ImmPort Webinar: Harnessing NIAID's ImmPort & NASA's GeneLab Through Computational and Systems Biology Approach: Determining female health risks for spaceflight driven by microRNAs

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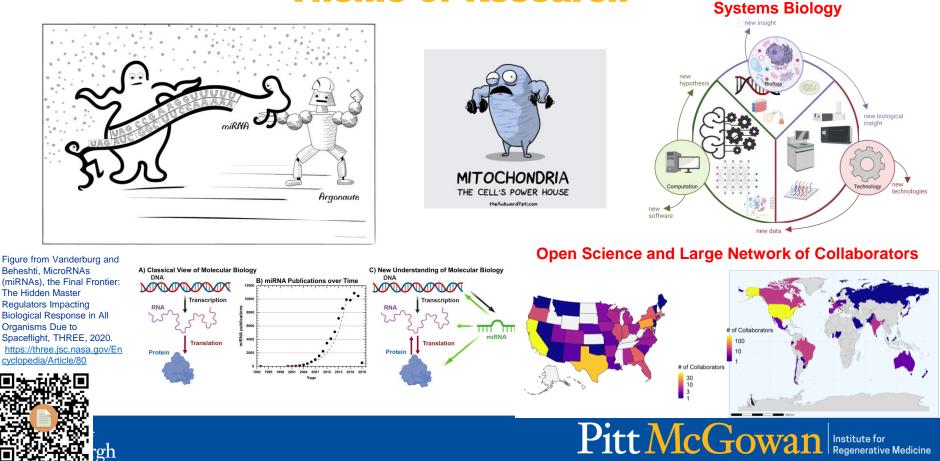
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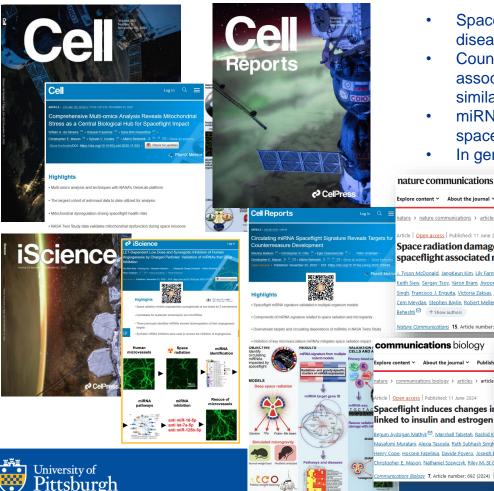


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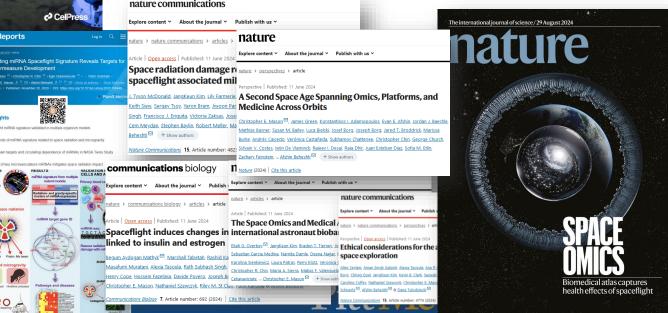
Work on Multiple Areas of Research: Central Theme of Research



Work on Multiple Areas of Research: Space Biology



- Space is an accelerated model for aging and mitochondrial disease
- Countermeasures and biomarkers developed for health risks associated with the space environment can easily be applied to similar clinical diseases
- miRNAs as a key biomarker for health risks associated with spaceflight and target for countermeasures
- In general understanding health risks due to spaceflight





Pitt Space Initiative

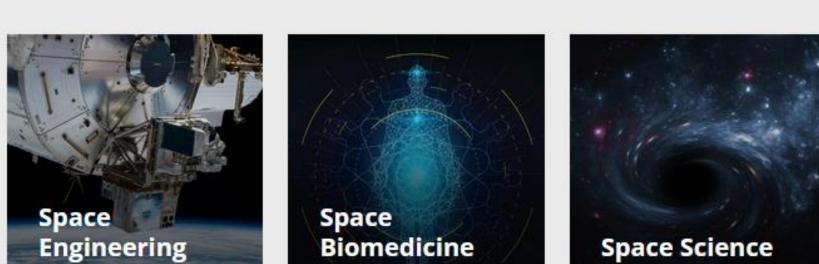
World-class research and graduates in space engineering, biomedicine, and science to meet the growing needs of the U.S. space community.

RESEARCH

EDUCATION







https://space.pitt.edu/



CORE STRENGTHS

University of Pittsburgh

Pitt Space



Ξ





The Space Biomedicine program at the University of Pittsburgh is at the forefront of integrating space biology with advanced biomedical research. Its mission is to develop innovative technologies to safeguard human health and optimize performance in space, while also translating the knowledge gained from space research into solutions for terrestrial healthcare. In addition to its research focus, the program has a second mission: to promote education and outreach in space biomedicine. It aims to establish a robust educational environment that not only supports the University of Pittsburgh but also engages domestic and global partners, preparing the next generation of space researchers and advancing knowledge in this critical field.

Advancing Human Health from Space to Earth

University of

Pittsburgh

As commercial and private spaceflight activities increase, particularly in low Earth orbit (LEO), the Space Biomedicine program is dedicated to generating impactful discoveries that not only address the challenges of space exploration but also provide tangible solutions for improving human health and environmental sustainability on Earth. The program's collaborative approach ensures that its research outcomes will have broad applications both in space and on Earth, while its educational initiatives will cultivate a new generation of experts in space biology and medicine.

The Space Biomedicine program is designed to foster interdisciplinary collaboration across a wide range of global challenges, as highlighted below.

Human Health and Physiology in Space	+
Mitochondrial and Metabolic Health	+
Radiation Exposure and Countermeasures	+
Advanced Medical Technologies for Space	+
Genetic, Omics, and Cellular Research	+
Microbiology and Immune System in Space	+
Pharmacology and Drug Development	+
Environmental and Sustainability Research	+
Technological Innovation and Translational Research	+
Al/ML-Driven Space Medicine Research	+

https://space.pitt.edu/about/space-biomedicine



Large Collaborative Model for Education and Outreach for the Space Biomedicine Program





Education and Outreach Space Biomedicine Program

The Global Education Certificate Space Program at the University of Pittsburgh (Pitt) aims to establish a cross-institutional and global education initiative that brings together leading academic, industry, and nonprofit entities to educate the next generation of space biology and biomedicine scientists. This innovative program will encompass student exchanges, joint seminars, integrated curricula, and co-teaching by faculty across multiple institutions globally, with Pitt as the central hub.







Education and Outreach Space Biomedicine Program

Initial Ideas for Implementation:

- 1. Degree Programs and Curriculum Development:
 - Develop a curriculum that enables students to earn a degree in Space Biomedicine/Biology. At Pitt, we've already introduced an "Introduction to Space Engineering" course, which has seen high demand. Building on this momentum, we could develop and offer Space Biomedicine courses in future semesters that will be applied as a cross-institutional approach, that would amplify our impact!
- 2. Credit Transfer and Course Structure:
 - Ensure course credits are transferable across all participating institutions. Classes will be available in both in-person and virtual formats. Faculty and scientists from various institutions could co-teach courses, allowing us to leverage diverse expertise and avoid overburdening any single instructor.
- 3. Industry and Non-Profit Collaboration:
 - Collaborate with industry partners to sponsor and support student programs. Industry experts could also provide courses on translating academic research into commercial applications, which is crucial for space biomedicine and rapid deployment of key technologies and countermeasures.
- 4. Space Industry Partnerships:
 - Engage space industry partners such as SpaceX, Axiom, and hardware developers like my collaborator from EcoAtoms and Ice Cubes. As the program develops, we can involve additional partners to broaden our network and capabilities.
- 5. Incorporating GeneLab for Universities (GL4U):
 - Utilize the existing GeneLab 4 University program. We can evolve this into a core component of our curriculum.
- 6. Global, Collaborative Effort:
 - Create a community-driven program that integrates space biomedicine/biology education across institutions. The program will cover foundational to advanced topics, reflecting the rapid advancements in this field.
- 7. Support from Space Agencies and Funding Opportunities:
 - I have had preliminary discussions with a couple people at NASA, and they mentioned there might be potential funds they can provide for such an effort, at least in the US. I will be exploring this further next week. This will probably take a while to put in place, BUT there is very positive and enthusiastic interest.

PittMcGowan Institute for Regenerative Medicine

- o I am also in touch with colleagues at ESA, who are very supportive and keen to participate. I will be discussing this with them in a few weeks.
- 8. Nonprofit and Industry Engagement:
 - Engaging nonprofits and industry stakeholders will be critical. With initial momentum, I believe we can secure their support fairly easily.



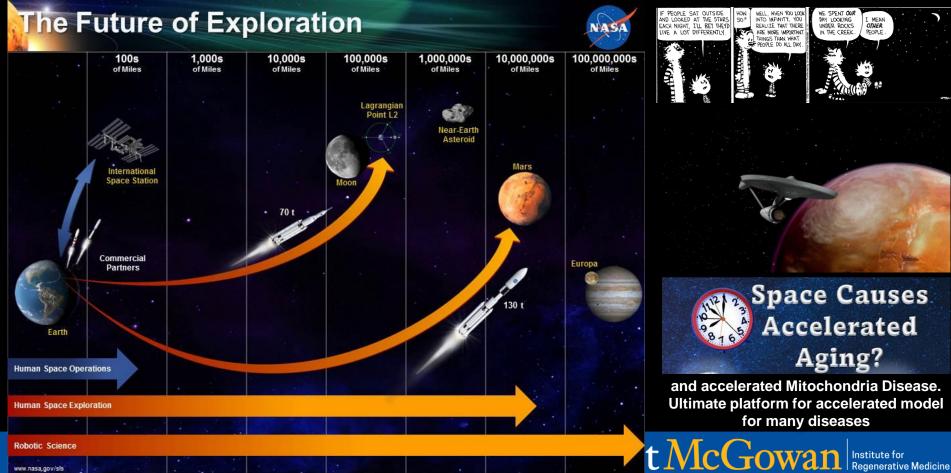
Interested Universities and Agencies for Education So Far





Pitt McGowan Institute for Regenerative Medicine

Why Care and Research Space?





WHEN YOU LOOK

INTO INFINITY, YOU

DEALIZE THAT THERE

ARE MORE IMPORTANT

THINGS THAN WHAT

WE SPENT OUR

DAY LOOKING

UNDER ROCKS

IN THE CREEK

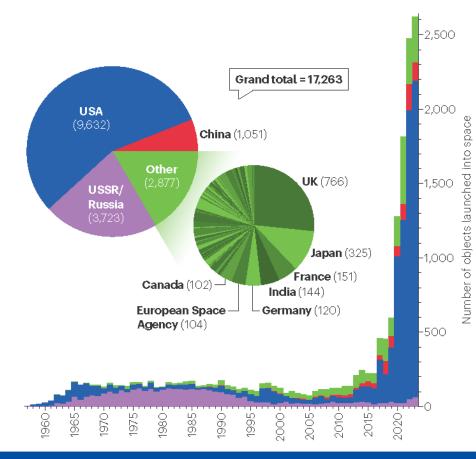
MEAt

OTHER PEOPLE

Aging?

and accelerated Mitochondria Disease. Ultimate platform for accelerated model for many diseases

The Second Space Age

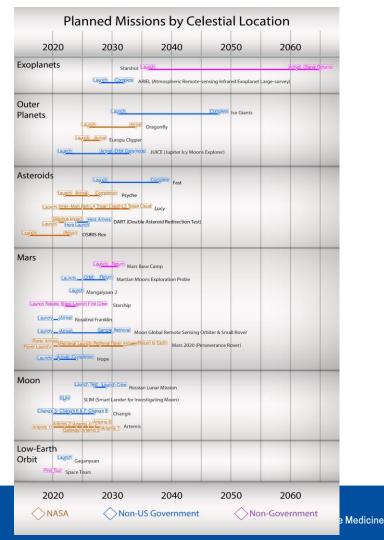




The Next Stage of Missions in Space: All Planned Future Space Missions













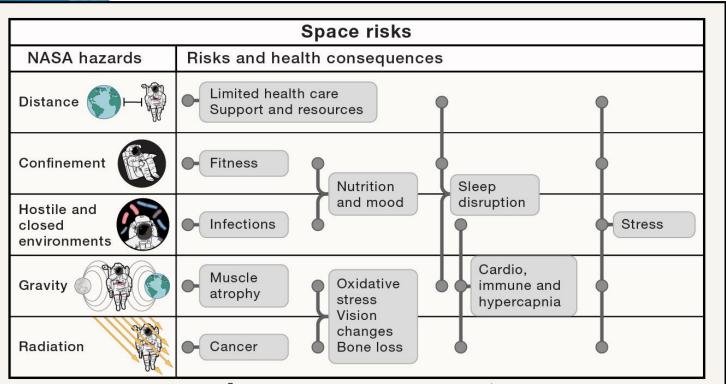
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Fundamental Biological Features of Spaceflight: Advancing the Field t Enable Deep-Space Exploration

Ebraham Ahahanakao $\frac{34}{2} + Ryan T. Scott. <math>\frac{34}{2} + Matthew J. MacKay <math>\frac{34}{2} + \dots$ Sylvain V. Costas. $\frac{34}{2} \frac{34}{100}$ Christopher E. Mason. $\frac{3}{2} \frac{35}{100} + Ahaha Bahashti. <math>\frac{3}{2} \frac{36}{200} + Show all authors + Show bodinetes$

DOI: https://doi.org/10.1016/j.cell.2020.10.050 - 👰 Check for updates

5 Hazards of Spaceflight



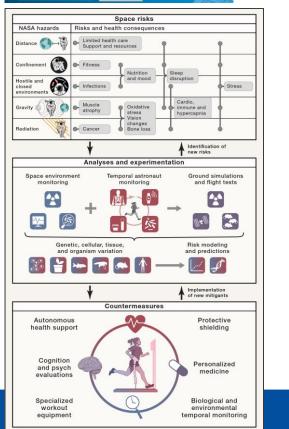


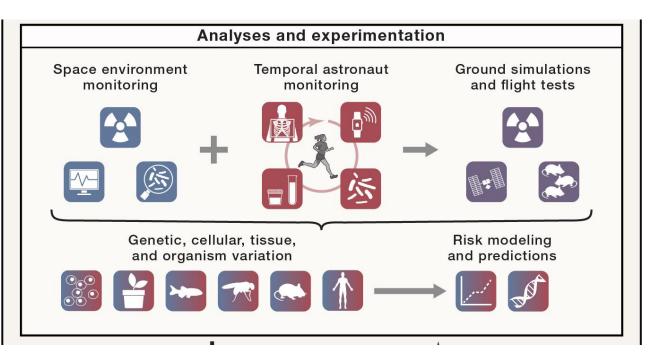
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Fundamental Biological Features of Spaceflight: Advancing the Field to Enable Deep-Space Exploration Estatem Advancekce ¹⁰ + Ryen 1 Soct ²¹ + Matter J Markov ²¹ + ... System 4 and to 1 + Stock Advance Onfrindere E Hanna A¹⁰ El + Advancekce J Social advance + Stock Advance DOI: https://doi.org/10.1016/j.col.200.01.000 + ... Col.200.01.000

5 Hazards of Spaceflight

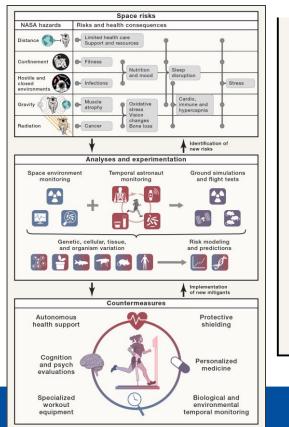


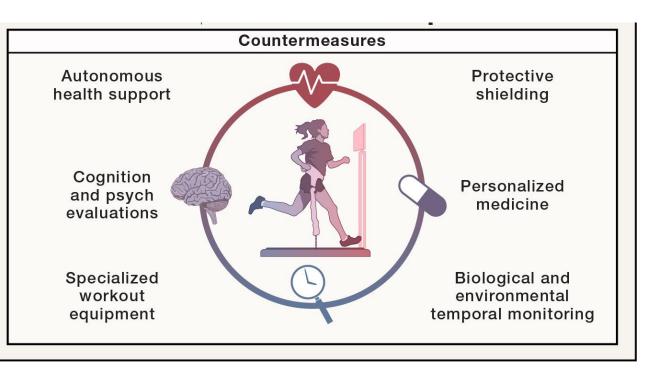


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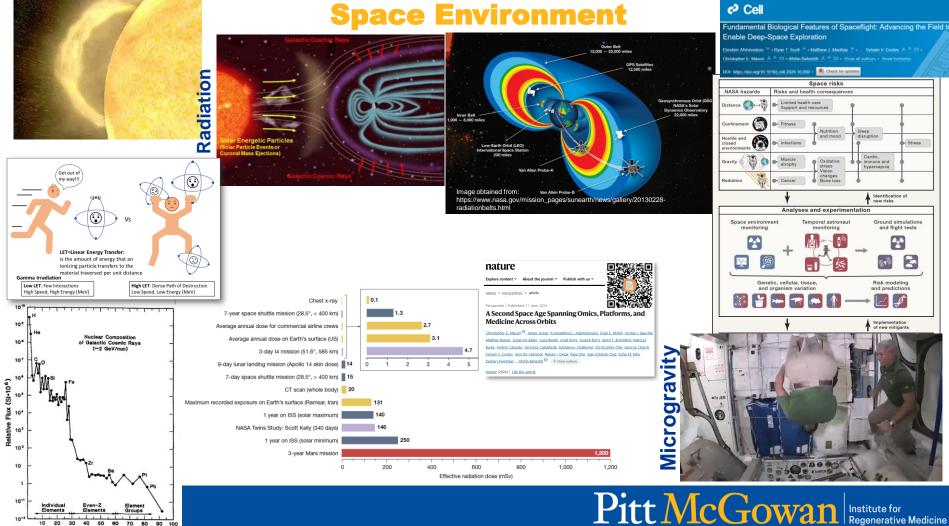
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5 Hazards of Spaceflight









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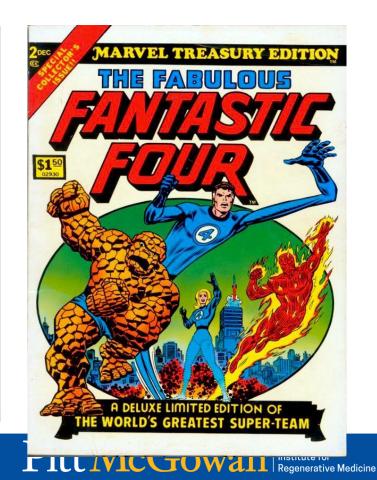
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Flements

Galactic Cosmic Radiation (High LET) – a cautionary tale

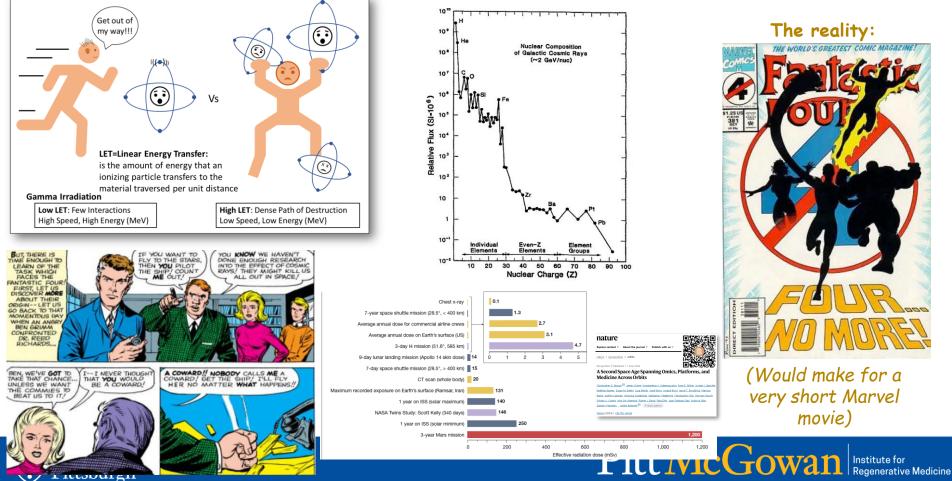






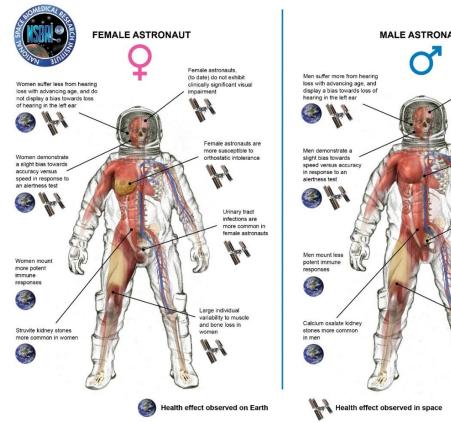


Galactic Cosmic Radiation (High LET) – a cautionary tale

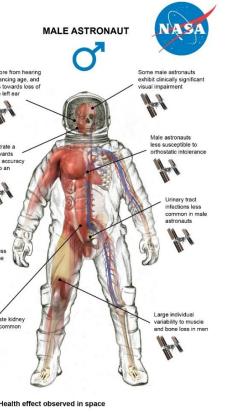


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Space Environment Health Risks On Astronauts



University of Pittsburgh



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Fundamental Biological Features of Spaceflight: Advancing the Field tt Enable Deep-Space Exploration

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Mission duration	6 mc	inths	12 months 1 month 12 months		onths	12 months		36 months				
Return duration	<= 1 day		<= 1 day		< 5 days		5 days		Weeks/ months		Months	
Radiation	Van	Allen	Van	Allen	Deep Space		Lunar	Deep Space	Variable			
Gravity	Mie	cro	Mi	cro	Mi	cro	1/6	òg	Mi	cro	Vari	able
Health risks	Mission	Long- term	Mission	Long- term	Mission	Long- term	Mission	Long- term	Mission	Long- term	Mission	Long- term
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Medical	0	0	0	0	0	•	0	0	•	•	۲	0
SANS	0	0	0	0	•	•	0	0	•	•	۲	۲
Arrhythmia	0	0	0	0	0	0	0	0	•	0	•	0
BMed	0	0	0	0	0	•	0	0	0	0	۲	•
Occupant protection	0	0	0	0	0	0	0	0	0	0	0	0
Hypobaric hypoxia	0	0	0	0	0	•	0	0	0	0	0	0
EVA	•	0	•	0	0	0	0	0	0	0	0	•
Degen	0	0	•	0	•	0	•	0	•	•	•	•
CNS	0	0	•	0	•	0	•	0	0	0	0	0
Team	0	0	0	•	0	•	0	•	0	0	•	0
Sleep	0	0	0	•	0	•	0	•	0	0	0	0
Sensorimotor	0	0	0	•	0	•	0	•	0	0	0	0
Cancer		0	0	0	•	•		0	•	•		•
Muscle	0	0	0	•	0	0	0	•	0	0	0	0
Aerobic	0	0	0	0	0	•	0	•	0	0	0	0
Immune	0	0	0	0	0	•	0	•	0	0	0	0
Microhost	0	0	0	•	0	•	0	•	0	•	0	0
DCS	0	0	•	•	0	•	0	•	0	0	0	۲
Stability	۲	0	•	•	•	•	•	•		0	•	•
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Type of Experiments Related to Space Biology

Experiments Done in Space



GENETICS

Platform

Research Center

University of

Pittsburgh

Space Radiation Simulated Experiments

Brookhaven National Laboratory

Advanced Q

Exploring the Effects of Spaceflight on Mouse Physiology using the Open Access NASA GeneLab

Afshin Beheshti¹, Yasaman Shirazi-Fard², Sungshin Choi¹, Daniel Berrios³, Samrawit G. Gebre¹, Jonathan M. Galazka², Sylvain V. Costes² ¹WYLE Labs, Space Biosciences Division, NASA Ames Research Center. ²Space Biosciences Division, NASA Ames Research Center. ³USRA, NASA Ames

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Microgravity Simulated Experiments



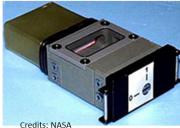
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PittMcGowan https://www.rutkovelab.org/nasa/

Mortreux

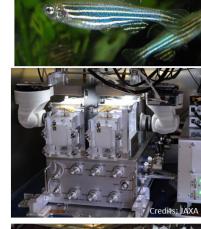
ype of Experiments Related to Space Biology





Credits: IAXA

C. elegans culture chambers for the Space Aging experiment aboard the ISS





The Zebrafish Muscle investigation employs the ISS Aquatic Habitat, an aquarium in microgravity.





rgence of mustard seedlings



Interior view of an incubator cassette from the Bioculture System

> SCIENCELIN Why fungi adapt so well to life in space

ATTHEW PHELAN + MARCH 7, 2018 . . .

Credits: NASA/Ames Research Cent

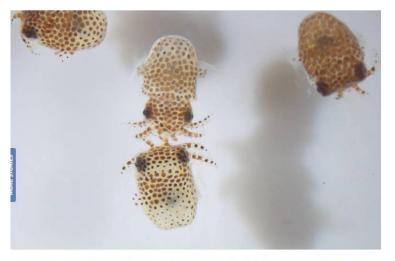




Type of Experiments Related to Space Biology



Squids and Other Research Heading to the Station. Yes, Squids!



In just over a week on June 3, 2021, these tiny squids will head to space along with many other scientific experiments aboard SpaceX's 22nd cargo resupply mission to the International Space Station. The squids are a part of the UMAMI study which examines the effects of spaceflight on interactions between beneficial microbes and their animal hosts. UMAMI stands for Understanding of Microgravity on Animal-Microbe Interactions. Microbes play a significant role in the normal development of animal tissues and in maintaining human health.



Newly hatched squid right before being added to the spaceflight hardware. (Photo credit: Jamie Foster)



Hatchling squid in their space aquariums. (Photo credit: Jamie Foster)



Space Omics/Data Platform that The Public can Use!!

https://osdr.nasa.gov

Help ~



Research & Resources v Home About ~ Data & Tools v Working Groups v

> GeneLab Open Science for Life in Space Keywords

Data & Tools - Research & Resources - Working Groups -Home About -Help -

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not possible on Earth.





Welcome to NASA GeneLab - the first comprehensive space-related omics database; users can upload, download, share, store, and analyze spaceflight and spaceflight-relevant data from experiments using model organisms.







GeneLab Multi-Omics Analysis Working Group

https://osdr.nasa.gov



https://www.nasa.gov/osdr-working-groups-awg-about/



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Analysis Working Groups (AWG)

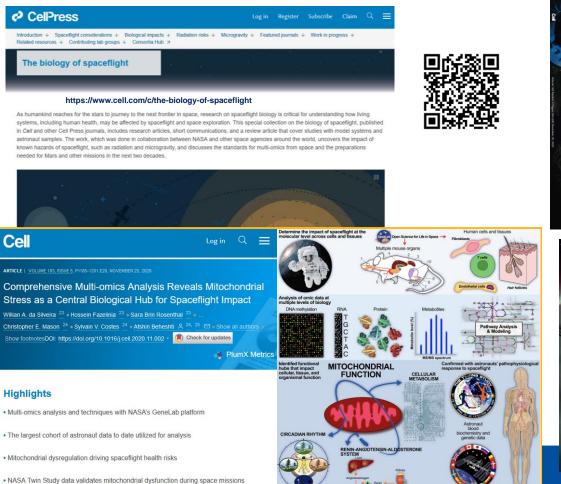
- About the Analysis Working Groups
- Charter
- · How to Join
- Current AWG Members
- AWG Forum

XX MVR

- AWG Annual Reports: 2018 2019
- AWG Workshops: 2018 2019 2021 2023
- AWG Symposia: 2022 2023 2024



Lots of Papers Published on Space Biology in 11/2020!!





CelPre





Afshin Beheshti University of Pittsburgh MeGowan Institute for





Susan Bailey



New Nature Portfolio Paper Package Launched on June 11th 2024!!

nature portfolio

Space Omics and Medical Atlas (SOMA) across orbits

New studies on astronauts and space biology bring humanity one step closer to the final frontier

SCIENCE

showstoppers

Animals

Health Environmen

Women appear to withstand the rigors of zero gravity better than men, report says.

Spaceflight is hard on humans, but scientists see no

The New York Times

3 Days in Space Were Enough to Change 4 Astronauts' Bodies and Minds

An extensive examination of medical data gathe private Inspiration4 mission in 2021 revealed te cognitive declines and genetic changes in the cre

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Jared Isaacman, left, and Hayley Arceneaux, two of the fou members, during the mission in 2021. spacex



acman and Hayley Arceneaux conduct research during the Inspiration4 SpaceX Mission. (SpaceX)



Afshin Beheshti



Chris Mason

Weill Cornell Medicine

- Central theme around the Inspiration 4 mission, JAXA missions, and commercial missions in general
- 44 space biology related papers total part of the package





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Article Open access Published: 11 June 2024 Cosmic kidney disease: an integrated pan-omic,	Article <u>Open access</u> Published: 11 June 2024 Aging and putative frailty biomarkers are altered b		Article <u>Open access</u> Published: 11 June 2024 Spaceflight induces changes in gene expression profiles
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A.C.Almeida, Elizabeth Blaber, Jonathan C. Schisler, Amelia J. Eisch, Masafumi Muratani, Sara R. Zwart,	underpinning spaceflight dermatology	Explore content Y About the journal Y Publish with us Y	Medicine Across Orbits
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Karolina Sienkiewicz, Laura Patras, Remi Klotz, Veronica Ortiz, Matthew MacKay, Annalise Schweickart	Article Open access Published: 11 June 2024	Nature Communications 15, Article number: 4862 (2024) Cite this article	nature > nature communications > articles > article
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	Singh, Francisco J. Enguita, Victoria Zaksas, Joseph W. Guarnieri, Michael Topper, Douglas C. V		
	Cem Meydan, Stephen Baylin, Robert Meller, Masafumi Muratani, D. Marshall Porterfield, Af		Nailil Husna, Tatsuya Aiba, Shin-Ichiro Fujita, Yoshika Saito, Dai Shiba, Takashi Kudo, Satoru Takahashi, Satoshi Furukawa & Masafumi Muratani
Jared Isaacman, left, and Hayley Arceneaux, two of the four Inspiration4 crew	Beheshti [™] + Show authors		
members, during the mission in 2021. spaceX	Nature Communications 15, Article number: 4825 (2024) Cite this article		Nature Communications 15, Article number: 4814 (2024) Cite this article

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Perspective | Published: 11 June 2024

A Second Space Age Spanning Omics, Platforms, and Medicine Across Orbits

<u>Christopher E. Mason</u> ^{ID}, James Green, Konstantinos I. Adamopoulos, Evan E. Afshin, Jordan J. Baechle, Mathias Basner, Susan M. Bailey, Luca Bielski, Josef Borg, Joseph Borg, Jared T. Broddrick, Marissa Burke, Andrés Caicedo, Verónica Castañeda, Subhamoy Chatterjee, Christopher Chin, George Church, Sylvain V. Costes, Iwijn De Vlaminck, Rajeev I. Desai, Raja Dhir, Juan Esteban Diaz, Sofia M. Etlin, Zachary Feinstein, ... Afshin Beheshti^{ID} + Show authors

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hristopher R. Chin, Maria A. Sierra, Matias F. Valenzuela, Ezequiel Dantas, Theodore M. Nelson, Egle ekanaviciute, ... Christopher E. Mason 😂 + Show authors



Jared Isaacman, left, and Hayley Arceneaux, two of the four Inspiration4 cremembers, during the mission in 2021. spaceX Space radiation damage rescued by inhibition of key spaceflight associated miRNAs

LTyson McDonald, Jangkeun Kim, Lily Farmerie, Meghan L. Johnson, Nidia S. Trovao, Shehbeel Arif, Keith Siew, Sergey Tsoy, Yaron Bram, Jiwoon Park, Ellah Overbey, Krista Ryon, Jeffrey Halton, Urminder Singh, Francisco J. Enguita, Victoria Zaksas, Joseph W. Guarnieri, Michael Topper, Douglas C. Wallace, Cem Meydana, Stephen Baylin, Robert Meller, Masafumi Muratani, D. Marshall Porterfield, ... Afshin Behesth ¹⁰ + Snow authors

Nature Communications 15, Article number: 4825 (2024) Cite this article

The international journal of science / 29 August 2024

nature

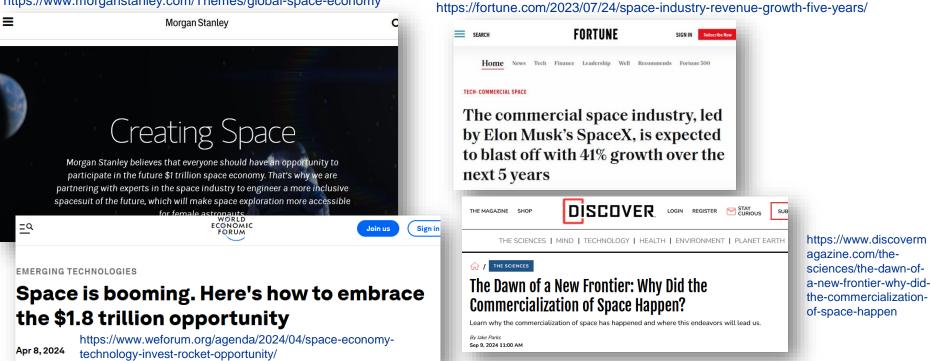
profiles

, and

Biomedical atlas captures health effects of spaceflight

The Second Space Age

https://www.morganstanley.com/Themes/global-space-economy







Question:

Can we leverage other publicly available data platforms to determine novel hypothesis and data for advancing both clinical and spaceflight related issues?





<u>Question:</u> Can we leverage multiple publicly available data platforms to determine novel hypothesis and data for advancing both clinical and spaceflight related issues?

WWW.IMMPORT.org

ImmPort is funded by the NIH, NIAID and DAIT in support of the NIH mission to share data with the public. Data shared through ImmPort has been provided by NIH-funded programs, other research organizations and individual scientists ensuring these discoveries will be the foundation of future research.

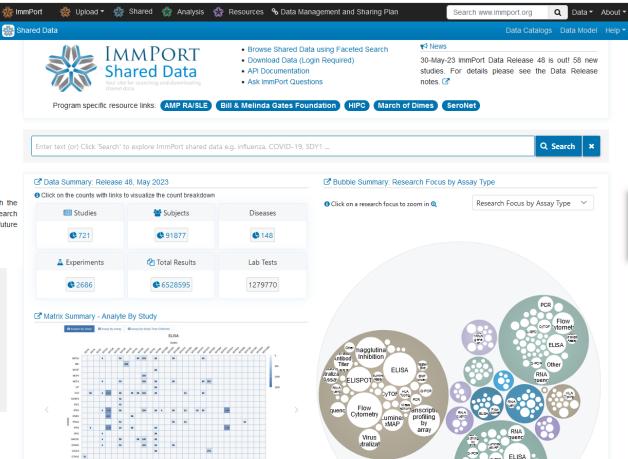
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Short Answer: Yes!!

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Space Omics Platform that The Public can Use!!



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https://osdr.nasa.gov



Welcome to NASA GeneLab - the first comprehensive space-related omics database; users can upload, download, share, store, and analyze spaceflight and spaceflight-relevant data from experiments using model organisms



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Dataset on ImmPort Related to Small-for-gestational-age fetuses (SGA)

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Download	Adverse Event Assessment Interventions Medications Substance Demographics Lab Tests Mechanistic Assays Study Files Maternal plasma samples were extracted from whole blood and collected	2000 LBW 2000 LBW PAPAPORTAR LBW LBW LBW Cestational Age 500 500 500 500 500 500 500 50
Accession	prospectively at three time-points; $12^{+0} - 14^{+6}$ (time-point A), $15^{+0} - 17^{+6}$ (time-point B) and/or $18^{+0} - 21^{+6}$ (time-point C) weeks gestation.	500 Ce⁵¹⁰ 24 26 28 30 32 34 36 38 40 42 44 46
Title	Maternal plasma miRNAs as potential biomarkers for detecting risk of SGA	Preterm Term Postterm Weeks of Gestation
DOI Brief Description	10.21430/M3TU8P1DQ0 To investigate the miRNA biomarkers associated with the <u>Small-for-gestational-age fetuses</u> (SGA) condition, maternal plasma samples from 29 women (N=16 normal, N=13 SGA) were selected to form a discovery cohort in which expression data for a total of 800 miRNAs was determined using the Nanostring nCounter miRNA assay. Differential expression of two miRNA markers; hsa-miR-374a-5p (p = 0?0176) and hsa-let-7d-5p (p = 0?0036), were validated in an independent population of 95 women (SGA n = 12, Control n = 83).	Elisabeles c2 (200) 103 141 Contents lists available at ScienceDirect EBioMedicine pourrait homepage: www.efsevier.com/locate/ebiom
Research Focus Condition Studied	Pregnancy Small for Gestational Age	Research paper Maternal plasma miRNAs as potential biomarkers for detecting risk of small-for-gestational-age births Sung Hye Kim ³⁰ , David A. MacIntyre ¹⁰ , Reem Binkhamis ⁴ , Joanna Cook ^{44,04} , Lynne Sykes ^{43,04} , Phillip R. Bennett ^{14,04} , Vasso Terzidou ^{14,04,04} ¹⁴ Protection Compared Mathematic Registric at Production, hunter of Reputations and Dordapportal Iting, to
Start Date Detailed	Small-for-gestational-age fetuses (SGA) (birthweight <10th centile) are at high risk for stillbirth or long-term adverse outcomes. Here, we investigate the	*Intrinsic Long, Experiment of Methodom, Experiment and Reproduction, Imperial College Landon, Robitar of Reproductive and Developmental Instage, Data *March of Gimmes Development Technical Instage, Line Lindon, Lindon Tabala, Charlos Calabana *Quero Charlosoft and Colles Linguid. Emperial College Instalhare NRS Trace, Landon, Lindon Edugion *Ausent: Department of Observice and Capaneology, Chelora and Westminer Empired, Lindon, Lindon Edugion *Ausent: Department of Observice and Capaneology, Chelora and Westminer Empired, Lindon, Lindon Edugion
Description	ability of circulating maternal plasma miRNAs to determine the risk of SGA births. Maternal plasma samples from 29 women of whom 16 subsequently delivered normally grown babies and 13 delivered SGA (birthweight <5th centile) were selected from a total of 511 women recruited to form a discovery cohort in which expression data for a total of 800 miRNAs was determined using the Nanostring nCounter miRNA assay. Validation by RT-qPCR was performed in an independent cohort. Findings: Partial least-squares discriminant analysis (PLS-DA) of the Nanostring nCounter miRNA assay initially identified seven miRNAs at 12?14+6 weeks gestation, which discriminated between SGA cases and controls. Four of these were technically validated by RT-qPCR. Differential expression of two miRNA markers; hsa-miR-374a-5p (p = 0?0176) and hsa-let-7d-5p (p = 0?0036), were validated in an independent population of 95 women (SGA n = 12, Control n = 83). In the validation cohort, which was enriched for SGA cases, the ROC AUCs were 0?71 for hsa-miR-374a-5p, and 0?77 for the two combined. Whilst larger population-wide studies are required to validate their performance, these findings highlight the potential of circulating miRNAs to act as biomarkers for early prediction of SGA births	ATTICLE INFO ADDATESTICS ADDAT

Dataset on ImmPort Related to Small-for-gestational-age fetuses (SGA)

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Condit Studied Start D	fter returning to Earth???	for-gestational- e Kim ^{3,b} , David A. M , Bennett ^{abbc} , Vasso zeu, Popartenet of Metalobon net 1922 of Kinel Eugen me's and Chebas Hospital Import	facIntyre ^{a,b} , Reem Binkhamis ^a , Joanna Cook ^{a,c,d} , Lynne Sykes ^{a,b,c} ,	
Detaile Description	ability of circulating maternal plasma miRNAs to determine the risk of SGA births. Maternal plasma samples from 29 women of whom 16 subsequently delivered normally grown babies and 13 delivered SGA (birthweight <5th centile) were selected from a total of 511 women recruited to form a discovery cohort in which expression data for a total of 800 miRNAs was determined using the Nanostring nCounter miRNA assay. Validation by RT-qPCR was performed in an independent cohort. Findings: Partial least-squares discriminant analysis (PLS-DA) of the Nanostring nCounter miRNA assay initially identified seven miRNAs at 12?14+6 weeks gestation, which discriminated between SGA cases and controls. Four of these were technically validated by RT-	ARTICLE INFO Ardic Houry: Berrier Angene 200 Academic Manager Analise Information 200 Analise Informations and Manager Manager Manager Seal Information and age	A B 5 T K A C T Background: Small-for gentational age fetures (SCA) (birthweight -10th centile) are at high ri- or long terms above automous. Here, we investigate the ability of circulating maternal plan Methods: Macroad plana samples from 29 women of whom 15 usbogenthy delivered in babies and 11 delivered SA (planar) and a statistical statistical of SD mathematical and of S1 m to form a discovery other in which expression data for a total of SD mathematical of S1 m to form a discovery other in which expression data for a total of SD mathematical of S1 m Nanoriting of automic miRMA analy. Validation by FF qC/Fer appendixed to the statistical of S1 m to the mathematical statistical of the statistical of S1 m S1	sma miRNAs to tormally grown omen recruited nined using the cohort. iRNA assay ini- t cases and con-

qPCR. Differential expression of two miRNA markers; hsa-miR-374a-5p (p = 0?0176) and hsa-let-7d-5p (p = 0?0036), were validated in an independent population of 95 women (SGA n = 12, Control n = 83). In the validation cohort, which was enriched for SGA cases, the ROC AUCs were 0?71 for hsamiR-374a-5p, and 0?74 for hsa-let-7d-5p, and 0?77 for the two combined. Whilst larger population-wide studies are required to validate their performance, these findings highlight the potential of circulating miRNAs to act as biomarkers for early prediction of SGA births

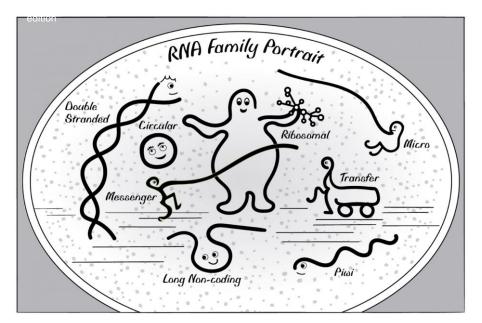
Interpretation: Whilst larger population-wide studies are required to validate their performance, these find-ings highlight the potential of circulating miRNAs to act as biomarkers for early prediction of SGA births. Funding: This work was supported by Genesis Research Trust, March of Dimes, and the National Institute for Health Research Biomedical Research Centre (NIHR BRC) based at Imperial Healthcare NHS Trust and Imperial College London

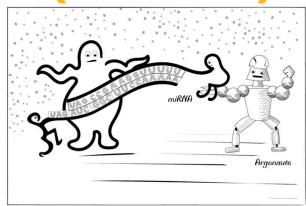
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What are microRNAs (miRNAs)?



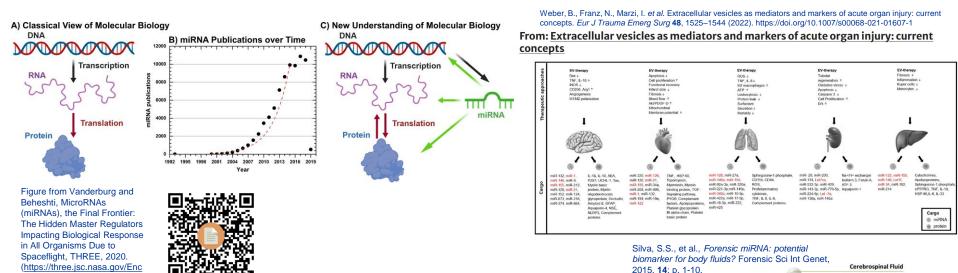


- MicroRNAs (miRNAs) are one of the many types of RNAs that don't code for proteins.
- Instead, they target and bind to sequences in specific mRNAs (i.e. genes) and can block the mRNA from being translated.
- MiRNAs don't travel alone: they pair up with a large protein called Argonaute, which protects them from destructive enzymes called nucleases in the cell.
 - Because of this protective protein, miRNAs can live in the cell for up to a week, floating around and targeting mRNAs for degradation.





What are miRNAs and why study miRNAs?

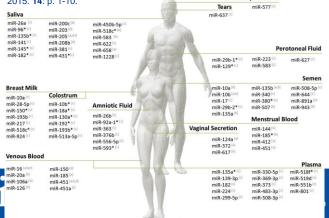


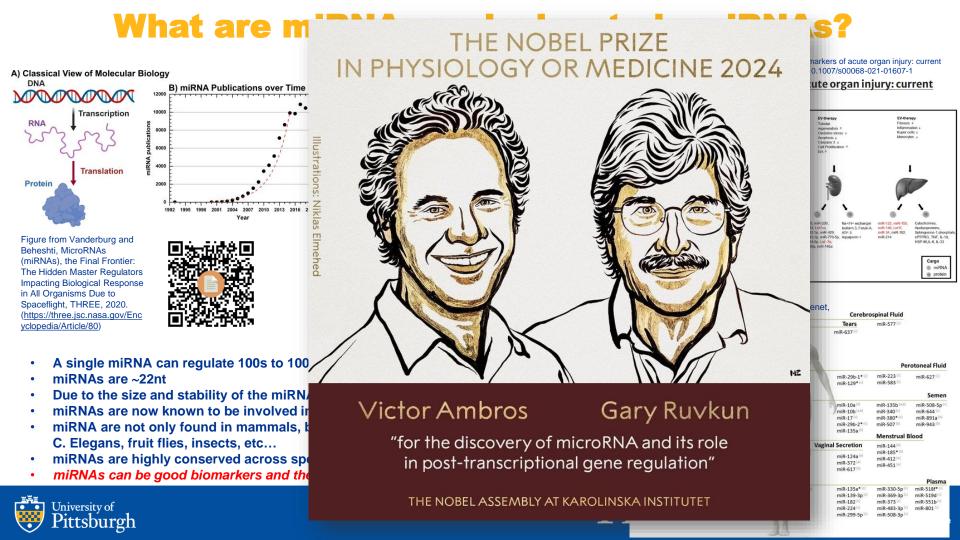
- A single miRNA can regulate 100s to 1000s of mRNAs.
- miRNAs are ~22nt

vclopedia/Article/80)

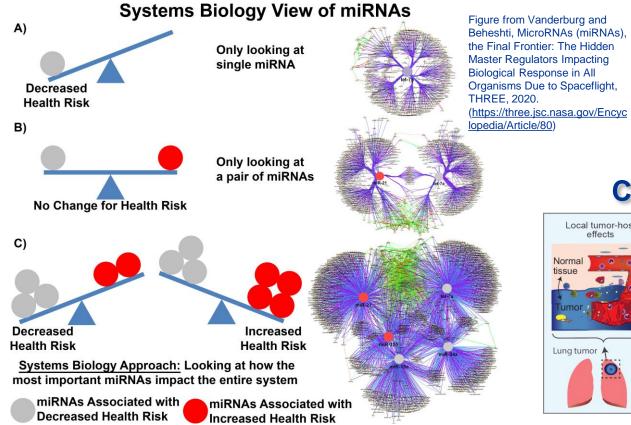
- Due to the size and stability of the miRNAs, it can float freely in the blood.
- miRNAs are now known to be involved in all aspects of diseases.
- miRNA are not only found in mammals, but everything else living: plants, microbes, fish, C. Elegans, fruit flies, insects, etc...
- miRNAs are highly conserved across species.
- miRNAs can be good biomarkers and therapeutic targets for many diseases







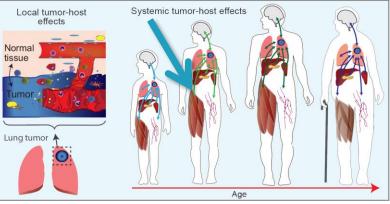
Systems Biology View of miRNAs



University of **Pittsburgh**



Circulating miRNAs



Beheshti, et al. Oncotarget 2015

Pitt McGowan Institute for Regenerative Medicine

miRNAs and Space: What I have done so far!

Cell Reports

ARTICLE | ONLINE NOW, 108448

Circulating miRNA Spaceflight Signature Reveals Targets for Countermeasure Development

Sherina Malkani 22 • Christopher R. Chin 22 • Egle Cekanaviciute 22 • ... Peter Grabham • Christopher E. Mason 🙁 23 🖂 🛛 Afshin Beheshti 😤 23, 24 🖂 🛛 Show all authors 🔹 Show footnotes Open Access • Published: November 25, 2020 • DOI: https://doi.org/10.1016/j.ceirep.2020.108448



PlumX Metrics

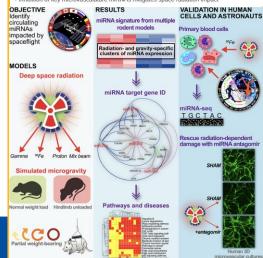
Highlights

 Spaceflight miRNA signature anism models

· Components of miRNA signature related to space radiation and microgravity

· Downstream targets and circulating dependence of miRNAs in NASA Twins Study

Inhibition of key microvasculature miRNAs mitigates space radiation impact





iScience

Peter

Grabham

COLUMBIA UNIVERSITY

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LET-Dependent Low Dose and Synergistic Inhibition of Human Angiogenesis by Charged Particles: Validation of miRNAs that Drive Inhibition

Yen-Ruh Wuu 🛚 Burong Hu 🗉 Hazeem Okunola 🛛 ... Margareth Cheng-Campbell 🖉 Afshin Beheshti 🙎 📼 🗰 eter Grabham 2 8 2 • Show all authors • Show footnotes

() Check for updates en Access + Published: November 25, 2020 + DOI: https://doi.org/10.1016/j.isci.2020.101771





· Space radiation inhibits angiogenesis synergistically at low doses by 2 mechanisms

Candidates for bystander transmission are microRNAs

 Three previously identified miRNAs showed downregulation of their angiogenesis targets

· Synthetic miRNA inhibitors were used to reverse the inhibition of angiogenesis

Space

radiation

Human microvessels



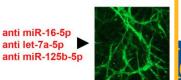


miRNA pathways



anti miR-16-5p anti let-7a-5p

Rescue of microvessels



miRNA

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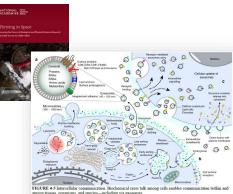
Article | Open access | Published: 11 June 2024

Space radiation damage rescued by inhibition of key spaceflight associated miRNAs

J. Tyson McDonald, JangKeun Kim, Lily Farmerie, Meghan L. Johnson, Nidia S. Trovao, Shehbeel Arif, Keith Siew, Sergey Tsoy, Yaron Bram, Jiwoon Park, Eliah Overbey, Krista Ryon, Jeffrey Haltom, Urminder Singh, Francisco J. Enquita, Victoria Zaksas, Joseph W. Guarnieri, Michael Topper, Douglas C. Wallace, Cem Meydan, Stephen Baylin, Robert Meller, Masafumi Muratani, D. Marshall Porterfield, ... Afshin Beheshti [™] + Show authors

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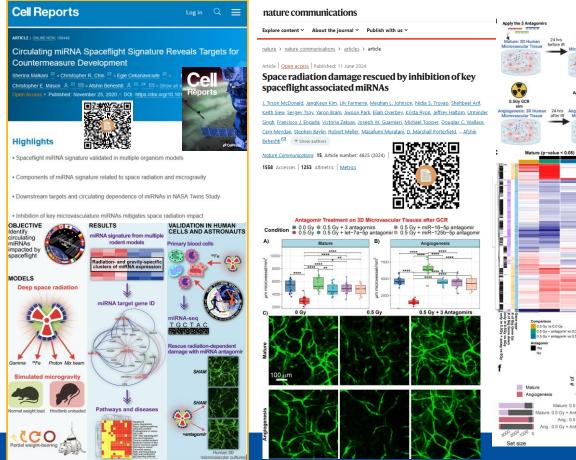
among tissues organisms and species-including via exosomes SOURCE: From Ni et al. (2020), https://doi.org/10.1038/s41413-020-0100-9. CC BY 4.0.

Impact on Extracellular Molecules and Extracellular Vesicles

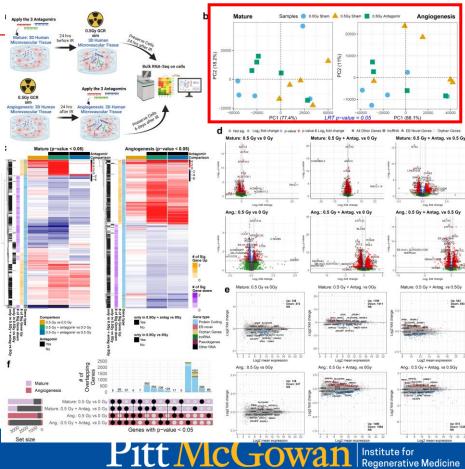
Extracellular vesicles are prime candidates for cross-talk vectors, and their study in organisms in space is critical for an understanding of the biological effects of the space environment. Extracellular molecules are the communicators in intra-organism cross talk and can be either small molecules, protein based, or nucleic acid-based. Some proteins like insulin or inflammatory response molecules like cytokines have been known for some time, whereas others are still being discovered (e.g., histone variants). Cell-free nucleic acids include several types of DNAs and RNAs, and also have shown responsiveness to spaceflight (e.g., mitochondrial DNA, mtDNA) (Lo et al. 2021). First recognized a narkers in cancer patients (Schwarzenbach et al. 2011), these molecules are potentially biomarkers fo any more pathologies and homeostasis changes in organisms in the space environment. Indeed, Malkar ad colleagues have identified and validated a spaceflight-associated microRNA (miRNA) signature that shared by rodents and humans in response to simulated short-duration and long-duration spaceflight (alkani at al. 2020). Additionally, a subset of these miRNAs was found to regulate vascular dama used by simulated deep-space radiatio

Extracellular vesicles are a heterogeneous group of membrane-limited vesicles loaded with us proteins, lipids, and nucleic acids. Release of extracellular vesicles from its cell of origin occurs

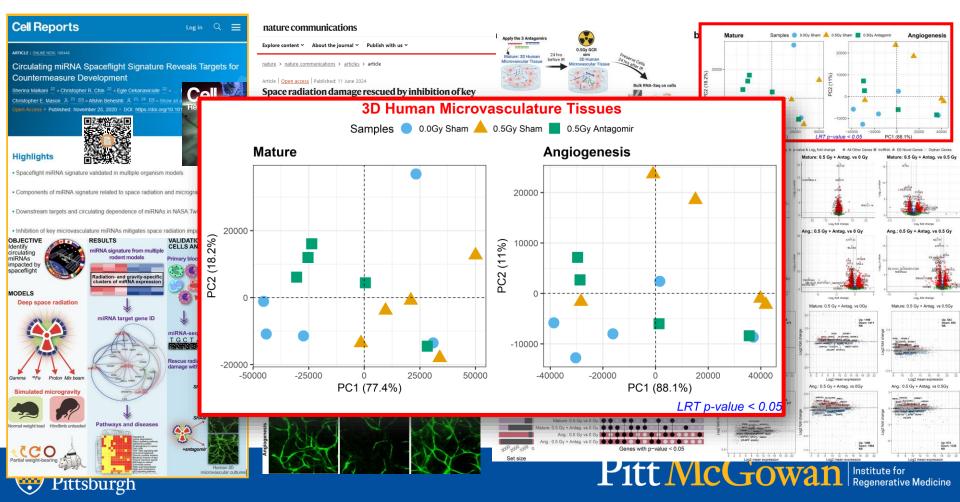
miRNAs and Space: What I have done so far!



Pittsburgh



miRNAs and Space: What I have done so far!



miRNAs Important Focus for Space Research in the next 10 years!!!

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Thriving in Space

Ensuring the Future of Biological and Physical Sciences Research Decadal Survey for 2023-2032



https://nap.nationalacademies.org/catalog/26750/thriving-in-space-ensuring-the-future-of-biological-andphysical-sciences-research-a-decadal-survey-for-2023-2032

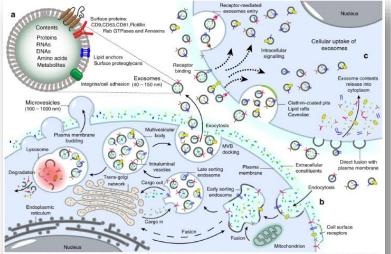


FIGURE 4-5 Intercellular communication. Biochemical cross talk among cells enables communication within and among tissues, organisms, and species-including via exosomes. SOURCE: From Ni et al. (2020), https://doi.org/10.1038/s41413-020-0100-9. CC BY 4.0.

Impact on Extracellular Molecules and Extracellular Vesicles

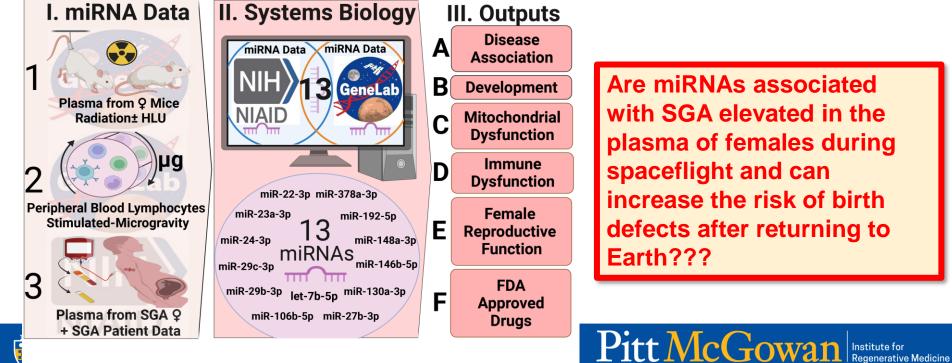
Extracellular vesicles are prime candidates for cross-talk vectors, and their study in organisms in space is critical for an understanding of the biological effects of the space environment. Extracellular molecules are the communicators in intra-organism cross talk and can be either small molecules, proteinbased, or nucleic acid-based. Some proteins like insulin or inflammatory response molecules like cytokines have been known for some time, whereas others are still being discovered (e.g., histone variants). Cell-free nucleic acids include several types of DNAs and RNAs, and also have shown responsiveness to spaceflight (e.g., mitochondrial DNA, mtDNA) (Lo et al. 2021). First recognized as biomarkers in cancer patients (Schwarzenbach et al. 2011), these molecules are potentially biomarkers for many more pathologies and homeostasis changes in organisms in the space environment. Indeed, Malkani and colleagues have identified and validated a spaceflight-associated microRNA (miRNA) signature that is shared by rodents and humans in response to simulated short-duration and long-duration spaceflight (Malkani et al. 2020). Additionally, a subset of these miRNAs was found to regulate vascular damage caused by simulated deep-space radiation.

Extracellular vesicles are a heterogeneous group of membrane-limited vesicles loaded with various proteins, lipids, and nucleic acids. Release of extracellular vesicles from its cell of origin occurs

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Hypothesis:

Does spaceflight increase the chance of potential birth defects?



Hypothesis:

Does spaceflight in oronge the change of not ential

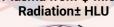
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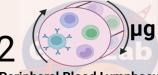


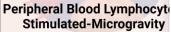
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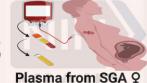
Article Open access Published: 05 October 2024











Plasma from SGA Q + SGA Patient Data

To boldly go where no microRNAs have gone before: spaceflight impact on risk for small-for-gestational-age infants

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Institute for Regenerative Medicine

<u>Giada Corti, JangKeun Kim, Francisco J. Enguita, Joseph W. Guarnieri, Lawrence I. Grossman, Sylvain V.</u> <u>Costes, Matias Fuentealba, Ryan T. Scott, Andrea Magrini, Lauren M. Sanders, Kanhaiya Singh,</u> Chandan K. Sen, Cassandra M. Juran, Amber M. Paul, David Furman, Jean Calleja-Agius, Christopher E.

Mason, Diego Galeano, Massimo Bottini & Afshin Beheshti 🖾

Communications Biology 7, Article number: 1268 (2024) Cite this article

Relating Spaceflight Data to Clinical Data



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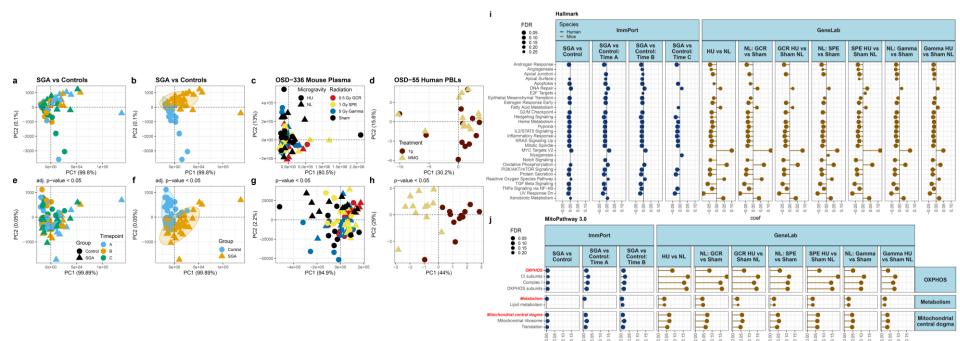
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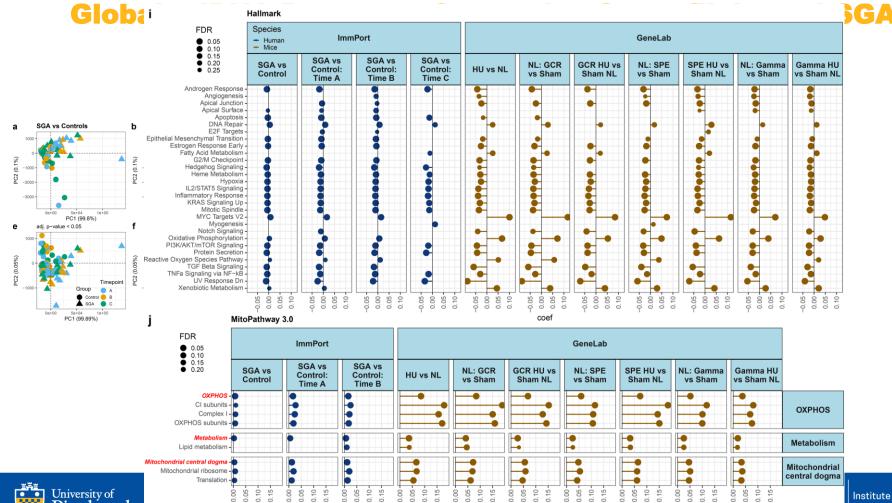
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Global miRNA Response Comparing Spaceflight and SGA



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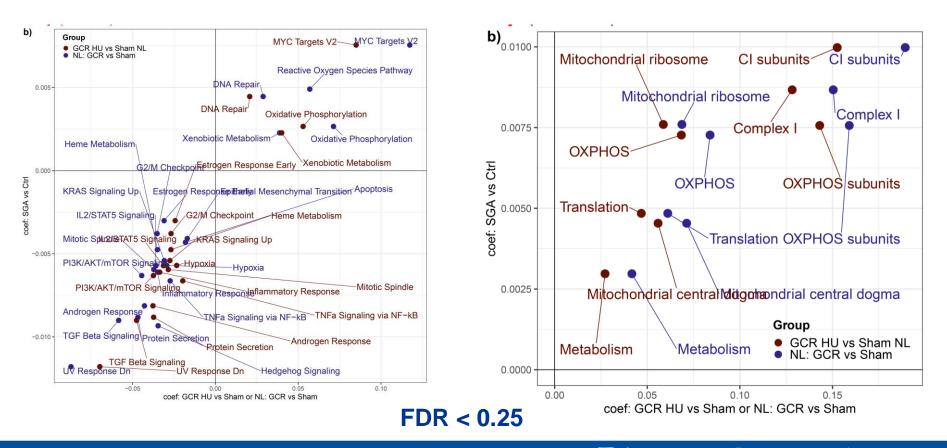


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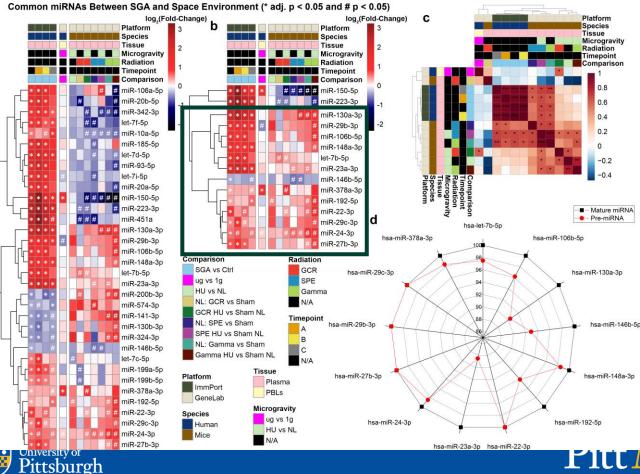
Global miRNA Response Comparing Spaceflight and SGA





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Common Circulating miRNAs Between SGA and



а

Percentage of homology (same nucleotides in the same positions) between mouse and human miRNAs shows the 13 mature miRNAs are 100% conserved between the two

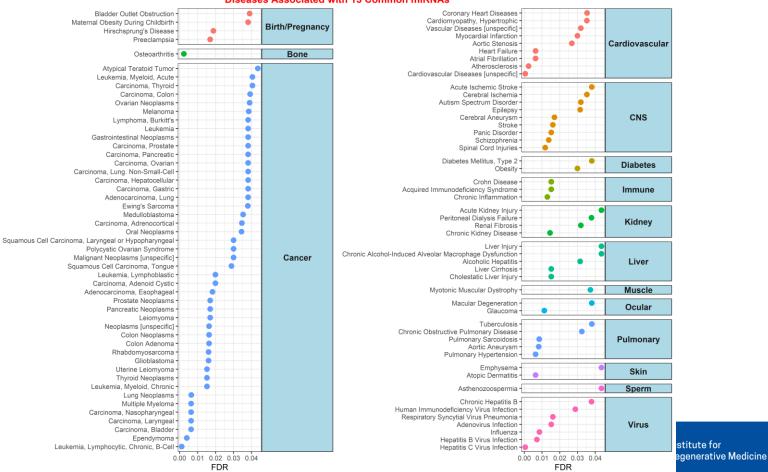
species!



Francisco "Paco" Enguita, PhD U LISBOA UNIVERSIDAD

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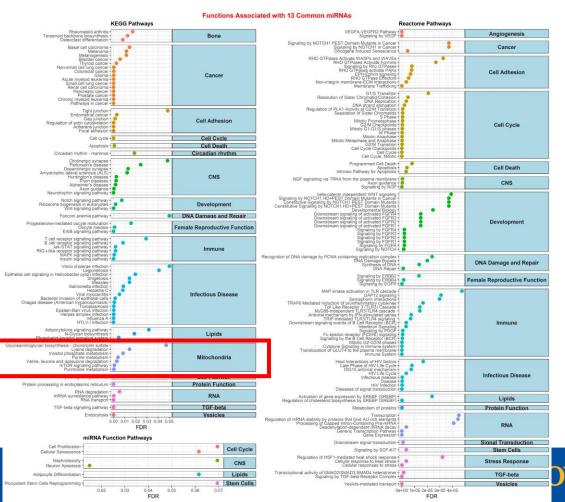
Health Risks Associated with the Common miRNAs



Diseases Associated with 13 Common miRNAs



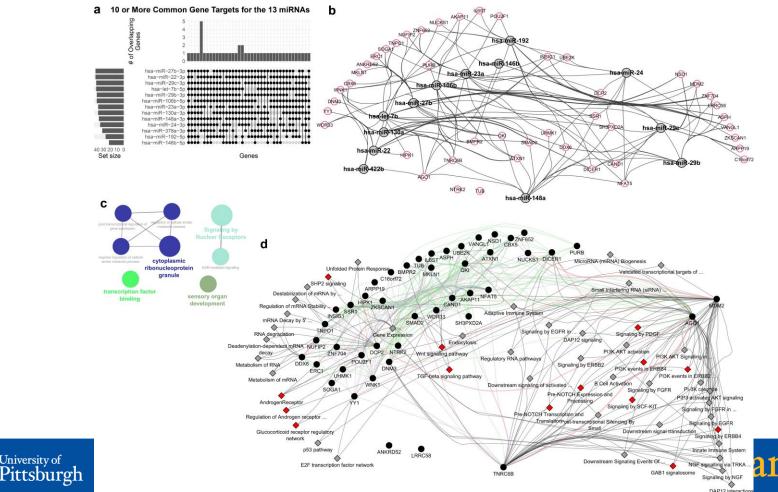
Biological Functions Associated with the Common miRNAs





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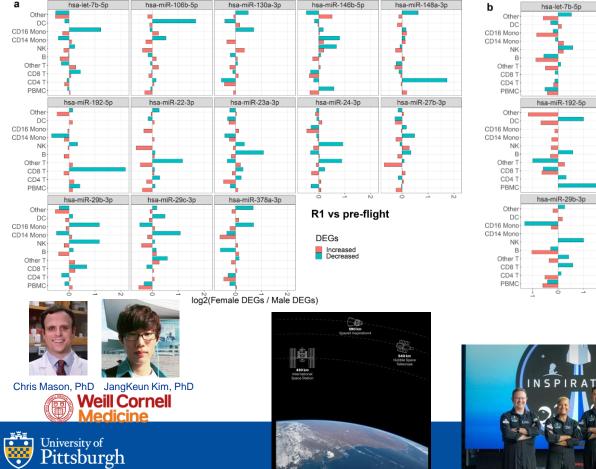
Gene Targets for the Common miRNAs

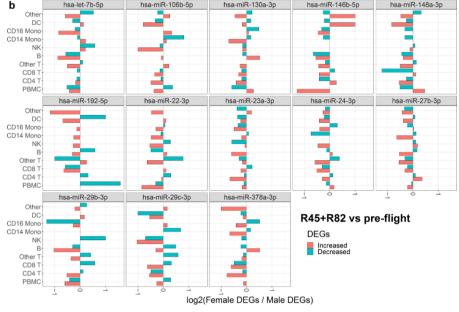


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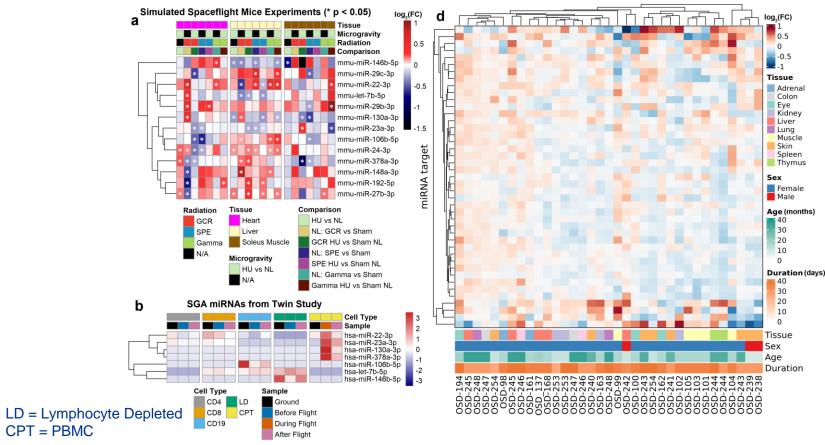
Gene Targets for the Common miRNAs in Astronauts







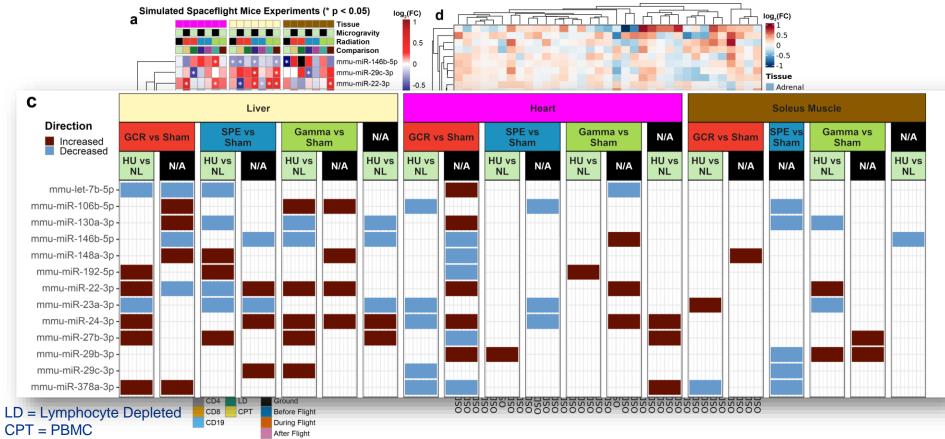
miRNAs and Gene Targets in other Tissues





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miRNAs and Gene Targets in other Tissues



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Can we determine potential countermeasures to mitigate the impact of SGA in females during spaceflight and the clinic???





sChemNET: A deep learning framework for predicting miRNA targets of small molecules based on chemical structure

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sChemNET: a deep learning framework for predicting small molecules targeting microRNA function

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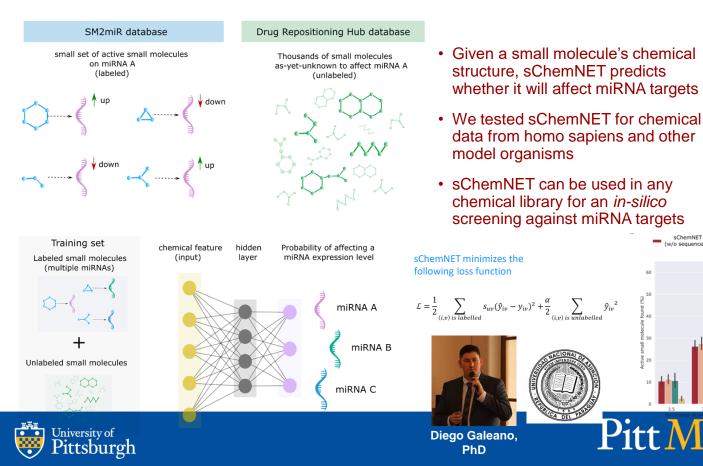


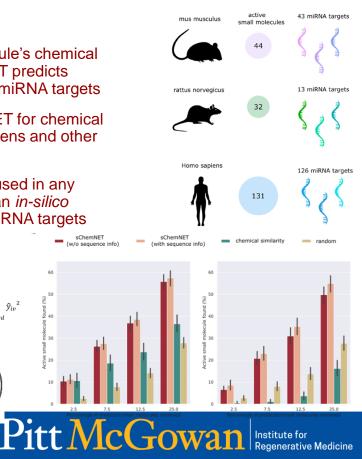
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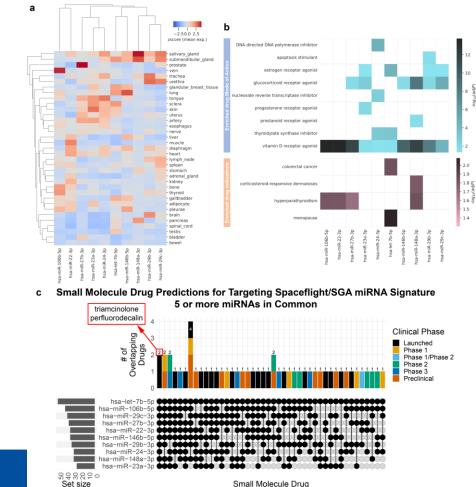
sChemNET: A deep learning framework for predicting miRNA targets of small molecules based on chemical structure





/o sequence info

sChemNET's predictions for our miRNA signature



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sChemNET's predictions for our miRNA signature

brain

Infants

Small Molecule Drug

triamcinolone

perfluorodecalin

Bu

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hsa-let-7b-5p

nsa-miR-106b-5p

hsa-miR-29c-3p

sa-miR-27b-3p

hsa-miR-22-3p

sa-miR-146b-5p

hsa-miR-148a-3p

hsa-miR-23a-3p

Set size

sa-miR-29b-3p hsa-miR-24-3p Open Access Article

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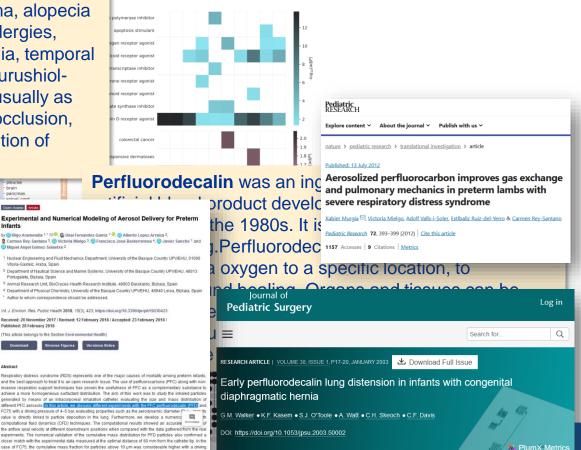
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vasive devices for the treatment of RDS in preterm infants

pressure of 5 bar. These numerical models could be a helpful tool to assist parametric studies of new non

Keywords: aerosol; CFD; inhalation catheter; perfluorocarbons; respiratory distress syndrome

Triamcinolone is a glucocorticoid used to treat a number of different medical conditions, such as eczema, alopecia areata, lichen sclerosus, psoriasis, arthritis, allergies, ulcerative colitis, lupus, sympathetic ophthalmia, temporal arteritis, uveitis, ocular inflammation, keloids, urushiolinduced contact dermatitis, aphthous ulcers (usually as triamcinolone acetonide), central retinal vein occlusion, visualization during vitrectomy and the prevention of asthma attacks.





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Matias David Furman, Fuentealba, PhD



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To boldly go where no microRNAs have gone before: spaceflight impact on risk for small-for-gestational-age infants

Giada Corti, JangKeun Kim, Francisco J. Enguita, Joseph W. Guarnieri, Lawrence I. Grossman, Sylvain V. Costes, Matias Fuentealba, Ryan T. Scott, Andrea Magrini, Lauren M. Sanders, Kanhaiya Singh, Chandan K. Sen, Cassandra M. Juran, Amber M. Paul, David Furman, Jean Calleja-Agius, Christopher E. Mason, Diego Galeano, Massimo Bottini & Afshin Beheshti 🖾

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PhD



NASA Selects 11 Space Biology Research Projects to Inform Biological Research During Future Lunar Exploration Missions



https://science.nasa.gov/science-research/biological-physicalsciences/nasa-selects-11-space-biology-research-projects/

Animal Research Investigations

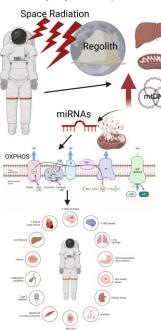
Cheryl Nickerson, Arizona State University

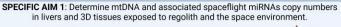
Effects of Lunar Dust Simulant on Human 3-D Biomimetic Intestinal Models, Enteric Microorganisms, and Infectious Disease Risks

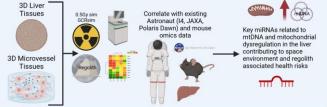
Afshin Beheshti, Ph.D. NASA Ames Research CenterSpaceflight and Regolith Induced Mitochondrial Stress Mitigated by miRNA-based Countermeasures

Current Space Funding

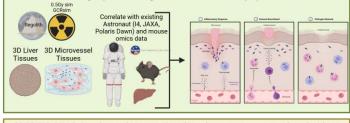
Hypothesis: We hypothesize during exposure to regolith and spaceflight, there is an increase in oxidative phosphorylation (OXPHOS) in the liver is due to increases in mitochondrial DNA (mtDNA) driven by microRNAs (miRNAs) creating a systemic impact on the body.







SPECIFIC AIM 2: Investigate the pathogen load, inflammation, immune, and DNA DSBs in the liver during exposure to regolith and simulated deep space environment.



SPECIFIC AIM 3: Develop and test a miRNA-based countermeasure with and without existing FDA-approved drugs to improve mitochondria and immune dysfunction during regolith exposure and spaceflight.



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