Systemic alterations with spaceflight associated health risks originating from both circulating miRNAs and mitochondrial biology

National Aeronautics and Space Administration

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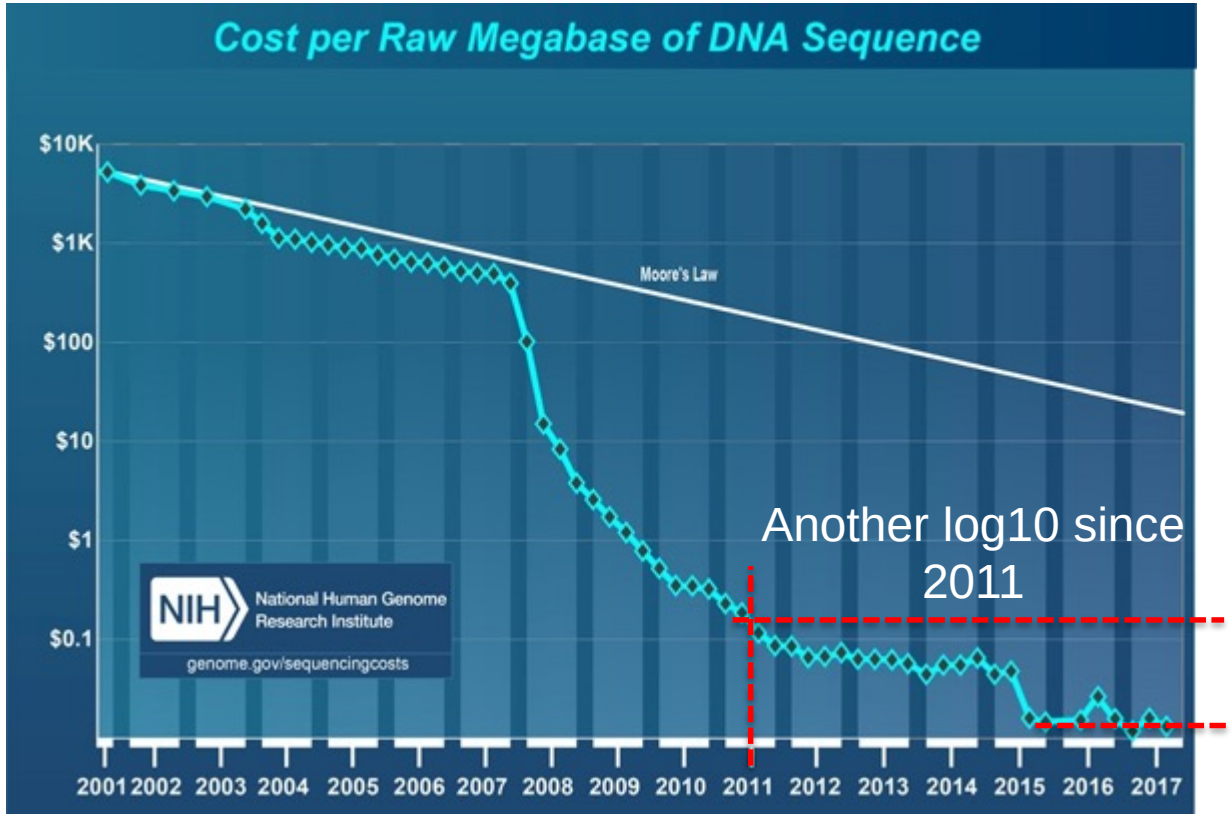
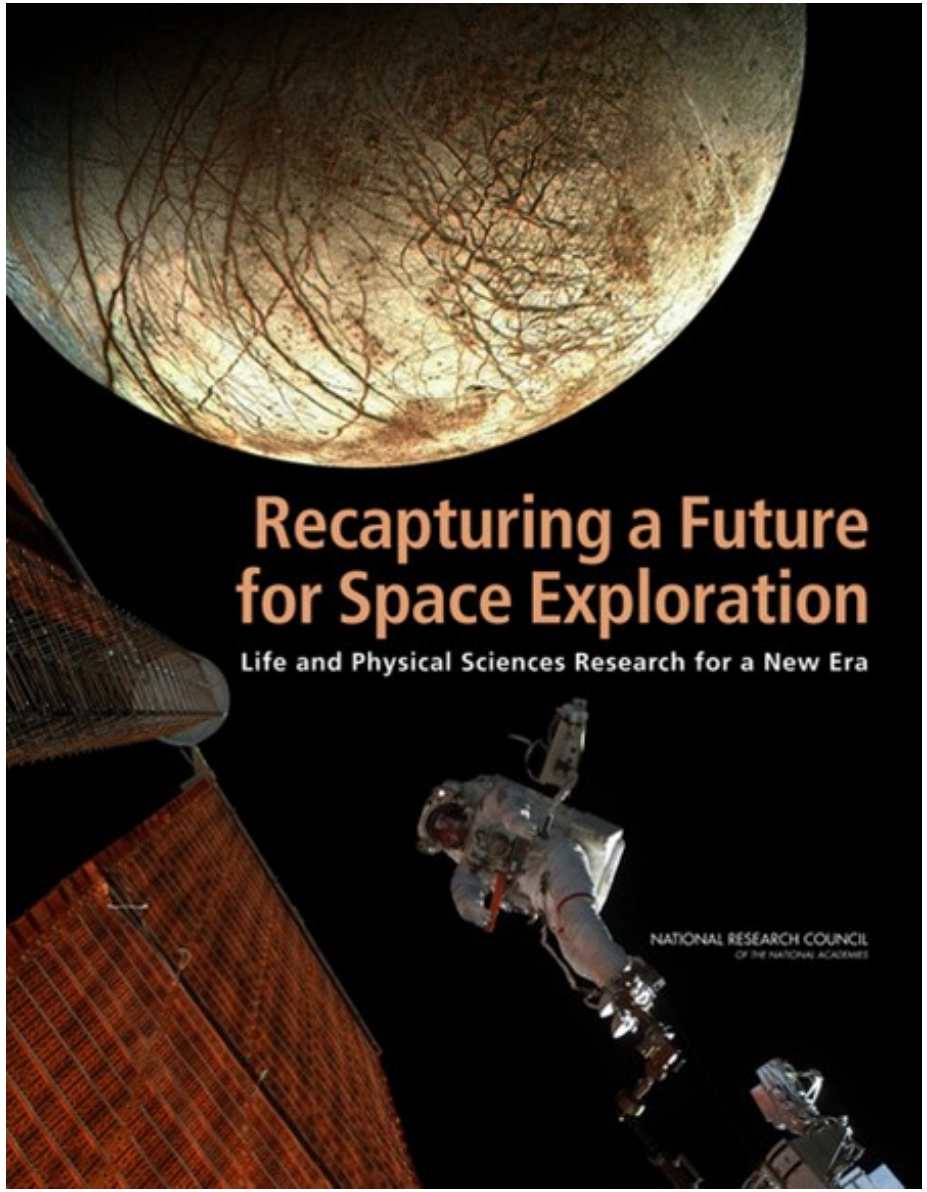
2011 NRC Decadal Survey and the Sequencing Paradigm Shift



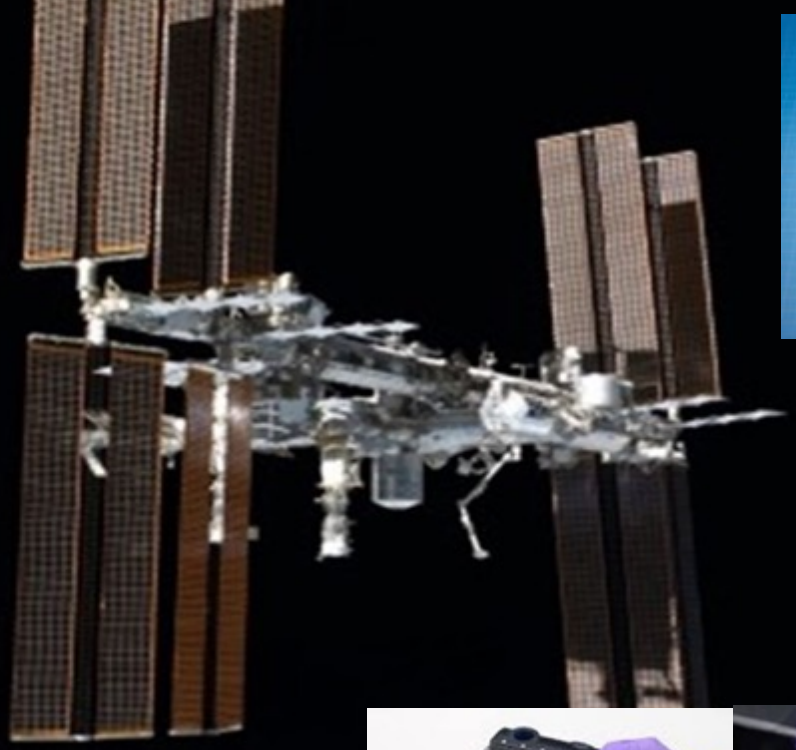
*"…**genomics, transcriptomics, proteomics, and metabolomics** offer an immense opportunity to understand the effects of spaceflight on biological systems…"*

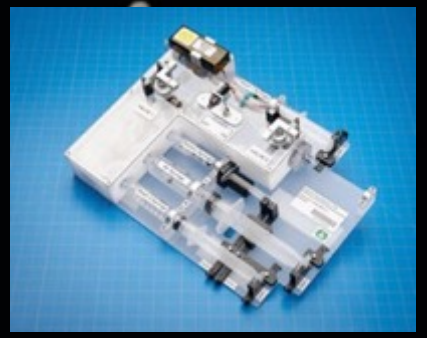
*"…Such techniques generate considerable amounts of **data that can be mined and analyzed** for information by multiple researchers…"*



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.



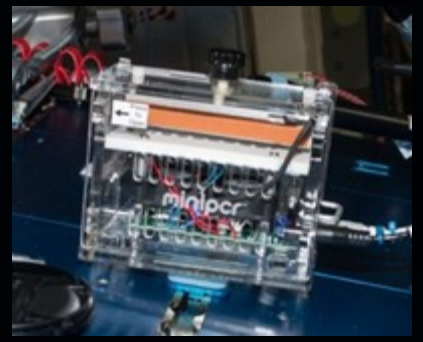


Sample Preparation Module

Oxford Nanopore MinION Gene Sequencer

Cepheid Smart Cycler qRT-PCR

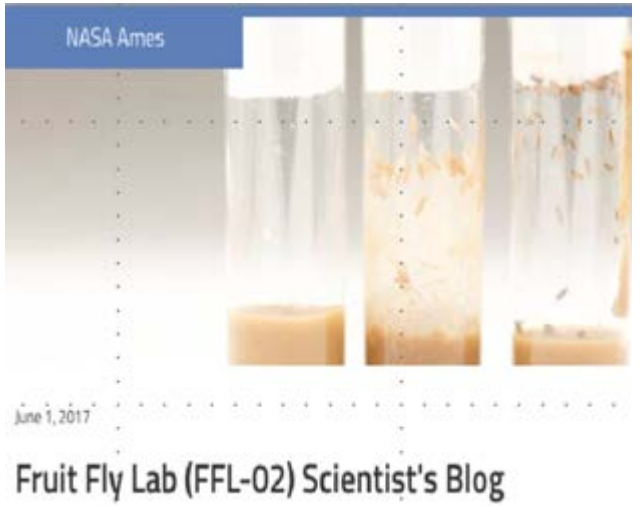
Reaction tube containing lyophilized chemical assay bead (proprietary)

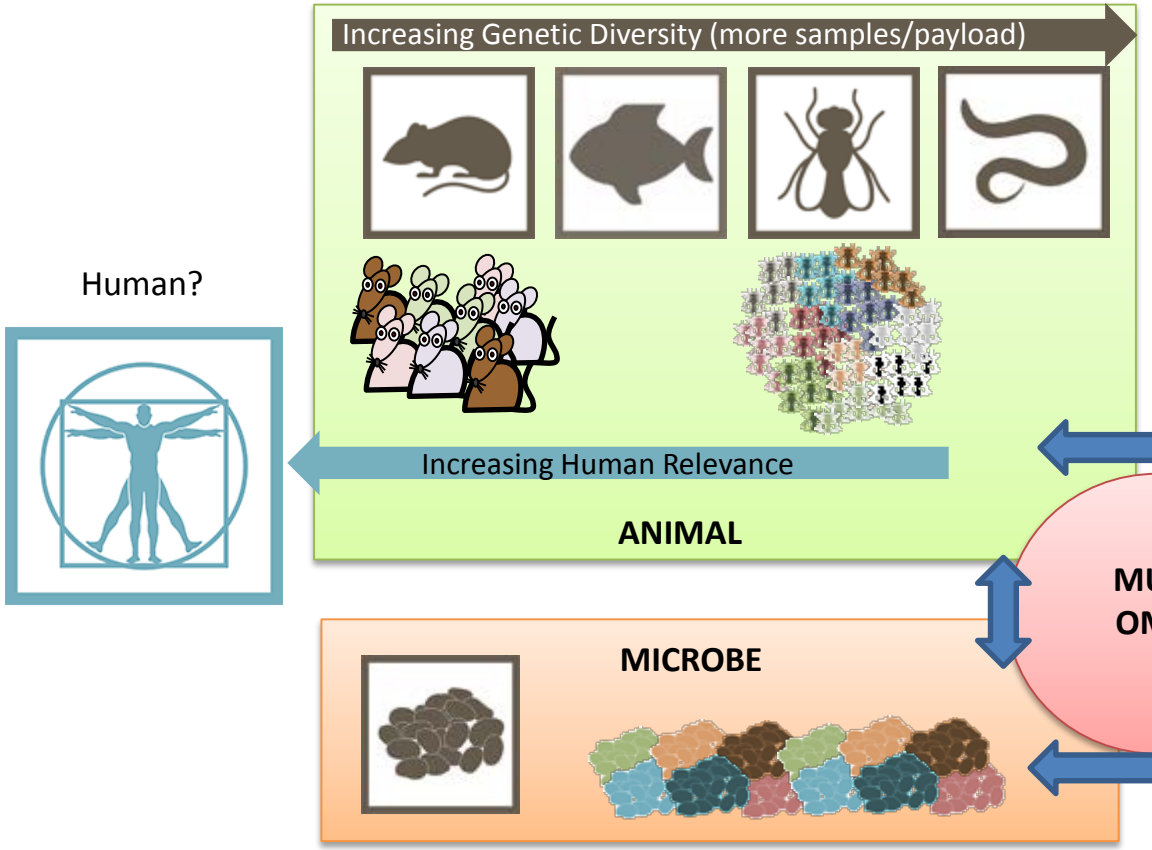


Mini-PCR

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





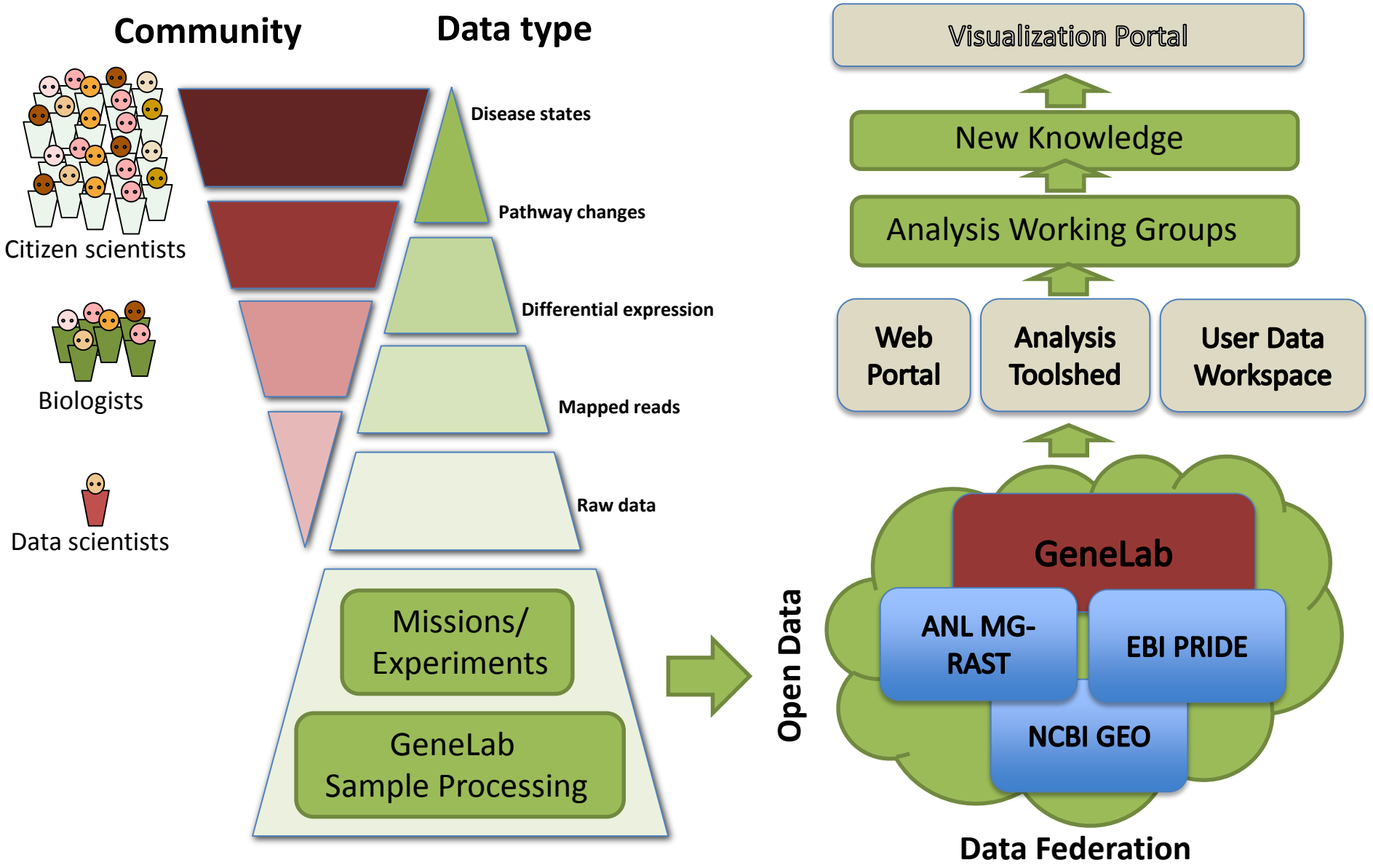
Identify Shared Processes/ Molecular Signatures

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

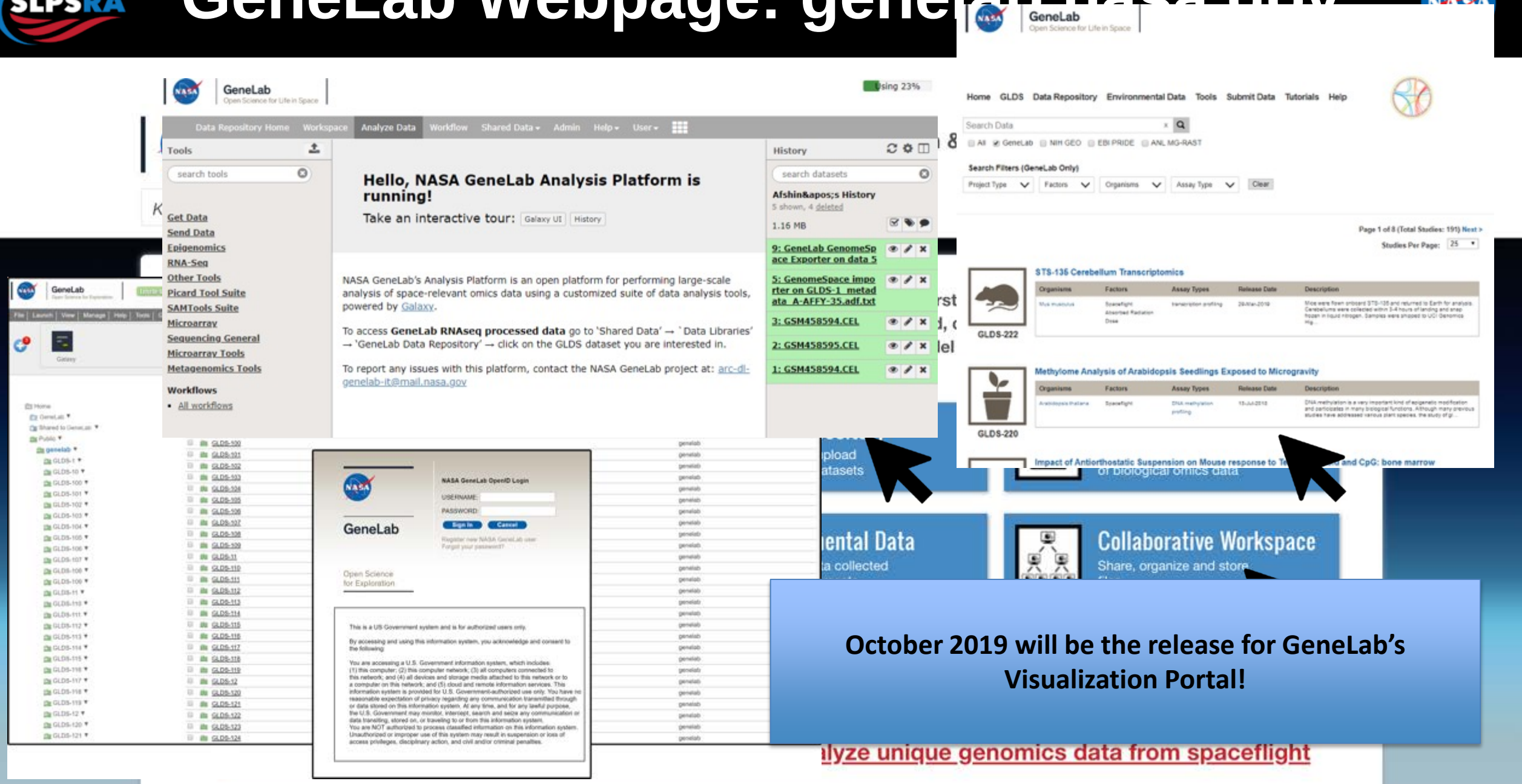
For Spaceflight

- 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.

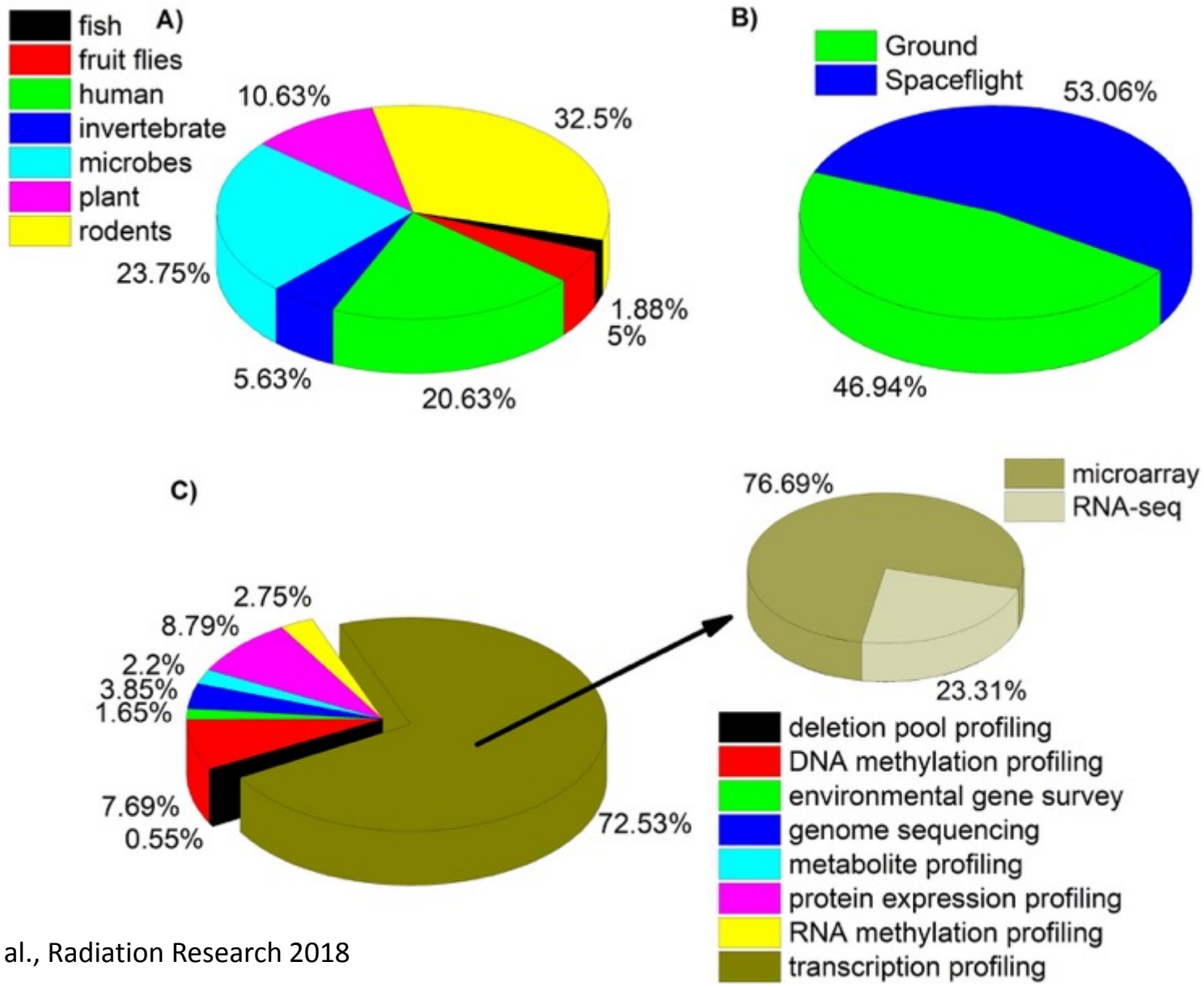
GeneLab Data Democratization



GeneLab Webpage: genelab.nasa.gov



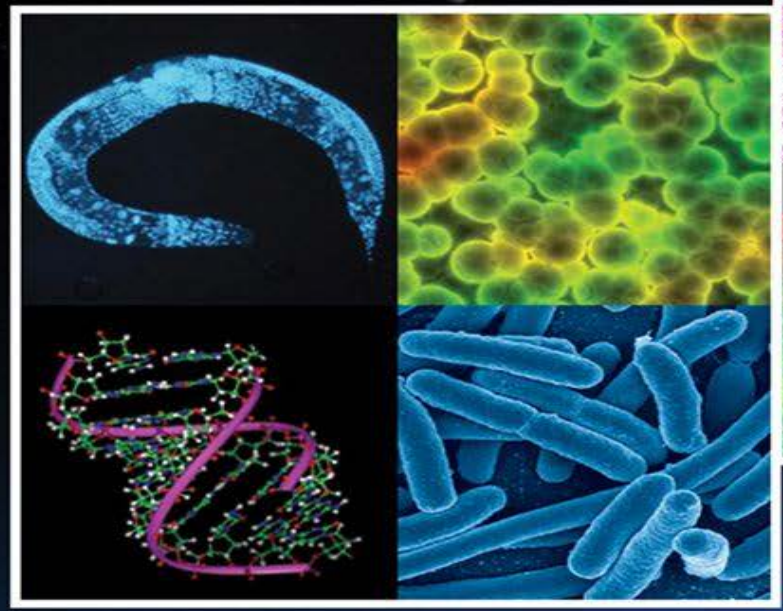
GeneLab Database: >200 data sets



Beheshti et al., Radiation Research 2018

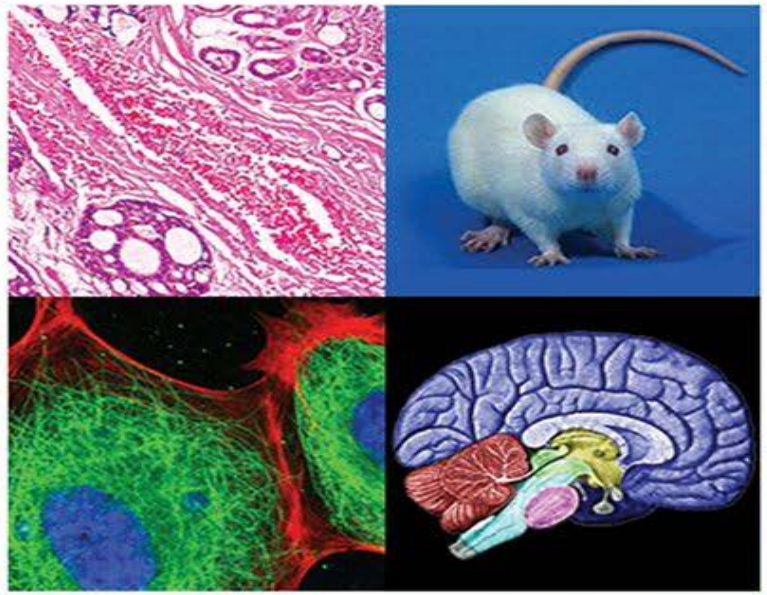
Space Biology Interest for NASA

Biological Systems



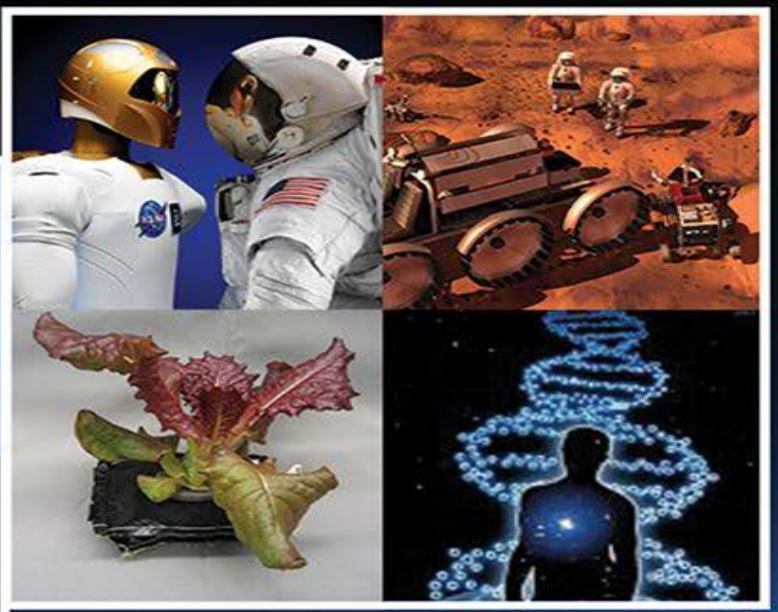
- Model Organisms
- Cell and Microbial Biology
- Biomolecules

Human Health



- Mammalian Cells
- Model Organisms

Human Exploration



- Exploration Subsystems
- Bioregenerative Life Support

npj Microgravity

www.nature.com/npjmgrav

PERSPECTIVE OPEN

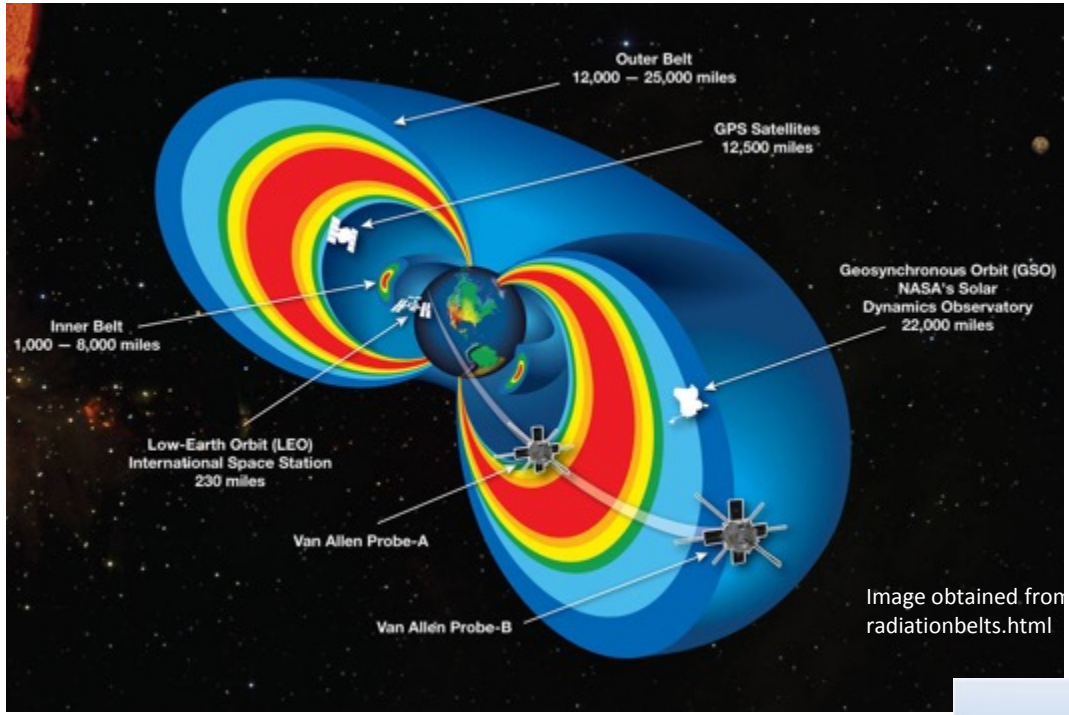
From the bench to exploration medicine: NASA life sciences translational research for human exploration and habitation missions

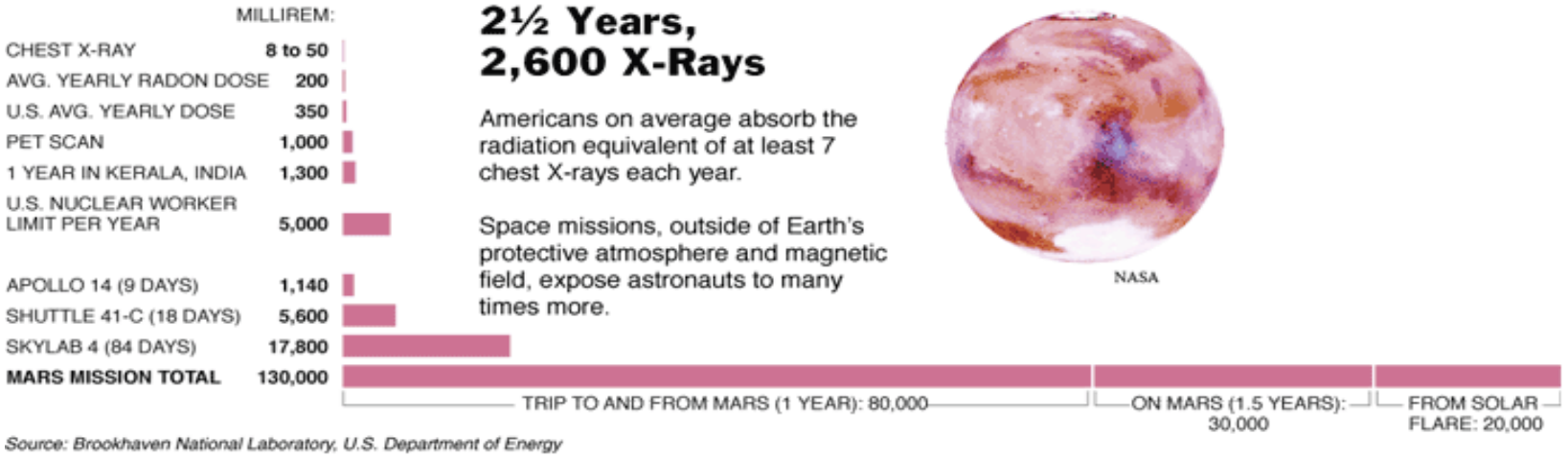
Joshua S. Alwood[1], April E. Ronca[1,2], Richard C. Mains[3], Mark J. Shelhamer[4], Jeffrey D. Smith[1] and Thomas J. Goodwin[1]

NASA's Space Biology and Human Research Program entities have recently spearheaded communications both internally and externally to coordinate the agency's translational research efforts. In this paper, we strongly advocate for translational research at NASA, provide recent examples of NASA sponsored early-stage translational research, and discuss options for a path forward. Our overall objective is to help in stimulating a collaborative research across multiple disciplines and entities that, working together, will more effectively and more rapidly achieve NASA's goals for human spaceflight.

npj Microgravity (2017)3:5 ; doi:10.1038/s41526-016-0002-8

Space Environment



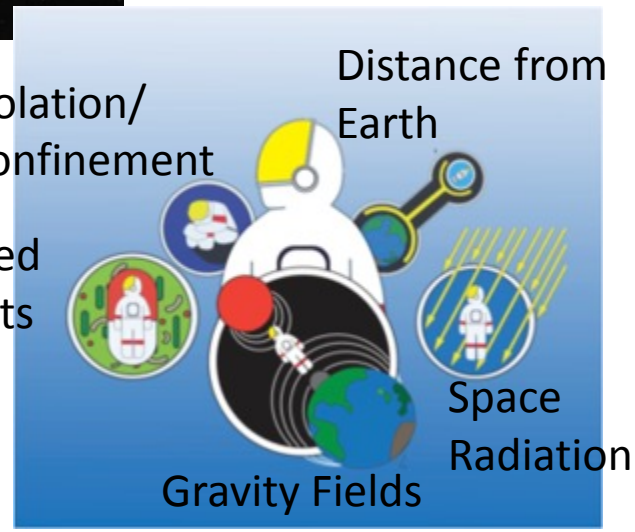


NASA

Isolation/
Confinement

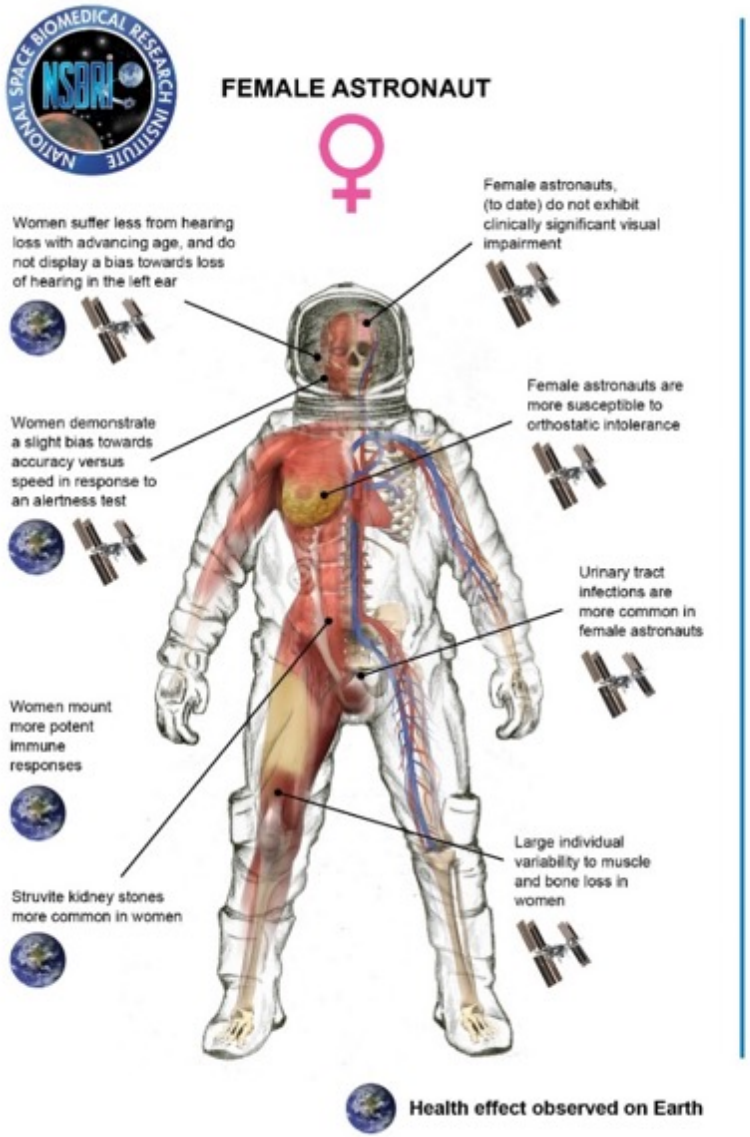
Distance from
Earth

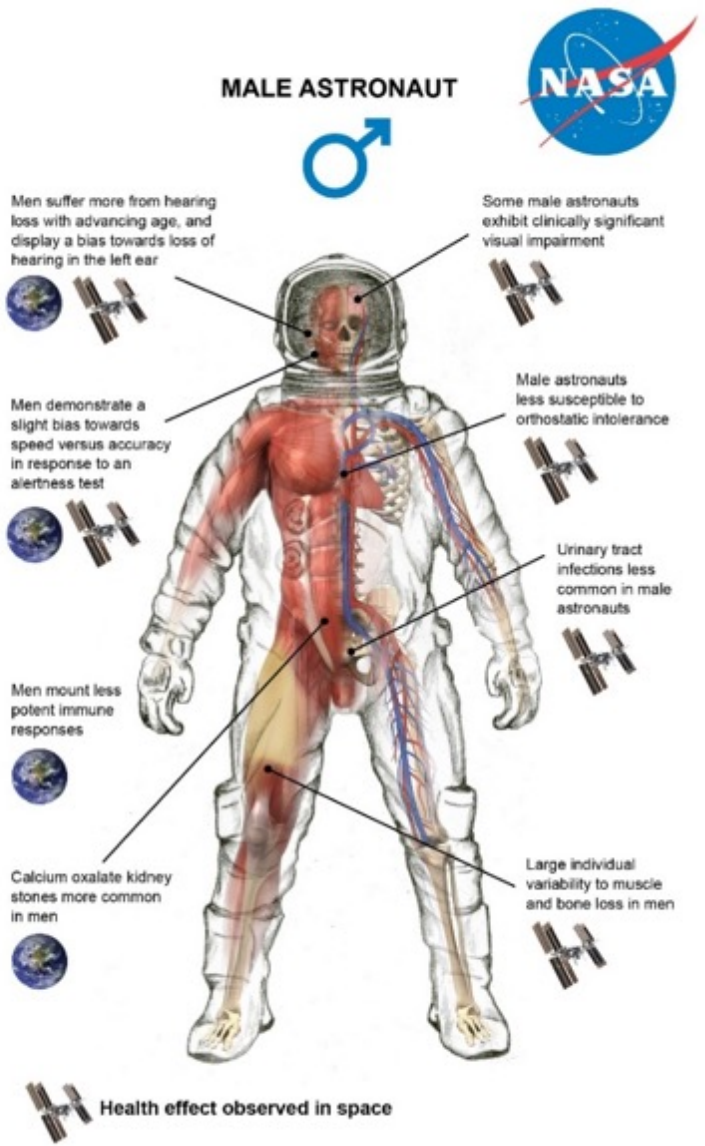
Hostile/closed
environments

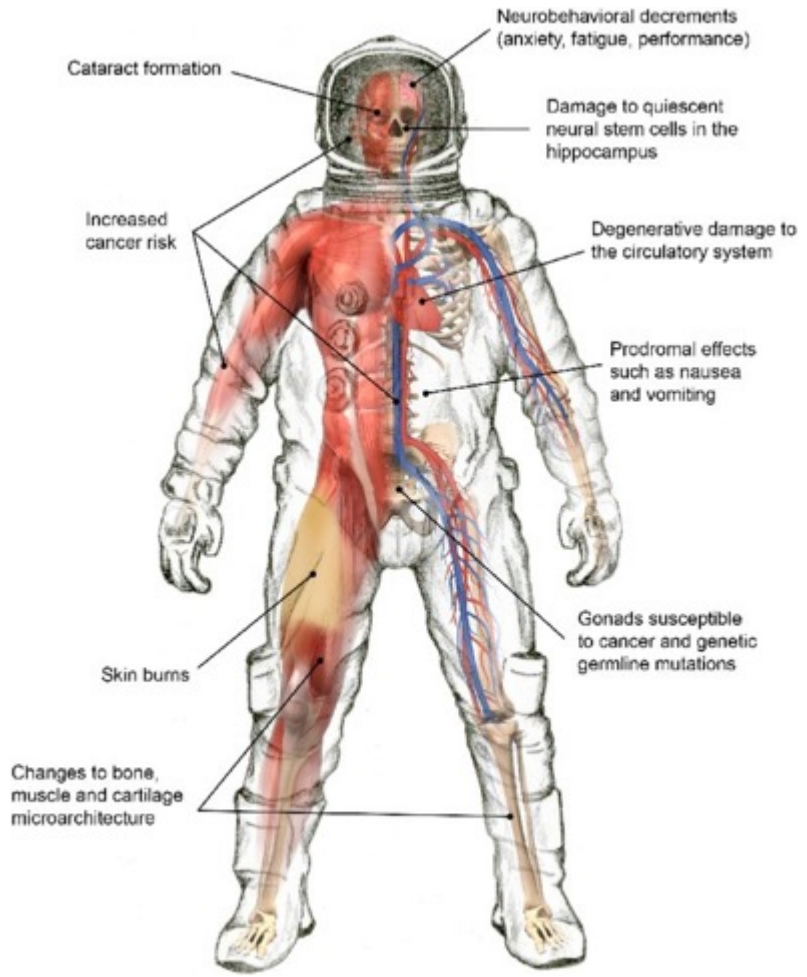


Credits: NASA

Space Health Risks On Astronauts





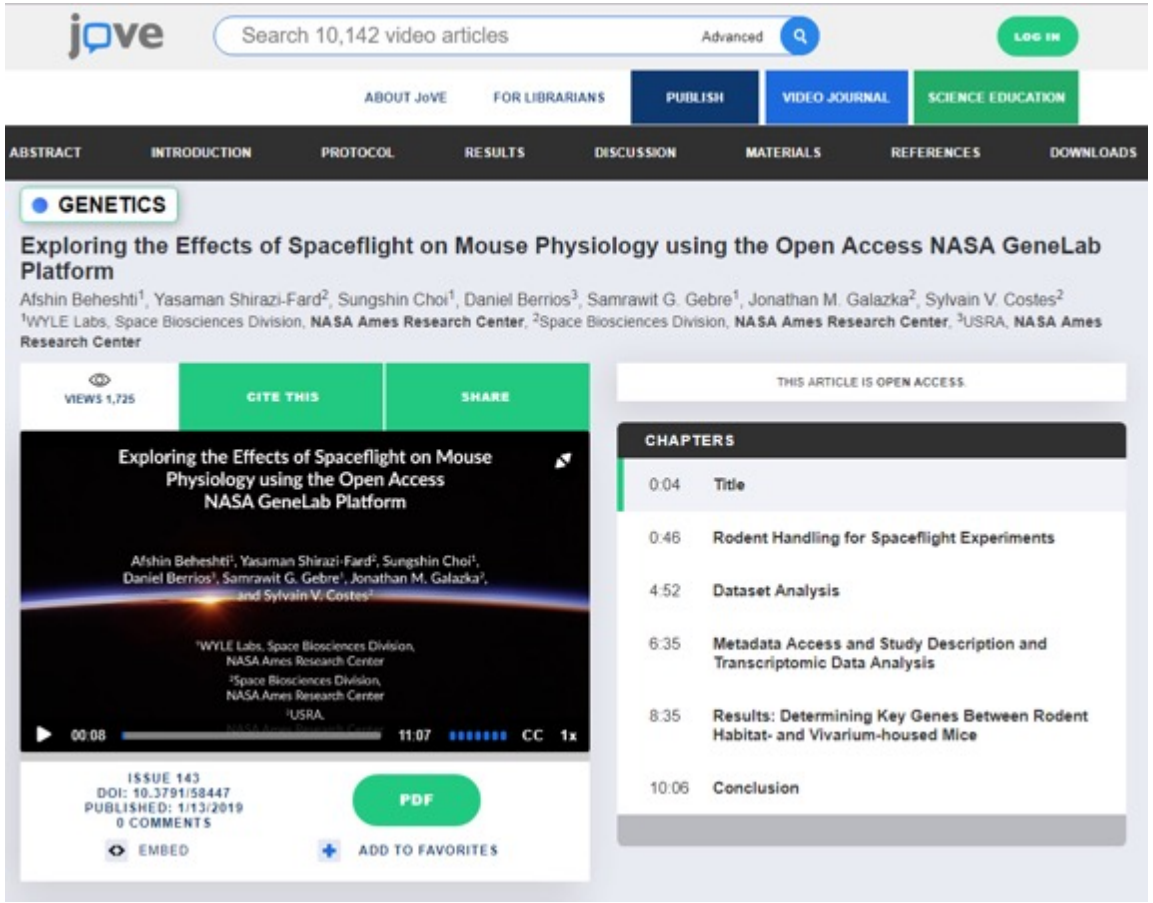


Select health effects due to space radiation exposures.

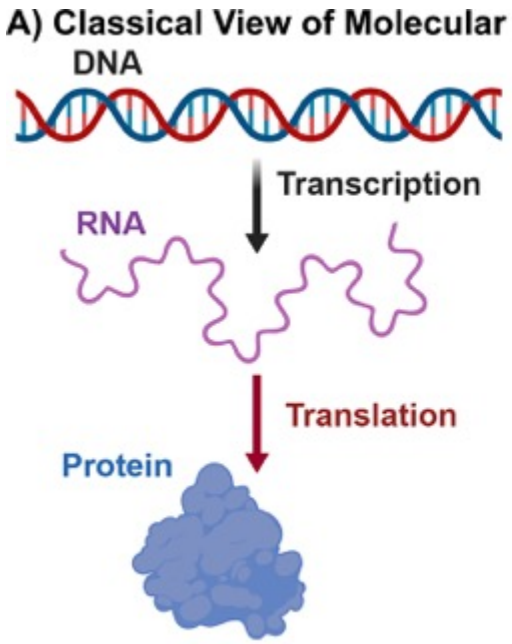
From: J. Chancellor et al., Space Radiation: The Number One Risk to Astronaut Health beyond Low Earth Orbit. *Life,* 4(3), 491-510;

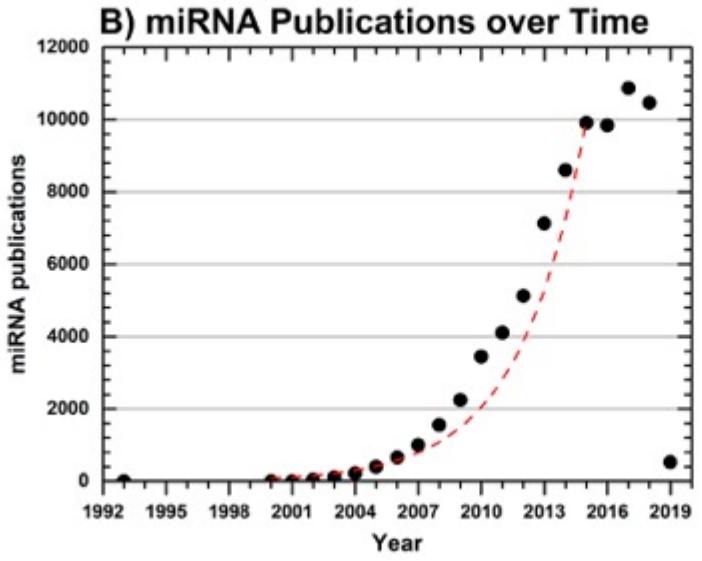
Systemic Alterations with Spaceflight Associated Health Risks: Determined Utilizing GeneLab datasets

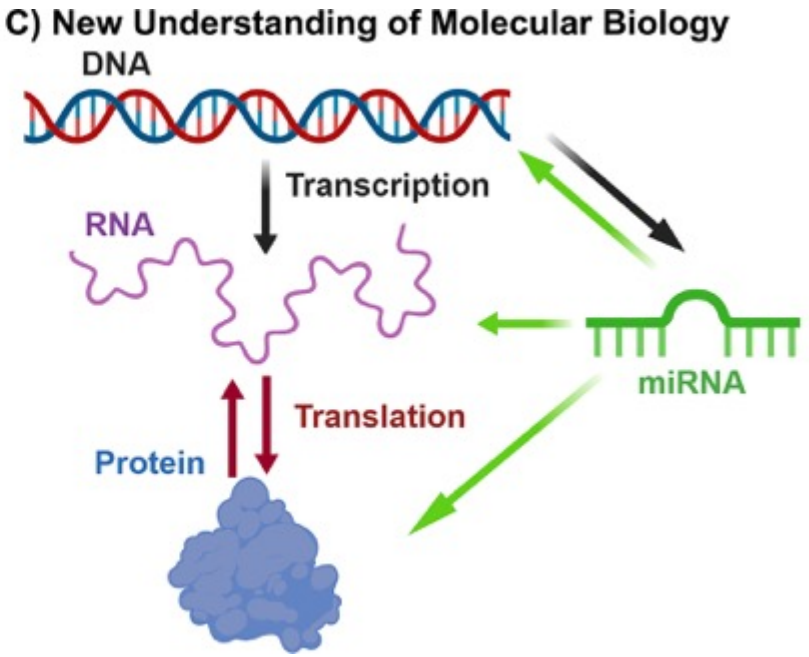
- **Circulating miRNA Signature Predicts Health Risks Associated with Radiation and Microgravity**
- **Multi-Omics Analysis using GeneLab database recognizes Mitochondrial Dysfunction as a mediator of spaceflight health risks**



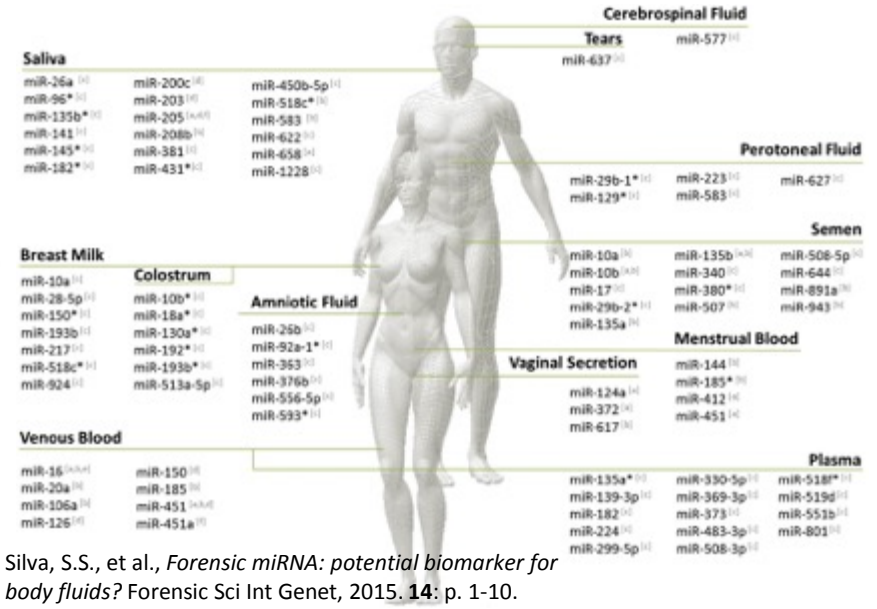
What are miRNAs and why study miRNAs





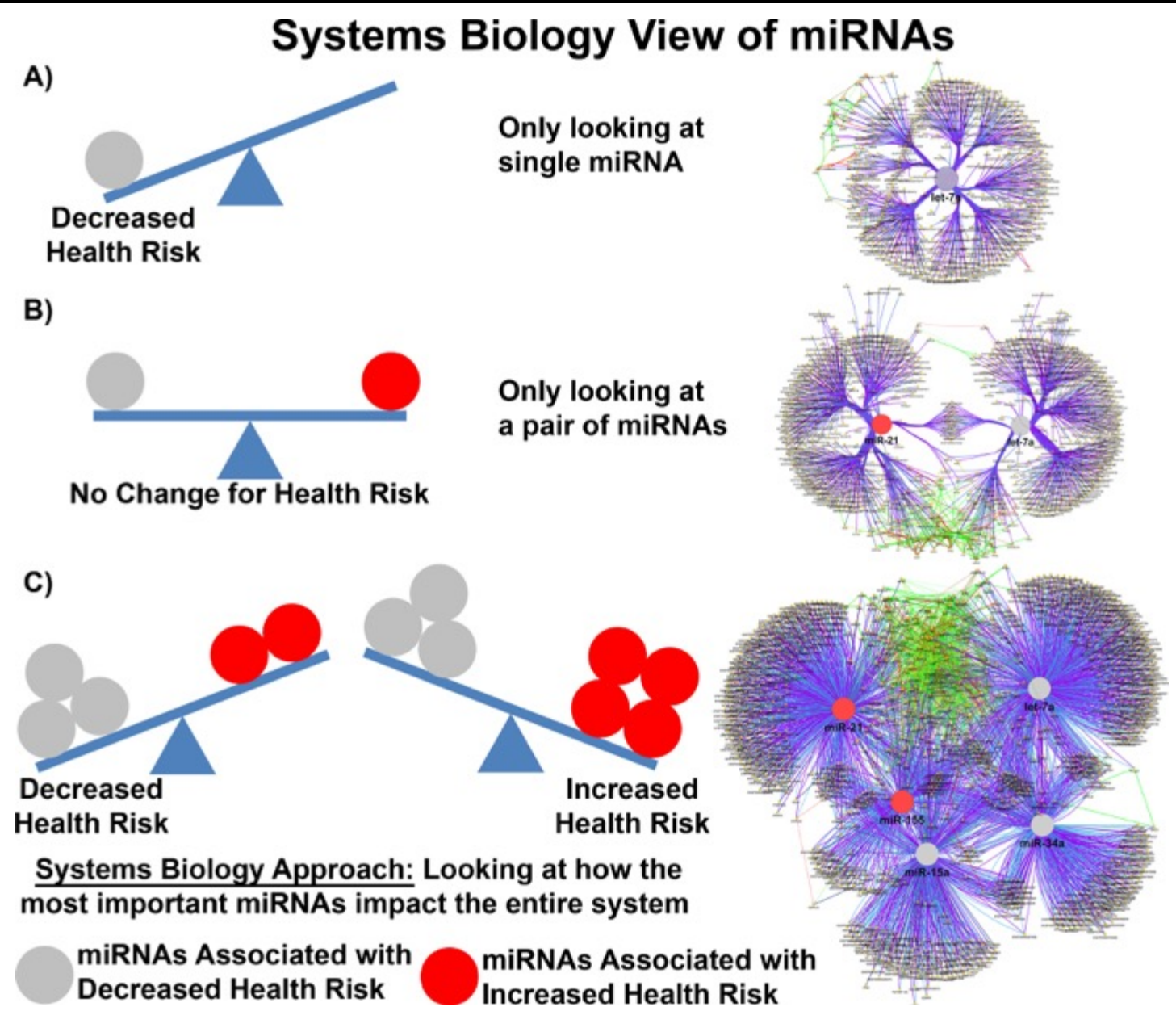


- **A single miRNA has been estimated to regulate up to 500 mRNAs.**
- **miRNAs are ~22nt**
- **Due to the size and stability of the miRNAs, it can float freely in the blood.**
- **miRNAs are now known to be involved in all aspects of diseases.**
- **miRNA are not only found in mammals, but everything else living: plants, microbes, fish, C. Elegans, fruit flies, insects, etc…**
- **miRNAs play a big role in radiation response (which also relates to space radiation).**



Silva, S.S., et al., *Forensic miRNA: potential biomarker for body fluids?* Forensic Sci Int Genet, 2015. **14**: p. 1-10.

Systems Biology View of miRNAs



PLOS ONE

RESEARCH ARTICLE

A microRNA signature and TGF-β1 response were identified as the key master regulators for spaceflight response

Afshin Beheshti[1☯*], Shayoni Ray[2☯*], Homer Fogle[1], Daniel Berrios[2], Sylvain V. Costes[3*]

1 WYLE, NASA Ames Research Center, Moffett Field, California, United States of America, 2 USRA, NASA Ames Research Center, Moffett Field, California, United States of America, 3 NASA Ames Research Center, Space Biosciences Division, Moffett Field, California, United States of America

☯ These authors contributed equally to this work.
* afshin.beheshti@nasa.gov (AB); sylvain.v.costes@nasa.gov (SVC)

Check for updates

OPEN ACCESS

Citation: Beheshti A, Ray S, Fogle H, Berrios D, Costes SV (2018) A microRNA signature and TGF-β1 response were identified as the key master regulators for spaceflight response. PLoS ONE 13 (7): e0199621. https://doi.org/10.1371/journal.pone.0199621

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Abstract

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International Journal of *Molecular Sciences*

MDPI

Article

GeneLab Database Analyses Suggest Long-Term Impact of Space Radiation on the Cardiovascular System by the Activation of *FYN* Through Reactive Oxygen Species

Afshin Beheshti [1,*], J. Tyson McDonald [2], Jack Miller [3], Peter Grabham [4] and Sylvain V. Costes [5,*]

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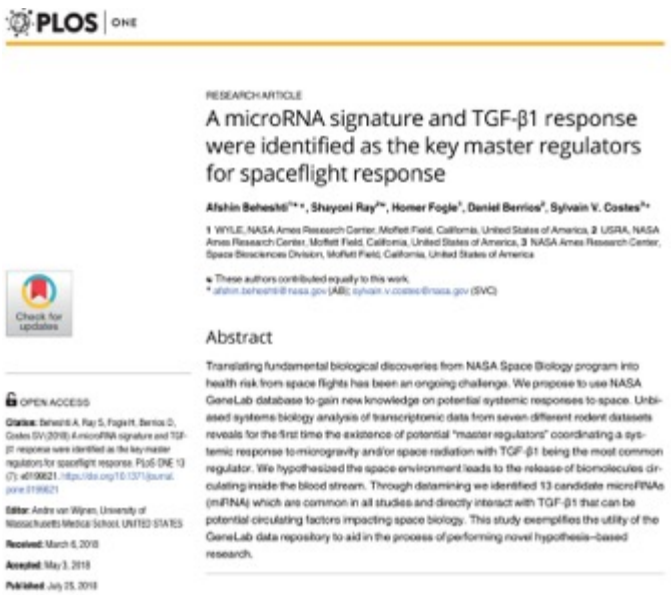
miRNA Signature Prediction Associated with Space Flight



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OPEN ACCESS

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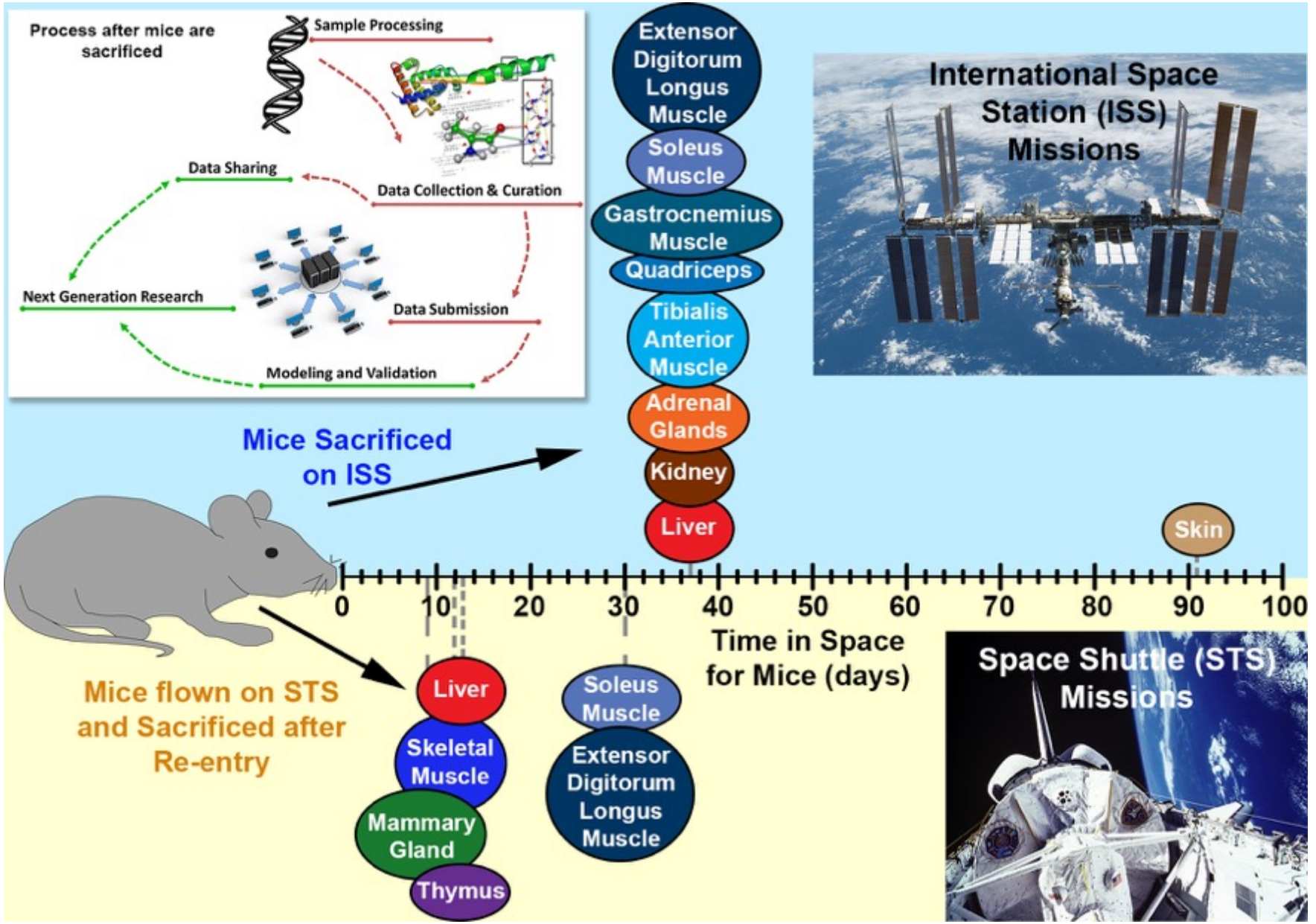
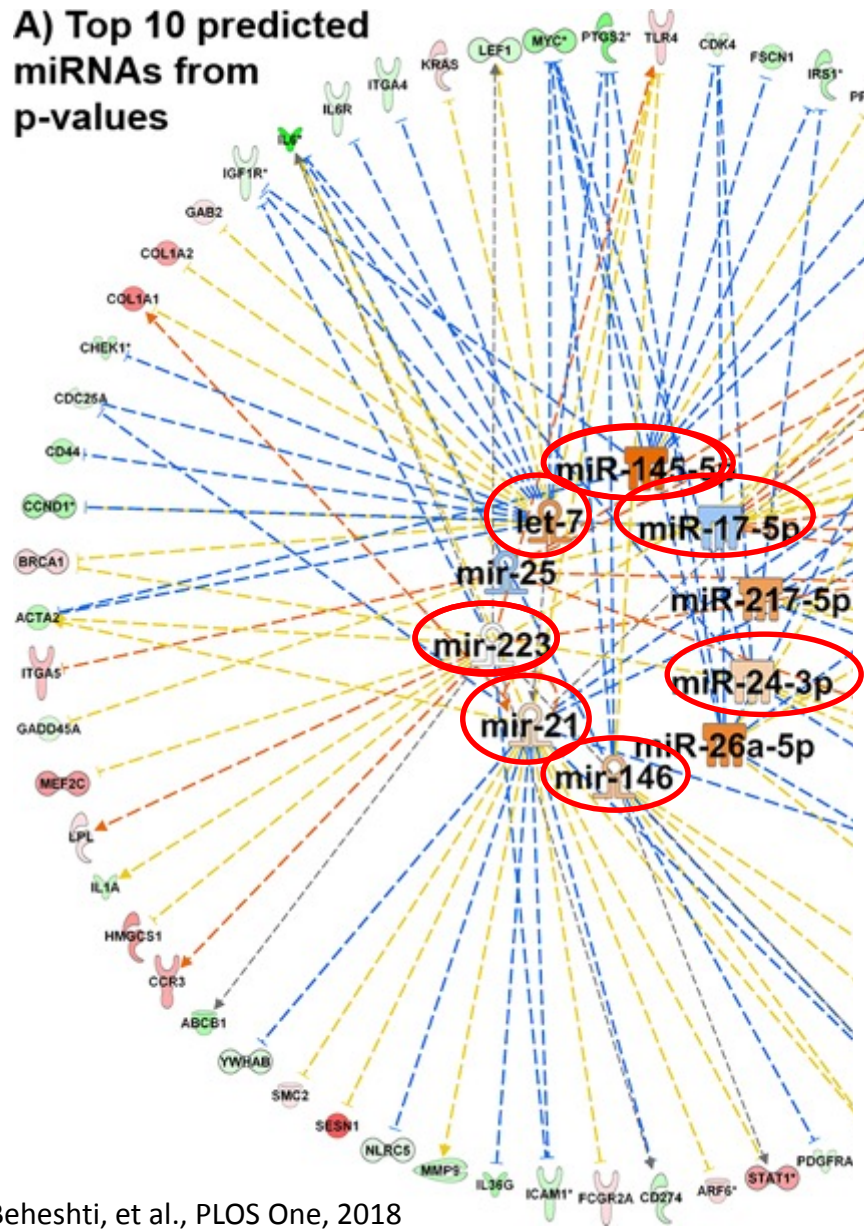
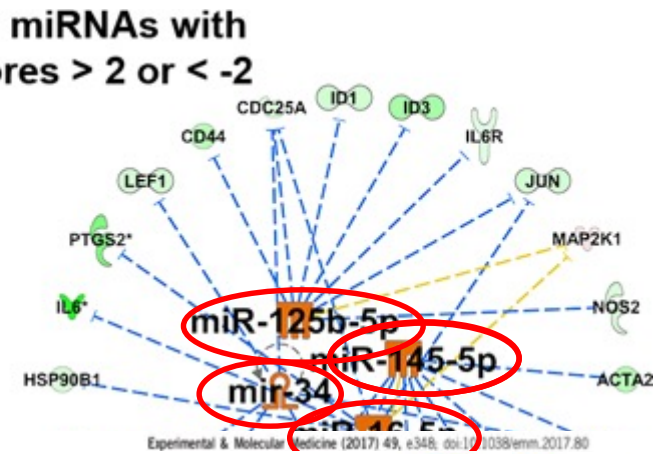
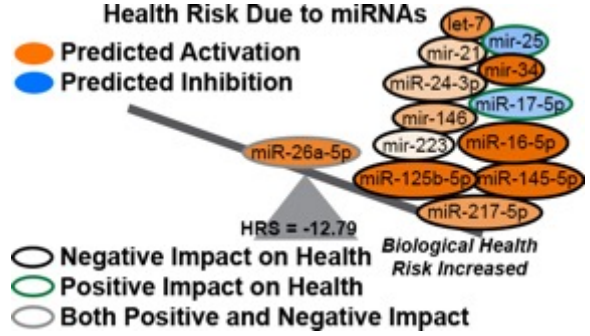


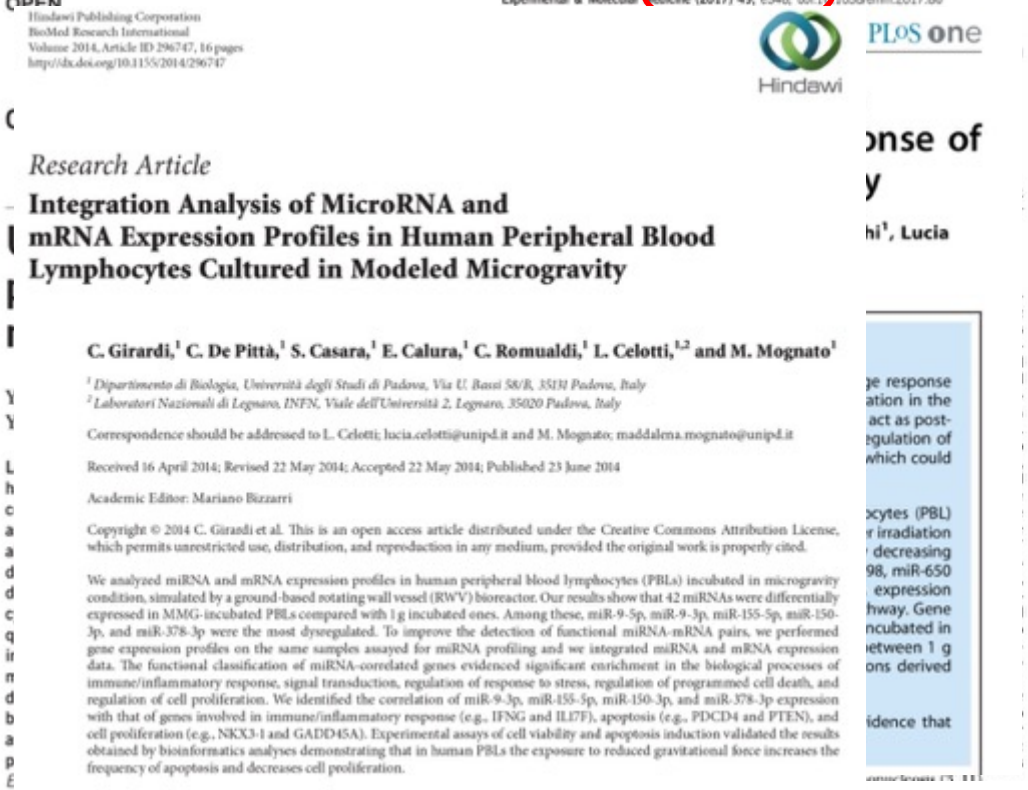
https://genelab.nasa.gov/

Predicted miRNAs Involved with Spaceflight









Hindawi Publishing Corporation
BioMed Research International
Volume 2014, Article ID 296747, 16 pages
http://dx.doi.org/10.1155/2014/296747

Research Article

Integration Analysis of MicroRNA and mRNA Expression Profiles in Human Peripheral Blood Lymphocytes Cultured in Modeled Microgravity

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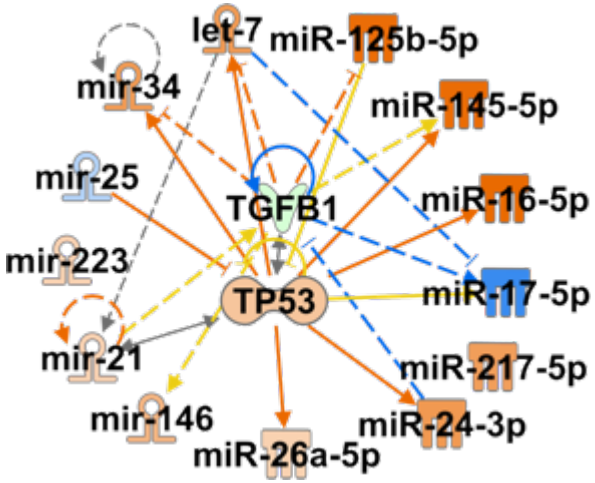
Academic Editor: Mariano Bizzarri

We analyzed miRNA and mRNA expression profiles in human peripheral blood lymphocytes (PBLs) incubated in microgravity condition, simulated by a ground-based rotating wall vessel (RWV) bioreactor. Our results show that 42 miRNAs were differentially expressed in MMG-incubated PBLs compared with 1 g incubated ones. Among these, miR-9-5p, miR-9-3p, miR-155-5p, miR-150-3p, and miR-378-3p were the most dysregulated. To improve the detection of functional miRNA-mRNA pairs, we performed gene expression profiles on the same samples assayed for miRNA profiling and we integrated miRNA and mRNA expression data. The functional classification of miRNA-correlated genes evidenced significant enrichment in the biological processes of immune/inflammatory response, signal transduction, regulation of response to stress, regulation of programmed cell death, and regulation of cell proliferation. We identified the correlation of miR-9-3p, miR-155-5p, miR-150-3p, and miR-378-3p expression with that of genes involved in immune/inflammatory response (e.g., IFNG and IL17F), apoptosis (e.g., PDCD4 and PTEN), and cell proliferation (e.g., NKX3-1 and GADD45A). Experimental assays of cell viability and apoptosis induction validated the results obtained by bioinformatics analyses demonstrating that in human PBLs the exposure to reduced gravitational force increases the frequency of apoptosis and decreases cell proliferation.



Beheshti, et al., PLOS One, 2018

Predict miRNAs with Space Radiation Cardiovascular Risk

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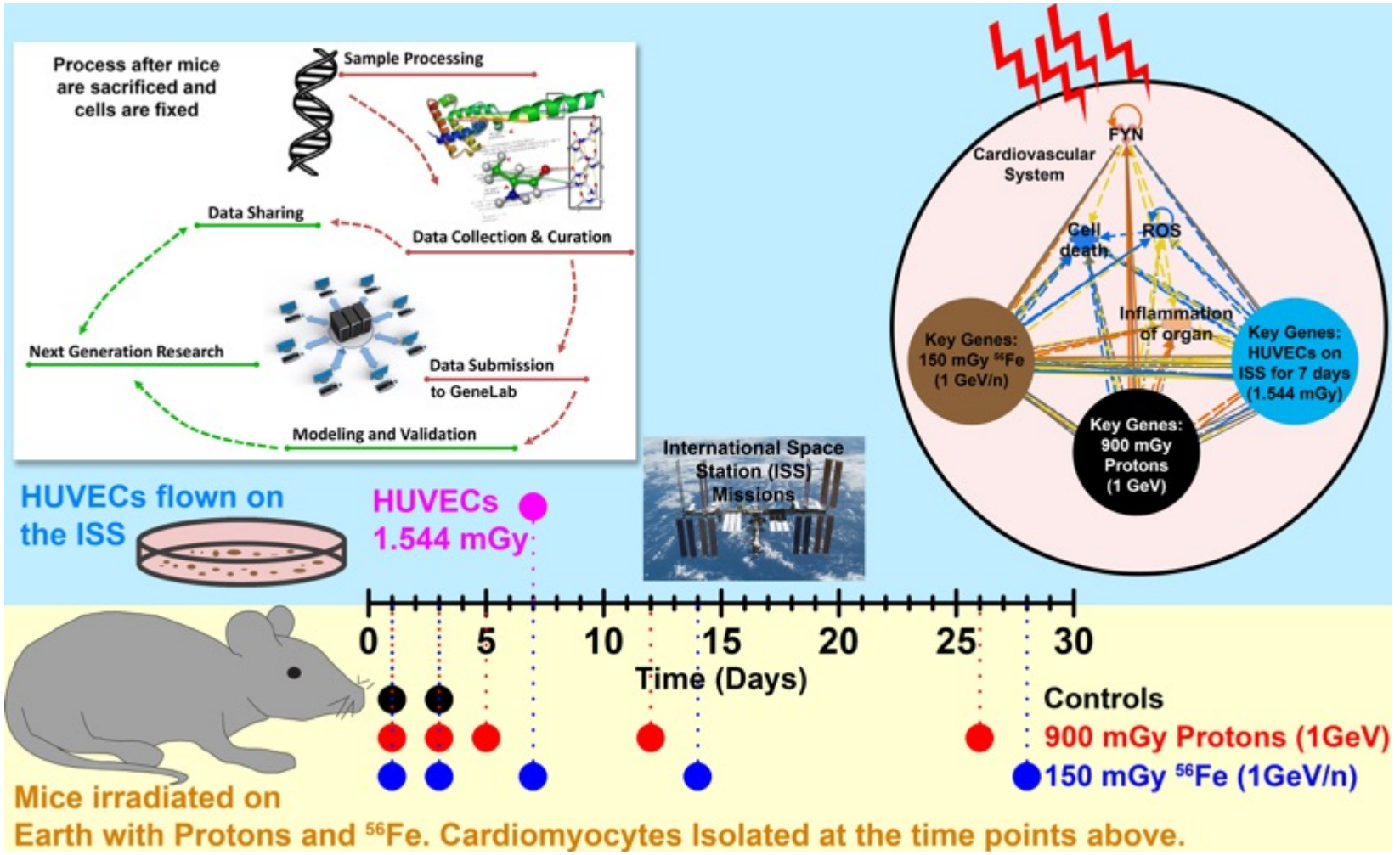
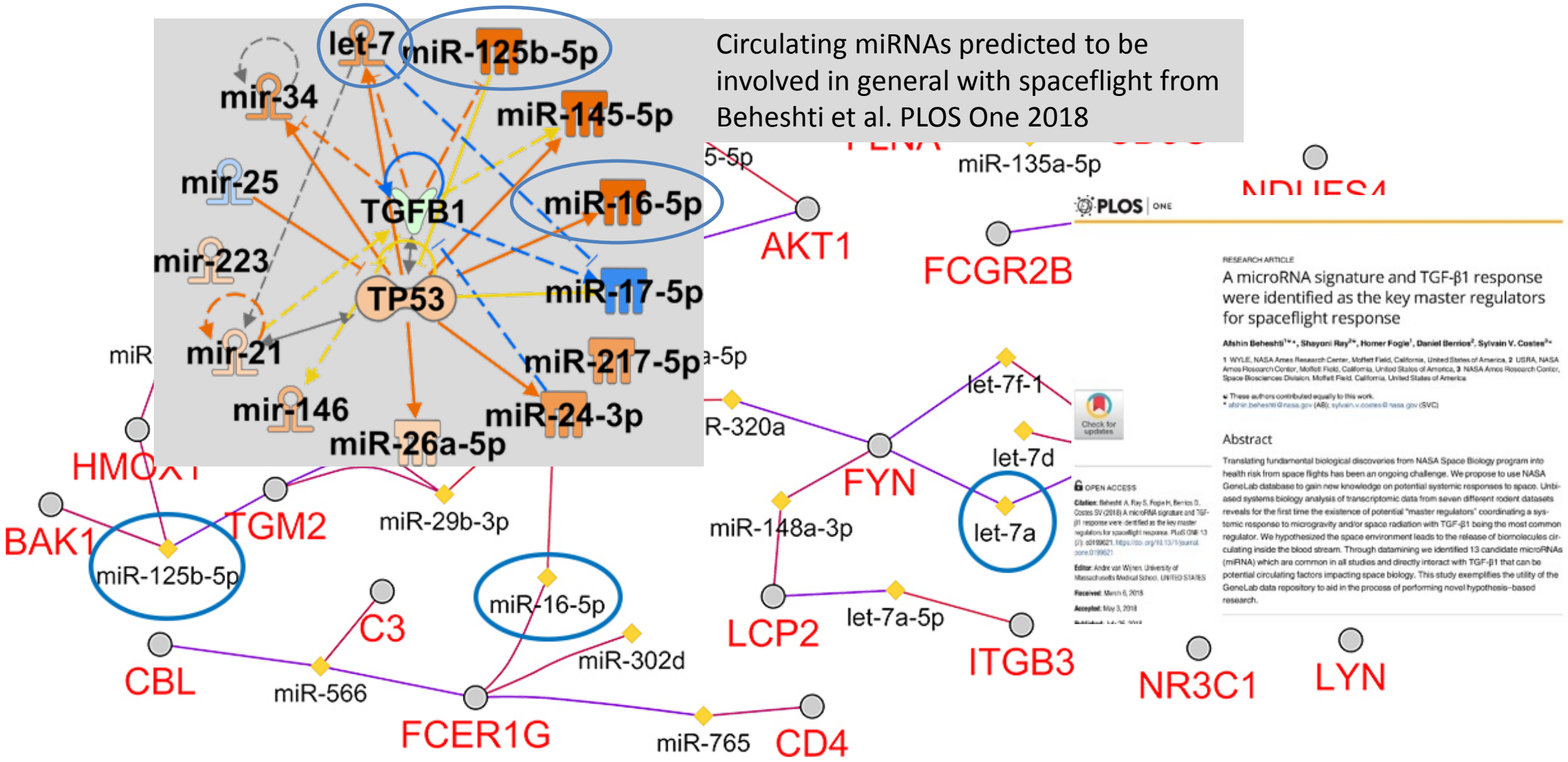
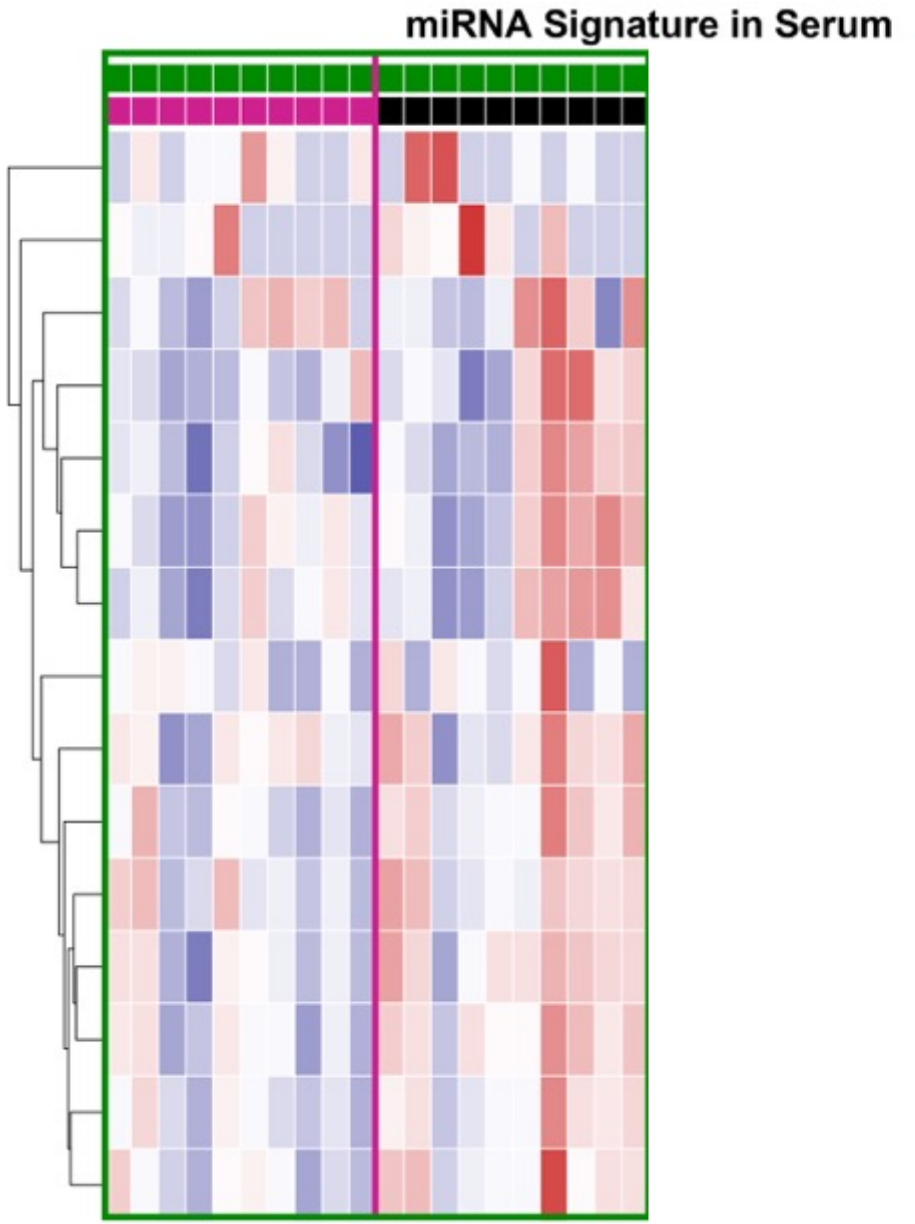


Predict miRNAs with Space Radiation Cardiovascular Risk

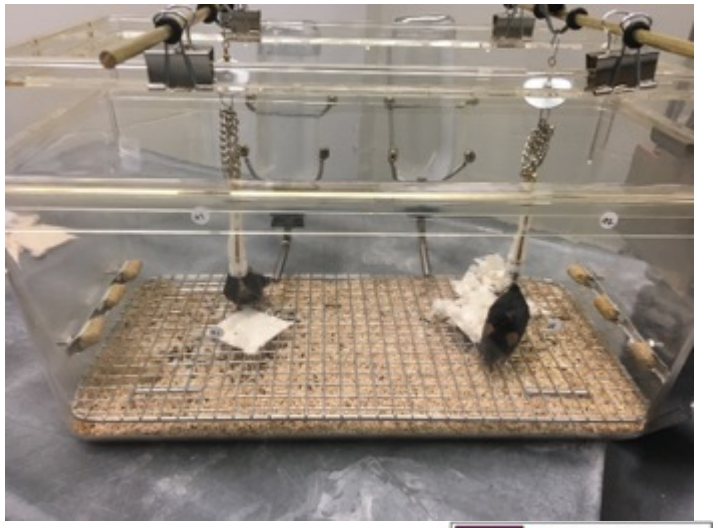
Circulating miRNAs predicted to be involved in general with spaceflight from Beheshti et al. PLOS One 2018

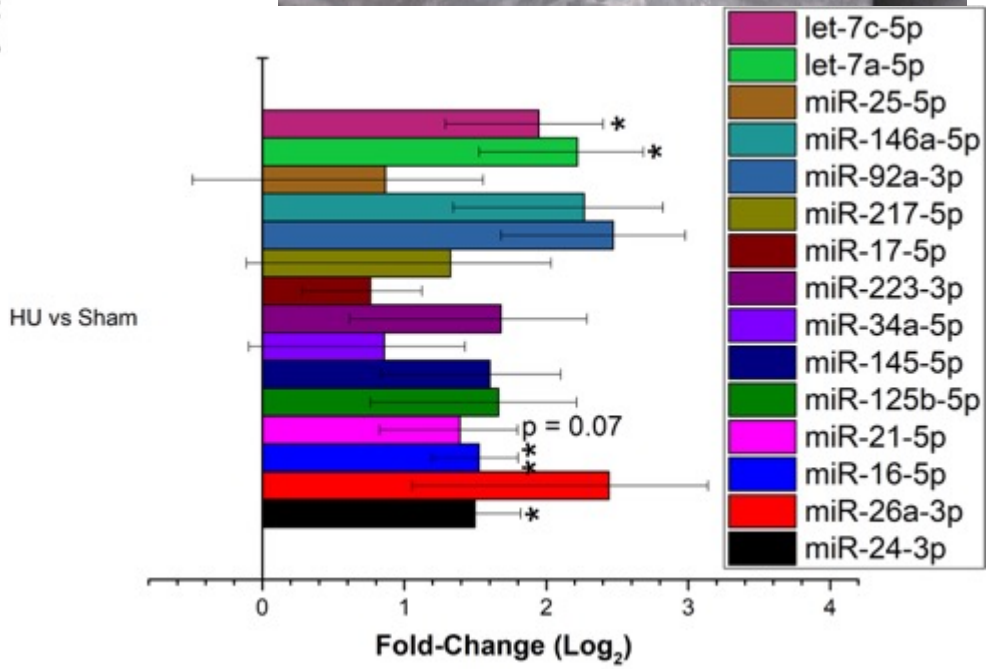


Presence of miRNA signature in Serum of Mice in Simulated Space Environment



Hindlimb Unloading

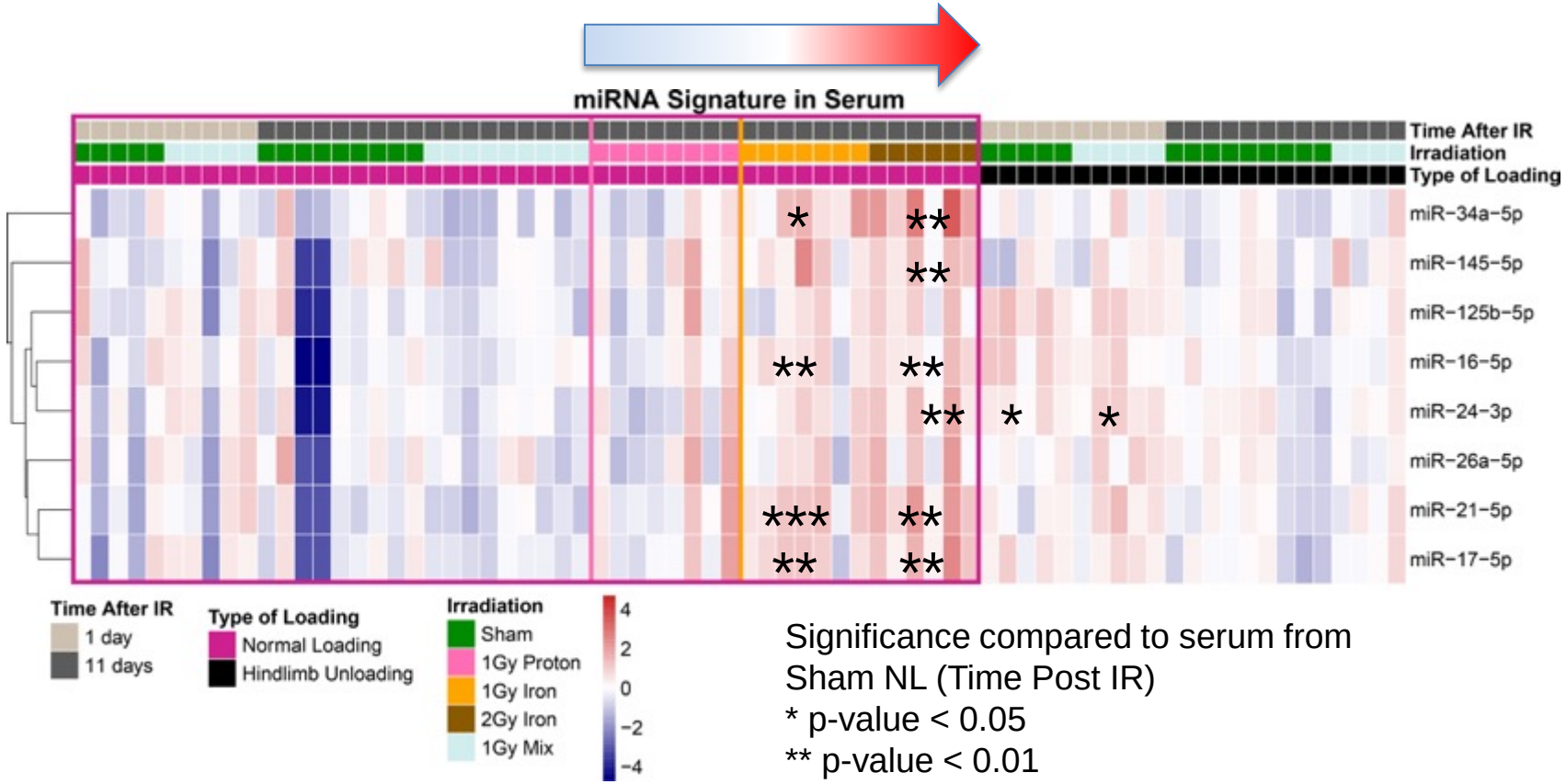




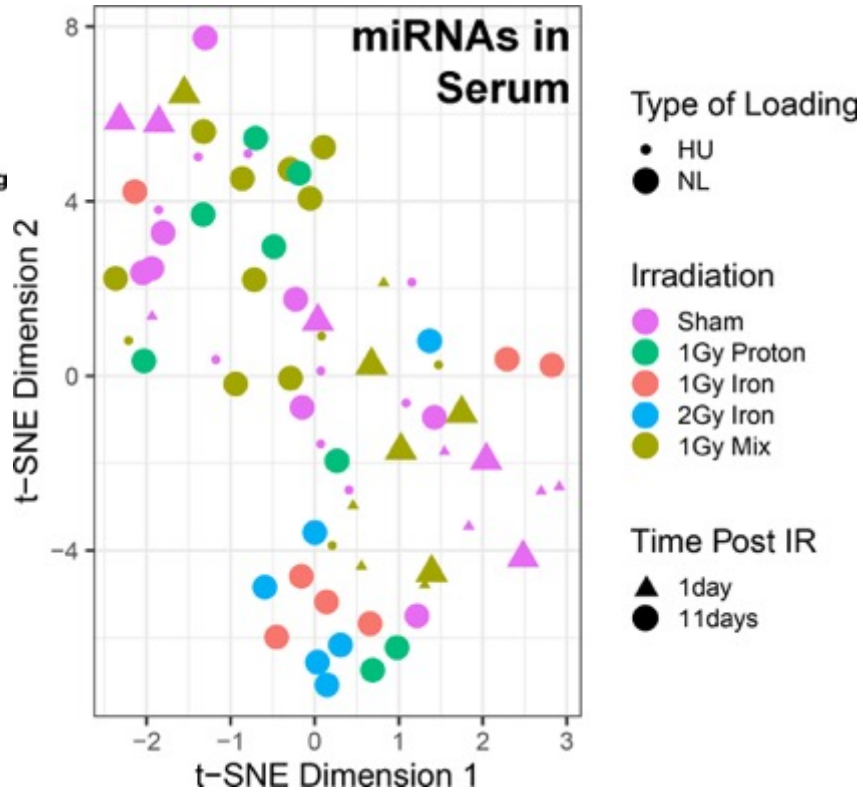
Preliminary data on miRNA signature Presence with Space Radiation

- HU for an initial three days followed by IR and continuation of HU for another 1 or 11 days
- Radiation exposure: Total body irradiation, conscious mice, 600 MeV/n ^{56}Fe (1 Gy and 2 Gy), 150 MeV Proton (1Gy) or '1Gy Mix' (0.5Gy ^{56}Fe and 0.5Gy Proton)

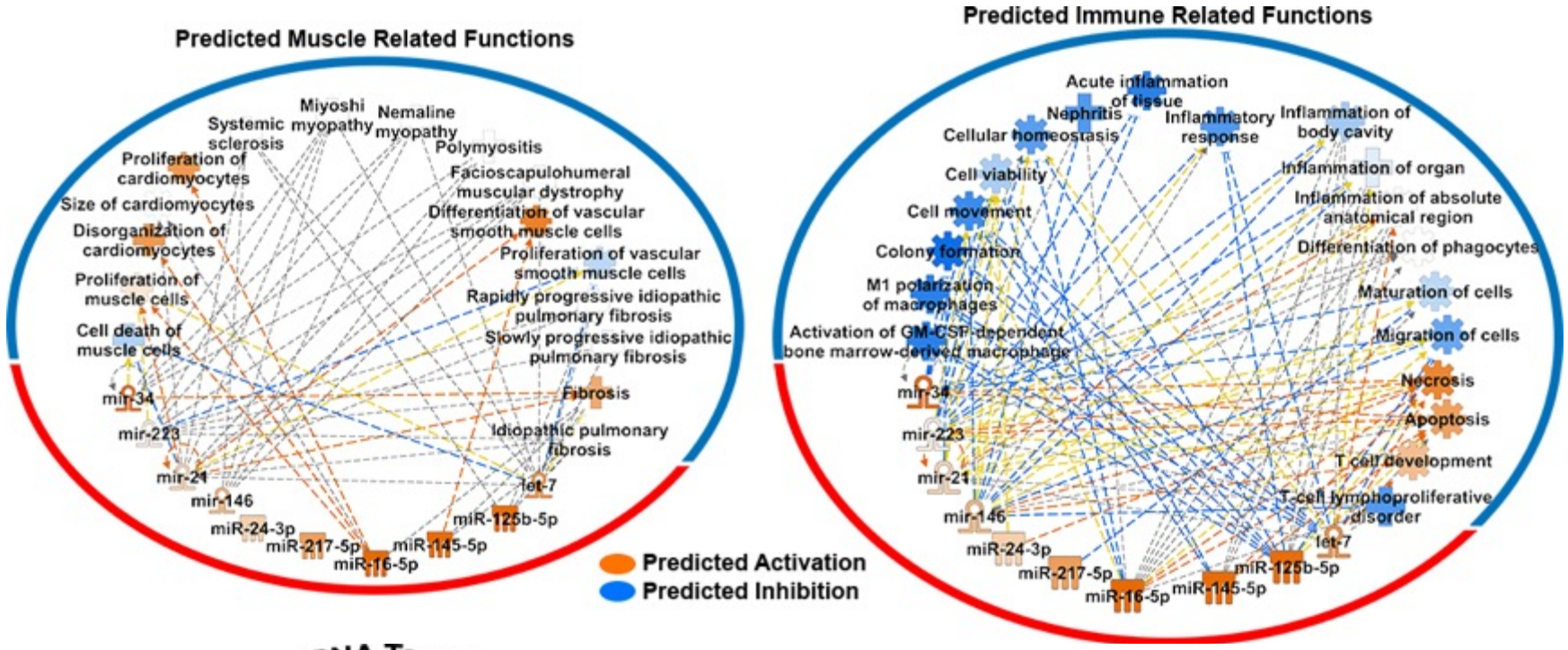
Increasing Dose and Ions causes increase miRNAs in serum

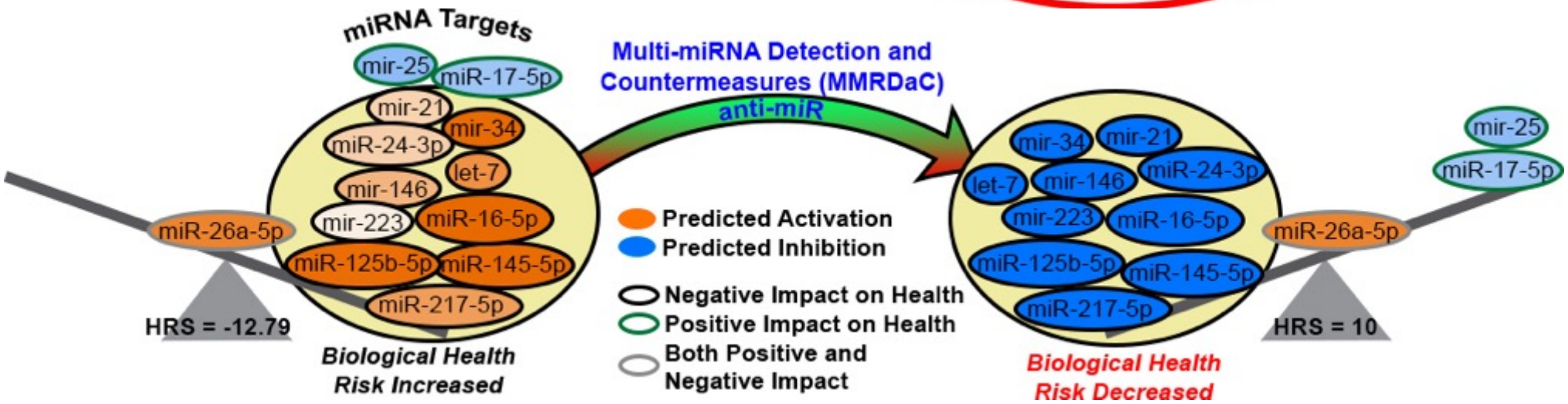


Significance compared to serum from Sham NL (Time Post IR)
* p-value < 0.05
** p-value < 0.01
*** p-value < 0.001



Impact of the Space Biology miRNA Signature on Functions and potential use for a novel Countermeasure





Acknowledgments for miRNA Studies

Sylvain Costes
Space Bio miRNAs

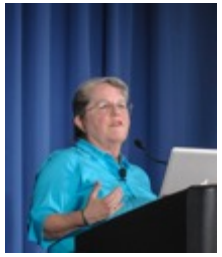
Egle Cekanaviciute
Quantifying miRNAs

Sherina Malkani
Quantifying miRNAs

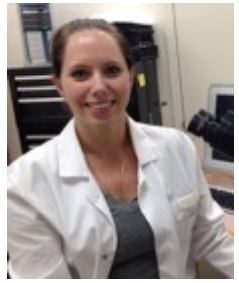
Ann-Sofie Schreurs
Provided Archived Tissues

Margareth Cheng-Campbell
Quantifying miRNAs

Yasaman Shirazi
Provided Archived Tissues



Ruth Globus
Provided Archived Tissues



Elizabeth Blaber
Space Bio miRNAs

J. Tyson McDonald
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Charles Vanderburg
BROAD INSTITUTE

Peter Grabham
COLUMBIA UNIVERSITY
IRVING MEDICAL CENTER

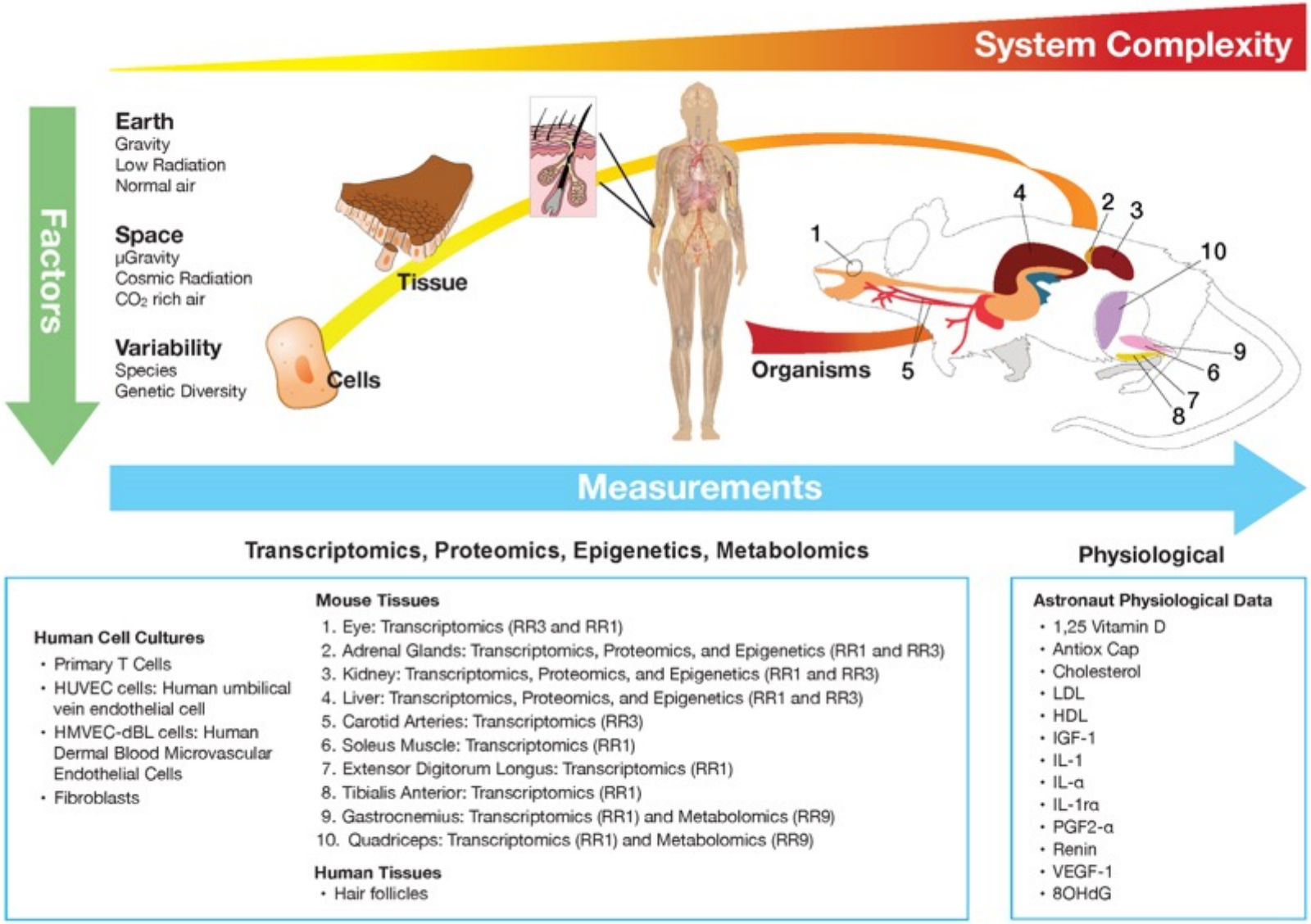
This work is supported by:

16-ROSBFP GL-0005: NNH16ZTT001N-FG Appendix G: Solicitation of Proposals for Flight and Ground Space Biology Research

The Translational Research Institute through NASA Cooperative Agreement NNX16AO69A (T-0404)

TRANSLATIONAL RESEARCH INSTITUTE FOR SPACE HEALTH

Multi-Omics Analysis using GeneLab database recognizes Mitochondrial Dysfunction as a mediator of spaceflight health risks



- Paper being written
- Plan to submit paper by end of September
- Target journal to submit is *New England Journal of Medicine*
  - Contacted the editor of the journal and he was interested in the paper and encouraged submission to their journal.

AWG Members Involved

Kathleen Fisch

Brin Rosenthal

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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

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J. Tyson McDonald

HAMPTON UNIVERSITY
THE STANDARD OF EXCELLENCE

Gary Hardiman

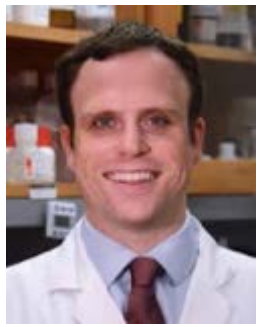
Willian da Silveira

QUEEN'S UNIVERSITY BELFAST

Jeffrey Scott Willey

WAKE FOREST UNIVERSITY

AWG Members Involved



Chris Mason

Cem Meydan

Jonathan Foox

Flavia Rius

Yared Kidane

Evagelia C. Laiakis

Robert Meller, D.Phil

Cornell University

Texas Scottish Rite Hospital for Children

Georgetown University Medical Center

Morehouse School of Medicine

Susana Zanello

Scott Smith

Sara Zwart

Sonja Schrepfer

Dong Wang

Afshin Beheshti

Sylvain Costes

Space Center Houston

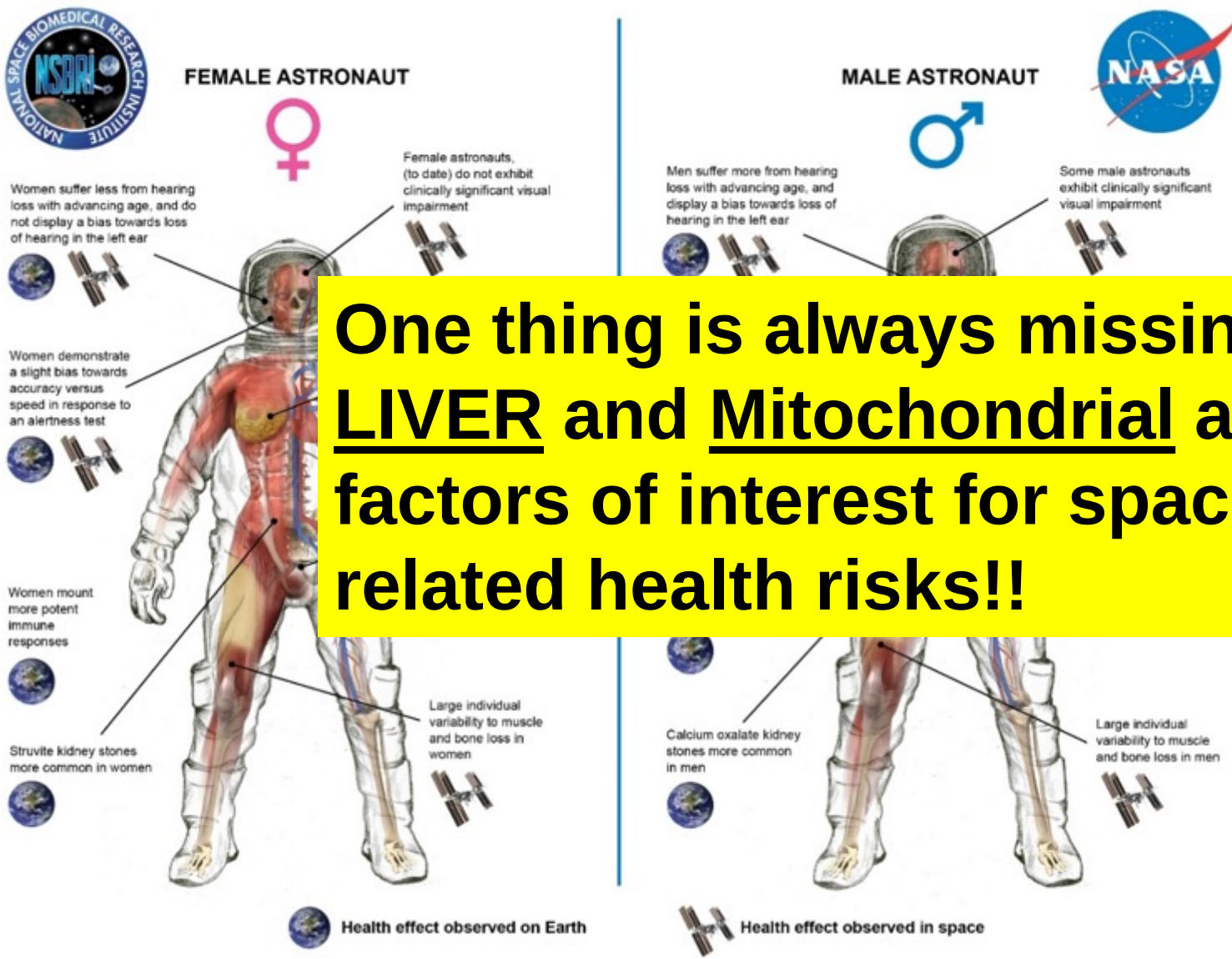
Manned Space Flight Education Foundation

UCSF

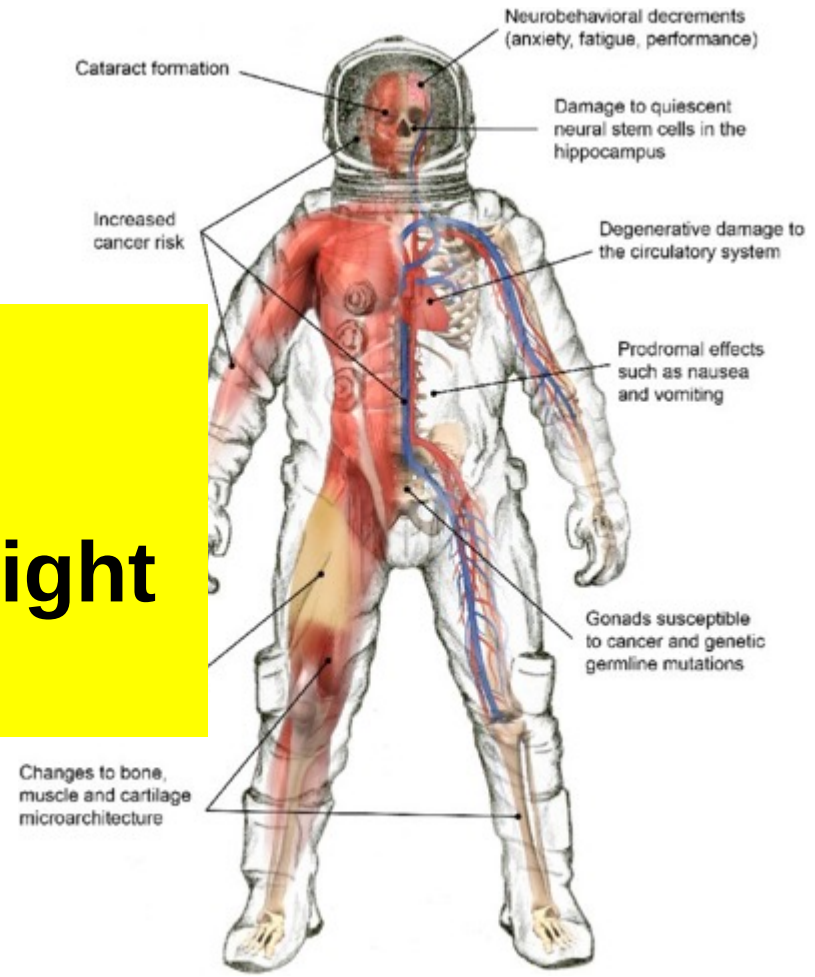
University of California San Francisco

Ames Research Center

Health Risks On Astronauts in Space



One thing is always missing: LIVER and Mitochondrial as factors of interest for spaceflight related health risks!!



Select health effects due to space radiation exposures.

From: J. Chancellor et al., Space Radiation: The Number One Risk to Astronaut Health beyond Low Earth Orbit. *Life,* 4(3), 491-510;

The Mitochodrial Stress Response

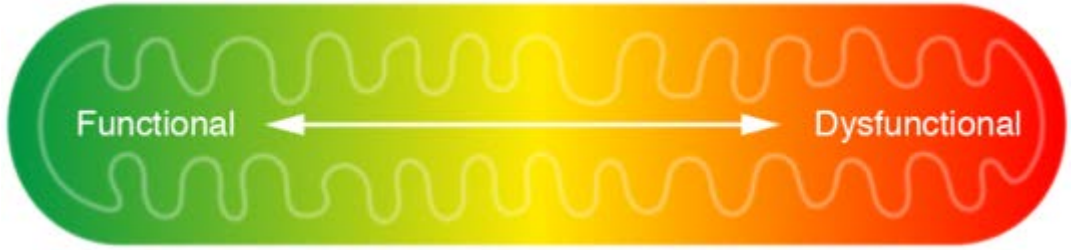
ATP
Energy

Growth/adaptation
Biosynthesis
Protein modification
Mitochondrial-nuclear communication

Thermogenesis

Inflammation
mtDNA or peptides
ROS

Cell death
mPTP opening
Cytochrome *c* release
Energy deprivation



Ca^{2+} transport
Metabolic stimulation
Stress response
Ca^{2+} homeostasis

ROS
Oxidative stress
Redox regulation
Cell signaling

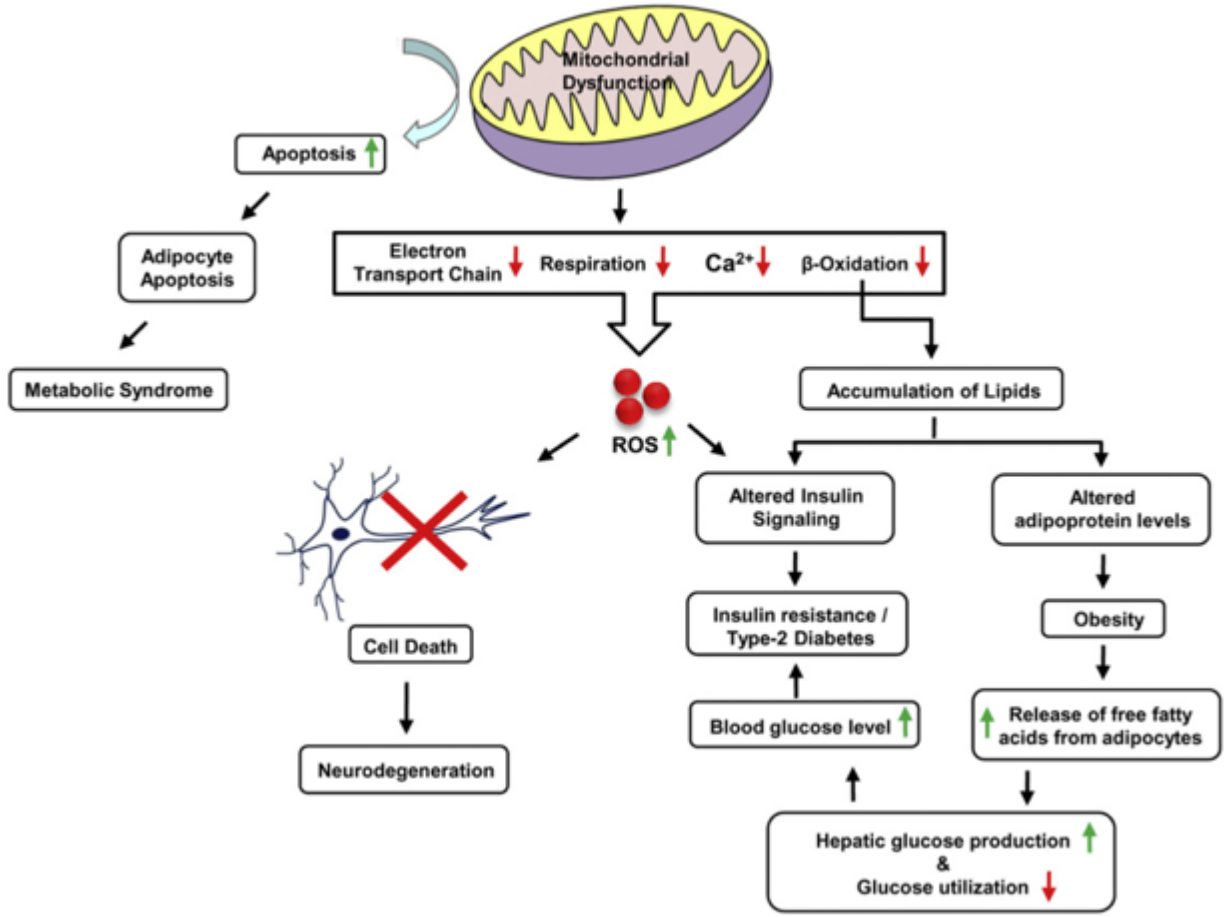
JCI The Journal of Clinical Investigation

Mitochondrial dysfunction in pathophysiology of heart failure

Bo Zhou, Rong Tian

J Clin Invest 2018;128(9):3716-3726. https://doi.org/10.1172/JCI120849.

Review Series

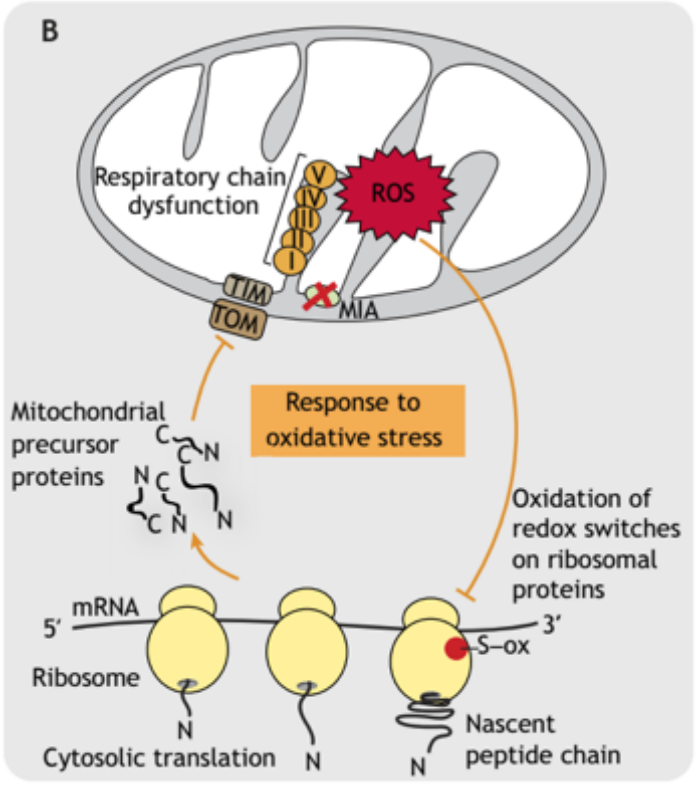


Linking mitochondrial dysfunction, metabolic syndrome and stress signaling in Neurodegeneration☆

Saurabh Kumar Jha [1], Niraj Kumar Jha [1], Dhiraj Kumar, Rashmi K. Ambasta, Pravir Kumar *

The Mitochodrial Stress Response

Respiratory Chain Dysfunction resulting in halt of translation



Cell arrest in response to oxidative stress

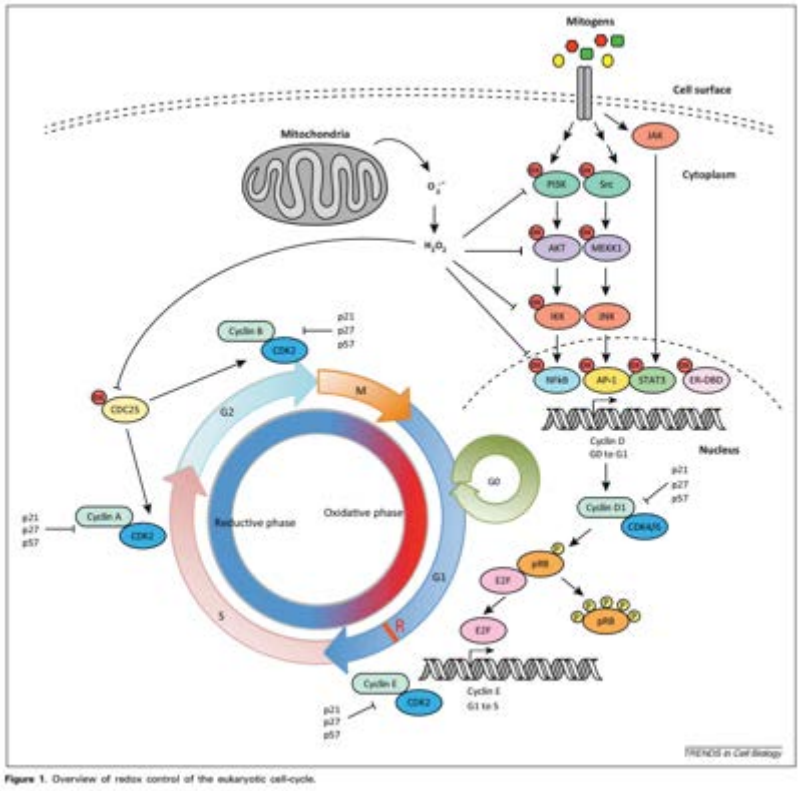
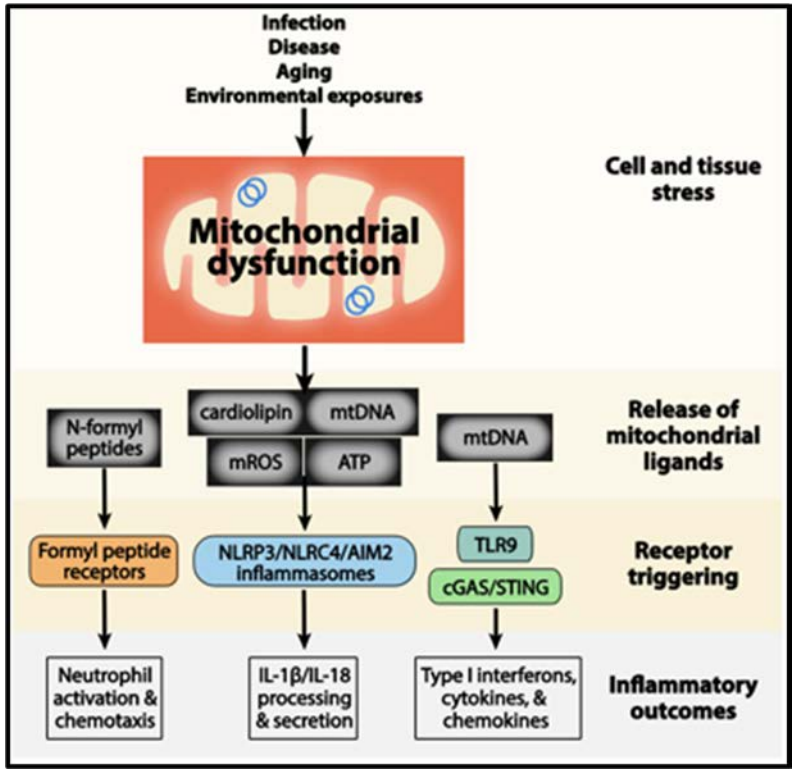


Figure 1. Overview of redox control of the eukaryotic cell-cycle.

Mitochondrial stress as a trigger innate immune responses



Journal of Cell Science

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REVIEW

Mitochondrial stress-dependent regulation of cellular protein synthesis

Ulrike Topf, Barbara Uszczynska-Ratajczak, Agnieszka Chacinska

Journal of Cell Science 2019 132: jcs226258 doi: 10.1242/jcs.226258 Published 26 April 2019

Trends in Cell Biology

REVIEW | VOLUME 22, ISSUE 11, P592-601, NOVEMBER 01, 2012

Redox control of cell proliferation

Joyce Chiu • Ian W. Dawes

Published: August 28, 2012 • DOI: https://doi.org/10.1016/j.tcb.2012.08.002

Toxicology

Volume 391, 1 November 2017, Pages 54-63

Mitochondrial dysfunction as a trigger of innate immune responses and inflammation

A. Phillip West

Show more

https://doi.org/10.1016/j.tox.2017.07.016

JCI The Journal of Clinical Investigation

Mitochondrial dysfunction in pathophysiology of heart failure

Bo Zhou, Rong Tian

J Clin Invest. 2018;128(9):3716-3726. https://doi.org/10.1172/JCI120849.

Review Series

The Mitochodrial Stress Response

Mitochondrial Dysfunction Impacts Many Organs

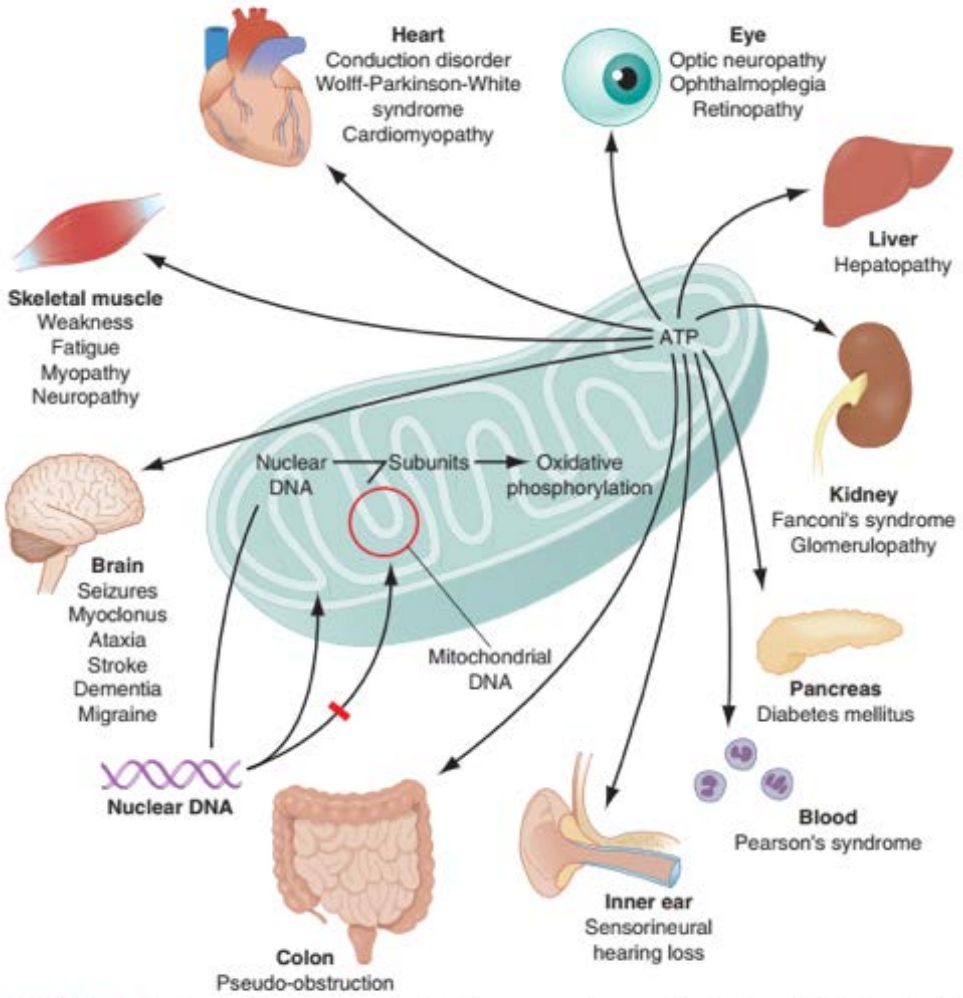


FIGURE 85e-1 **Dual genetic control and multiple organ system manifestations of mitochondrial disease.** *(Reproduced with permission from DR Johns: Mitochondrial DNA and disease. N Engl J Med 333:638, 1995.)*

Mitochondrial Dysfunction May Differ Between Organs

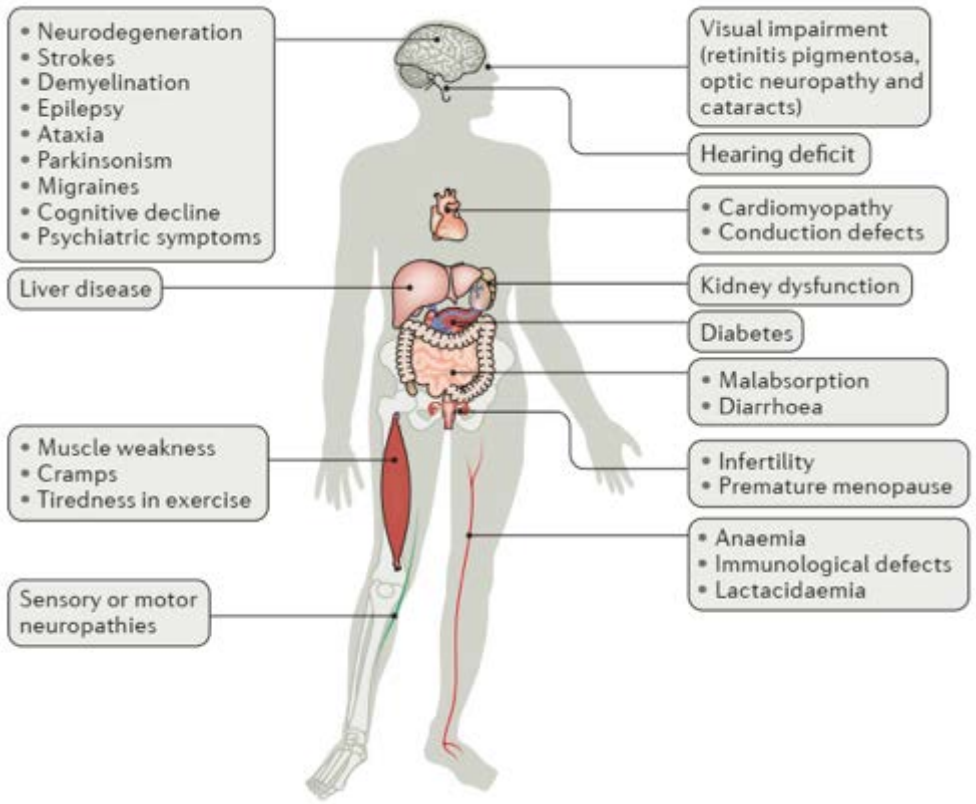
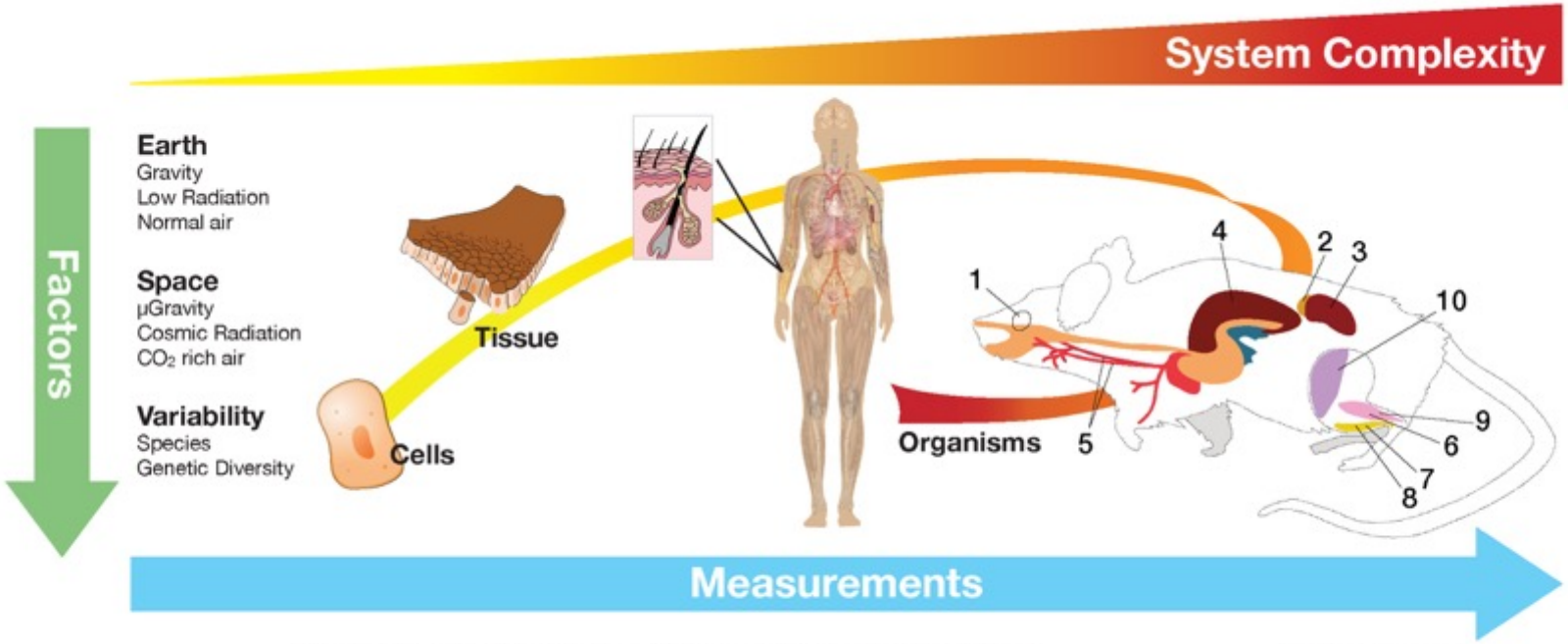


Figure 1 | **The variability of mitochondrial disease manifestations.** Mitochondrial diseases can manifest both in children and in adults, and can present in various organs, including in multiple organs that may have no apparent functional links to each other, such as the brain and liver, or pancreatic β-cells and the auditory system. Sometimes manifestations only affect one tissue, such as the heart or the optic nerve. Children may recover from one phenotype and later develop another — for example, in Pearson syndrome, the primary manifestation is exocrine pancreatic dysfunction and megaloblastic anaemia, and the survivors may later develop brain disease. Typically, these disorders are progressive.

Nat Rev Mol Cell Biol. 2018 Feb;19(2):77-92. doi: 10.1038/nrm.2017.66.

Multi-Omics Analysis using GeneLab database recognizes Mitochondrial Dysfunction as a mediator of spaceflight health risks



Transcriptomics, Proteomics, Epigenetics, Metabolomics

Human Cell Cultures

- Primary T Cells
- HUVEC cells: Human umbilical vein endothelial cell
- HMVEC-dBL cells: Human Dermal Blood Microvascular Endothelial Cells
- 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. Carotid Arteries: Transcriptomics (RR3)
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

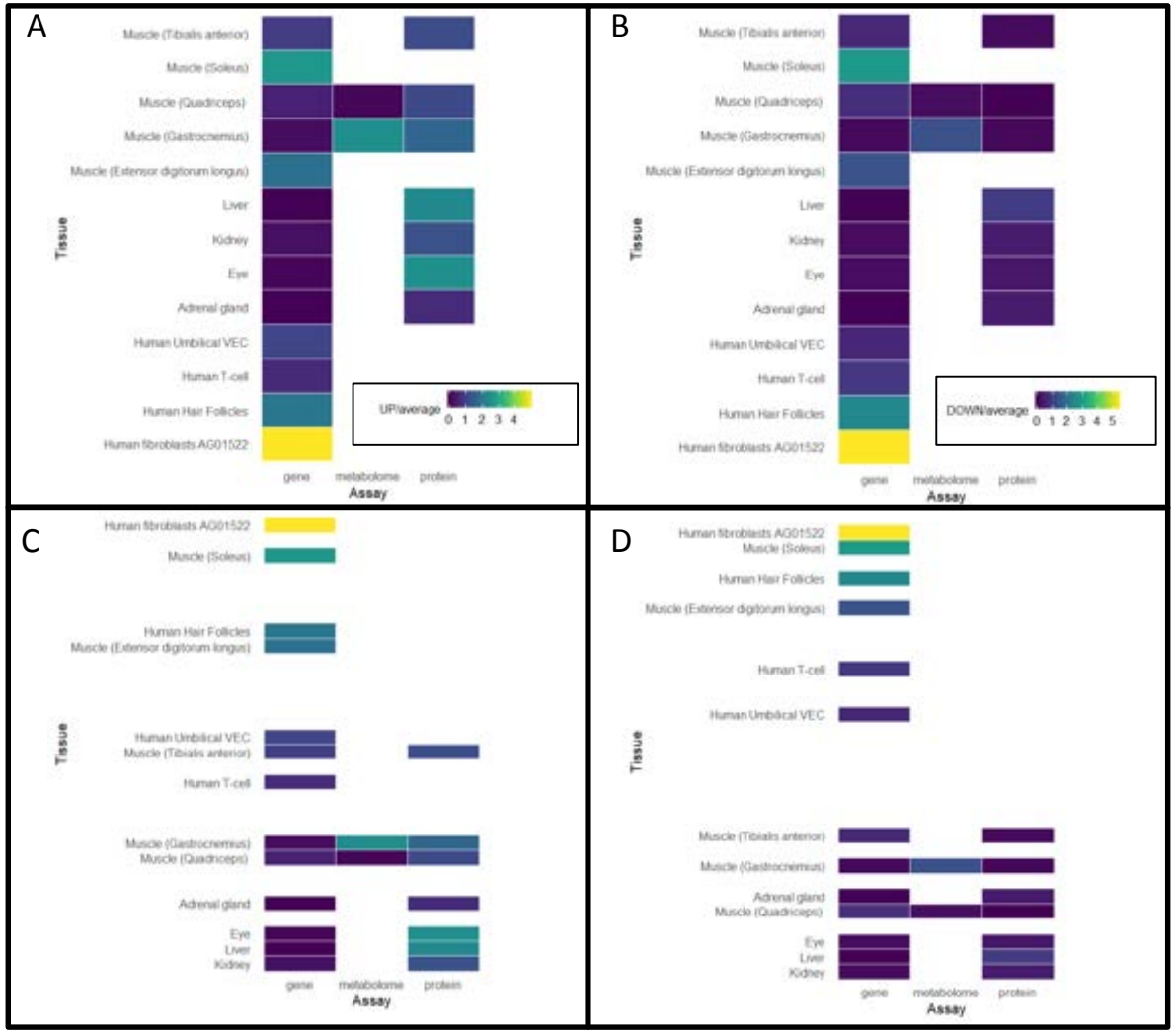
- Hair follicles

Physiological

Astronaut Physiological Data

- 1,25 Vitamin D
- Antiox Cap
- Cholesterol
- LDL
- HDL
- IGF-1
- IL-1
- IL-α
- IL-1rα
- PGF2-α
- Renin
- VEGF-1
- 8OHdG

Quantitative Response to Spaceflight Global view of the data



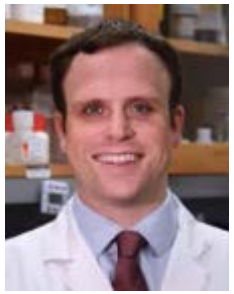
Deanne Taylor

Hossein Fazelinia

Komal Rathi

Children's Hospital of Philadelphia

Perelman School of Medicine University of Pennsylvania



Chris Mason

Cem Meydan

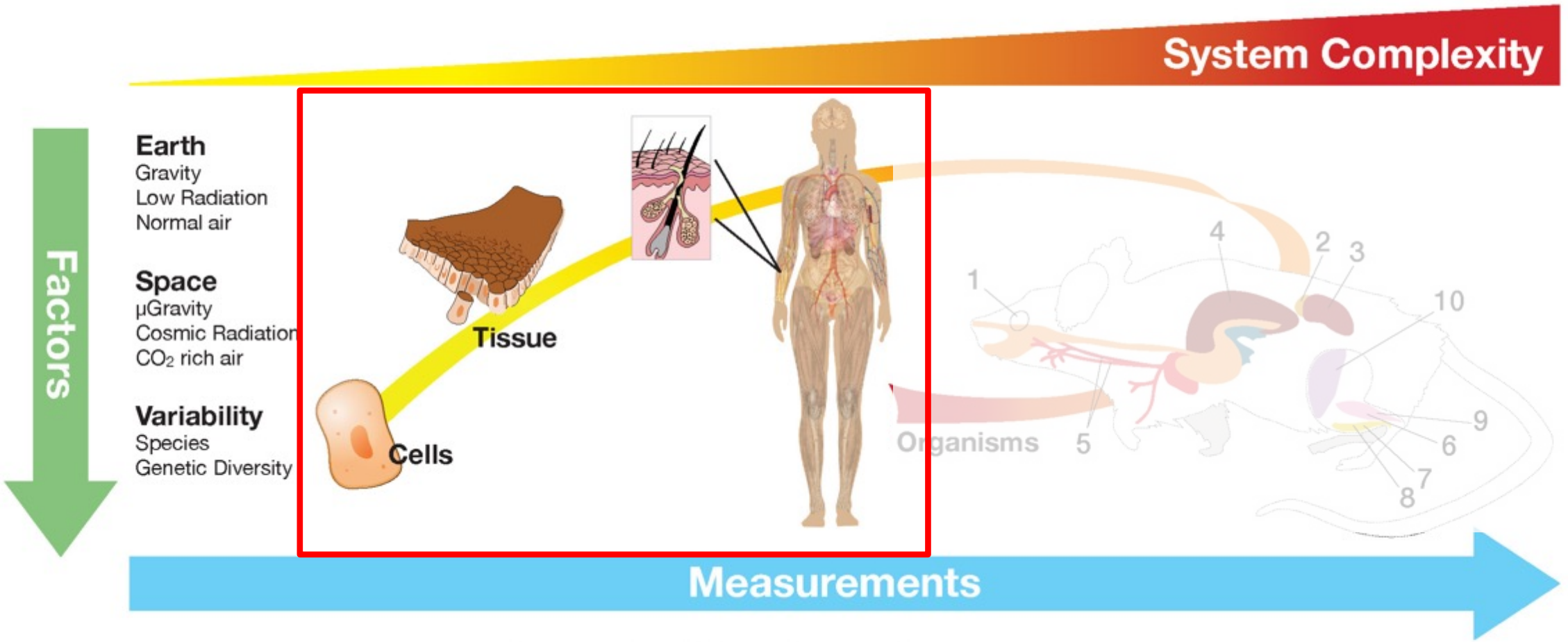
Jonathan Foox

Cornell University

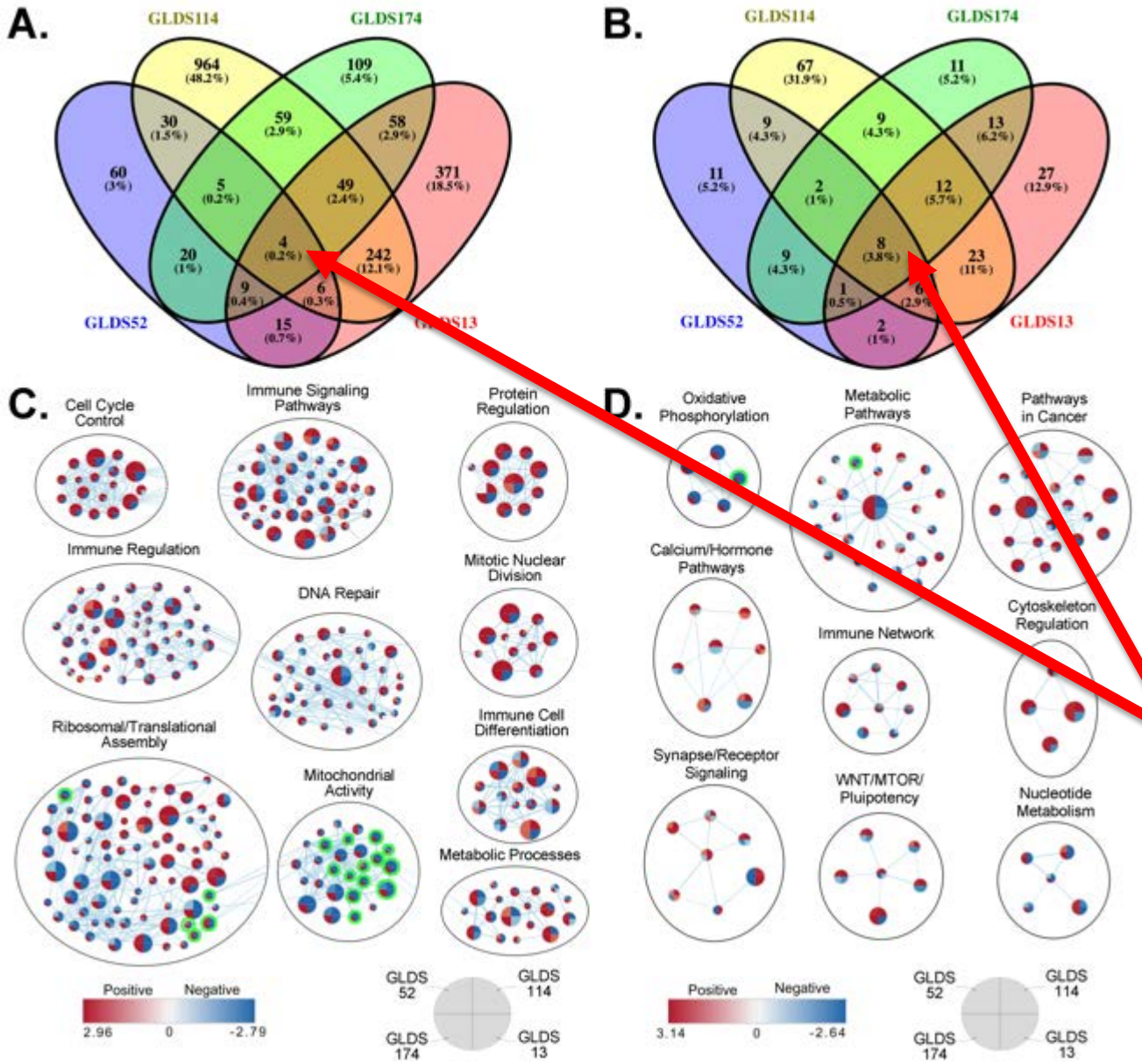
Sylvain Costes

NASA Ames Research Center

In Vitro Human Dataset Analyses Reveals Conserved Mitochondrial Response to Spaceflight



In Vitro Human Dataset Analyses Reveals Conserved Mitochondrial Response to Spaceflight



Gene Set Enrichment Analysis (GSEA) of human microarray datasets GLDS-13, GLDS-52, GLDS-114, and GLDS-174 comparing flight to ground treatments. (**A,B**) Venn diagrams of statistically significant GSEA (**A**) Gene Ontology (GO) and (**B**) Kyoto Encyclopedia of Genes and Genomes (KEGG) gene sets with FDR < 10%. (C,D) Cytoscape enrichment maps of (**C**) GO sets with FDR <10% in at least two GLDS datasets and (**D**) KEGG gene sets with FDR < 10% in at least one GLDS dataset. Green Highlights indicate all pathways involved with

Common significant dysregulation of the gene ontology genes sets for:

- mitochondrial ATP synthesis
- mitochondrial electron transport
- oxidative phosphorylation
- hydrogen ion transmembrane transportation

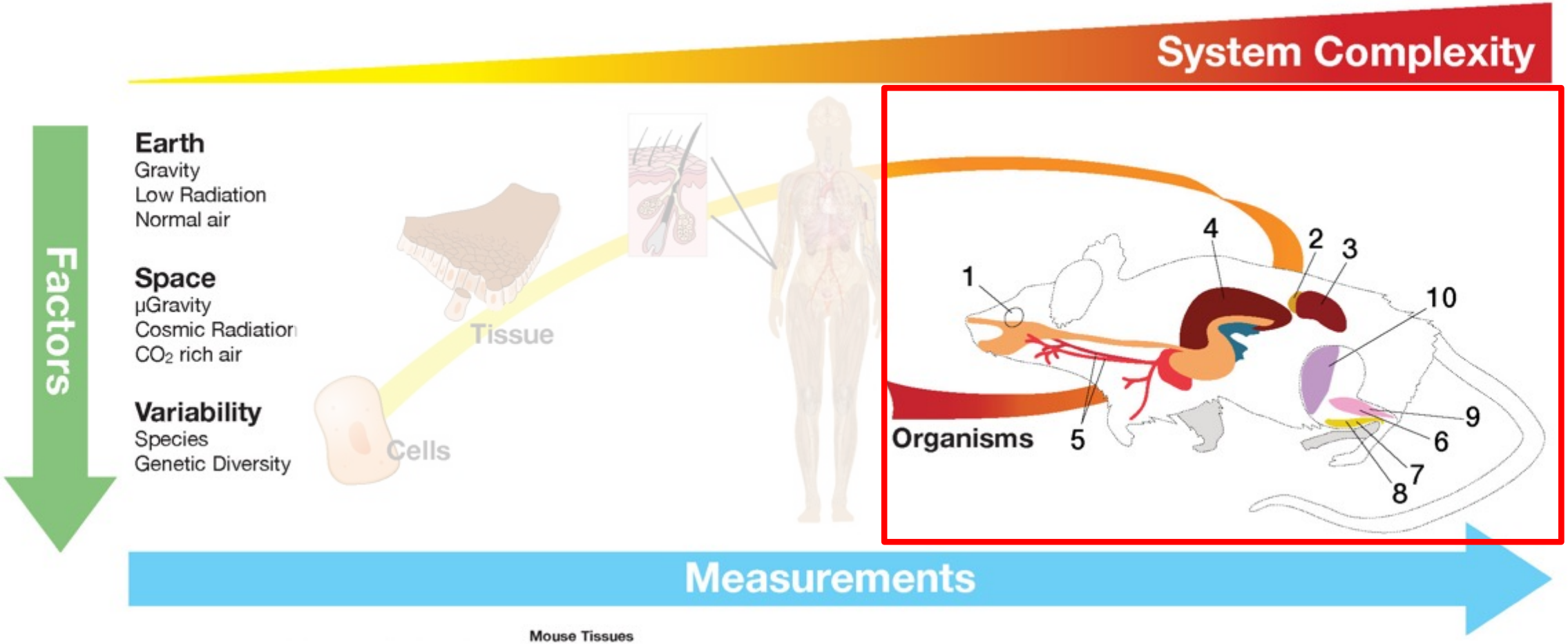
Dermal Blood Microvascular Endothelial Cells
- Fibroblasts

Yared Kidane

SCOTTISH RITE HOSPITAL FOR CHILDREN

HAMPTON UNIVERSITY
THE STANDARD OF EXCELLENCE

Multi-Omics Analysis on mice flown to ISS reveals Mitochondrial driven response stemming from the liver



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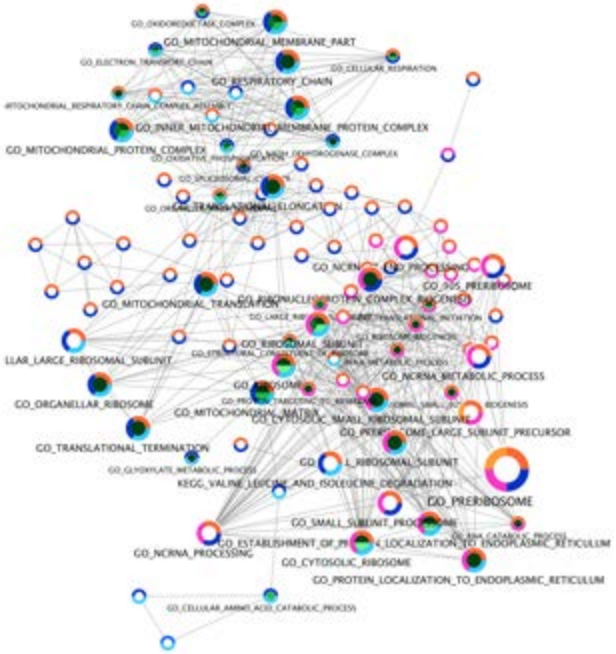
7. Extensor Digitorum Longus: Transcriptomics (RR1)
8. Tibialis Anterior: Transcriptomics (RR1)
9. Gastrocnemius: Transcriptomics (RR1) and Metabolomics (RR9)
10. Quadriceps: Transcriptomics (RR1) and Metabolomics (RR9)

RR1 mice: Female C57BL/6, 32 weeks old at launch
RR3 mice: Female BALB/C, 18 weeks old at launch
RR9 mice: Male C57BL/6, 9 weeks old at launch

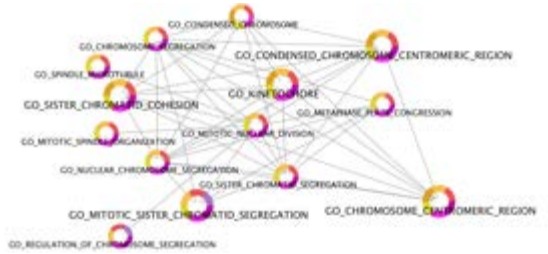
Multi-Omics Analysis on mice flown to ISS reveals Mitochondrial driven response stemming from the liver

A) Mitochondrial Activity

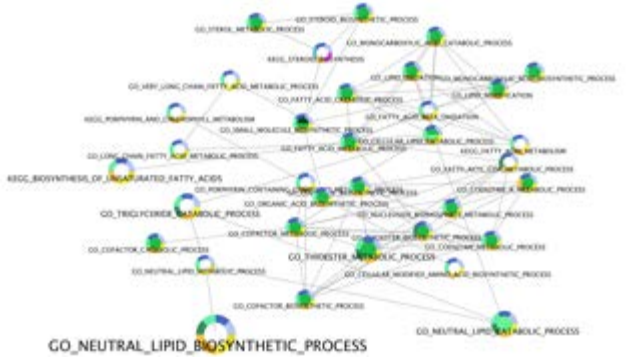


B) Ribosome and Translation

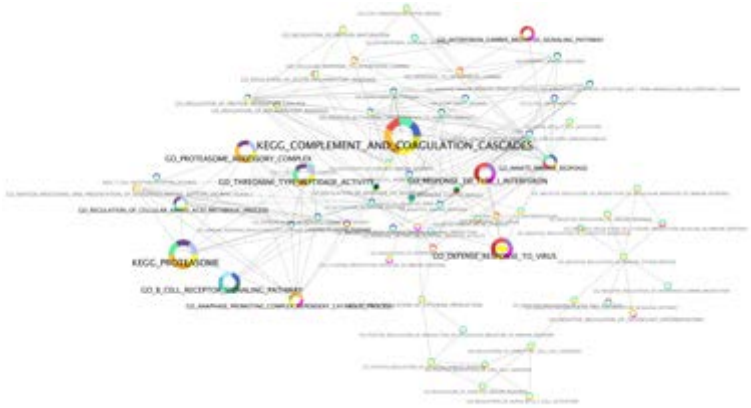
C) Cell Cycle



D) Lipid Metabolism



E) Immune Response



F) Photoreceptor Activity / Circadian Rhythm

Node size- RNAseq differential expression (RR1+RR3)

- Pathway enriched in all 8 DE tissues
- Pathway enriched in 7 DE tissues
- Pathway enriched in 7 DE tissues
- Pathway enriched in 5 DE tissues

Node outer colors- RNAseq differential expression (RR1+RR3)

Down in liver RR1	Up in liver RR1
Down in liver RR3	Up in liver RR3
Down in kidney RR1	Up in kidney RR1
Down in kidney RR3	Up in kidney RR3
Down in eye RR1	Up in eye RR1
Down in eye RR3	Up in eye RR3
Down in adrenal RR1	Up in adrenal RR1
Down in adrenal RR3	Up in adrenal RR3

Node inner colors- Differential proteomics (RR3)

- Enriched in liver proteomics
- Enriched in kidney proteomics
- Enriched in eye proteomics
- Enriched in adrenal proteomics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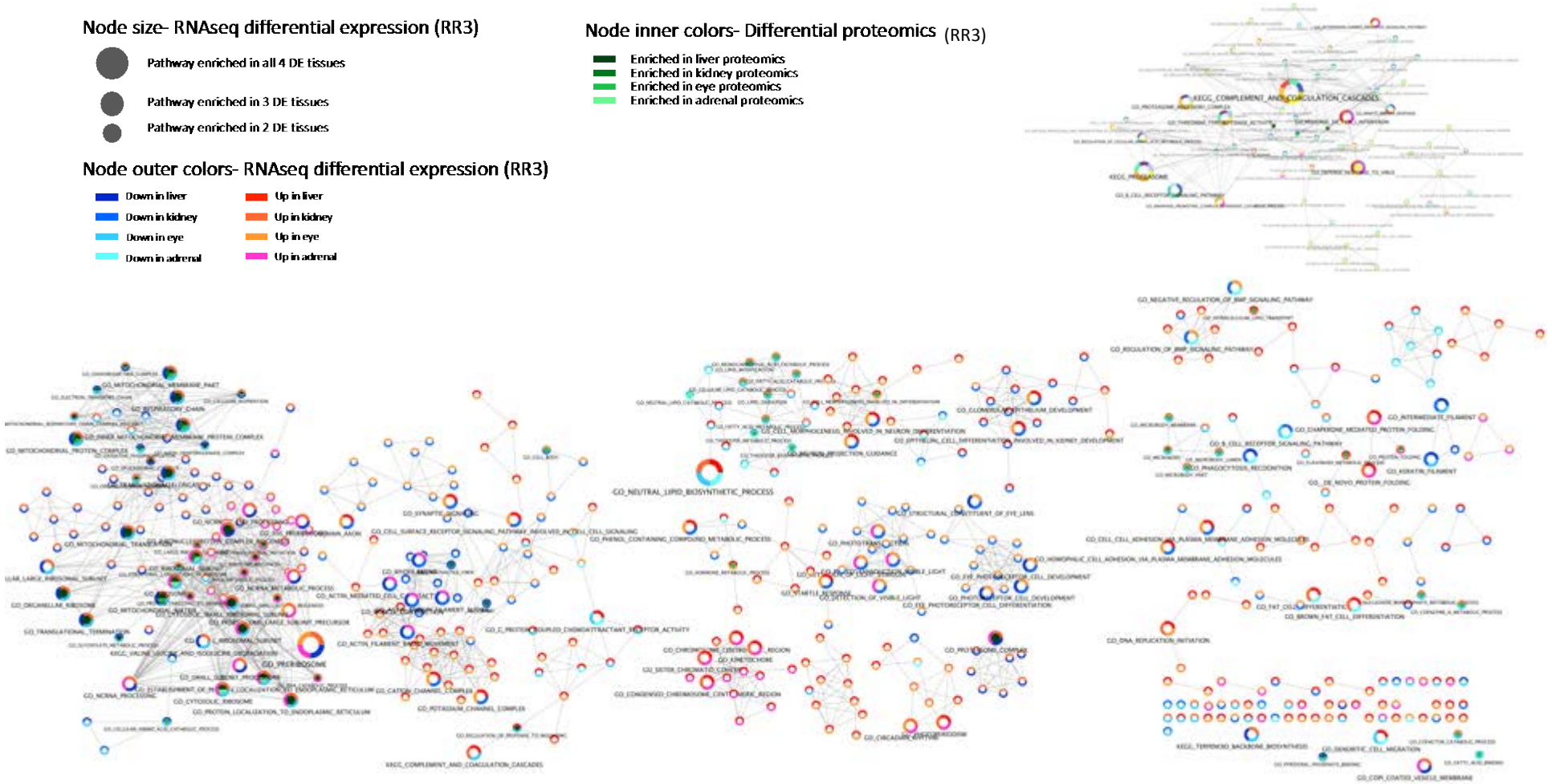
QUEEN'S UNIVERSITY BELFAST

Cross-tissue, cross-omics pathway analysis reveals a convergence on key dysregulated processes

Supplementary Figure in Paper showing the entire pathway multi-omic pathway analysis

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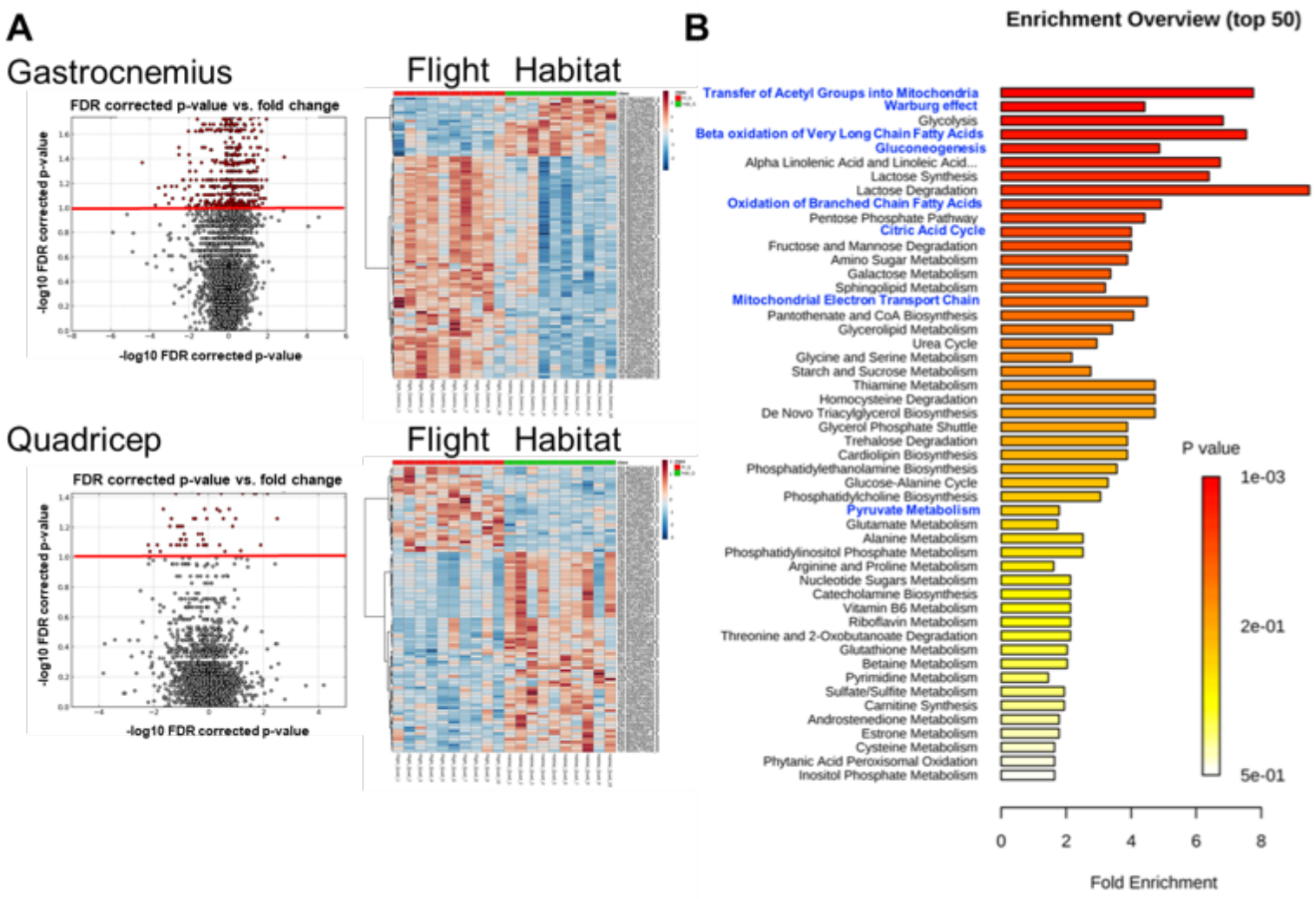
Gary Hardiman


Willian da Silveira

QUEEN'S UNIVERSITY BELFAST

Metabolomics on muscles reveal mitochondrial factors as top biological factors being regulated by spaceflight



Panel A - Volcano plots and heatmaps from analysis of habitat ground control versus flight samples. Panel B – Enrichment pathway analysis based on the subset of putative metabolites from Supplementary Table 2. Blue letters highlight pathways with mitochondrial involvement.

- RR1 mice: Female C57BL/6, 32 weeks old at launch
- RR3 mice: Female BALB/C, 18 weeks old at launch
- **RR9 mice: Male C57BL/6, 9 weeks old at launch**

Evagelia C. Laiakis

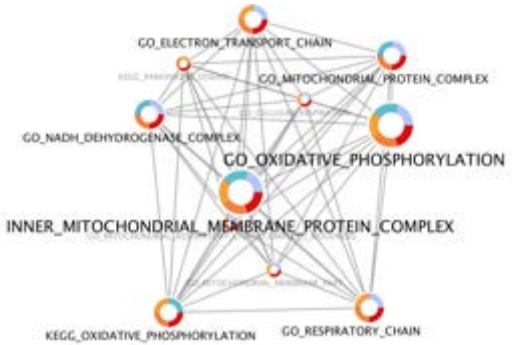
GEORGETOWN UNIVERSITY
Georgetown University Medical Center

Jeffrey Scott Willey

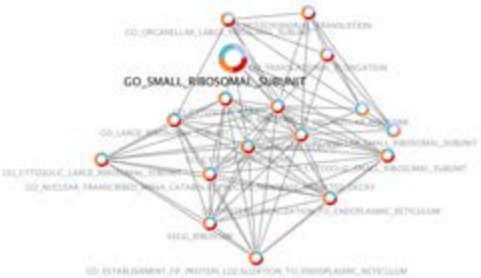
WAKE FOREST UNIVERSITY

Metabolomics Related to Proteomic and Transcriptomic data

C) Mitochondrial Activity

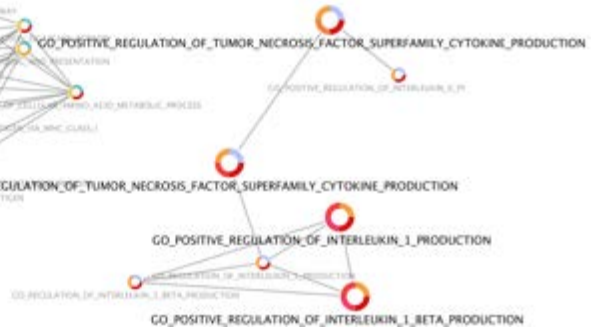


D) Ribosome and Translation



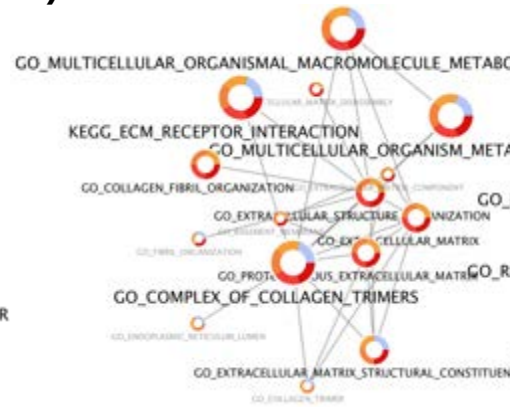
E) Proteasome

F) TNF/IL1 Response

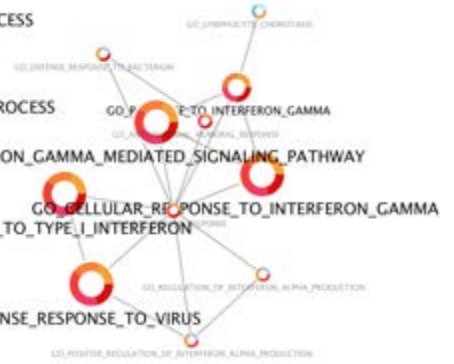


G) Sympathetic and Feeding Behavior

H) Metabolism and ECM



I) Interferon Response



Node outer colors- RNAseq differential expression

Node outer colors- RNAseq differential expression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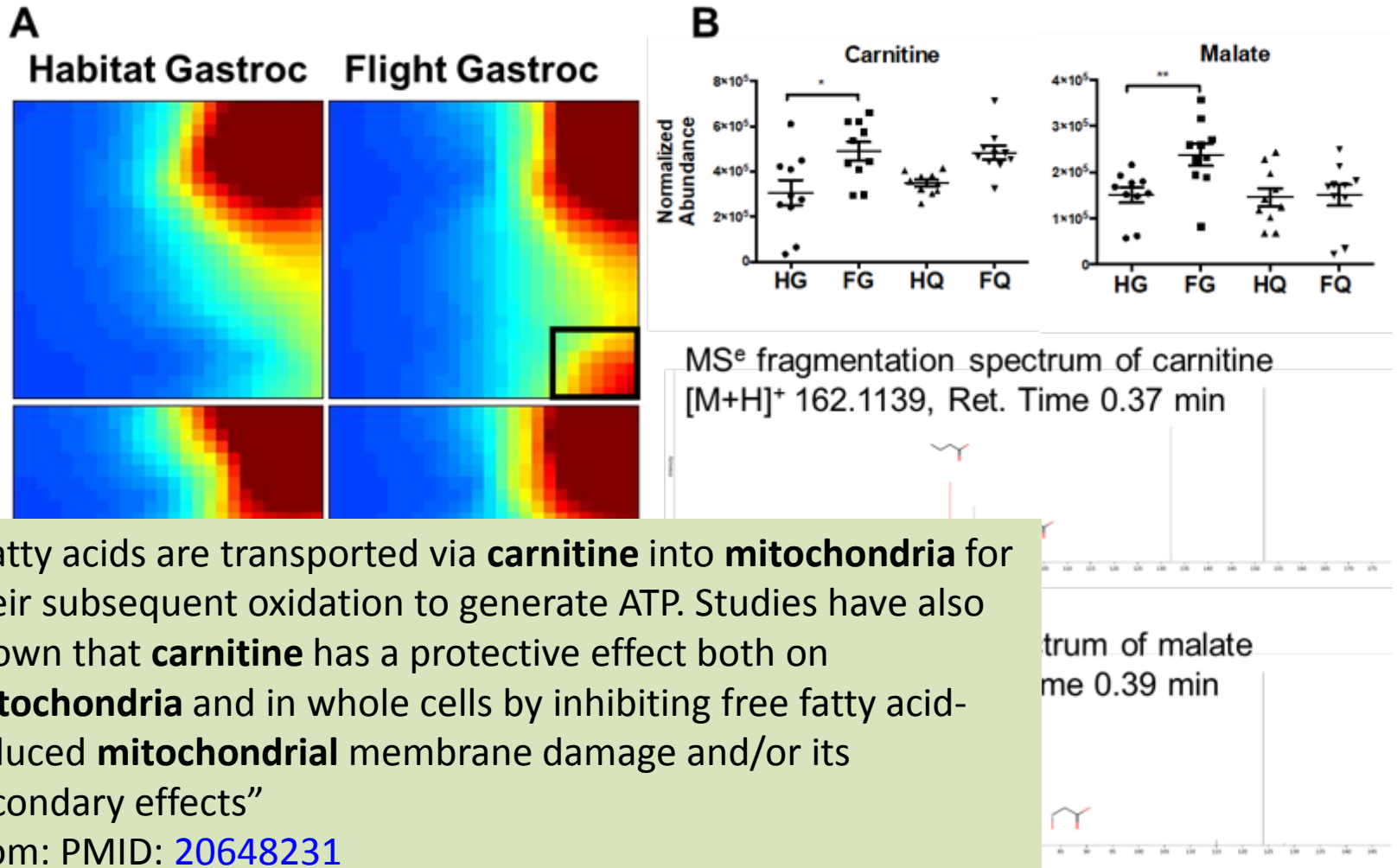
Global Metabolomic Shifts and Specific Mitochondrial related factors



"Fatty acids are transported via **carnitine** into **mitochondria** for their subsequent oxidation to generate ATP. Studies have also shown that **carnitine** has a protective effect both on **mitochondria** and in whole cells by inhibiting free fatty acid-induced **mitochondrial** membrane damage and/or its secondary effects"
From: PMID: 20648231

Supplementary Figure 2: Panel A – GEDI self organizing maps showing global metabolomic shifts due to the effects of spaceflight. Panel B - Carnitine and malate levels with their theoretical fragmentation spectra from Progenesis QI. Levels are depicted as mean ± standard error of the mean. * p<0.05, ** p<0.01.

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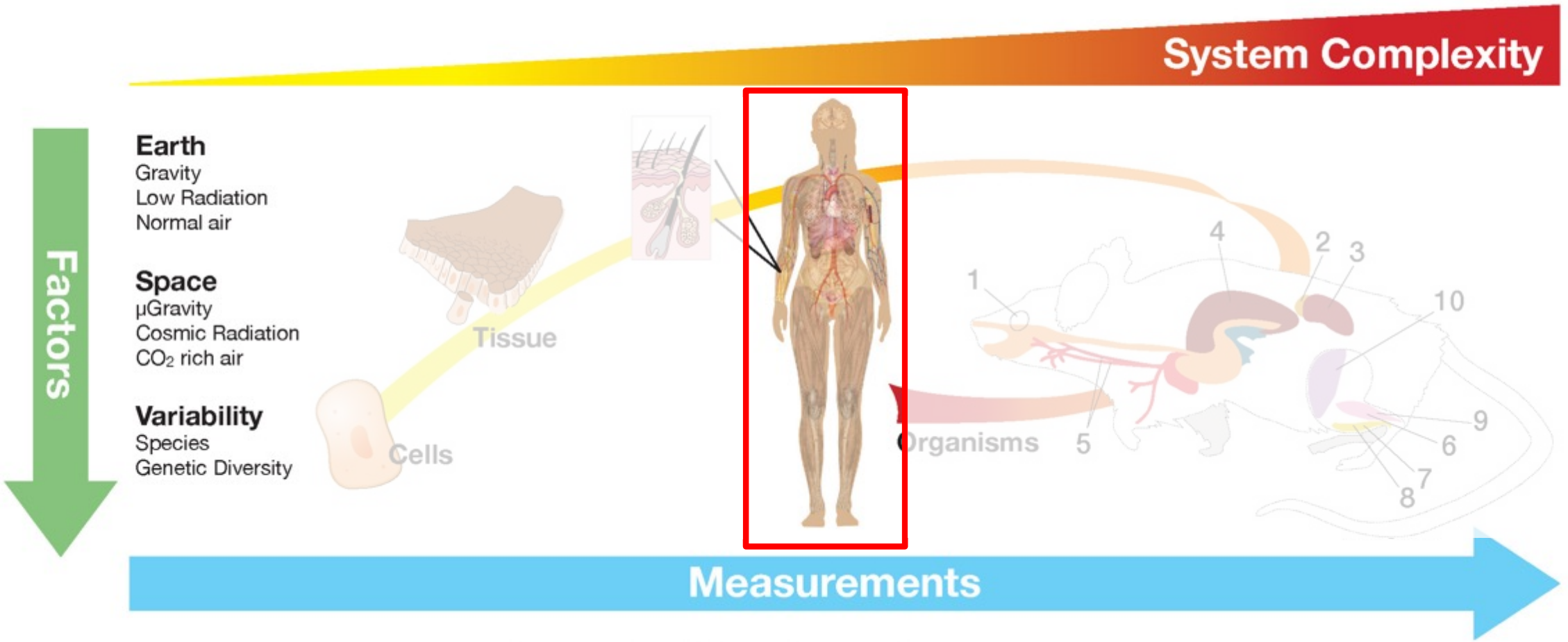
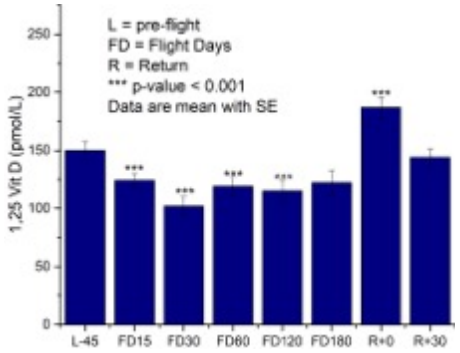
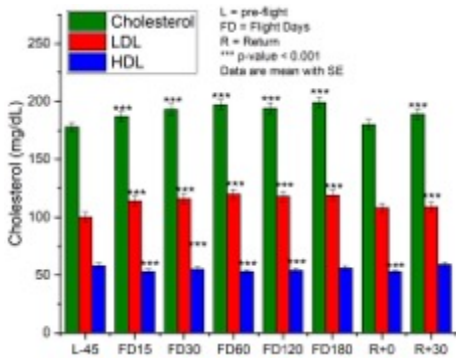
Astronaut Physiological Factors Confirm Omics *in vitro* and *in vivo* analysis!

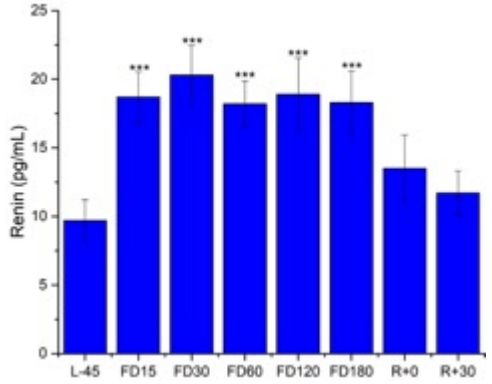


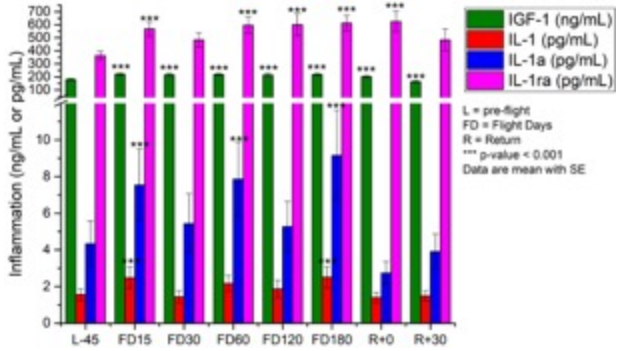
Astronaut Physiological Factors Confirm Omics *in vitro* and *in vivo* analysis!

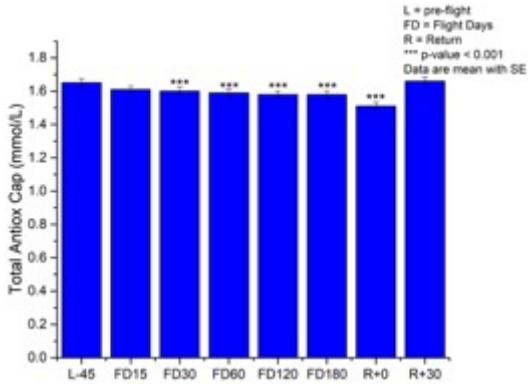
Can cause bone loss

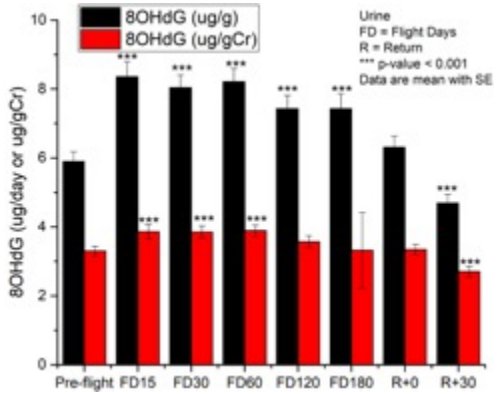


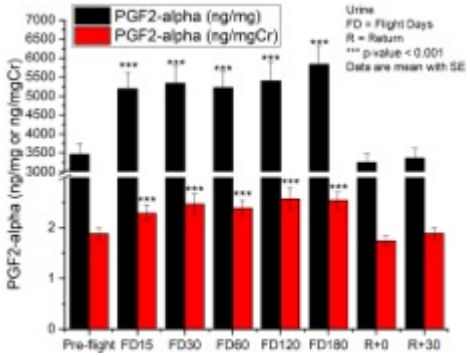


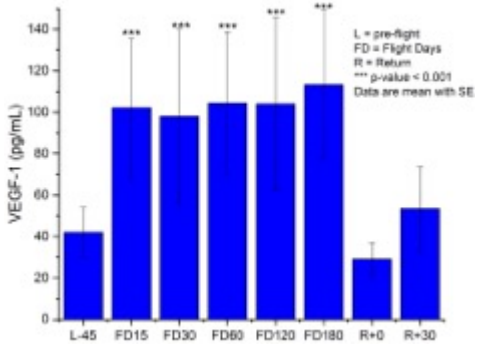












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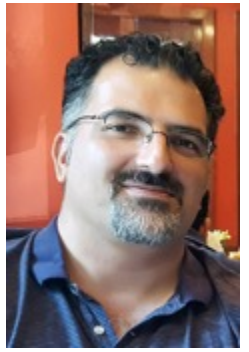

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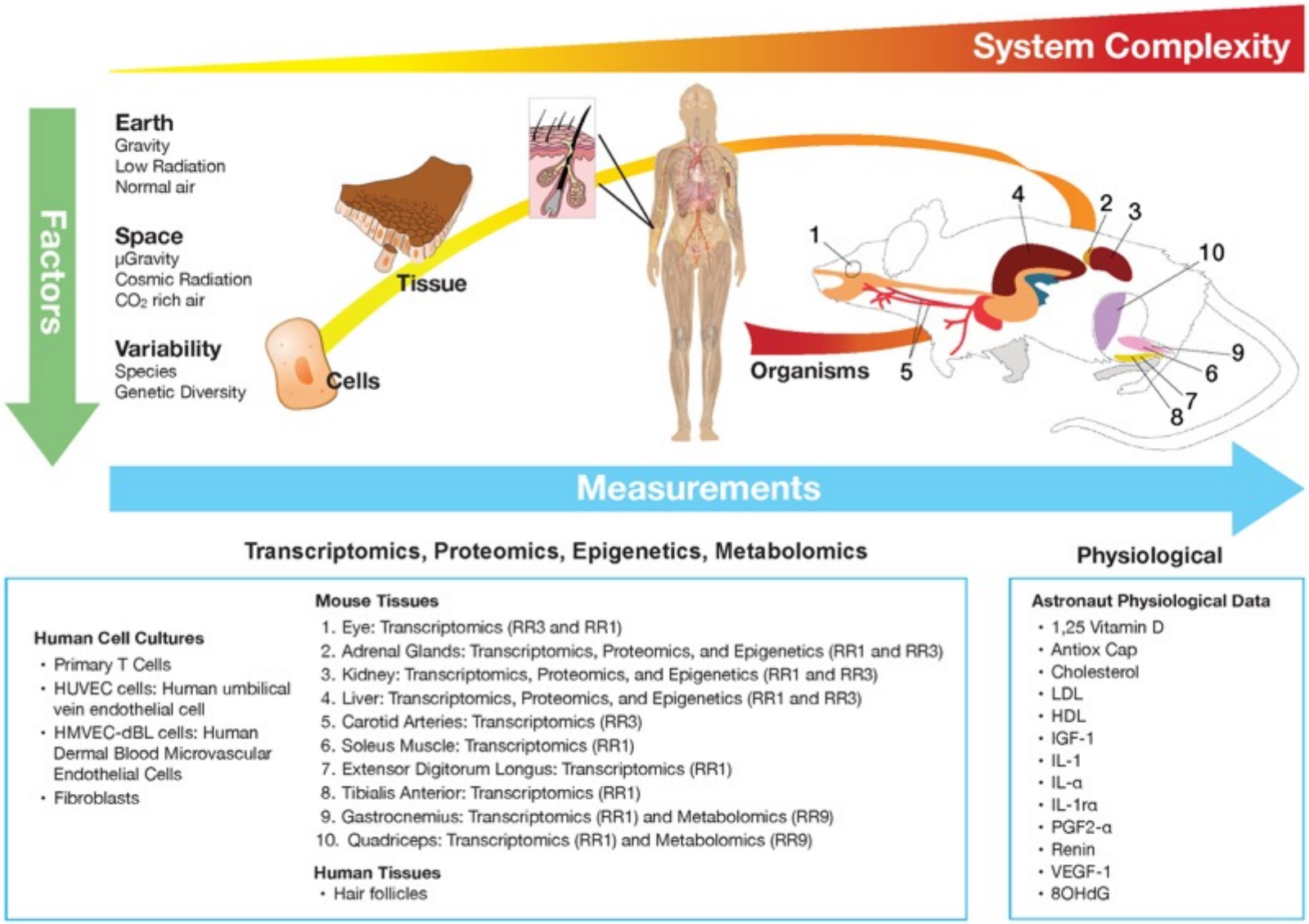
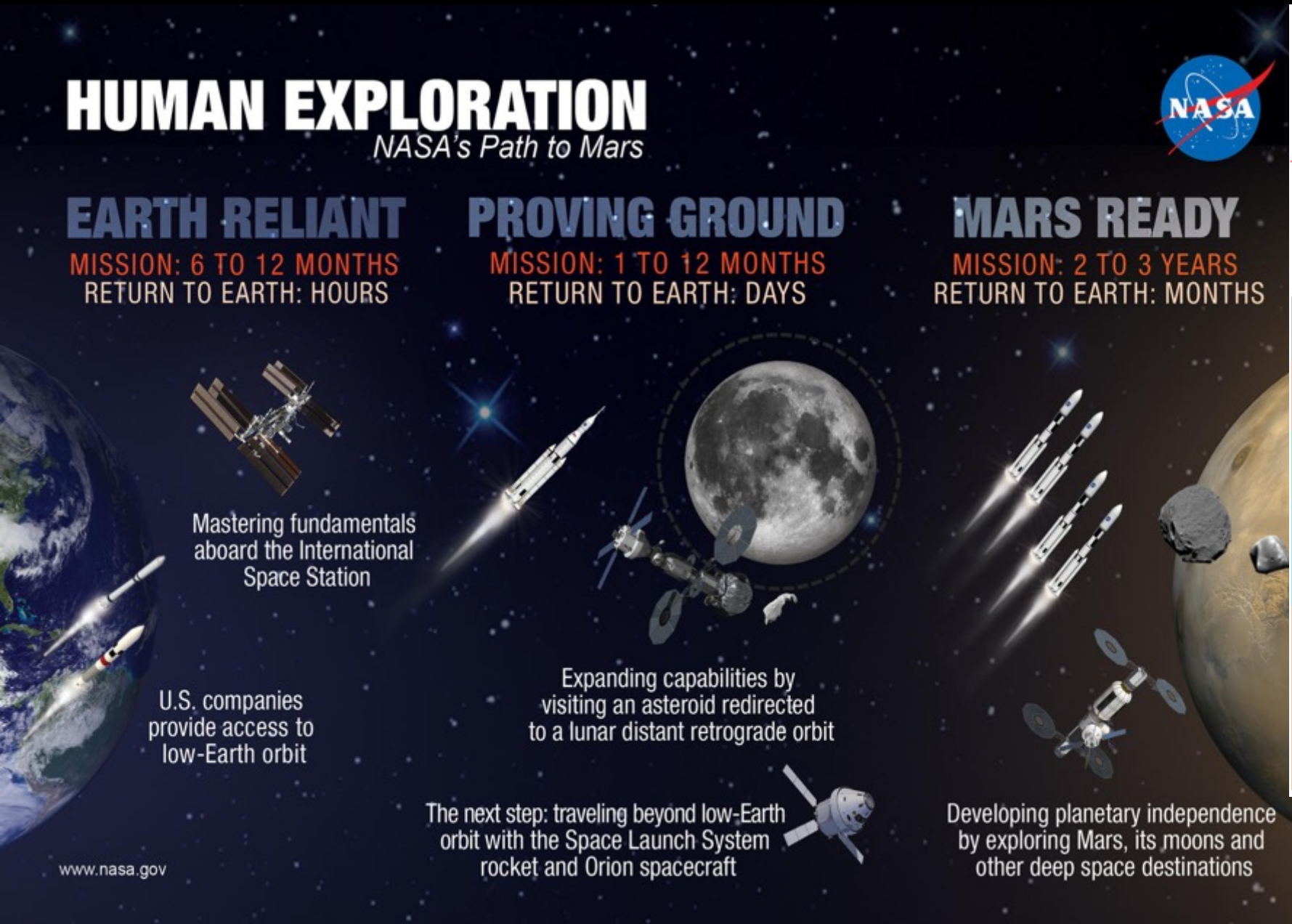
Ames Research Center

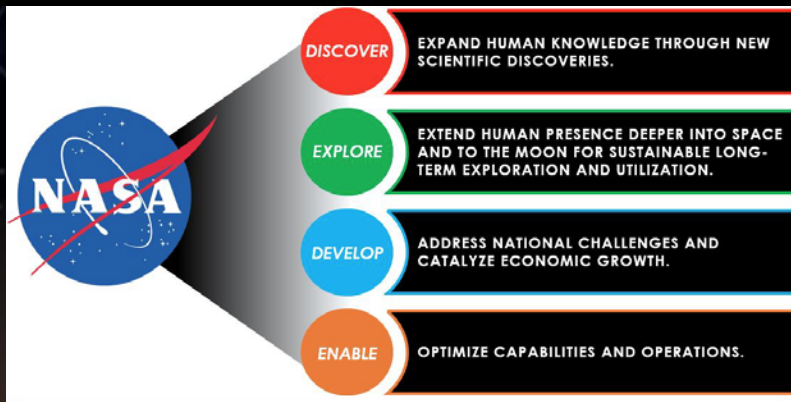
Mitochondrial Driven Factors Might be Key to Systemic Spaceflight Associated Increase in Health Risk



- **GeneLab was instrumental to determine this universal response!**
- **No other possible way to piece the puzzle together without the power of GeneLab**
- **The large collaborative nature of the AWG was essential to drive this work!!**

Many Space Biology Questions and Challenges Still Need to Addressed!





NASA 2018 Strategic Plan Framework

Theme	Strategic Goal	Strategic Objective
DISCOVER	EXPAND HUMAN KNOWLEDGE THROUGH NEW SCIENTIFIC DISCOVERIES.	1.1: Understand the Sun, Earth, Solar System, and Universe. 1.2: Understand Responses of Physical and Biological Systems to Spaceflight.
EXPLORE	EXTEND HUMAN PRESENCE DEEPER INTO SPACE AND TO THE MOON FOR SUSTAINABLE LONG-TERM EXPLORATION AND UTILIZATION.	2.1: Lay the Foundation for America to Maintain a Constant Human Presence in Low Earth Orbit Enabled by a Commercial Market. 2.2: Conduct Exploration in Deep Space, Including to the Surface of the Moon.
DEVELOP	ADDRESS NATIONAL CHALLENGES AND CATALYZE ECONOMIC GROWTH.	3.1: Develop and Transfer Revolutionary Technologies to Enable Exploration Capabilities for NASA and the Nation. 3.2: Transform Aviation Through Revolutionary Technology Research, Development, and Transfer. 3.3: Inspire and Engage the Public in Aeronautics, Space, and Science.
ENABLE	OPTIMIZE CAPABILITIES AND OPERATIONS.	4.1: Engage in Partnership Strategies. 4.2: Enable Space Access and Services. 4.3: Assure Safety and Mission Success. 4.4: Manage Human Capital. 4.5: Ensure Enterprise Protection. 4.6: Sustain Infrastructure Capabilities and Operations.

Acknowledgements

https://genelab.nasa.gov/