Mapping astronauts' clonal hematopoiesis and stem cell dynamics to prepare for Mars missions

@mason_lab

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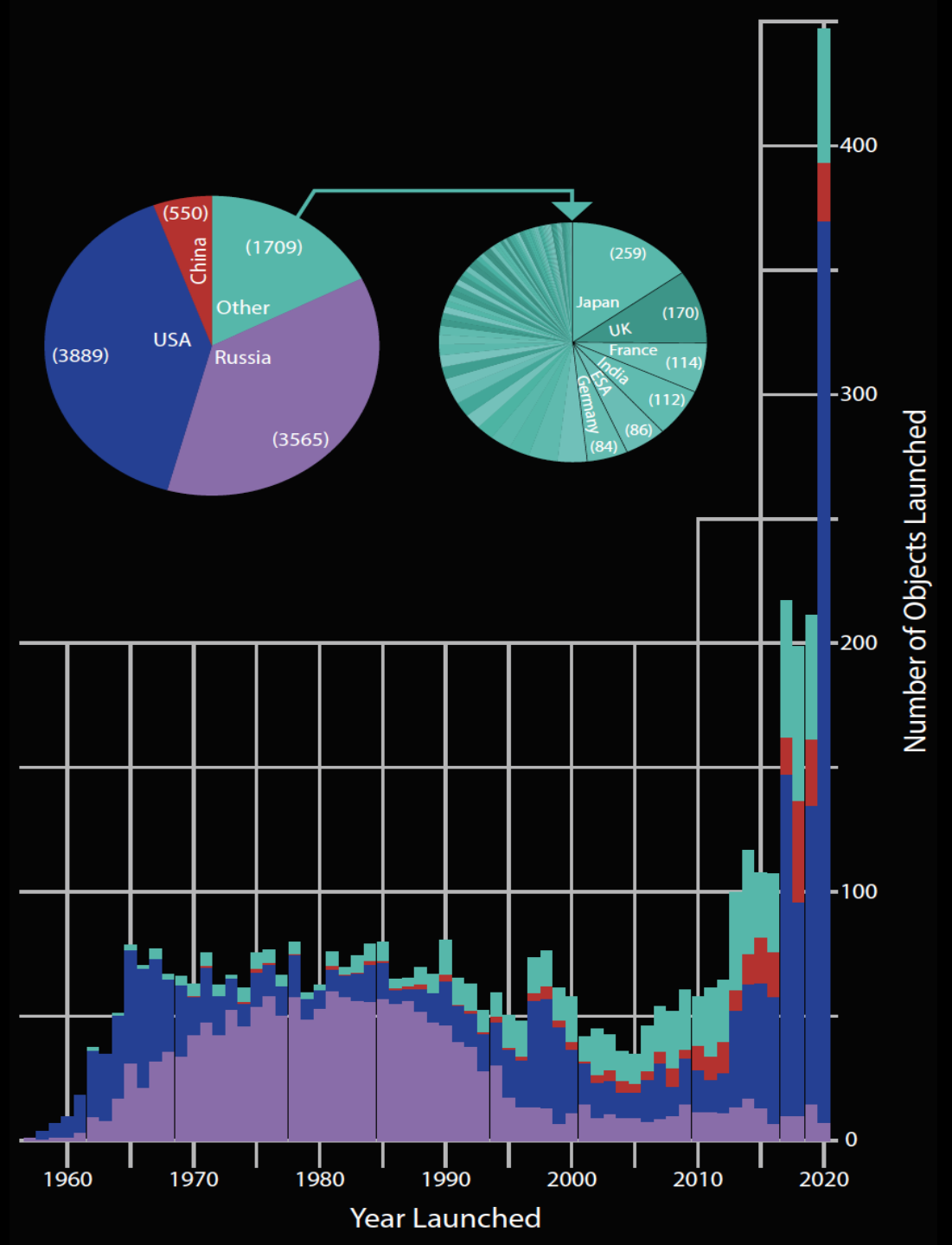
Meyer Cancer Center, Feil Family Brain and Mind Research Institute,
at Weill Cornell Medicine,
Affiliate, New York Genome Center (NYGC) and Yale Law School

November 16th 2021

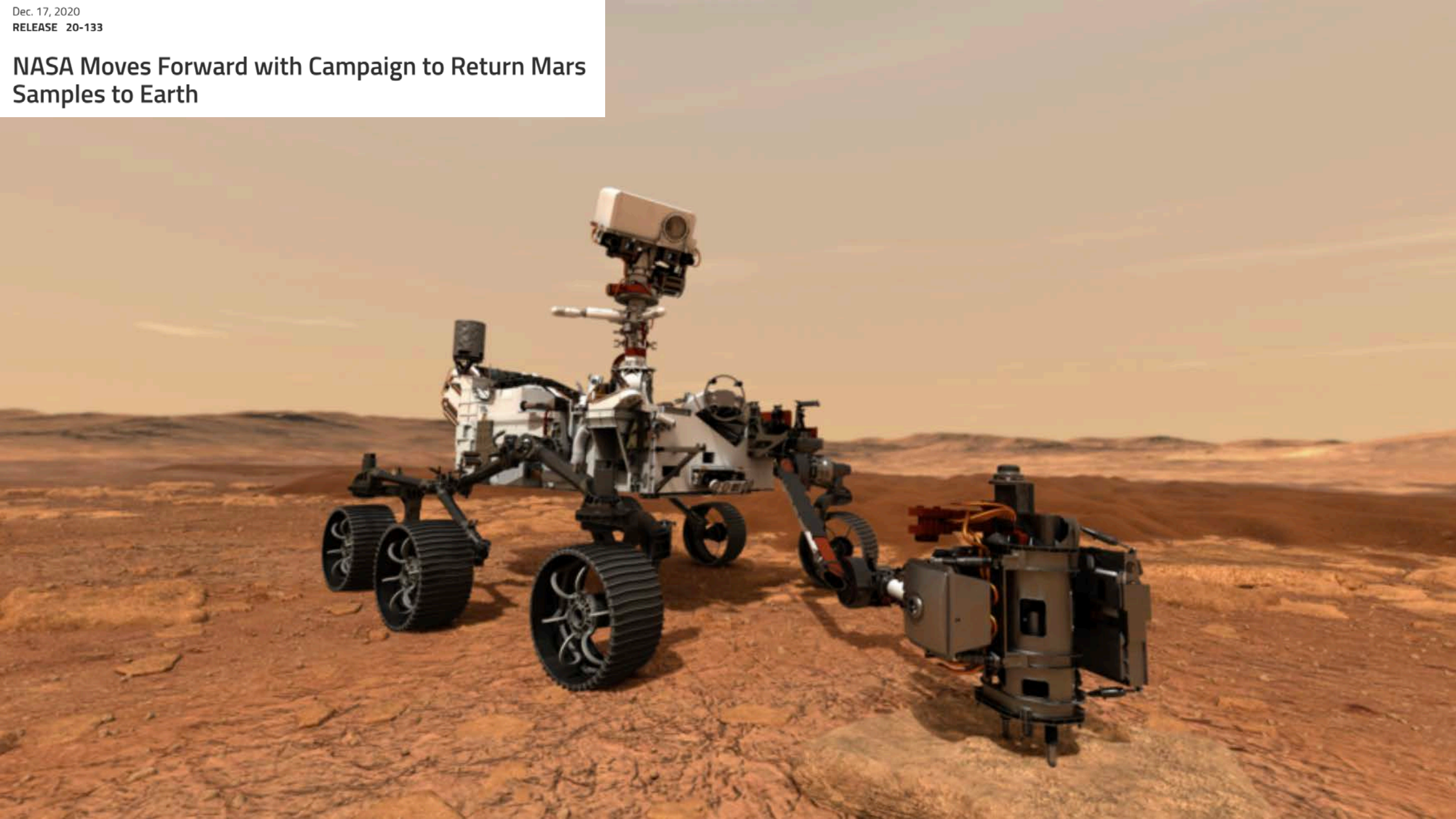
More than ever, we are a space-faring species

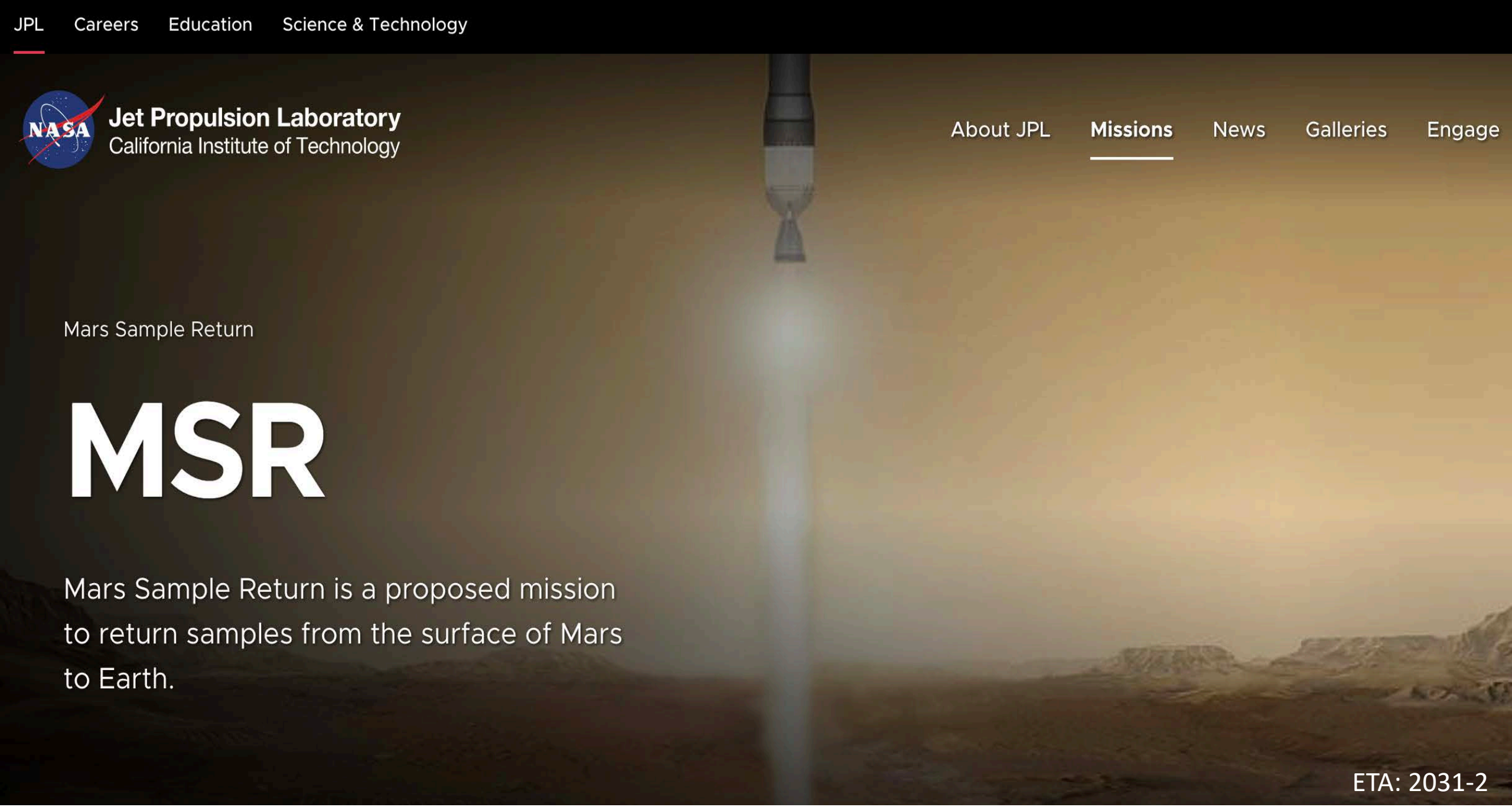


Mason CE
The Next 500 Years

Dec. 17, 2020
RELEASE 20-133

NASA Moves Forward with Campaign to Return Mars Samples to Earth



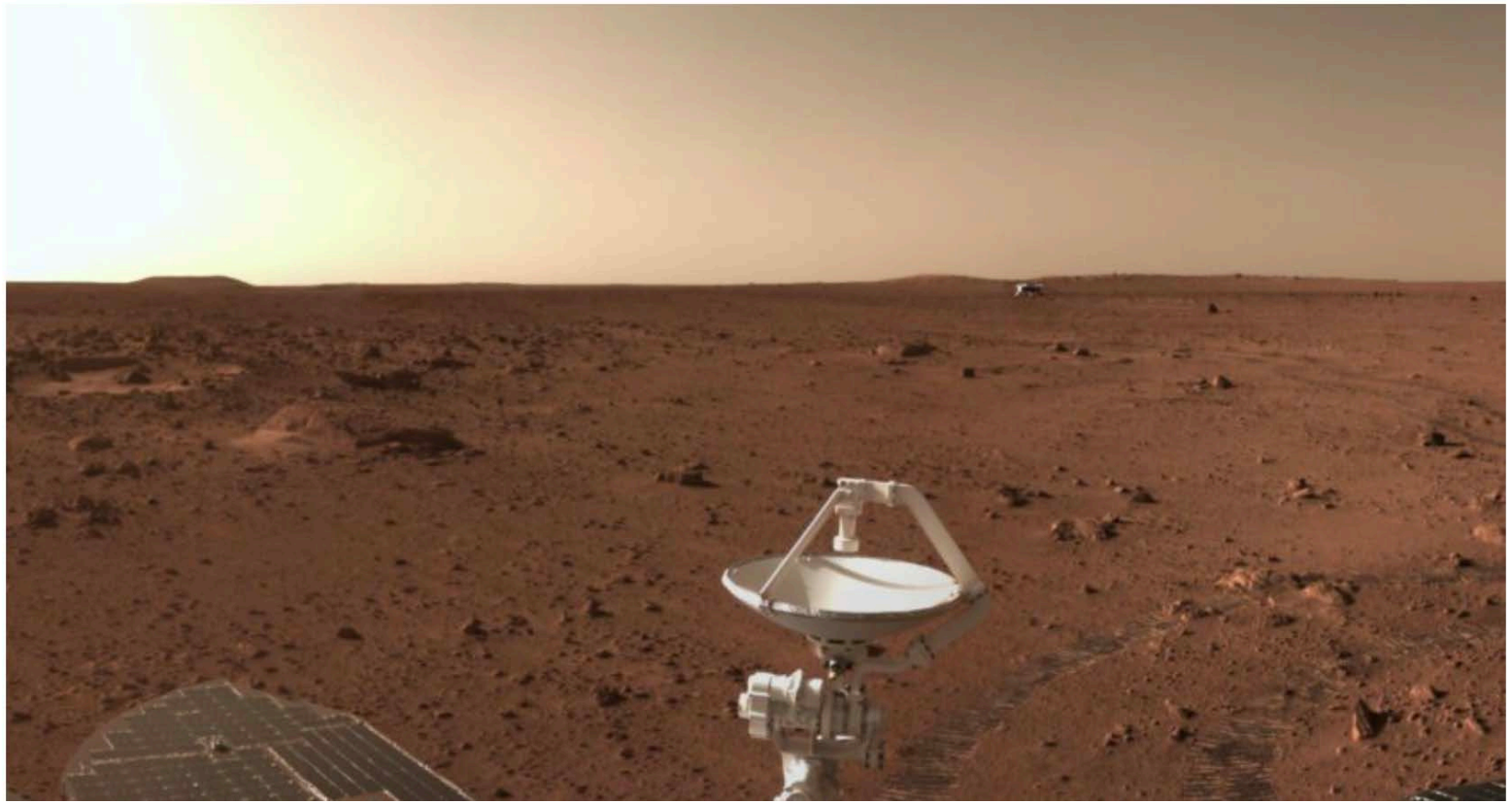


https://www.jpl.nasa.gov/missions/mars-sample-return-msr/

China is aiming for samples back by 2030

China is planning a complex Mars sample return mission

by **Andrew Jones** — November 4, 2021



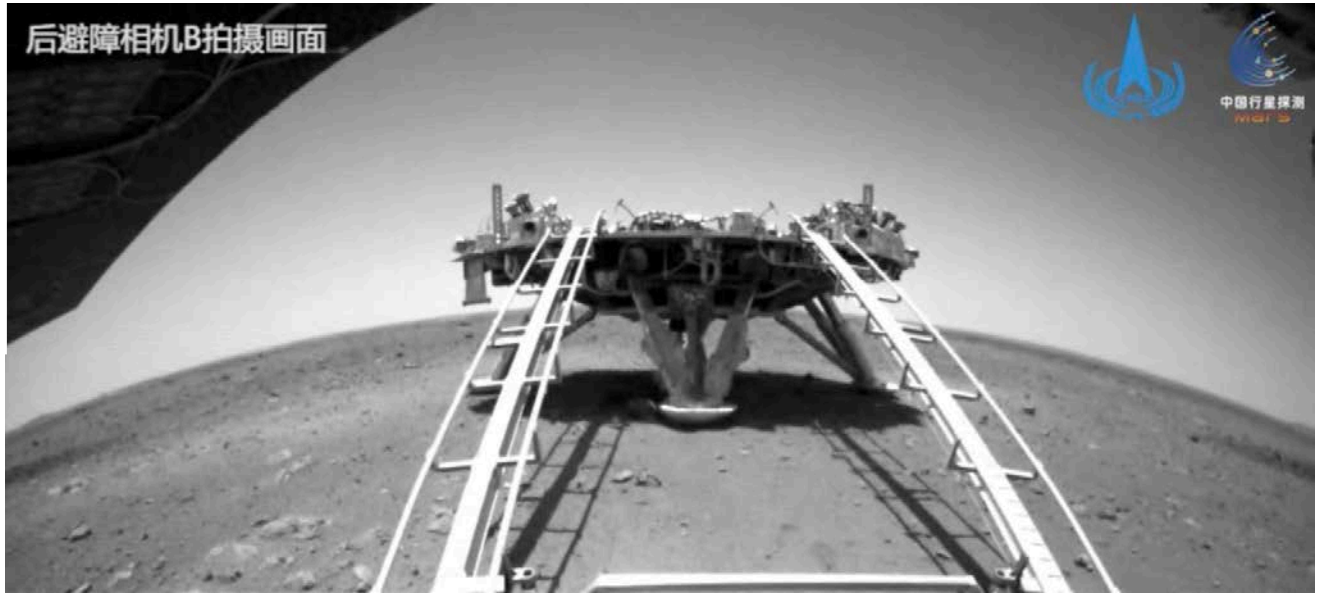
https://spacenews.com/china-is-planning-a-complex-mars-sample-return-mission/

And boots on the ground in 2033

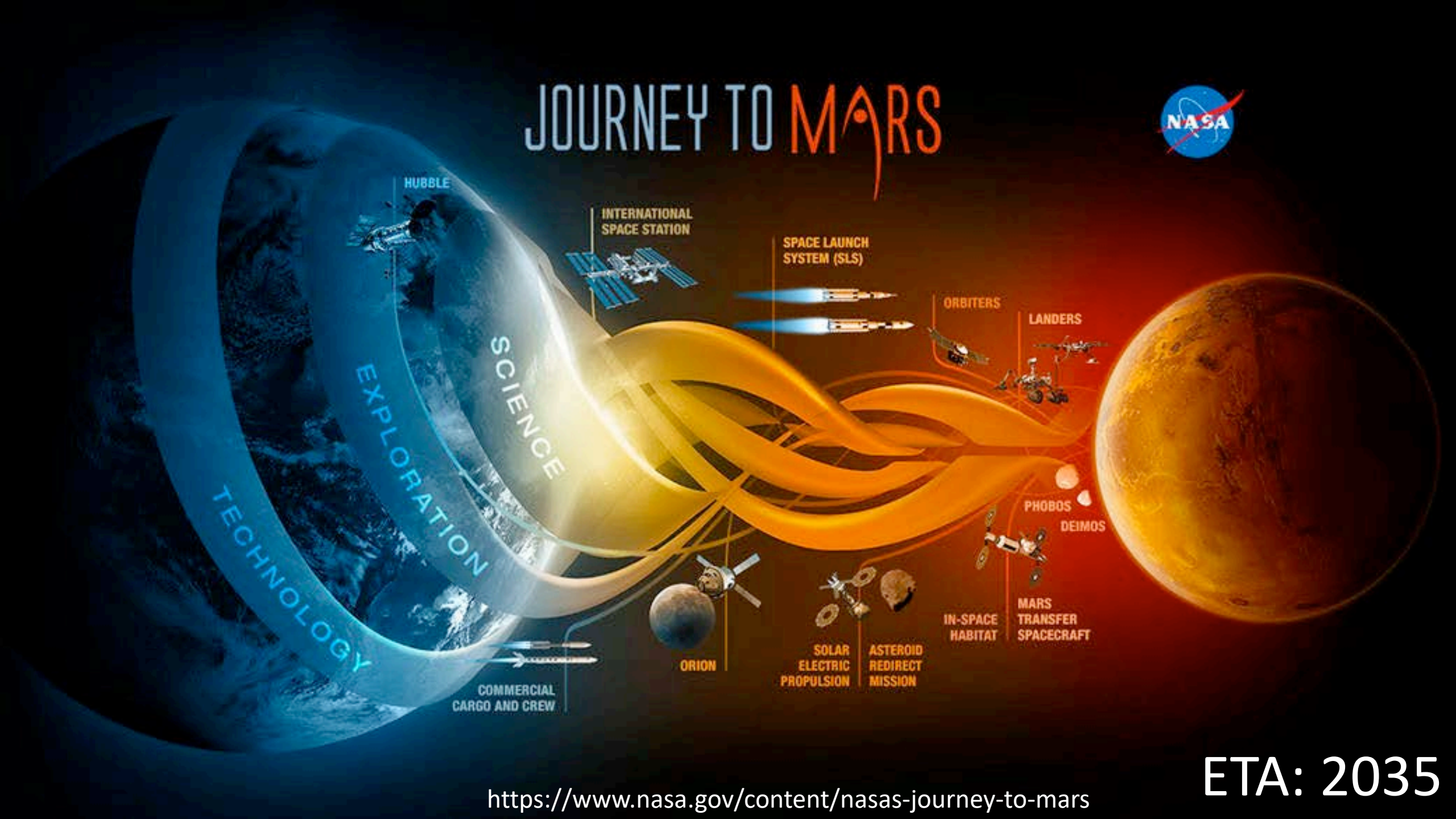
June 24, 2021
12:58 AM EDT

Aerospace & Defense

China plans its first crewed mission to Mars in 2033



https://www.reuters.com/business/aerospace-defense/china-plans-its-first-crewed-mission-mars-2033-2021-06-24/

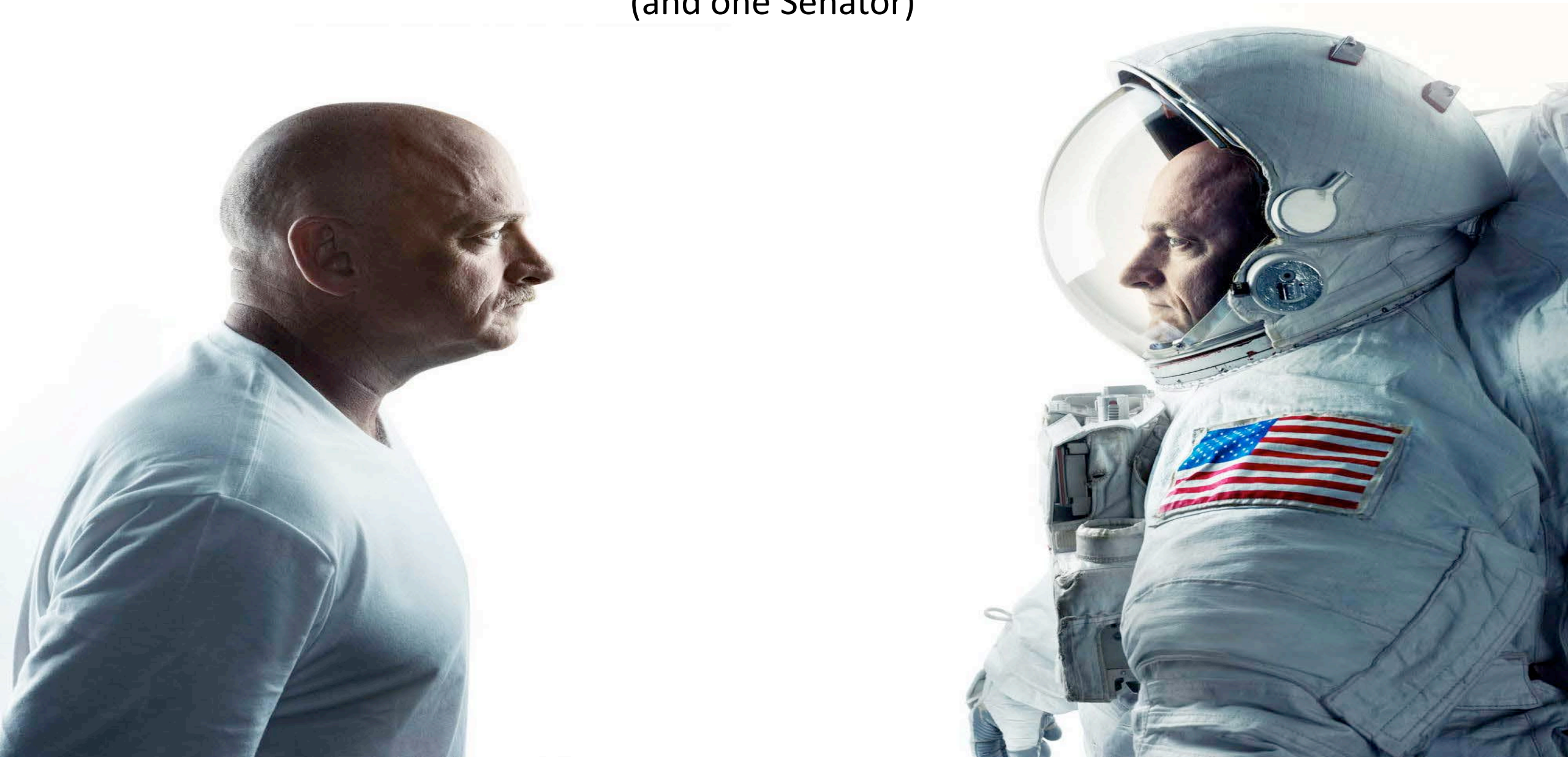


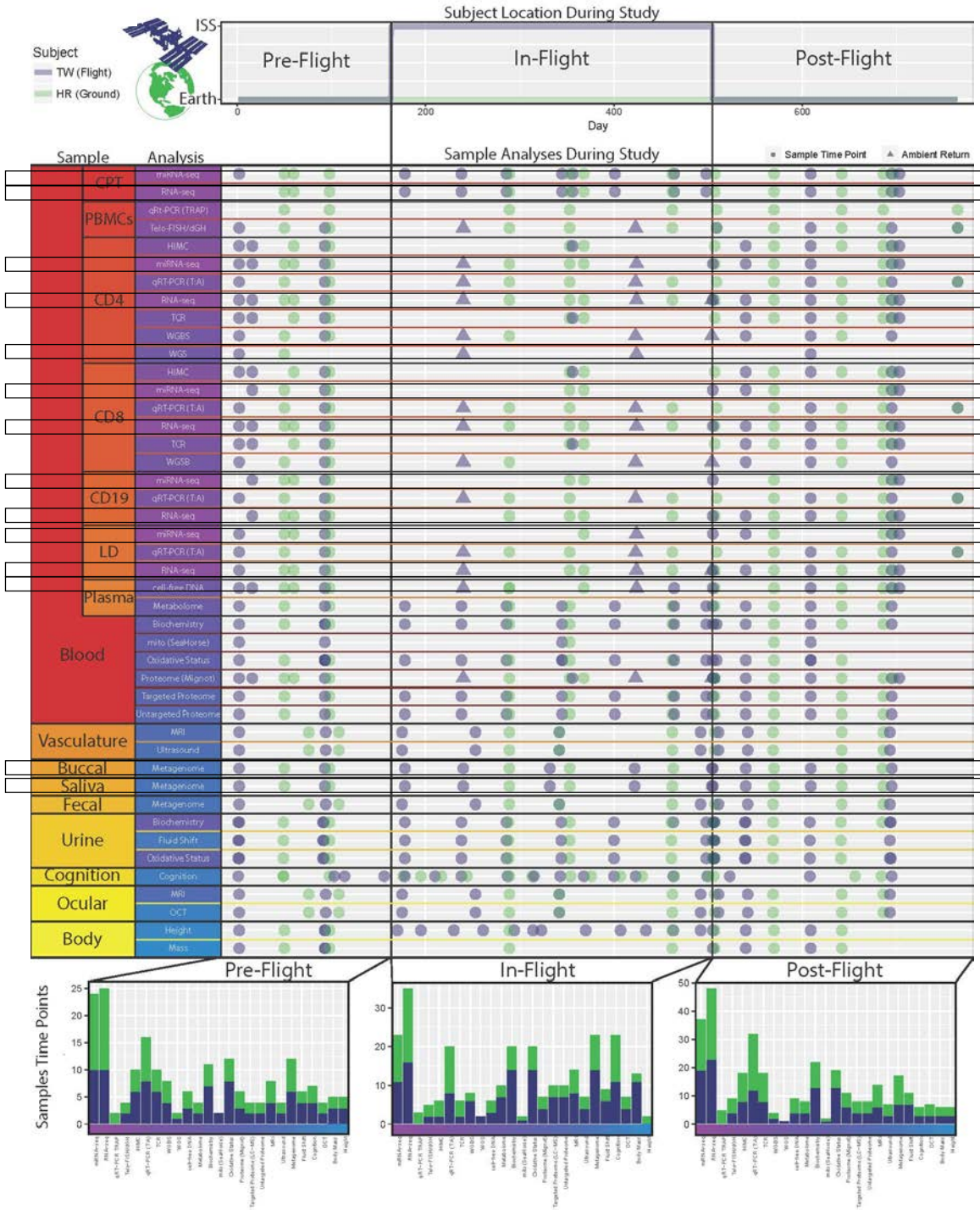
https://www.nasa.gov/content/nasas-journey-to-mars

ETA: 2035

Integrative medicine with twin astronauts

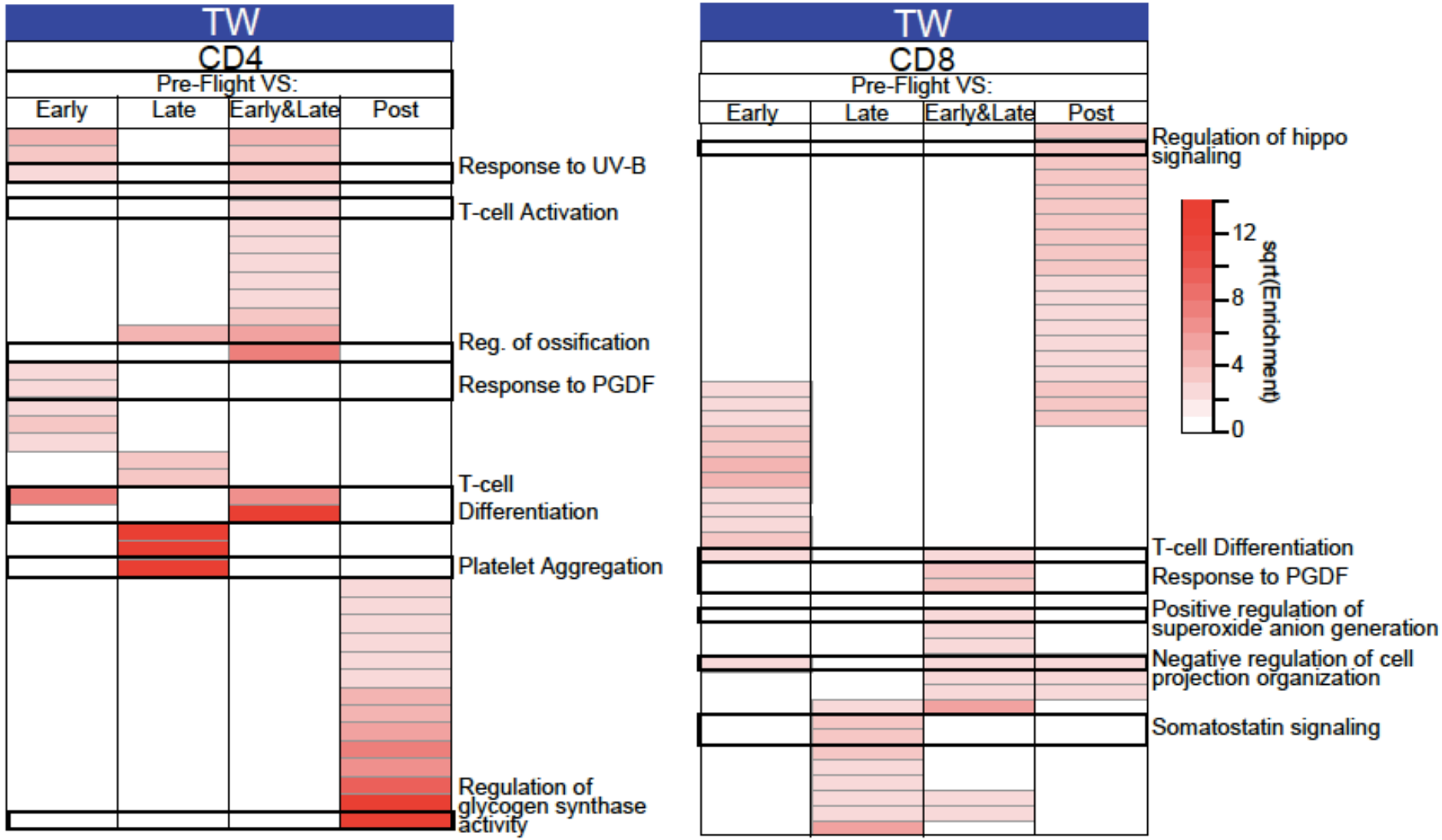
(and one Senator)





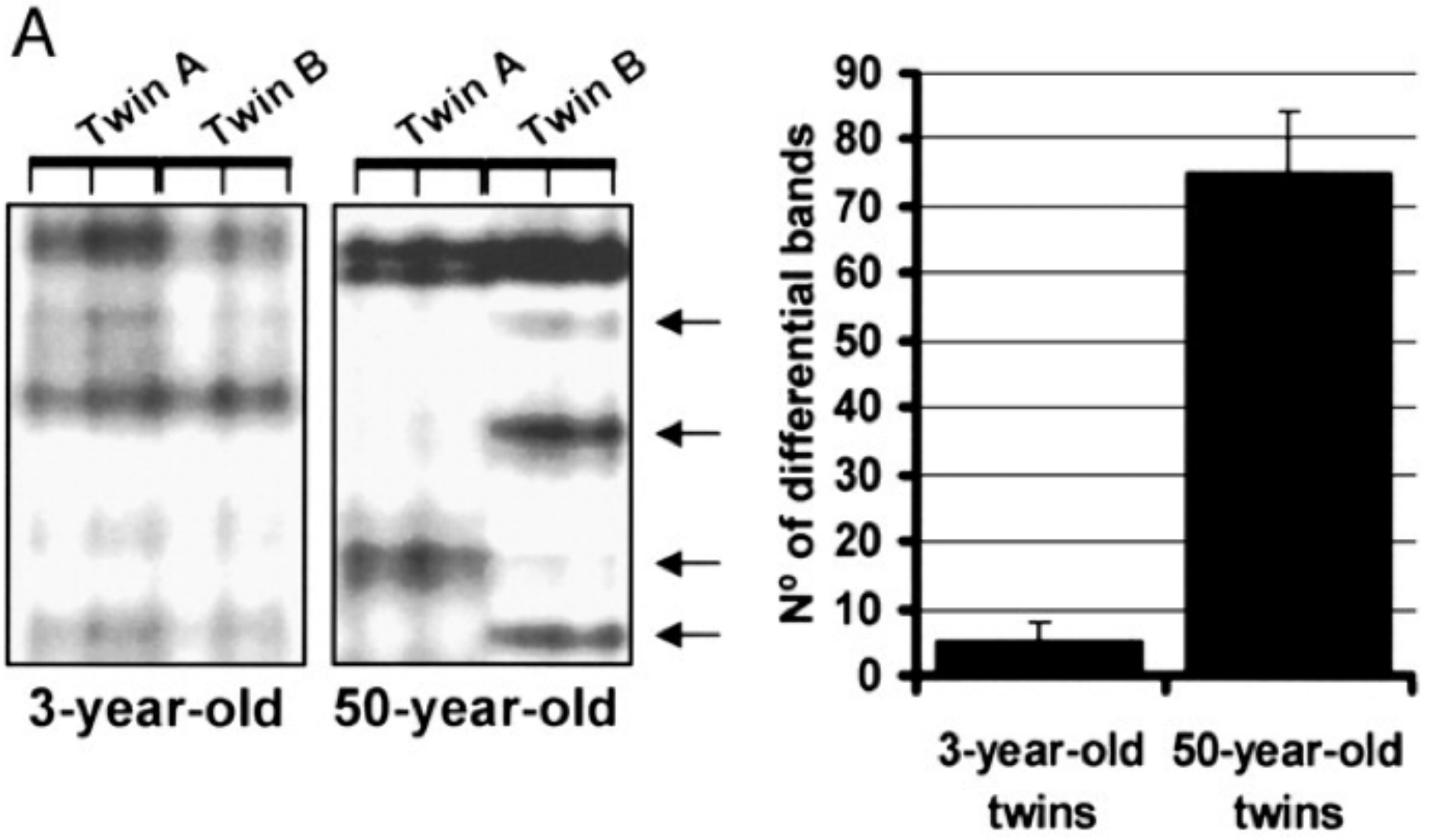
The NASA Twins Study
Garrett-Bakelman *et al*., 2019

Broad epigenetic changes observed, especially in the immune system



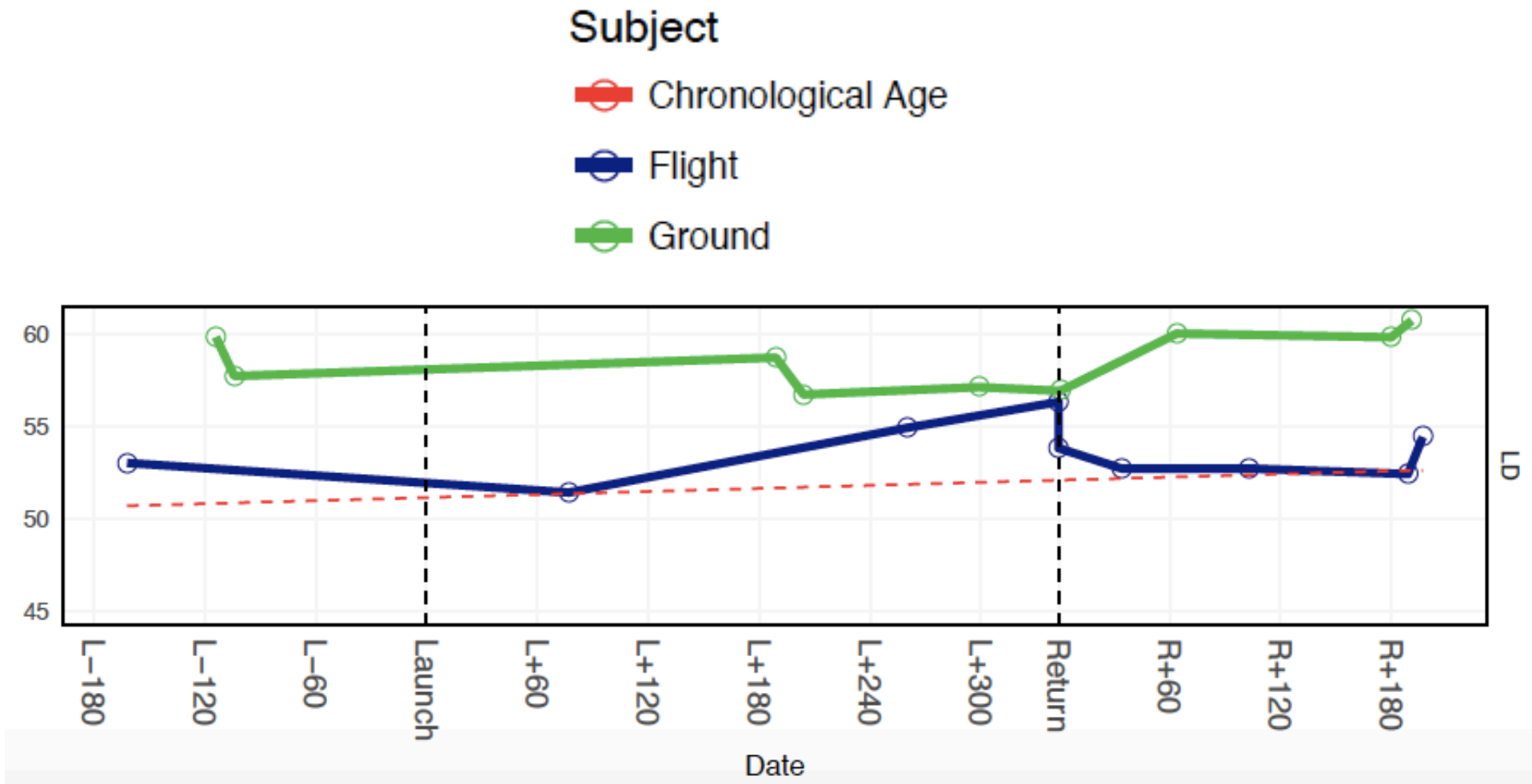
Lindsay Rizzardi, Andy Feinberg

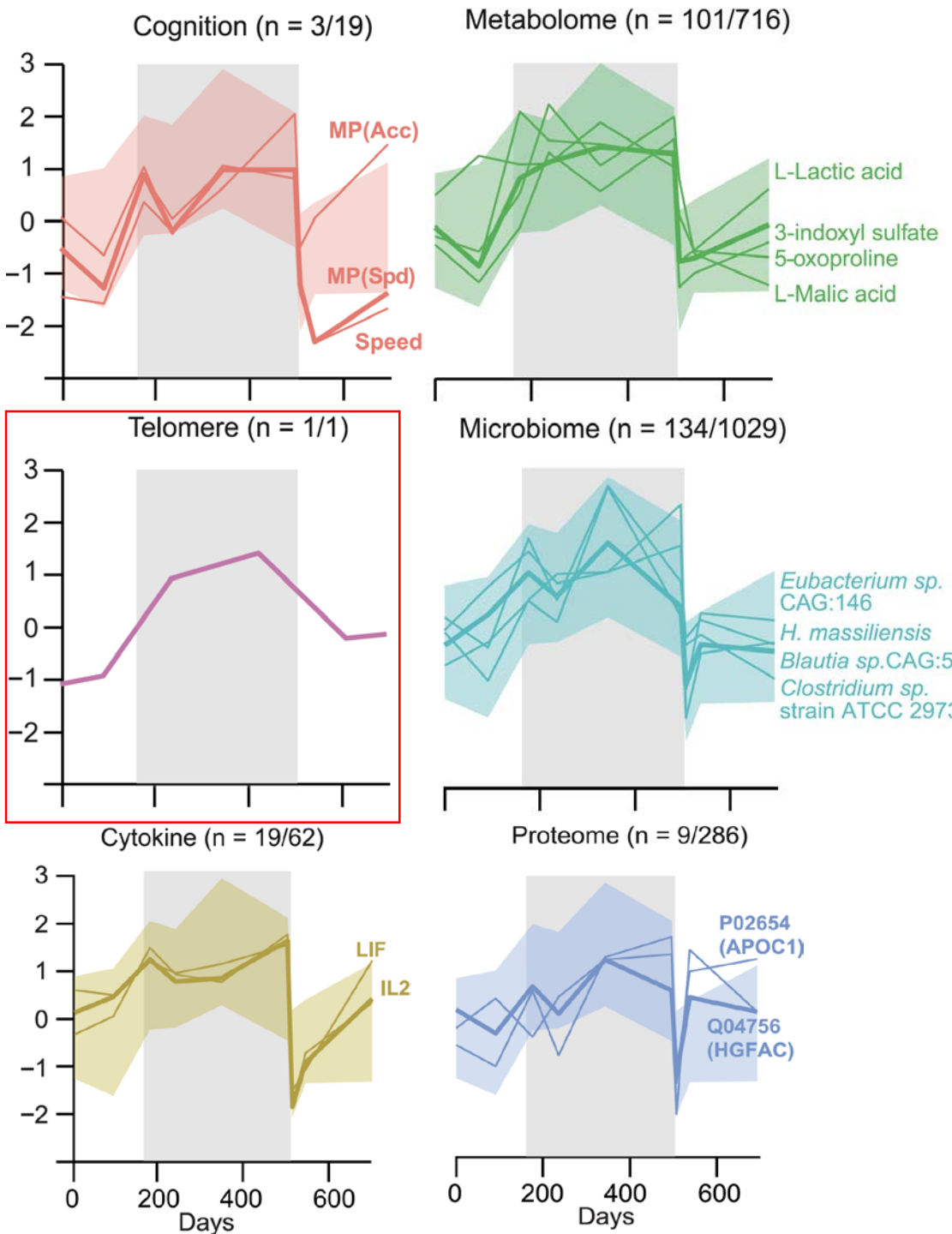
Epigenetic Drift in Twins



Mario F. Fraga et al. PNAS 2005;102:10604-10609

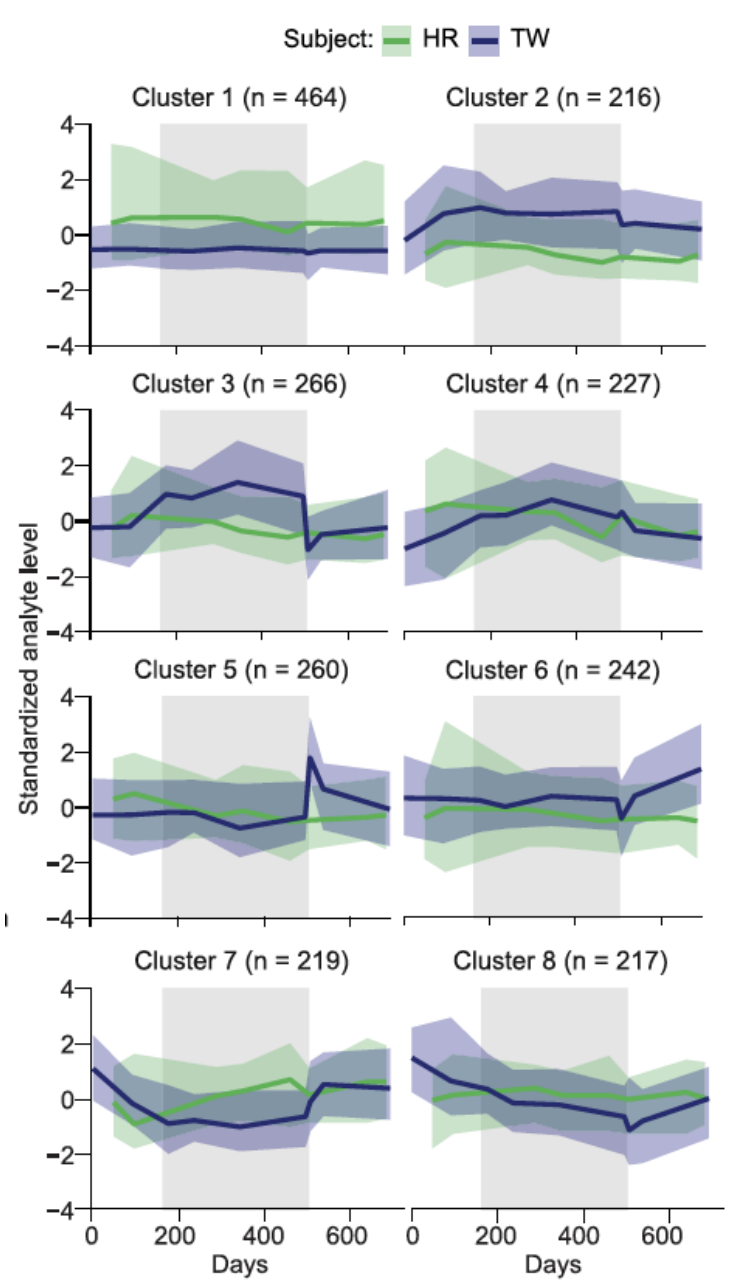
Epigenetic age
is almost the same after two years.





Analyte Type
- Cognition
- Cytokine
- Metabolite
- Microbiome
- Proteome
- Telomere

2019



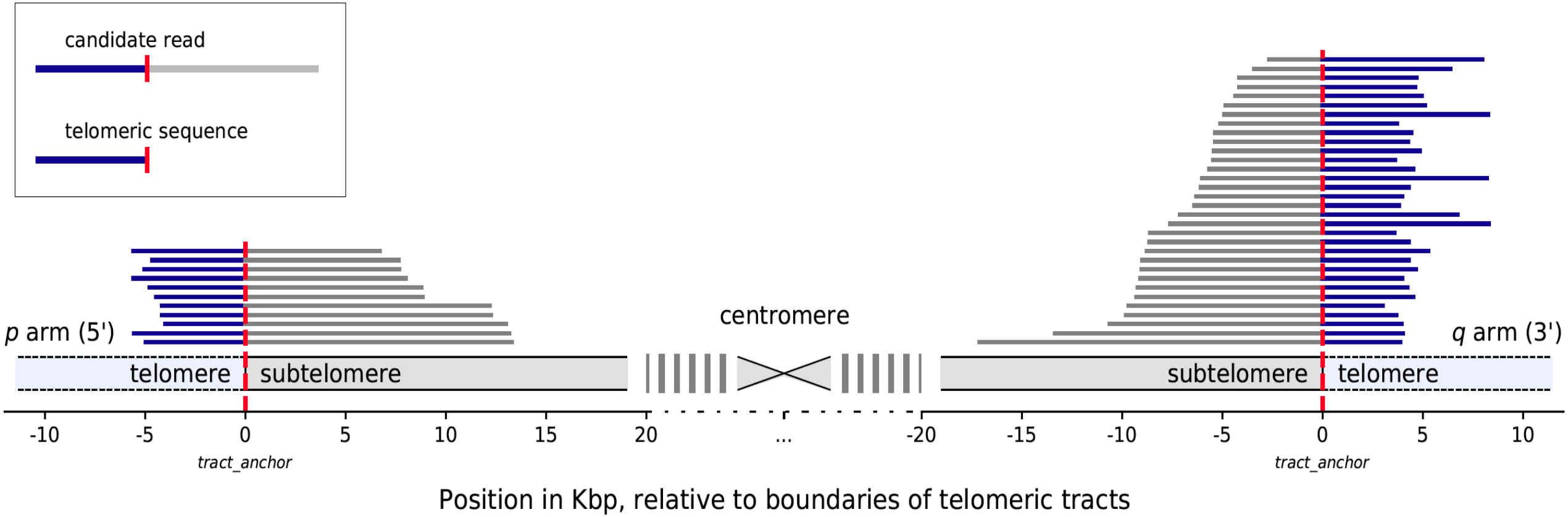
Garrett-Bakelman *et al.*, *Science*, 2019

TL;DR

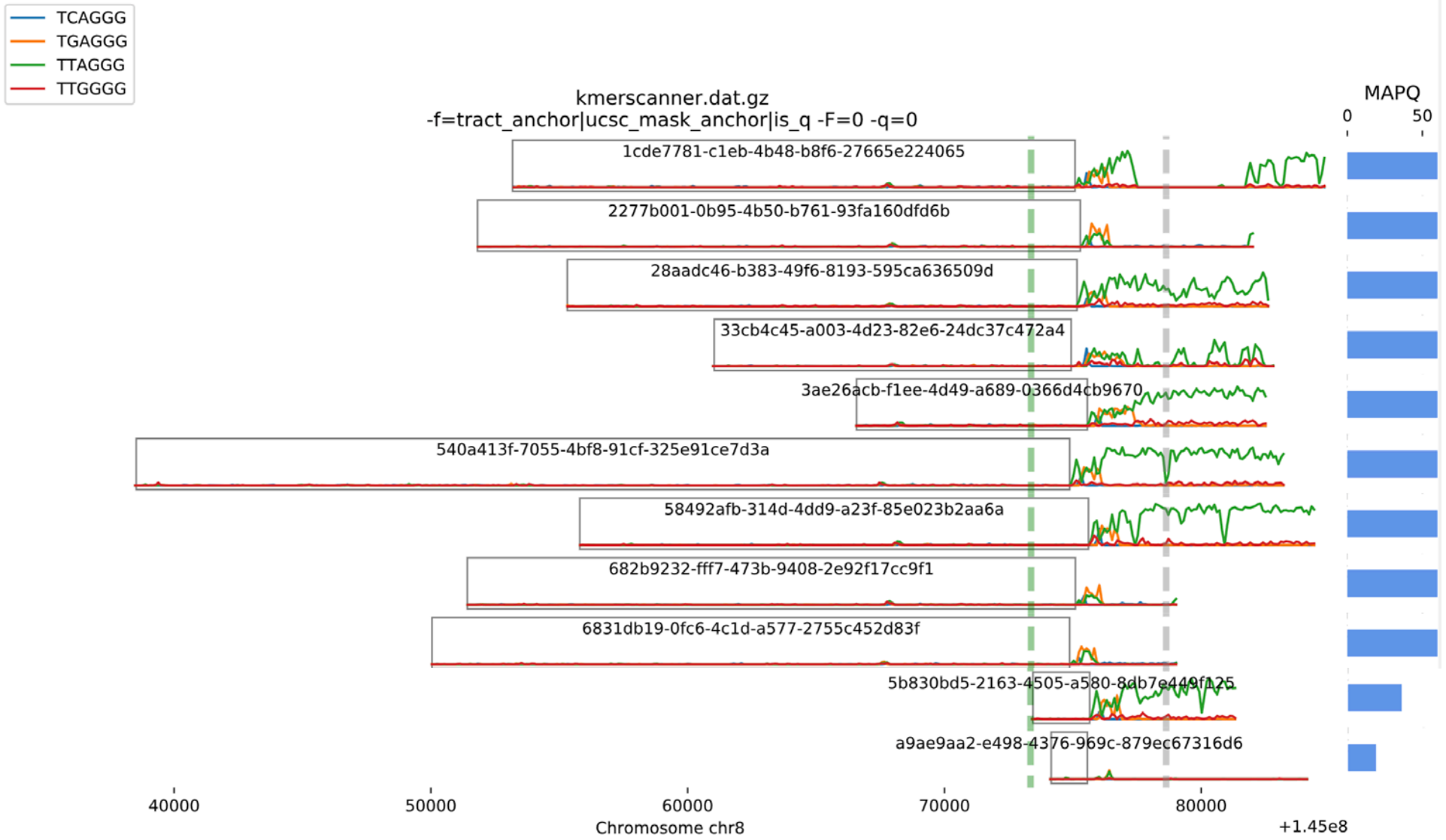
Space made Scott Kelly taller and younger

By Loren Grush on March 3, 2016 03:15 pm @lorengrush

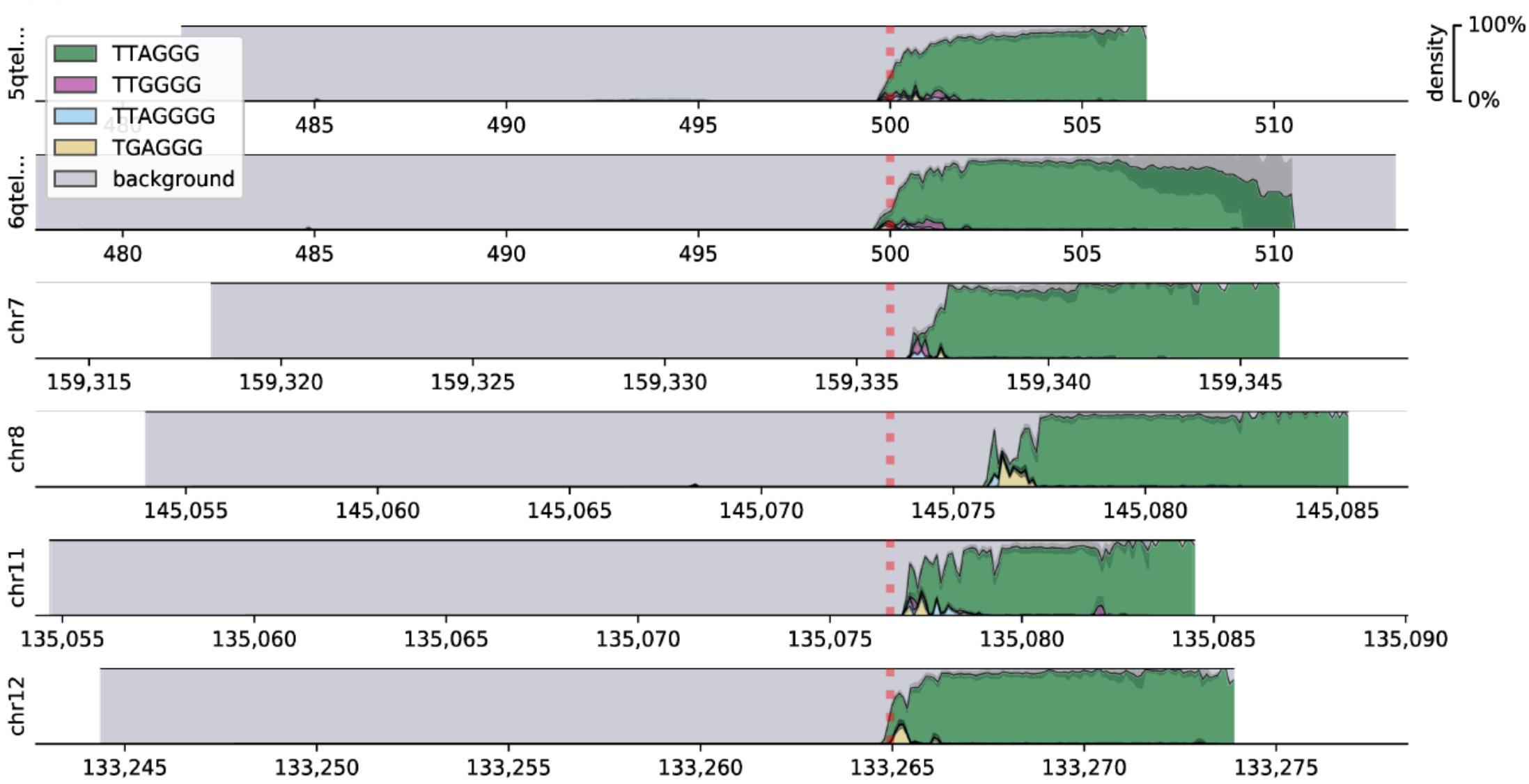
Line up the reads



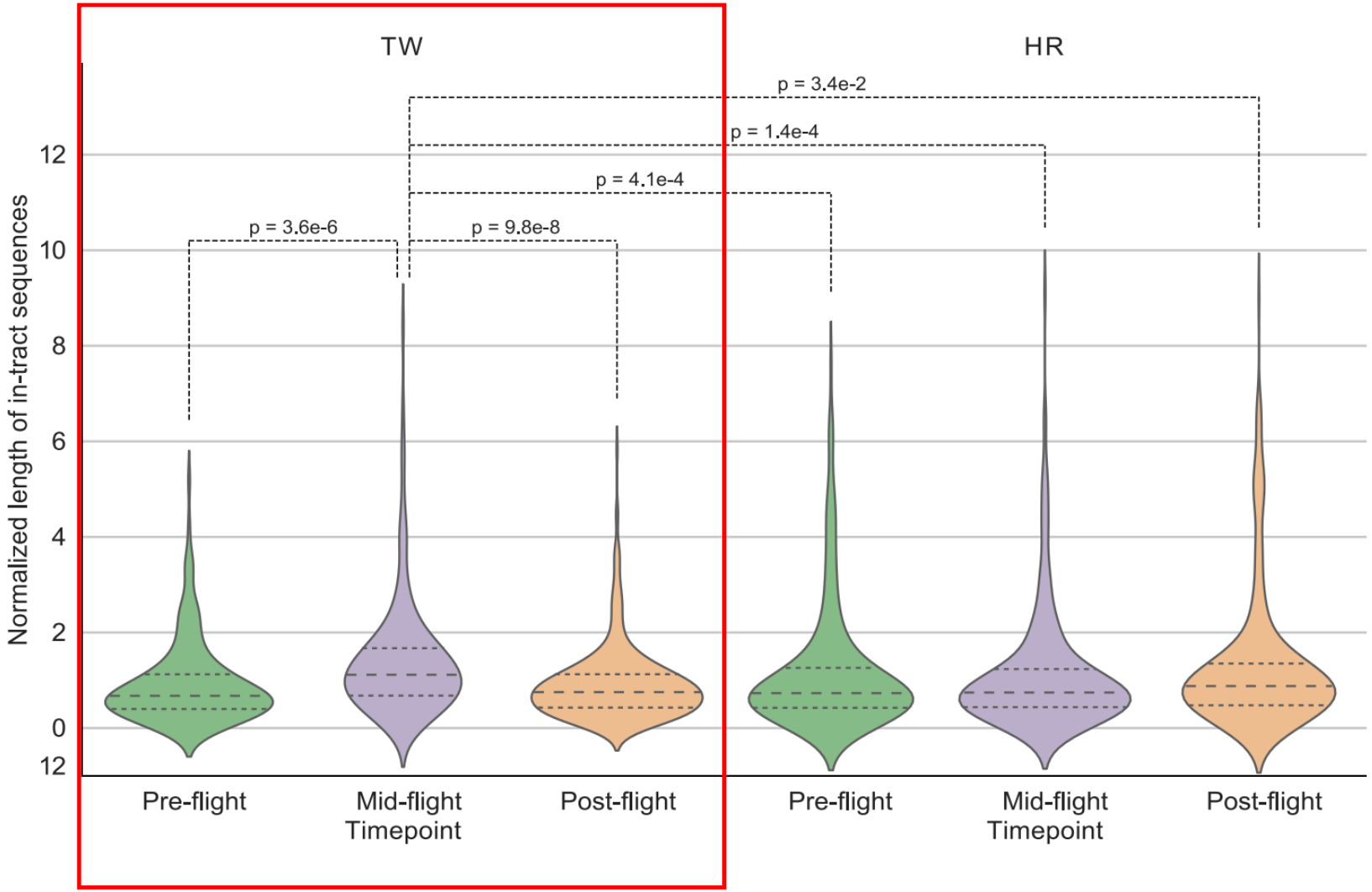
Can see it in nanopore data….



and PacBio HiFi reads



Indeed, the nanopore-based telomeres are longer in flight (TW)



Luxton et al., *Cell Reports*, 2020
https://pubmed.ncbi.nlm.nih.gov/33242411/

But, telomeres still have many stories to tell…

Haplotype diversity and sequence heterogeneity of human telomeres

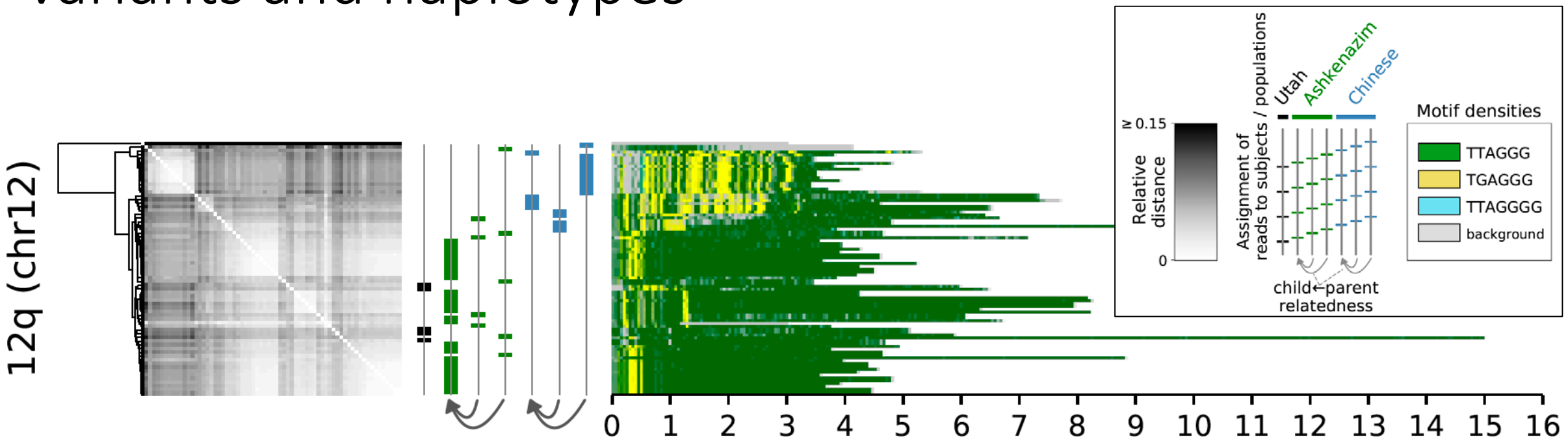
Kirill Grigorev[1,2,10], Jonathan Foox[1,2,3,10], Daniela Bezdan[1,2,3,4,5], Daniel Butler[1], Jared J. Luxton[6,7], Jake Reed[1], Miles J. McKenna[6,7], Lynn Taylor[6], Kerry A. George[8], Cem Meydan[1,2,3], Susan M. Bailey[6,7] and Christopher E. Mason[1,2,3,9]

Published in Advance June 23, 2021, doi: 10.1101/gr.274639.120

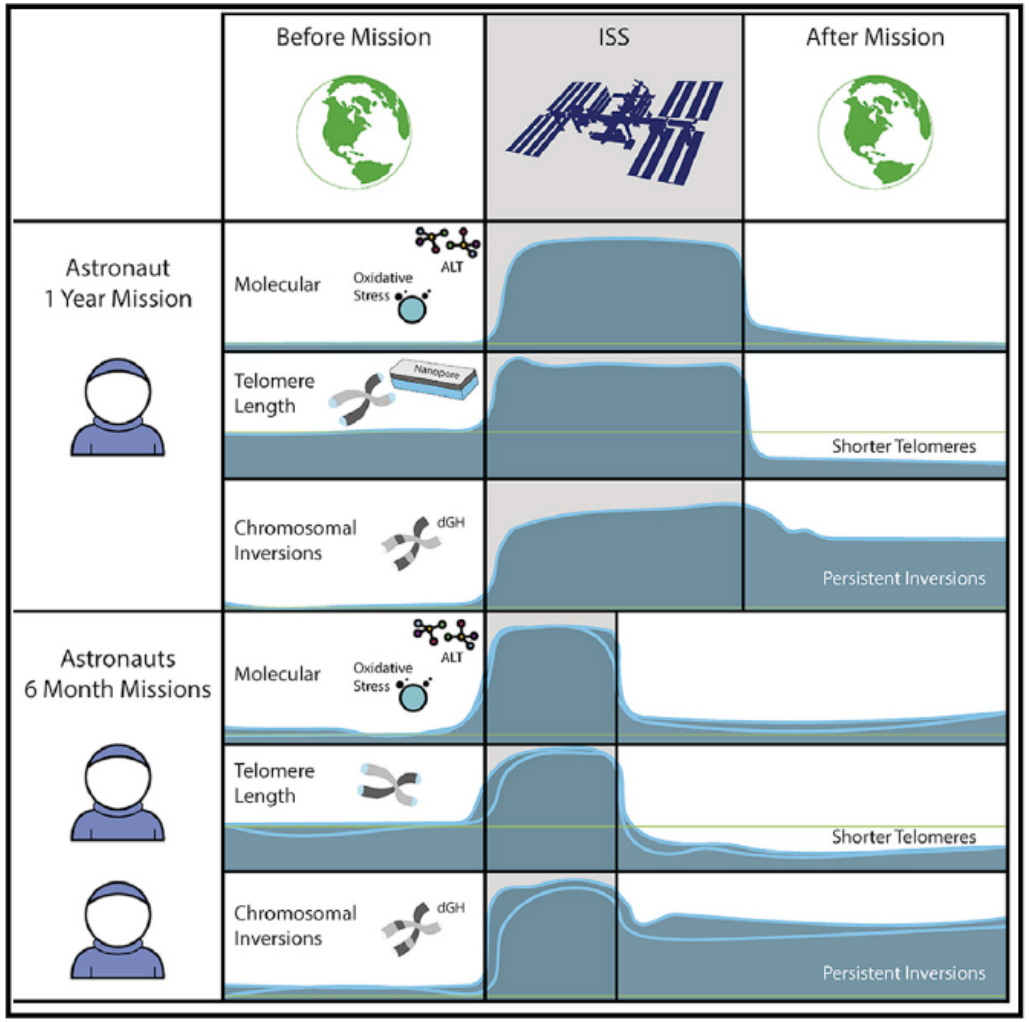
Genome Res. 2021. 31: 1269-1279

https://genome.cshlp.org/content/31/7/1269

Population-specific, non-canonical variants and haplotypes



Telomere elongation validated in two other astronauts



Luxton *et al.*, *Cell Reports*, 2020

w/ Susan Bailey

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817

28

Matt Moniz (right) ascends the world's sixth-tallest peak, Mount Cho Oyu, during a 2014 climb. WILLIE BENEGAS

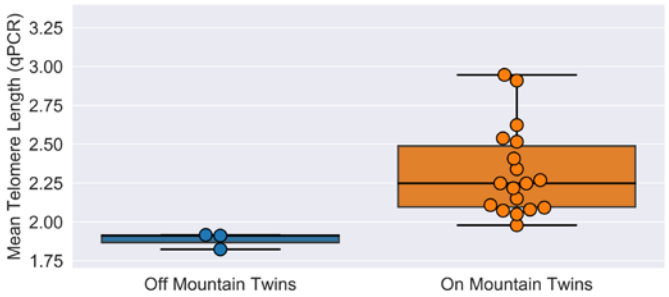
Two mountaineers are trying to recreate NASA's twin study—on Mount Everest

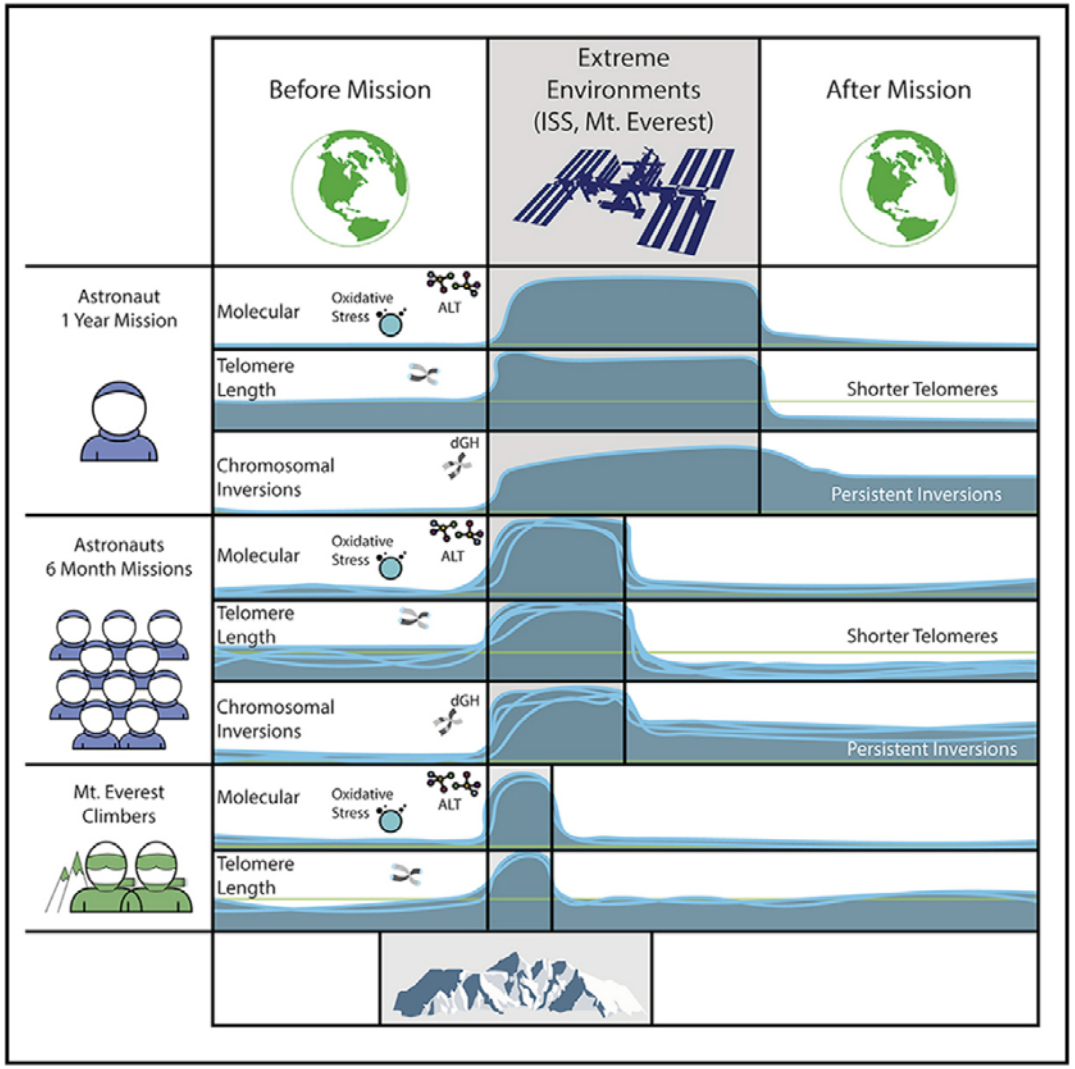
By Vedrana Simicevic | May. 4, 2018 , 12:15 PM

NASA's widely publicized twin study—which compared astronaut Scott Kelly's bodily functions to

http://www.sciencemag.org/news/2018/05/two-mountaineers-are-trying-recreate-nasa-s-twin-study-mount-everest

Then 11 other astronauts & on Mt. Everest



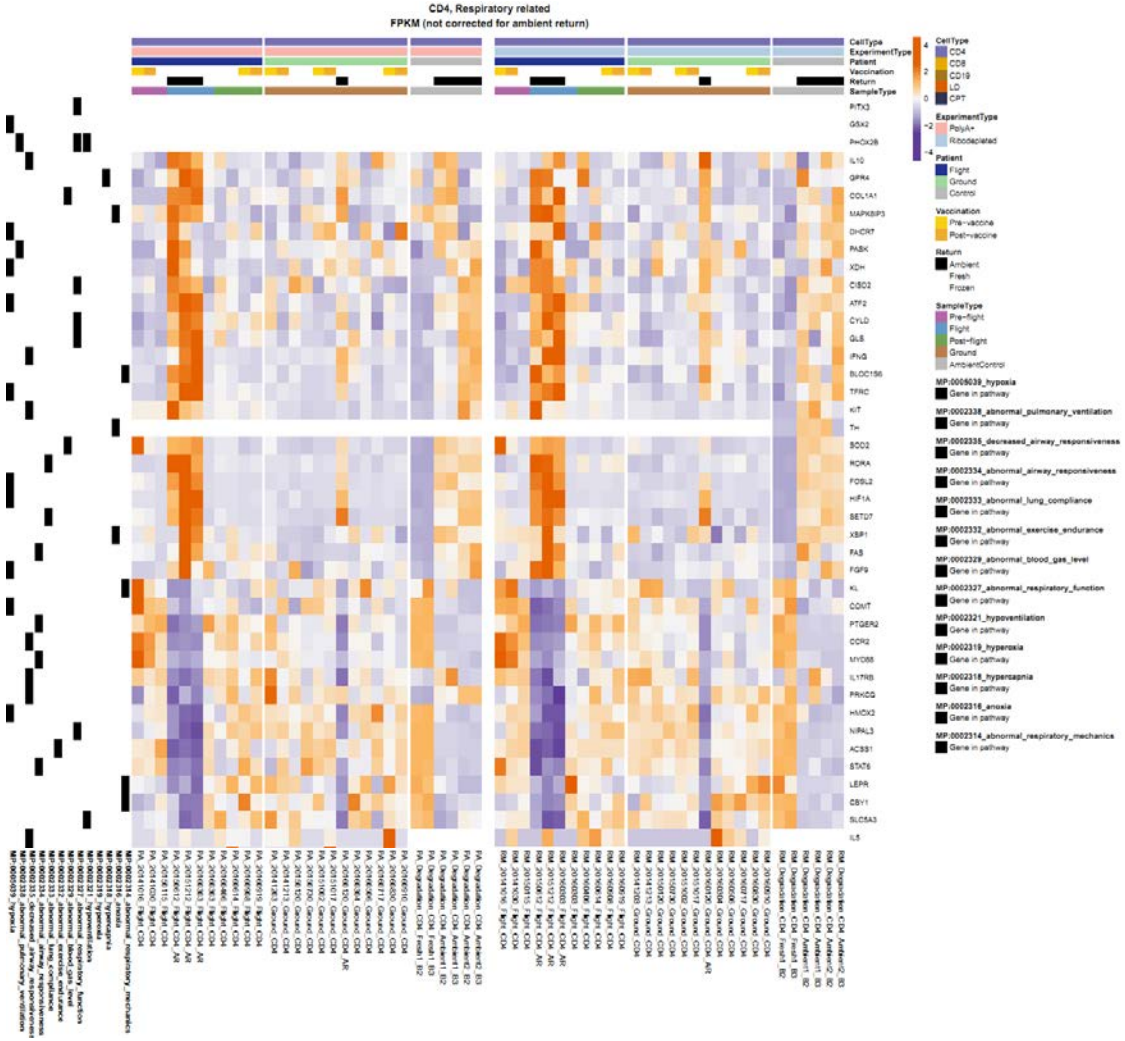


Luxton *et al.*, *Cell Reports*, 2020

https://www.cell.com/cell-reports/fulltext/S2211-1247(20)31446-7

w/ Susan Bailey

Gene expression changes in flight and after: Immune system, DNA repair, and hypercapnia



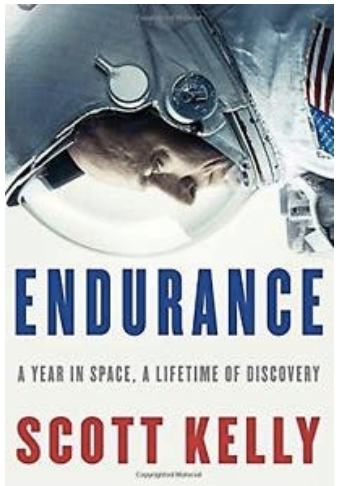
Relationship Between Carbon Dioxide Levels and Reported Headaches on the International Space Station

Jennifer Law, MD, MPH, Mary Van Baalen, MS, Millennia Foy, PhD, Sara S. Mason, BS, Claudia Mendez, MPH, Mary L. Wear, PhD, Valerie E. Meyers, PhD, DABT, and David Alexander, MD

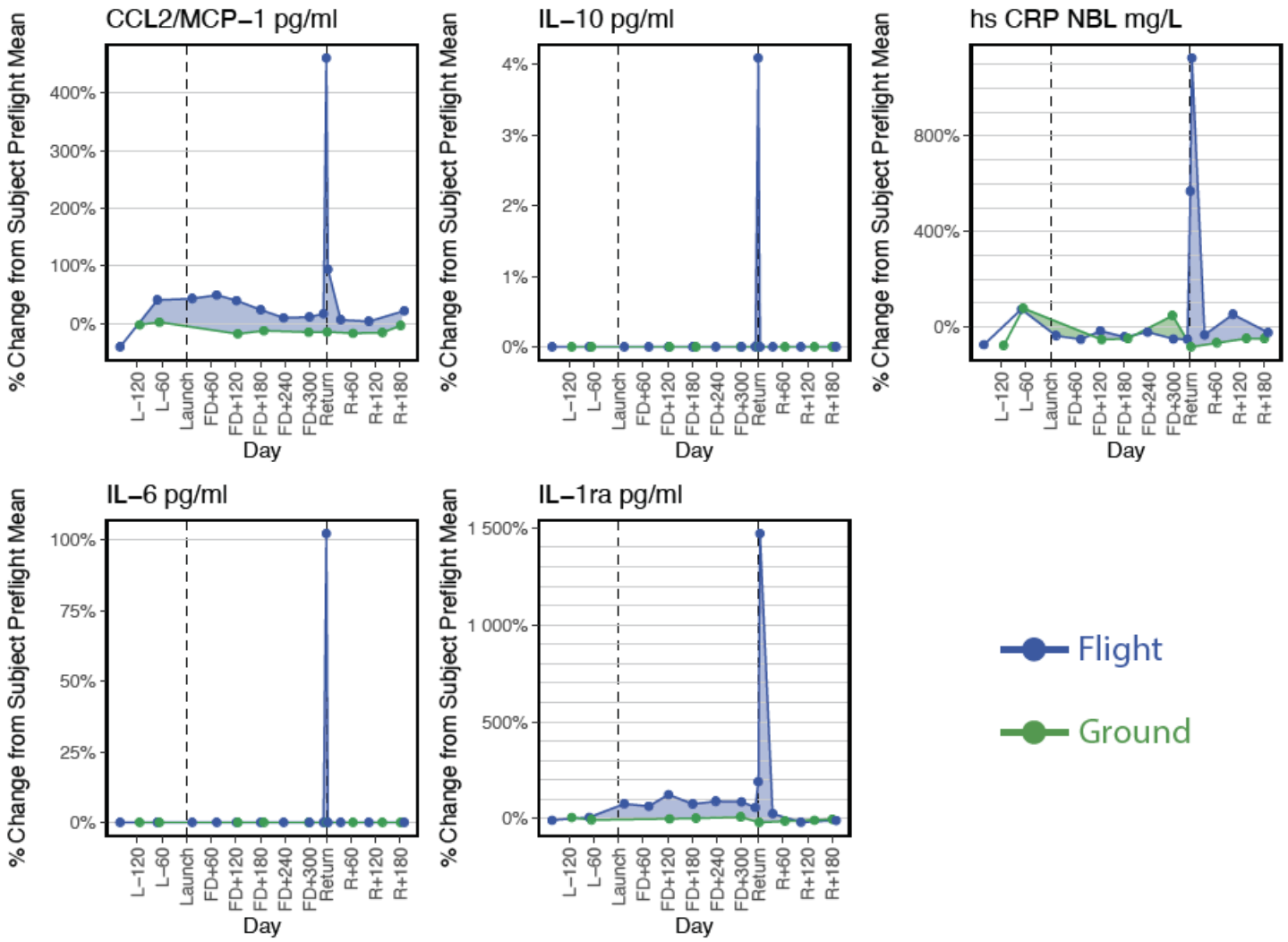
Objective: Because of anecdotal reports of CO_2-related symptoms onboard the International Space Station (ISS), the relationship between CO_2 and in-flight headaches was analyzed. **Methods:** Headache reports and CO_2 measurements were obtained, and arithmetic means and single-point maxima were determined for 24-hour and 7-day periods. Multiple imputation addressed missing data, and logistic regression modeled the relationship between CO_2, headache probability, and covariates. **Results:** CO_2 level, age at launch, time in-flight, and data source were significantly associated with headache. For each 1-mm Hg increase in CO_2, the odds of a crew member reporting a headache doubled. To keep the risk of headache below 1%, average 7-day CO_2 would need to be maintained below 2.5 mm Hg (current ISS range: 1 to 9 mm Hg). **Conclusions:** Although headache incidence was not high, results suggest an increased susceptibility to physiological effects of CO_2 in-flight.

were similar for the two levels of exposure, headache complaints were more frequent during the early days of exposure to the higher level. Furthermore, CBFv increased at days 1 and 5 after discontinuation of hypercapnia. In addition, although CBF and cerebral blood volume (CBV) change similarly during hypercapnia on the Earth,[11] CBF and CBV may not have the same relationship in spaceflight because of impaired venous drainage caused by the cephalad fluid shift; therefore, increased flow may increase the volume.

Terrestrially, healthy males can tolerate CO_2 levels below 7.5 mm Hg indefinitely and up to 480 minutes at 11 mm Hg without acute health effects. Individuals begin to experience headache



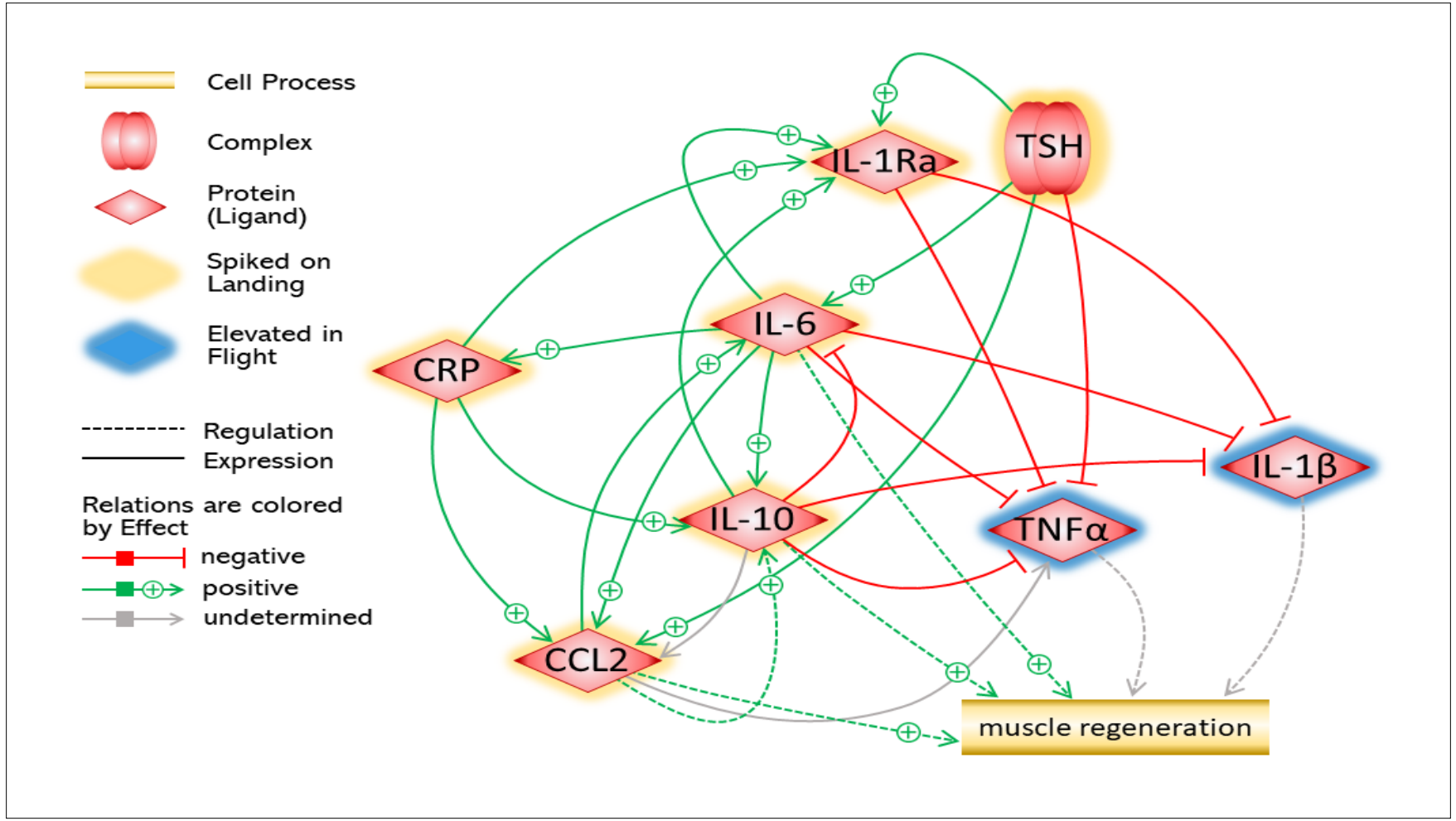
Space is hard; landing is harder



https://www.cell.com/cell-reports/fulltext/S2211-1247(20)31418-2

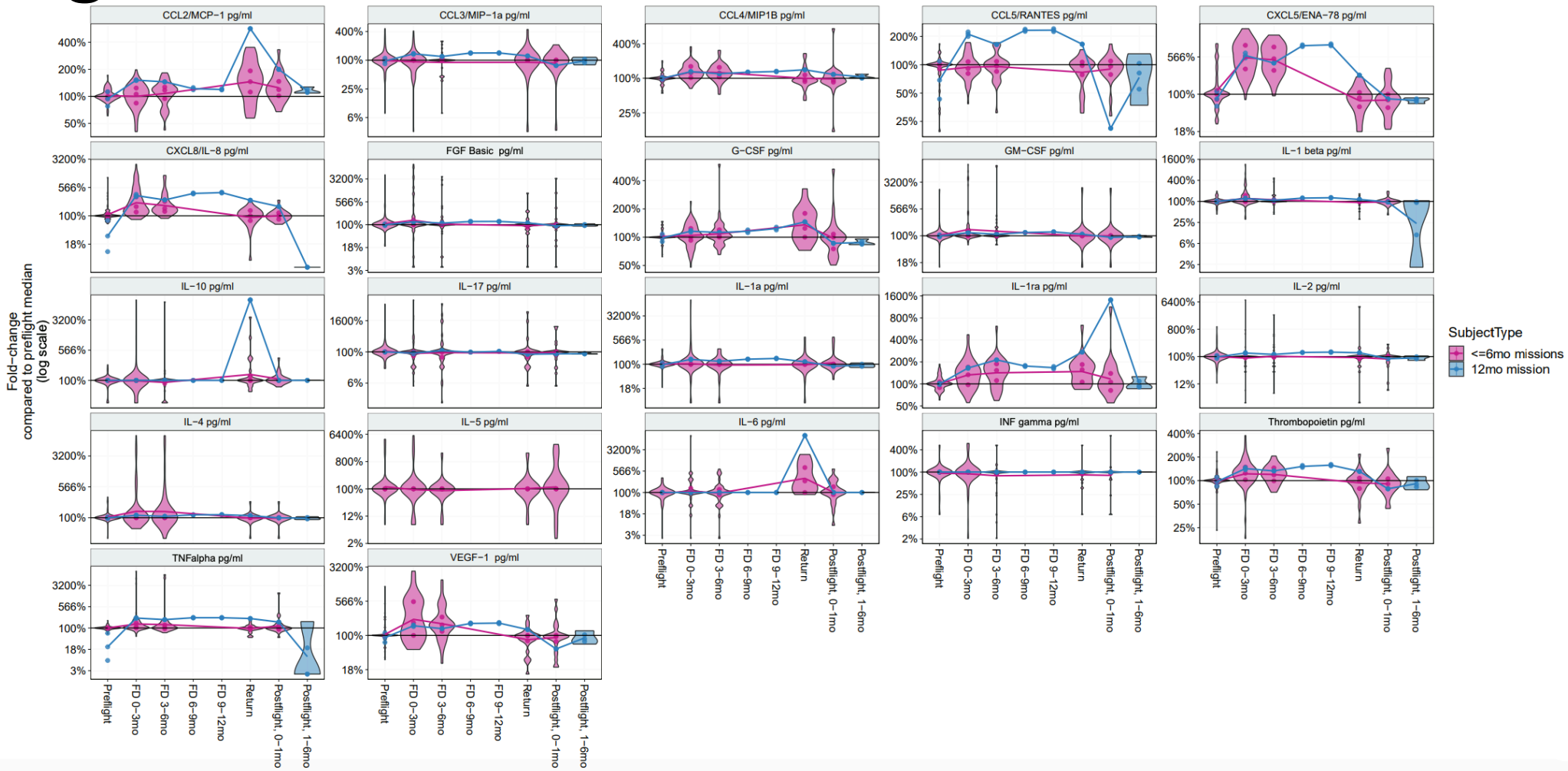
Gertz *et al.*, *Cell Reports*, 2020

The return of muscles' use



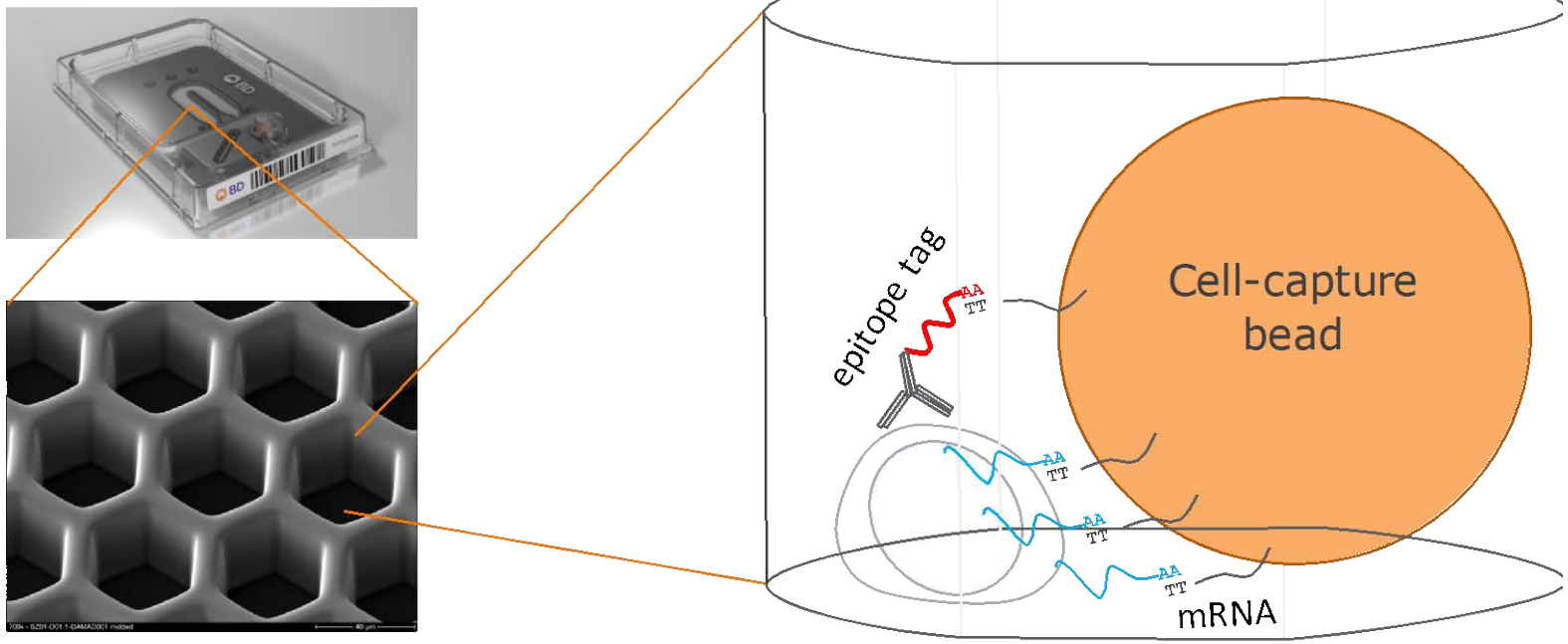
Gertz *et al.*, *Cell Reports*, 2020

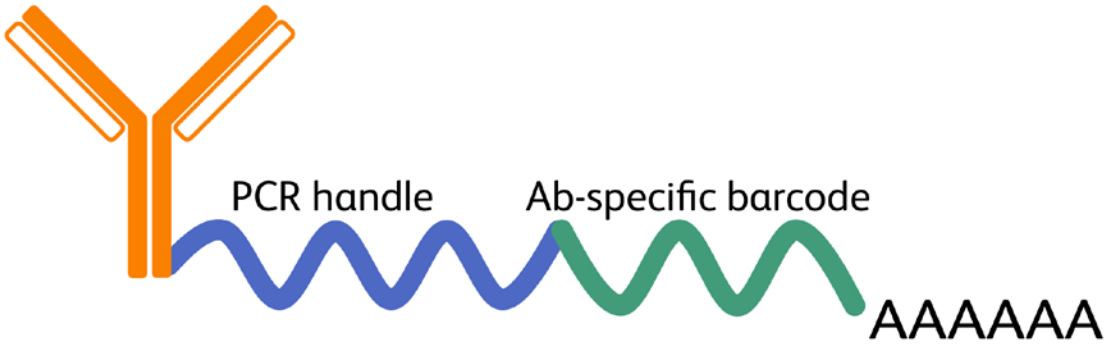
Some differences as a function of mission length



Gertz *et al.*, *Cell Reports*, 2020

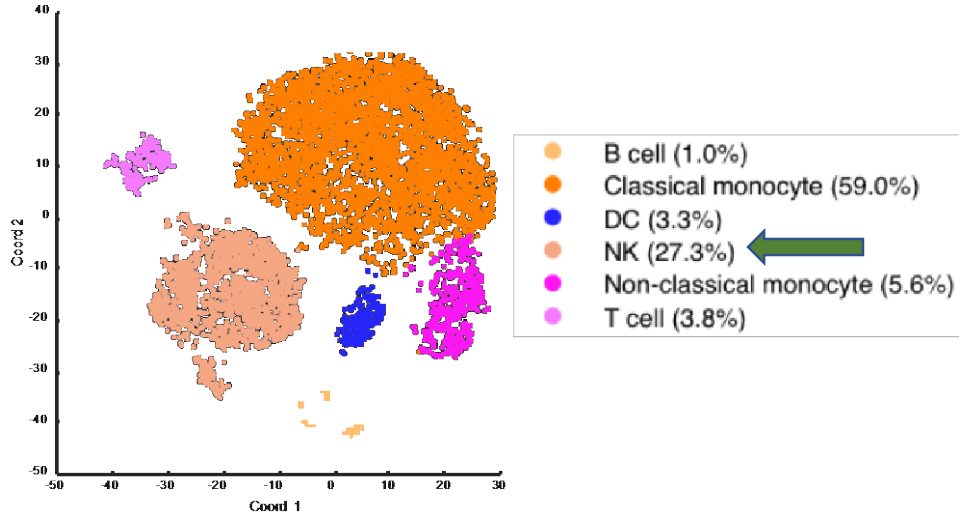
Single-cell expression and 100-plex protein epitope tagging at the same time (BD Rhapsody AbSeq)



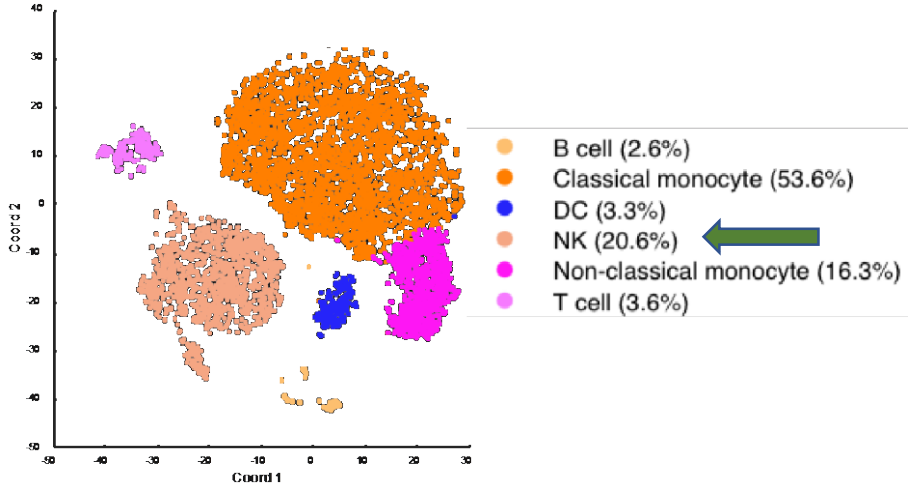


Shifts found in the immune cell types : NK cells, monocytes

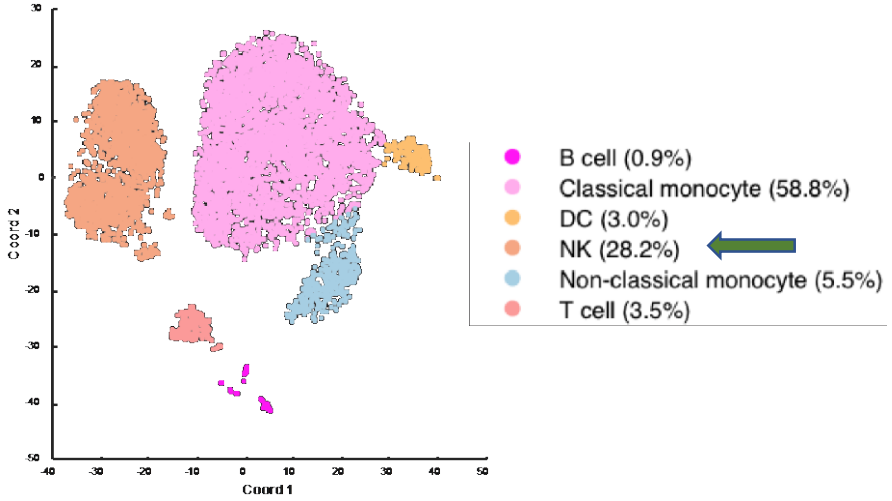
Pre-flight Cells (epitope)



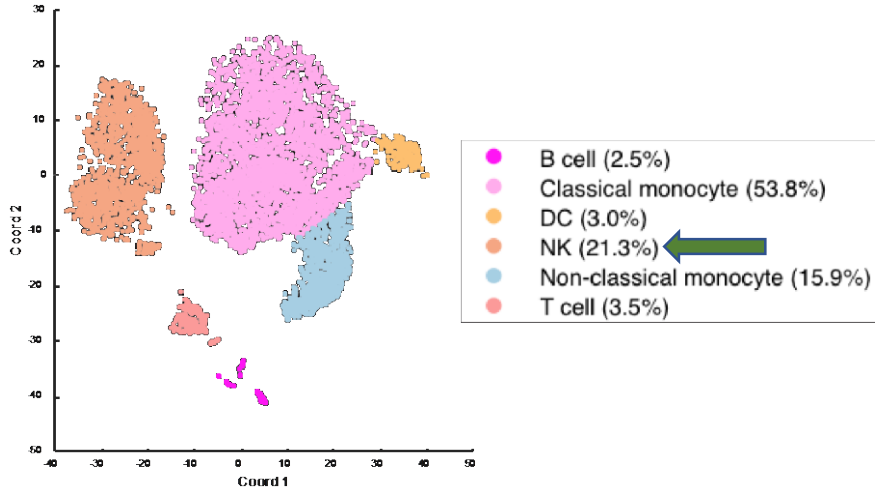
Post-flight Cells (epitope)



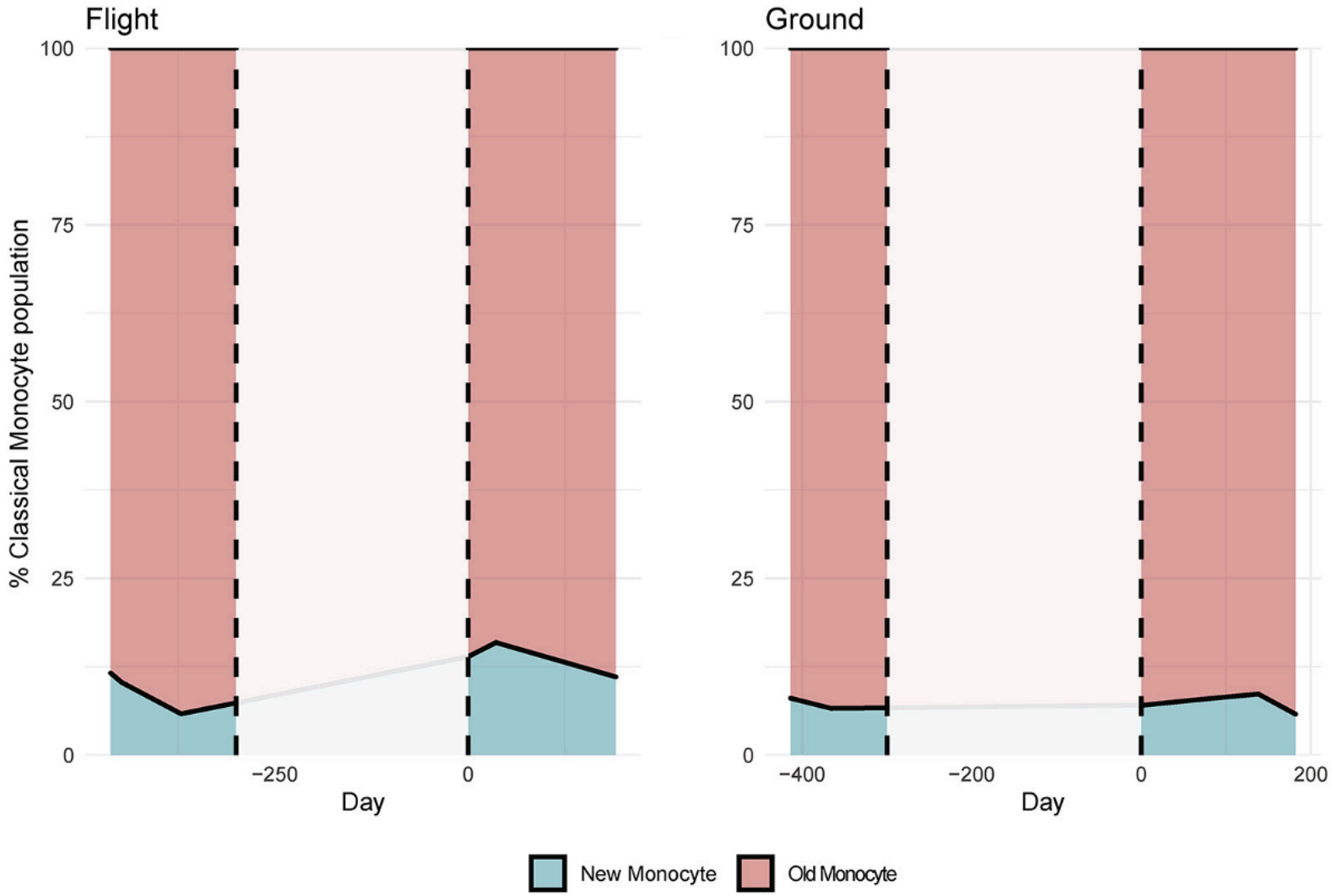
Pre-flight Cells (mRNA)



Post-flight Cells (mRNA)



Increase of monocytes upon landing



Inflammation and aging?

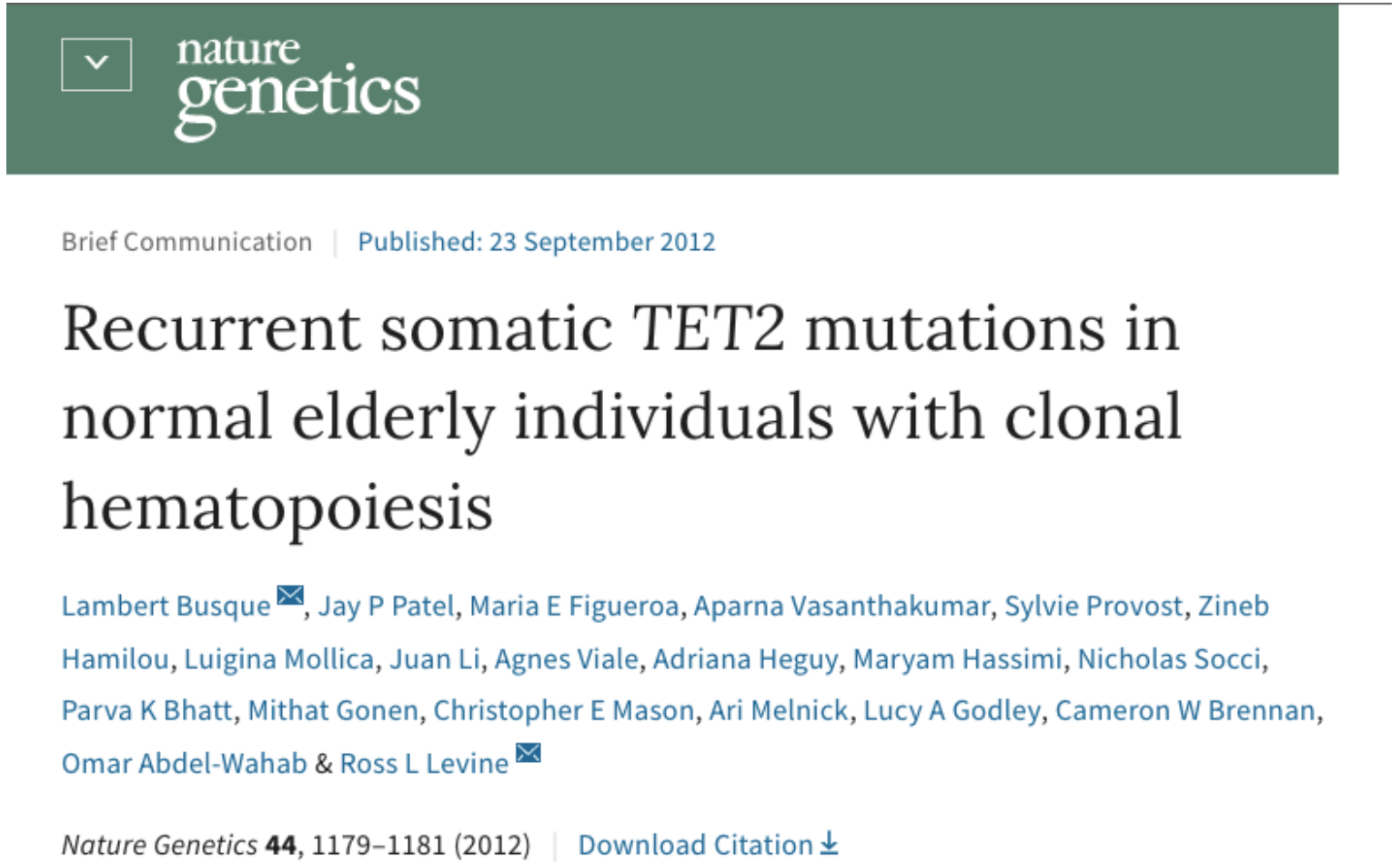
What is Inflammaging?

What is Inflammaging?

https://drheathermd.com/wellness/what-is-inflammaging

🔥 🔥 🔥 This is a HOT topic! 🔥 🔥 🔥

Everyone has some mutations…



nature genetics

Brief Communication | Published: 23 September 2012

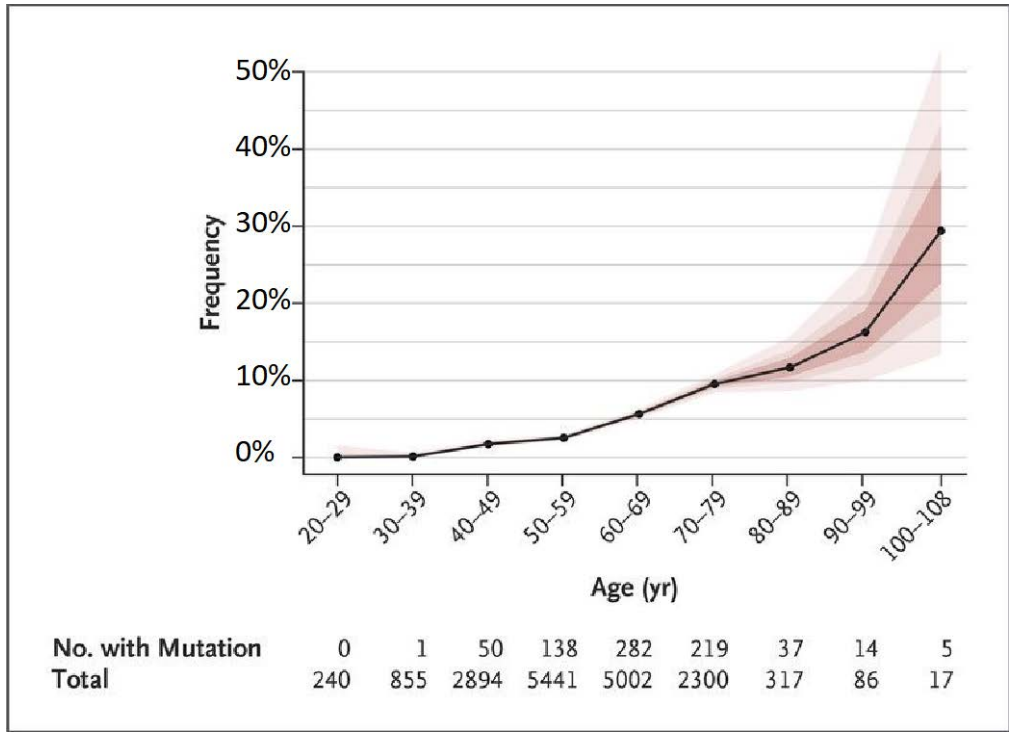
Recurrent somatic *TET2* mutations in normal elderly individuals with clonal hematopoiesis

Lambert Busque, Jay P Patel, Maria E Figueroa, Aparna Vasanthakumar, Sylvie Provost, Zineb Hamilou, Luigina Mollica, Juan Li, Agnes Viale, Adriana Heguy, Maryam Hassimi, Nicholas Socci, Parva K Bhatt, Mithat Gonen, Christopher E Mason, Ari Melnick, Lucy A Godley, Cameron W Brennan, Omar Abdel-Wahab & Ross L Levine

Nature Genetics **44**, 1179–1181 (2012) | Download Citation

https://www.nature.com/articles/ng.2413

Inevitable Mutations?
Clonal Hematopoiesis of Indeterminate Potential (CHIP)



nature medicine

Article | Published: 09 July 2018

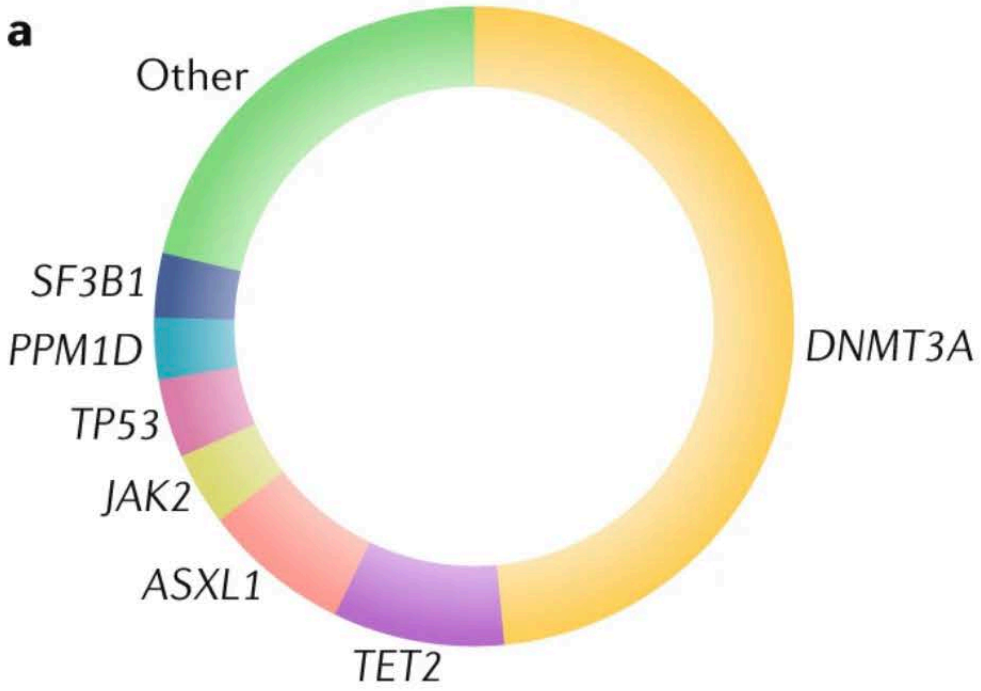
Somatic mutations precede acute myeloid leukemia years before diagnosis

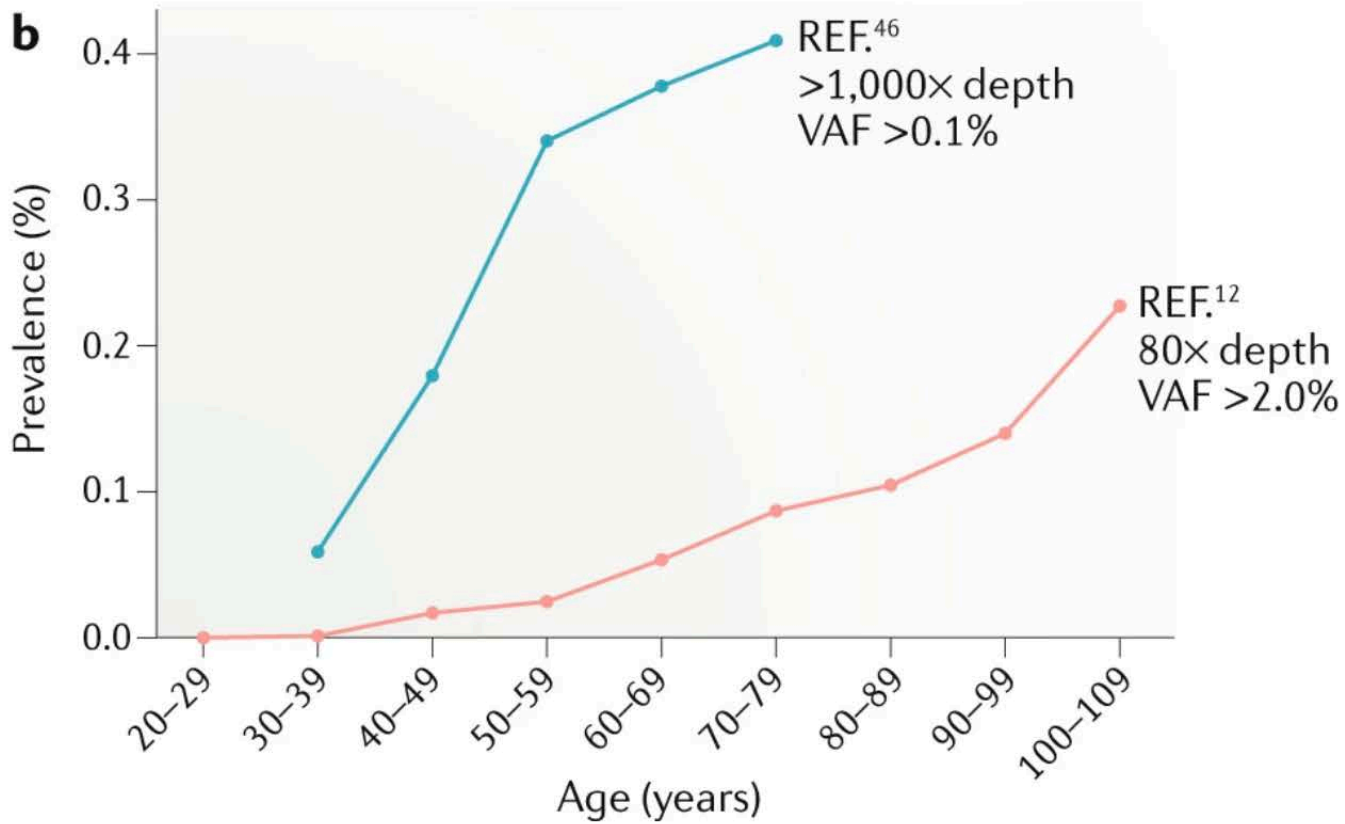
Pinkal Desai, Nuria Mencia-Trinchant, Oleksandr Savenkov, Michael S. Simon, Gloria Cheang, Sangmin Lee, Michael Samuel, Ellen K. Ritchie, Monica L. Guzman, Karla V. Ballman, Gail J. Roboz & Duane C. Hassane

Nature Medicine **24**, 1015–1023 (2018) | Download Citation

https://www.nature.com/articles/s41591-018-0081-z

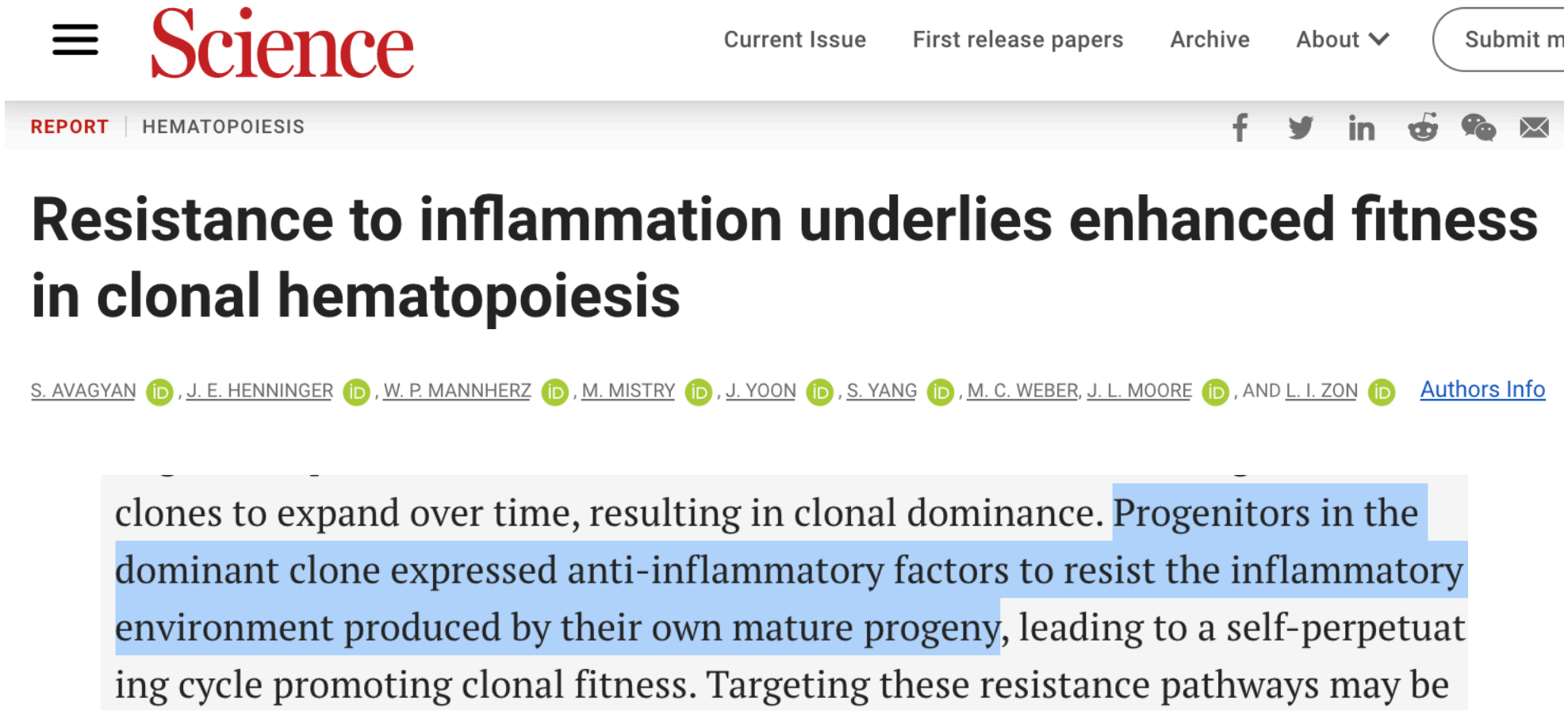
Interaction between the immune system and CHIP; if you sequence deep enough, you find it





https://www.nature.com/articles/s41569-019-0247-5

The stem cells encode their own dominance



Science

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REPORT | HEMATOPOIESIS

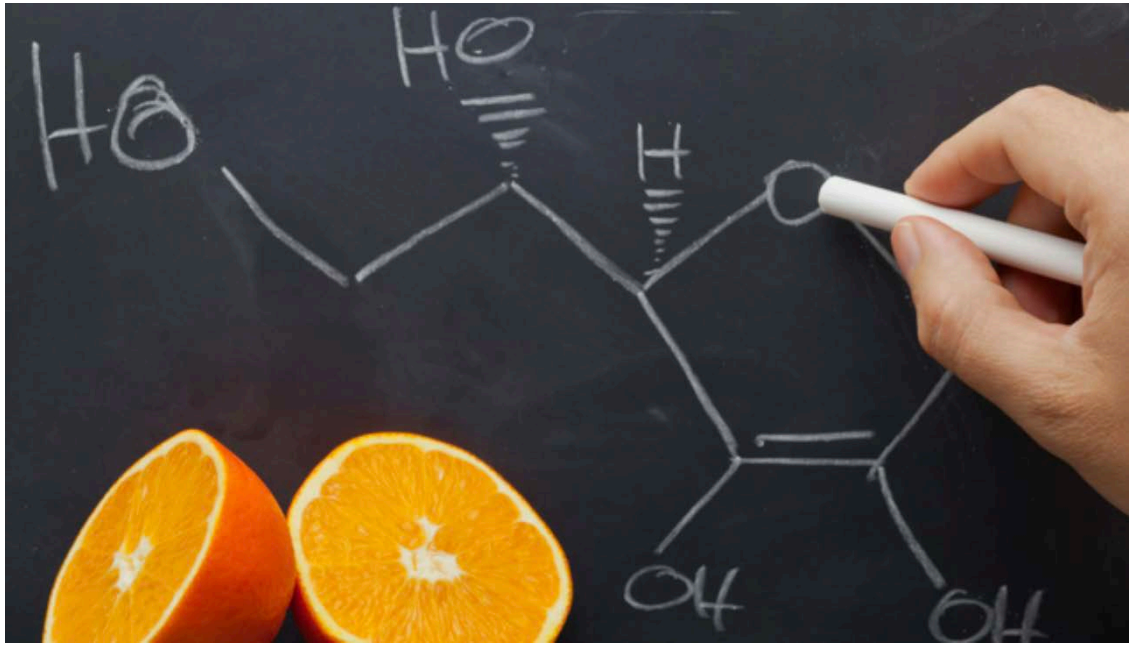
Resistance to inflammation underlies enhanced fitness in clonal hematopoiesis

S. AVAGYAN, J. E. HENNINGER, W. P. MANNHERZ, M. MISTRY, J. YOON, S. YANG, M. C. WEBER, J. L. MOORE, AND L. I. ZON Authors Info

clones to expand over time, resulting in clonal dominance. Progenitors in the dominant clone expressed anti-inflammatory factors to resist the inflammatory environment produced by their own mature progeny, leading to a self-perpetuat ing cycle promoting clonal fitness. Targeting these resistance pathways may be

https://www.science.org/doi/10.1126/science.aba9304

Maybe some ways to reduce it: such as Vitamin C (in mice)?



- Vitamin C treatment mimics *Tet2* restoration to block leukemia progression
- Vitamin C treatment in leukemia cells enhances their sensitivity to PARP inhibition

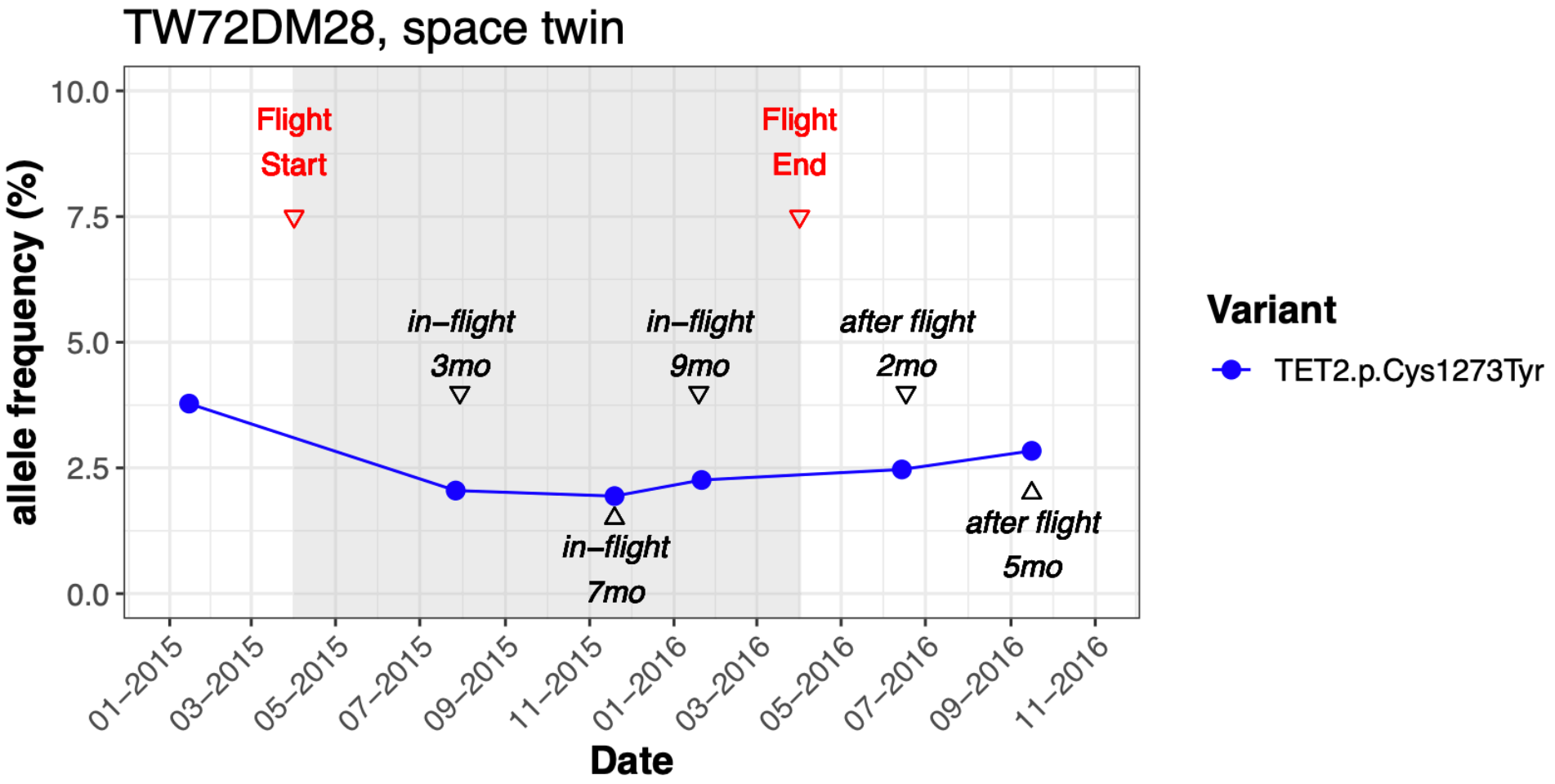
Restoration of TET2 Function Blocks Aberrant Self-Renewal and Leukemia Progression

Luisa Cimmino • Igor Dolgalev • Yubao Wang • ... Aristotelis Tsirigos • Benjamin G. Neel [8]
Iannis Aifantis [8, 9] • Show all authors • Show footnotes

Cell

https://linkinghub.elsevier.com/retrieve/pii/S0092867417308681

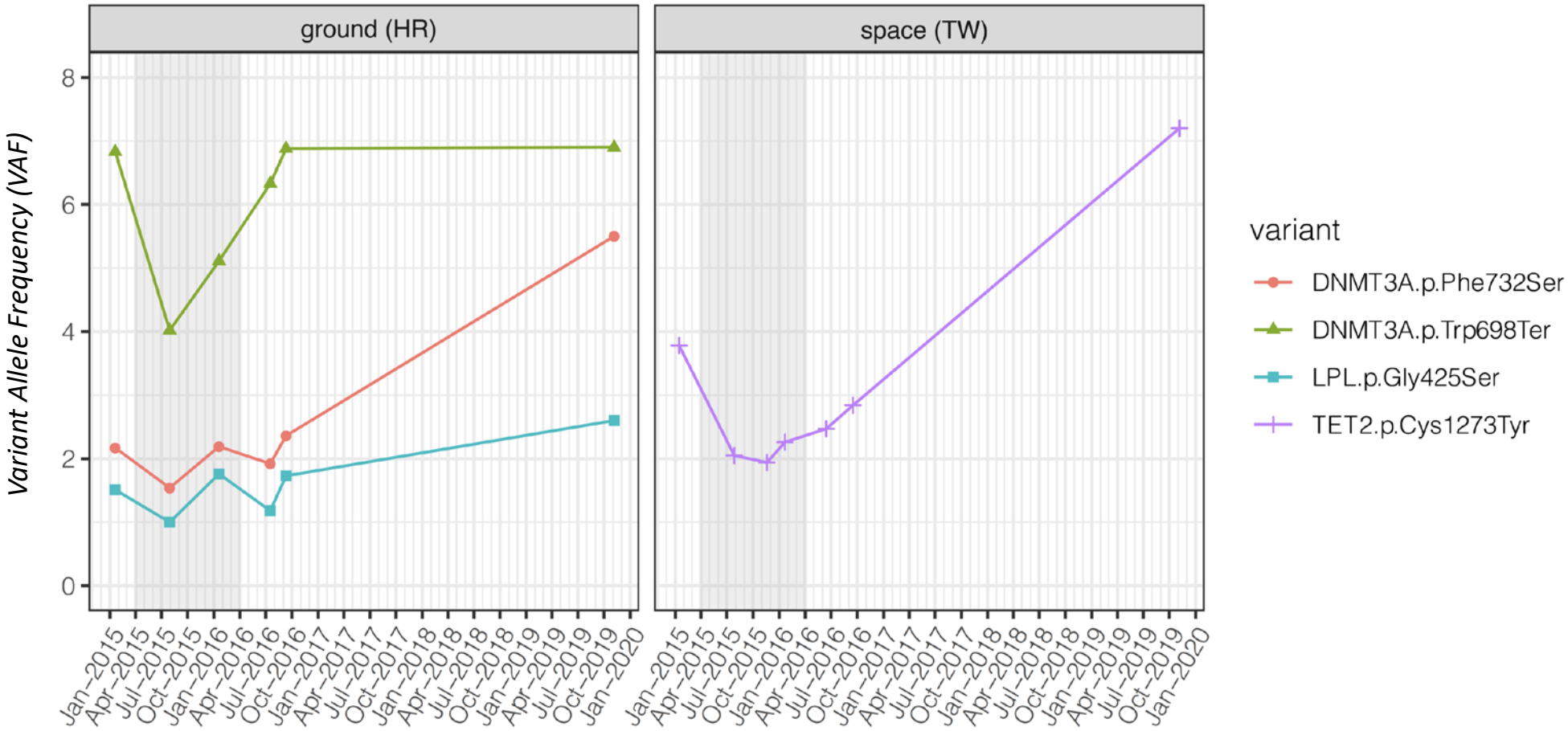
And…CHIP gets a little better in space



Trinchant *et al.*, *Cell Reports*, 2020

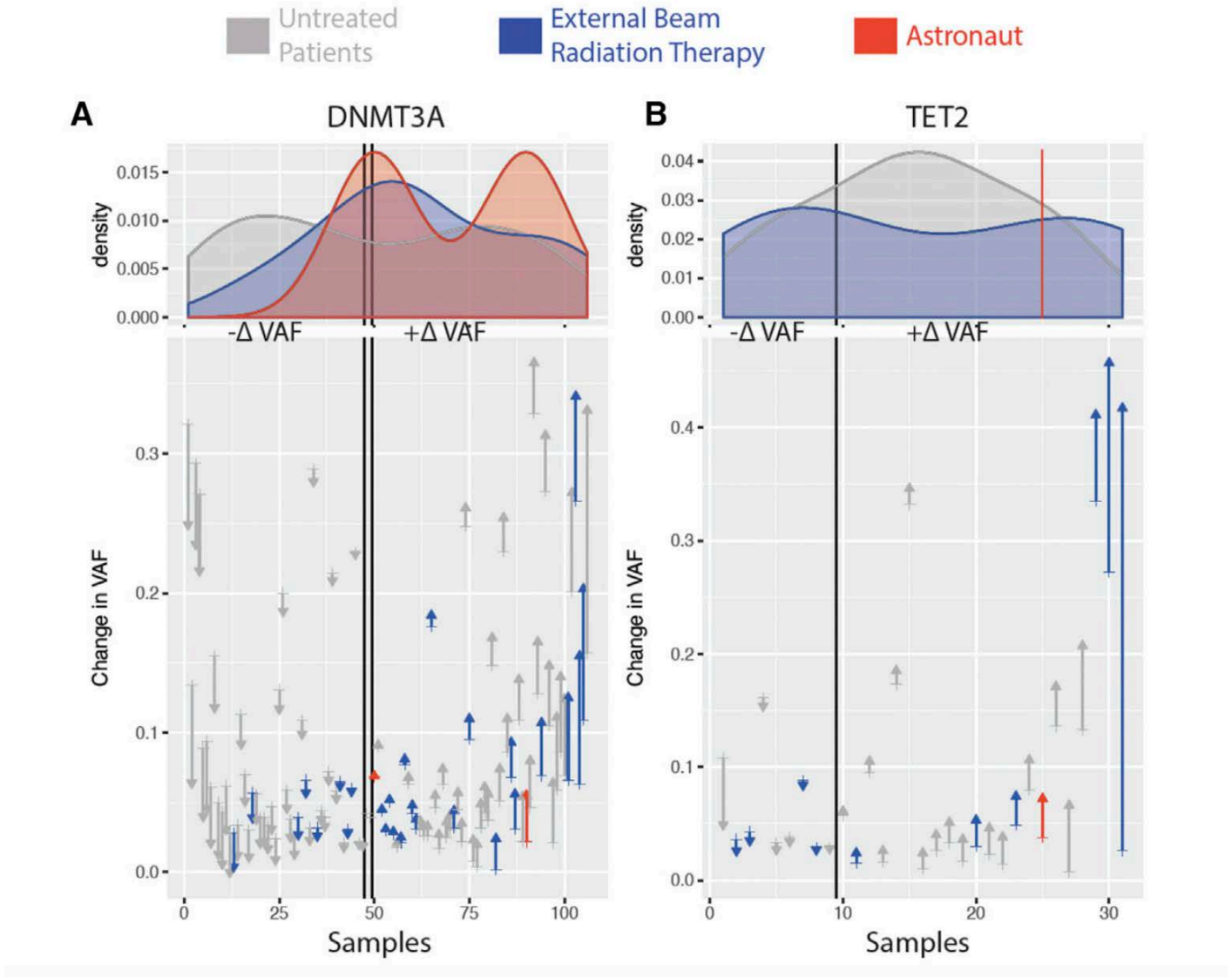
But…

It came back



Trinchant *et al.*, *Cell Reports*, 2020

Compared to beam radiation, mid-rage VAF changes

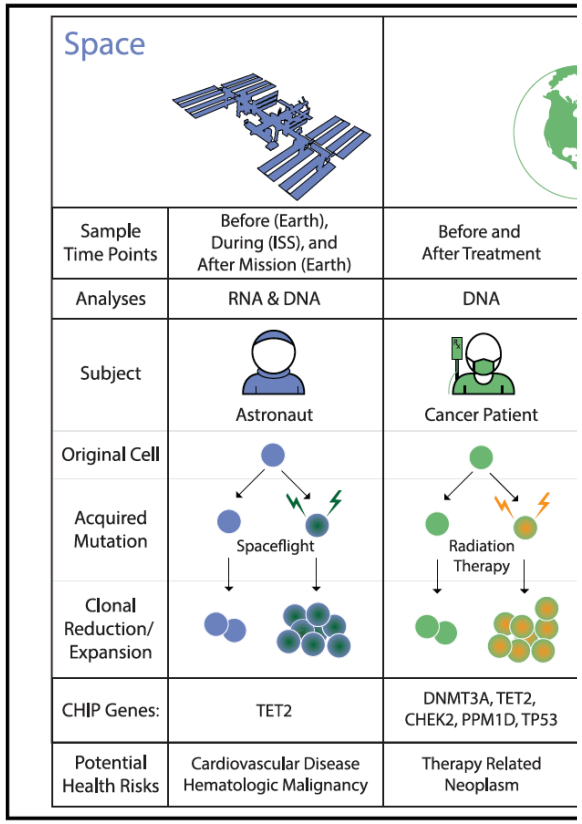


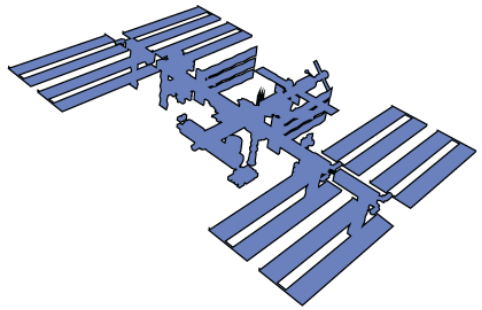
Now onlir

Cell Reports

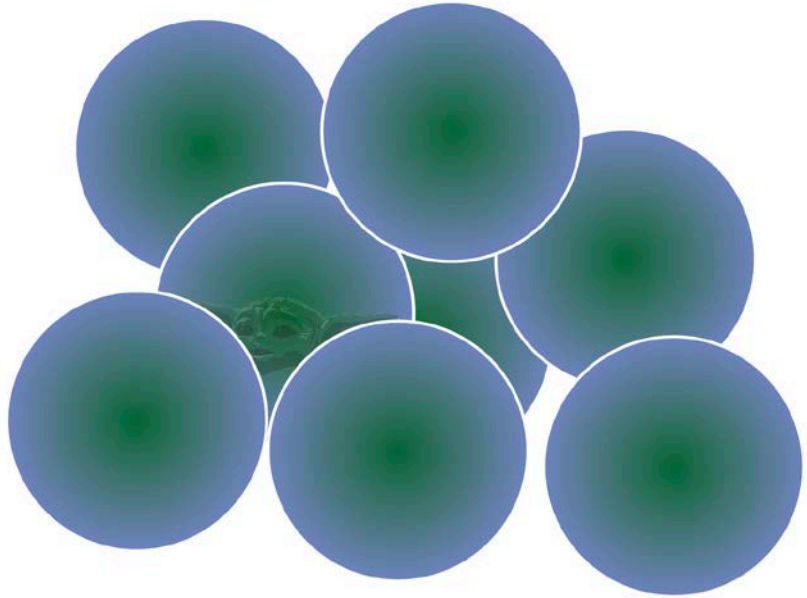
Clonal Hematopoiesis
Human Spaceflight

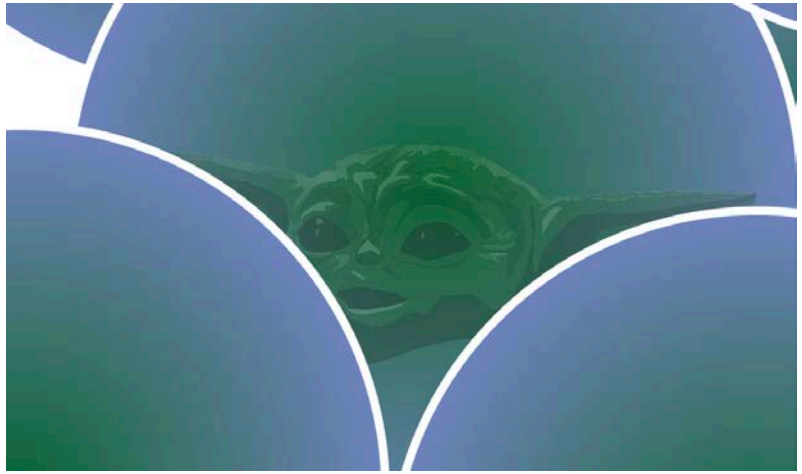
Graphical Abstract



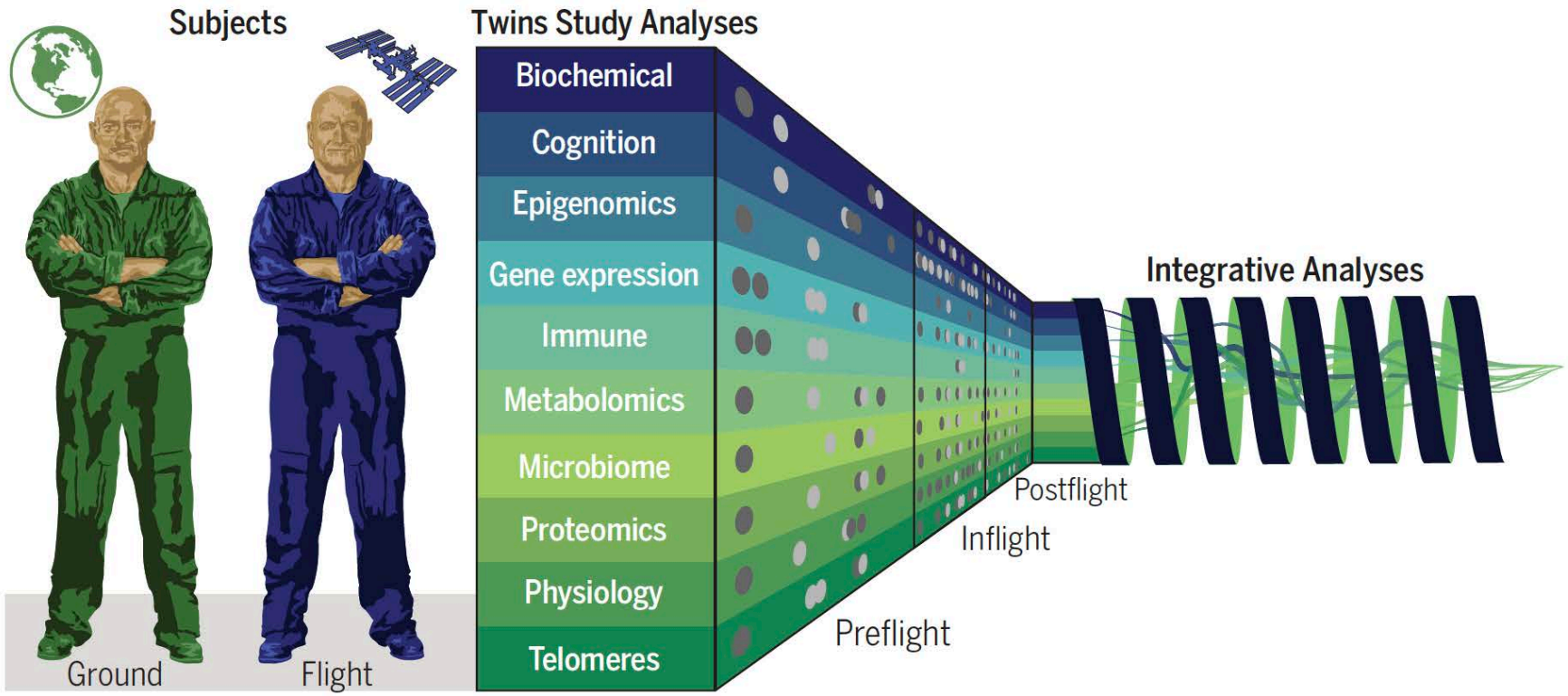


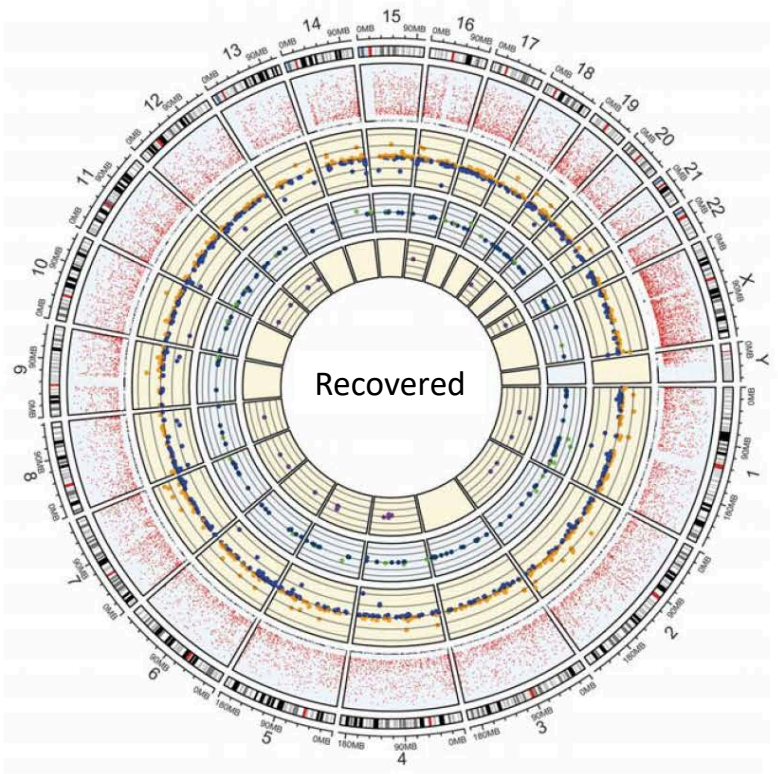
Sample Time Points	Before (Earth), During (ISS), and After Mission (Earth)
Analyses	RNA & DNA
Subject	Astronaut
Original Cell	
Acquired Mutation	Spaceflight
Clonal Reduction/ Expansion	





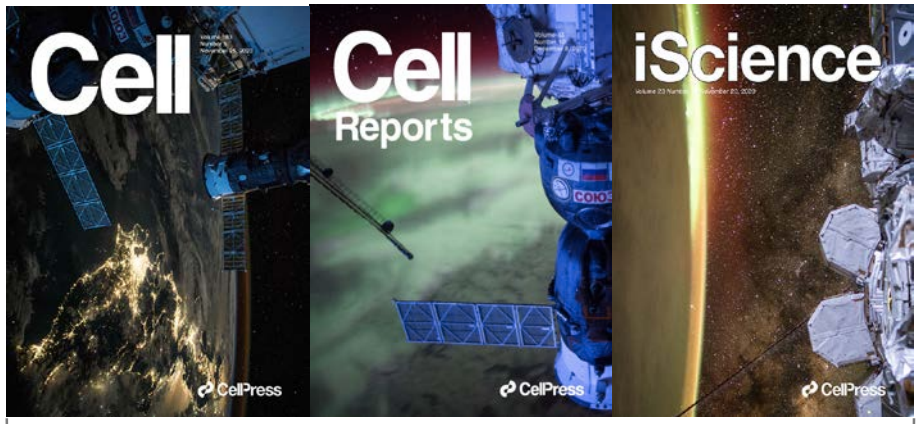
Overall good news





Garrett-Bakelman *et al.*, Science, 2019

59 more astronauts' data released in the Aerospace Medicine & Spaceflight Biology Package (30 papers)



Dr. Afshin Beheshti
Dr. Susan Bailey

In-flight photos from Scott Kelly

https://www.cell.com/c/the-biology-of-spaceflight

>N

Informed Consent Form (ICF) and active IRB

Weill Cornell Medicine | NewYork-Presbyterian

TITLE: Multi-Omics, Physiological, and Clinical Analysis of Human Spaceflight

IRB Protocol #: 21-05023569
Version Date: 05/15/2021
Funding Source(s):
National Aeronautics and Space Administration (NASA) 80NSSC20K1841
Status: Active
Principal Investigators: Monica Guzman/Christopher Mason

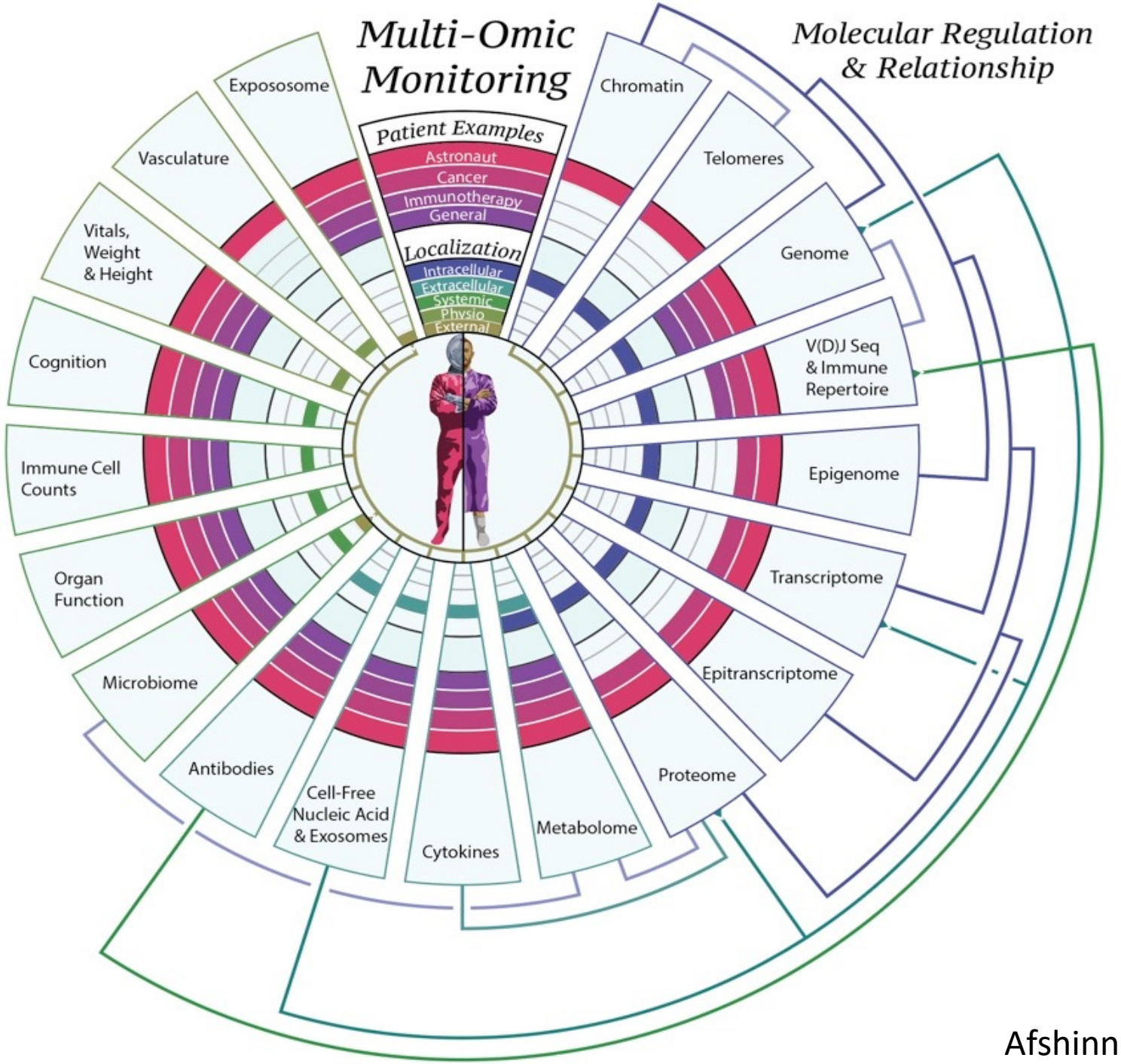
NASA 80JSC019N0001
Status: Pending
Principal Investigator: Christopher Mason

WorldQuant Initiative for Quantitative Prediction (WQIQP)
Status: Active
Principal Investigator: Christopher Mason

Institutional Review Board at:
(646) 962-8200
1300 York Avenue
Box 89
New York, New York 10065

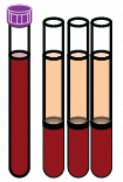
8.30.2021

Inspiration4 Crew Will Conduct Health Research to Further Human Exploration of Space



Afshinnekoo *et al*., *Cell*, 2020

Standard Omics Measures for Astronauts (SOMA)



4 Vials & 1 Card

2 Vials

1 Sample

1 Sample

1 Skin Punch
10 Swabs

1 Sample

Tests

10 Swabs

Space-

Earth-

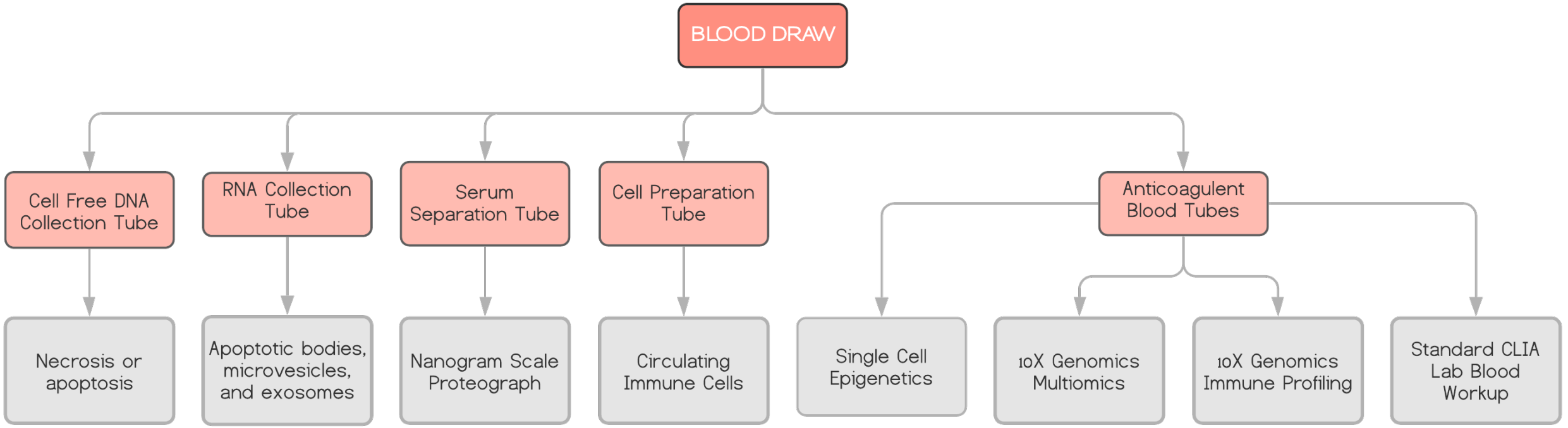
Subject Location During Study

In-Flight

Pre-Flight

Post-Flight

Sample	Analysis	June 14th	July 5th	July 26th	Sept 13th	FD 1-3	R+ 0-7	R+ 14	R+ 30	R+ 6m	R+ 1y	R+ 2y
PBMCs	WGS	●	●	●	●	◇◇◇	●	●	●	○	●	○
	Epigenome	●	●	●	●	◇◇◇	●	●	●	○	●	○
	scRNA/scATAC	●	●	●	●	◇◇◇	●	●	●	○	●	○
Sorted Blood (CD4+, CD8+, CD19+, LD)	Epigenome	●	●	●	●	◇◇◇	●	●	●	○	●	○
	RNA-seq	●	●	●	●	◇◇◇	●	●	●	○	●	○
	TCR *	●	●	●	●	◇◇◇	●	●	●	○	●	○
	Telomeres	●	●	●	●	◇◇◇	●	●	●	○	●	○
Plasma	Biochemistry **	●	●	●	●	◇◇◇	●	●	●	○	●	○
	Cytokines **	●	●	●	●	◇◇◇	●	●	●	○	●	○
	Metabolomics **	●	●	●	●	◇◇◇	●	●	●	○	●	○
	Proteomics **	●	●	●	●	◇◇◇	●	●	●	○	●	○
	cfDNA/cfRNA **	●	●	●	●	◇◇◇	●	●	●	○	●	○
	Exosomes	●	●	●	●	◇◇◇	●	●	●	○	●	○
Stool	Metagenomics	●	●	●	○	◇◇◇	●	●	●	○	●	○
	Metabolomics	●	●	●	○	◇◇◇	●	●	●	○	●	○
Urine	Biochemistry	●	●	●	○	◇◇◇	●	●	●	○	●	○
	cfDNA	●	●	●	○	◇◇◇	●	●	●	○	●	○
	Exosomes	●	●	●	○	◇◇◇	●	●	●	○	●	○
Saliva/Buccal	RNA-seq	●	●	●	●	◇◇◇	●	●	●	○	●	○
	Metagenomics	●	●	●	●	◇◇◇	●	●	●	○	●	○
	PCR	●	●	●	●	◇◇◇	●	●	●	○	●	○
Skin	Spatial-Omics	●	○	●	○	◇◇◇	●	●	●	○		
	Functional	●	○	●	○	◇◇◇	●	●	●	○		
	Metagenomics ***	●	●	●	○	◇◇◇	●	●	●	○	○	○
Reproductive Tissue	WGS	○	○	○	○	◇◇◇	○	○	○	○	○	○
	WGBS	○	○	○	○	◇◇◇	○	○	○	○	○	○
	RNA-seq	○	○	○	○	◇◇◇	○	○	○	○	○	○
Cognition	Cognition	●	●	●	●	◇◇◇	●	●	●	●	○	
Environment	Metagenomics				●	◇◇◇	●				○	



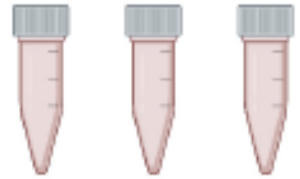




Tube Type	Streck cfDNA	PaxGene RNA	Serum Separation	Cell Preparation	K2EDTA	Total
# of Tubes	1	1	1	2	4	9
Volume	10 mL	2.5 mL	7.5 mL	20 mL	16 mL	56 mL

Stool, saliva, urine genomics and metabolomics

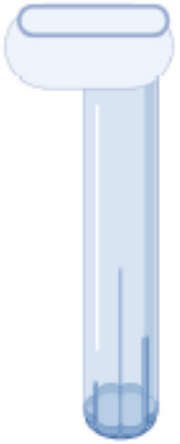
A



3 Collection TImepoints
(1) Morning
(2) Afternoon
(3) Evening

Collection Container 5mL Screw-Top Vials	
Collection Amount 1-3mL	
Biospecimen(s) (1) Crude Saliva	**Storage Conditions** (1) -80°C

B



1 Collection Timepoint
Anytime of day

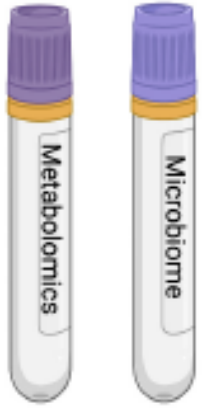
Collection Container Saliva Microbiome Stabilization Kit	
Collection Amount Fill to collection line	
Biospecimen(s) (1) Stabilized Saliva	**Storage Conditions** (1) -80°C

C

2 Collection Timepoints
(1) Morning/Midday
(2) Evening/Night

Collection Container 120 mL Screw-Top Container	
Collection Amount Full bladder or until cup is filled	
Biospecimen(s) (1) Crude Urine (2) Urine with preservative conditioning buffer added	**Storage Conditions** (1) -80°C (2) -80°C

D



1 Collection Timepoint
Anytime of day

Collection Container Stool Stabilization Kits	
Collection Amount A few grams per tube	
Biospecimen(s) (1) Stool in metabolomic preservative (2) Stool in microbiome preservative	**Storage Conditions** (1) -80°C (2) -80°C


V/SPEED


V/SPEED


FWD


Budweiser
BUD LIGHT
BUD LIGHT
BUD LIGHT
BUD LIGHT

Microbiomes can come from unexpected places

SpaceX's private Inspiration4 astronauts had some toilet trouble in space

By Amy Thompson 2 days ago

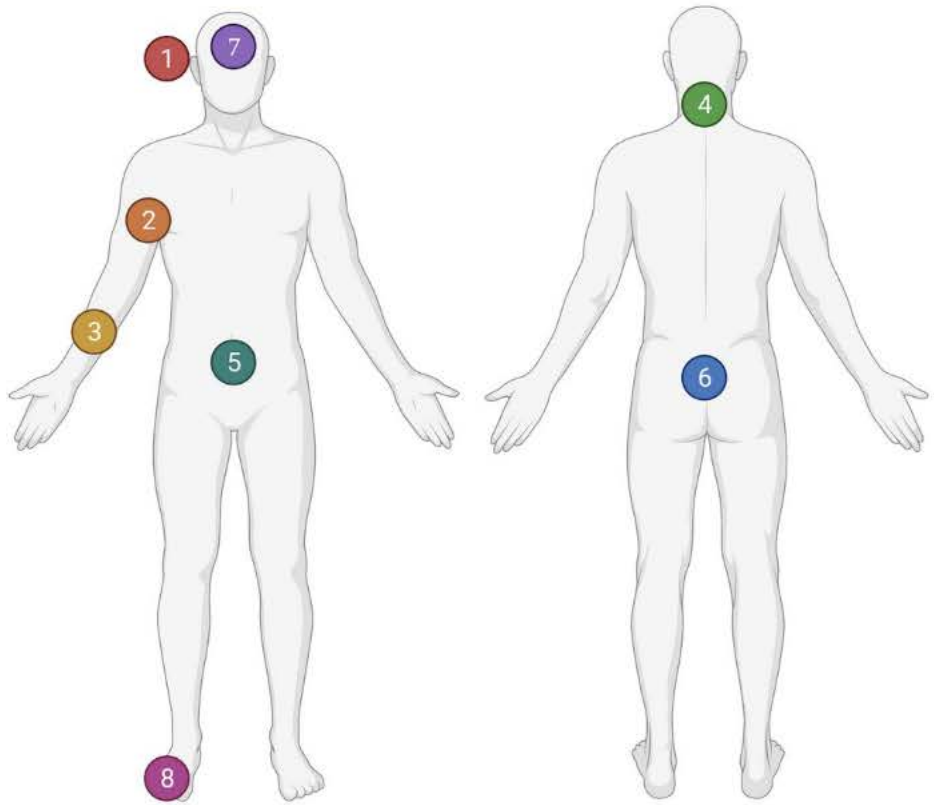
In space, even basic amenities are difficult.

https://www.space.com/inspiration4-spacex-toilet-trouble-in-space

A

Wet Swab Locations

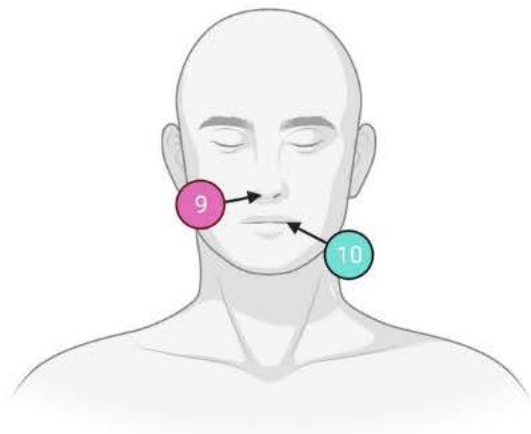
1. **Post-Auricular** Behind the Ear
2. **Axillary Vault** Armpit
3. **Volar Forearm** Underside of Forearm
4. **Occiput** Upper Back/Nape of Neck
5. **Umbilicus** Belly Button
6. **Gluteal Crease** Upper Crack
7. **Glabella** T-Zone
8. **Toe Web Space** Between the Toes



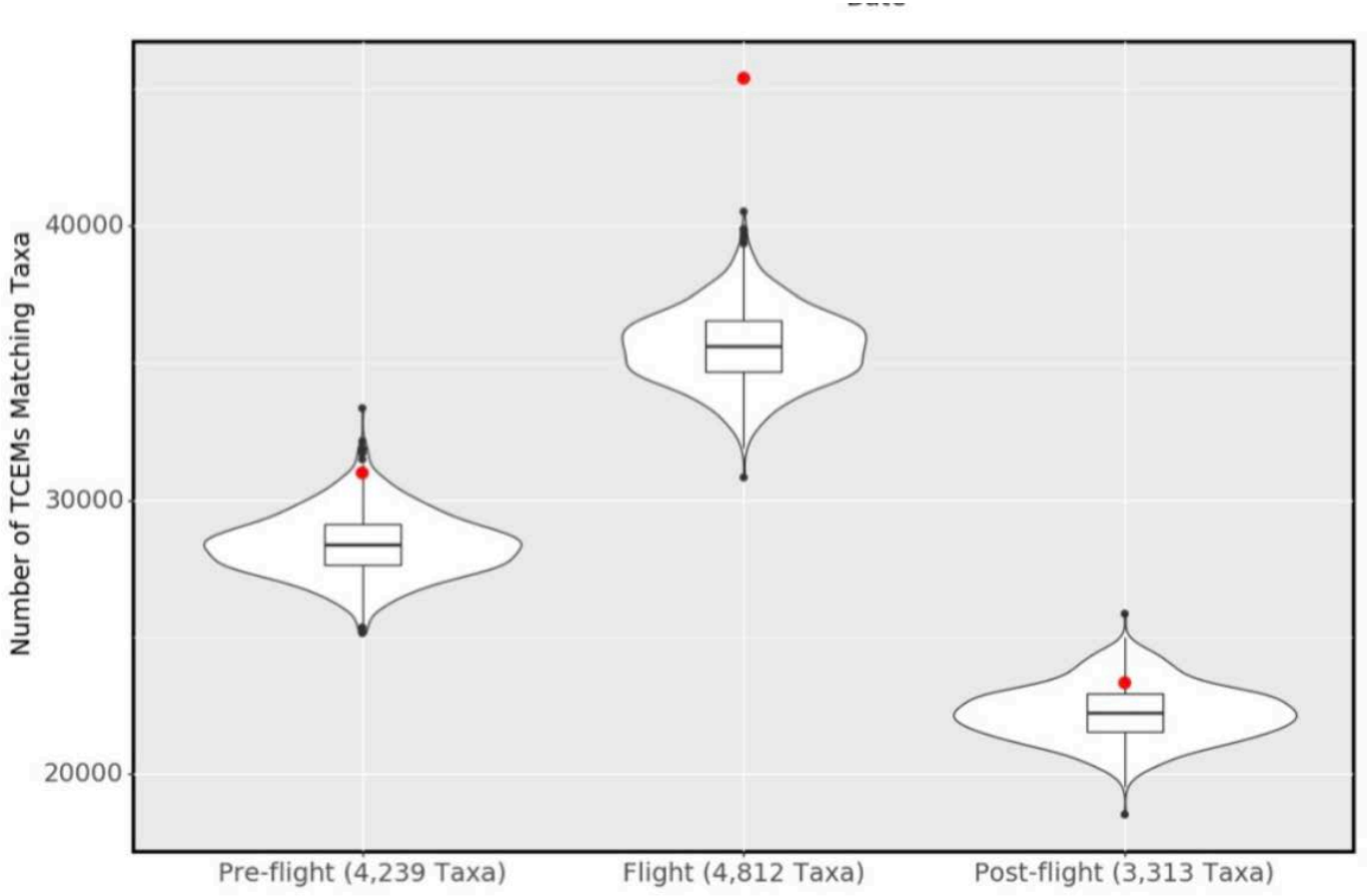
B

Dry Swab Locations

9. **Nasal Swab** Swab Lower Nasal Cavity
10. **Oral Swab** Swab Sides of Cheeks

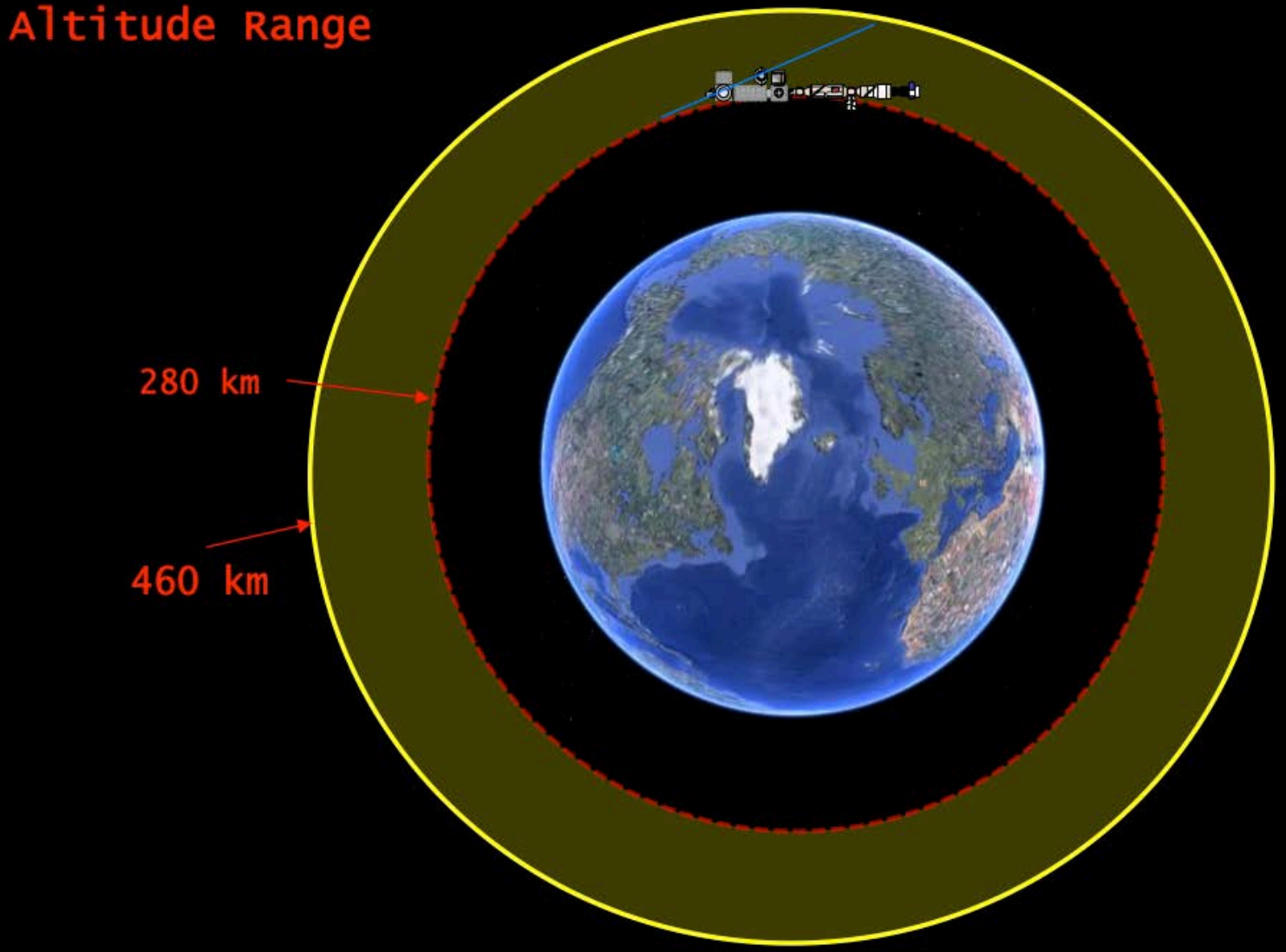


T-cells' Expressed Motifs (TCEMs) may respond to microbes inside the Dragon capsule, just like Scott Kelly's did to the walls of the ISS



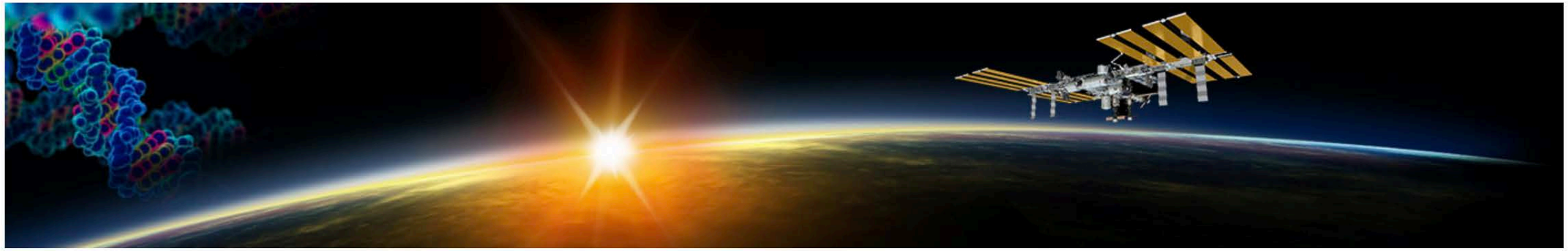
Danko et al., 2021
https://www.biorxiv.org/content/10.1101/2020.11.10.376954v2

Radiation impact of 575km vs. 400km



Up Next…

Compare to model organisms: GeneLab



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.

Data Repository
Search and upload spaceflight datasets

Analyze Data
Perform large-scale analysis of biological omics data

Environmental Data
Radiation data collected during experiments conducted in space

Collaborative Workspace
Share, organize and store files

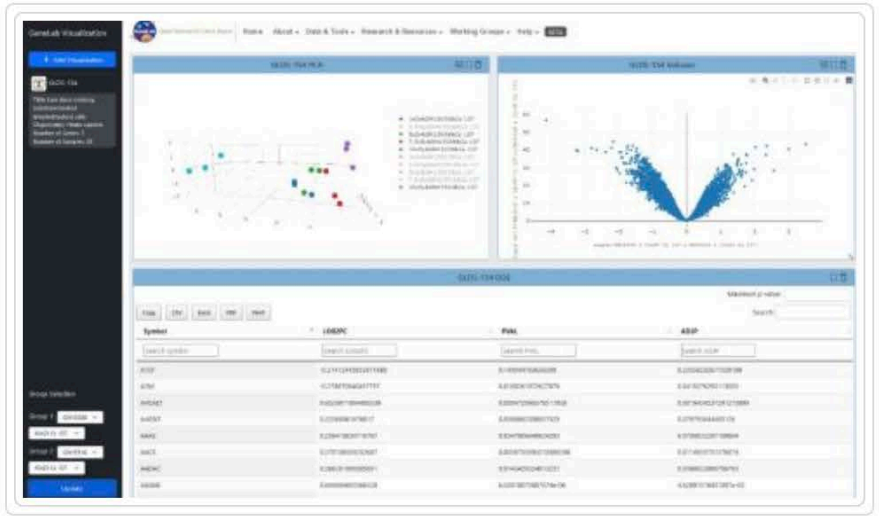
Submit Data
Have space-relevant data to submit to GeneLab?

Visualize Data
Interact with GeneLab processed data

https://genelab.nasa.gov/

New Visualization Portal is Here

GeneLab's latest software release includes a new visualization portal to interact with gene expression data from space-related omics experiments. The enhanced portal includes a new search interface, new plots and layout, and advanced settings to customize the plots.



The tools in this latest version include:

- **Gene Expression query table**
  - This table provides the normalized gene expression values for microarray datasets and normalized count values for RNA-seq datasets for each sample in the dataset.
- **Pair plot**
  - This plot allows a user to compare overall gene expression data between to two samples from that dataset.
- **Volcano plot**
  - This is a scatter plot that compares the significance (i.e. p-values) vs the log fold-change values for the genes. This plot allows for a quick view of the most significantly regulated genes for each dataset.
- **Heatmap**
  - This is a graphical representation of the individual samples displaying how the overall genes are up- and down-regulated across all samples in the dataset. Clustering of both the genes and the samples are also

This release also includes updates to the GeneLab Open API wrapper and an interactive user interface to parse metadata and data. The API wrapper was developed by Kirill Grigorev. To query the GeneLab database, click here.

Ax1 Mission - Feb 2022

Michael Lopez-Alegria
Ax1 Commander

Larry Connor
Ax1 Pilot

Eytan Stibbe
Ax1 Mission Specialist

Mark Pathy
Ax1 Mission Specialist

Axiom 2 Mission, then 3 & 4, maybe 5…

Axiom Space Ax-2 Commander Peggy Whitson and Pilot John Shoffner. (Download)

https://www.axiomspace.com/press-release/ax2

A 500-day mission in space; planned for 2025

Beginning a New Twin Study

We are now in the genomic era. Numerous changes were observed from NASA Astronaut Scott Kelly's comprehensive and molecular genetic data during his 340 consecutive days in space.[17] Ninety-one percent (91%) of the gene expression changes returned to normal within six months of returning to Earth. Yet, there was still a "molecular echo" from his time in space, wherein the cells in his body could be seen actively working to maintain DNA stability. Some genes were still disrupted in their expression while adapting to life back on Earth. Numerous indicators gave us a guide as to which genes may need to be accelerated, decelerated, or otherwise altered to help response to spaceflight in future astronauts. Limitations on our scientific progress towards the stars is no longer a matter of laboratory investigation and research. We need more samples, and that begins with additional sets of identical siblings. A second pathfinder twins study is the logical and essential next step.

Paradigm Shifts in Astronaut Monitoring and Countermeasures

A second Twins Study will begin a new era in monitoring and addressing real-time astronaut health conditions. There are groundbreaking improvements for inflight data and sample collection strategies (while in orbit). We have the technology to perform continual genetic-based monitoring of twins at the

Below: Identical twins, Drs. Brad (left) and Brent West (right).

https://www.newscientist.com/round-up/mars500/

Thanks to Funding from:

BILL & MELINDA GATES foundation

ALFRED P. SLOAN FOUNDATION 1934

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STARR CANCER CONSORTIUM

genome.gov National Human Genome Research Institute National Institutes of Health

Weill Cornell Medical College Clinical & Translational Science Center

National Institute of Neurological Disorders and Stroke National Institutes of Health

NIH NATIONAL CANCER INSTITUTE

Deep Gratitude to Many People:

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Yared Bayleyen
Chandrima Bhattacharya
Daniel Butler
Chris Chin
Rafael Colon
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Ceyda Durmaz
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Deena Najjar
Eliah Overbey
Jiwoon Park
Krista Ryon
Maria Sierra
Braden Tierney
Delia Tomoiaga
Craig Westover

Cornell/WCM
Alain Borczuk
David Erickson
Selina Chen-Kiang
Iwijn De Vlaminck
Olivier Elemento
Samie Jaffrey
Iman Hajirasouliha
Marcin Imielinksi
Ari Melnick (Melnick Lab)
Margaret Ross
Rob Schwartz

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Elizabeth Hénaff

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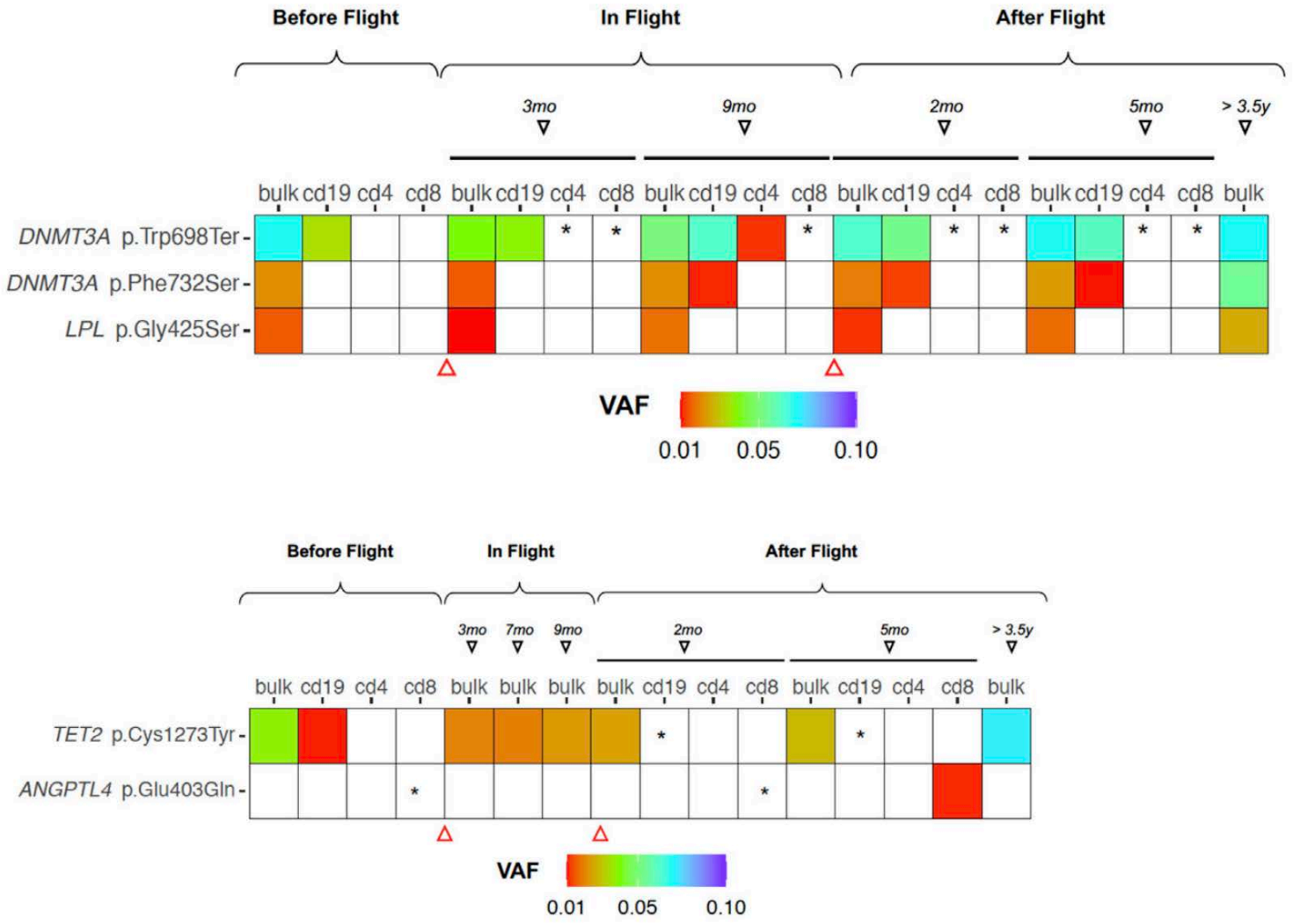
MIT Media Lab
Kevin Slavin
Devora Najjar

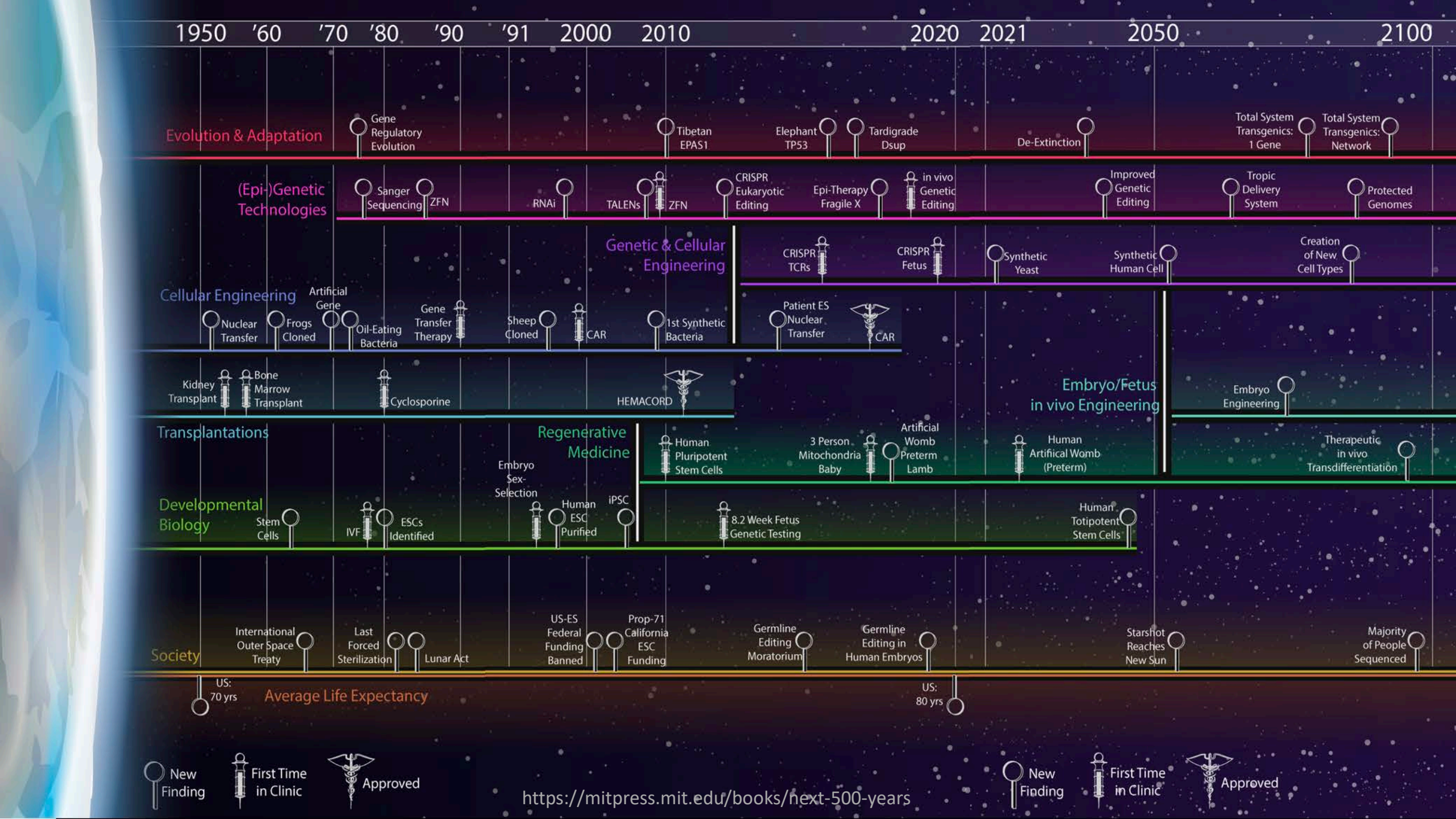
FDA/SEQC/Fudan.
Leming Shi

ABRF/Vermont
Scott Tighe
Don Baldwin

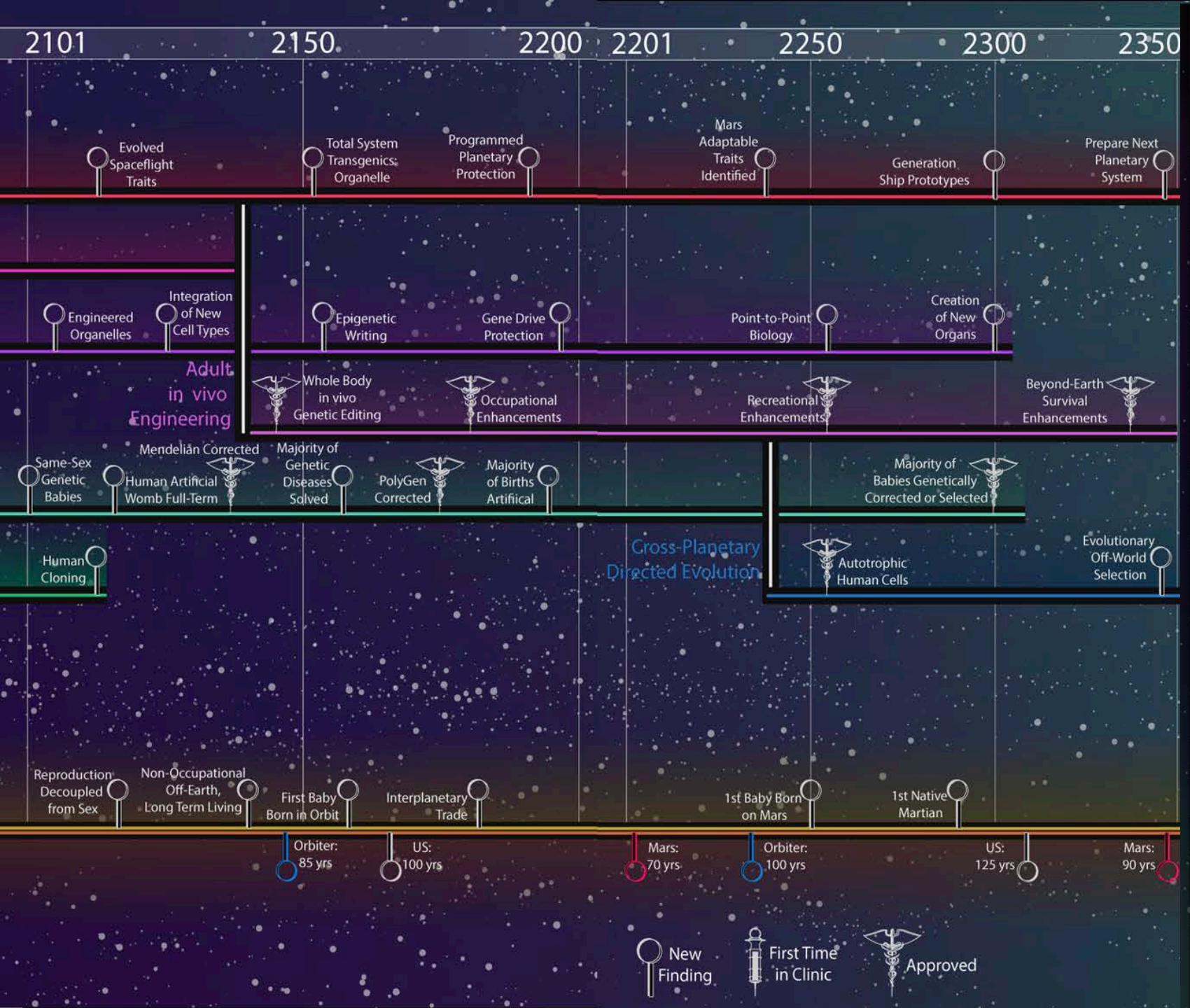
Kennedy Space Center, Florida

Found in most cell types





https://mitpress.mit.edu/books/next-500-years


2101
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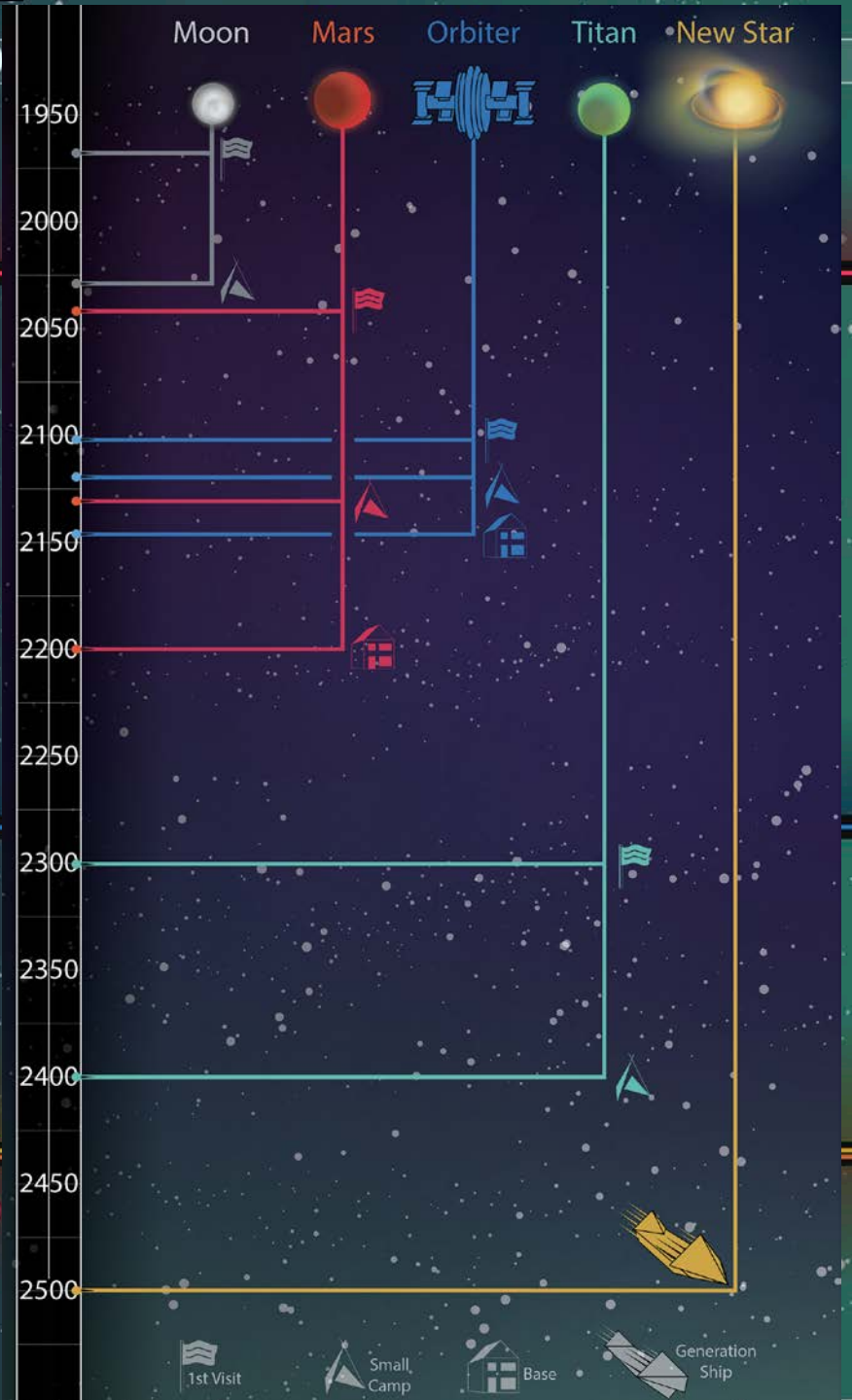
Evolved Spaceflight Traits
Total System Transgenics; Organelle
Programmed Planetary Protection
Mars Adaptable Traits Identified
Generation Ship Prototypes
Prepare Next Planetary System
Engineered Organelles
Integration of New Cell Types
Epigenetic Writing
Gene Drive Protection
Point-to-Point Biology
Creation of New Organs
Adult in vivo Engineering
Whole Body in vivo Genetic Editing
Occupational Enhancements
Recreational Enhancements
Beyond-Earth Survival Enhancements
Same-Sex Genetic Babies
Mendelian Corrected
Human Artificial Womb Full-Term
Majority of Genetic Diseases Solved
PolyGen Corrected
Majority of Births Artifiical
Majority of Babies Genetically Corrected or Selected
Human Cloning
Cross-Planetary Directed Evolution
Autotrophic Human Cells
Evolutionary Off-World Selection
Reproduction Decoupled from Sex
Non-Occupational Off-Earth, Long Term Living
First Baby Born in Orbit
Interplanetary Trade
1st Baby Born on Mars
1st Native Martian
Orbiter: 85 yrs
US: 100 yrs
Mars: 70 yrs
Orbiter: 100 yrs
US: 125 yrs
Mars: 90 yrs
New Finding
First Time in Clinic
Approved


Moon
Mars
Orbiter
Titan
New Star
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2250
2300
2350
2400
2450
2500
1st Visit
Small Camp
Base
Generation Ship