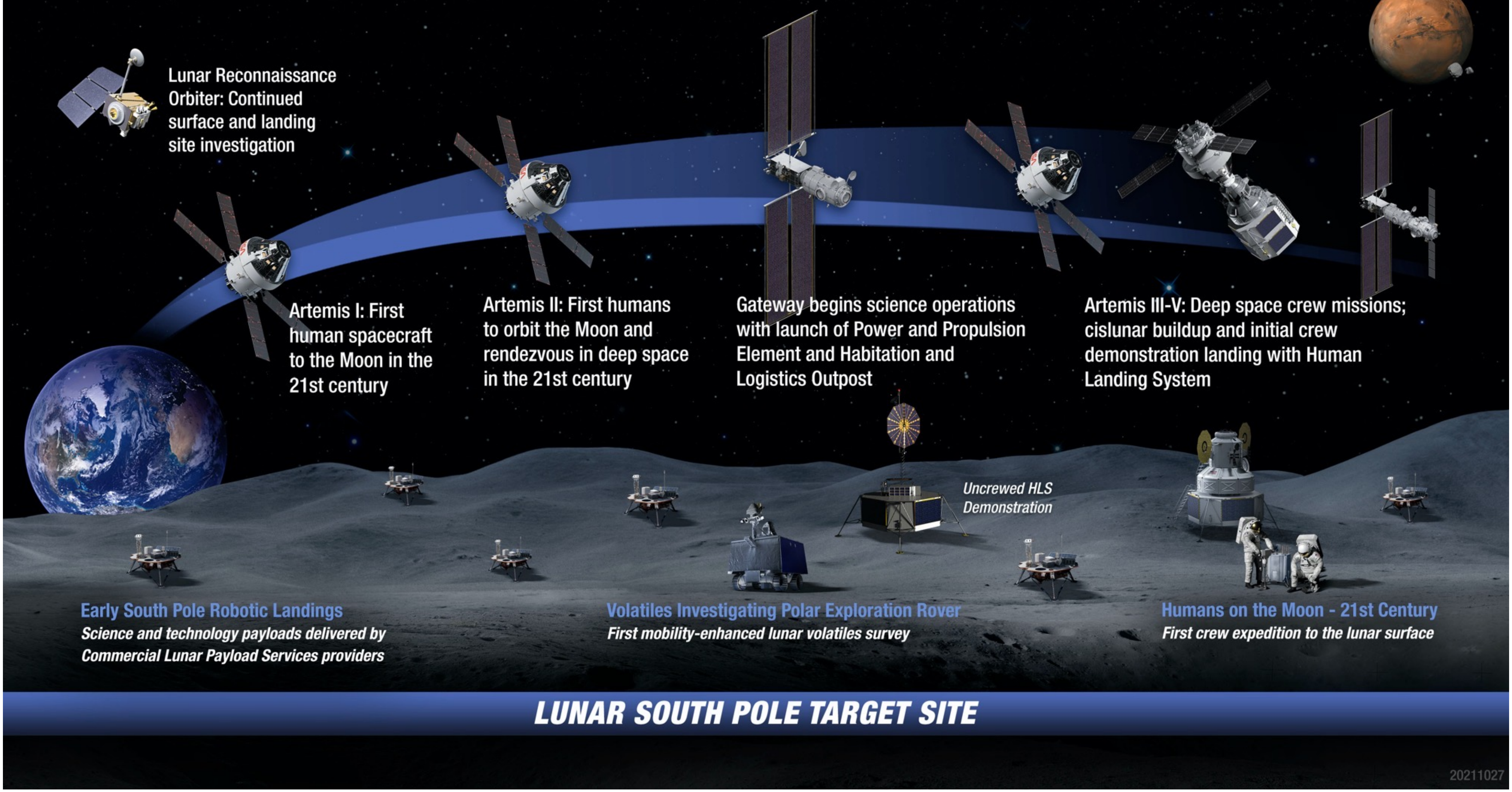

The Gateway in Lunar Orbit


Orion

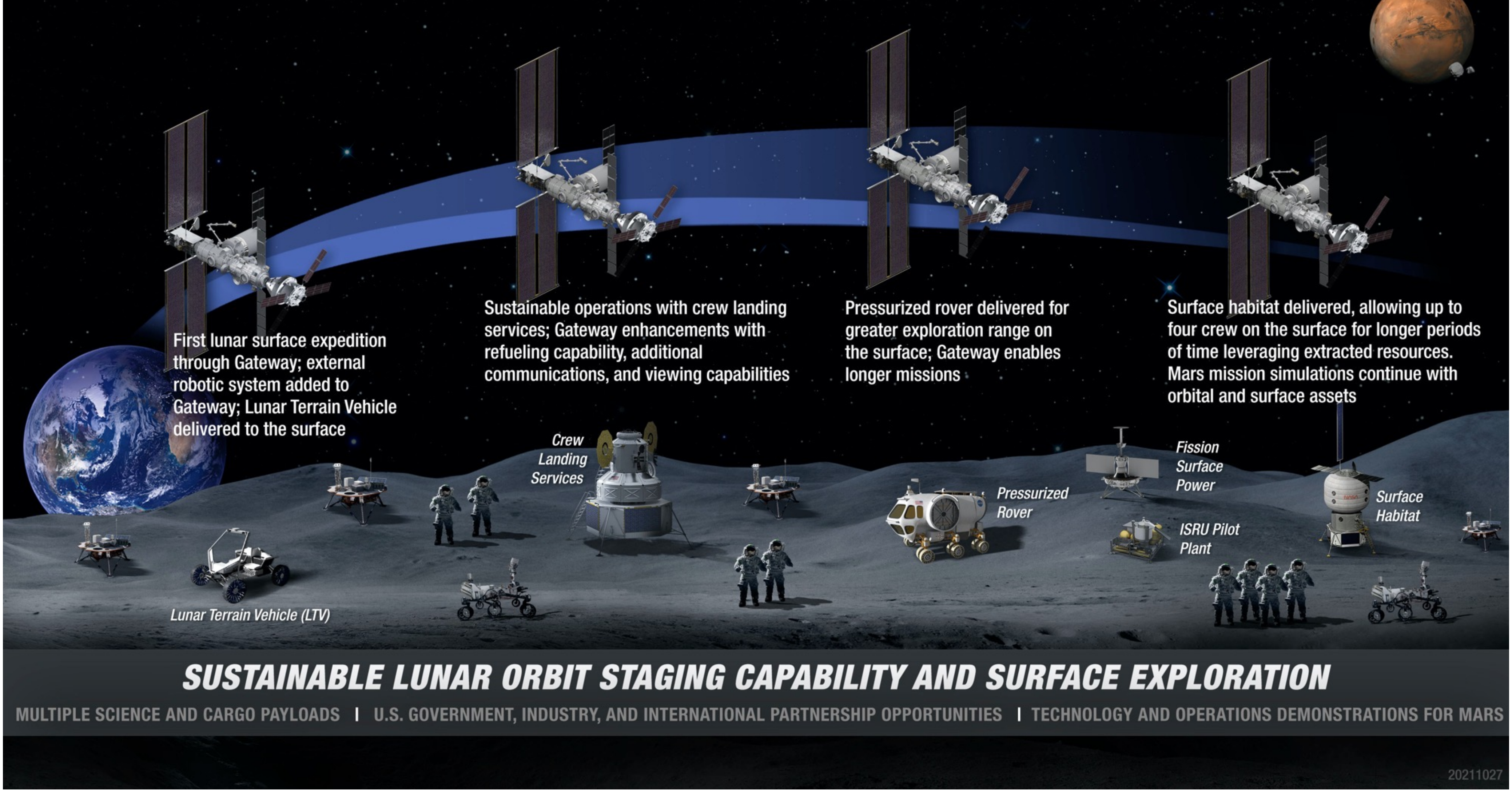

Back to the Moon


Artemis Base Camp

Artemis Missions (Beyond LEO): Landing Humans on the Moon

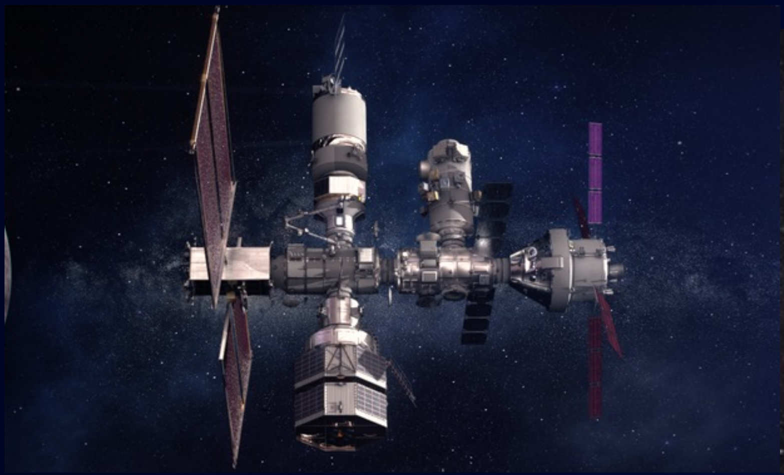


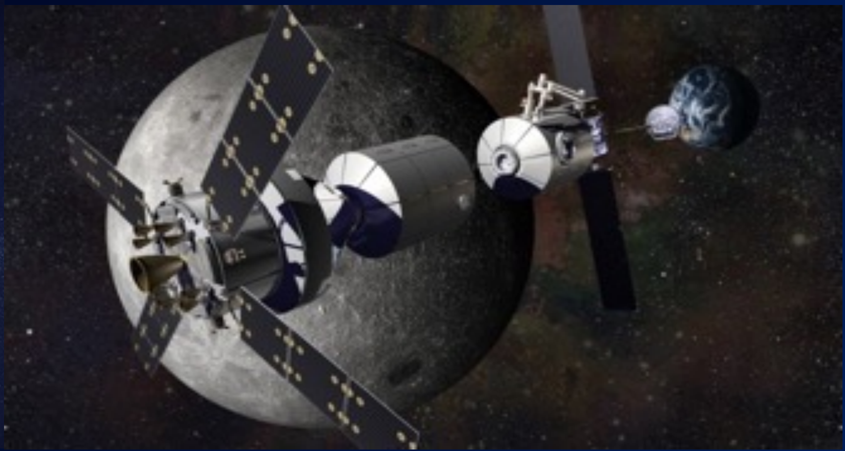
Artemis Missions (Beyond LEO): Artemis Base Camp Buildup



Lunar Gateway (Future)

The Gateway will be an outpost orbiting the Moon that provides vital support for a long-term human return to the lunar surface, as well as a staging point for deep space exploration. It is a critical component of NASA's Artemis program.



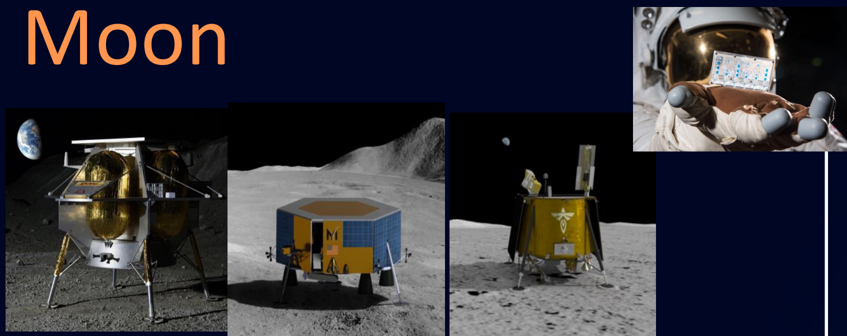


The Gateway is a vital part of NASA's deep space exploration plans. Gaining new experiences on and around the Moon will prepare NASA to send the first humans to Mars in the coming years, and the Gateway will play a vital role in this process. It is a destination for astronaut expeditions and science investigations, as well as a port for deep space transportation such as landers en route to the lunar surface or spacecraft embarking to destinations beyond the Moon.

NASA has focused Gateway development on the initial critical elements required to support the landing – the Power and Propulsion Element, the Habitation and Logistics Outpost (HALO) and logistics capabilities.

Notional Facilities in Space that Could Benefit Space Biology

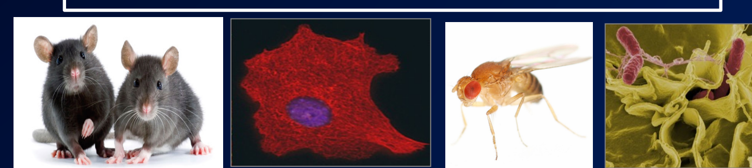
Capabilities for Animal & Model Organism Studies on the Moon

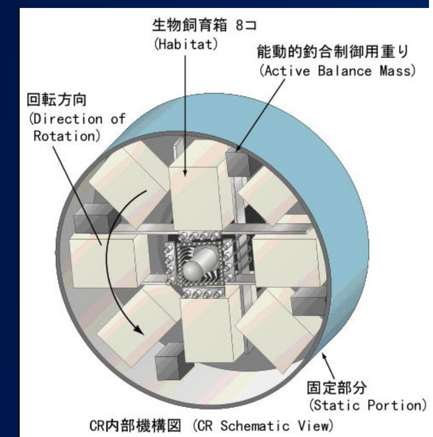


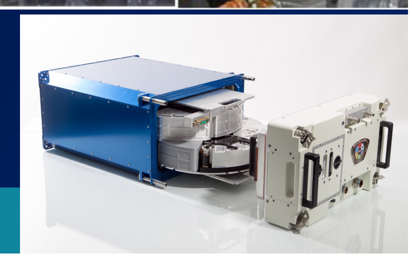
Taking science to the lunar surface

Habitats & analytical tools for research

- Use well-characterized animal model organisms & cellular systems to understand the complex biological consequences of exposure to deep space's unique environment.
- Facilities/equipment/habitats required for lunar surface experimentation with animals and related systems, need to be developed for Space Biology.
- Centrifuges that can simulate 1g or fractional g loads, can be used to differentiate between the biological effects of altered gravity vs other stressors like radiation.







Growing Plants on the Moon

Develop a plant growth facility on the lunar surface to understand the complex biological consequences of exposure to deep space's unique environment and validate the ability to produce supplemental nutrients for future space explorers

Other Resources

Need to obtain correct link from NAS for the video recordings for both talks

- **Bhattacharya Presentation for the National Academy at the Committee on Biological and Physical Sciences in Space - 2021 Fall Virtual Meeting (Oct. 13, 2021) can be accessed here [see 3rd talk for a presentation on "Other Transformative Areas" section].**

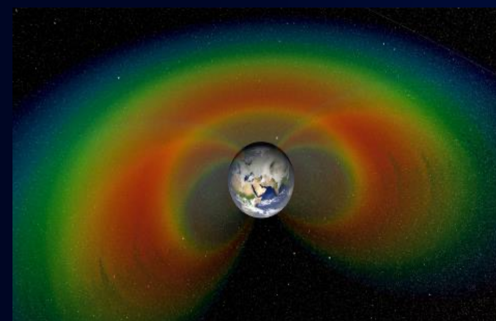
- **Bhattacharya Presentation for the National Academy at the Committee on Biological and Physical Sciences (CBPSS) in Space - 2020 Fall Virtual Meeting (Oct. 27, 2020) can be accessed here [see 3rd talk for a presentation of the effects of combined stressors such as radiation and altered gravity].**

BACKUP

Biologically Relevant Environmental Factors Encountered in Spaceflight

Microgravity/Reduced Gravity

Ionizing Radiation

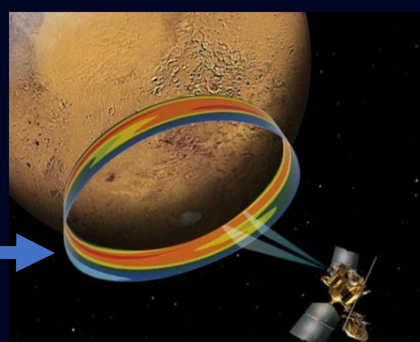


Credits: NASA/Goddard Space Flight Center/Scientific Visualization Studio

Altered Day/Night Cycles: Circadian Rhythm Changes

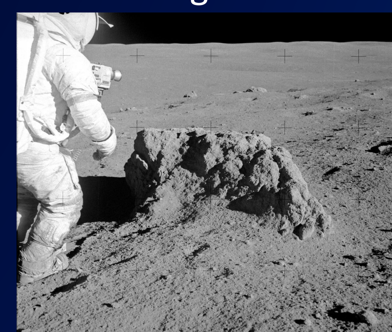
- Elevated CO2
- Reduced atmospheric pressure and elevated volumetric fraction of oxygen

Altered Temperature and Atmosphere



Isolation

Regolith

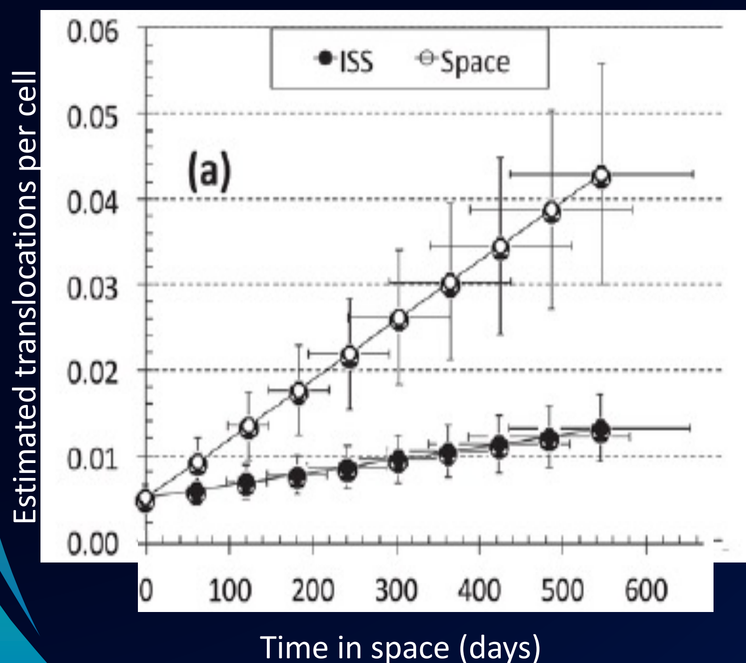


COMBINATION OF MULTIPLE STRESSORS

Ionizing radiation-induced DNA damage

Radiation & spaceflight damages chromosomes as measured in astronauts' white blood cells (lymphocytes) – **expect effect to be greater in deep space than on ISS**

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



- Astronauts have ⬆ in # chromosomal abnormalities, even at low Earth orbits, during ISS, Mir & STS (Hubble shuttle) missions
- The relative increase in frequency of these chromosomal abnormalities ranges from 1.5 to 1.8 times more than pre-flight levels (95 % CL)
- > 80% of organ dose equivalents on ISS are from galactic cosmic rays (GCR) which are difficult to shield
  - ***GCR will be more abundant as astronauts go to higher orbits beyond Earth's protective magnetosphere***

Spaceflight Induces Oxidative Damage to Blood-Brain Barrier Integrity in a Mouse Model

Xiao W. Mao*, Nina C. Nishiyama, Stephanie D. Byrum, Seta Stanbouly, Tamako Jones, Jacob Holley, Vijayalakshmi Sridharan, Marjan Boerma, Alan J. Tackett, Jeffrey S. Willey, Michael J. Pecaut, Michael D. Delp (2020) DOI:https://doi.org/10.1096/fj.202001754R

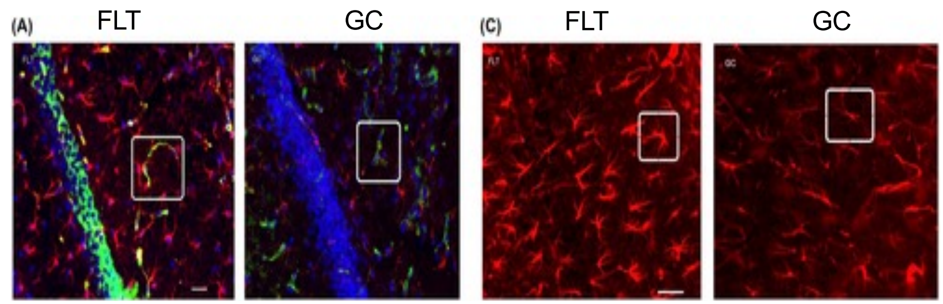
Impact: Spaceflight-induced neuronal damage and potential adverse neurovascular effects constitute a significant health risk for astronauts, particularly for long-duration missions into deep space.

- This study investigated spaceflight effects on oxidative in the mouse brain and its impact on the blood-brain-barrier (BBB) integrity
- Brain samples were collected from 10-week-old male mice launched on SpaceX-12 and maintained onboard the ISS for 35 days

Results:

- Quantitative assessment of brain tissue demonstrated that spaceflight caused an up to 2.2-fold **increase in apoptosis in the hippocampus** compared to the control group
- **Increased oxidative damage and disruption in BBB integrity**, as evidenced by changes in the expression of BBB-related proteins
- Spaceflight-induced **changes in proteomic profiles** and pathways, including functional changes such as cell cycle progression, apoptosis, mitochondrial function, metabolism, and behavior were also found

These findings may provide insight into cellular mechanisms that underlie the effects of oxidative stress-mediated structure and functional damage induced by spaceflight conditions.



A. Representative micrographs of brain sections (hippocampus) after immunostaining with anti-GFAP and AQP4 antibodies on flight (FLT) and ground control (GC) samples. AQP4 positive staining was identified by green fluorescence, GFAP with red, and the cell nuclei with blue (DAPI).

C. Representative images of GFAP immunoreactivity of mouse FLT hippocampus show more GFAP-positive astrocytes with larger in size than those in the GC group. Note that many GFAP-positive astrocytes exhibited hypertrophic morphology.