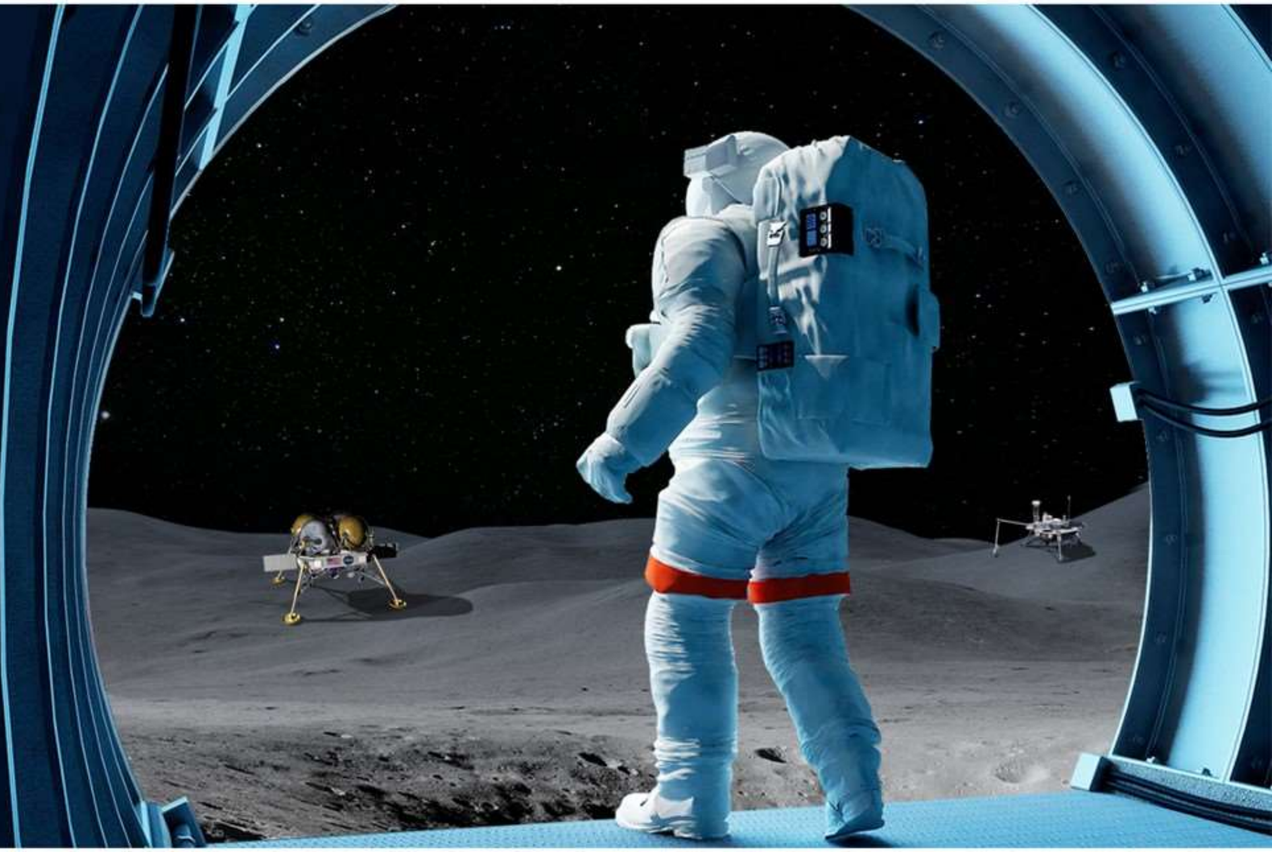
GeneLab: A Systems Biology Platform for Omics Analysis

National Aeronautics and
Space Administration

Disseminate and reuse data, tools, and samples post-project

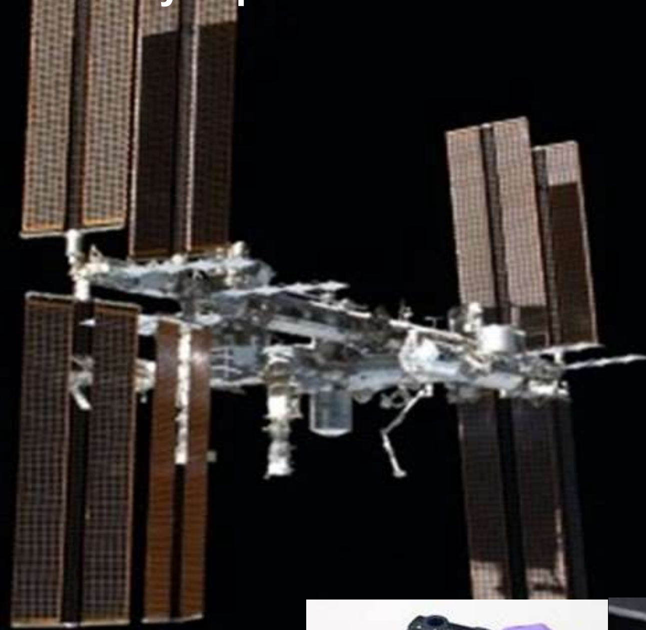
Sylvain V. Costes, PhD
GeneLab Project Manager

AAAS-2019
February 15th 2019



Omics Acquisition in Space is Now a Reality

This is truly an exciting time for cellular and molecular biology, omics and biomedicine research on ISS with these amazing additions to the suite of ISS Laboratory capabilities.



Sample Preparation Module

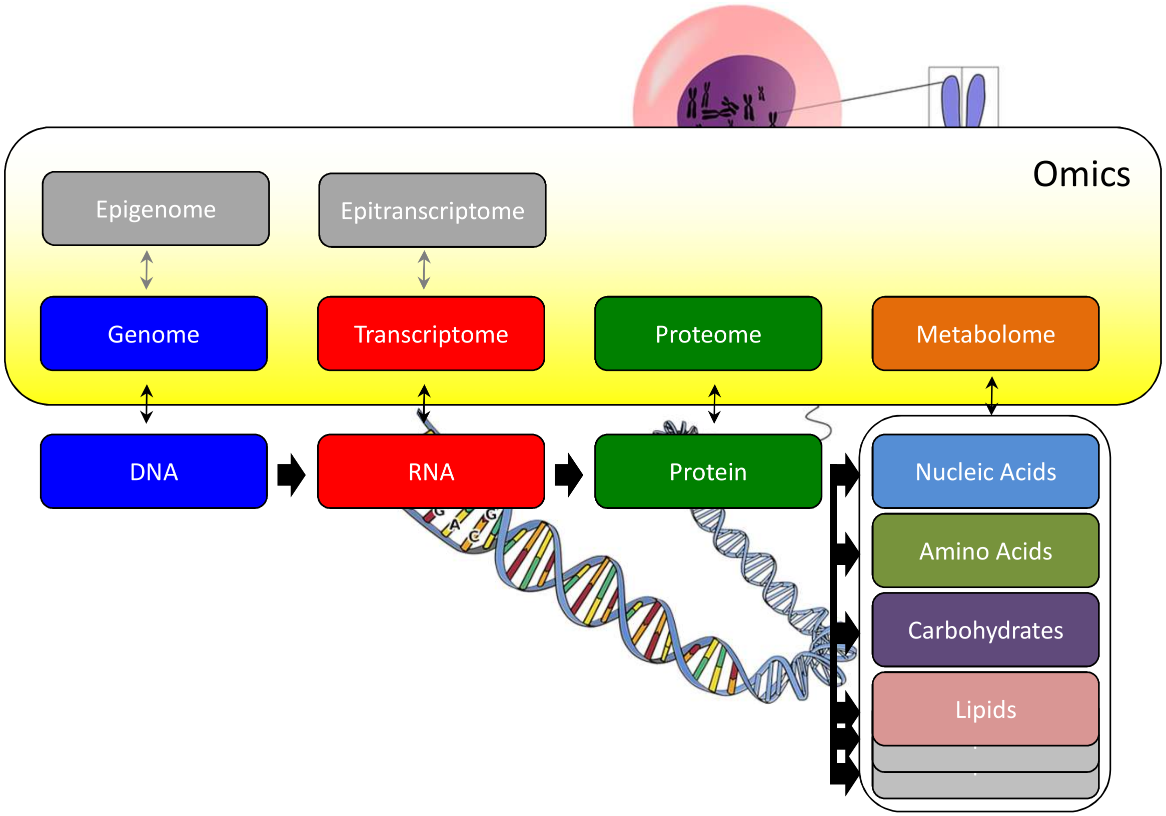
Oxford Nanopore MinION Gene Sequencer

Mini-PCR

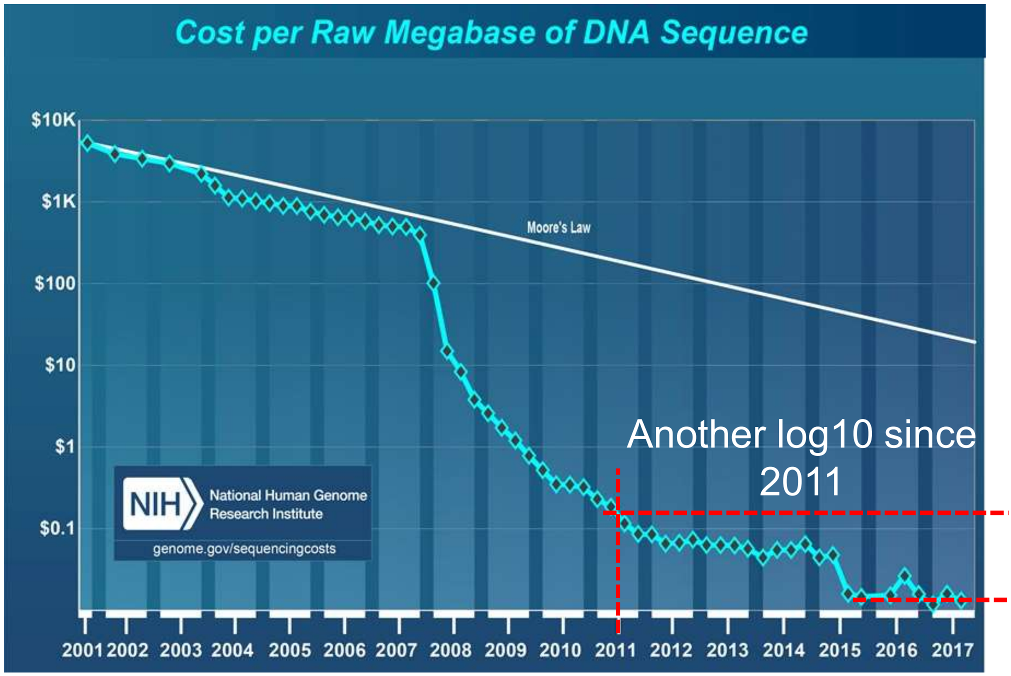
Cepheid Smart Cycler qRT-PCR

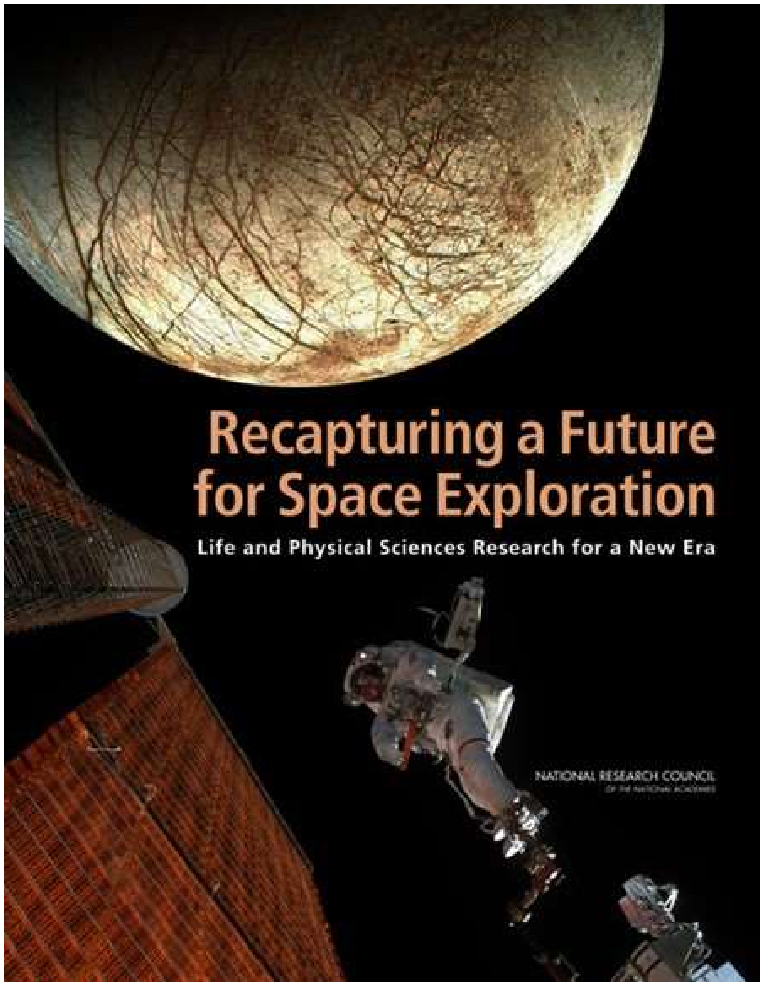
Reaction tube containing lyophilized chemical assay bead (proprietary)

What is Omics?



2011 NRC Decadal Survey and the Sequencing Paradigm Shift



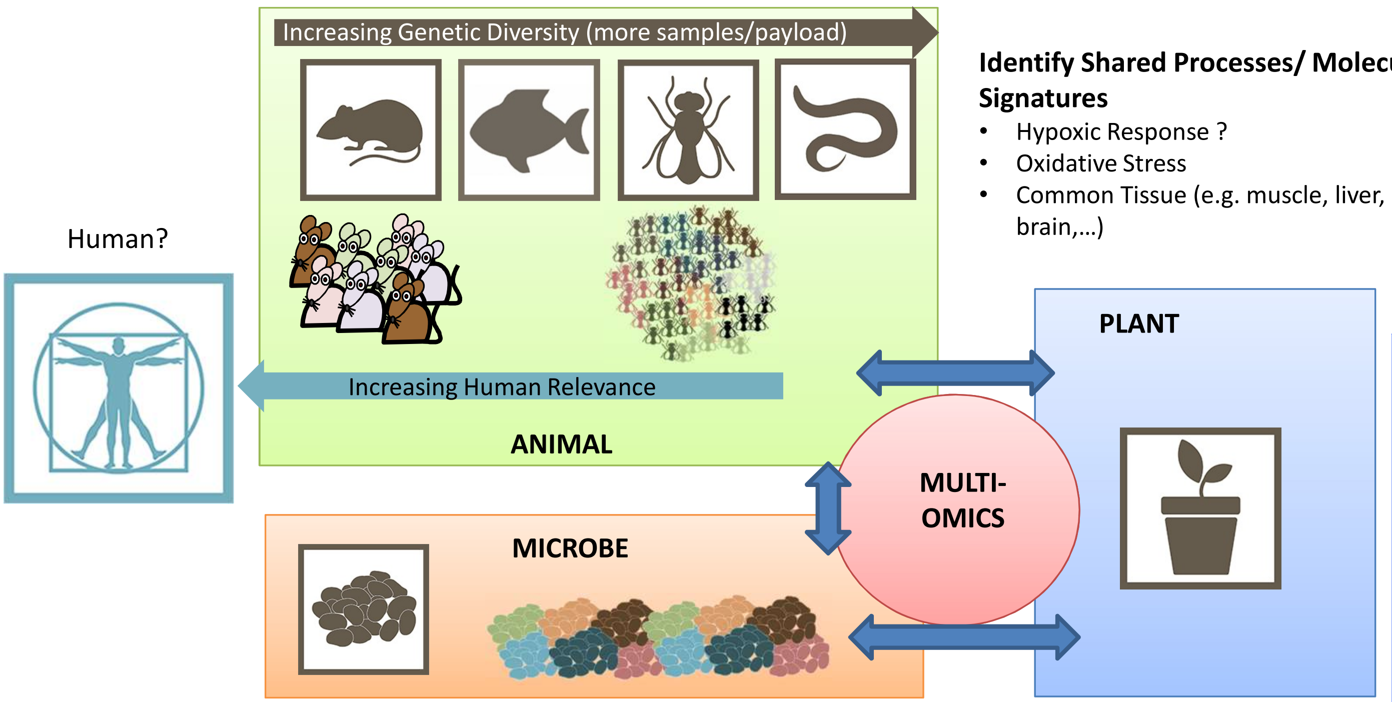


*"…**genomics, transcriptomics, proteomics, and metabolomics** offer an immense opportunity to understand the effects of spaceflight on biological systems…"*

*"…Such techniques generate considerable amounts of **data that can be mined and analyzed** for information by multiple researchers…"*

GeneLab ecosystem: maximizing knowledge by bringing experiments together as a system

- **Sequencing on ISS is still limited in the amount of data generated**
  - Most of the work needs to happen on earth
- **Measurements on human cannot be too invasive and limited in numbers**
  - Usage of animals



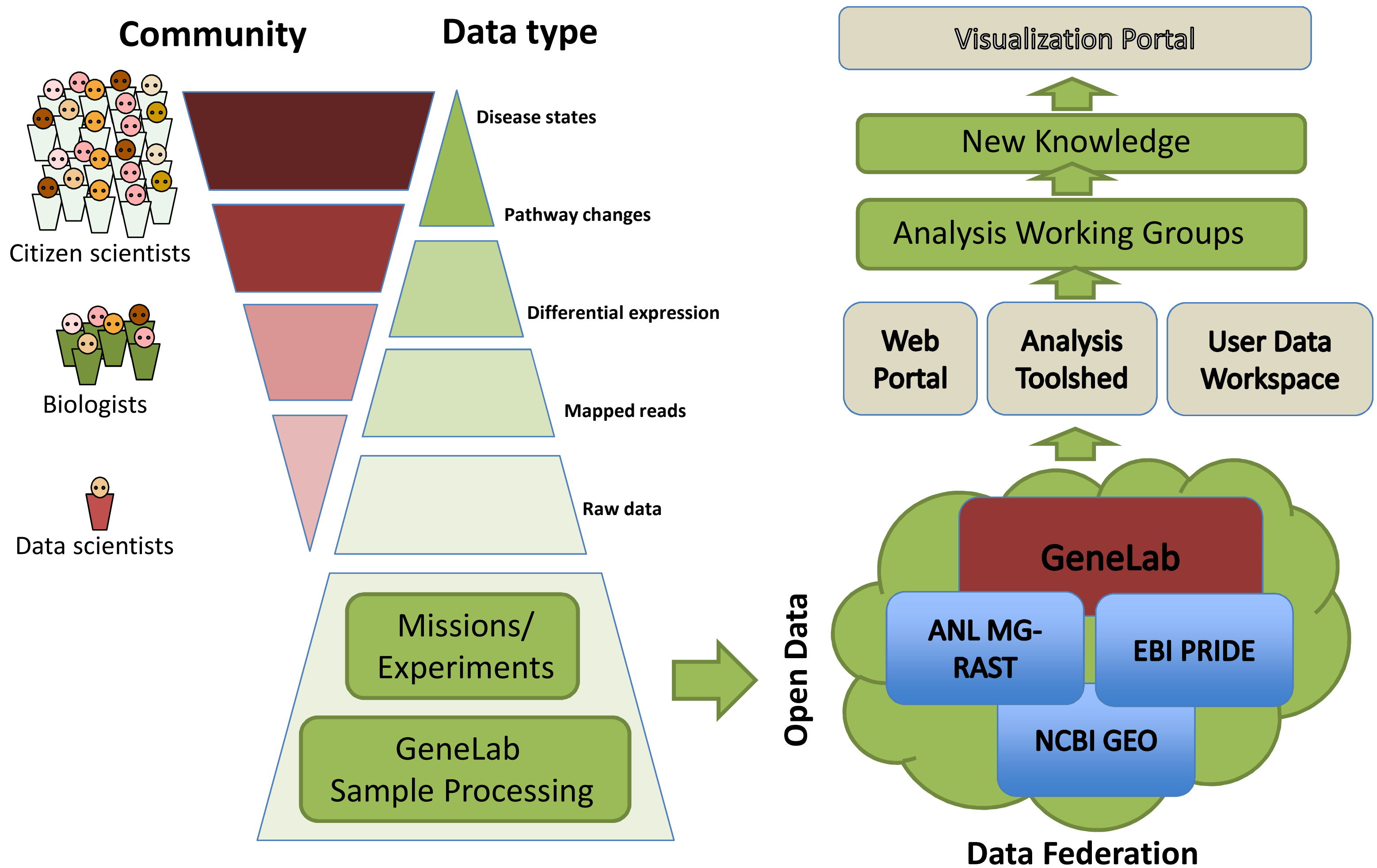
Identify Shared Processes/ Molecular Signatures

- Hypoxic Response ?
- Oxidative Stress
- Common Tissue (e.g. muscle, liver, heart, eyes brain,…)

For Spaceflight

- High "n" number – statistically significant data
- Genetically identical animals
- Low resource requirements
- Short life cycle - multiple generations
- Measure response of a whole multicellular animal
- **Flies used as a model for humans for innate immunity, circadian rhythm, oxidative stress, neurobehavior, development, genetics, GWAS, "omics" studies etc.**

GeneLab Data Democratization

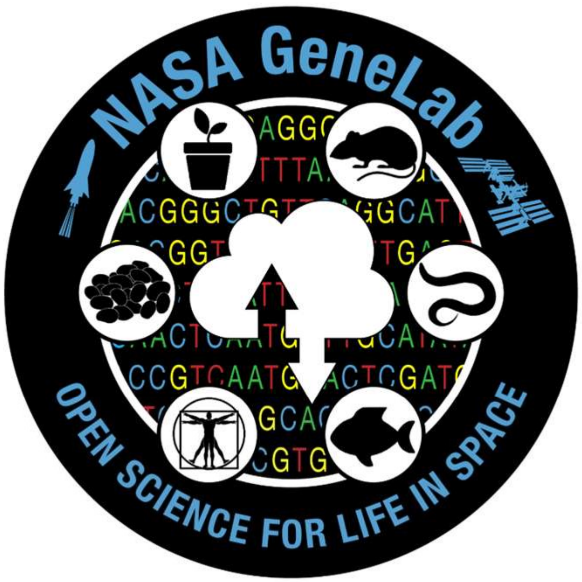


GeneLab Webpage: genelab.nasa.gov

GeneLab
Open Science for Life in Space

Home | About | Data & Tools | Research & Resources | Help

Keywords



Welcome to NASA GeneLab – the first comprehensive space-related omics database in which users can upload, download, share, store, and analyze spaceflight and corresponding model organism data.

Data Repository
Search and upload spaceflight datasets

Analyze Data
Perform large-scale analysis of biological omics data

Environmental Data
Radiation data collected during experiments conducted in space

Collaborative Workspace
Share, organize and store files

Submit Data
Have space-relevant data to submit to GeneLab?

Tutorials
New to GeneLab?

WATCH: NASA's new GeneLab video - Access and analyze unique genomics data from spaceflight

GeneLab Data Repository

Home GLDS Data Repository Environmental Data Tools Submit Data Tutorials Help

Search Data

☐ All ☑ GeneLab ☐ NIH GEO ☐ EBI PRIDE ☐ ANL MG-RAST

Search Filters (GeneLab Only)

Project Type | Factors | Organisms | Assay Type | Clear

Page 1 of 8 (Total Studies: 178) Next >

Studies Per Page: 25

Low dose (0.4 Gy) irradiation (LDR) and hindlimb unloading (HLU) microgravity in mice (RRBS Methyl-Seq)

Organisms	Factors	Assay Types	Release Date	Description
Mus musculus	Ionizing Radiation Hindlimb unloading	DNA methylation profiling	19-Sep-2018	The purpose of the present study was to evaluate damage in brain and eye in a ground-based model for spaceflight which includes prolonged unloading and low-dose radiation. Low-dose/Low-dose-rate (LDR…

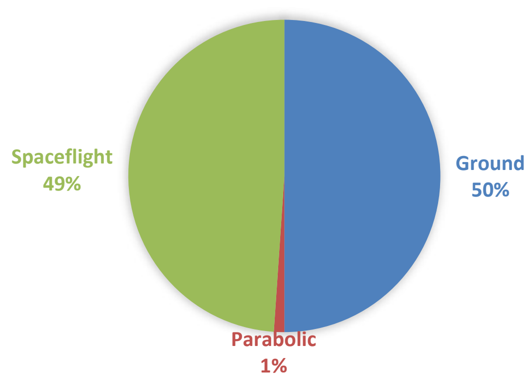
GLDS-203

Low dose (0.4 Gy) irradiation (LDR) and hindlimb unloading (HLU) microgravity in mice (RNA-Seq)

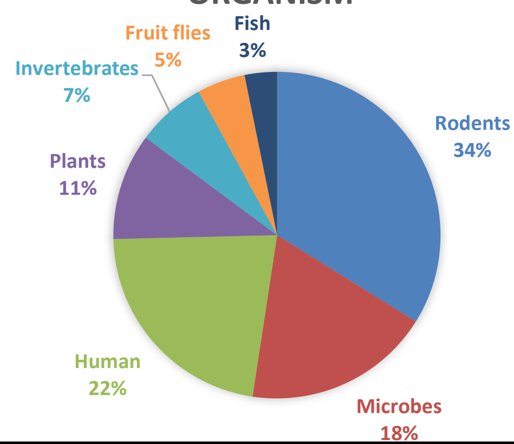
Organisms	Factors	Assay Types	Release Date	Description
Mus musculus	Ionizing Radiation Hindlimb Unloading	transcription profiling	19-Sep-2018	The purpose of the present study was to evaluate damage in brain and eye in a ground-based model for spaceflight which includes

Overview: Database content

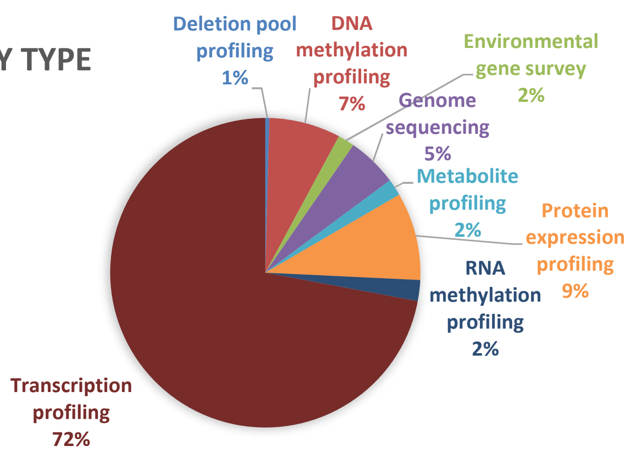
STUDY TYPE



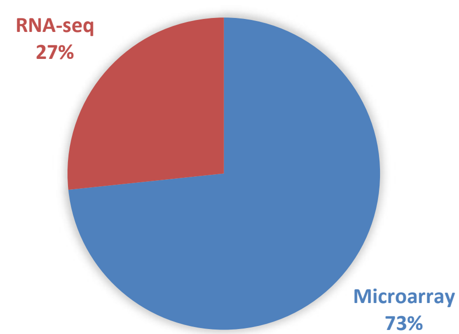
ORGANISM



ASSAY TYPE



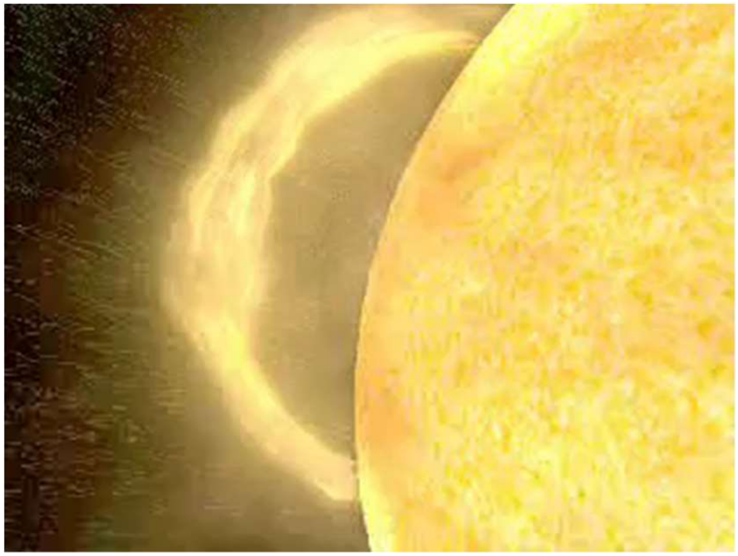
TRANSCRIPTION PROFILING

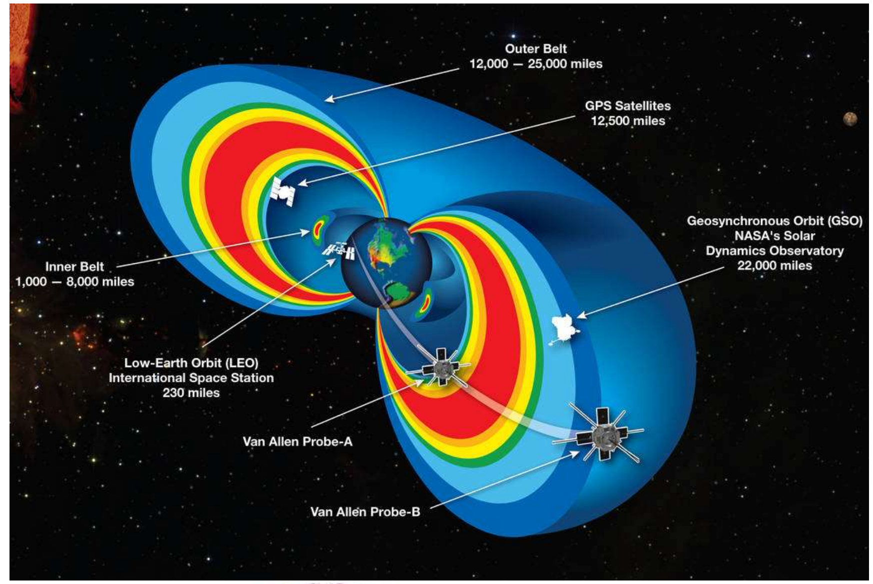


Title

Total # of studies: 186

The Radiation Factor





2½ Years, 2,600 X-Rays

Americans on average absorb the radiation equivalent of at least 7 chest X-rays each year.

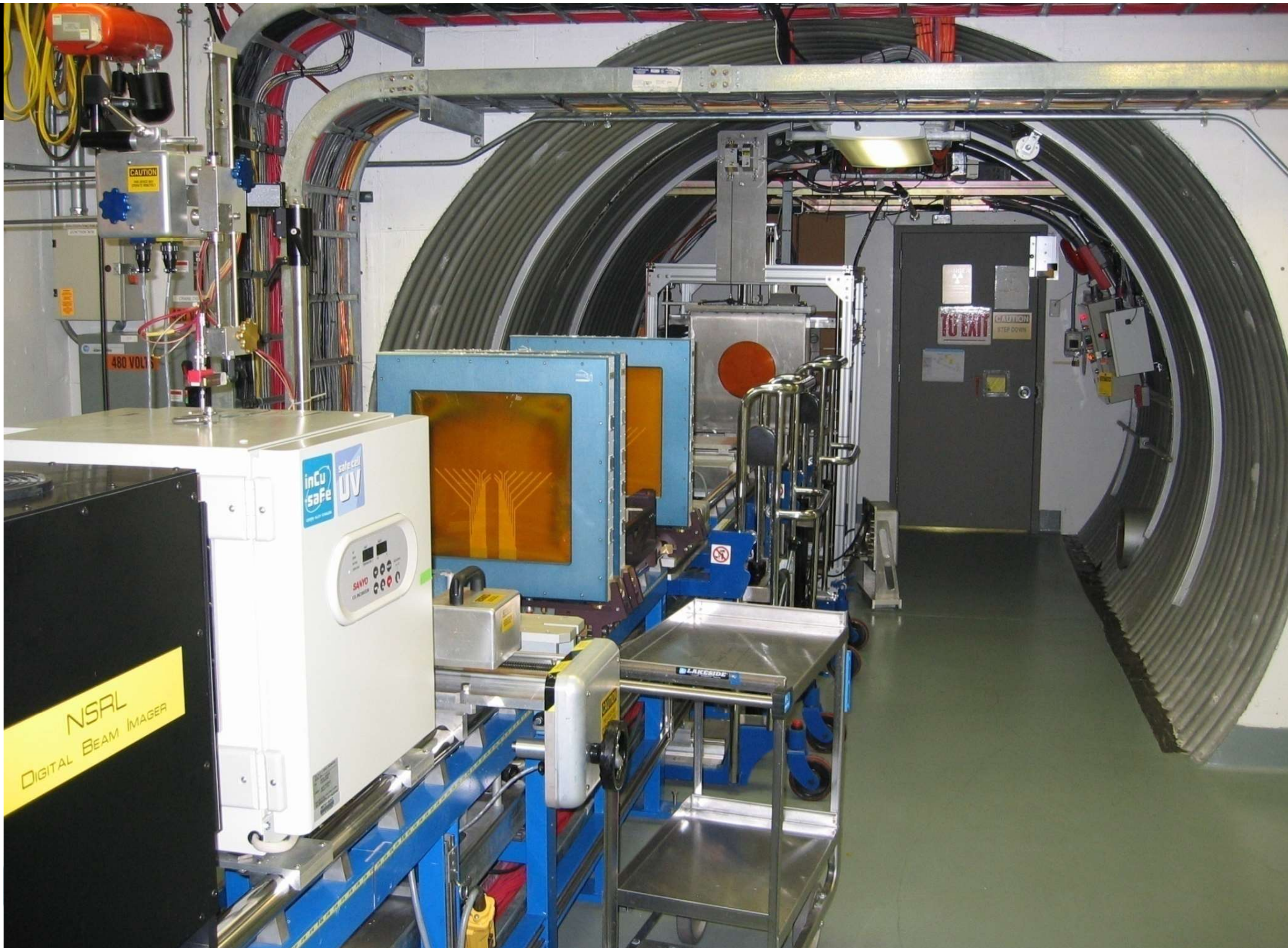
Space missions, outside of Earth's protective atmosphere and magnetic field, expose astronauts to many times more.

	MILLIREM:
CHEST X-RAY	8 to 50
AVG. YEARLY RADON DOSE	200
U.S. AVG. YEARLY DOSE	350
PET SCAN	1,000
1 YEAR IN KERALA, INDIA	1,300
U.S. NUCLEAR WORKER LIMIT PER YEAR	5,000
APOLLO 14 (9 DAYS)	1,140
SHUTTLE 41-C (18 DAYS)	5,600
SKYLAB 4 (84 DAYS)	17,800
MARS MISSION TOTAL	130,000

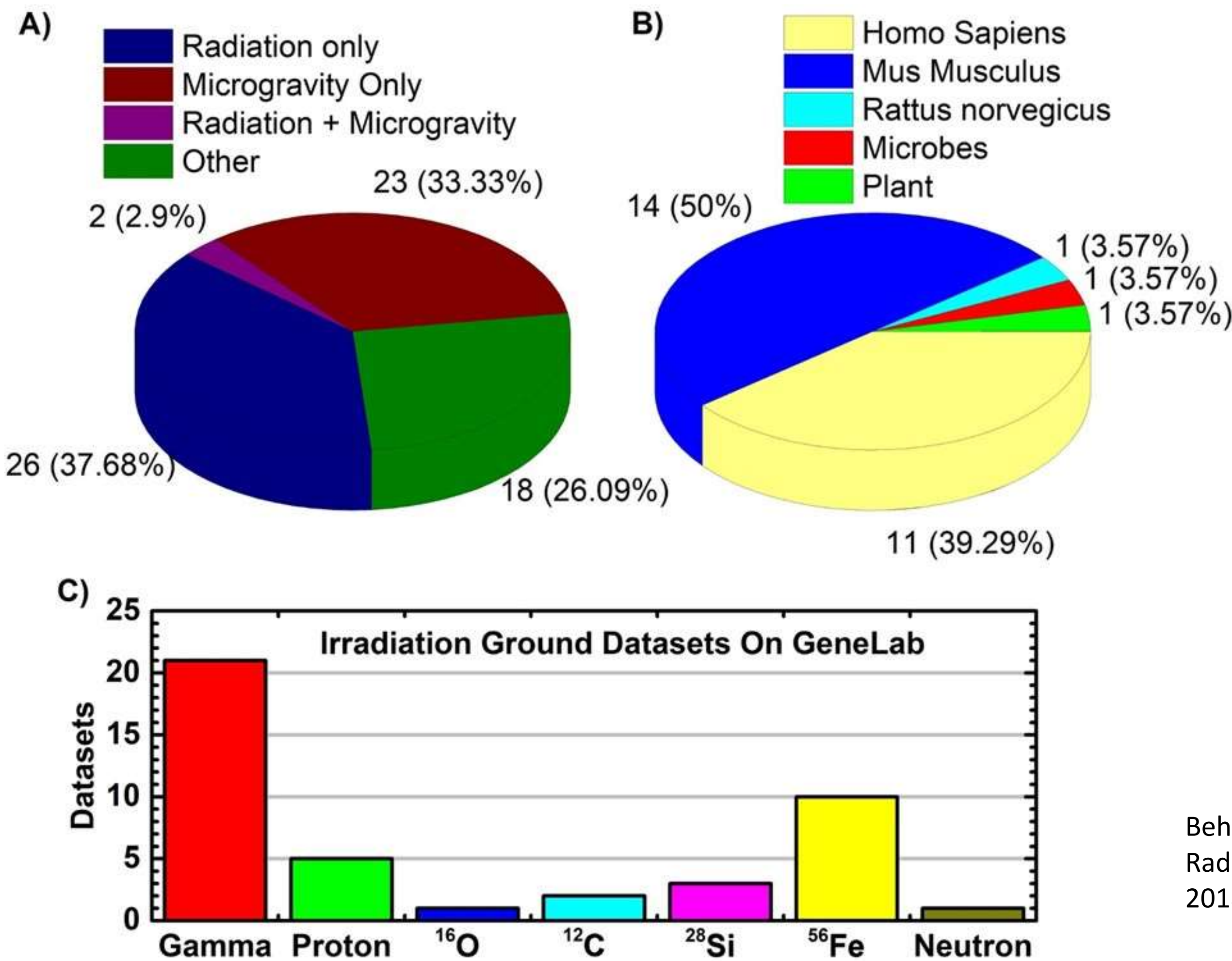
TRIP TO AND FROM MARS (1 YEAR): 80,000 — ON MARS (1.5 YEARS): 30,000 — FROM SOLAR FLARE: 20,000

Source: Brookhaven National Laboratory, U.S. Department of Energy

NASA


NSRL
DIGITAL BEAM IMAGER
480 VOLTS
TO EXIT
CAUTION
STEP DOWN
inCu saFe
safe cell UV
SANYO
LAKESIDE

69 Ground Data Sets: Radiation and simulated microgravity



Beheshti et al.,
Radiation Research
2018

GeneLab Environmental Data

Home GLDS Data Repository Environmental Data Tools Submit Data Tutorials Help

Search Data

All GeneLab NIH GEO EBI PRIDE ANL MG-RAST

Search Filters (GeneLab Only)

Project Type | Factors | Organisms | Assay Type | Clear

Environmental Data for Spaceflight Experiments

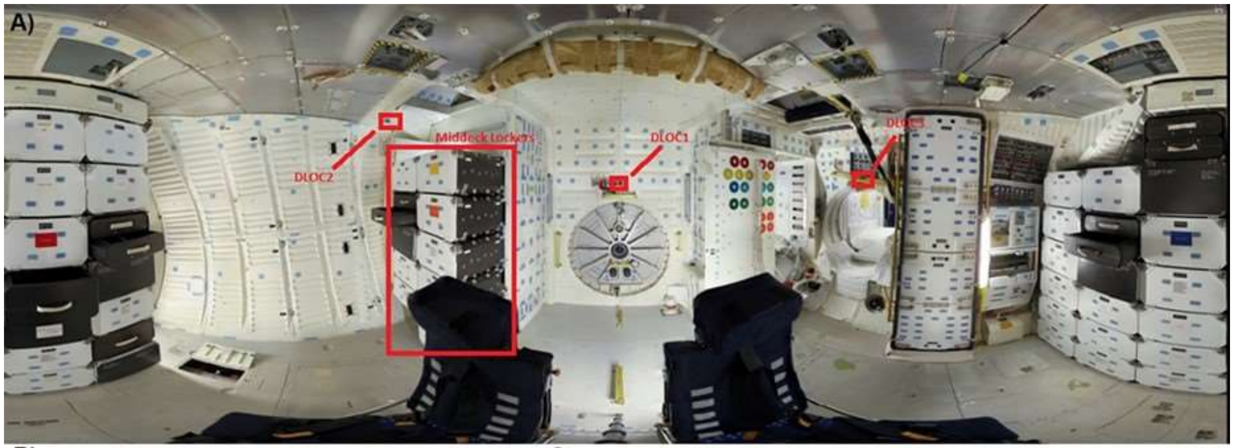
Any and all data regarding the conditions under which an experiment is conducted may have bearing on how the data produced during the experiment are interpreted; these conditions, explicitly documented or not, are a part of the experiment design. Therefore, GeneLab is taking actions, where possible and policies and available resources permit, to collect and publish data on these conditions. We have grouped these conditions into the areas listed below.

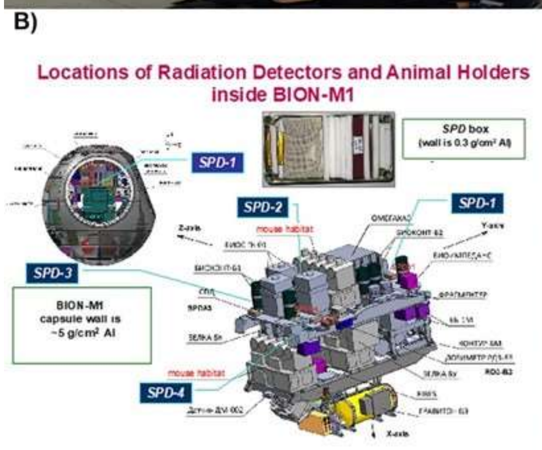
Space Radiation Dosimetry

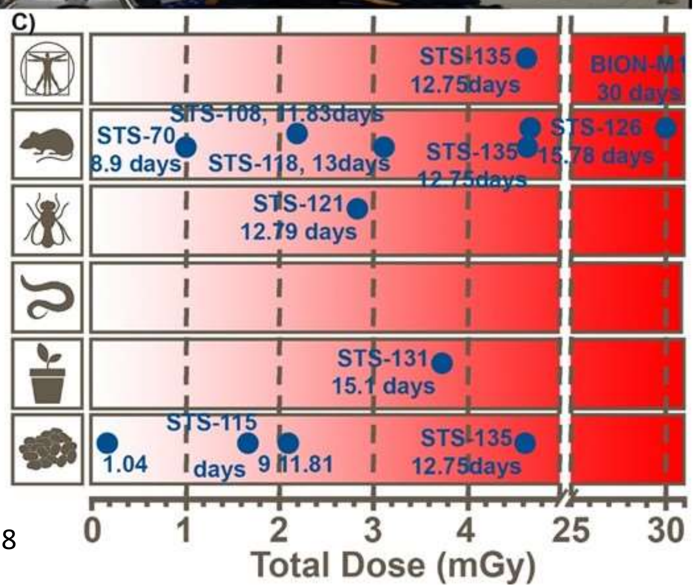
Dosimetry measuring techniques vary depending on the particular experiment environment. Through 2018, most flight experiments have not employed "dedicated" dosimeters (i.e. dosimeters integrated into experiment platform housing). Therefore, doses to which study samples are exposed frequently must be interpolated and/or extrapolated from close-by dosimeters. Two qualities of radiation were considered: low-LET (photons and electrons) and high-LET (charged nuclei). Both passive (thermoluminescent dosimeters: TLD, or plastic nuclear track detectors: PNTD) and active (solid state, tissue equivalent proportional counters) have been used. For passive dosimeters, TLD are sensitive to low-LET charged particles (< 10 keV/μm) and PNTD to high-LET (> 10 keV/μm). Active dosimeters are sensitive to a wider range in LET and, depending on the detector, can provide time resolution, LET spectra and some particle identification. By integrating the dose from the time-resolved data over the duration of the experiment, the total absorbed dose can be calculated. Depending on the configuration of dosimeters in the vicinity of the samples, absorbed dose may be reported as averaged with other detectors, or individually.

Datasets in the GeneLab repository with samples flown in space have corresponding metadata which includes the exposure duration, and the average, minimum and maximum absorbed dose received, broken out into low LET and high LET charged particles (when LET resolution is available). The duration of the exposure is defined as

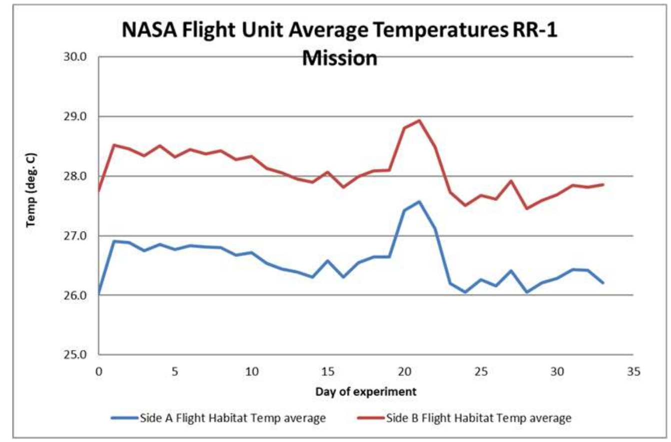
Radiation Dosimetry for STS samples (ISS to follow)

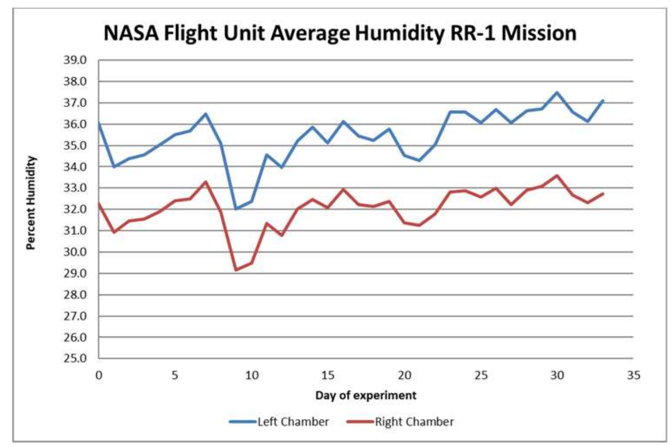






Beheshti et al., Radiation Research 2018





GeneLab Analysis Working Groups:
Letting the scientific community take the lead

AWG Members represent:

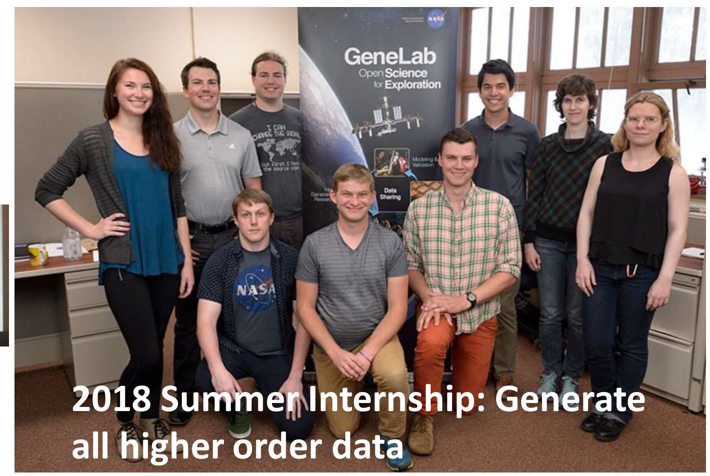
- 48 US Universities
- 4 NASA Centers
- 4 Other Government-funded Organizations
- 3 Institutes or Private Industry
- 3 International Universities

Total AWG Members: **114**

AWG Members Per Group:	
Animal	47
Multi-Omics/System Biology	33
Plants	24
Microbes	21

**Some members are in multiple groups*

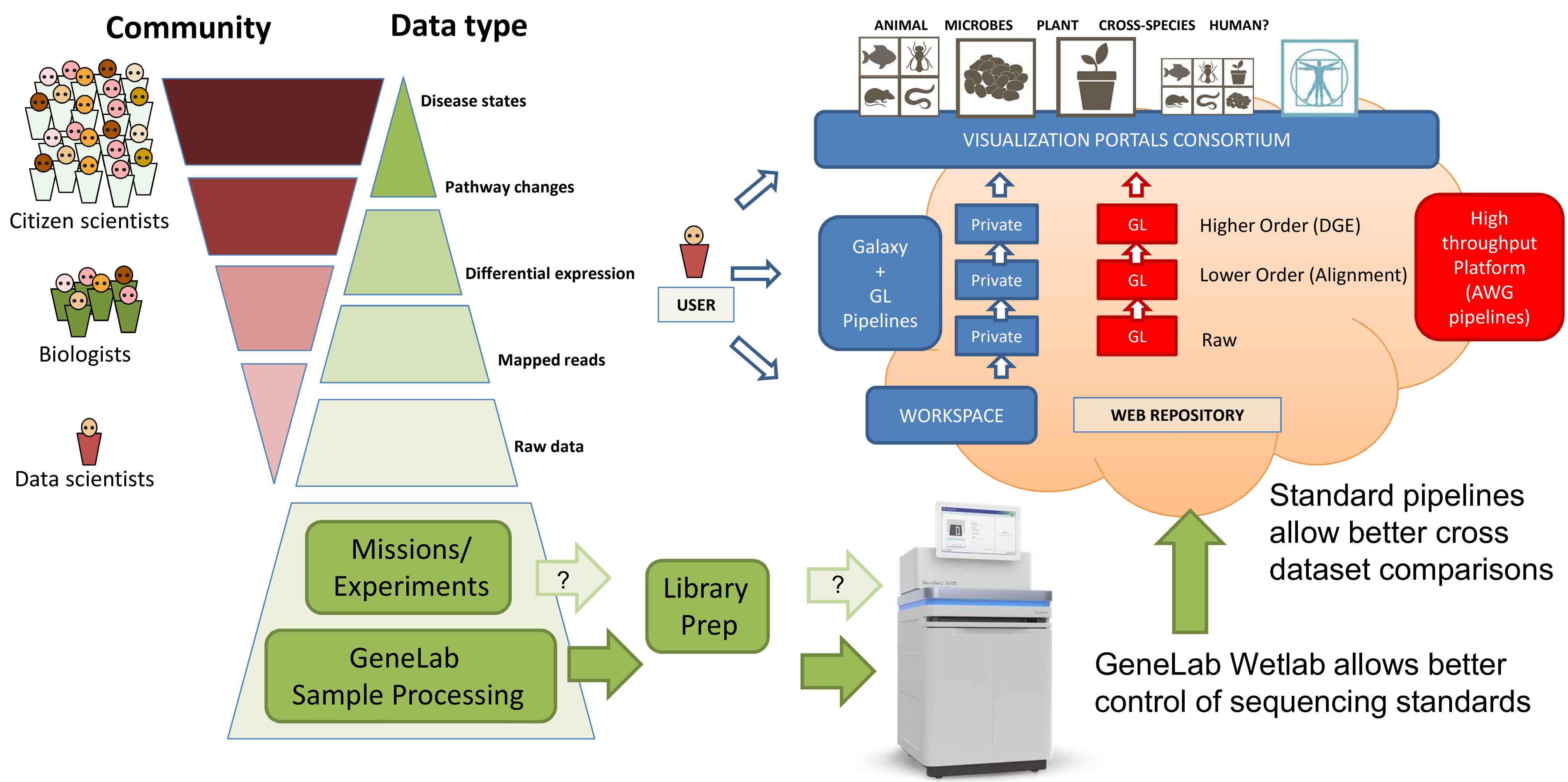
Annual Workshop (April 2018)



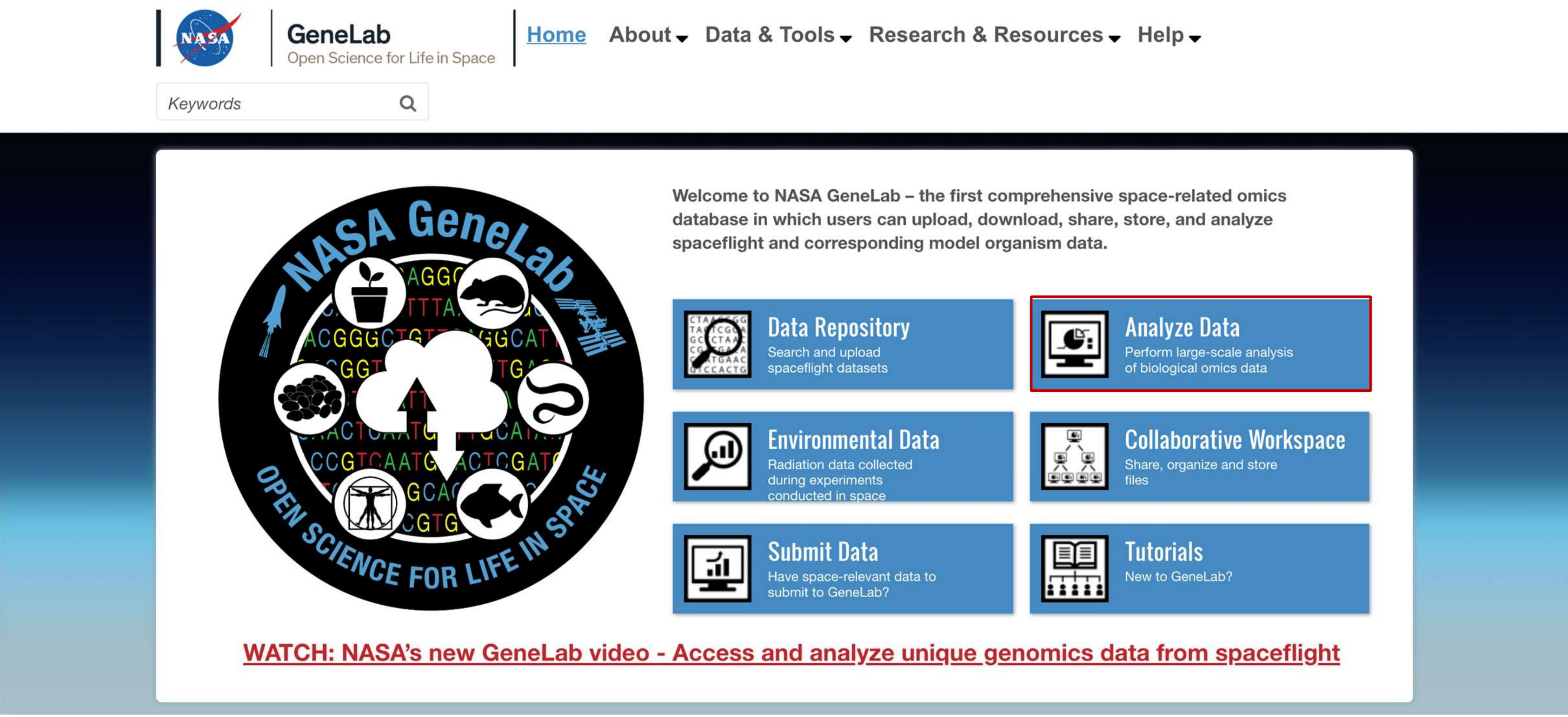
2018 Summer Internship: Generate all higher order data

- **Monthly meetings + "Homework"**
- **Deliverables:**
  - Consensus pipelines for primary analysis of data (Microarray, RNASeq, Bisulfite sequencing, Proteomics, 16S metagenomics, Whole genome metagenomics)
  - Recommendations for visualization of data

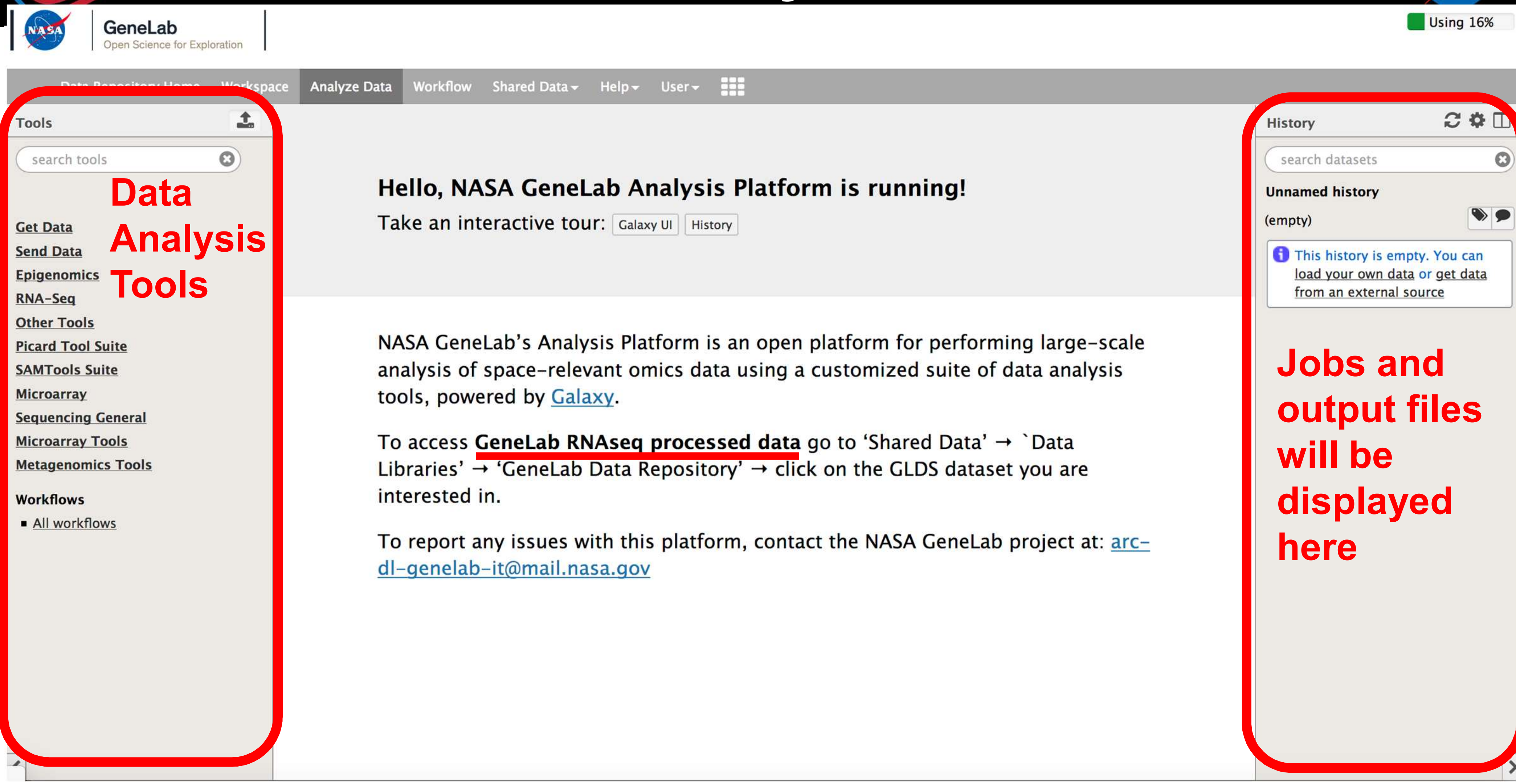
Data Standardization – Sequencing Workflow



GeneLab Galaxy toolshed



GeneLab Analysis Platform

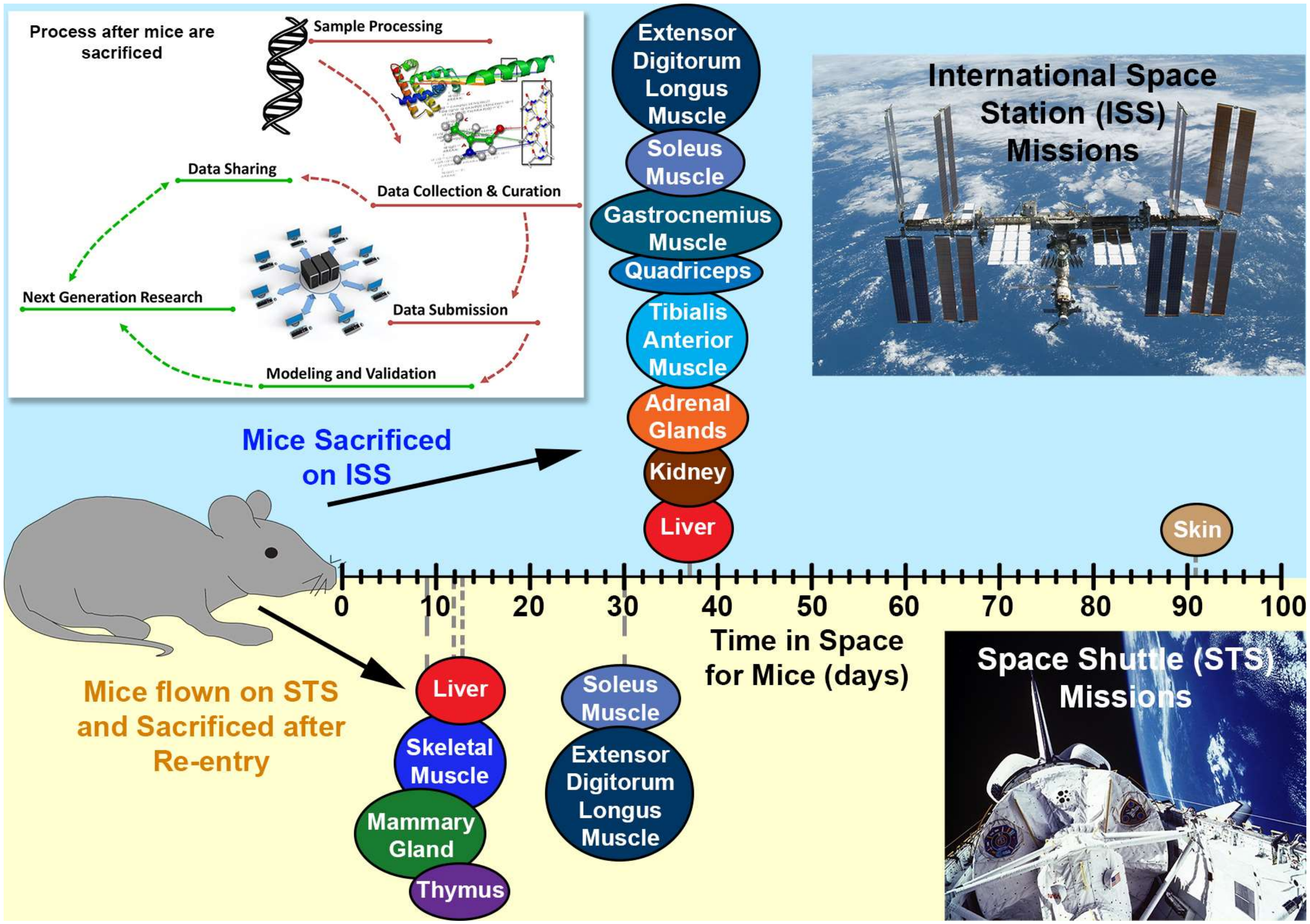


SLPSRA

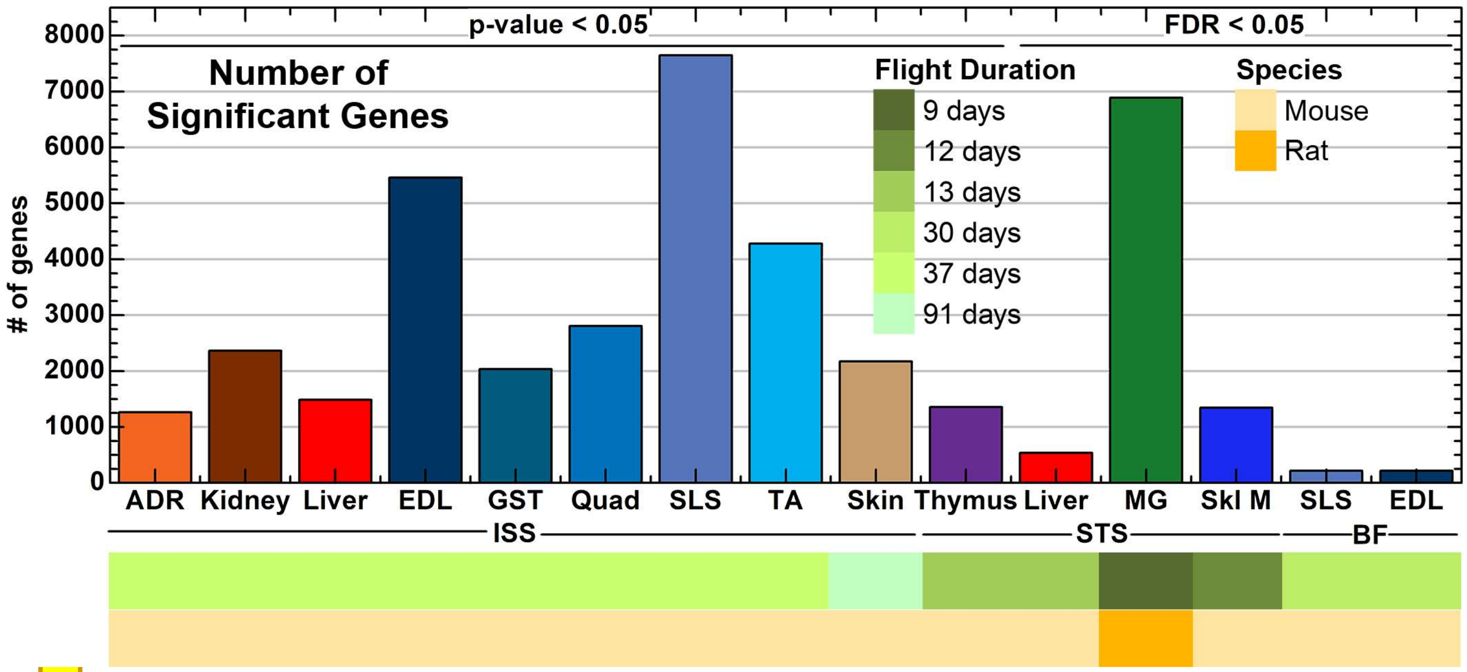
Publications using GeneLab

#	Year	Title	Journal	Authors	Status
1	2017	Validation of Methods to Assess the Immunoglobulin Gene Repertoire in Tissues Obtained from Mice on the International Space Station.	Gravit Space Res.	Rettig TA, Ward C, Pecaut MJ, Chapes SK	Published
2	2018	A microRNA signature and TGF-β1 response were identified as the key master regulators for spaceflight response	PLoS One	Beheshti A, Ray S, Fogle H, Berrios D, Costes SV	Published
3	2018	NASA GeneLab Project: Bridging Space Radiation Omics with Ground Studies Project: Bridging Space Radiation Omics with Ground Studies	Radiation Research	Beheshti A, Miller J, Kidane Y, Berrios D, Gebre SG, Costes SV	Published
4	2018	Global transcriptomic analysis suggests carbon dioxide as an environmental stressor in spaceflight: A GeneLab case study	Scientific Reports	Beheshti A, Cekanaviciute E, Smith DJ, Costes SV	Published
5	2018	Meta-analysis of data from spaceflight transcriptome experiments does not support the idea of a common bacterial "spaceflight response"	Scientific Reports	Michael D. Morrison & Wayne L. Nicholson	Published
6	2018	GeneLab: Omics database for spaceflight experiments	Bioinformatics	S Ray, S Gebre, H Fogle, D Berrios, PB Tran , JM Galazka, SV Costes	Published
7	2019	Exploring the Effects of Spaceflight on Mouse Physiology using the Open Access NASA GeneLab Platform	JoVE	A Beheshti, Y Shirazi-Fard, S Choi, D Berrios, SG Gebre, JM Galazka, SV Costes	Published
8	2019	GeneLab database analyses suggest a long term impact of Space Radiation on the Cardiovascular System by the activation of FYN through Reactive Oxygen Species	International Journal of Molecular Sciences	A Beheshti, J. T. McDonald, J. Miller, P. Grabham, SV Costes	Published

GeneLab Data Used to Generate Results



Number of Significant Genes from Each Dataset



Fold-Change ≥ |1.2|

Pathway/Functional Predictions:
Ingenuity Pathway Analysis (IPA)
Gene Set Enrichment Analysis (GSEA)

Beheshti, et al., PLOS One, 2018

Ground Control (GC) Experiment

KSC ISS Environmental Simulator (ISSES; CO_2, O_2, Temp, RH)

AEM vs Vivarium Control

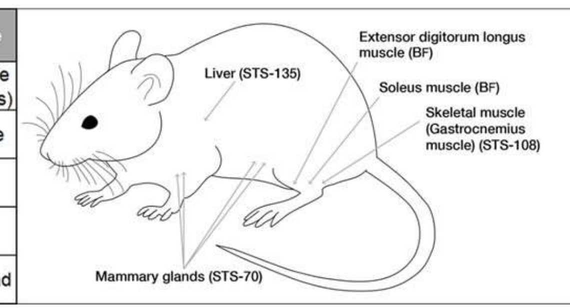
A) Cage Types

Animal Enclosure Module (AEM)

Sample vivarium cage

B)

GeneLab Study	Mission	Species	CO_2 (ppm)	Duration (days)	Tissue Type
GLDS-21	STS-108	mouse	~3000	11.8	skeletal muscle (gastrocnemius)
GLDS-111	BF	mouse	~600	30	soleus muscle
GLDS-111	BF	mouse	~600	30	extensor digitorum
GLDS-25	STS-135	mouse	~3000	13	liver
GLDS-63	STS-70	rat	~3000 (est)	9	mammary gland

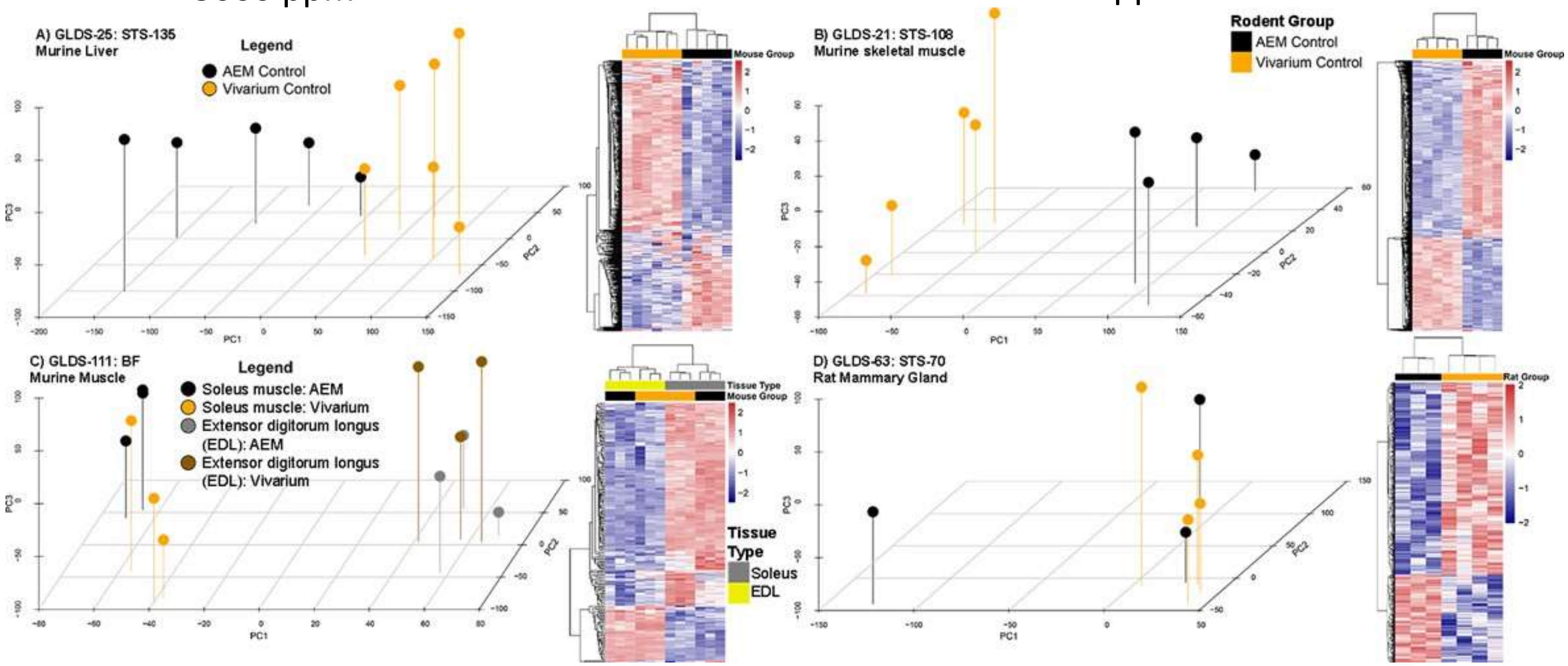


Beheshti, et al., Scientific Reports, 2018

Carbon Dioxide as an Environmental Stressor in Spaceflight

3000 ppm

3000 ppm



600 ppm

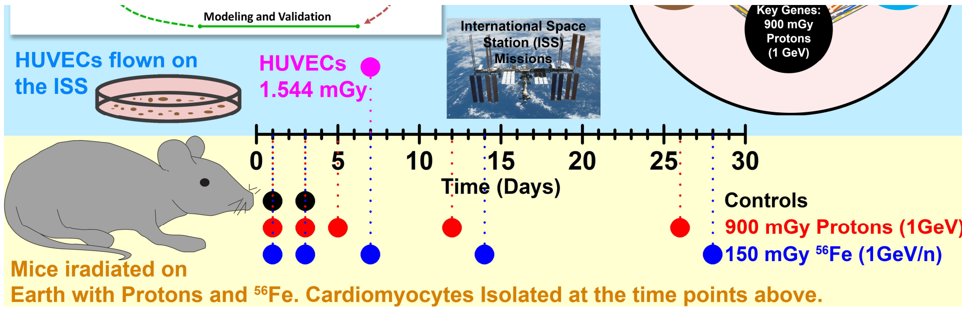
3000 ppm

AEM = Animal Enclosure Modules (now referred to as Rodent Habitats)

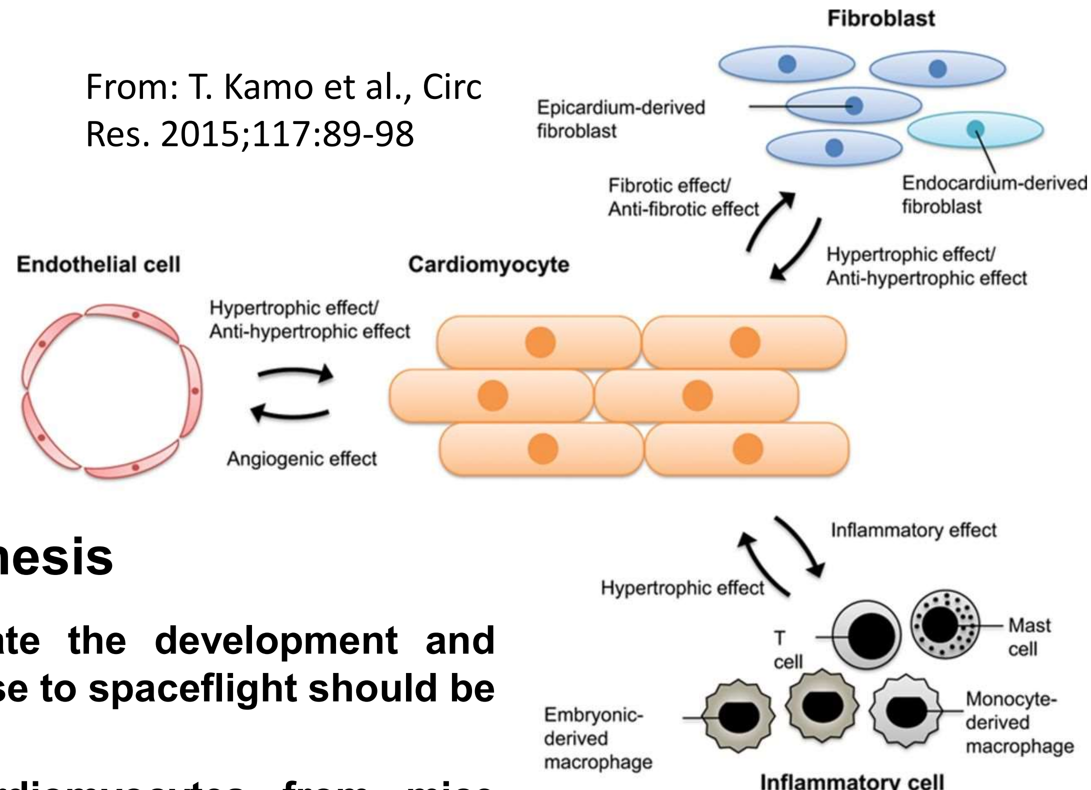
Vivarium = normal ground based rodent cages

Even though simulated levels up to 3000 ppm CO_2 are considered safe without detectable physiological impacts, hypoxic responses are detected from such exposure in mouse tissue

Space Radiation induces long term impact on the cardiovascular system by the activation of FYN through Reactive Oxygen Species



From: T. Kamo et al., Circ Res. 2015;117:89-98

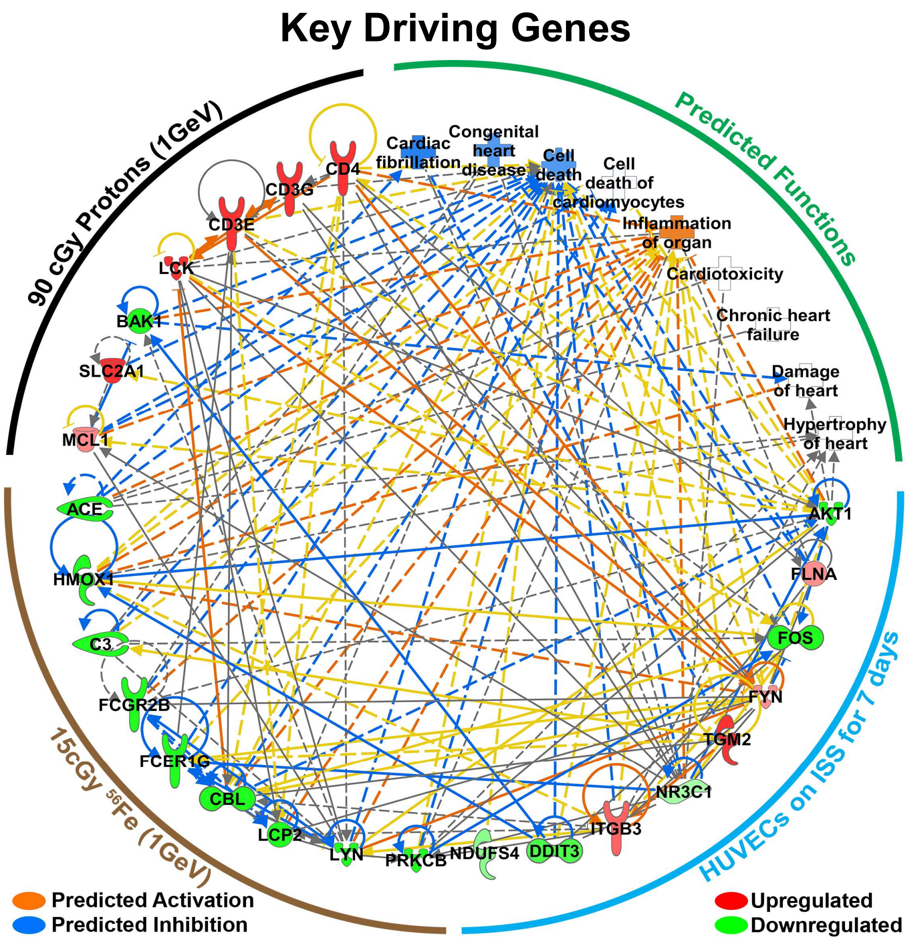


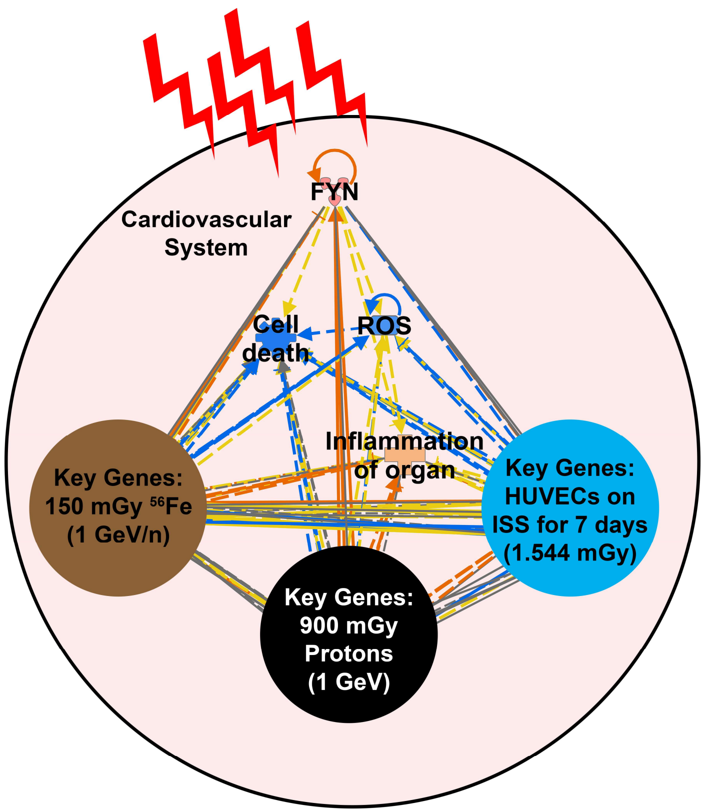
GeneLab Data Used and Hypothesis

- **Endothelial cells are known to directly regulate the development and activity of cardiomyocytes, and thus their response to spaceflight should be highly correlated with cardiomyocytes.**
- **Compare differential gene expression in cardiomyocytes from mice exposed to cosmic radiation on earth with endothelial cells flown on the ISS**
- **Use System Biology to observed common response and synergism**

Beheshti, et al. IJMS, 2019

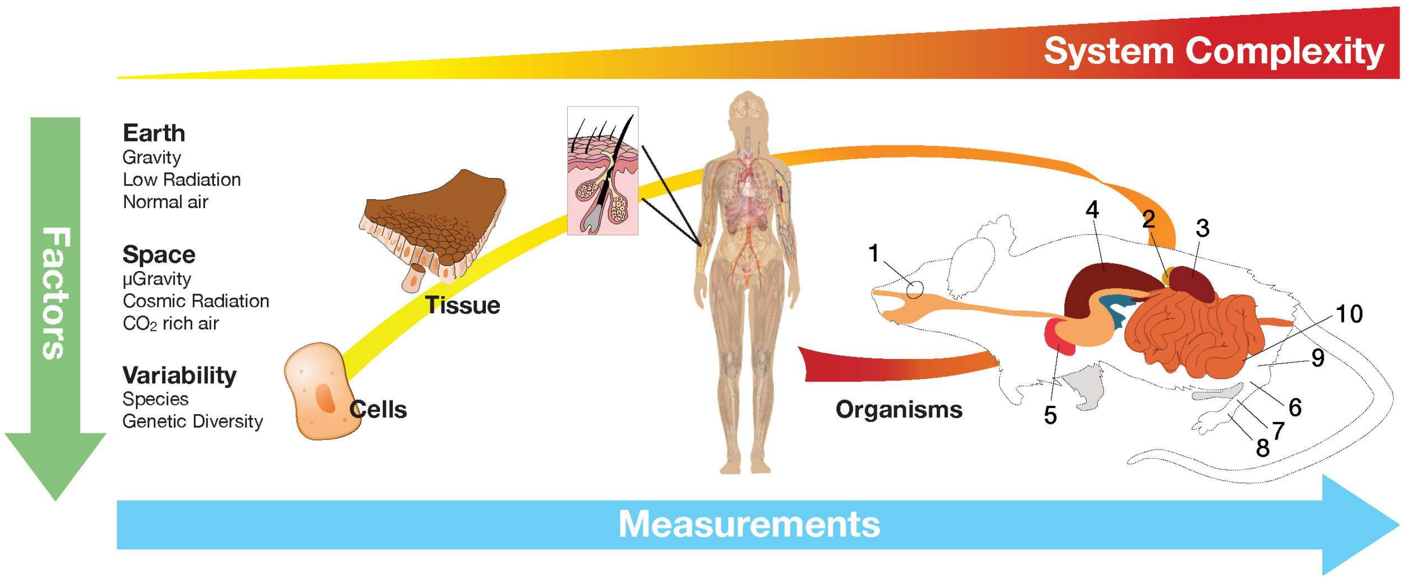
Space Radiation induces long term impact on the cardiovascular system by the activation of FYN through Reactive Oxygen Species





Beheshti, et al. IJMS, 2019

Multi-Omics Multi-Strain Multi-Species AWG Meta Analysis



Transcriptomics, Proteomics, Epigenetics

Human Cell Cultures

1. Primary T Cells
2. HUVEC cells: Human umbilical vein endothelial cell
3. HMVEC-dBL cells: Human Dermal Blood Microvascular Endothelial Cells
4. Fibroblasts

Mouse Tissues

1. Eye: Transcriptomics (RR3 and RR1)
2. Adrenal Glands: Transcriptomics, Proteomics, and Epigenetics (RR1 and RR3)
3. Kidney: Transcriptomics, Proteomics, and Epigenetics (RR1 and RR3)
4. Liver: Transcriptomics, Proteomics, and Epigenetics (RR1 and RR3)
5. Heart: Transcriptomics (RRx)
6. Soleus Muscle: Transcriptomics (RR1)
7. Extensor Digitorum Longus: Transcriptomics (RR1)
8. Tibialis Anterior: Transcriptomics (RR1)
9. Gastrocnemius: Transcriptomics (RR1) and Metabolomics (RR9)
10. Quadriceps: Transcriptomics (RR1) and Metabolomics (RR9)

Human Tissues

1. Hair follicles

Physiological

Astronaut Physiological Data

1. 1,25 Vitamin D
2. Antiox Cap
3. Cholesterol
4. LDL
5. HDL
6. IGF-1
7. IL-1
8. IL-α
9. IL-1rα
10. PGF2-α
11. Renin
12. VEGF-1
13. 8OHdG

All Tissues Network Analysis from RR1 data

Jan. 31, 2018

NASA Twins Study Investigators to Release Integrated Paper in 2018

Significant responses were found for at least five biological pathways in Scott during his time in space. These responses are important for future missions: hypoxia (likely from lack of oxygen and high CO_2 levels); mitochondrial stress and increased levels of mitochondria in the blood

AWG Members Involved


Kathleen Fisch
Brin Rosenthal

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SCHOOL OF MEDICINE





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Hossein Fazelinia
Komal Rathi
Douglas Wallace
Larry Singh

Children's Hospital of Philadelphia

Perelman School of Medicine
UNIVERSITY of PENNSYLVANIA


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J. Tyson McDonald

HAMPTON UNIVERSITY
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Afshin Beheshti


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NASA

Ames Research Center

GeneLab Team