

GeneLab: A Systems Biology Platform for Omics Analysis

National Aeronautics and
Space Administration



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

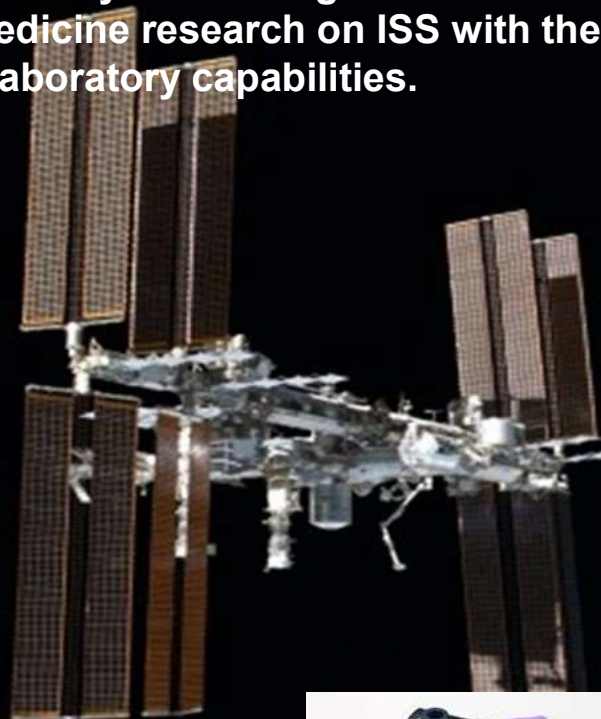
Sylvain V. Costes, PhD
GeneLab Project Manager

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



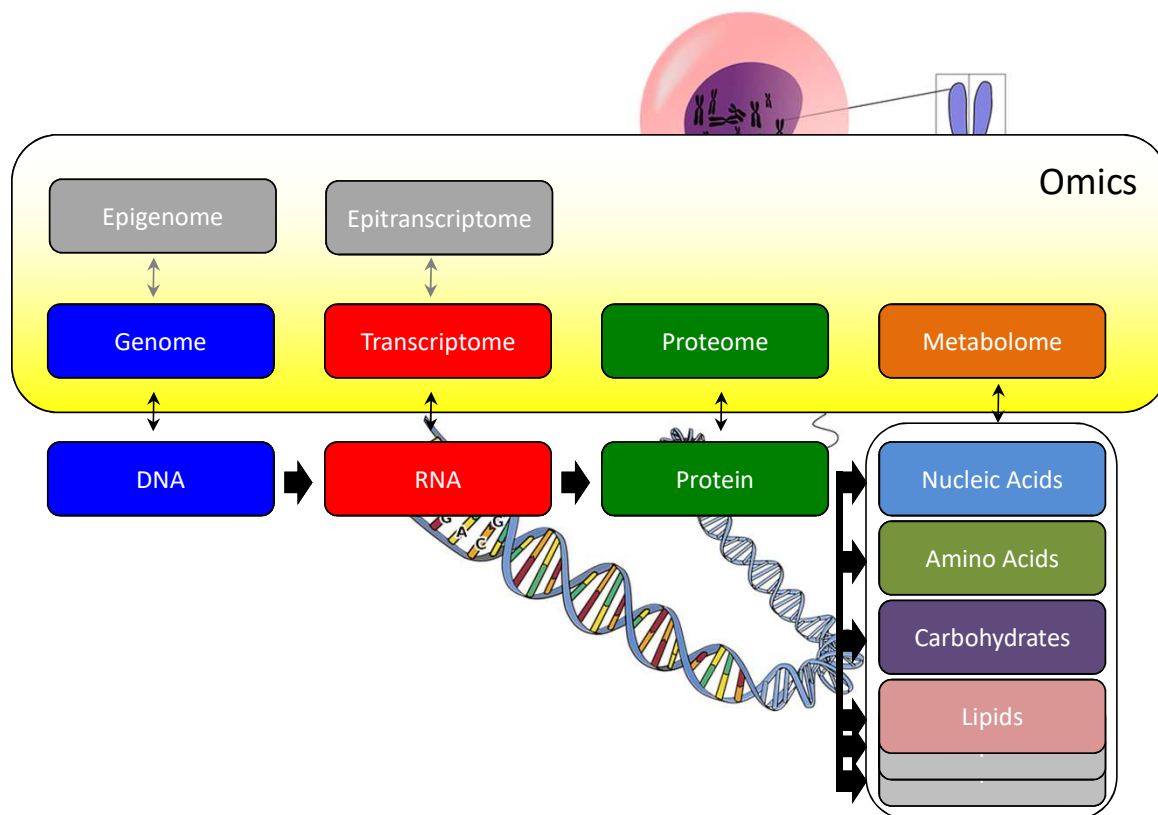
Cepheid Smart Cycler qRT-PCR

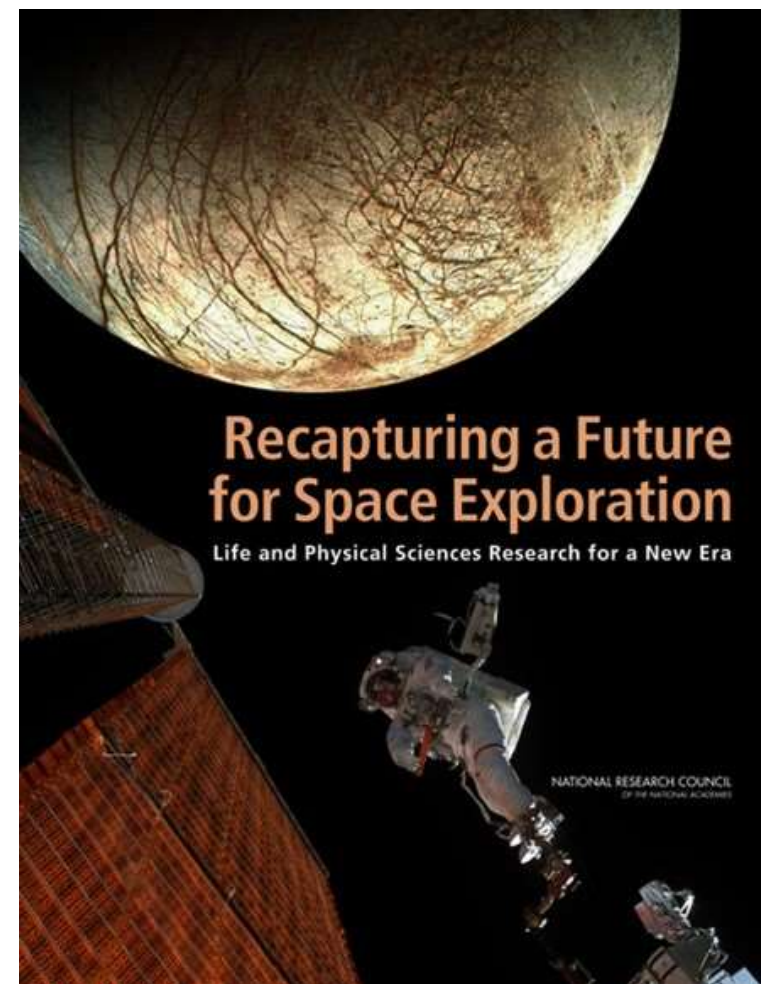
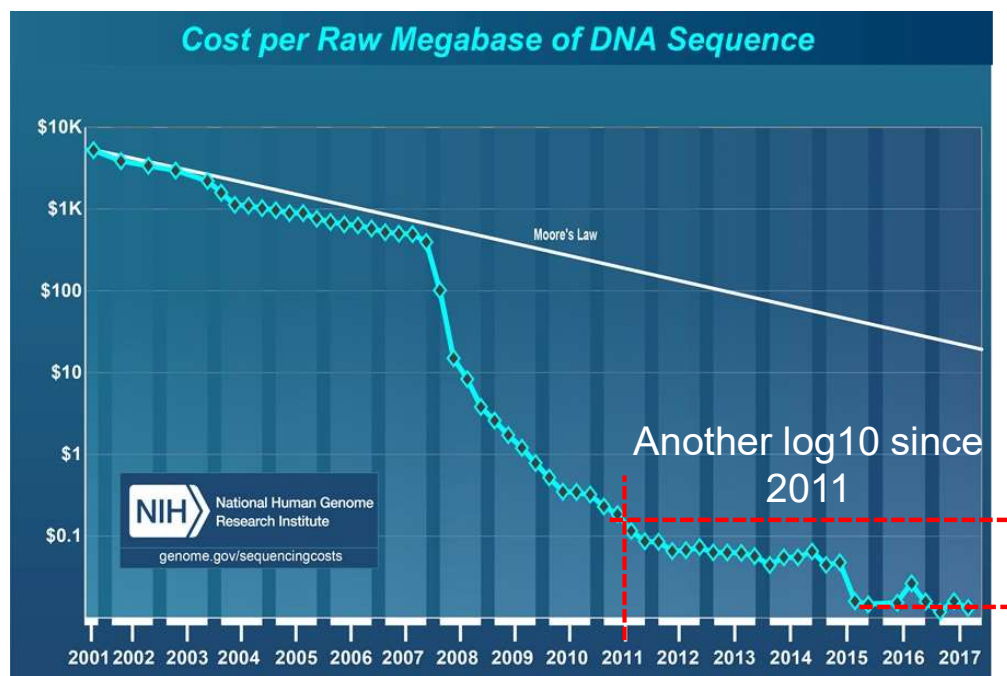


Reaction tube containing lyophilized chemical assay bead (proprietary)



Mini-PCR



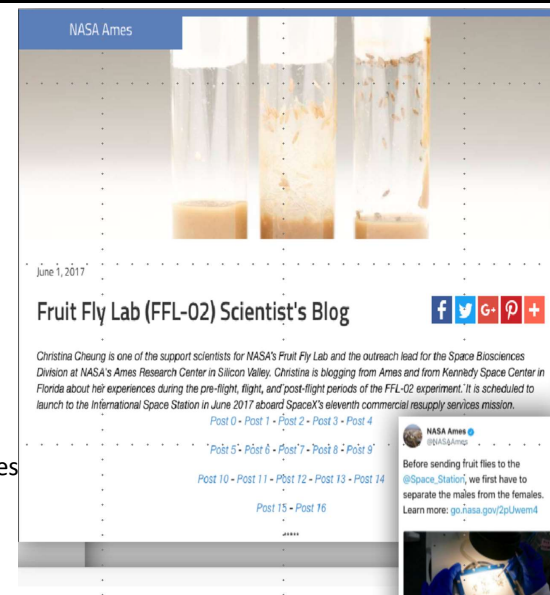
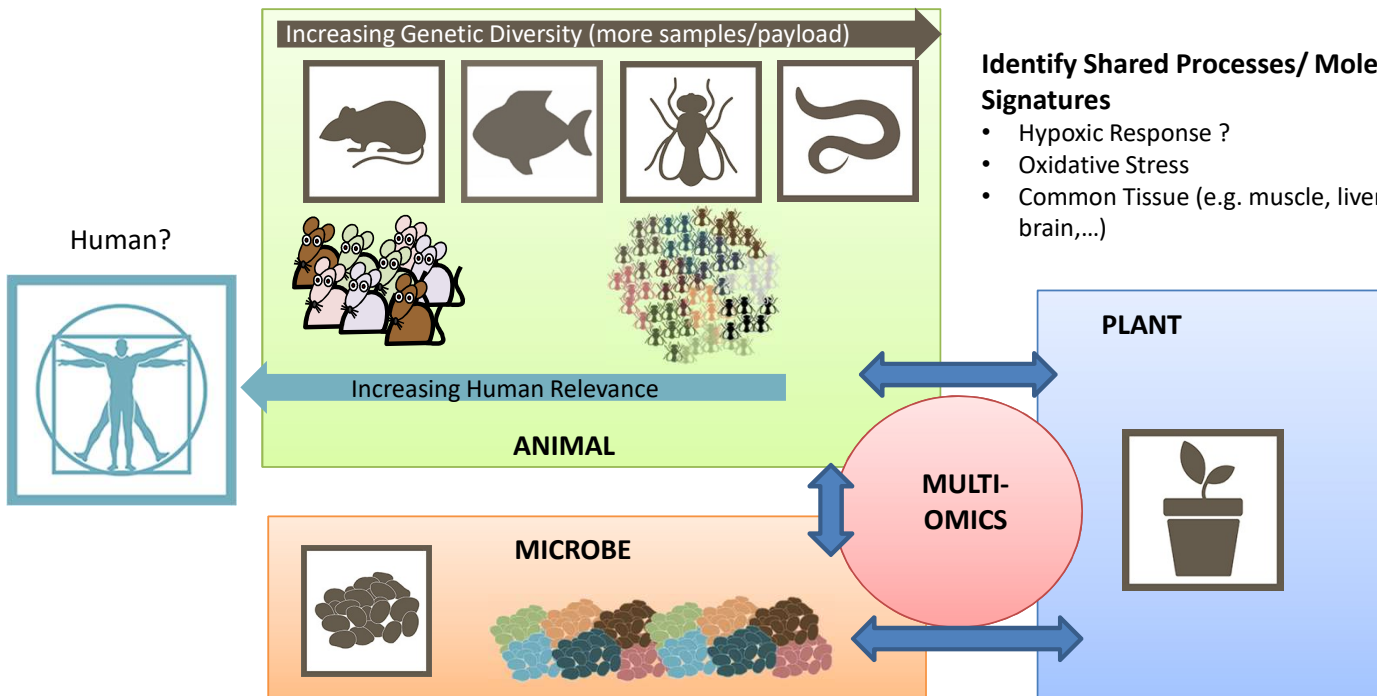


“...genomics, transcriptomics, proteomics, and metabolomics offer an immense opportunity to understand the effects of spaceflight on biological systems...”

*“...Such techniques generate considerable amounts of **data that can be mined and analyzed** for information by multiple researchers...”*

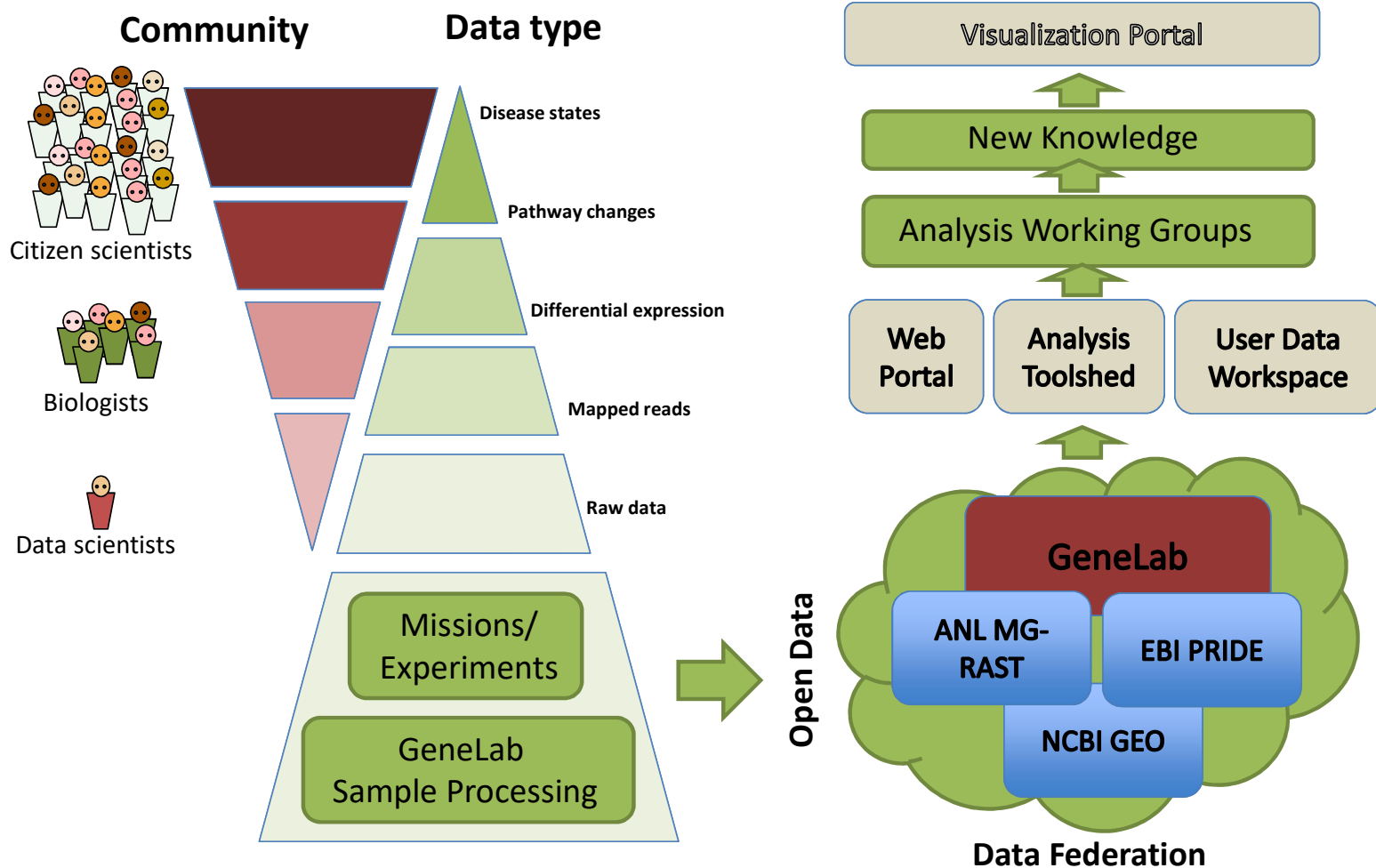
GeneLab ecosystem: maximizing knowledge by bringing experiments together as a system

- 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



- 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

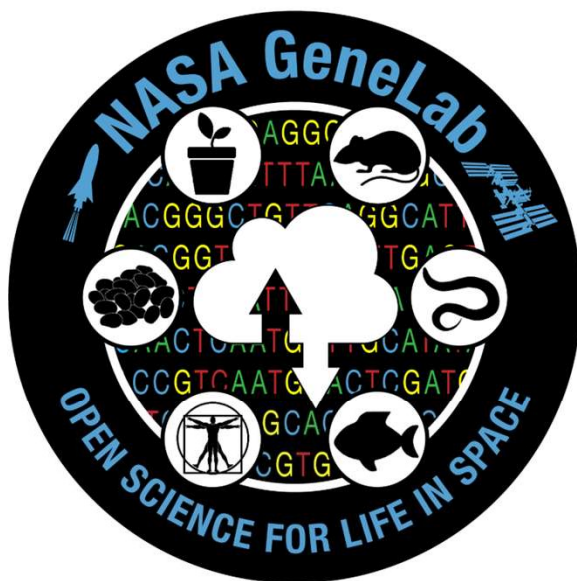


GeneLab

Open Science for Life in Space

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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

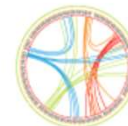
Have space-relevant data to submit to GeneLab?



Tutorials

New to GeneLab?

[WATCH: NASA's new GeneLab video - Access and analyze unique genomics data from spaceflight](#)



Search Data x

All
 GeneLab
 NIH GEO
 EBI PRIDE
 ANL MG-RAST

Search Filters (GeneLab Only)

Project Type
 Factors
 Organisms
 Assay Type

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

Studies Per Page:



GLDS-203

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

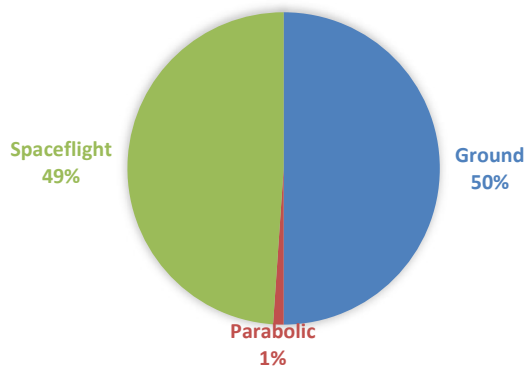
Organisms	Factors	Assay Types	Release Date	Description
Mus musculus	Ionizing Radiation Hindlimb unloading	DNA methylation profiling	19-Sep-2018	The purpose of the present study was to evaluate damage in brain and eye in a ground-based model for spaceflight which includes prolonged unloading and low-dose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



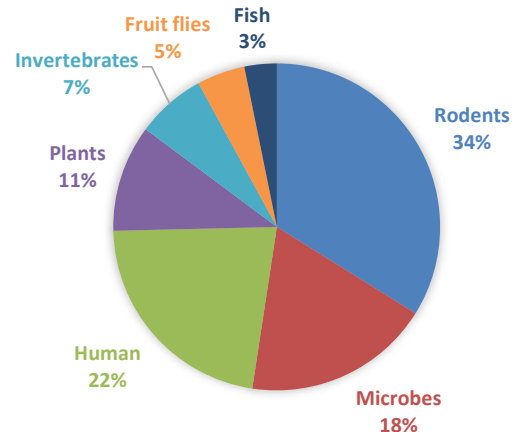
Low dose (0.4 Gy) irradiation (LDR) and hindlimb unloading (HLU) microgravity in mice (RNA-Seq)

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

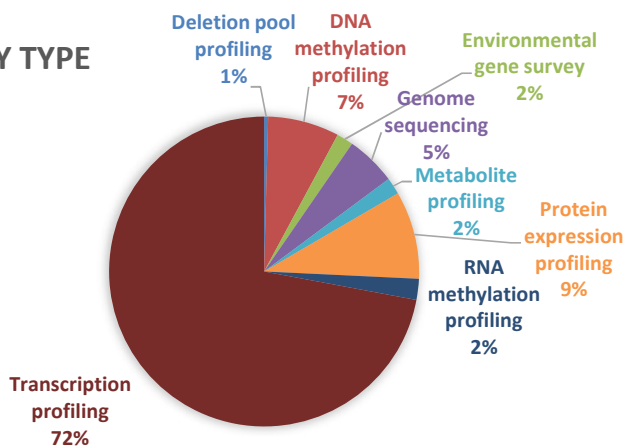
STUDY TYPE



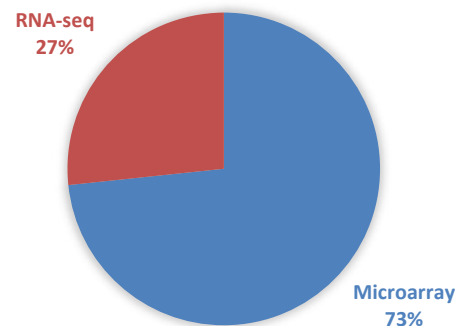
ORGANISM



ASSAY TYPE

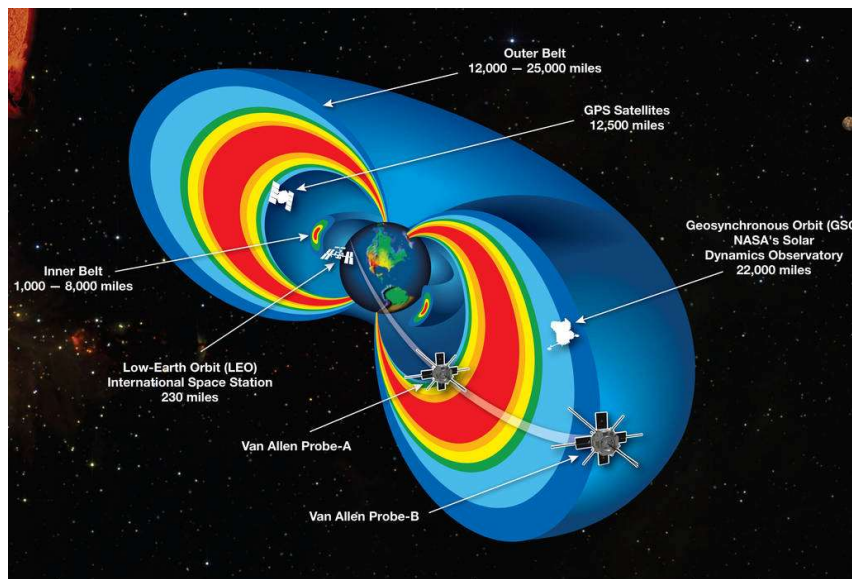


TRANSCRIPTION PROFILING



Total # of studies: 186

Title



	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

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.

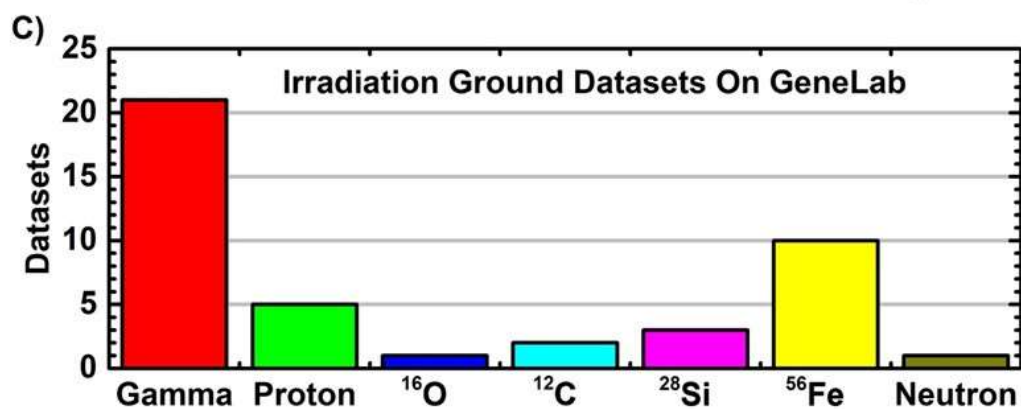
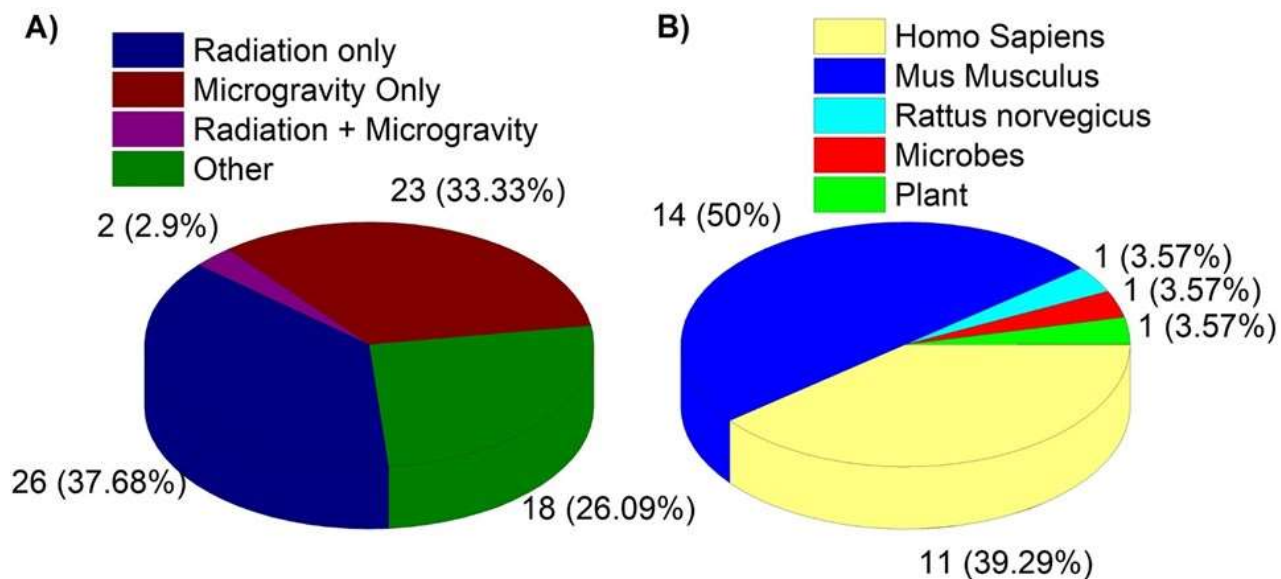


NASA

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







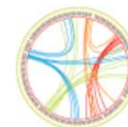
Beheshti et al.,
Radiation Research
2018



GeneLab Environmental Data



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Search Data x

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Search Filters (GeneLab Only)

Project Type Factors Organisms Assay Type

Environmental Data for Spaceflight Experiments

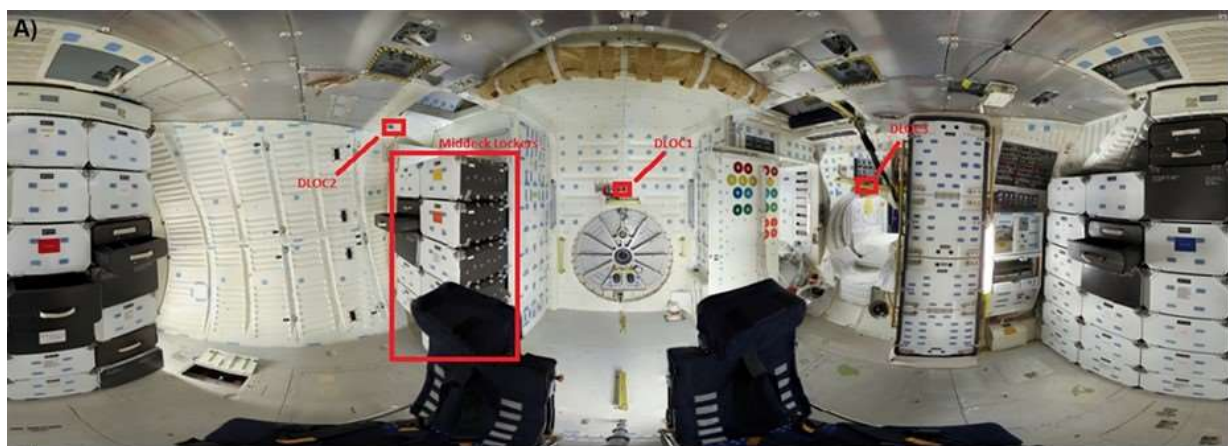
Any and all data regarding the conditions under which an experiment is conducted may have bearing on how the data produced during the experiment are interpreted; these conditions, explicitly documented or not, are a part of the experiment design. Therefore, GeneLab is taking actions, where possible and 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

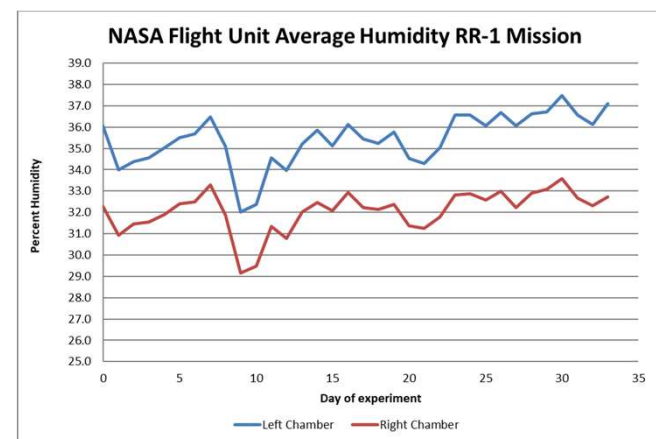
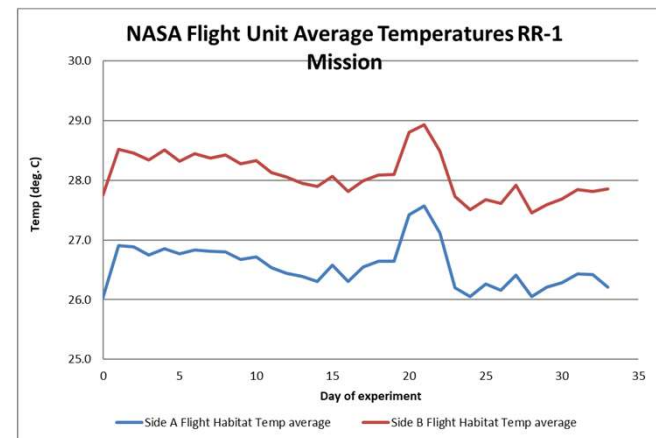
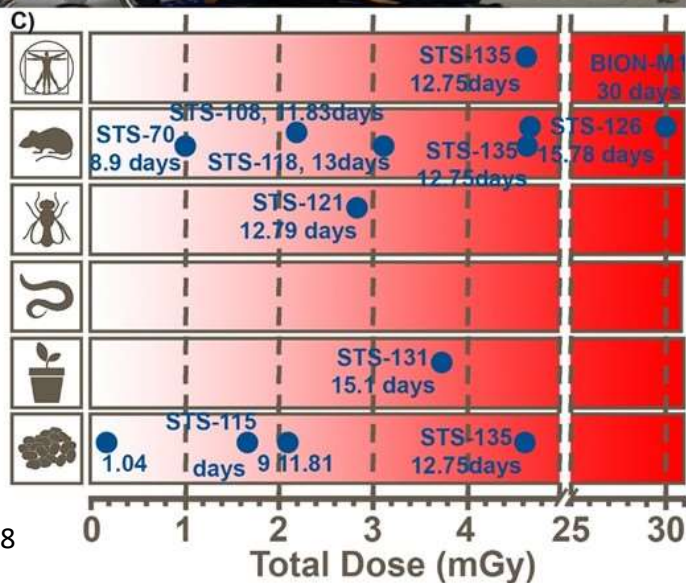
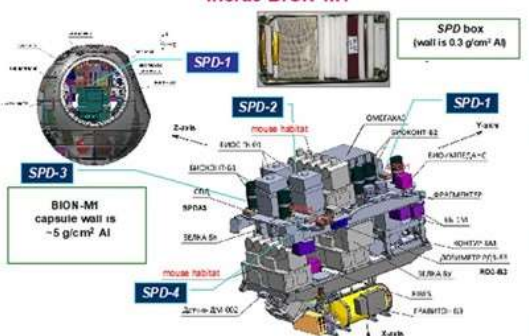
Dosimetry measuring techniques vary depending on the particular experiment environment. Through 2018, most flight experiments have not employed "dedicated" dosimeters (i.e. dosimeters integrated into experiment platform housing). Therefore, doses to which study samples are exposed frequently must be 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 ($< 10 \text{ keV}/\mu\text{m}$) and PNTD to high-LET ($> 10 \text{ keV}/\mu\text{m}$). 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)



B) Locations of Radiation Detectors and Animal Holders inside BION-M1



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*

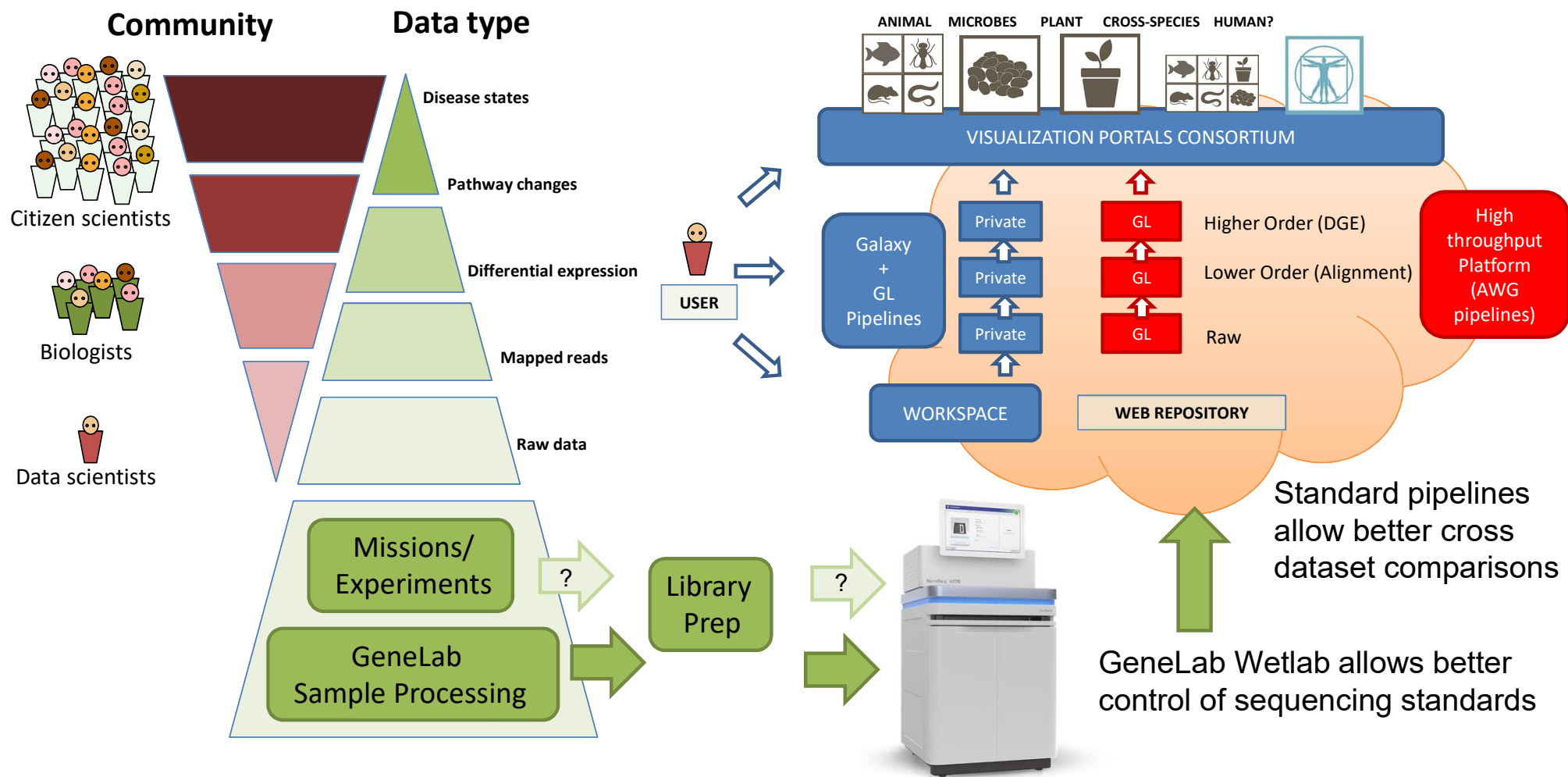


Annual Workshop (April 2018)



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



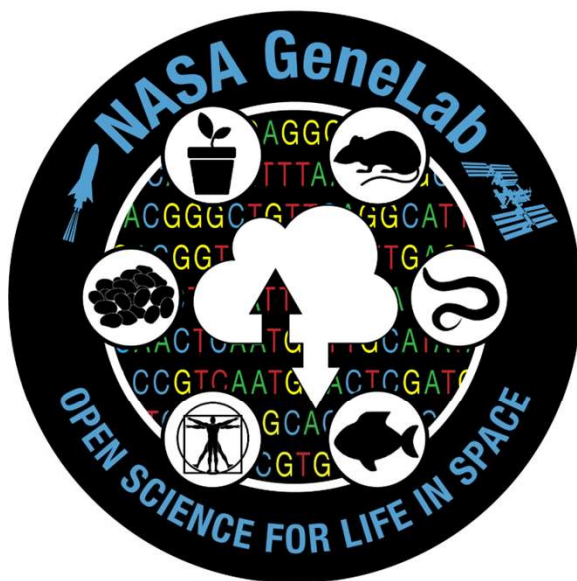


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GeneLab Analysis Platform



Using 16%

Data Depository Home Workspace Analyze Data Workflow Shared Data Help User

Tools

Data Analysis Tools

- Get Data
- Send Data
- Epigenomics
- RNA-Seq
- Other Tools
 - Picard Tool Suite
 - SAMTools Suite
 - Microarray
 - Sequencing General
 - Microarray Tools
 - Metagenomics Tools
- Workflows
 - All workflows

Hello, NASA GeneLab Analysis Platform is running!

Take an interactive tour: [Galaxy UI](#) [History](#)

NASA GeneLab's Analysis Platform is an open platform for performing large-scale analysis of space-relevant omics data using a customized suite of data analysis tools, powered by [Galaxy](#).

To access GeneLab RNAseq processed data go to 'Shared Data' → 'Data Libraries' → 'GeneLab Data Repository' → click on the GLDS dataset you are interested in.

To report any issues with this platform, contact the NASA GeneLab project at: arc-dl-gene-lab-it@mail.nasa.gov

History

Unnamed history (empty)

Jobs and output files will be displayed here

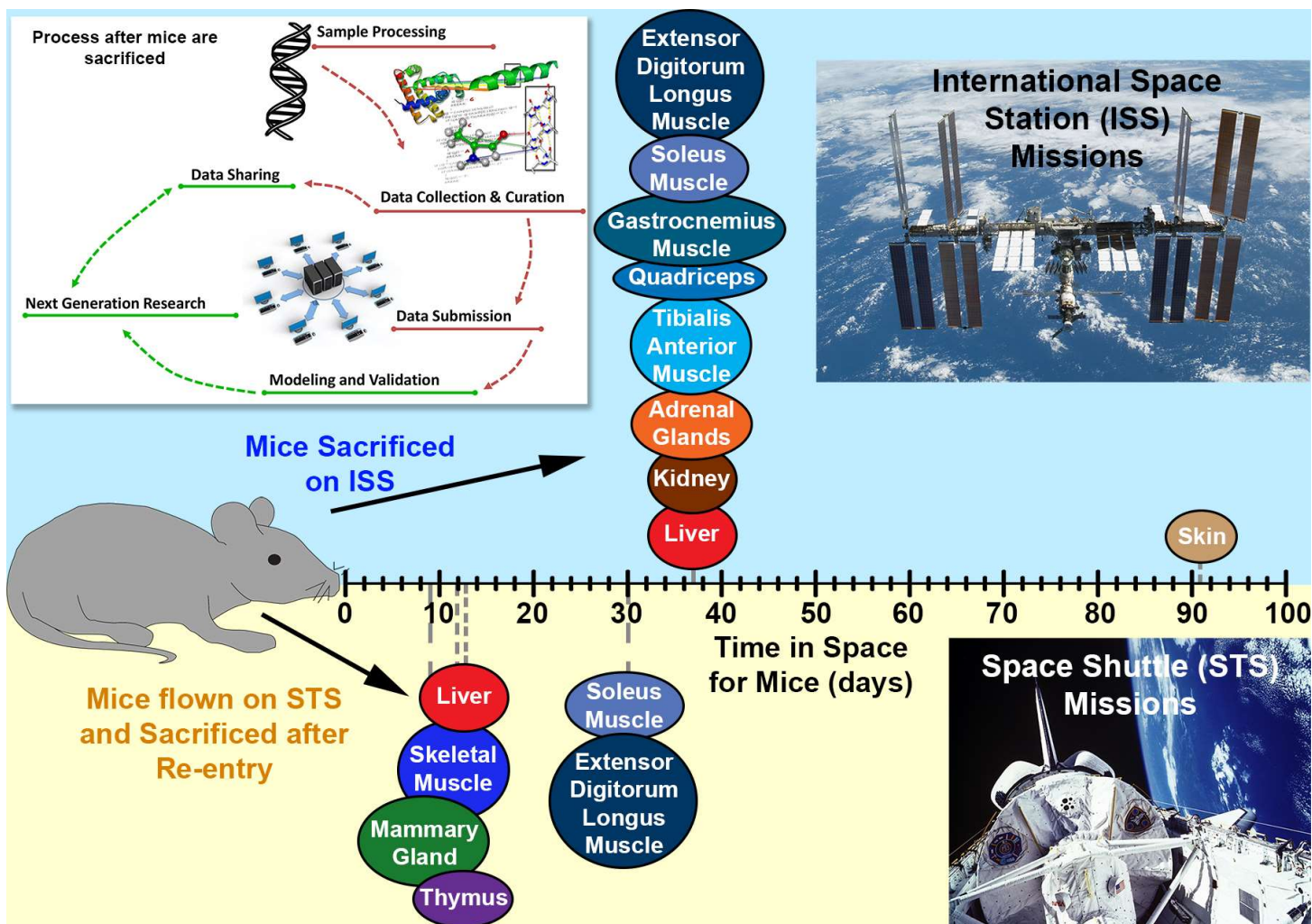
This history is empty. You can [load your own data](#) or [get data from an external source](#)



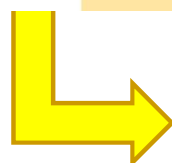
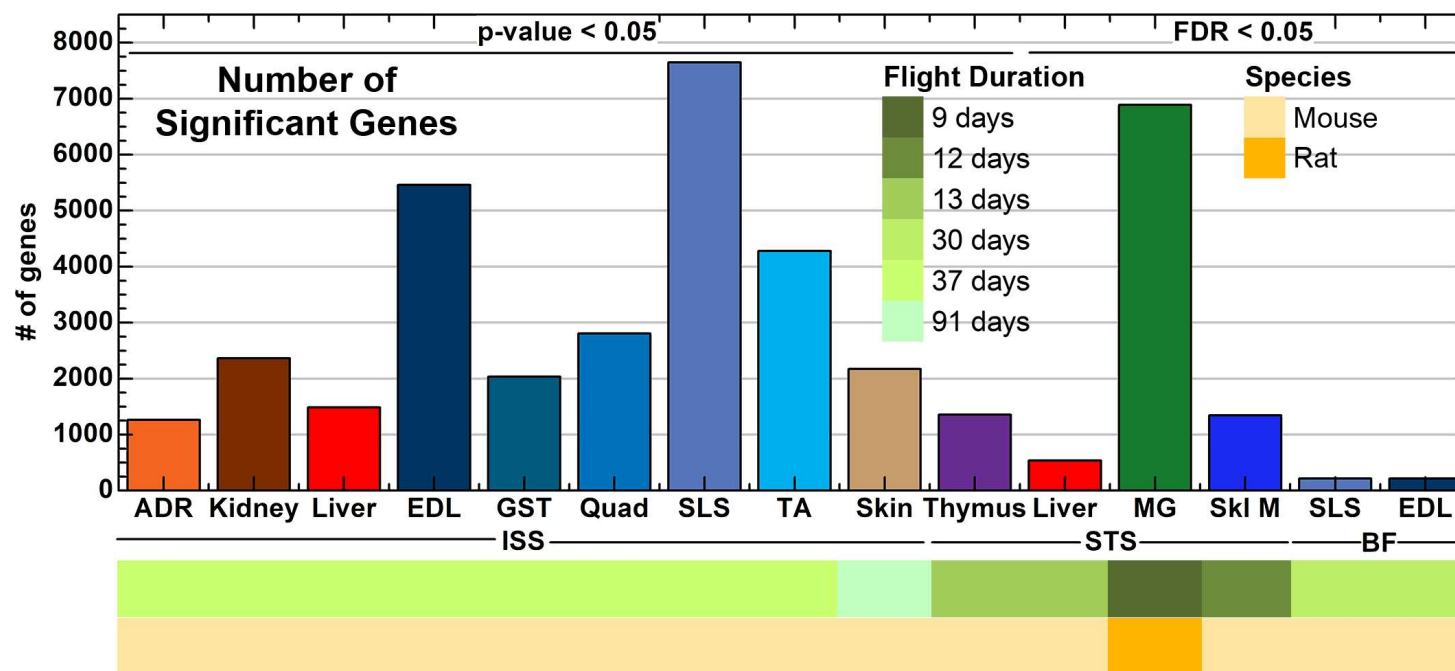
Publications using GeneLab



#	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



Number of Significant Genes from Each Dataset



Fold-Change $\geq |1.2|$



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

KSC ISS Environmental Simulator (ISSES; CO₂, O₂, Temp, RH)

AEM vs Vivarium Control



A) Cage Types



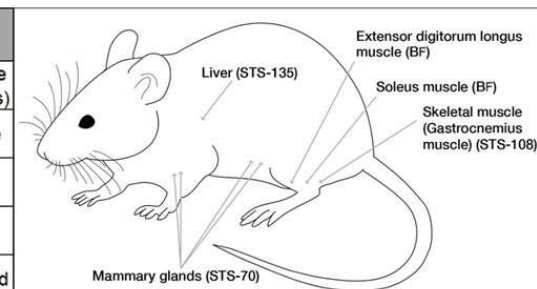
Animal Enclosure Module (AEM)



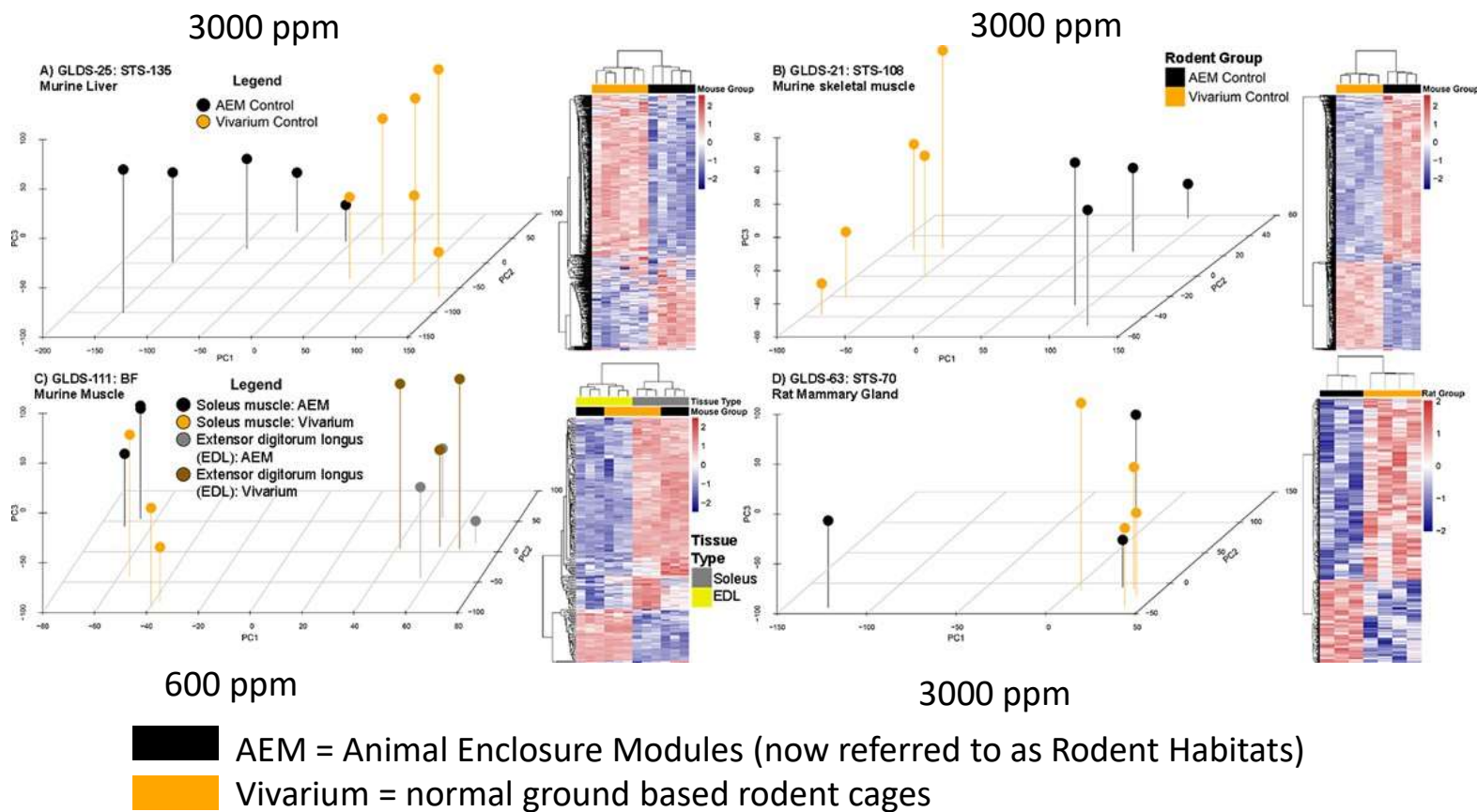
Sample vivarium cage

B)

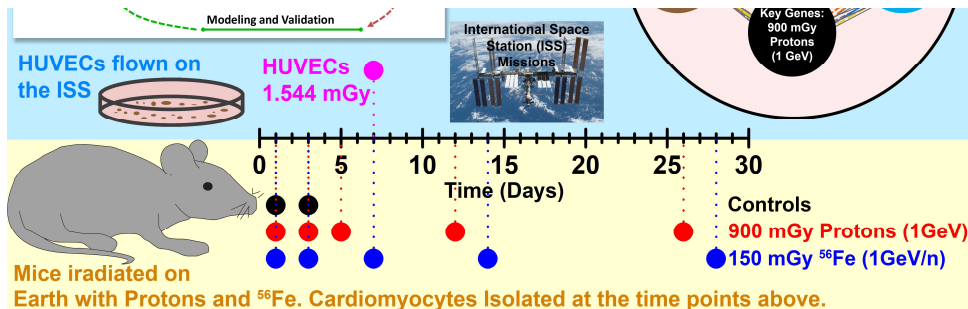
GeneLab Study	Mission	Species	CO ₂ (ppm)	Duration (days)	Tissue Type
GLDS-21	STS-108	mouse	~3000	11.8	skeletal muscle (gastrocnemius)
GLDS-111	BF	mouse	~600	30	soleus muscle
GLDS-111	BF	mouse	~600	30	extensor digitorum
GLDS-25	STS-135	mouse	~3000	13	liver
GLDS-63	STS-70	rat	~3000 (est)	9	mammary gland



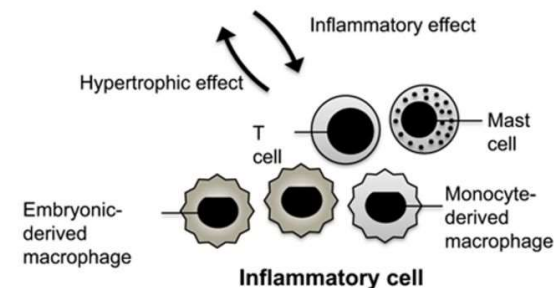
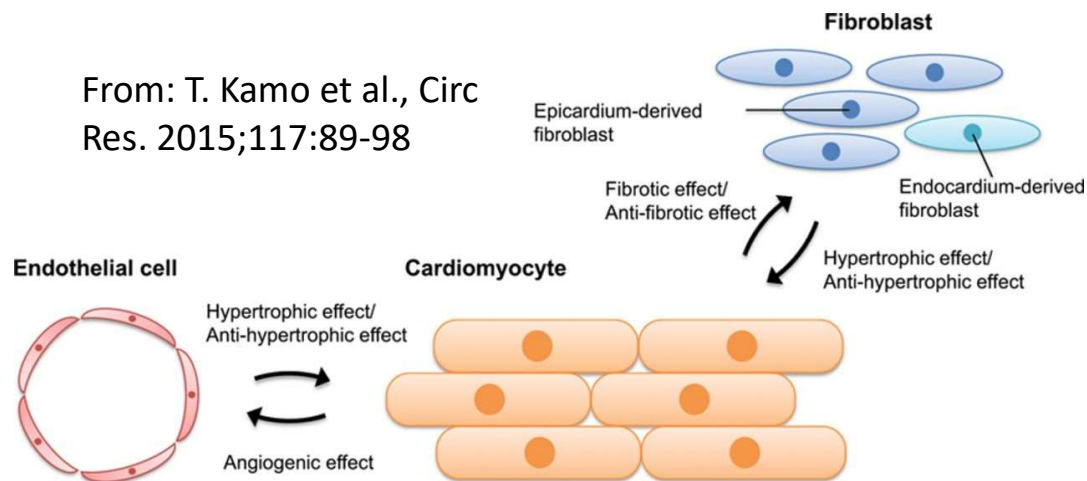
Beheshti, et al., Scientific Reports, 2018



Even though simulated levels up to 3000 ppm CO₂ are considered safe without detectable physiological impacts, hypoxic responses are detected from such exposure in mouse tissue



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

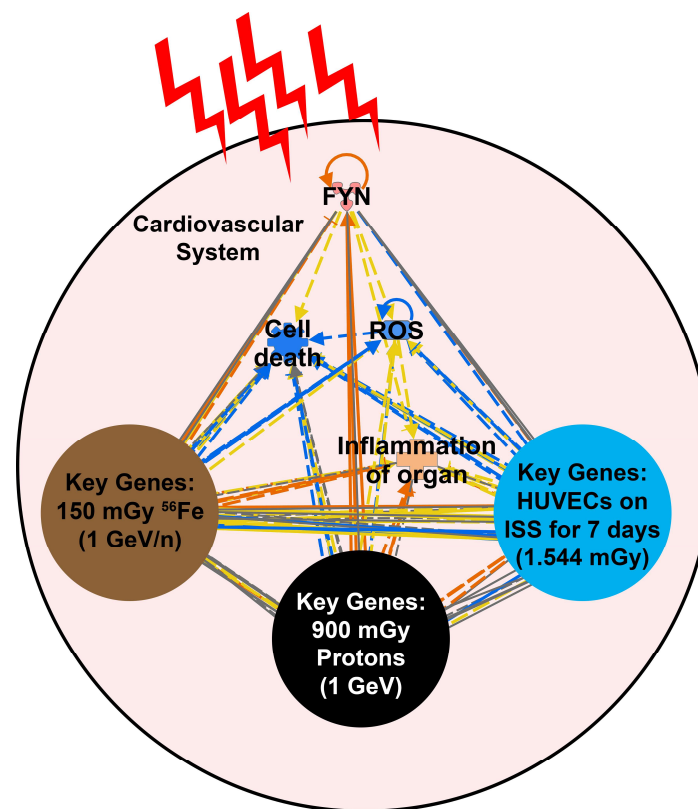
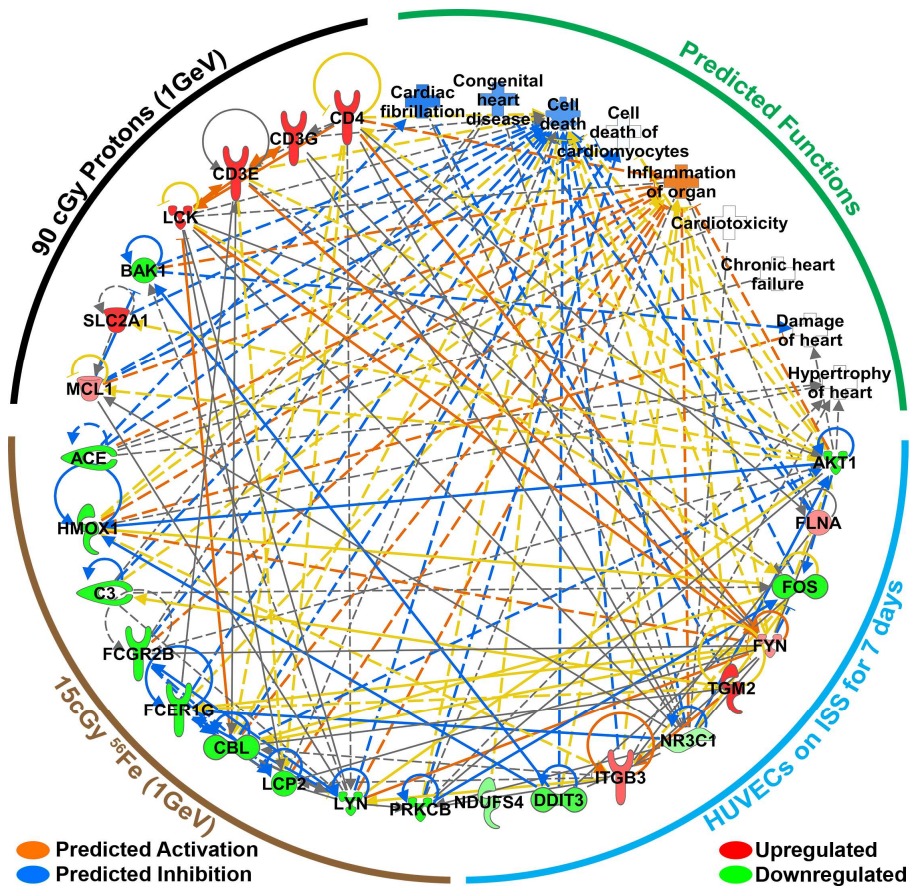


GeneLab Data Used and Hypothesis

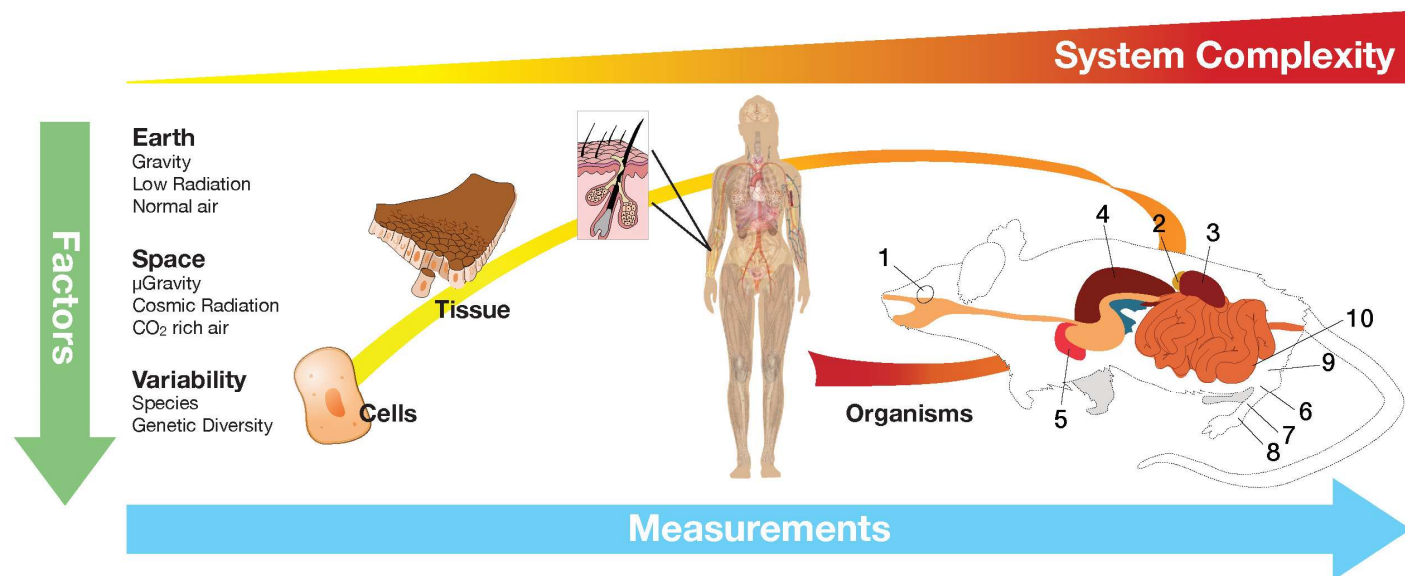
- Endothelial cells are known to directly regulate the development and activity of cardiomyocytes, and thus their response to spaceflight should be highly correlated with cardiomyocytes.
- Compare differential gene expression in cardiomyocytes from mice exposed to cosmic radiation on earth with endothelial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

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

Key Driving Genes



Beheshti, et al. IJMS, 2019



Transcriptomics, Proteomics, Epigenetics

Physiological

Transcriptomics, Proteomics, Epigenetics	Physiological
<p>Human Cell Cultures</p> <ol style="list-style-type: none"> 1. Primary T Cells 2. HUVEC cells: Human umbilical vein endothelial cell 3. HMVEC-dBL cells: Human Dermal Blood Microvascular Endothelial Cells 4. Fibroblasts 	<p>Astronaut Physiological Data</p> <ol style="list-style-type: none"> 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-1α 10. PGF2-α 11. Renin 12. VEGF-1 13. 8OHdG
<p>Mouse Tissues</p> <ol style="list-style-type: none"> 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) <p>Human Tissues</p> <ol style="list-style-type: none"> 1. Hair follicles 	

Human Research



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 CO₂ levels); mitochondrial stress and increased levels of mitochondria in the blood



AWG Members Involved



Kathleen Fisch Brin Rosenthal



UNIVERSITY of CALIFORNIA, SAN DIEGO
SCHOOL OF MEDICINE



Deanne Taylor Hossein Fazelinia Komal Rathi Douglas Wallace Larry Singh



Children's Hospital
of Philadelphia™



Perelman
School of Medicine
UNIVERSITY of PENNSYLVANIA



Helio Costa Kathryn Grabek



STANFORD
UNIVERSITY



J. Tyson McDonald Gary Hardiman Willian da Silveira Jeffrey Scott Willey



HAMPTON
UNIVERSITY
THE STANDARD OF EXCELLENCE



QUEEN'S
UNIVERSITY
BELFAST



WAKE FOREST
UNIVERSITY

AWG Members Involved



Chris Mason



Cem Meydan



Jonathan Foox



Flavia Rius



Cornell University



Yared Kidane



Evagelia C. Laiakis



GEORGETOWN UNIVERSITY
Georgetown University Medical Center



Susana Zanella



Scott Smith



Manned Space Flight Education Foundation



Sara Zwart



Sonja Schrepfer



University of California
San Francisco



Dong Wang



Afshin Beheshti



Sylvain Costes





GeneLab Team

