National Aeronautics and Space Administration

Biological and Physical Sciences

SPACE BIOLOGY PROGRAM

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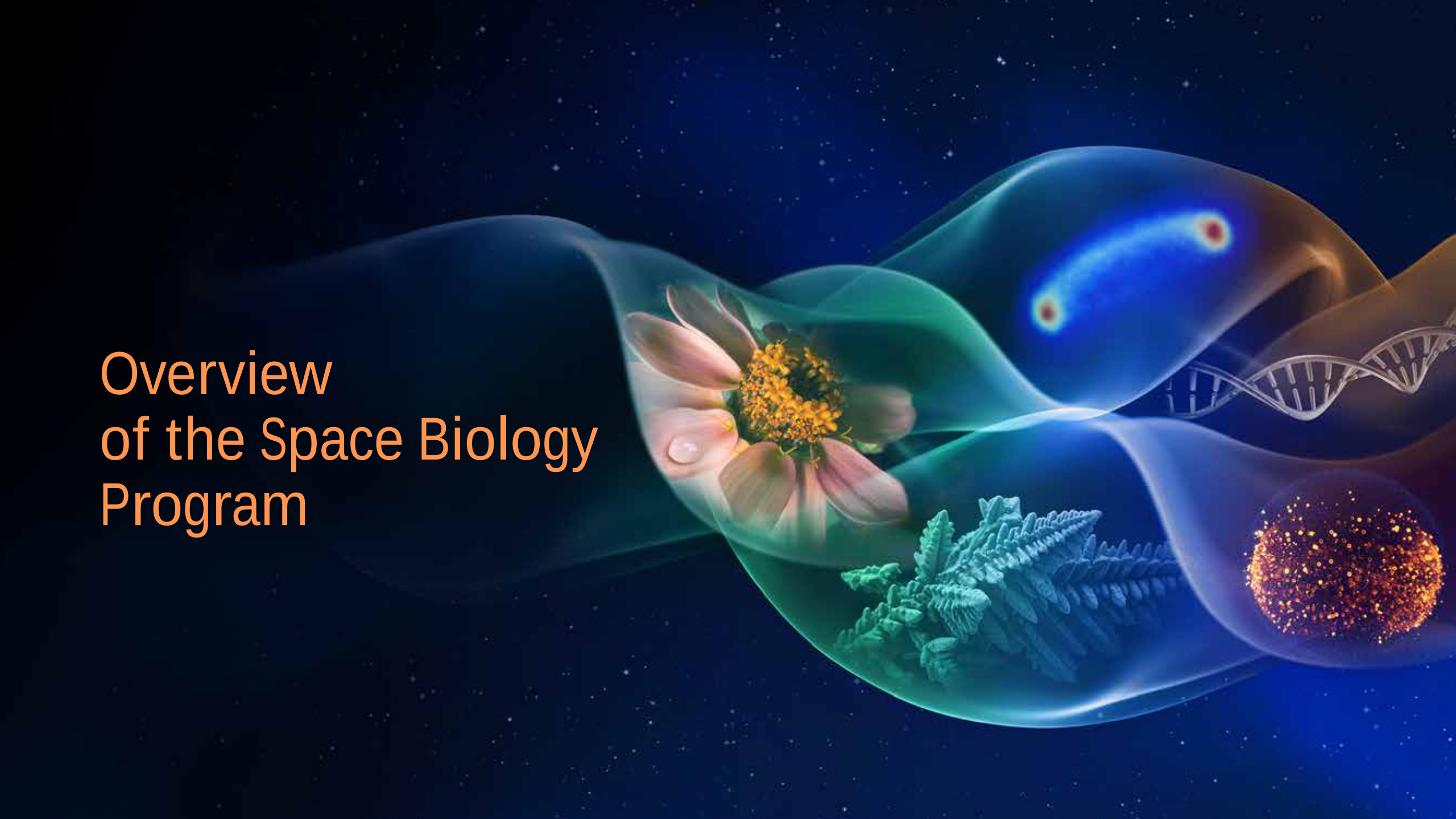
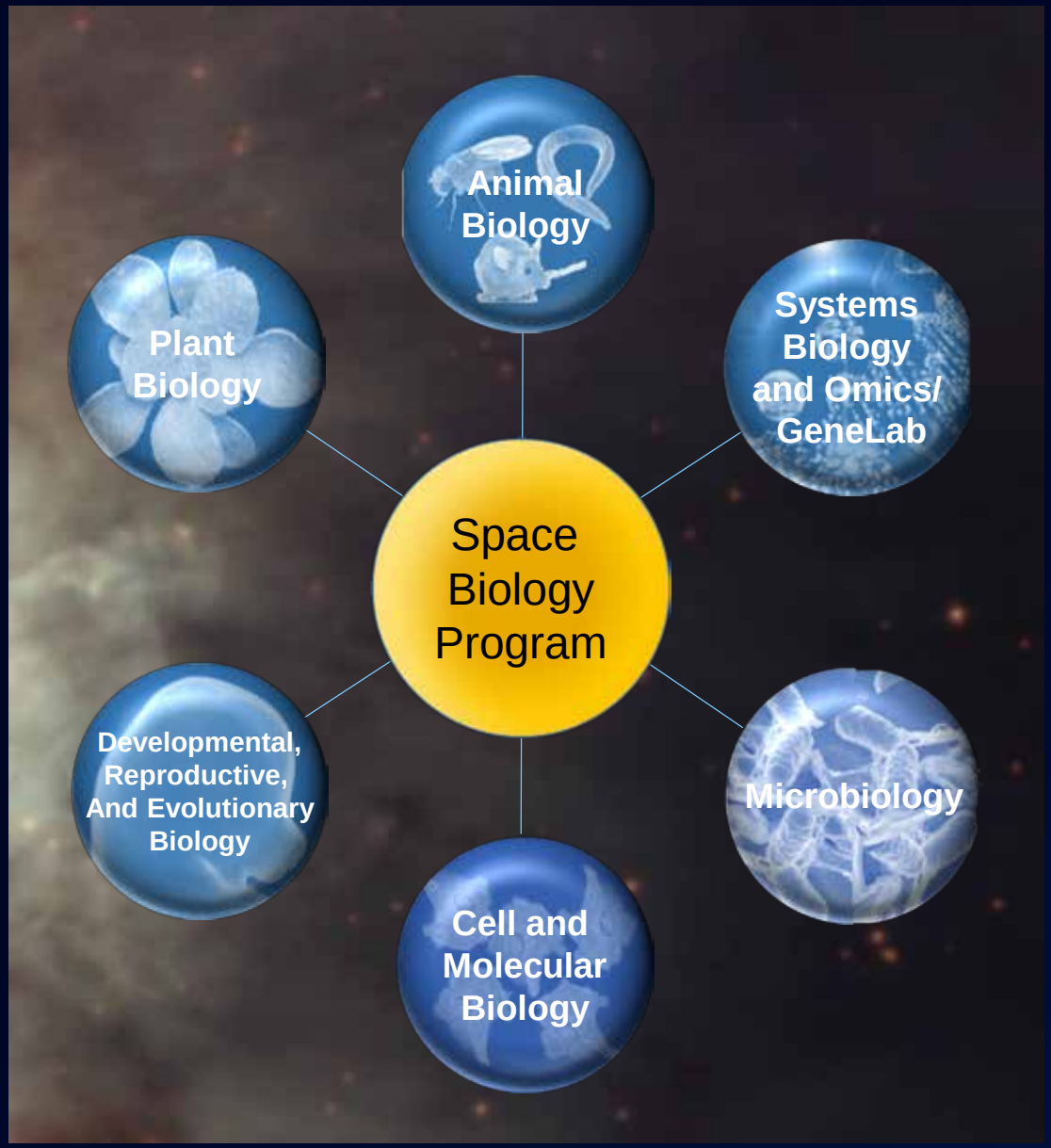
Space Biology Program Scientist

Decadal Survey Committee Meeting
Jan 12, 2022

Overview of the Space Biology Program





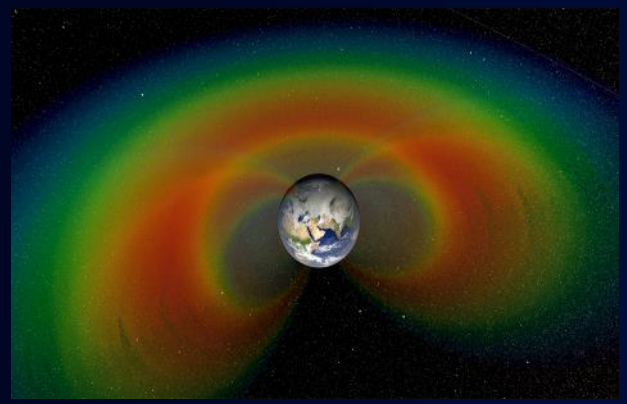
Objectives

- **Discover how biological systems respond to the space environment**
- **Identify the underlying mechanisms and develop models for biological systems in space**
- **Provide mechanistic understanding to support human health in space**
- **Promote open science through the GeneLab Data System and Life Sciences Data Archive**
- **Develop technologies to enable spaceflight research**
- **Transfer the knowledge and technology of space-based research to benefit life on Earth**

Biologically Relevant Environmental Factors Encountered in Spaceflight

Microgravity/Reduced Gravity

Ionizing Radiation

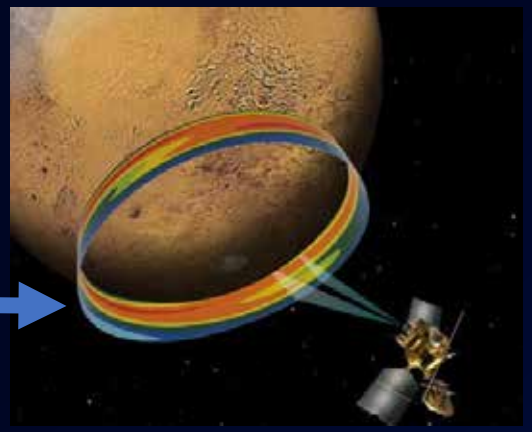


Credits: NASA/Goddard Space Flight Center/Scientific Visualization Studio

Altered Day/Night Cycles: Circadian Rhythm Changes

Altered Temperature and Atmosphere

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



Isolation

Regolith

COMBINATION OF MULTIPLE STRESSORS

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

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

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

+

Build the Blocks to Support Human Life

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

=

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 | Isolation

PLATFORM PROGRESSION

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

MODEL ORGANISM PROGRESSION

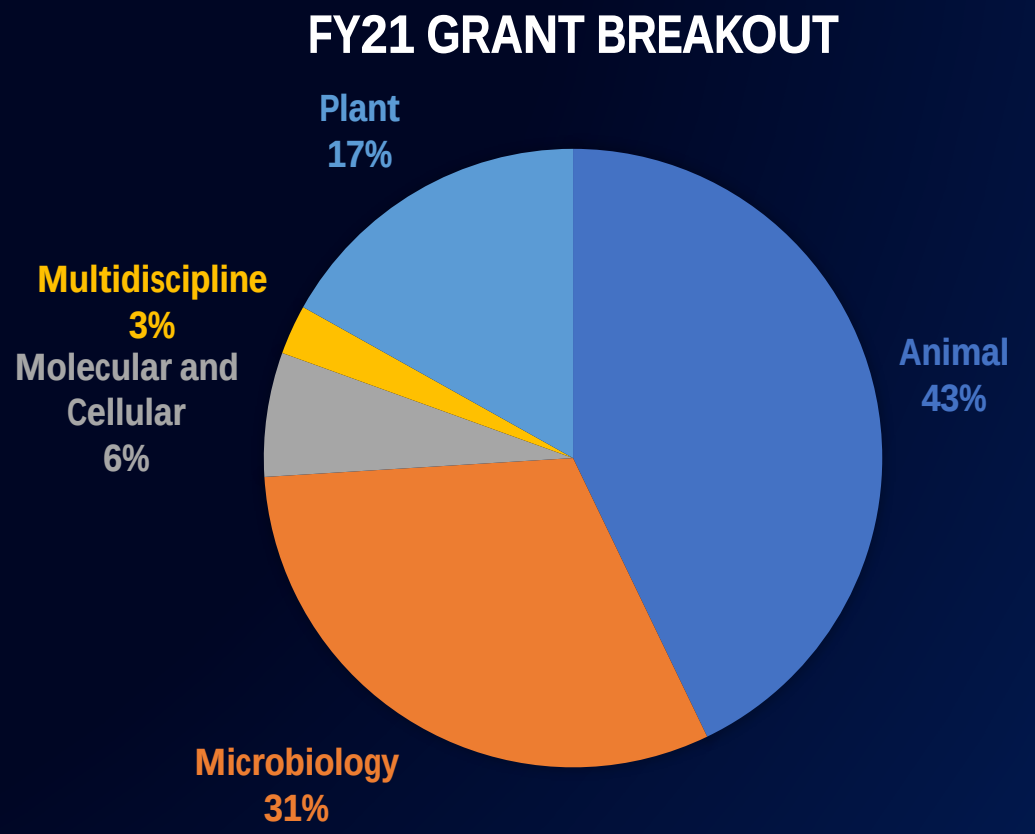
Unicellular (e.g., yeast, fungi)

Invertebrates (e.g., flies, worms, tardigrades) → Vertebrates (e.g., mice, fish; tissue chips)

Simple model plants (e.g., *Arabidopsis*) → Edible & others (for micronutrients, etc.)

→ Humans

Space Biology Content



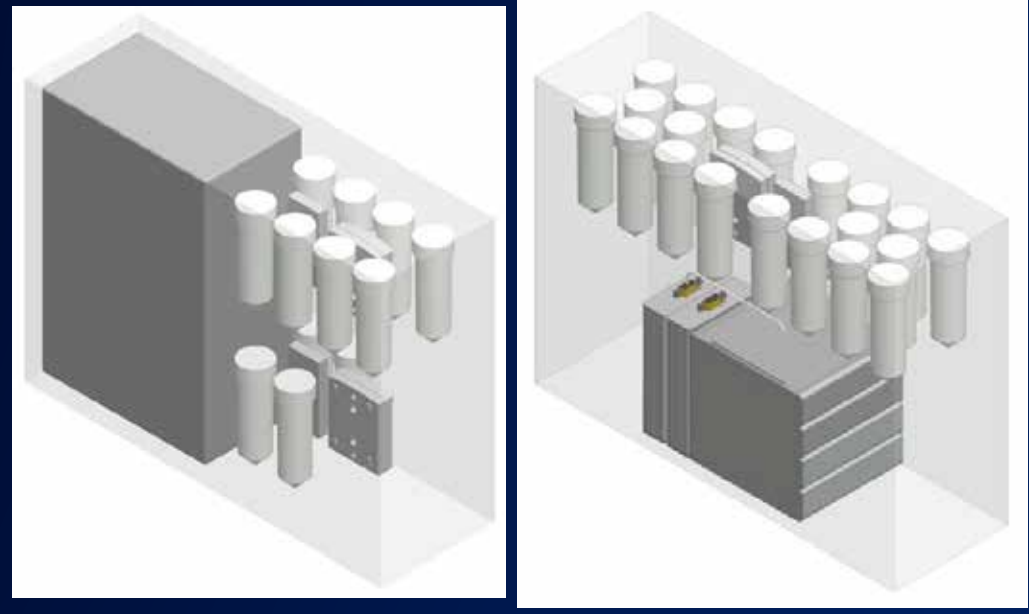
Total SB FY21 Grants	135
Flight	74
Ground	61

Number Directed vs Competed	
Directed	4
Competed	131

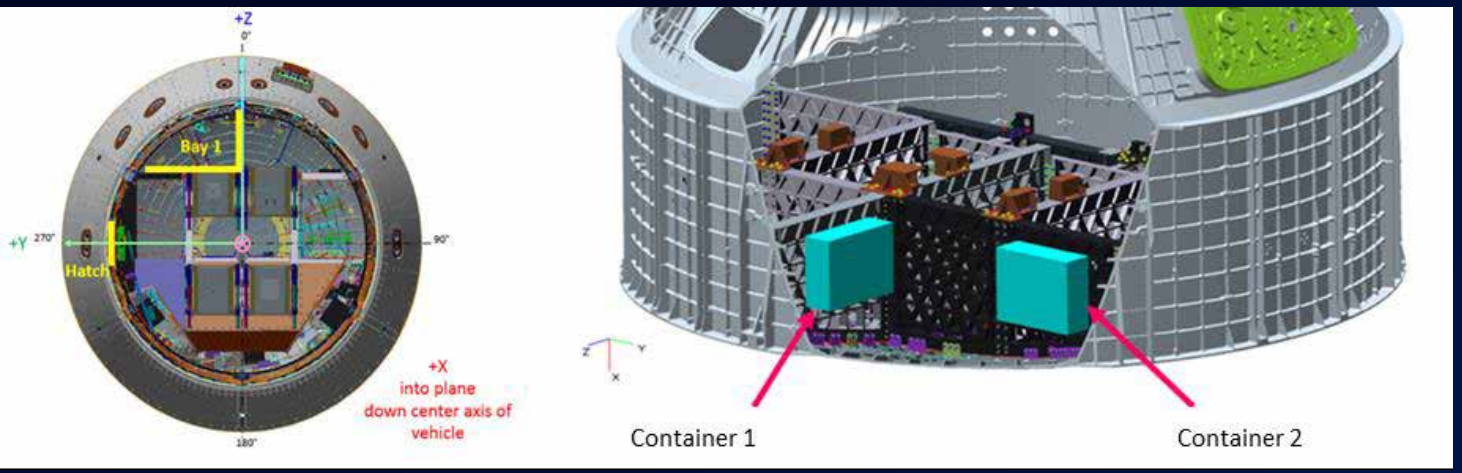
taskbook.nasaprs.com

BioExpt-1: Flying on Artemis-1

- Plant seeds *Arabidopsis thaliana*: *Life Beyond Earth: Effect of Space Flight on Seeds with Improved Nutritional Value*; PI Federica Brandizzi, Michigan State University
- Algae *Chlamydomonas reinhardtii*: *Fuel to Mars*; PI Timothy Hammond, Institute for Medical Research; *Chlamydomonas reinhardtii*
- Fungi *Aspergillus niger*: *Investigating the Roles of Melanin and DNA Repair on Adaptation and Survivability of Fungi in Deep Space*; PI Zheng Wang, Naval Research Laboratory
- Yeast *Saccharomyces cerevisiae*: *Multi-Generational Genome-Wide Yeast Fitness Profiling Beyond and Below Earth's Van Allen Belts*; PI Luis Zea, University of Colorado-Boulder



SBP Payload Container Assembly configuration for Drs. Zea & Brandizzi (left) and Drs. Wang & Hammond (right).

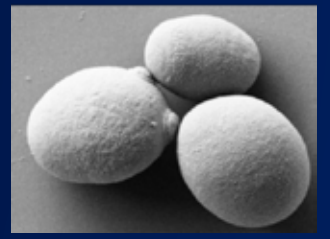


The SBP Payload Container Assemblies are installed onto backbone panels 1 and 2 in Bay 1 of the Orion capsule.

3D printed ½ scale mockup of SBP Payload Container Assembly with blue Science Bag contained within.

Lunar Explorer Instrument for Space Biology Applications (LEIA)

- LEIA is based on the 6U BioSentinel Small Sat
- Modified 4U Biosensor with a 2U “Pseudo Bus” to provide thermal control for the lunar surface and data conditioning

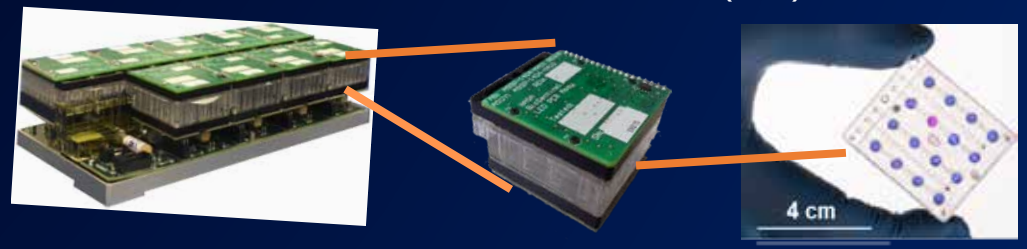


Accommodates yeast and related cellular systems

4U BioSensor Payload

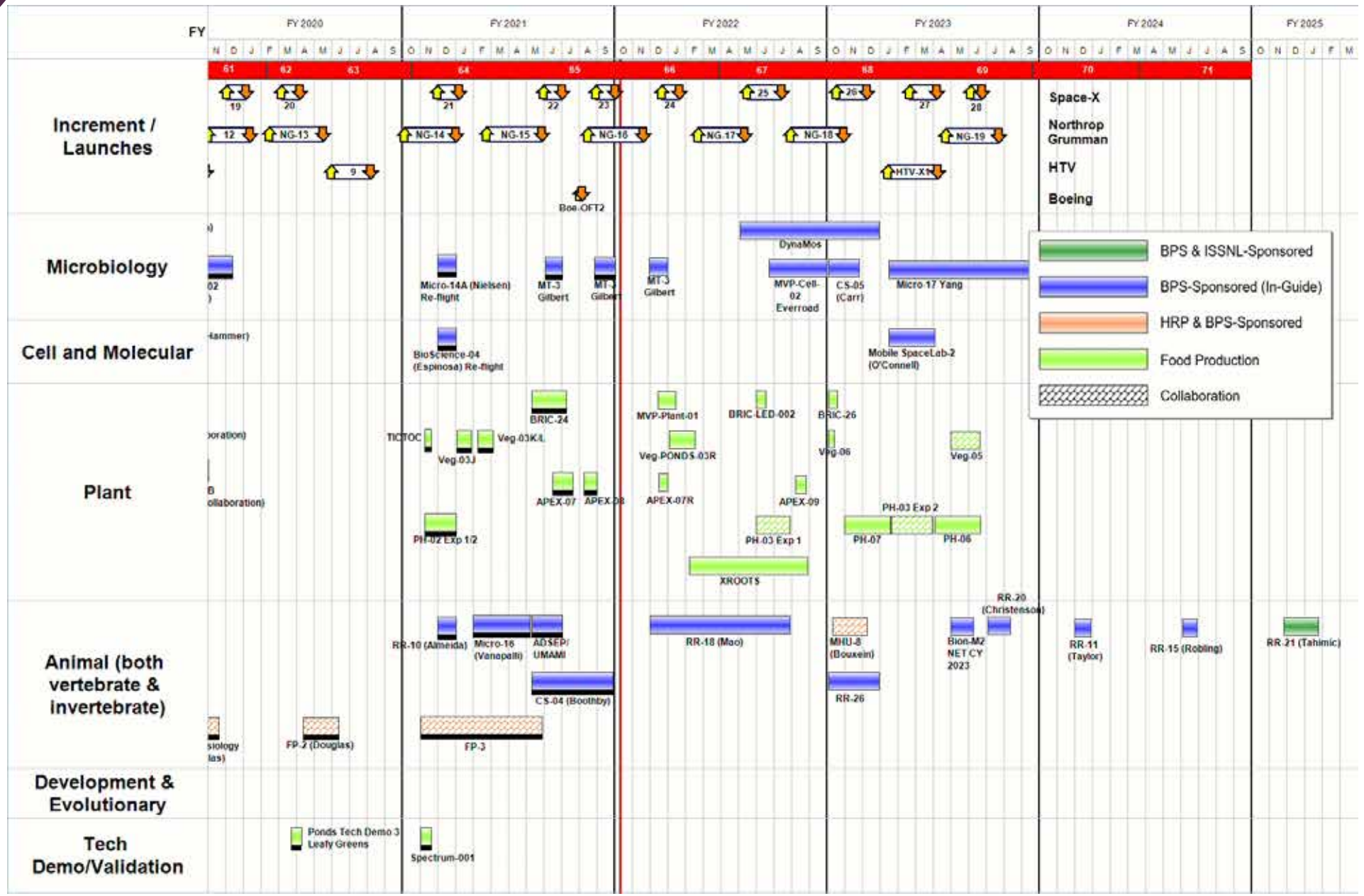
(2U Pseudo Bus not shown in diagrams below)

LET spectrometer attached at one end of payload



Biosensor payload with fluidic cards and optical sensors

ISS Utilization

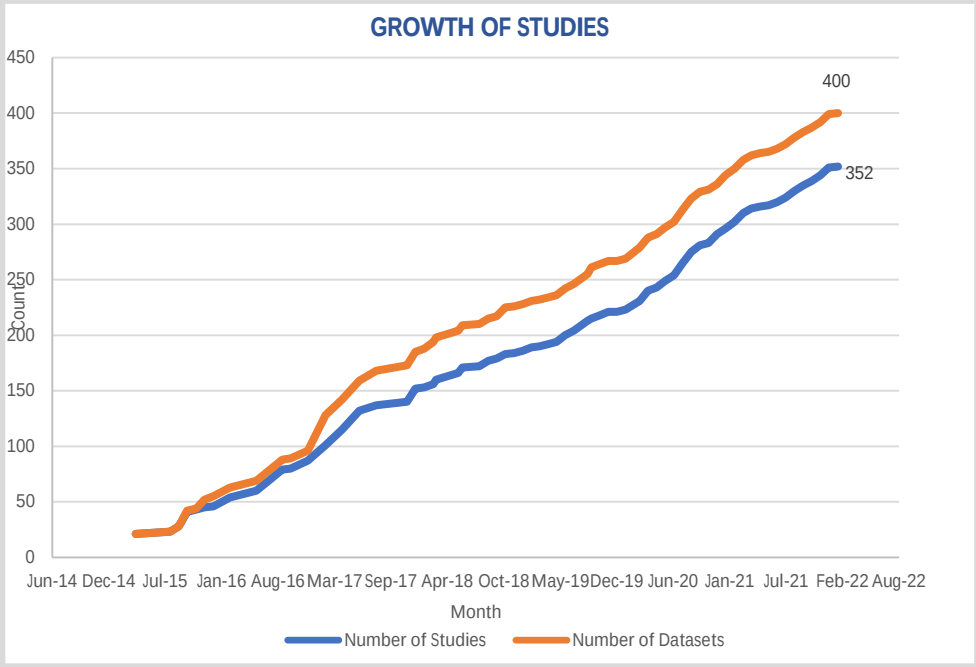


As of 11/12/21

Open Science

- **GeneLab** is an effort to maximize the value of spaceflight experiments through meticulous curation, augmentation with additional data, and widespread distribution to a motivated community. **(https://genelab.nasa.gov/)**

- **NBISC (NASA Biological Institutional Scientific Collection)** archive of spaceflight-relevant vertebrate and invertebrate animal tissues, cells, data, etc. (https://www.nasa.gov/ames/research/space-biosciences/alsda)



GeneLab

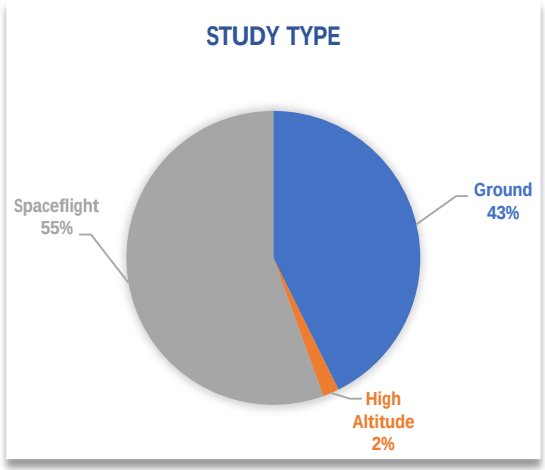
352
Studies

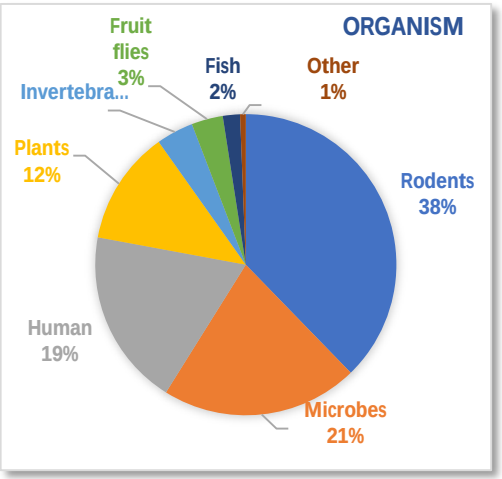
400
Datasets

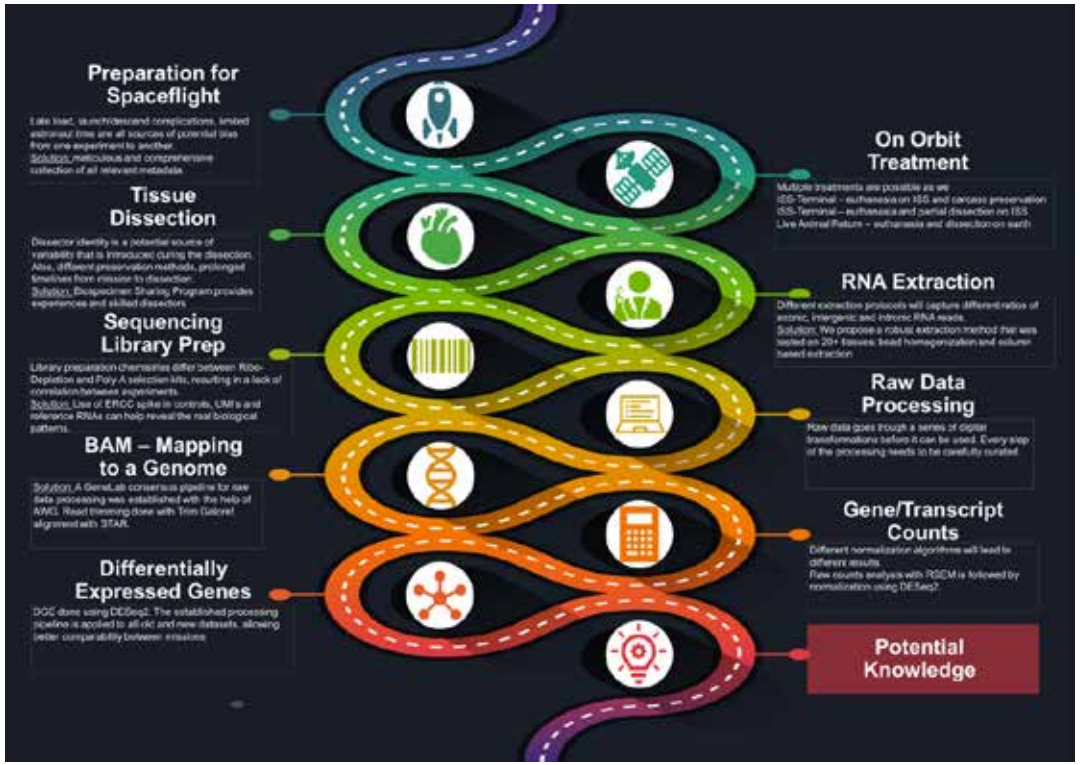
45
Species

>10
Assays

>135TB
Data

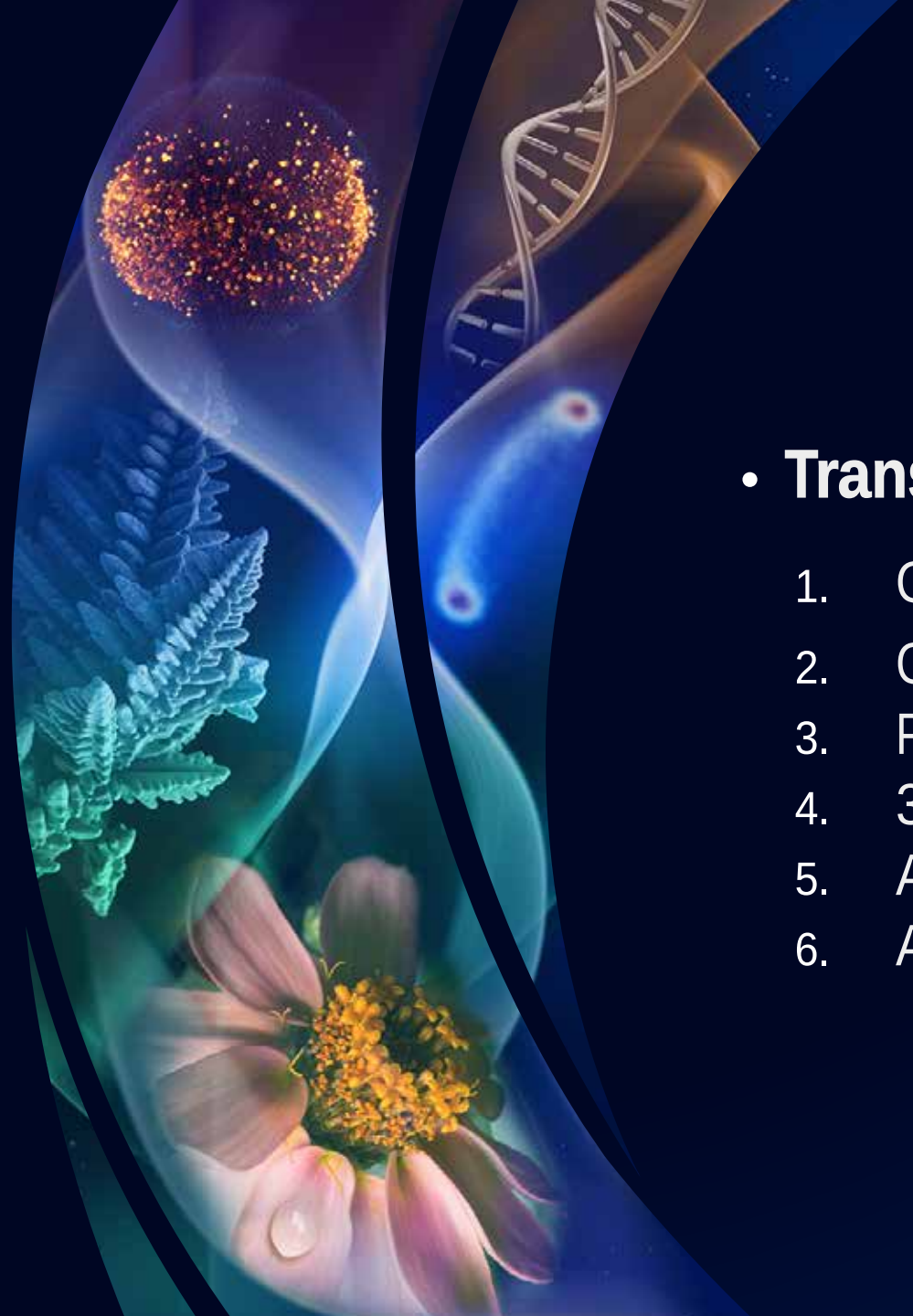






Utilizing Different Platforms in Space

- Lunar surface experiments – partial gravity (1/6g), long-duration experiments (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/small 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-long), 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.



....For Next Time

- **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

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

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

ØEnable exploration,

ØBenefit Earth: human health & controlled environment agriculture.

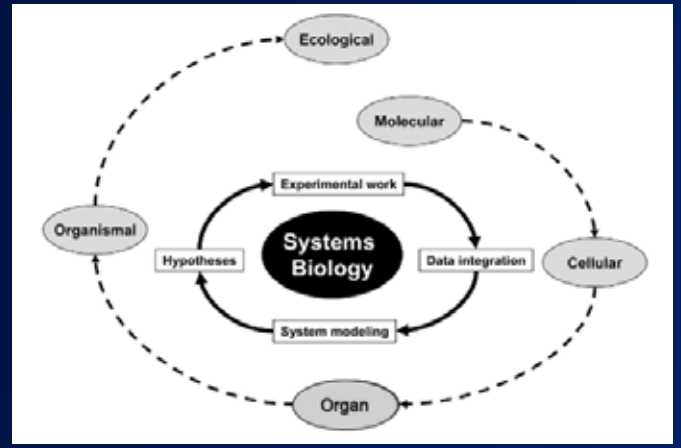
Thank you!

Anthony Hickey, Lisa Carnell, 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.

Transformative Science Areas

1. Transformative area: "Omics" and Systems Biology

- **Changes in the field as a whole**
  - Enhancement/development of methodologies:
    - "Omics"
    - Systems biology
    - Quantitative genomics



- **Changes in NASA-funded research**
  - 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 Ames Life Sciences Data Archive – 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 (NASA Biological Institutional Scientific Collection) to facilitate efficient curation of samples along with ancillary data
      (desire to include microbiological samples 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 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).

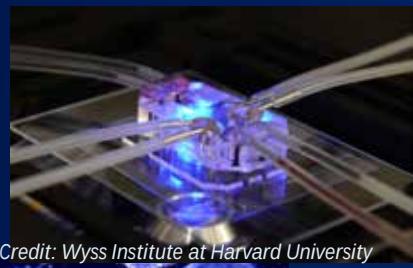
- Rodent studies conducted indicate that **the intratracheal instillation of LDS in rats** causes inflammatory damage that affects autonomic function, leading to **inflammatory myocardial fibrosis** (Sun et al., *Toxicol Res.* 2019), and the aggregation and **infiltration of lymphocytes and neutrophils in the lung** which **may lead to inflammatory pulmonary fibrosis** (Sun et al., *Environ Toxicol.* 2018).

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

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

Background and Advances in Last 10 years

- **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.



Credit: Wyss Institute at Harvard University

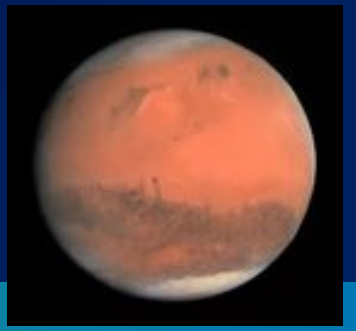
Credit: NASA

Changes in the field as a whole:

- ***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.

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

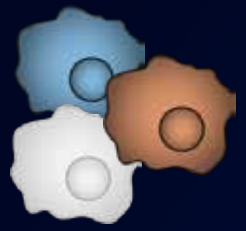


4. 3D Tissues & Organ-on-Chip Models (cont.)

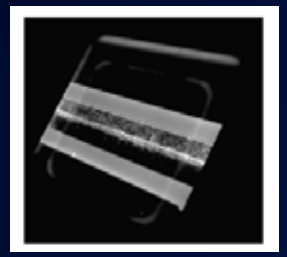
Personalized models:

- Genomic and epigenetic associations à mechanisms à targets for countermeasures and biomarkers
- Individual astronaut's risk

Donors



iPSC-derived cells



3D Tissue/Organ Models

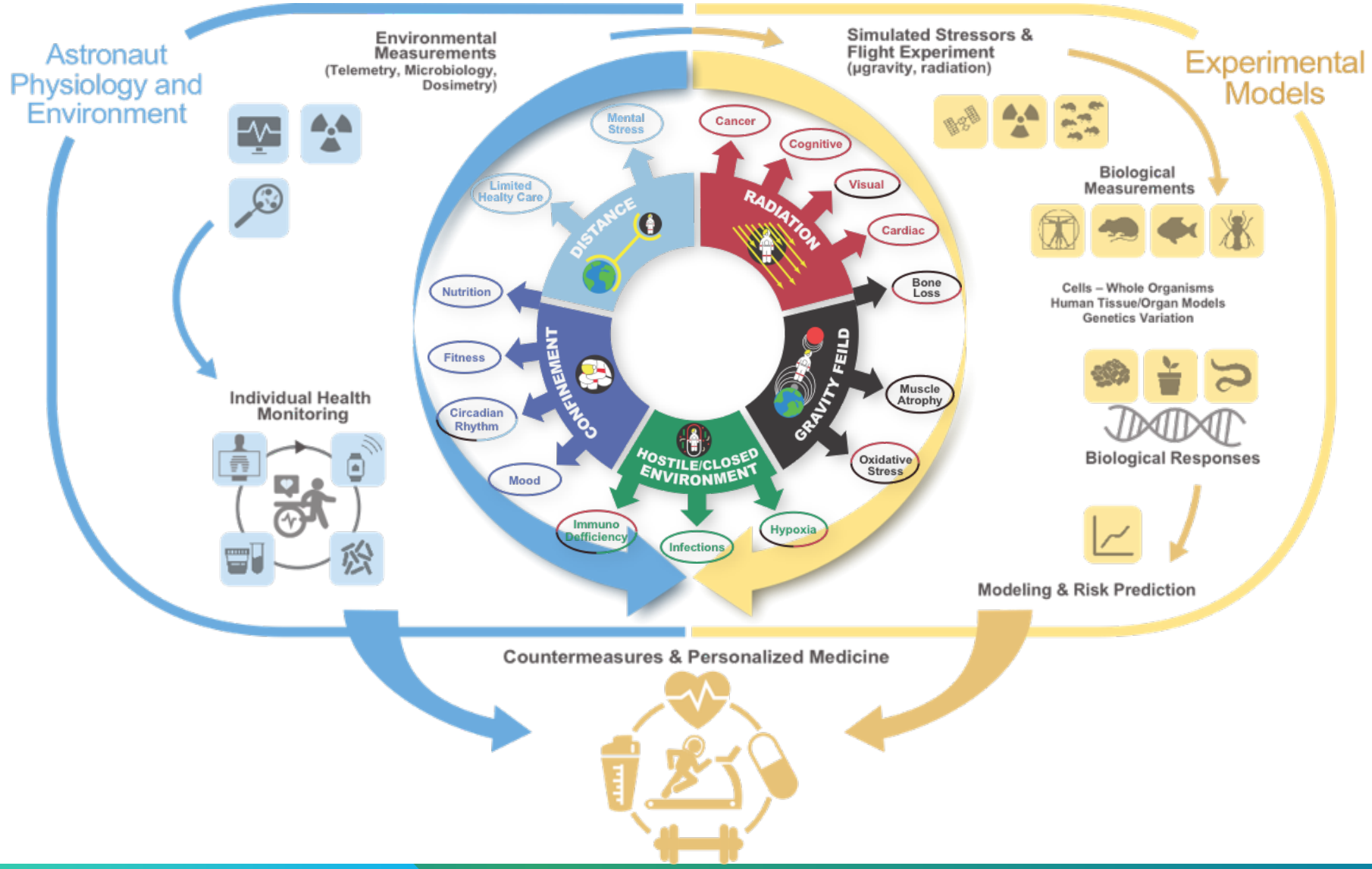
Simulated spaceflight stressors: microgravity, ionizing radiation

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.
- **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., distributed across many hospitals/institutes at once).
- **xAI (Explainable AI) – is a paradigm shift in AI/ML 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 free-flyer missions, Gateway, lunar orbit, and lunar surface:**

    - 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

Other Resources

- **Bhattacharya Presentation at the Committee on Biological and Physical Sciences in Space - 2020 Fall Virtual Meeting (Oct. 27, 2020) can be accessed here.**