National Aeronautics and
Space Administration

Adapting to Space

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CBPSS Panel on Adapting to Space

Washington, DC

BPS

Biological & Physical Sciences

Adapting to Space

- Fluid shifts
- Unloading
- Radiation

- ISS Microbiome

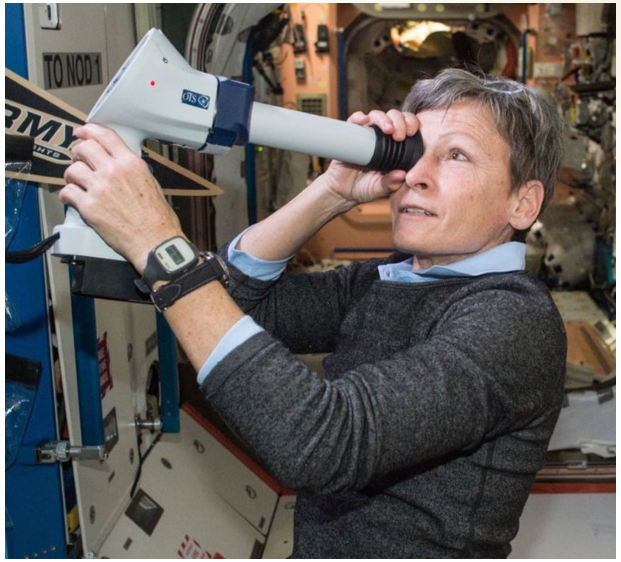
- Genetic background
- Sex
- Microbiome
- Lifestyle
- Life history

Jessica Watkins and Bob Hines, aboard the ISS. Credit NASA.

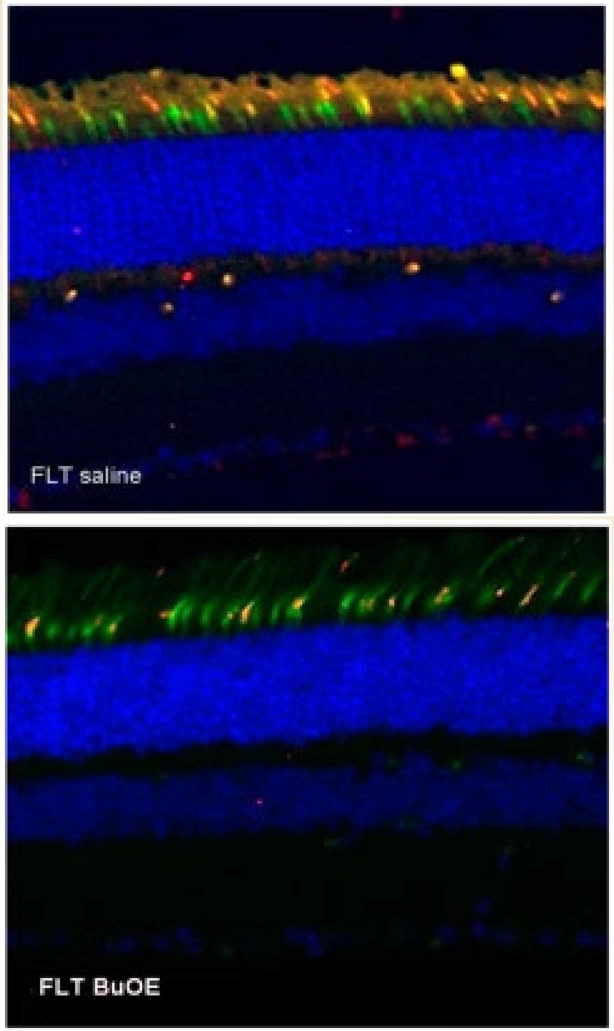
1. How Spaceflight Impacts Vision.
2. How Genetic Background Impacts Muscle Loss.
3. How Unloading and Irradiation Combine to Impact Muscle Loss.
4. How Open Science is Accelerating Discovery.

Evidence of Spaceflight-Induced Adverse Effects on Photoreceptors and Retinal Function in the Mouse Eye.

- Spaceflight induces neuro-ocular changes in astronauts during and after space flight.
- The RR-18 mission (PI Dr. Vivien Mao, Loma Linda U.) characterized acute oxidative damage in ocular structure and retinal function of mice and evaluated the efficacy of an antioxidant in reducing spaceflight-induced changes in the retina.
- **Postflight evaluations showed increases in retinal oxidative stress and apoptotic cell death after spaceflight** and decreases in the amplitudes of alpha and beta waves.
- **Treatment with the antioxidant, BuOE (superoxide dismutase mimic), significantly reduced levels of oxidative stress**, but levels of apoptotic cell death, and ERG metrics remained unchanged.



Peggy Whitson performing an eye check aboard the International Space Station. Credit NASA.

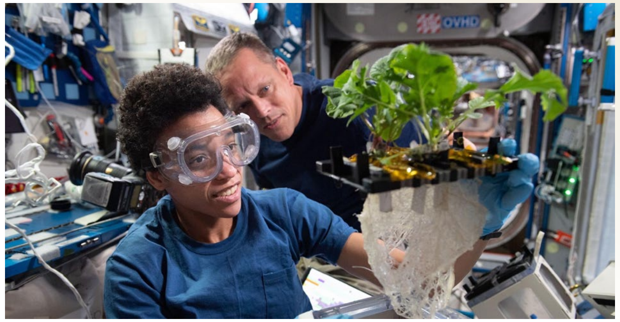


Flight induced oxidative stress in cones (yellow signal) which was mitigated by treatment with the antioxidant, BuOE.s

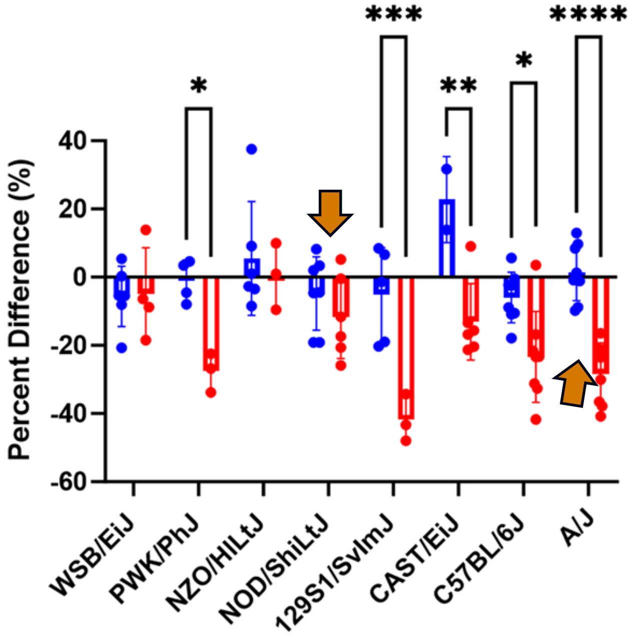
Citation: Mao, X.; Stanbouly, S.;Holley, J.; Pecaut, M.; Crapo, J. **Evidence of Spaceflight-Induced Adverse Effects on Photoreceptors and Retinal Function in the Mouse Eye**. Int. J. Mol. Sci. 2023, 24, 7362. **Funding**: Space Biology award NNX15AB41G to Dr. Vivien Mao.

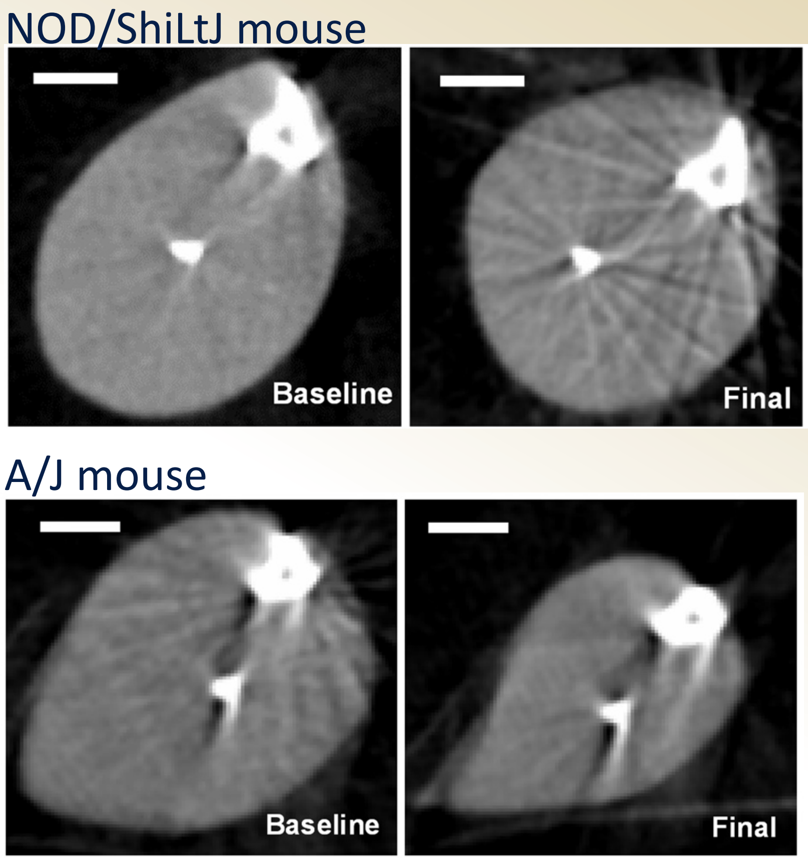
Genetic diversity modulates the physical and transcriptomic response of skeletal muscle to simulated microgravity in male mice

- Astronaut data shows considerable variation in muscle loss in response to microgravity[1].
- Strength losses vary from 0–55% for missions between 30-380 days[2,3,4].
- Study compared response of muscle in 8 mouse strains to 3 weeks of hind limb unloading (PI H. Donahue at VCU).
- **Saw substantial differences in muscle loss between strains.**
- Differences are reflected in the magnitude and pattern of changes within muscles from each strain.



Astronauts aboard the ISS. Credit NASA.





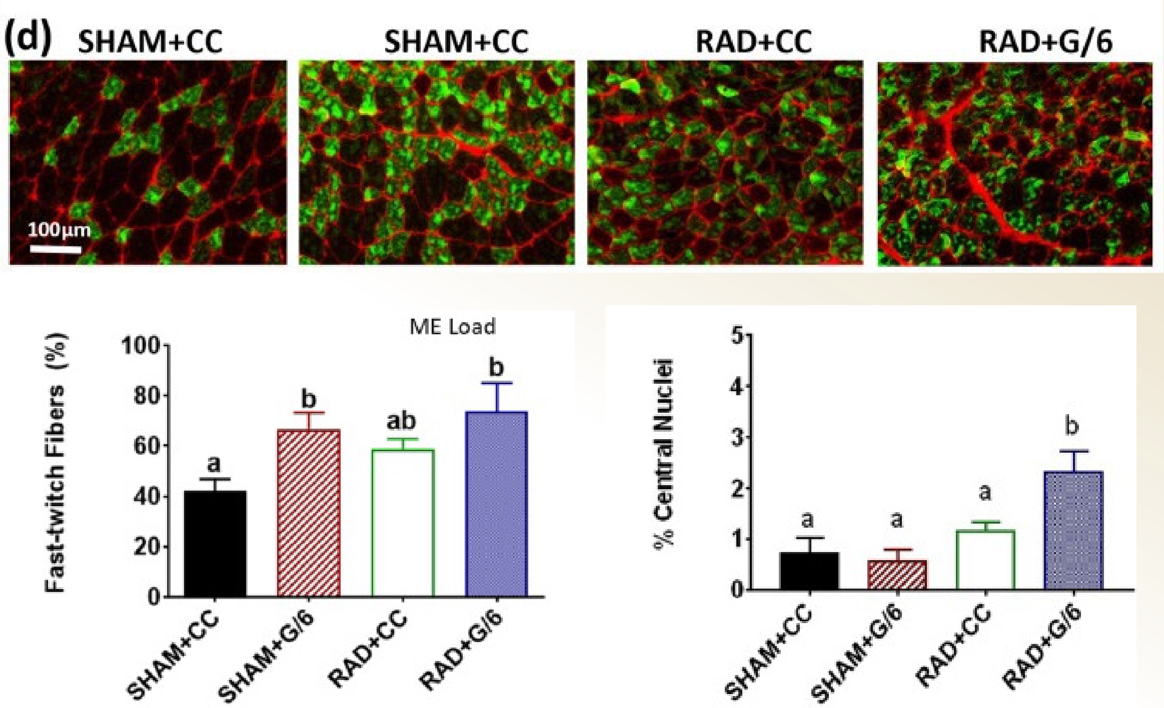
Red is unloaded. Blue is control. Adapted from Figure 3 of Zeineddine et al. 2023.

Citation: Zeineddine, Y., Friedman, M.A., Buettmann, E.G. et al. Genetic diversity modulates the physical and transcriptomic response of skeletal muscle to simulated microgravity in male mice. npj Microgravity 9, 86 (2023) **Funding:** Space Biology grant 80NSSC18K1473 (Gap Junctions and Microgravity Induced Bone Loss) to Dr. Henry Donahue at VCU.

Combined effects of heavy ion exposure and simulated Lunar gravity on skeletal muscle

- Mice exposed to a single 0.5 Gy ^{28}Si dose at a rate of 0.25 Gy min^{-1} (similar to Mars mission) or sham treatment.
- Mice then spent 21 days at 1 or 1/6 g.
- **Partial weight bearing causes muscle atrophy and fiber type switching.**
- **Irradiation combined with unloading did not exacerbate muscle atrophy or fiber switching**.
- However, the proportion of fibers with central nuclei (indicative of muscle regeneration or repair) was impacted irradiation and there was a significant interaction between loading and irradiation.

Luca Parmitano on treadmill aboard the International Space Station. Credit NASA.



Citation: Wiggs et al. Combined effects of heavy ion exposure and simulated Lunar gravity on skeletal muscle. Life Sci Space Res (Amst). 2023 May;37:39-49. **Funding:** Space Biology grant 80NSSC19K0432 to Dr. Lawler.

How Open Science is Accelerating Discovery

RR-1

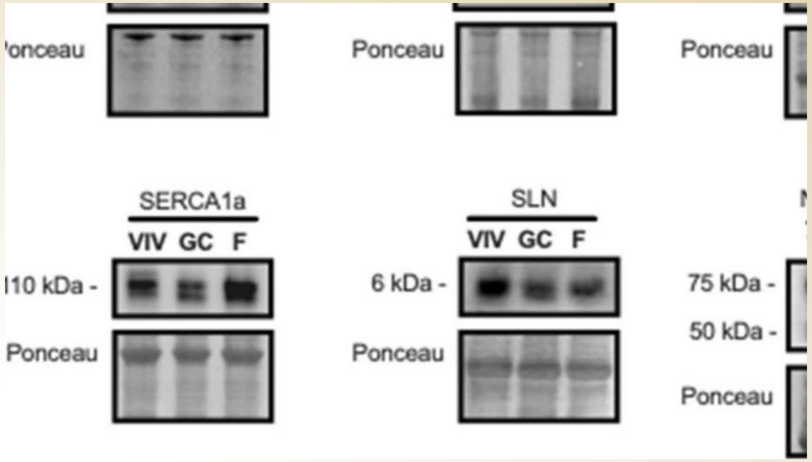
RR-9

Tissue collection

Archiving

Tissue request by PI

Biospecimen Sharing Program
NASA Biological Institutional Science Collection



Braun, J.L.; Geromella, M.S.; Hamstra, S.I.; Messner, H.N.; Fajardo, V.A. Characterizing SERCA Function in Murine Skeletal Muscles after 35–37 Days of Spaceflight. Int. J. Mol. Sci. 2021, 22, 11764.

Primary data deposited

PI deposits secondary data

Team accesses primary and secondary data

Soleus (SOL) Muscle Data:
- Proteomics (quantitative mass spectrometry)
- Transcriptomics (bulk RNA-seq)
- Epigenomics (DNA methylation)
- Calcium Reuptake

Tibialis Anterior (TA) Muscle Data:
- Transcriptomics (bulk RNA-seq)
- Epigenomics (DNA methylation)
- Calcium Reuptake

Explainable ML to identify genetic targets that explain patterns between flight and ground.

Li, K., Desai, R., Scott, R.T. et al. Explainable machine learning identifies multi-omics signatures of muscle response to spaceflight in mice. npj Microgravity 9, 90 (2023).

Conclusion

- Four examples of how Space Biology is advancing:
  - How spaceflight impacts Vision.
  - How genetic background impacts muscle loss.
  - How unloading and irradiation combine to impact muscle loss.
  - How Open Science is accelerating discovery.

- These four examples are the “tip of the iceberg” in recent Space Biology advances:
  - Spaceflight studies
  - Ground studies
  - Diverse model organisms
  - Data science
  - Open science

- Thank you for your attention!