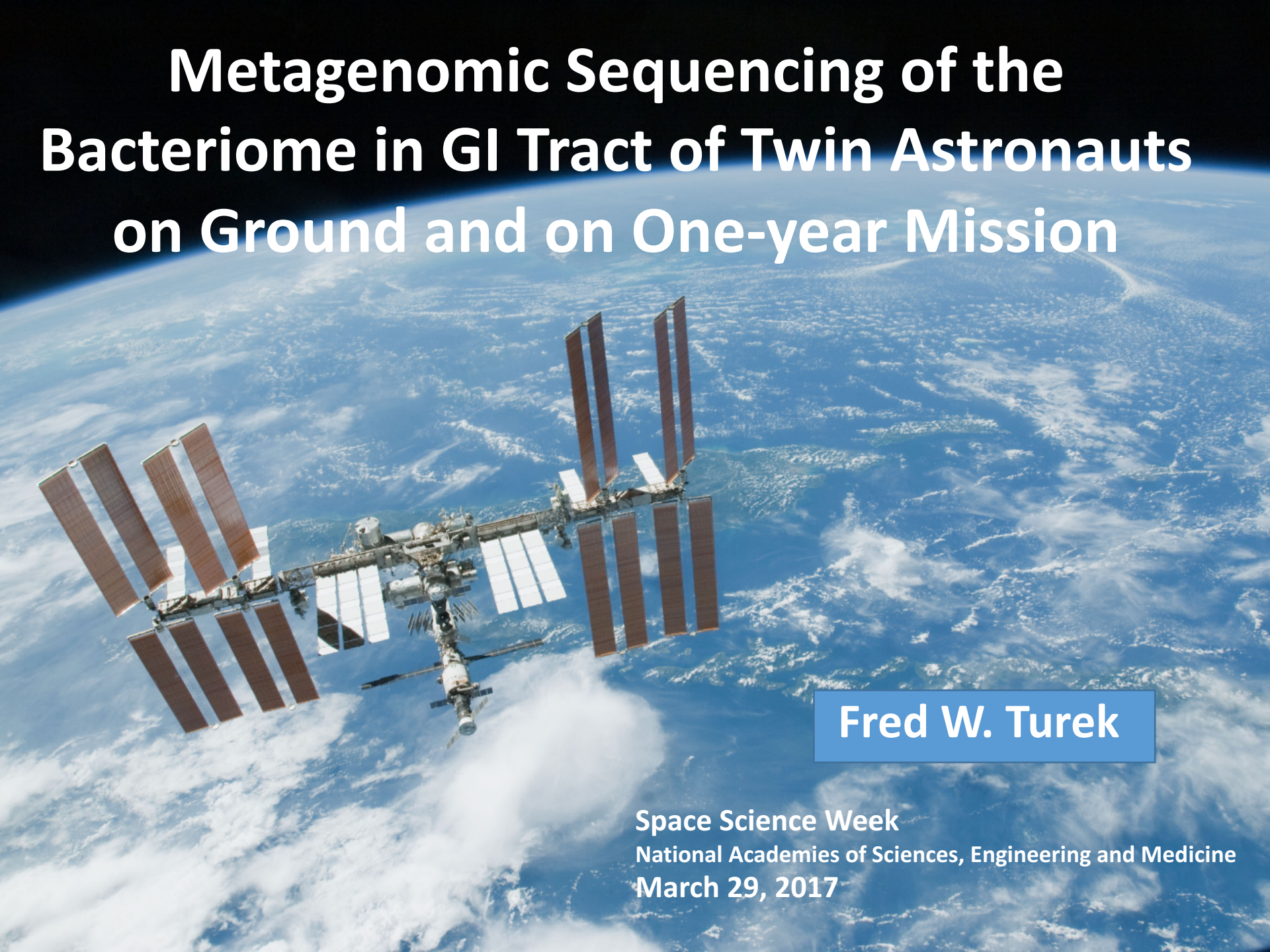
# Metagenomic Sequencing of the Bacteriome in GI Tract of Twin Astronauts on Ground and on One-year Mission



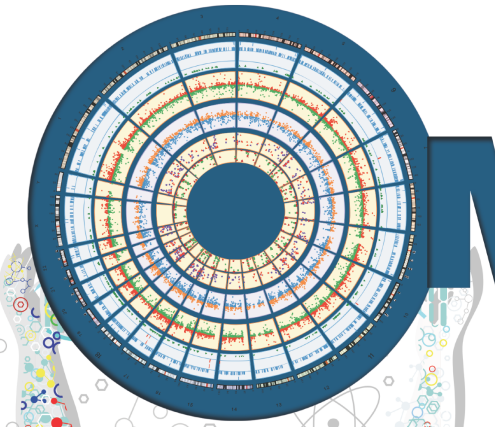
**Fred W. Turek**

**Space Science Week**
**National Academies of Sciences, Engineering and Medicine**
**March 29, 2017**

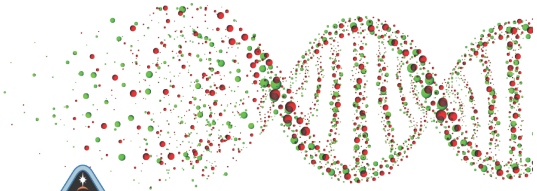
# THE TWINS STUDY




# INVESTIGATORS



# OMICS



## Exploring Space Through You

### VOCABULARY

1. _____ OMICS
2. _____ GENOMICS
3. _____ TRANSCRIPTOMICS
4. _____ PROTEOMICS
5. _____ EPIGENOMICS
6. _____ METABOLOMICS
7. _____ MICROBIOMICS

a. The study of the genetic ecosystem in our body including bacteria, viruses, fungi, etc. that keep our body healthy or give our body disease

b. The study of the complete set of DNA within a single cell of an organism

c. The study of all RNA that was produced from a genome

d. The study of all proteins in an organism that enables scientists to find and target disease within that organism

e. An integrative field of study that helps scientists determine what each part of someone's genetic instruction does, how it relates to the other parts, and how each part is expressed

f. The study of the chemical processes that happen in a cell, tissue, organ, or organism to help maintain life and help stop disease by monitoring those processes

g. The study of how an organism's environment influences changes in the expression of the gene without changing the actual DNA sequence

Journey into the vastness of the human body and explore the endless possibilities of omics on Earth and in space. Omics integrates fields of study of biomolecules allowing researchers to investigate and see more than ever before. On the front of this poster is a depiction of the interrelation of Earth, humans and space. The graph surrounding Earth shows a genomic circular visualization used by scientists to analyze data representative of human biomolecules. Biomolecules are shown flowing through an astronaut to demonstrate the makeup of the human body. The unwinding DNA within the chromosome represents the journey from Earth to Mars and deep space and is analogous to the dual missions of protecting astronaut health to ensure a successful journey to Mars and beyond. The NASA Twins Study enables researchers to compare identical twin DNA to discover molecular changes within the human body. Join us on this exciting adventure at www.nasa.gov/hrp.

NW-2016-12-019-JSC

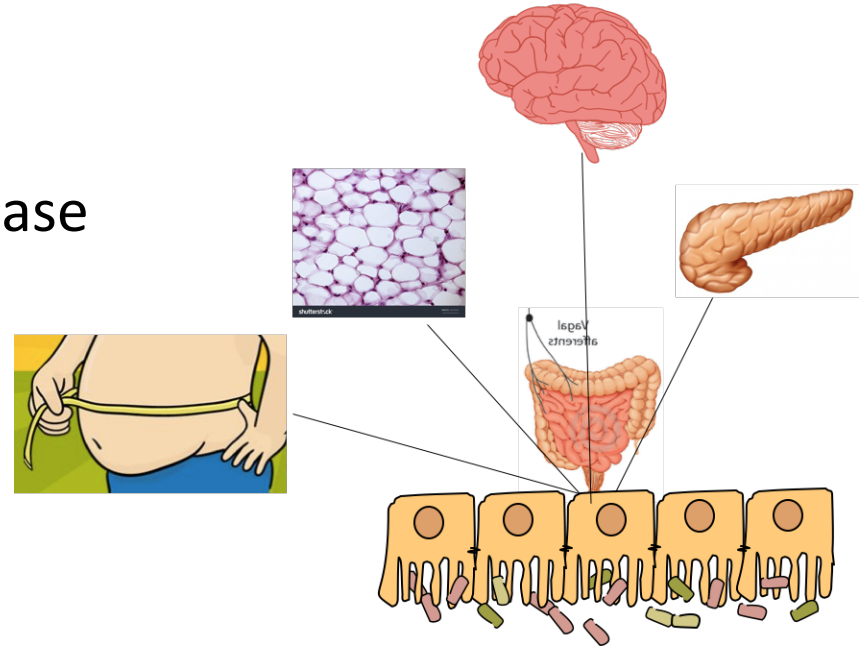
http://www.nasa.gov/content/exploring-space-through-you-omics | http://www.nasa.gov/twins-study | http://www.nasa.gov/hrp

Acknowledgement: Alex Munoz, NASA Intern, vocabulary quiz

ANSWERS: a. Microbiomics, b. genomics, c. transcriptomics, d. proteomics, e. omics, f. metabolomics, g. epigenomics

# The Microbiome and Health

- Disruption in the microbiota (dysbiosis) has been associated with:
  - Obesity
  - Type 2 Diabetes
  - Inflammatory Bowel Disease
  - Stress
  - Depression and Anxiety
  - Autism
  - Parkinson's



# Background: The Gut Microbiota

- Latest Estimate:

  38 trillion microbial cells vs.
  30 trillion human cells

  (Sender et al. 2016)

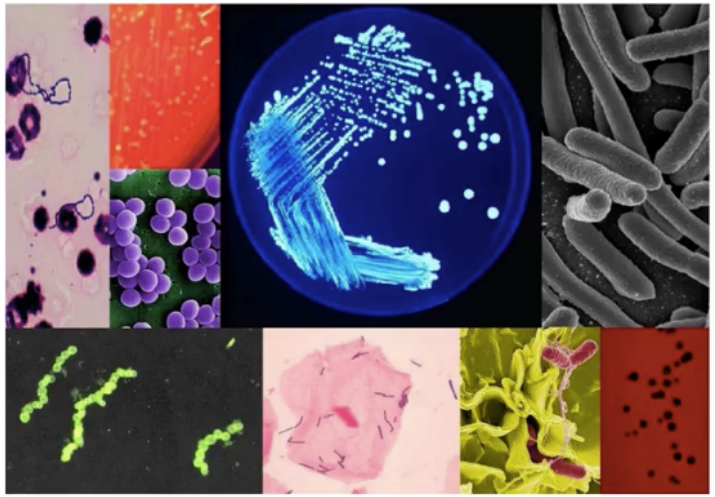


Photo credit: PeskyPlummer, Creative Commons License

~$3.8 \cdot 10^{13}$ Bacterial Cells
(~0.2 kg)

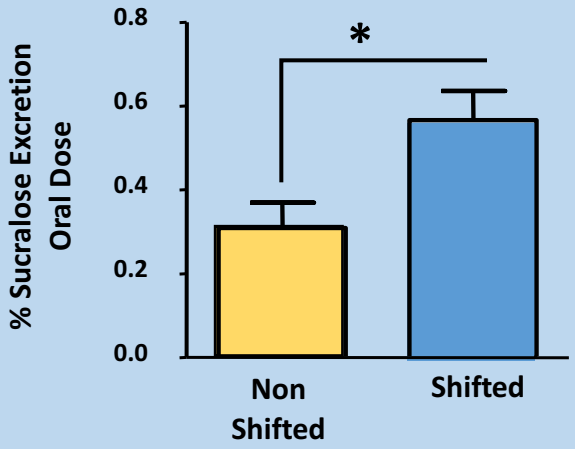
vs

~$3.0 \cdot 10^{13}$ Human Cells
(~70 kg)

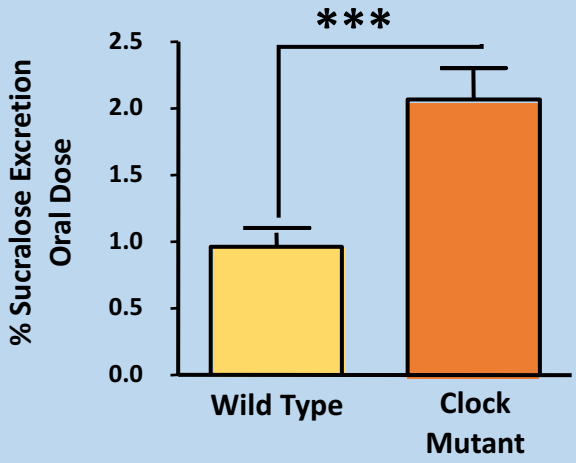
**Source: Sender et al. 2016. PLOS BIOLOGY.**

# Gut Leakiness

**Environmental Disruption**

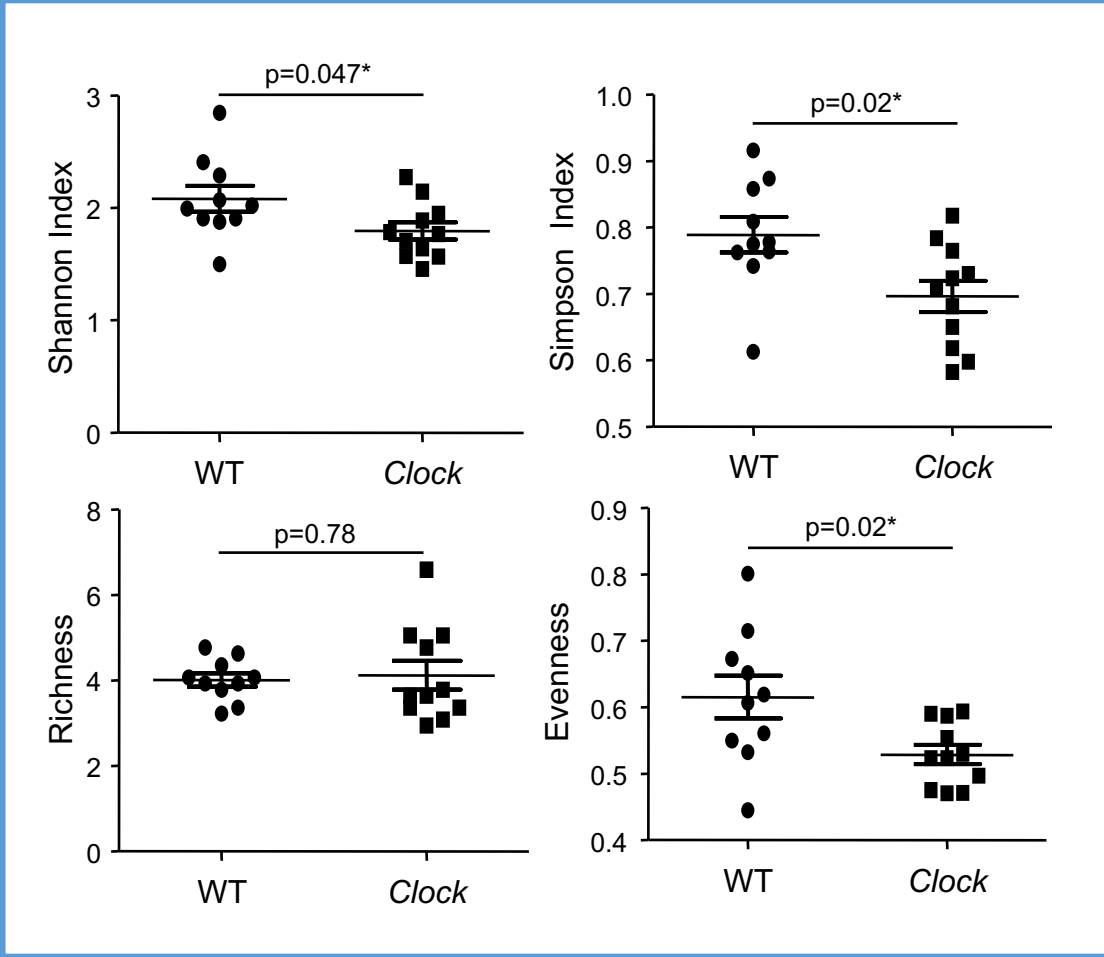



**Genetic Disruption**



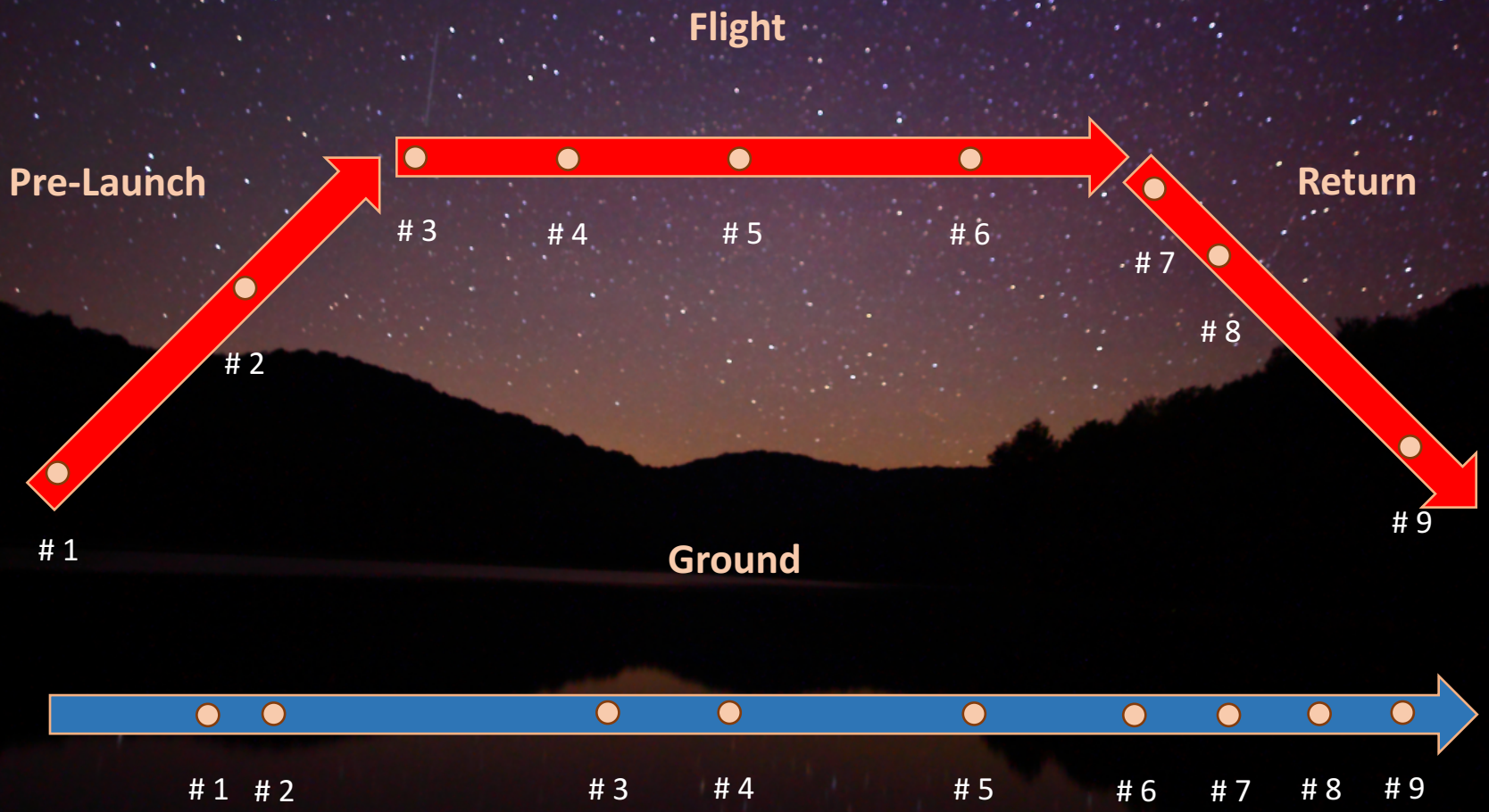

Environmental and genetic circadian rhythm disruption increases gut permeability in response to chronic alcohol

# *Clock*$^{\Delta 19}$ reduces microbiome diversity and evenness

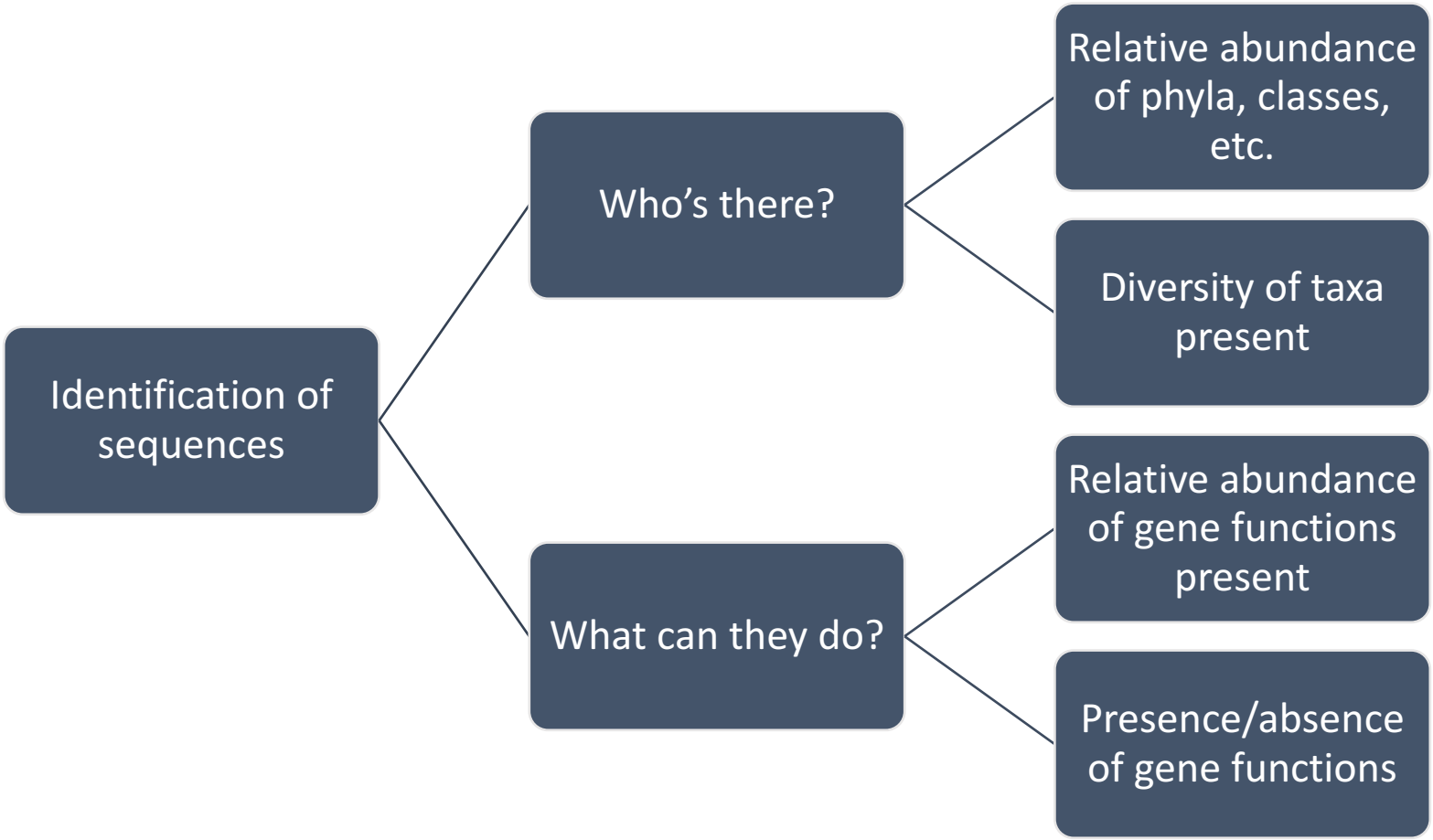



Voigt, Summa, Forsyth, Green, Engen, Naqib, Vitaterna, Turek, Keshavarzian *In Press,* ACER

# Sampling Before, During & After One Year in Space or On Ground

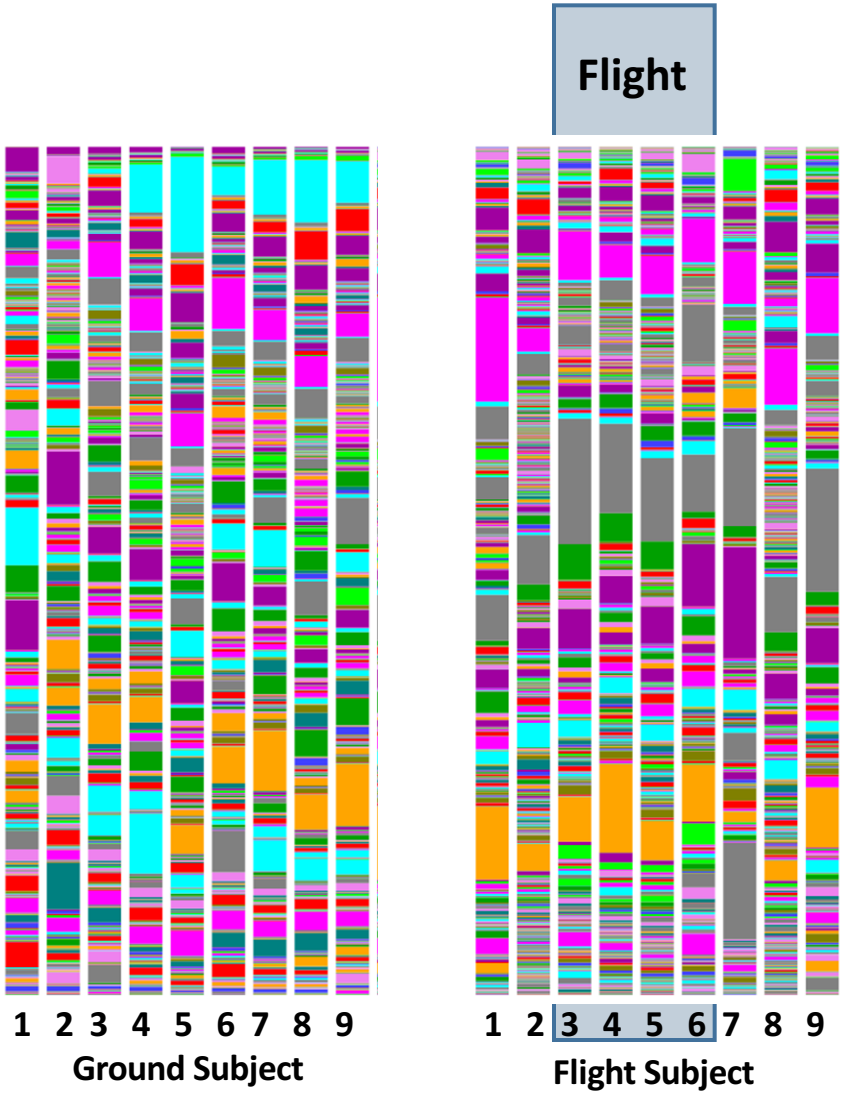


# Analysis of Metagenomic Sequence Data



## *Who is there?*

High taxonomic diversity of microorganisms present in both twins.

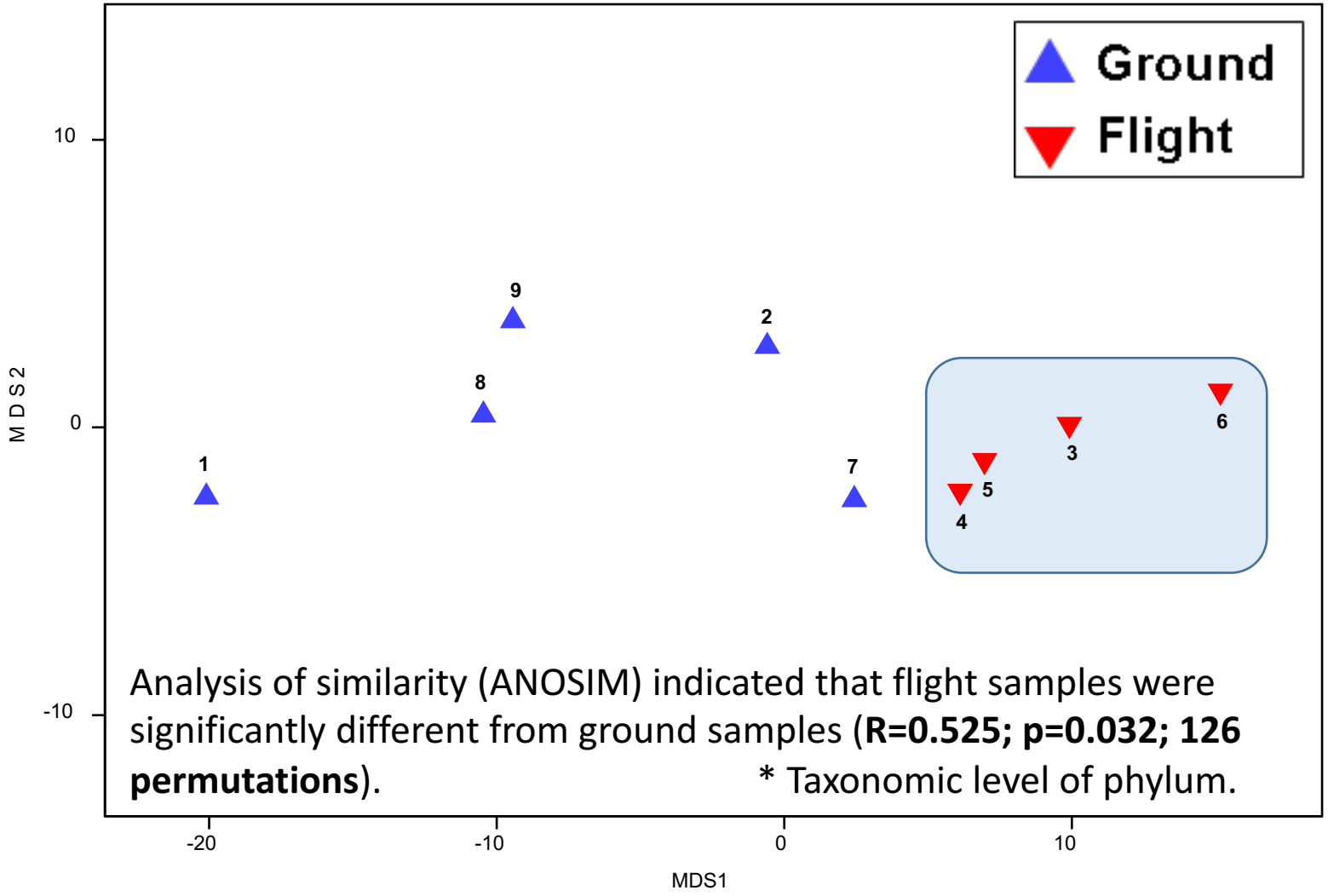



At the taxonomic level of "species" –

>7,000 Bacteria
>300 Archaea
>150 Fungi
>200 Viruses

- **No significant diversity differences between subjects.**
- **No significant diversity differences between flight and ground samples in the flight subject.**
- **Communities of two subjects are always significantly different**

# Taxonomic Composition of Flight Samples is Significantly Different From Ground Samples in Flight Subject*

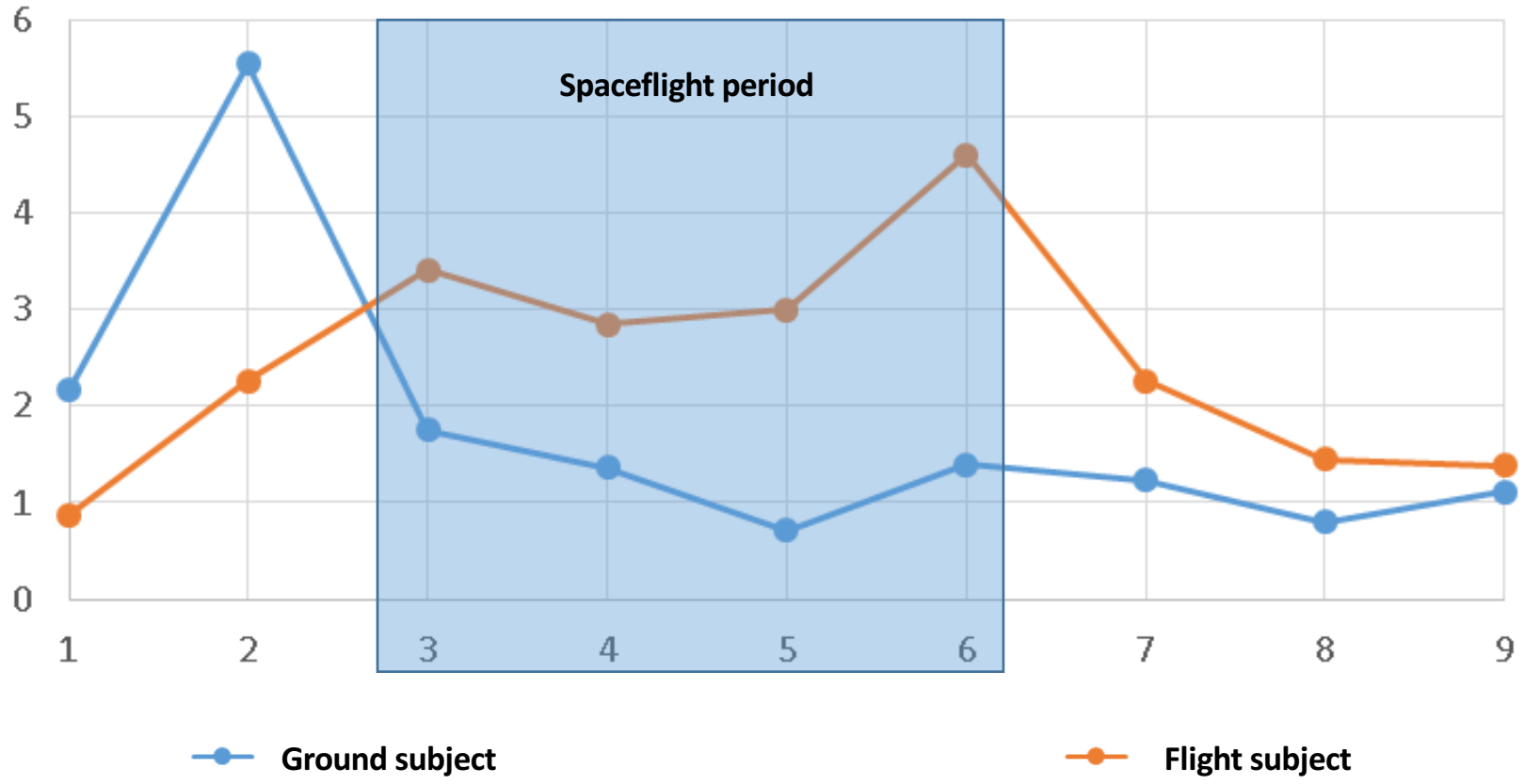



Analysis of similarity (ANOSIM) indicated that flight samples were significantly different from ground samples (**R=0.525; p=0.032; 126 permutations**).

* Taxonomic level of phylum.

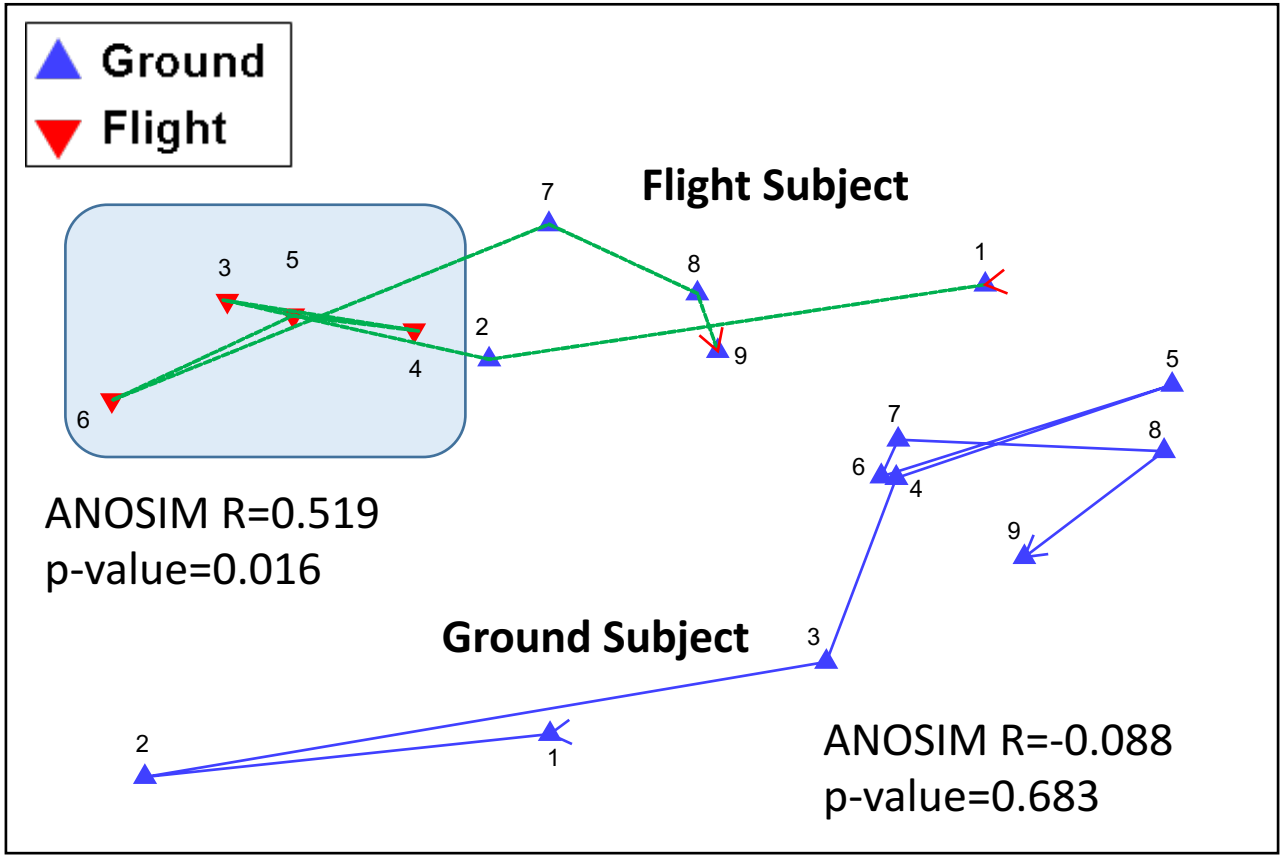
# Change in Firmicutes-Bacteroidetes Ratio

Firmicutes and Bacteroidetes are the two dominant phyla of bacteria in the human GI tract.



*What can they do?*

# Gene Function of Flight Samples is Significantly Different From Ground Samples In Flight Subject




Ordination (nMDS) plot: Similarity of gene pathway content between samples

# Changes in Microbial Gene Functions Content Correlated* with Flight in Flight Subject

- Categories ***Increased*** during Spaceflight
  - Stress Response
  - Iron acquisition and metabolism
  - Central Metabolism
  - DNA Metabolism
  - Phosphorus Metabolism
  - Cell Division and Cell Cycle
  - Protein Metabolism
  - Fatty Acids, Lipids, Isoprenoids
  - Cofactors, Vitamins, Prosthetic Groups, Pigments
  - Phages, Prophages, Transposable elements
  - Dormancy and Sporulation
- Categories ***Decreased*** during Spaceflight
  - Phages, Prophages, Transposable Elements, Plasmids
  - Carbohydrates
  - Secondary Metabolism
  - Membrane Transport
  - Virulence
  - Sulfur Metabolism
  - Cell Wall and Capsule
  - Photosynthesis

*Pearson's correlation coefficient $\geq 0.9$

# Summary

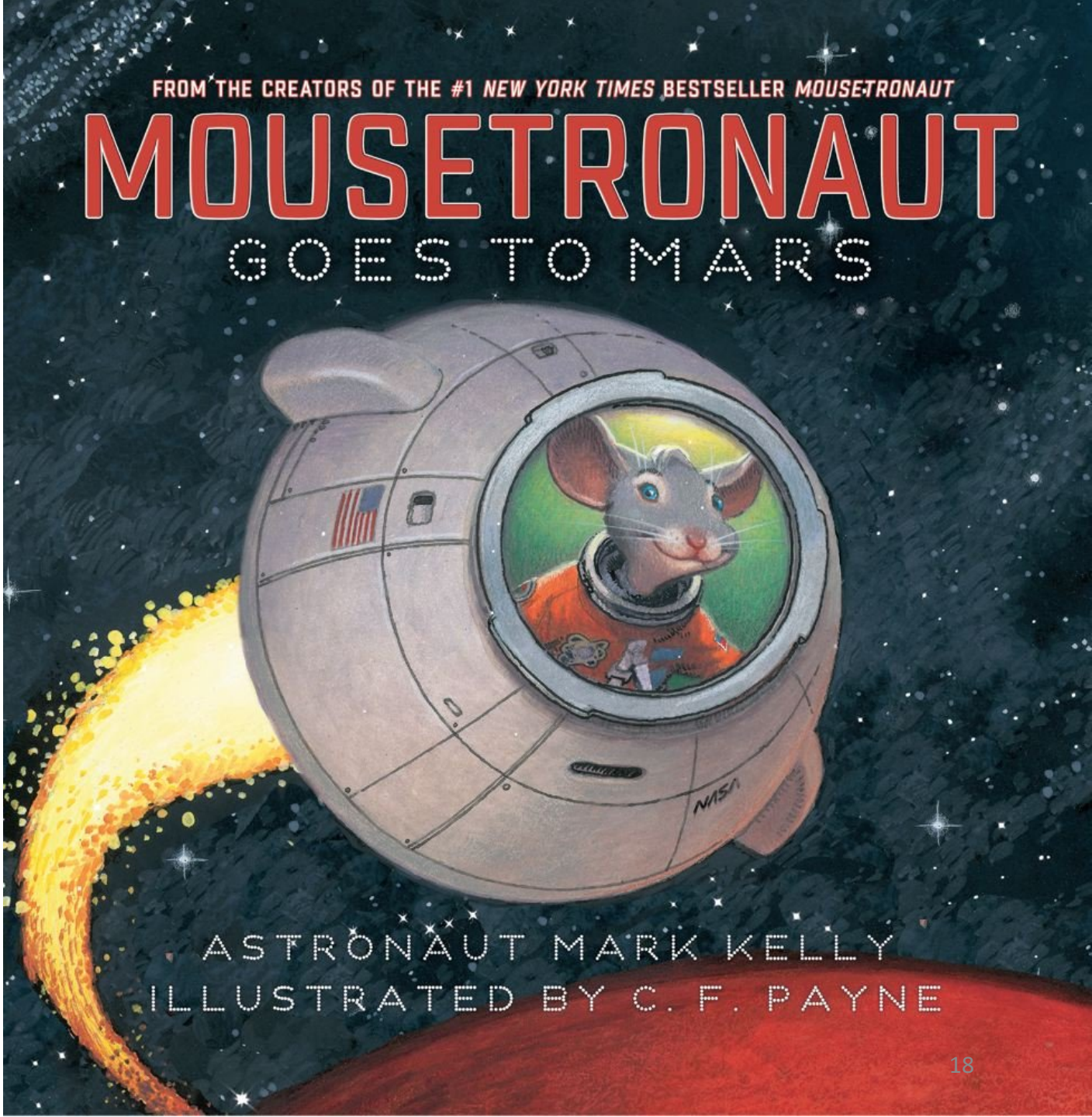
- Both subjects had highly diverse GI microbiota at all sample times – high diversity associated with good health.
- For the bacteriome, virome, (and fungal mycobiome), differences between the two subjects were pronounced at all time points.
- Within the FLIGHT subject, differences in taxonomic composition and functional gene composition were observed between flight and ground samples.
- Spaceflight-associated microbiota changes did not appear to persist post-return (i.e., effects not permanent).

# Conclusions

- Spaceflight-associated changes in GI microbiota composition and functional gene composition were observed.
- However, it is not clear what the changes in gut microbes associated with spaceflight mean.
- Further study is needed to determine what countermeasures should be utilized to protect astronaut health for long-term spaceflight.

**Newly selected Project:**

"Effects of Spaceflight on Gastrointestinal Microbiota in Mice: Mechanisms and Impact on Multi-System Physiology"



# TAKING FLIGHT ON SPACEX-15

## APRIL 2018

## KENNEDY SPACE CENTER