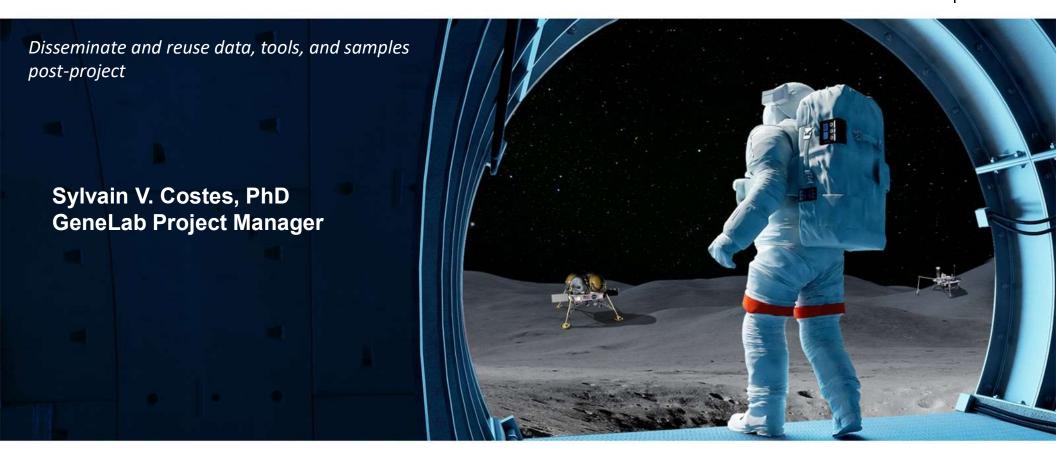
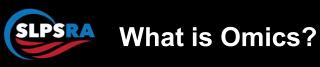
GeneLab: A Systems Biology Platform for Omics Analysis

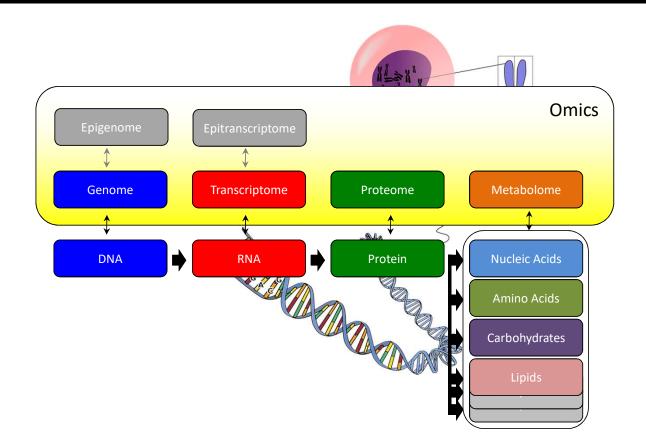
National Aeronautics and Space Administration







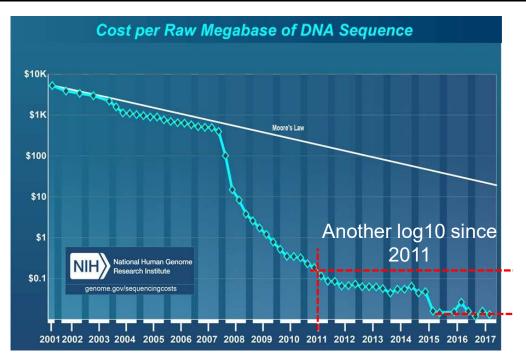
NASA





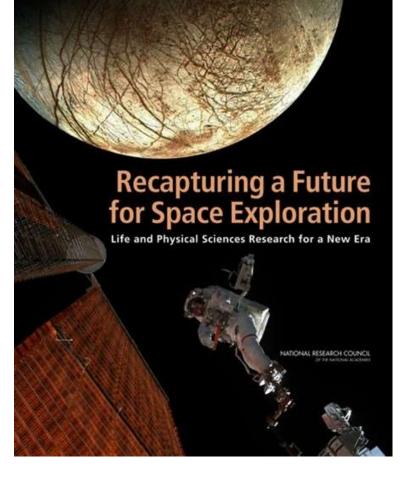
2011 NRC Decadal Survey and the Sequencing Paradigm Shift





"...**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..."





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

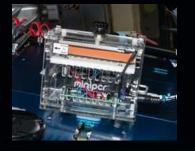


Oxford Nanopore MinION Gene Sequencer

Cepheid Smart Cycler qRT-PCR



Reaction tube containing lyophilized chemical assay bead (proprietary)



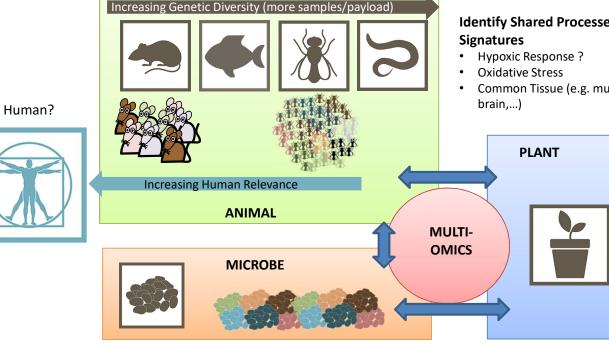
Mini-PCR



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

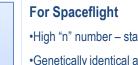


- Sequencing on ISS is still limited in the amount of data generated
 - Most of the work needs to happen on earth
- Measurements on human cannot be too invasive and limited in numbers
 - Usage of animals



Identify Shared Processes/ Molecular

Common Tissue (e.g. muscle, liver, heart, eyes,



•High "n" number - statistically significant data

•Genetically identical animals

June 1, 2017

•Low resource requirements

•Short life cycle - multiple generations

•Measure response of a whole multicellular animal

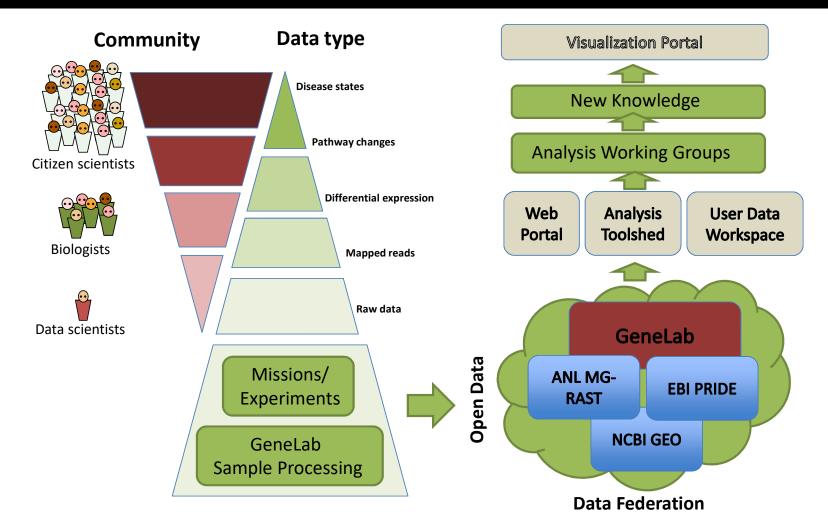
•Flies used as a model for humans for innate immunity. circadian rhythm, oxidative stress, neurobehavior, development, genetics, GWAS, "omics" studies etc.

Fruit Fly Lab (FFL-02) Scientist's Blog



GeneLab Data Democratization

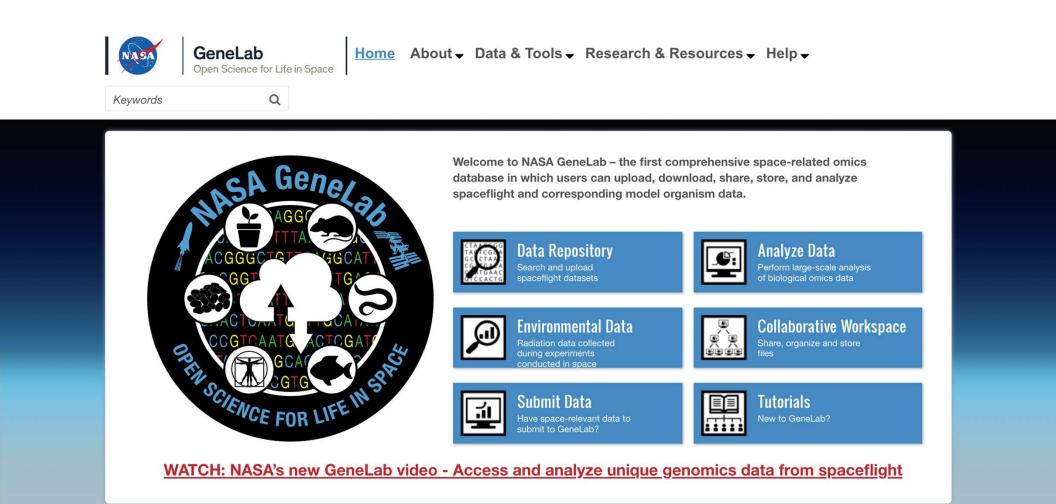






GeneLab Webpage: genelab.nasa.gov







GeneLab Data Repository



Home	GLDS	Data Repository	Environmental Data	Tools	Submit Data	Tutorials	Help	
Search	Data		x Q					
	GeneLal	D NIH GEO 🗆 E	BI PRIDE 🗌 ANL MG-RA	ST				
Search	Filters (G	eneLab Only)						
Project T	ype 🗸	Factors V	Organisms 🗸 Assa	ау Туре	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	lonizing 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

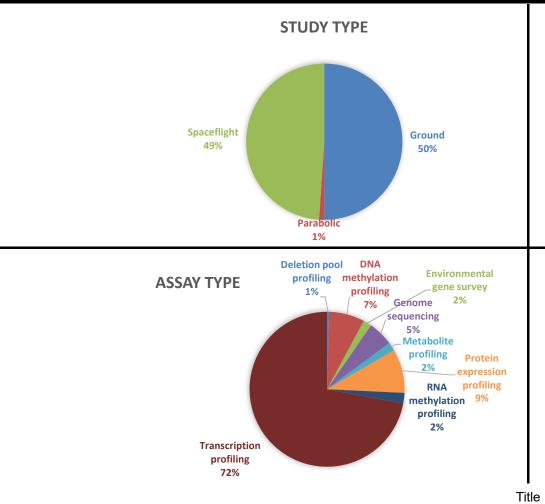
Low dose (0.4 Gy) irradiation (LDR) and hindlimb unloading (HLU) microgravity in mice (RNA-Seq)

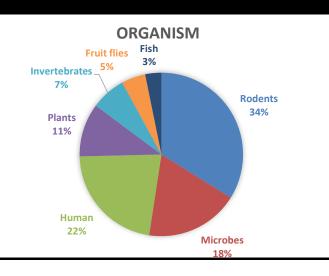
	Organisms	Factors	Assay Types	Release Date	Description
\ge	Mus musculus	lonizing Radiation Hindlimb Unloading	transcription profiling	19-Sep-2018	The purpose of the present study was to evaluate damage in brain and eye in a ground-based model for spaceflight which includes



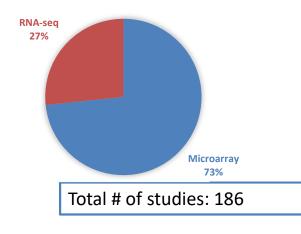
Overview: Database content



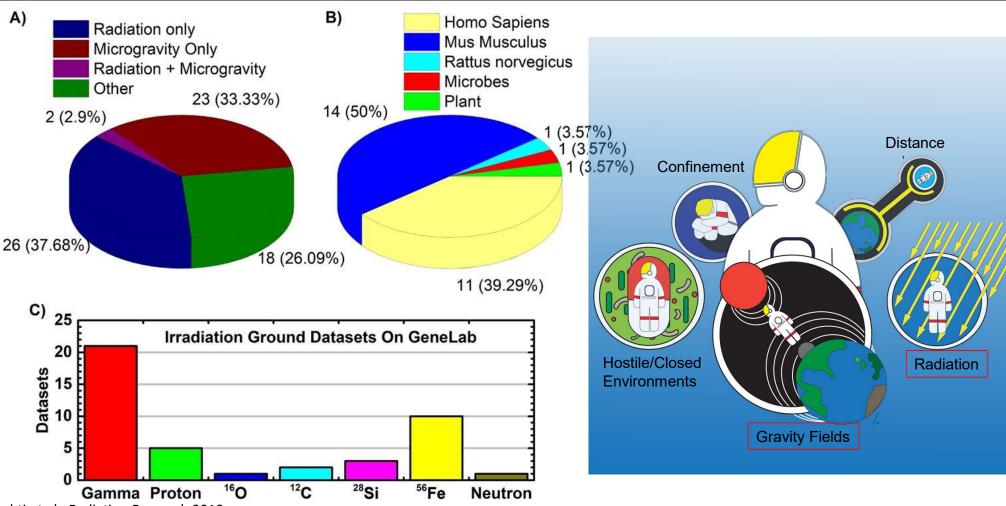




TRANSCRIPTION PROFILING



69 Ground Data Sets: Radiation and simulated microgravity



Beheshti et al., Radiation Research 2018

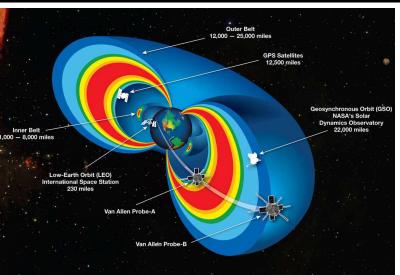
SLPSRA



The Radiation Factor





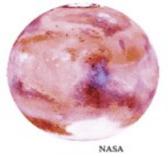


MI	LLINEM.	
CHEST X-RAY	8 to 50	1
AVG. YEARLY RADON DOS	E 200	1
U.S. AVG. YEARLY DOSE	350	1
PET SCAN	1,000	
1 YEAR IN KERALA, INDIA	1,300	
U.S. NUCLEAR WORKER LIMIT PER YEAR	5,000	
APOLLO 14 (9 DAYS)	1,140	
SHUTTLE 41-C (18 DAYS)	5,600	
SKYLAB 4 (84 DAYS)	17,800	
MARS MISSION TOTAL	130,000	

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.



ARS MISSION TOTAL	130,000			
		TRIP TO AND FROM MARS (1 YEAR): 80,000	ON MARS (1.5 YEARS):	FROM SOLAR - FLARE: 20,000
			00,000	

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





GeneLab Environmental Data



Home GLDS	Data Repository	Environmental Data	Tools	Submit Data	Tutorials	Help
Search Data		X Q				
🗆 All 🗹 GeneL	ab 🗌 NIH GEO 🗌 E	BI PRIDE O ANL MG-RA	ST			
Search Filters (GeneLab Only)					
Project Type	✓ Factors ✓	Organisms 🗸 Ass	ay 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

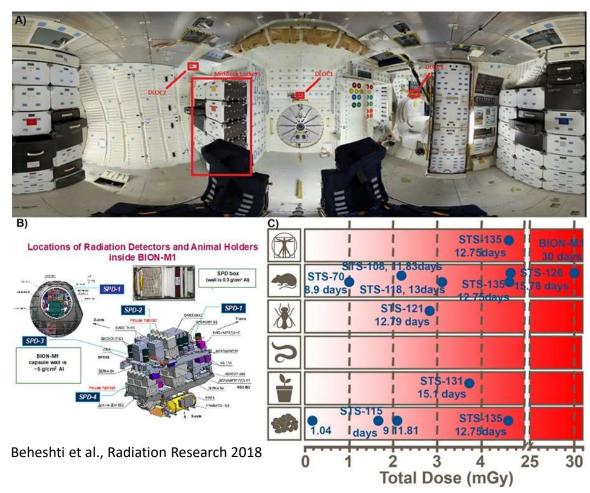
Dosimetry measuring techniques vary depending on the particular experiment environment. Through 2018, most flight experiments have not employed "dedicated" dosimeters (i.e. dosimeters integrated into experiment platform housing). Therefore, doses to which study samples are exposed frequently must be 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

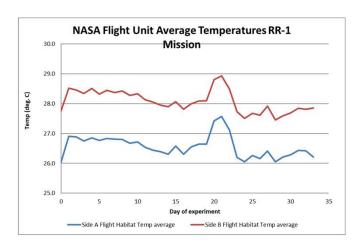


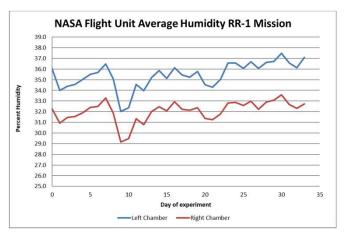
Radiation Dosimetry for STS samples (ISS to follow)





STS = Space Transportation System (Shuttle Program)







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	



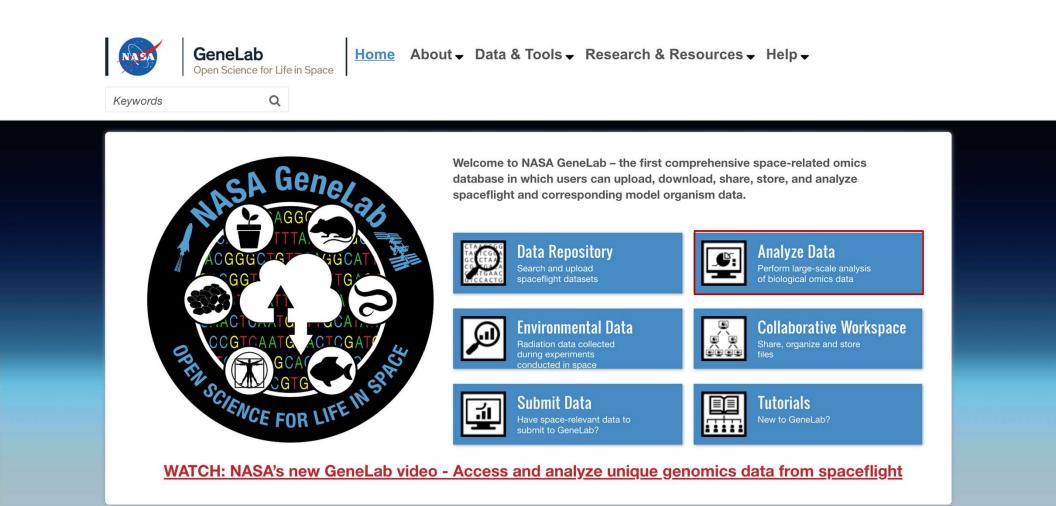
- Monthly meetings + "Homework"
- Deliverables:

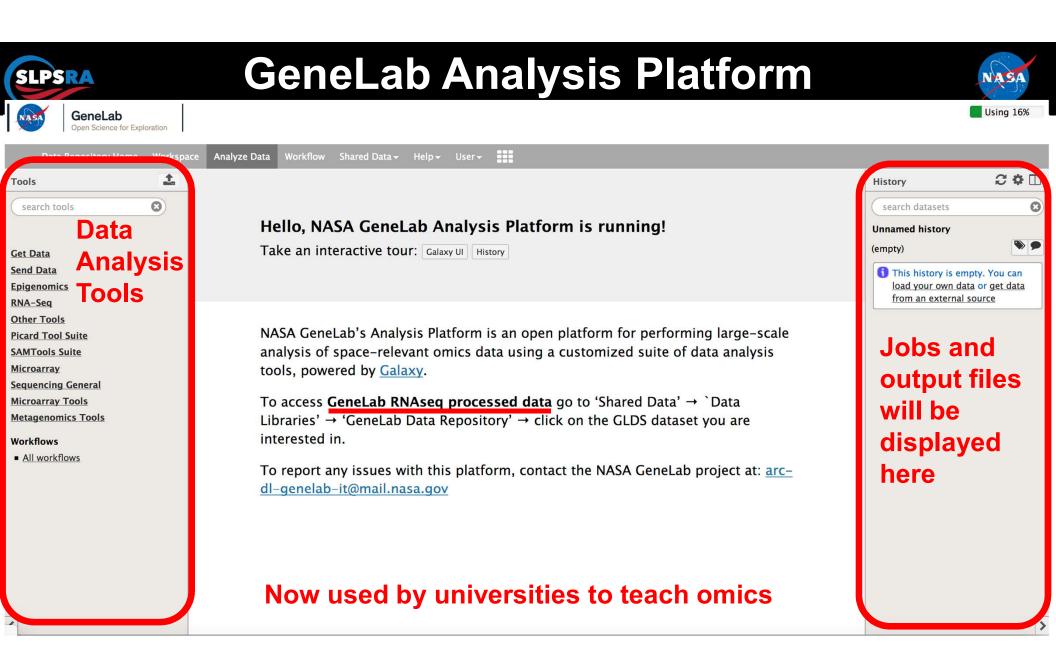
- Content of the second of the s
- Consensus pipelines for primary analysis of data (Microarray, RNASeq, Bisulfite sequencing, Proteomics, 16S metagenomics, Whole genome metagenomics)
- Recommendations for visualization of data



GeneLab Analysis Platform









Publications using GeneLab

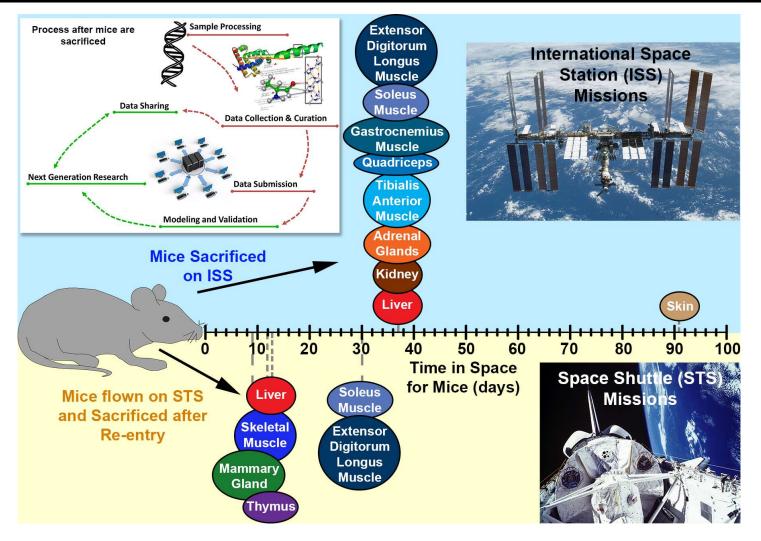


#	Year	Title	Journal	Authors	Status
1	2017	Validation of Methods to Assess the Immunoglobulin Gene Repertoire in Tissues Obtained from Mice on the International Space Station.	Gravit Space Res.	Rettig TA, Ward C, Pecaut MJ, Chapes SK	Published
2	2018	A microRNA signature and TGF-β1 response were identified 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		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

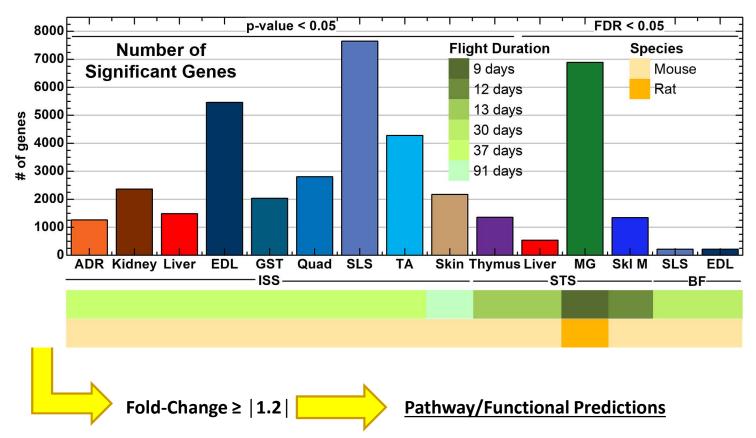






Number of Genes Significantly Expressed (FLT vs GC) varies with duration, species and tissue





Beheshti, et al., PLOS One, 2018



Ground Control (GC) Experiment



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



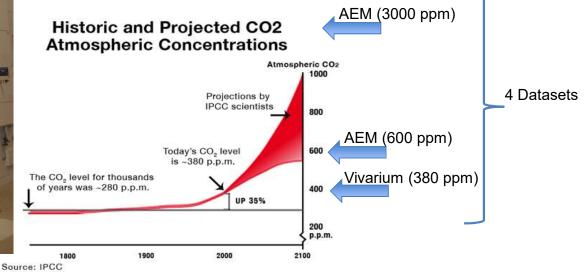
AEM vs Vivarium Control



7.5" 11.5"

Animal Enclosure Module (AEM)

Sample vivarium cage

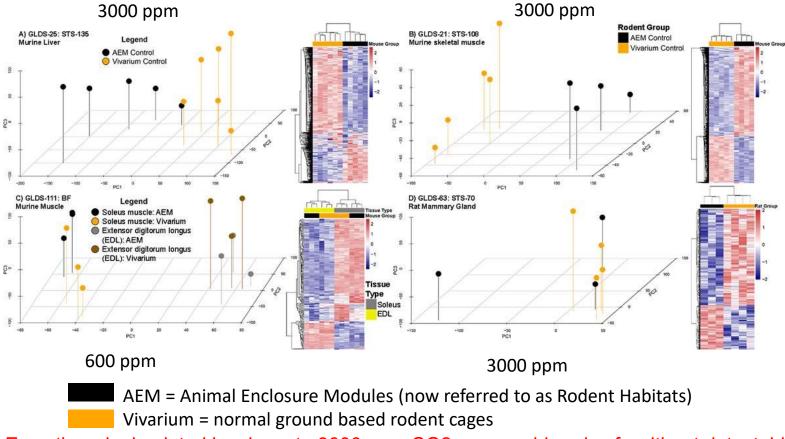


http://www.ipcc.ch/present/graphics.htm



Carbon Dioxide as an Environmental Stressor in Spaceflight





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

Beheshti, et al., Scientific Reports, 2018



Jan. 31, 2018

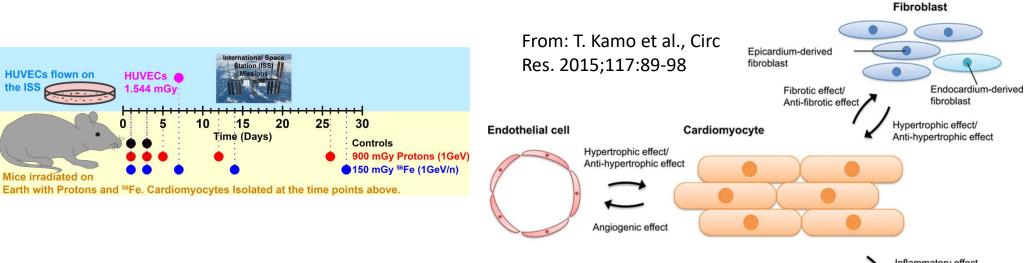
NASA Twins Study Investigators to Release Integrated Paper in 2018



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

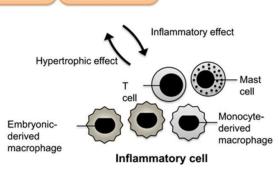


Space Radiation induces long term impact on the cardiovascular system by the activation of FYN through Reactive Oxygen Species



GeneLab Data Used and Hypothesis

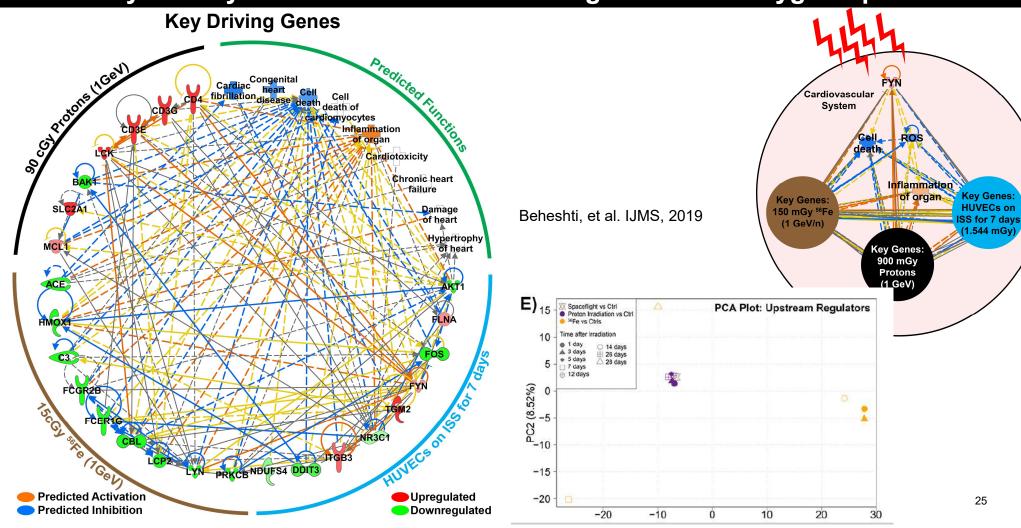
- Endothelial cells are known to directly regulate the development and activity of cardiomyocytes, and thus their response to spaceflight should be highly correlated with cardiomyocytes.
- Compare differential gene expression in cardiomyocytes from mice exposed to cosmic radiation on earth with endothelial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

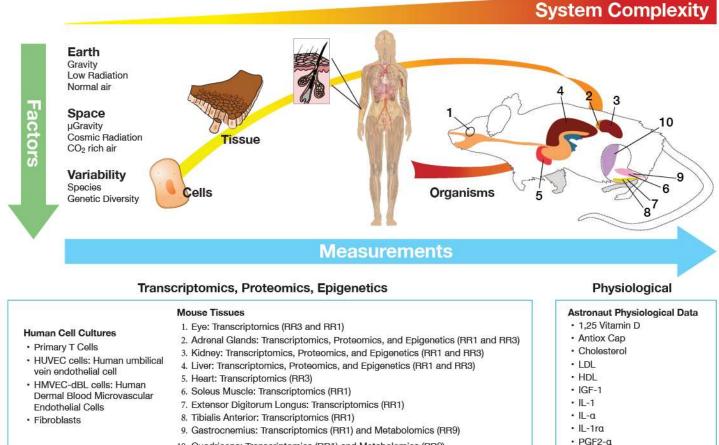






Multi-Omics Multi-Strain Multi-Species AWG Meta Analysis





Renin

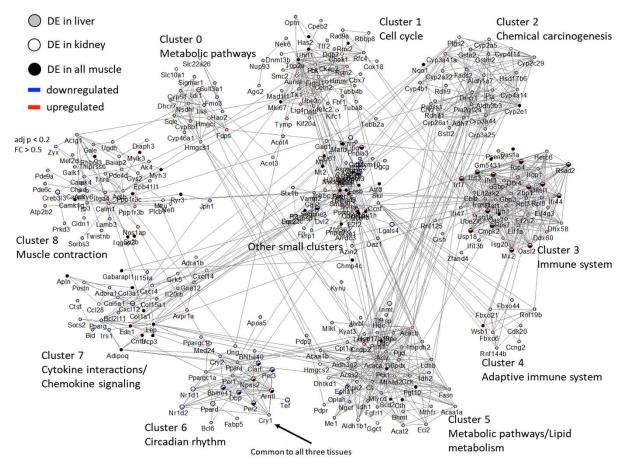
VEGF-1
8OHdG

10. Quadriceps: Transcriptomics (RR1) and Metabolomics (RR9)

Human Tissues • Hair follicles

All Tissues Network Analysis from RR1 data





SLPSRA

Mitochondrial stress and metabolomics changes are captured across the various tissues and strains





Kathleen Fisch Brin Rosenthal



UNIVERSITY of CALIFORNIA, SAN DIEGO SCHOOL OF MEDICINE





Gary Hardiman Willian da Silveira

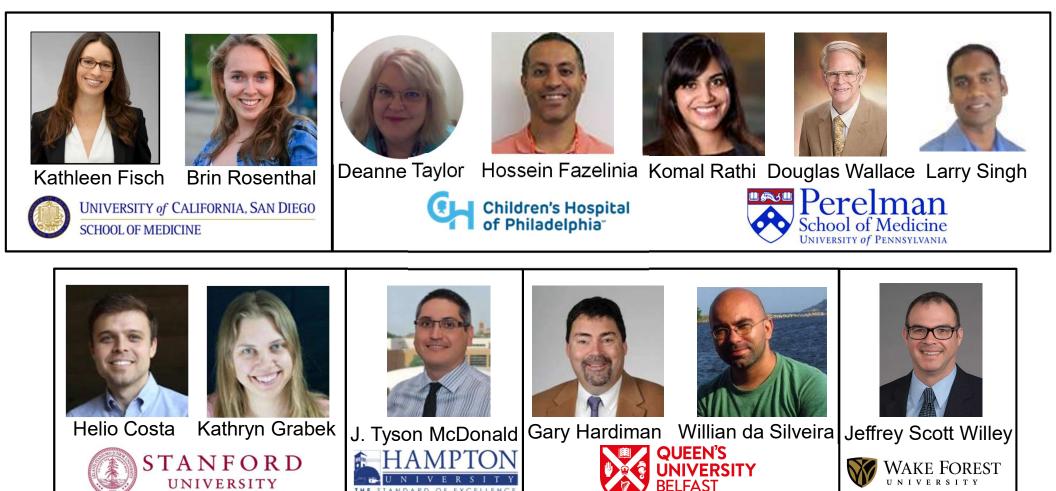






AWG Members Involved

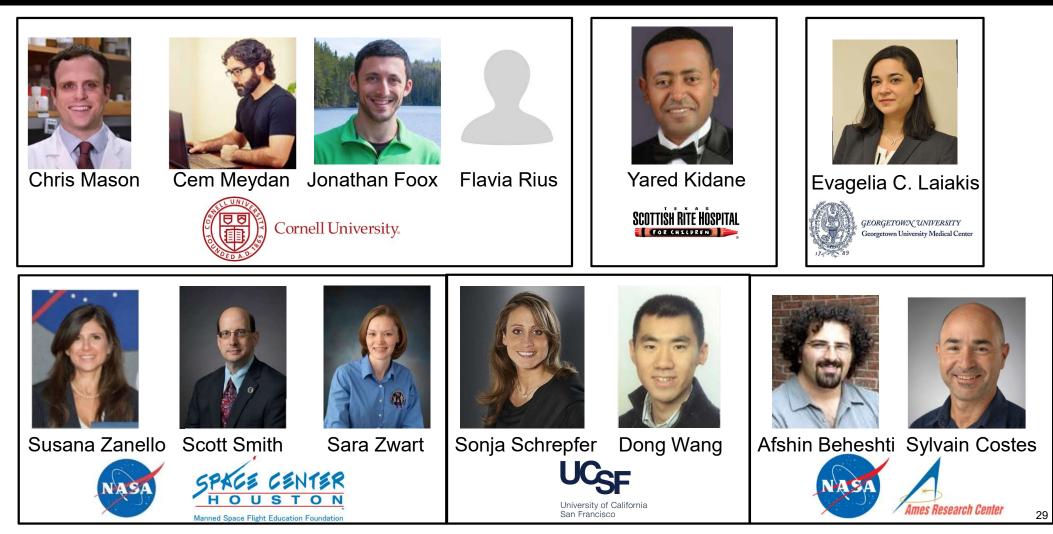






AWG Members Involved







GeneLab Team



