National Aeronautics and Space Administration

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

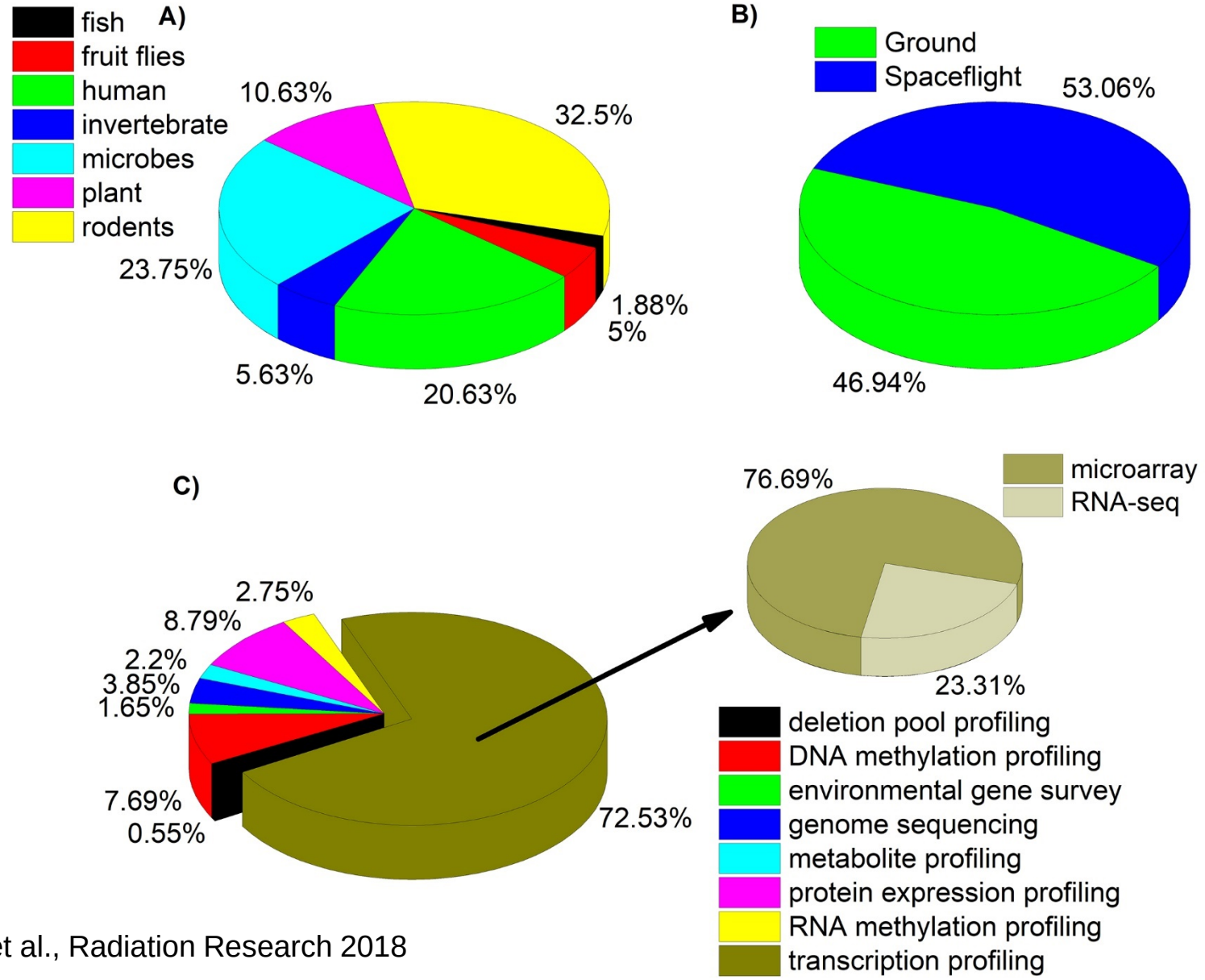
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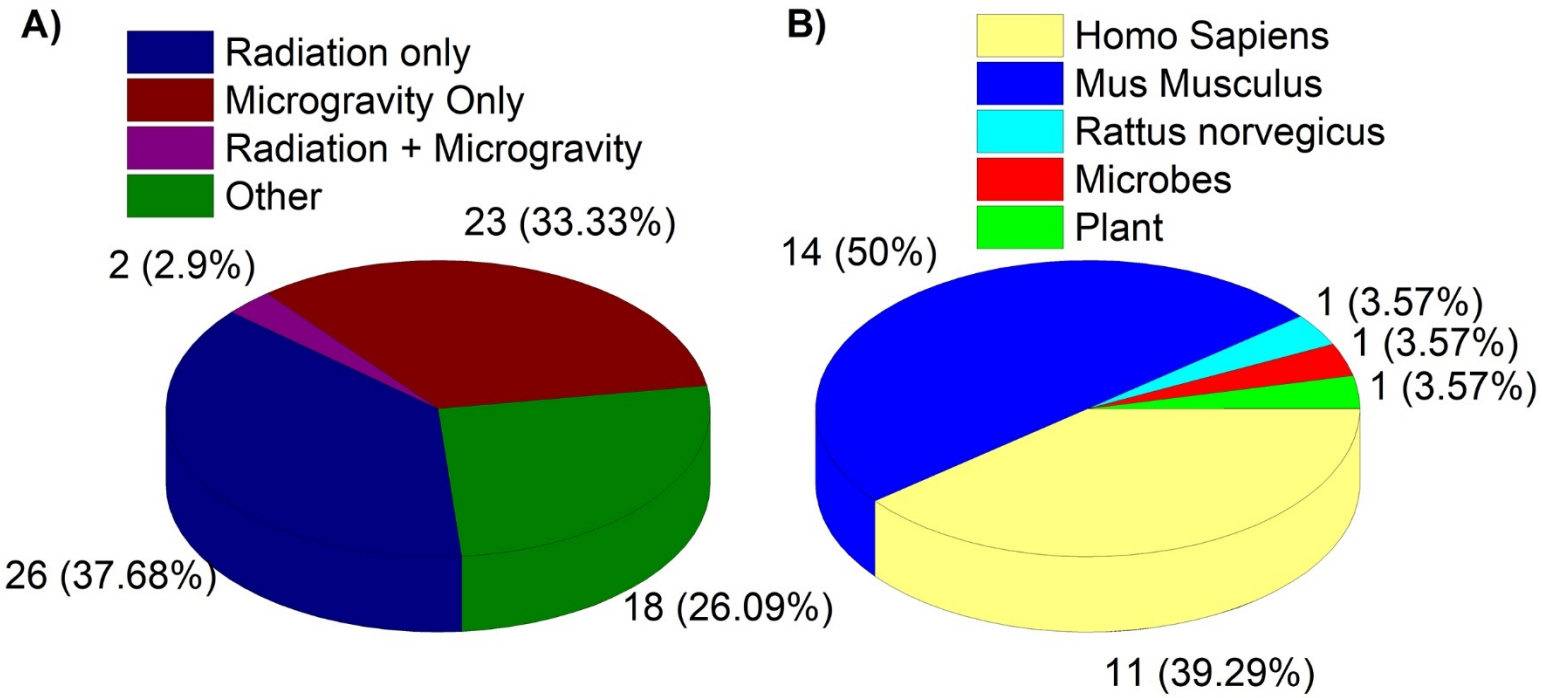
GeneLab (genelab.nasa.gov)

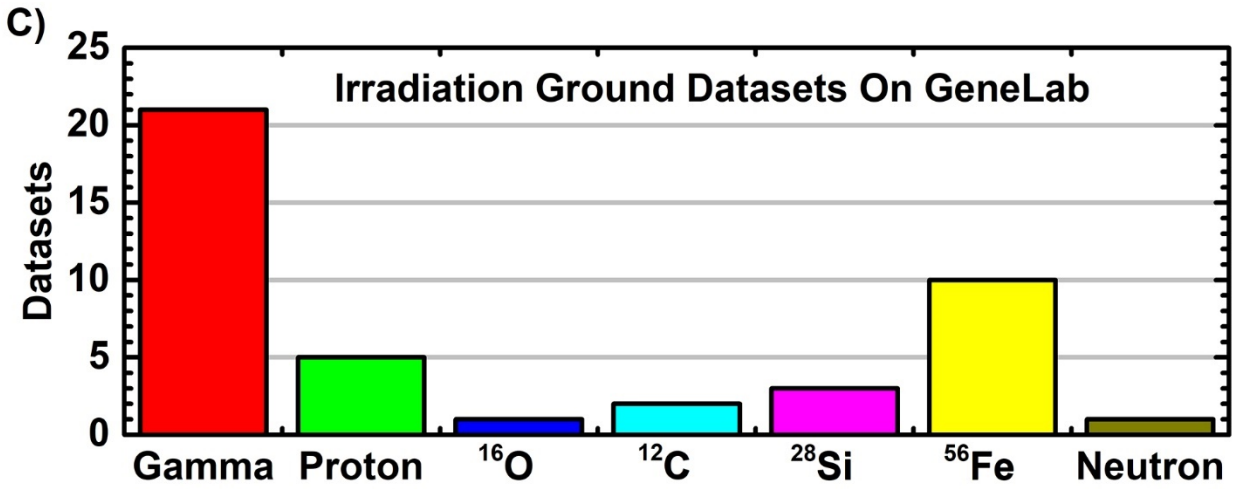


Beheshti et al., Radiation Research 2018

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69 Ground Data Sets: Radiation and simulated microgravity

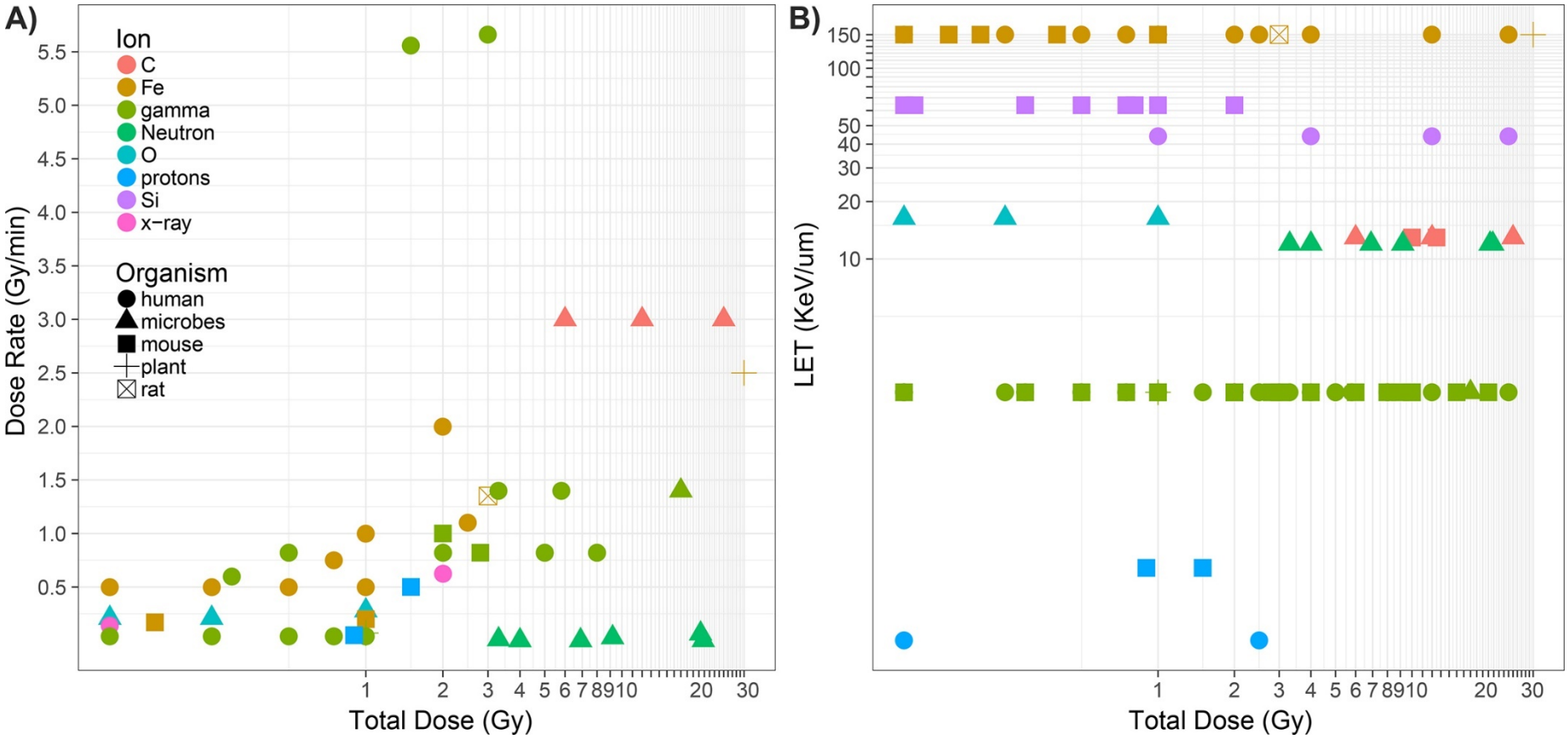




Beheshti et al., Radiation Research 2018

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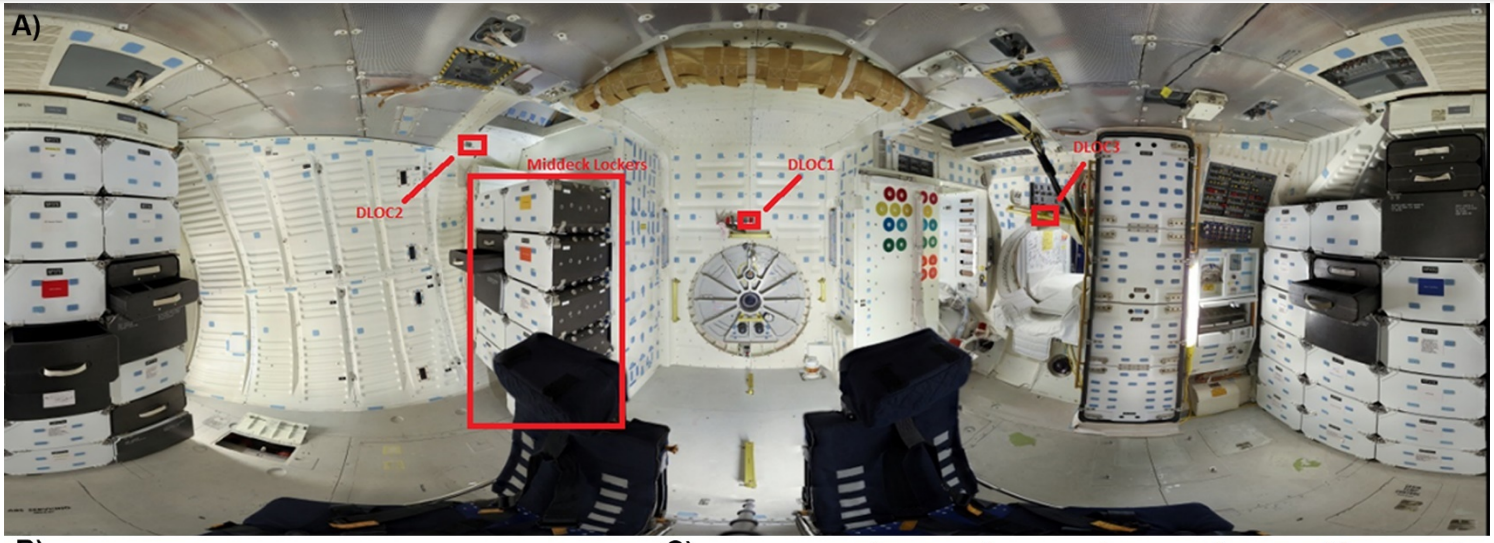
Radiation Ground Studies

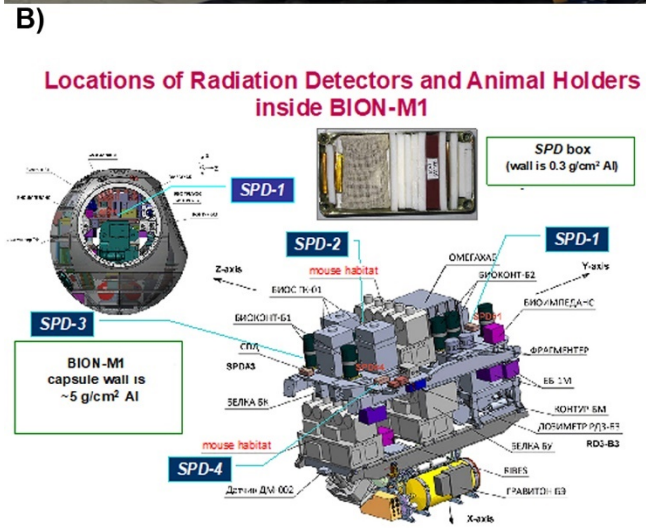


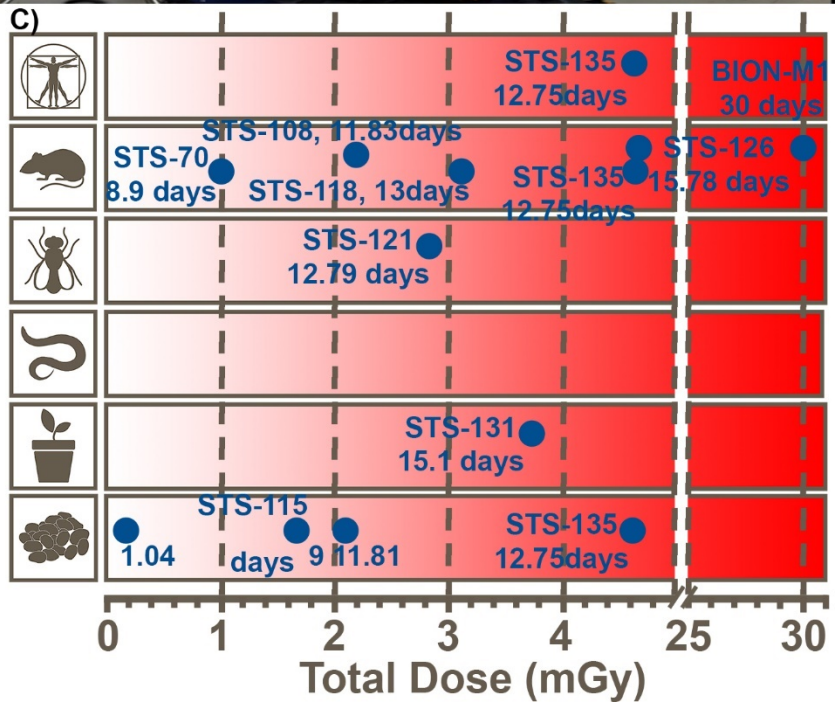
Beheshti et al., Radiation Research 2018

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Radiation Dosimetry for STS samples (ISS to follow)







Beheshti et al., Radiation Research 2018

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Space Radiation

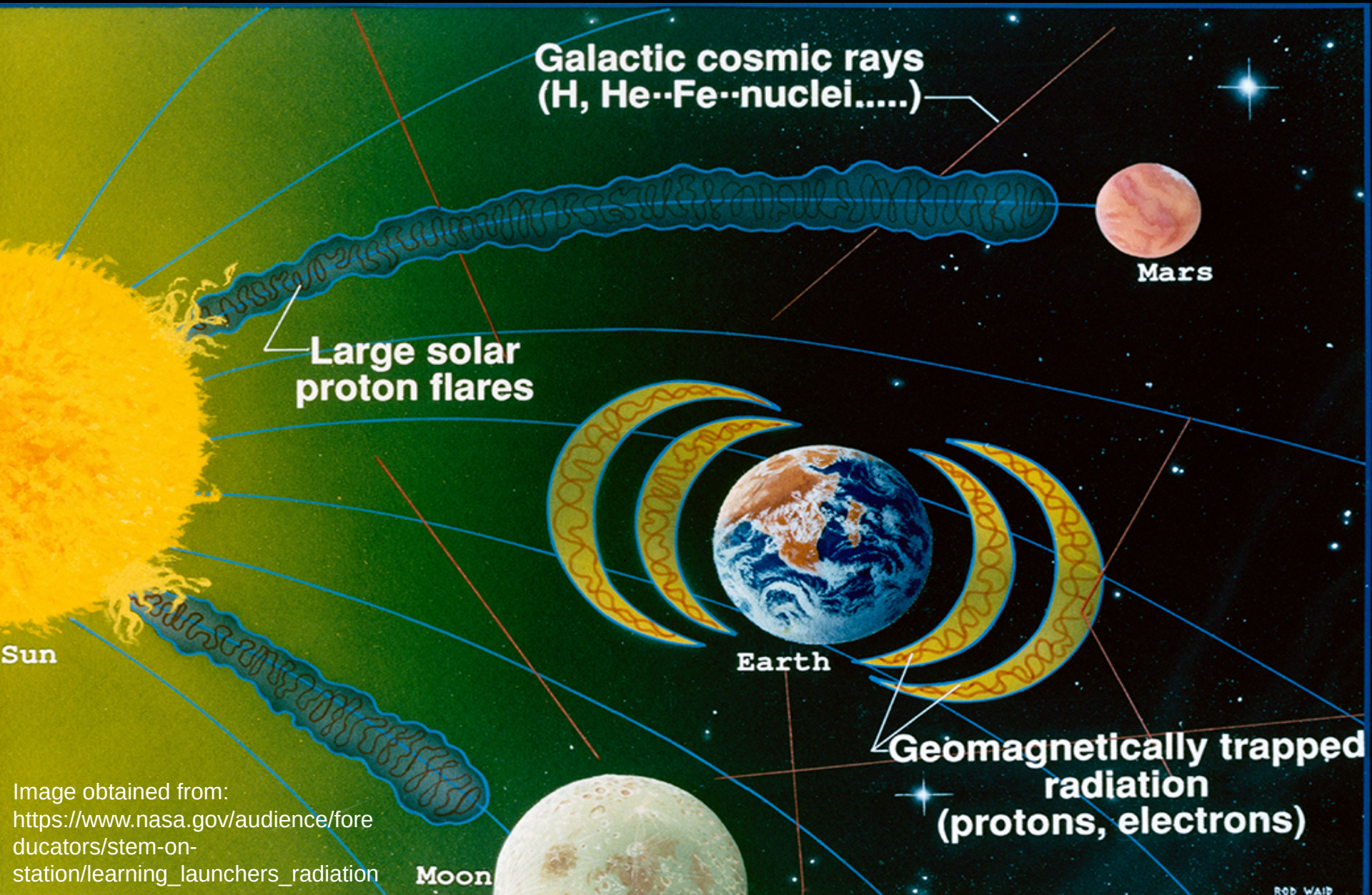


Image obtained from:
https://www.nasa.gov/audience/foreducators/stem-on-station/learning_launchers_radiation

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Space Radiation: Van Allen Belt

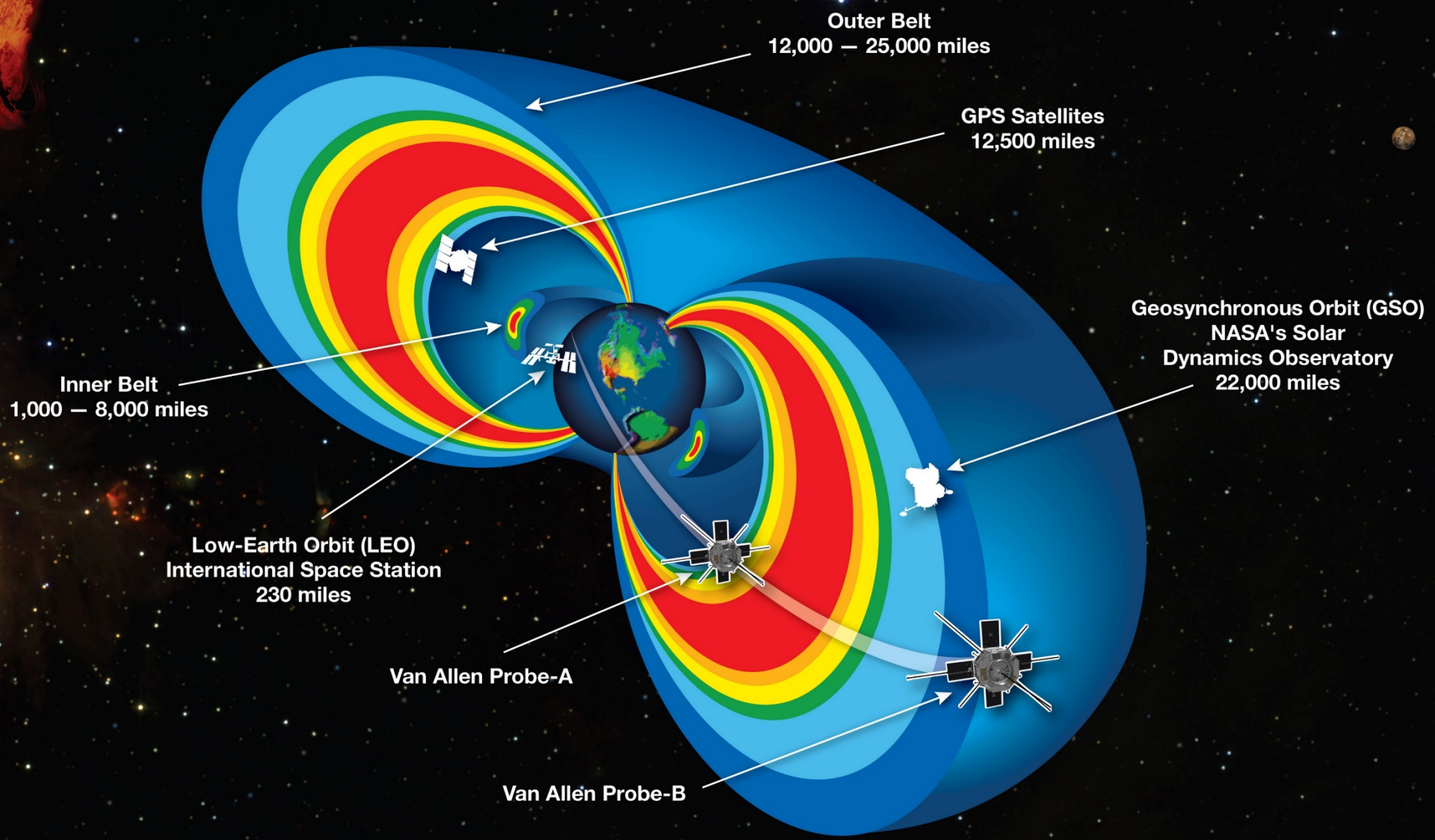
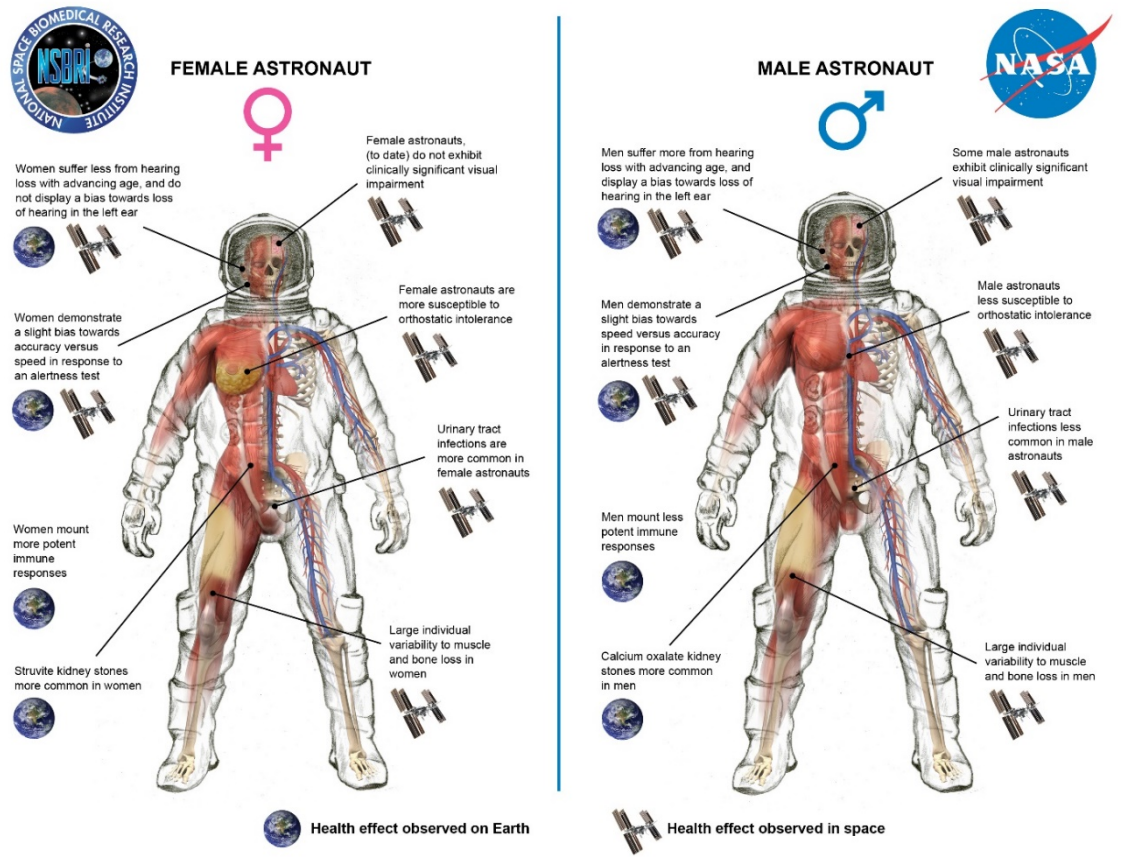
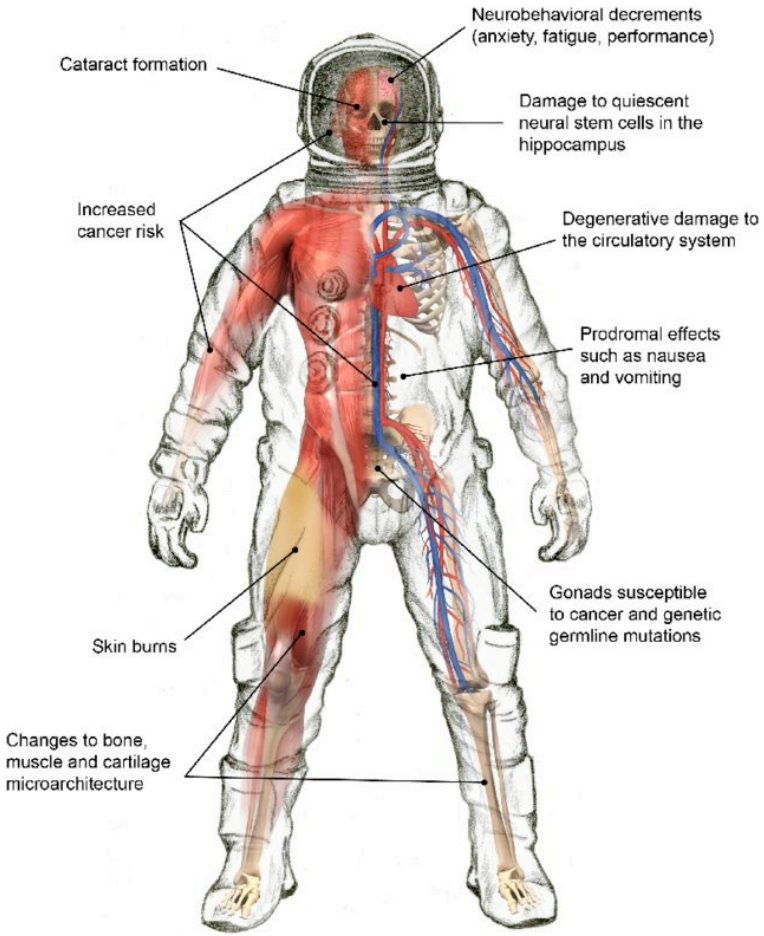


Image obtained from: https://www.nasa.gov/mission_pages/sunearth/news/gallery/20130228-radiationbelts.html

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Space Radiation Risk 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;

GeneLab Data Used and Hypothesis

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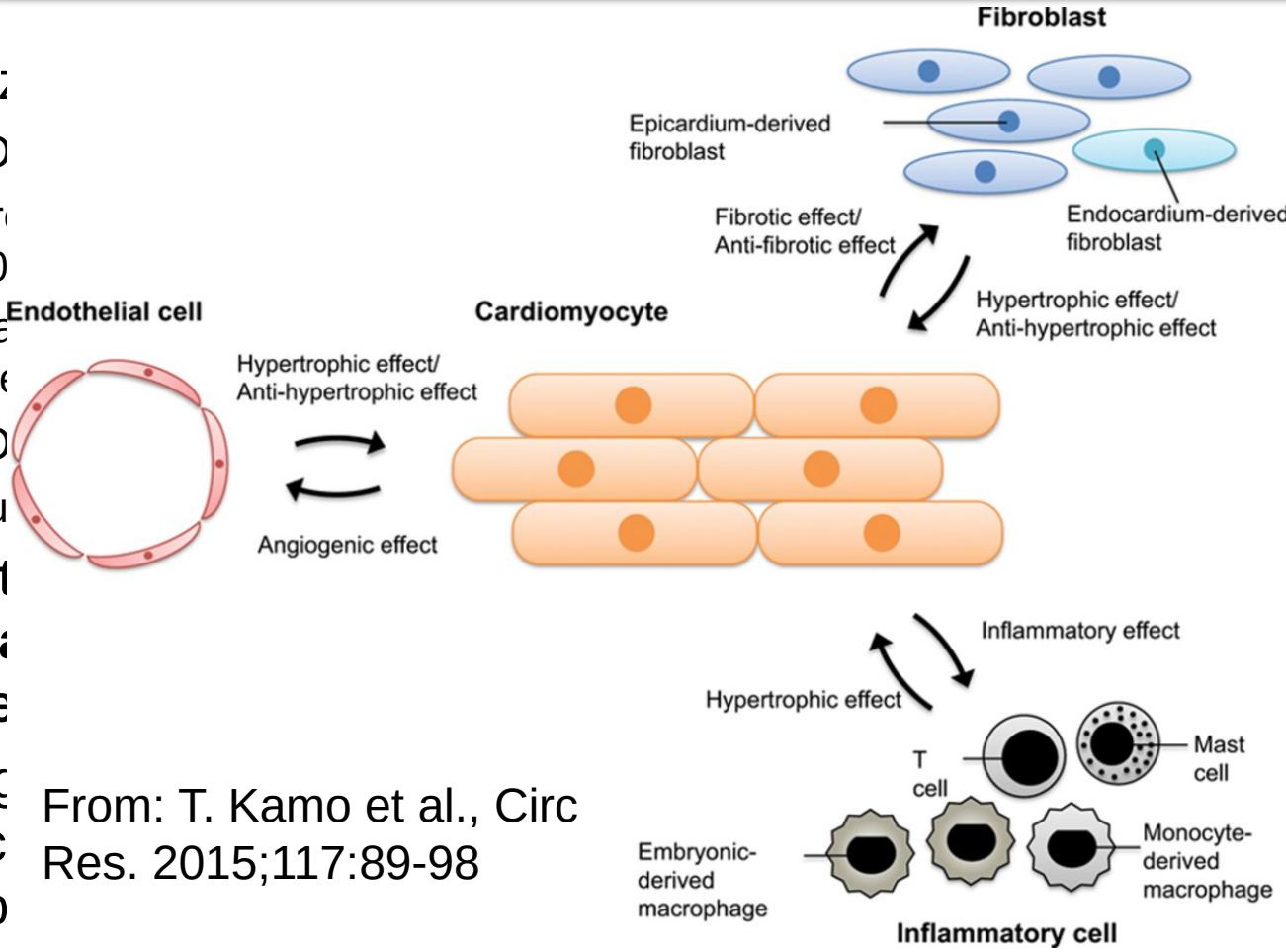
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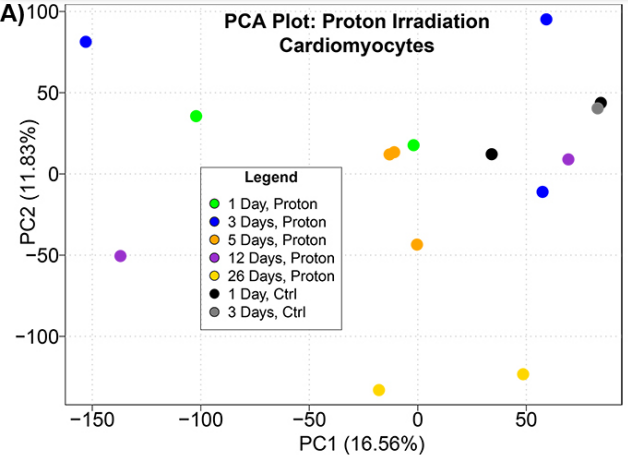


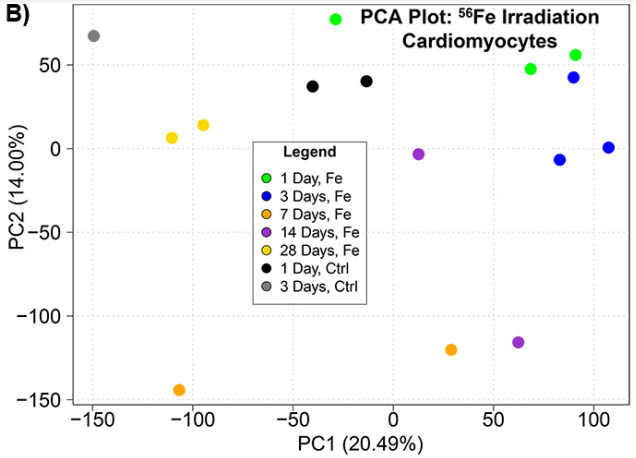
From: T. Kamo et al., Circ Res. 2015;117:89-98

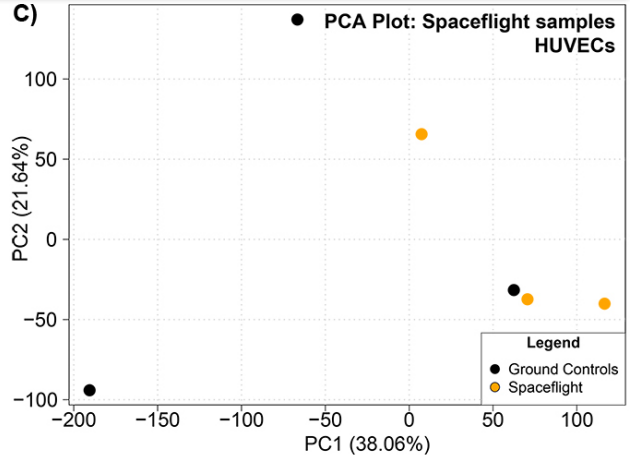
- Our analysis was guided by the hypothesis that there are common persistent molecules affecting the cardiovascular system due to radiation effects during spaceflight.

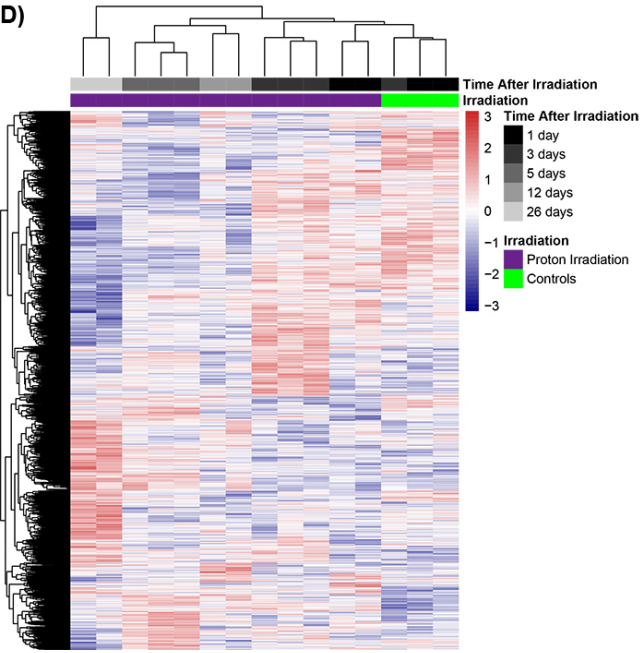
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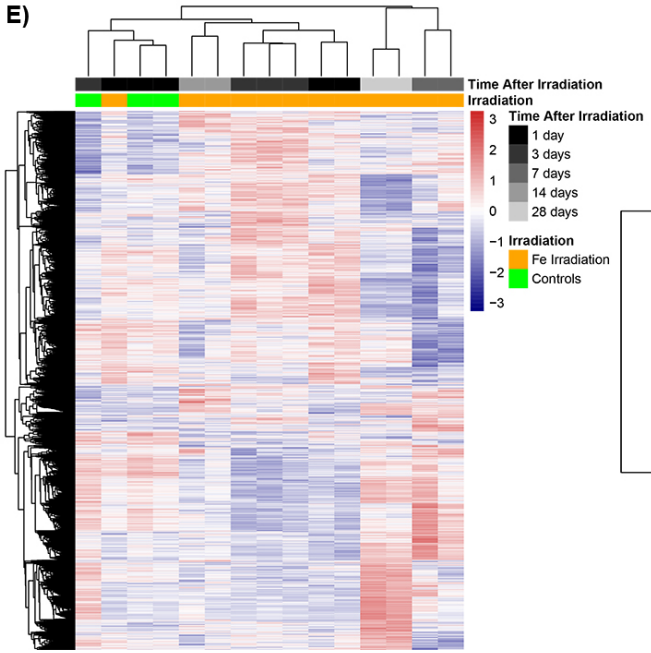
Global View of Impact of Space Irradiation

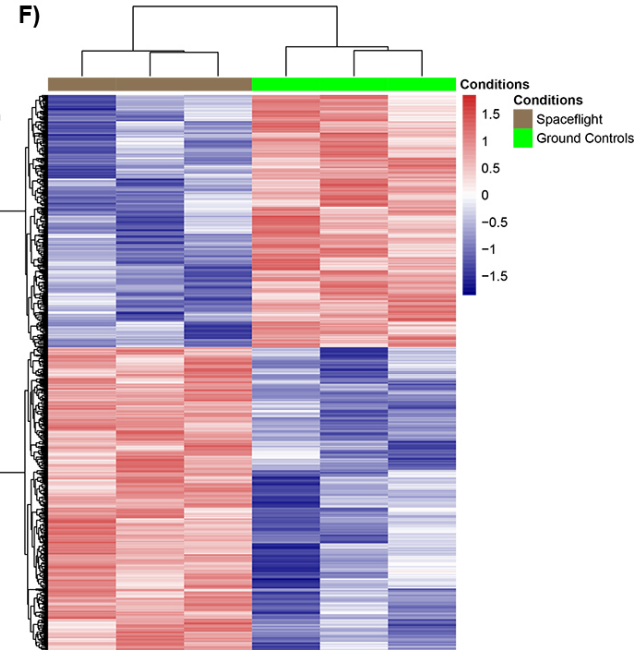








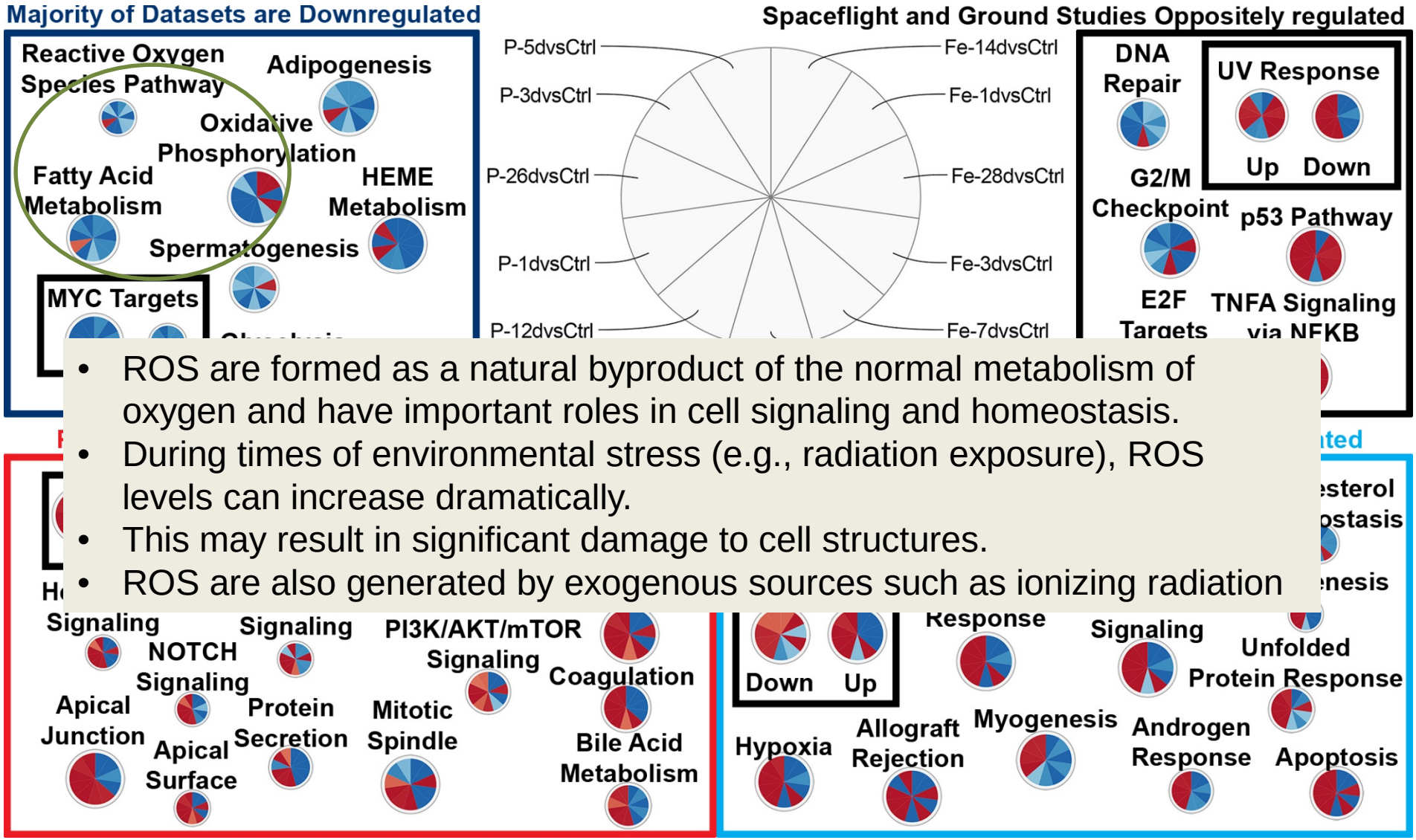




Focused on biological factors that will continue to have impact for all time points after irradiation.

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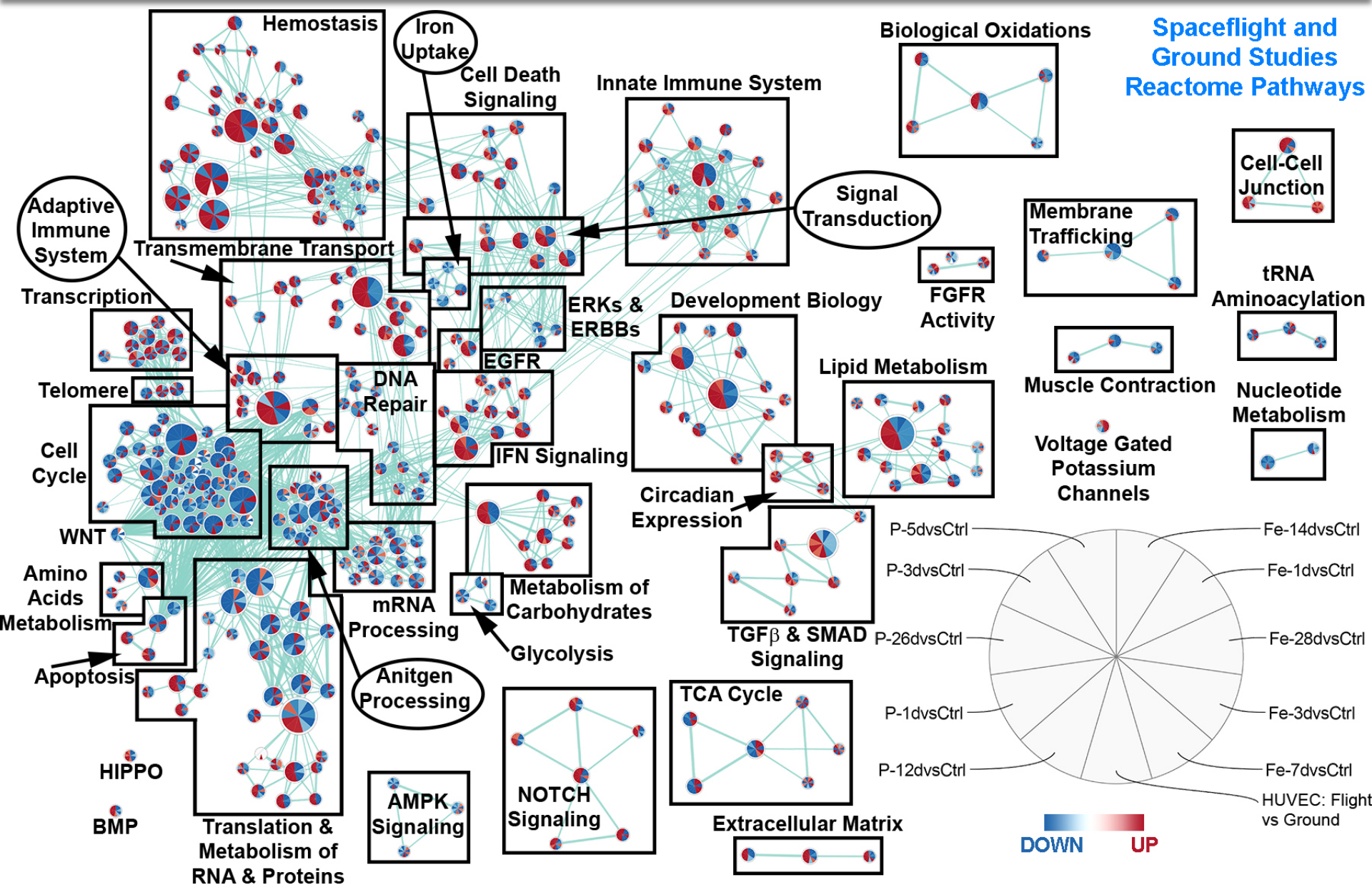
Functional Impact on Health: GSEA



- ROS are formed as a natural byproduct of the normal metabolism of oxygen and have important roles in cell signaling and homeostasis.
- During times of environmental stress (e.g., radiation exposure), ROS levels can increase dramatically.
- This may result in significant damage to cell structures.
- ROS are also generated by exogenous sources such as ionizing radiation

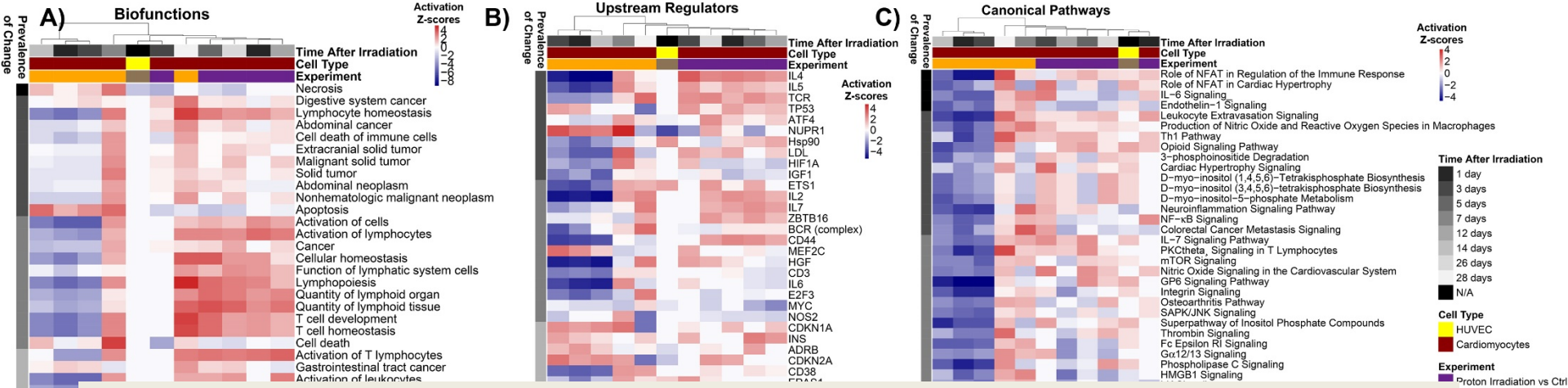
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Functional Impact on Health: GSEA

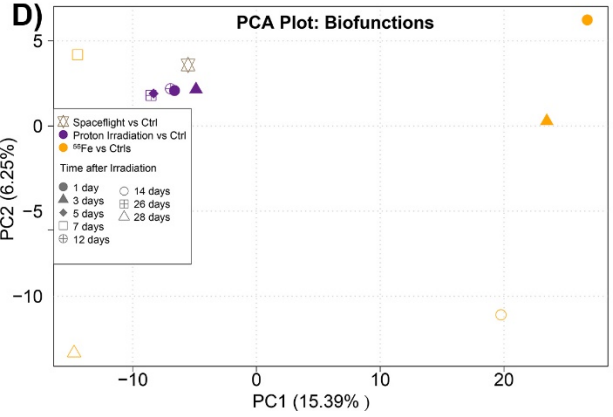


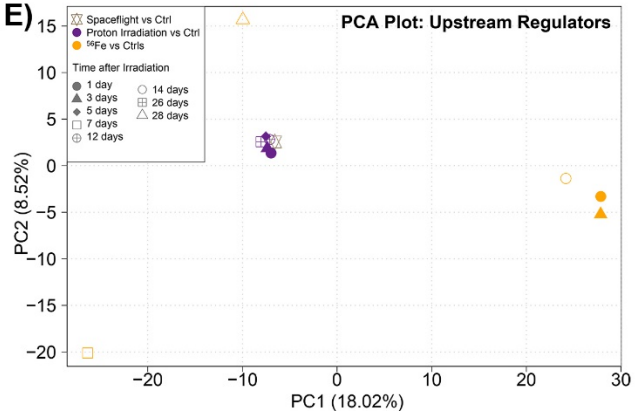
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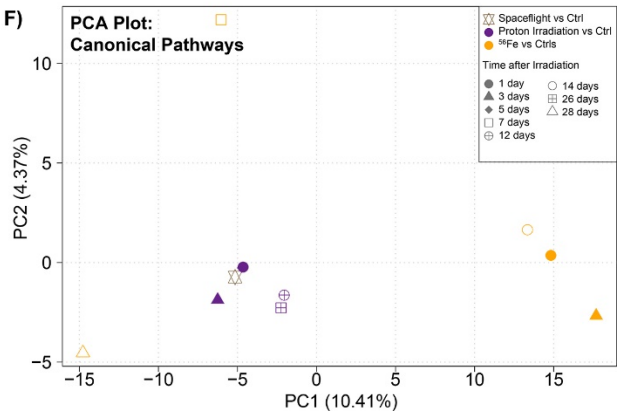
Functional Impact on Health: IPA



- It is interesting to note that the functional predictions show that the spaceflight samples cluster (or behave) very similar to the proton irradiated samples.
- Possible indication (and hypothesis) that in general samples from the ISS may be experiencing more proton ions than other type of ions.

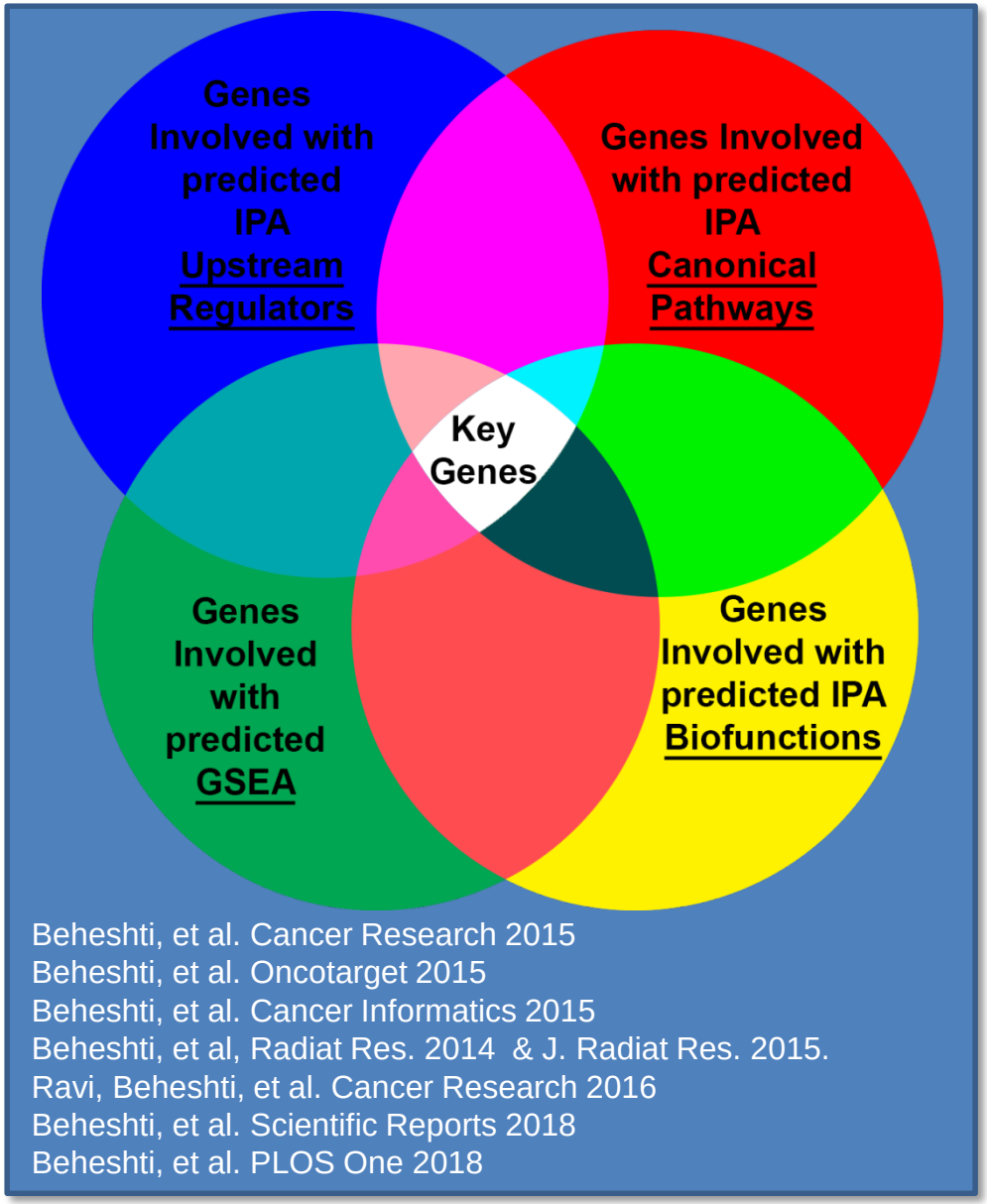






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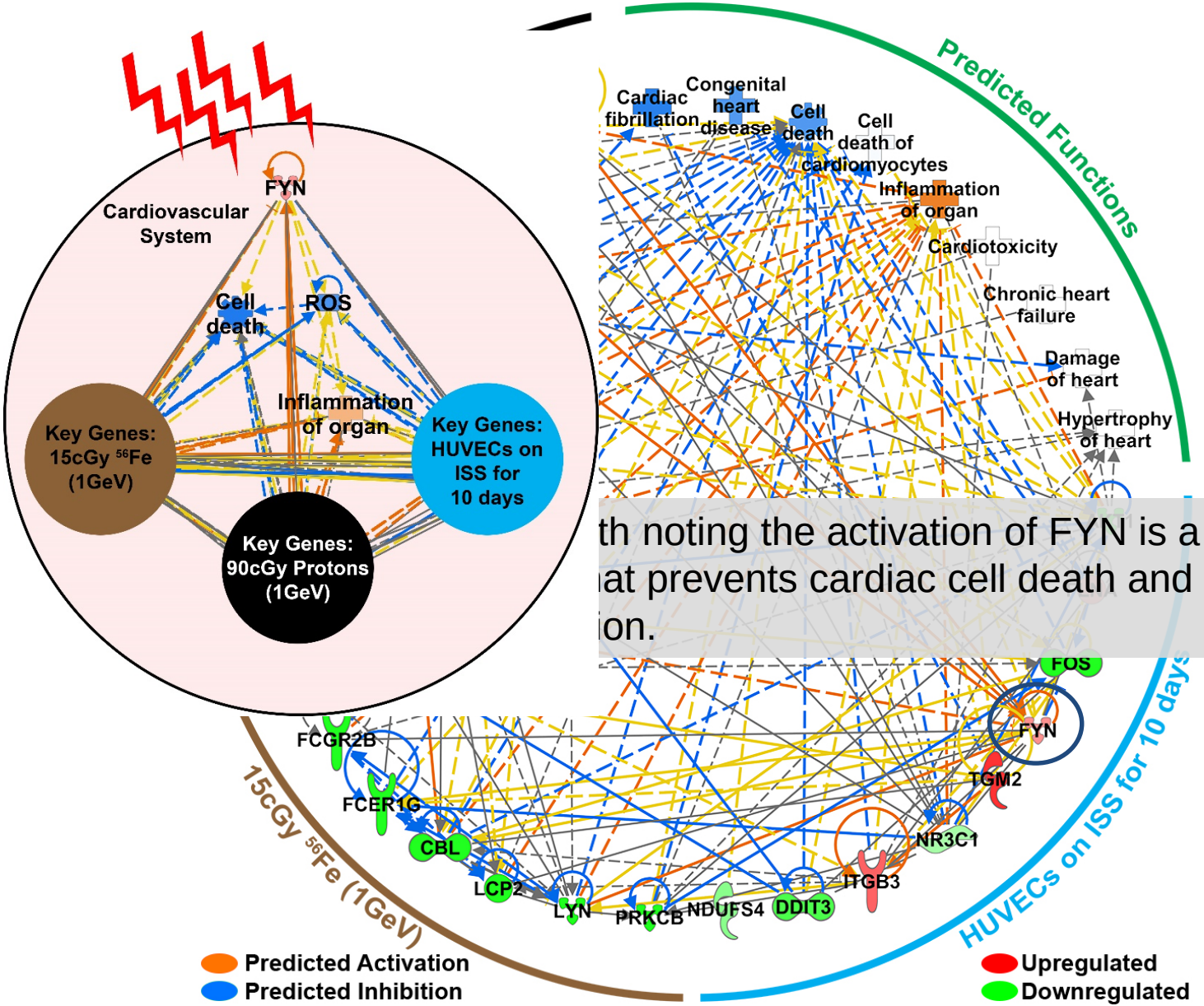
Determination of Key Driving Genes

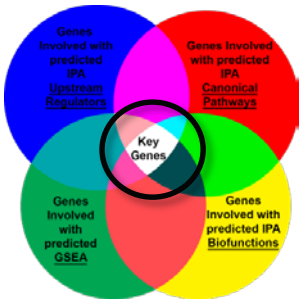


Beheshti, et al. Cancer Research 2015
Beheshti, et al. Oncotarget 2015
Beheshti, et al. Cancer Informatics 2015
Beheshti, et al, Radiat Res. 2014 & J. Radiat Res. 2015.
Ravi, Beheshti, et al. Cancer Research 2016
Beheshti, et al. Scientific Reports 2018
Beheshti, et al. PLOS One 2018

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Key Drivers Involved with Space Radiation Induced Cardiovascular Risk

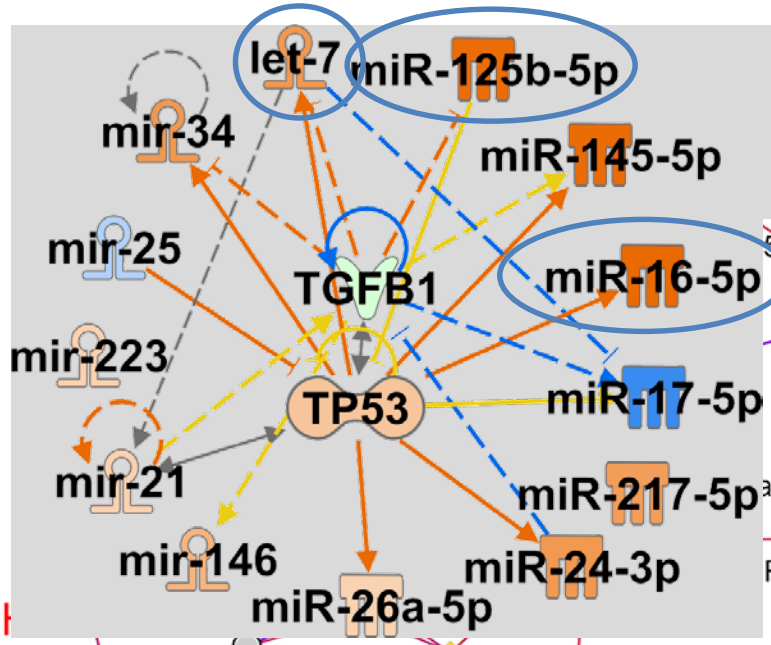


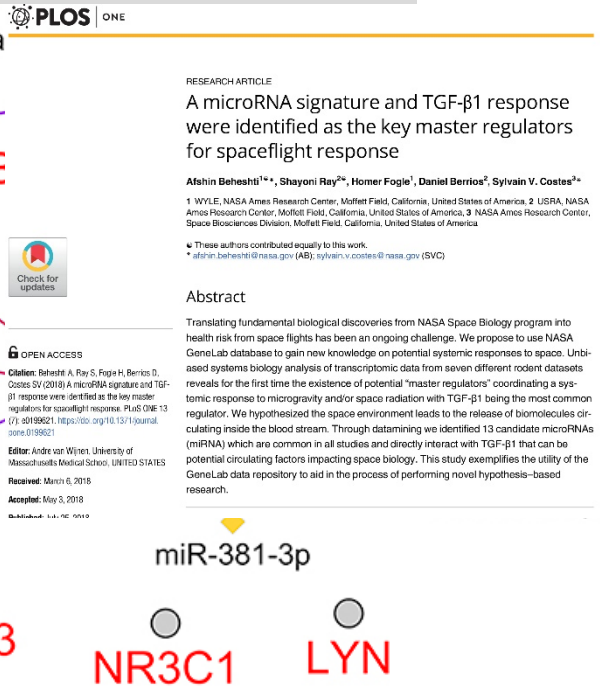


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miRNA impact?

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





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)

Abstract

Translating fundamental biological discoveries from NASA Space Biology program into health risk from space flights has been an ongoing challenge. We propose to use NASA GeneLab database to gain new knowledge on potential systemic responses to space. Unbiased systems biology analysis of transcriptomic data from seven different rodent datasets reveals for the first time the existence of potential "master regulators" coordinating a systemic response to microgravity and/or space radiation with TGF-β1 being the most common regulator. We hypothesized the space environment leads to the release of biomolecules circulating inside the blood stream. Through datamining we identified 13 candidate microRNAs (miRNA) which are common in all studies and directly interact with TGF-β1 that can be potential circulating factors impacting space biology. This study exemplifies the utility of the GeneLab data repository to aid in the process of performing novel hypothesis–based research.

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

Editor: Andre van Wijnen, University of Massachusetts Medical School, UNITED STATES

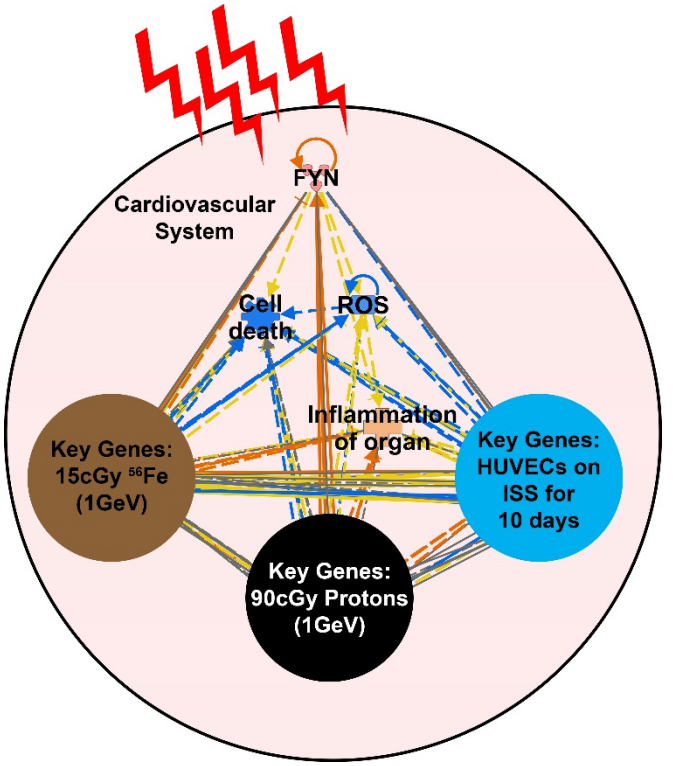
Received: March 6, 2018

Accepted: May 3, 2018

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Conclusions from this Study

- Space radiation causes downregulation of ROS functions in the cardiovascular system
- Astronauts and samples on the ISS might be experiencing more proton IR than any other type of space radiation.
- Key/driving genes: FYN, LCK, AKT1 are upregulated and LYN and FOS are downregulated with FYN being the central driver/hub for the cardiovascular response to space radiation.
  - FYN is a key event that prevents cardiac cell death and ROS production.
- From our study we thus hypothesize that a feedback loop occurs from the oxidative stress caused by space radiation that upregulates FYN which in turn reduces ROS levels and thus ROS pathways, preventing cardiomyocyte and endothelial cell death and thus protecting the cardiovascular systems.
- We believe that this is a novel mechanism for space radiation induced cardiovascular risk directly linking radiation ground studies to spaceflight.



Acknowledgements



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Columbia University Irving Medical Center



J. Tyson McDonald

Hampton University — The Standard of Excellence



Sylvain Costes

NASA Ames Research Center

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