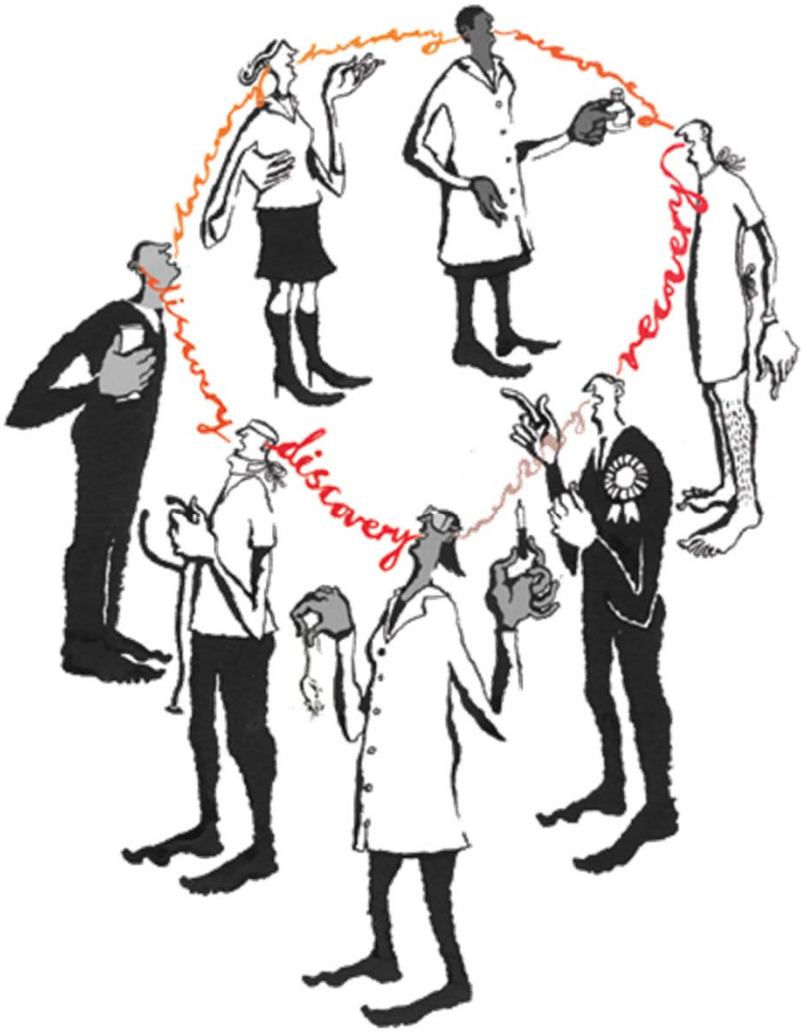
Space Research in the Age of Translational Science

Jim Pawelczyk, PhD

PennState



Nature 453:840, 2008

Who am I?

- a biologist who conducts preclinical and clinical research
- a former astronaut
- I train clinical and translational scientists
- I review a lot of NASA life sciences programs

Disclaimers:

- All views expressed are my own.
- I serve on the HEO Research Subcommittee to the NAC, the LMS Mid-term decadal, and the NAM's Review of NASA Evidence Books.
- I have plenty of biases, and no financial conflicts of interest.

http://belveal.net/

Outline

- Law of unintended consequences
- Framing the challenge
- What is translational science?
- Translational research needs for the future of human spaceflight
- Inferring NASA success as a translational science entity

Outline

- **Law of unintended consequences**
  - **An example from Neurolab (STS-90)**
- **Framing the challenge**
- **What is translational science?**
- **Translational research needs for the future of human spaceflight**
- **Inferring NASA success as a translational science entity**

Unique electrophysiological experiments on STS-90

Hippocampal place cells/3-D place field mapping

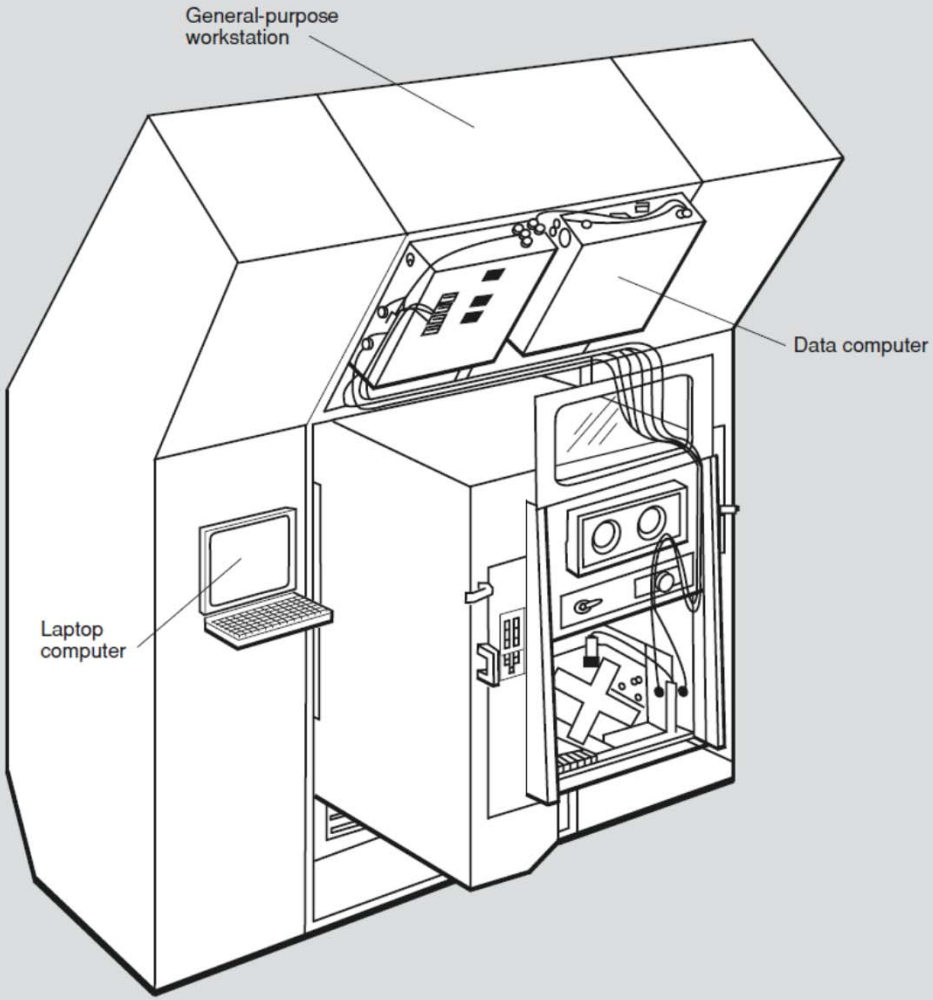
PI Bruce McNaughton, University of Arizona

Co-I's and Collaborators

- Jim Knierim
- Gina Poe
- Casey Stengel

McNaughton Lab
c. 1997

Extraordinary R&D …



Neurolab SP-2003-535, NASA

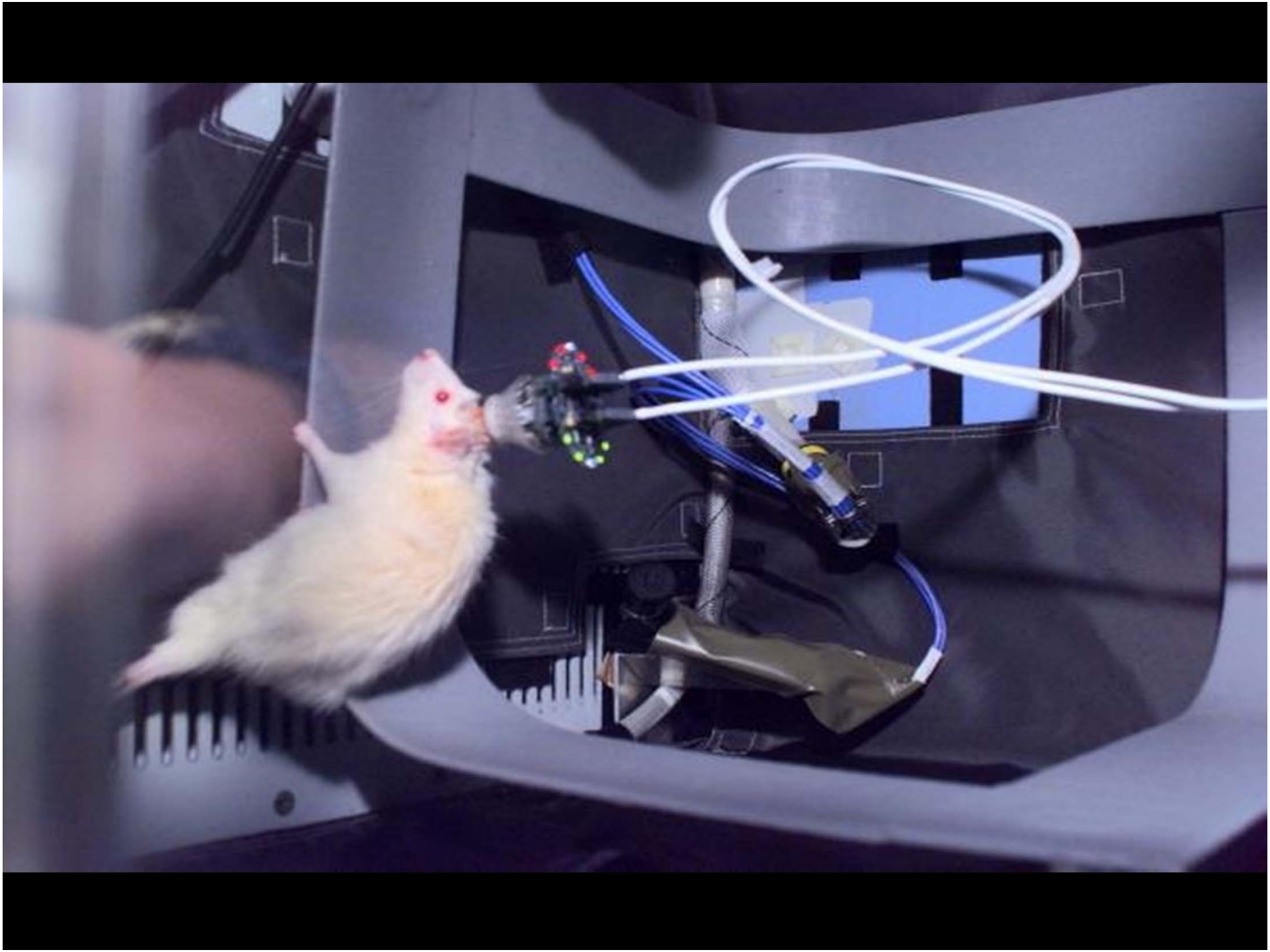
… and unique operational challenges

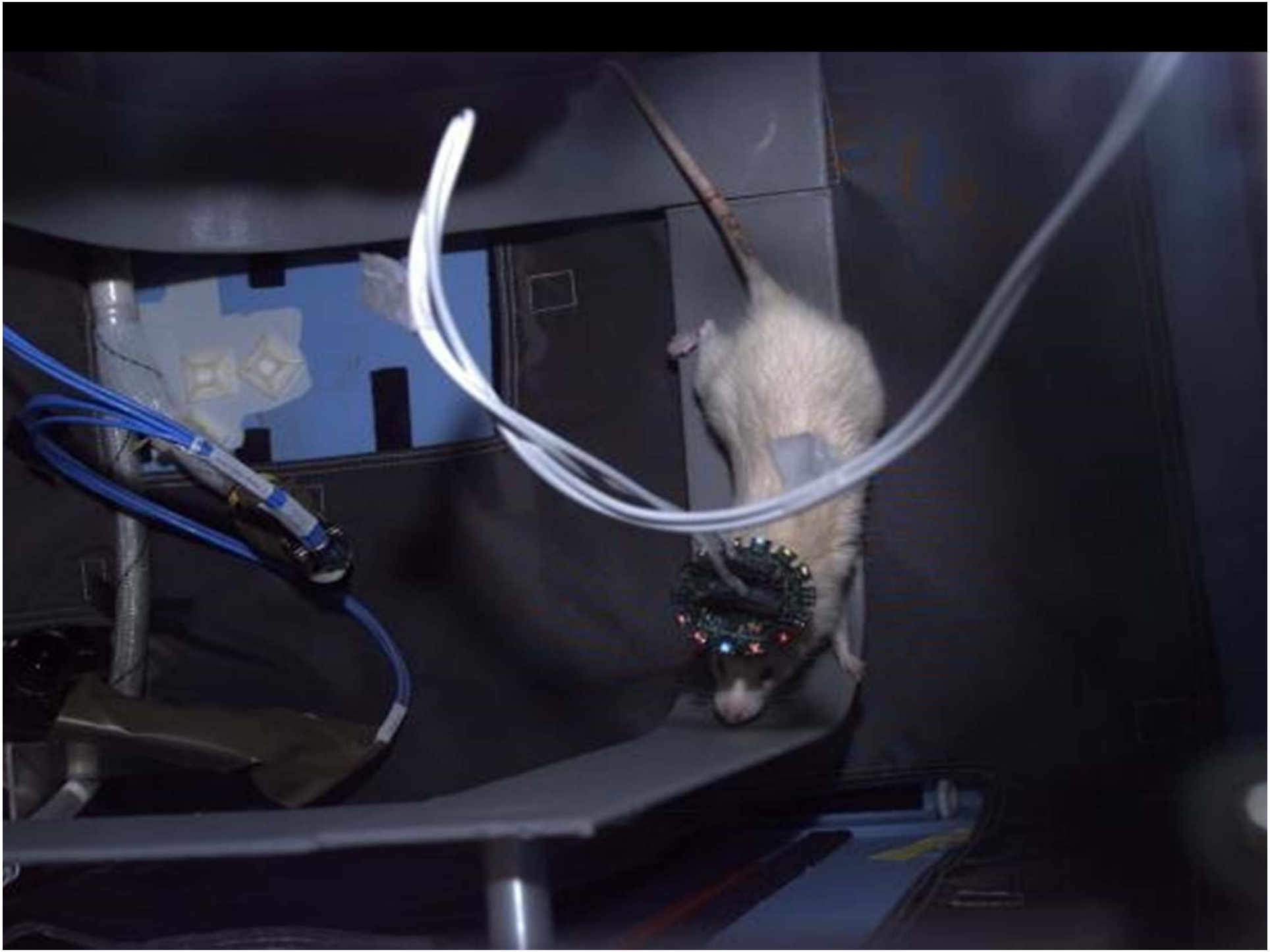
Jay Buckey, MD

Kay Hire

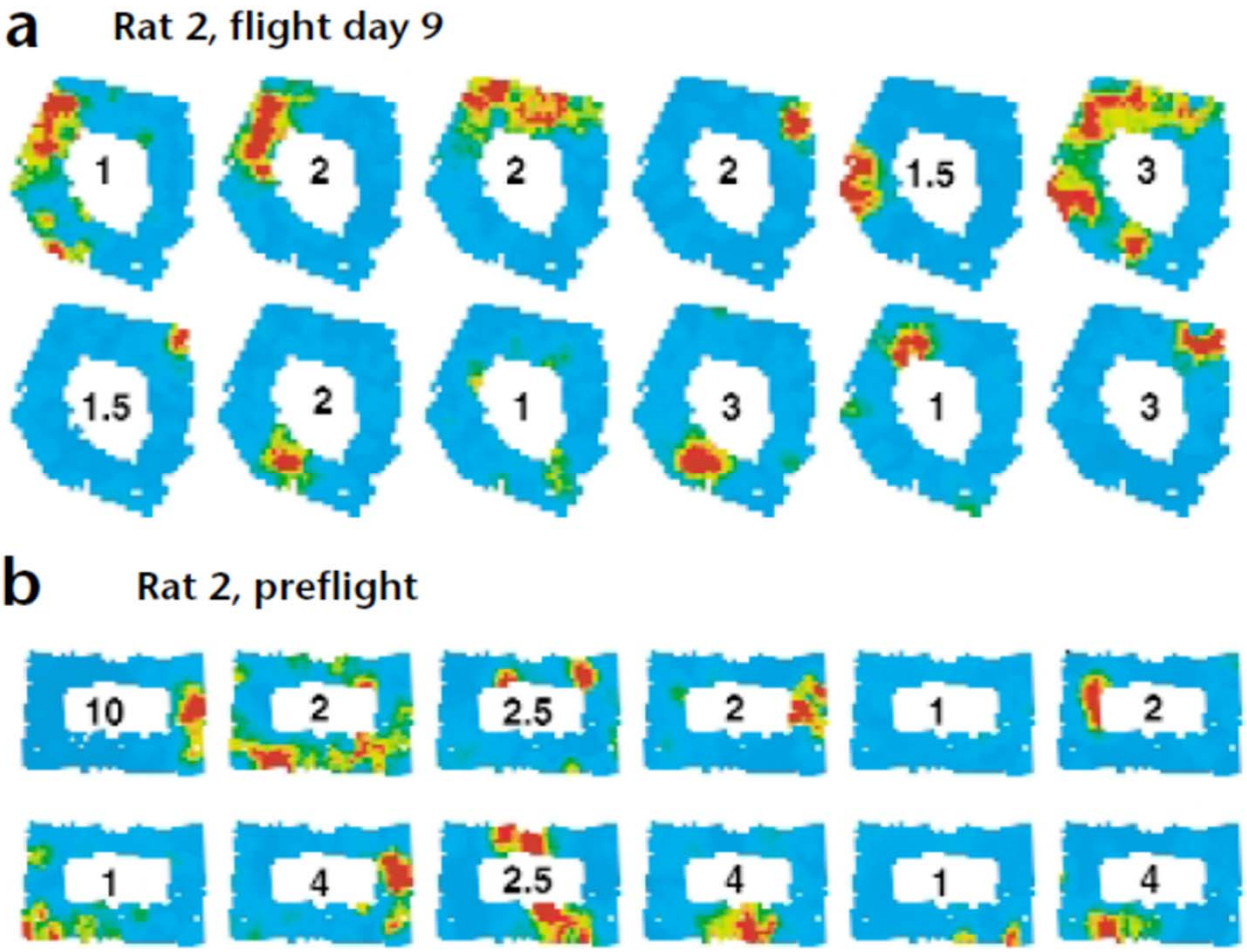
Dave Williams, MD

Jim Pawelczyk, PhD



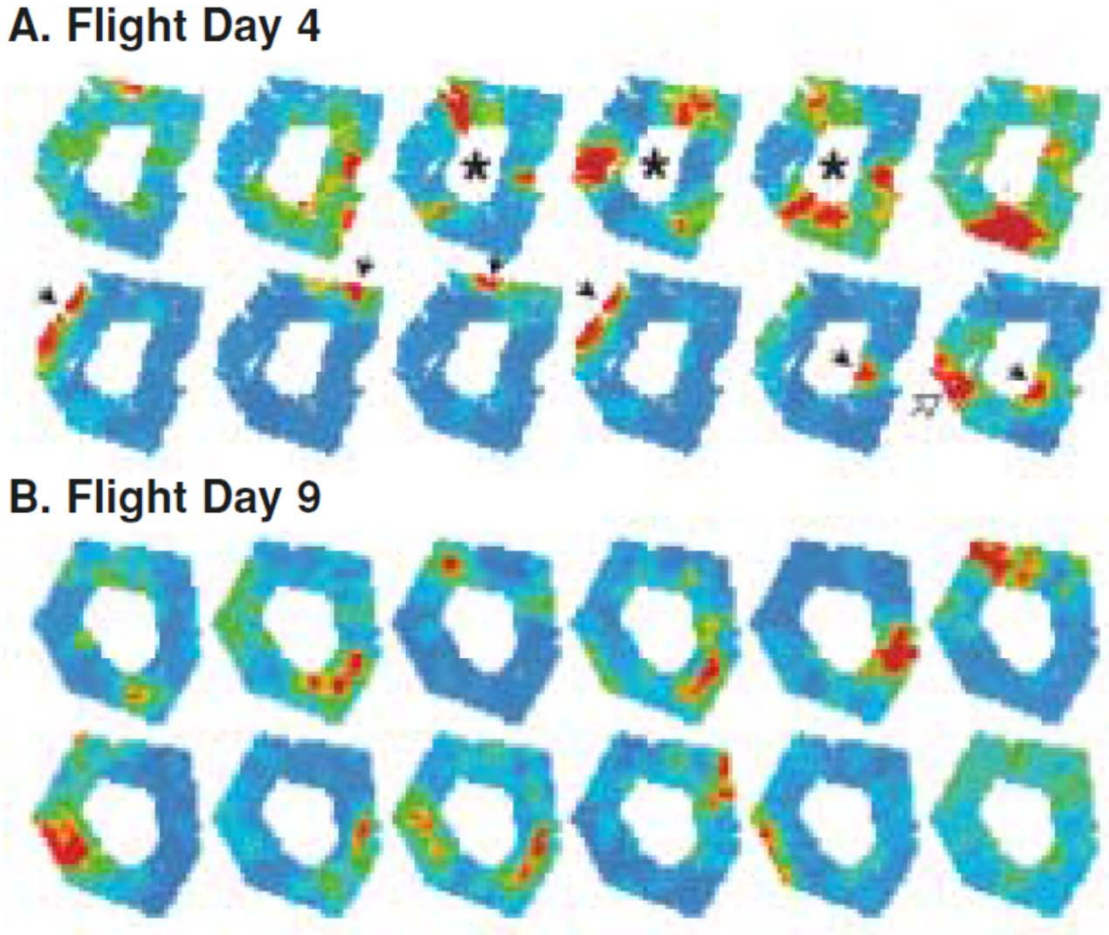


Normal place cell firing



Knierim, McNaughton, Poe. *Nature Neurosci*, 3:211, 2000.

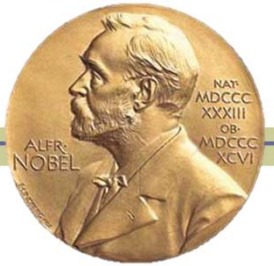
Abnormal place cell firing



29 citations to date

Knierim, McNaughton, Poe. *Nature Neurosci*, 3:211, 2000.

and facilitating a Nobel Prize



NeuraLynx

The Complete Solution for Electrophysiology Research

Company Products Software Support

Longtime Neuralynx Customers

May-Britt Moser &
Edvard I. Moser

along with their colleague
John O'Keefe

Awarded 2014 Nobel Prize in Medicine
for Discovery of the Brain's Global Positioning System

Congratulations,
May-Britt and Edvard,
from Neuralynx!

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It’s (still) OK to say, “Mars”

TITLE IV—Advancing human deep space exploration

subtitle A—Human space flight and exploration goals and objectives

SEC. 412. Key objectives.

Section 202(b) of the National Aeronautics and Space Administration Authorization Act of 2010 (42 U.S.C. 18312(b)) is amended (to add the following):

…

“(5) to achieve human exploration of Mars and beyond through the prioritization of those technologies and capabilities best suited for such a mission in accordance with the stepping stone approach to exploration under section 70504 of title 51, United States Code.”

One Hundred Fifteenth Congress
of the
United States of America

AT THE FIRST SESSION

Begun and held at the City of Washington on Tuesday, the third day of January, two thousand and seventeen

An Act

To authorize the programs of the National Aeronautics and Space Administration, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the “National Aeronautics and Space Administration Transition Authorization Act of 2017”.

(b) TABLE OF CONTENTS.—The table of contents of this Act is as follows:

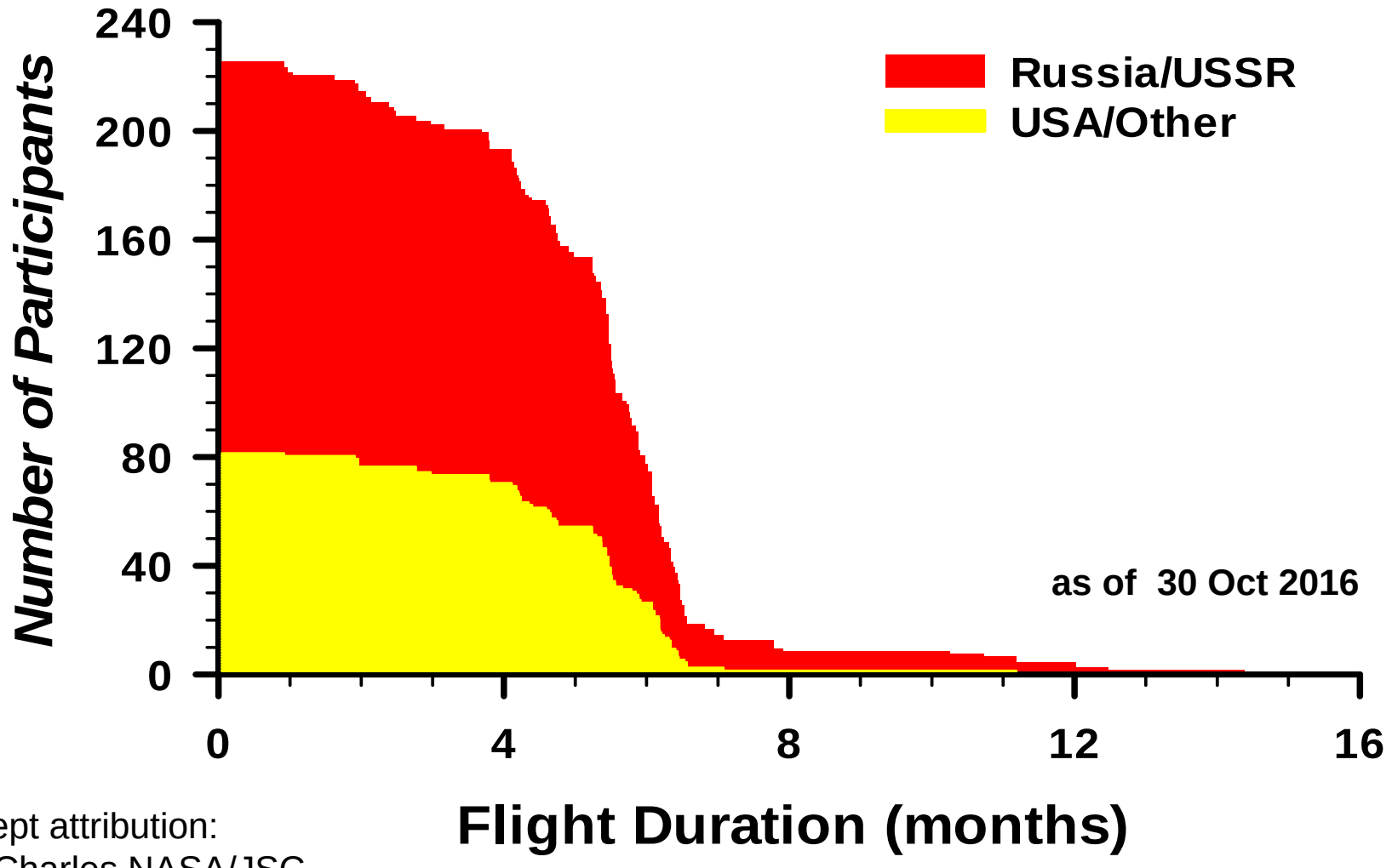
54 Years After Yuri Gagarin First Orbited the Earth …

we have rarely ventured far from Earth,

and never for very long.

Jeff Smith NASA/ARC

Summary of human long-duration spaceflight



Concept attribution:
John Charles NASA/JSC

Unique Stressors to Humans in the Space Environment (beyond LEO)

- **Altered Gravity Fields**
  Balance Disorders, Fluid Shifts, Visual Alterations, Cardiovascular Deconditioning, Decreased Immune Function, Muscle Atrophy, Bone Loss
- **Isolation/Confinement & Altered Light-dark Cycles**
  Behavioral & Performance aspects of isolation/confinement, Sleep disorders
- **Hostile/closed environment**
  Vehicle Design, Environment (CO_2 Levels, Toxicology, Microbiology, Water), Food, Microbiome
- **Space Radiation**
  Acute In-flight effects, Long-term cancer risk, CNS and Cardiovascular
- **Distance from Earth**
  Autonomous medical care capacity (cannot come home for treatment), Communication Delays

Steve Davison, NASA/HQ

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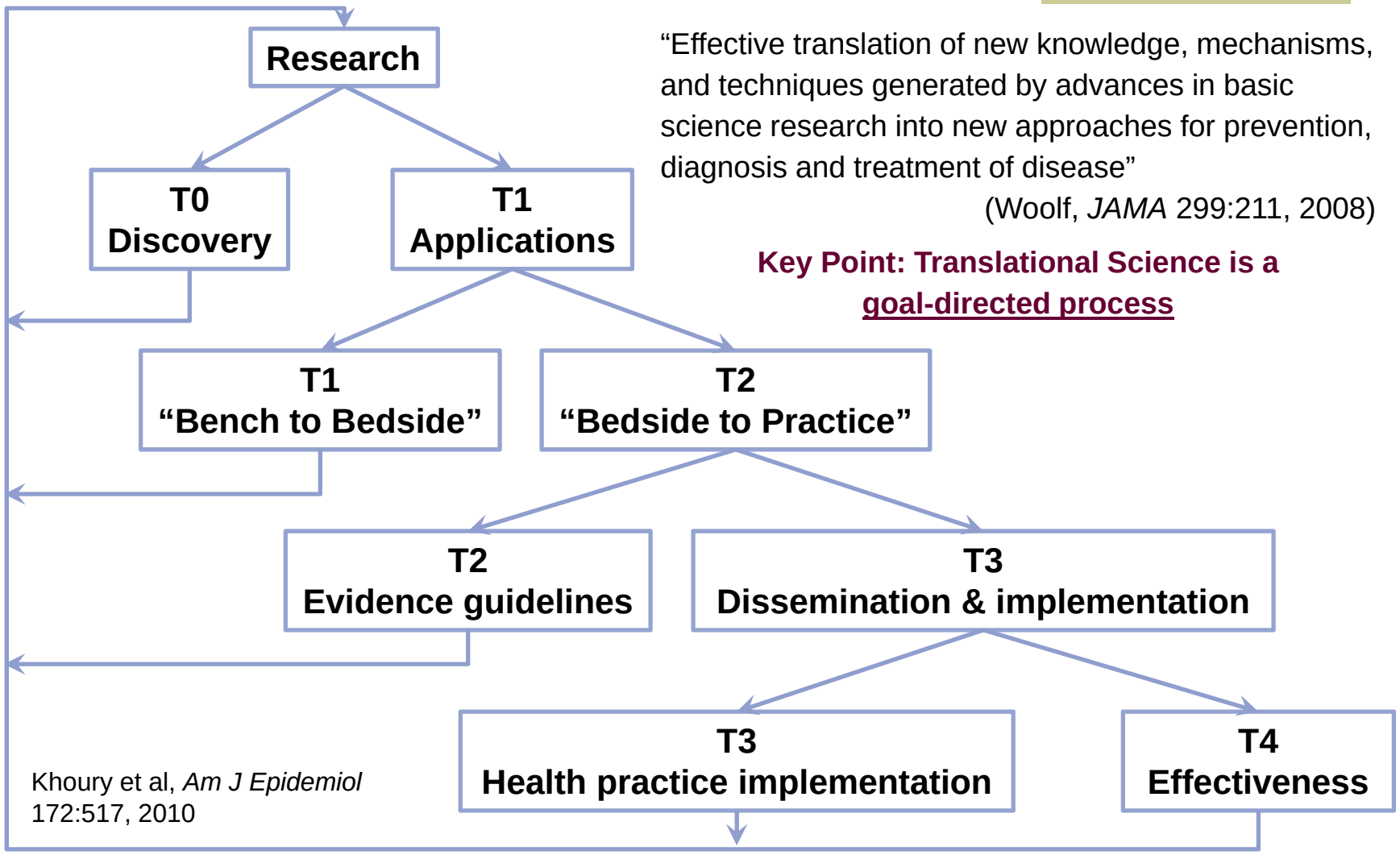
Translational Taxonomy



"Effective translation of new knowledge, mechanisms, and techniques generated by advances in basic science research into new approaches for prevention, diagnosis and treatment of disease"

(Woolf, *JAMA* 299:211, 2008)

Key Point: Translational Science is a goal-directed process

Khoury et al, *Am J Epidemiol* 172:517, 2010

Translation the NASA way

	TECHNOLOGY	T/CRL	COUNTERMEASURES
T3	Actual system 'flight proven'	9	Implementation in spaceflight
	Actual system 'flight qualified'	8	Validation in spaceflight
T2	Prototype demonstration in a space environment	7	Validation in spaceflight analogs
	Demonstration in a relevant environment (ground or space)	6	Application in human subjects
	Validation in relevant environment	5	Concept feasibility and efficacy
T1	Validation in laboratory environment	4	Concept development
	Proof of concept	3	Knowledge development
	Technology concept and/or application formulated	2	Hypothesis formulated
T0	Basic principles observed and reported	1	Phenomenon observed and defined

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- Law of unintended consequences
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- What is translational science?
- **Translational research needs for the future of human spaceflight**
  - **Beyond the genome**
  - **Biologically-inspired technology**
  - **Biomes**
  - **Loading**
- Inferring NASA success as a translational science entity

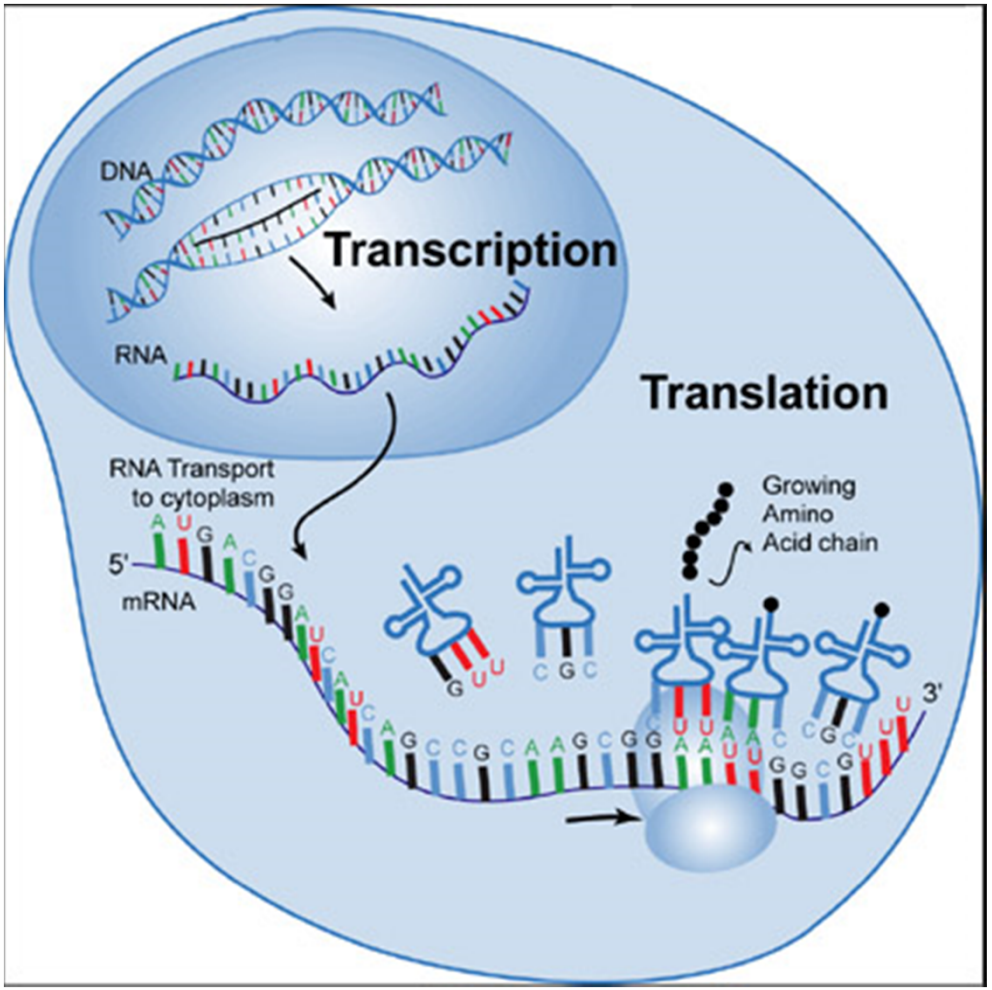
Beyond the Genome

The Central Dogma of Molecular Biology states that DNA makes RNA (transcription), and that RNA is the template for protein synthesis (translation).

These processes are highly regulated, error prone and correcting.

The spaceflight environment, especially radiation, affects many aspects of transcription and translation.

Understanding these influences within and between cells is still in its infancy.



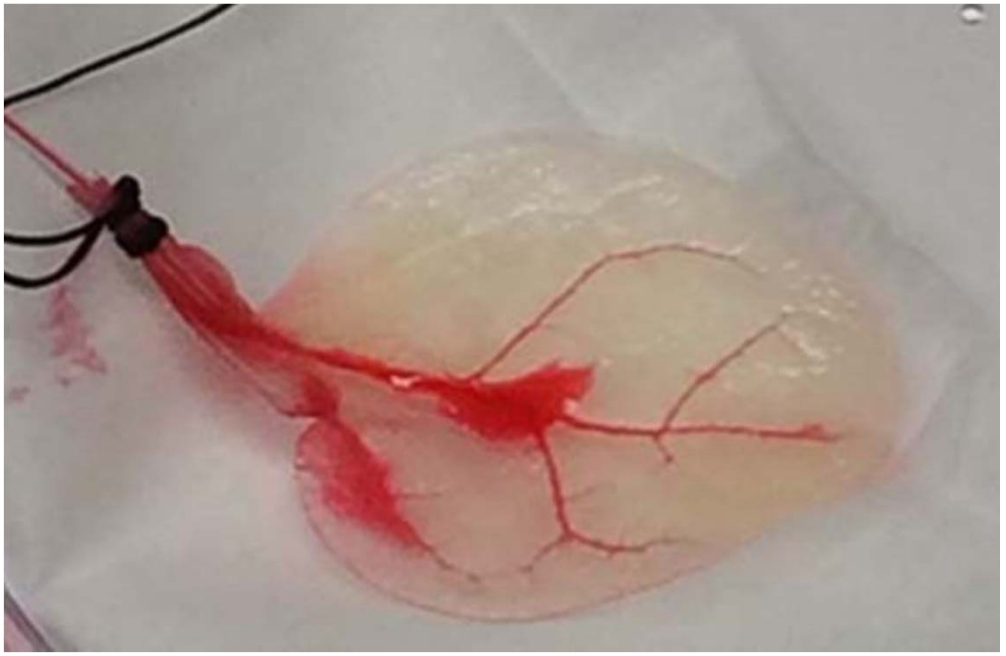
http://diagram.rogersvillegallery.com

Biologically-inspired technology

Biology is more than a science enabled by spaceflight. Biology engenders new technology that is applicable to space exploration and the terrestrial condition.

e.g.,

- Bioregenerative life support
- Thin-film biological transducers
  - optical
  - mechanical
  - magnetic
  - electrical
- Tissue engineering



"The development of decellularized plants for scaffolding opens up the potential for a new branch of science that investigates the mimicry between plant and animal … A highly vascularized plant tissue, such as the spinach leaf, might be better suited for a highly vascularized tissue, like cardiac tissue, whereas the cylindrical hollow structure of the stem might better suit an arterial graft. Conversely, the vascular columns of wood might be useful in bone engineering."

Gershlak et al, *Biomaterials* 125: 13-22, 2017

Microbiota

- A dynamic, evolving genomic environment orders of magnitude larger than our own
- Ecosystems relevant to space exploration
  - Spacecraft
  - Plant and soil specimens
  - Gut
  - Skin
  - Extraterrestrial
  - …

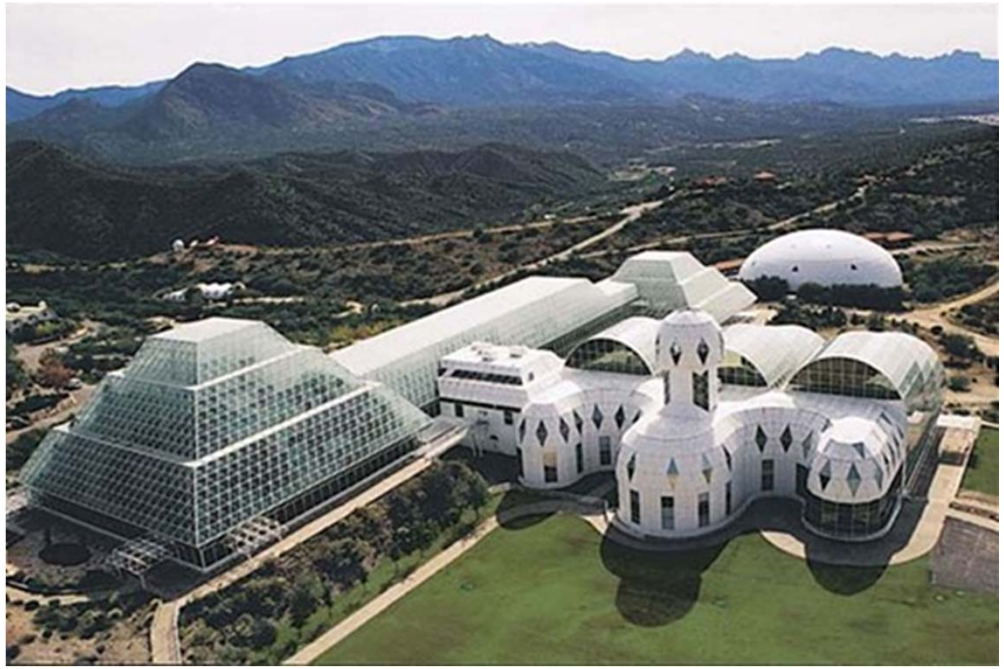
Biosphere 2

Constructed: 1987-1991

Inhabited: 1991-1993

Evacuated: Sept 1993

Score: Soil microbes 1, Humans 0



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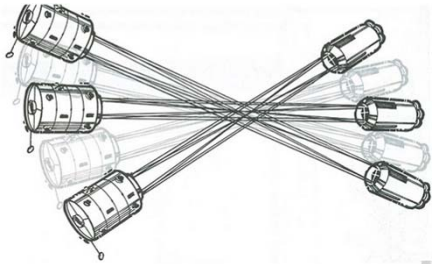

	Artificial Gravity	Exercise
Load	0-1+ G	0-1+ G
Load Control	precise	coarse
Metabolic Rate	near resting	near resting - maximal
Duration	sec - continuous	sec - hr
Therapeutic Range	unknown	somewhat known
Vestibular stimulation	High	High
Cost	$$-$$$$$	$-$$
Power requirements	Low - High	Low - High
Operational requirements	Low - High	Low - Moderate

“Comparative Effectiveness Research is designed to inform health-care decisions by providing evidence on the effectiveness, benefits, and harms of different treatment options.”

- Association for Health Research Quality

Amortizing the exercise prescription

Space Shuttle	International Space Station
$0.5 B/mission	$100 B (2006)
÷ 7 crew	÷ 99 crew-years
÷ 16 days	÷ 365 days/year
÷ 24 hr/day	÷ 24 hr/day
÷ 60 min/hr	÷ 60 min/hr
$3100 / person / minute	$1903 / person / minute

The most expensive gym membership ever created!

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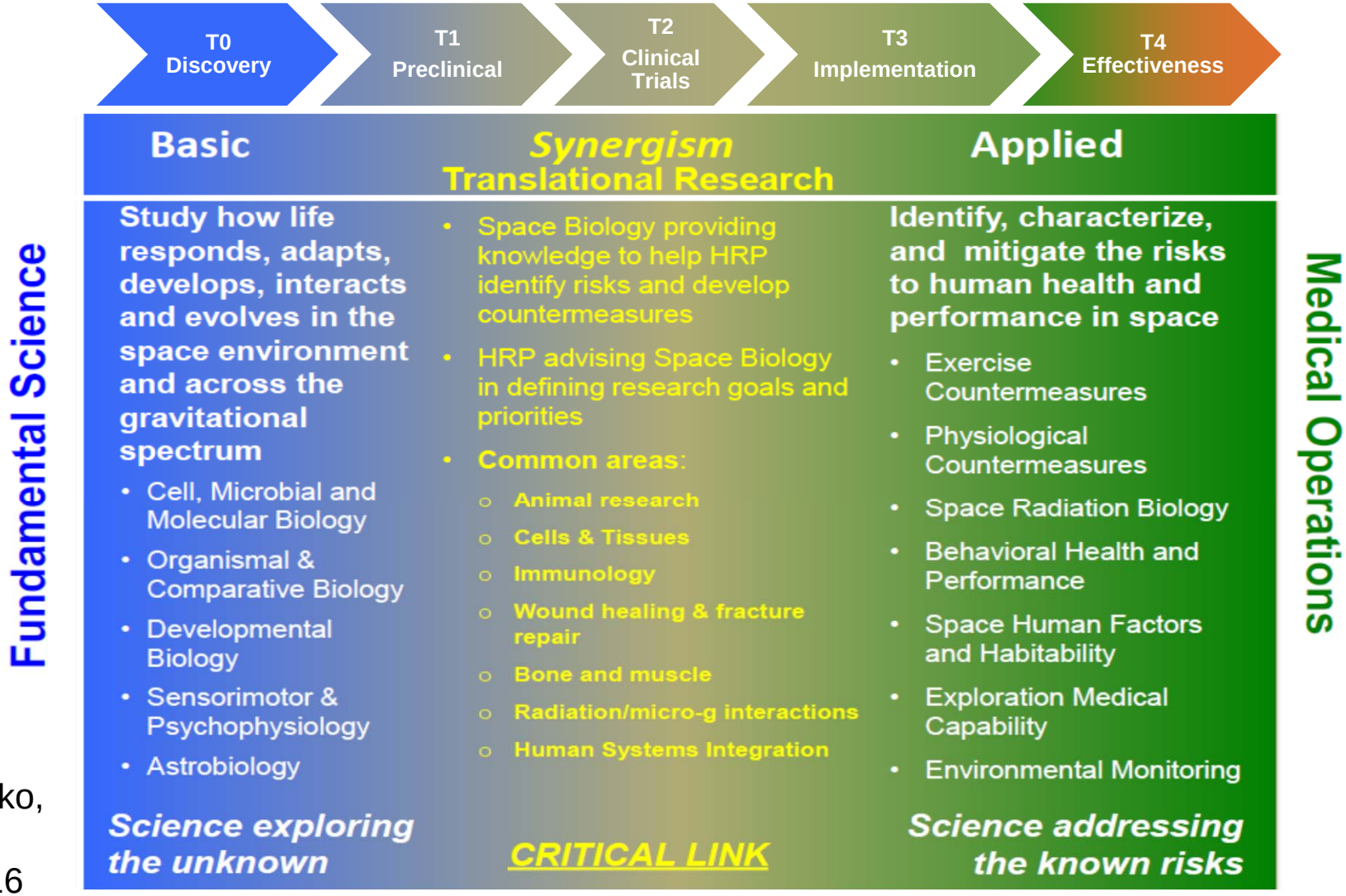
Inferences

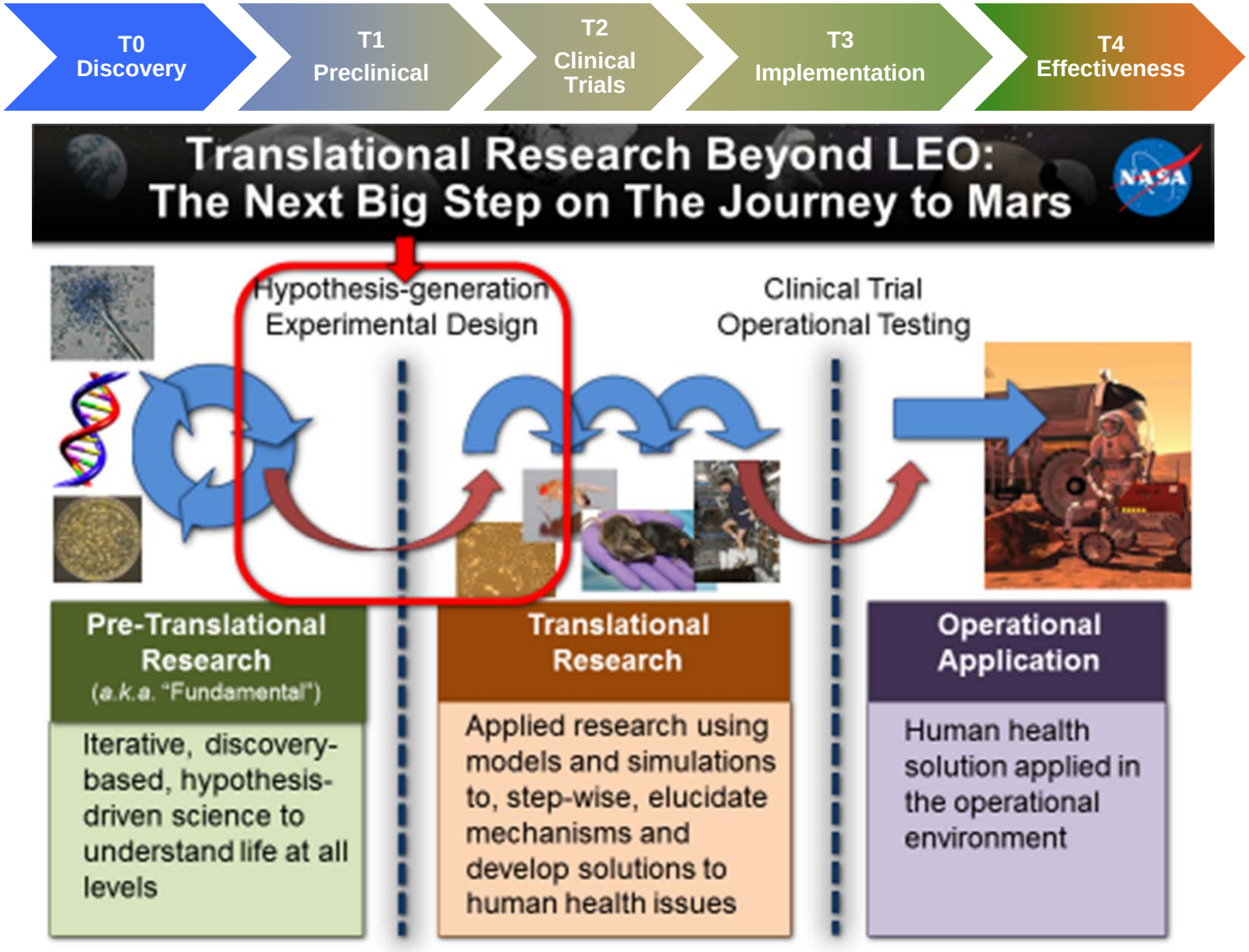
1. It's all translation! 2. There are multiple gaps in translation



David Tomko, NASA/HQ
ACTS, 2016

Inferences

3. NASA/SLPSRA is at risk to develop definition drift

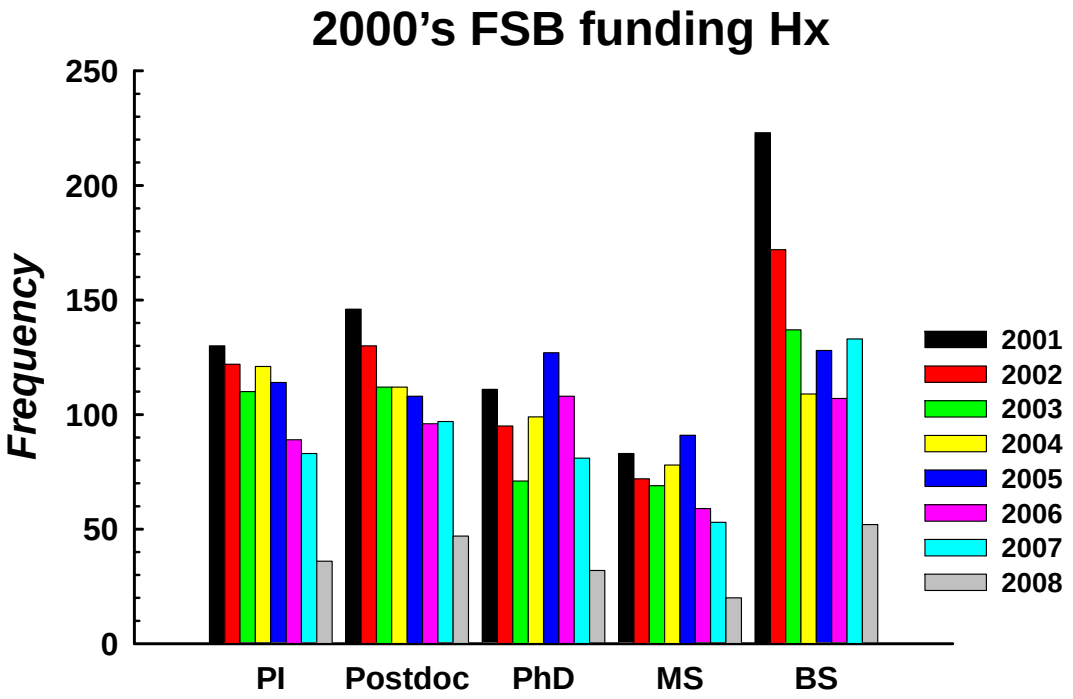


Jeff Smith
NASA/ARC
HRP Workshop
Feb 2016

Inferences

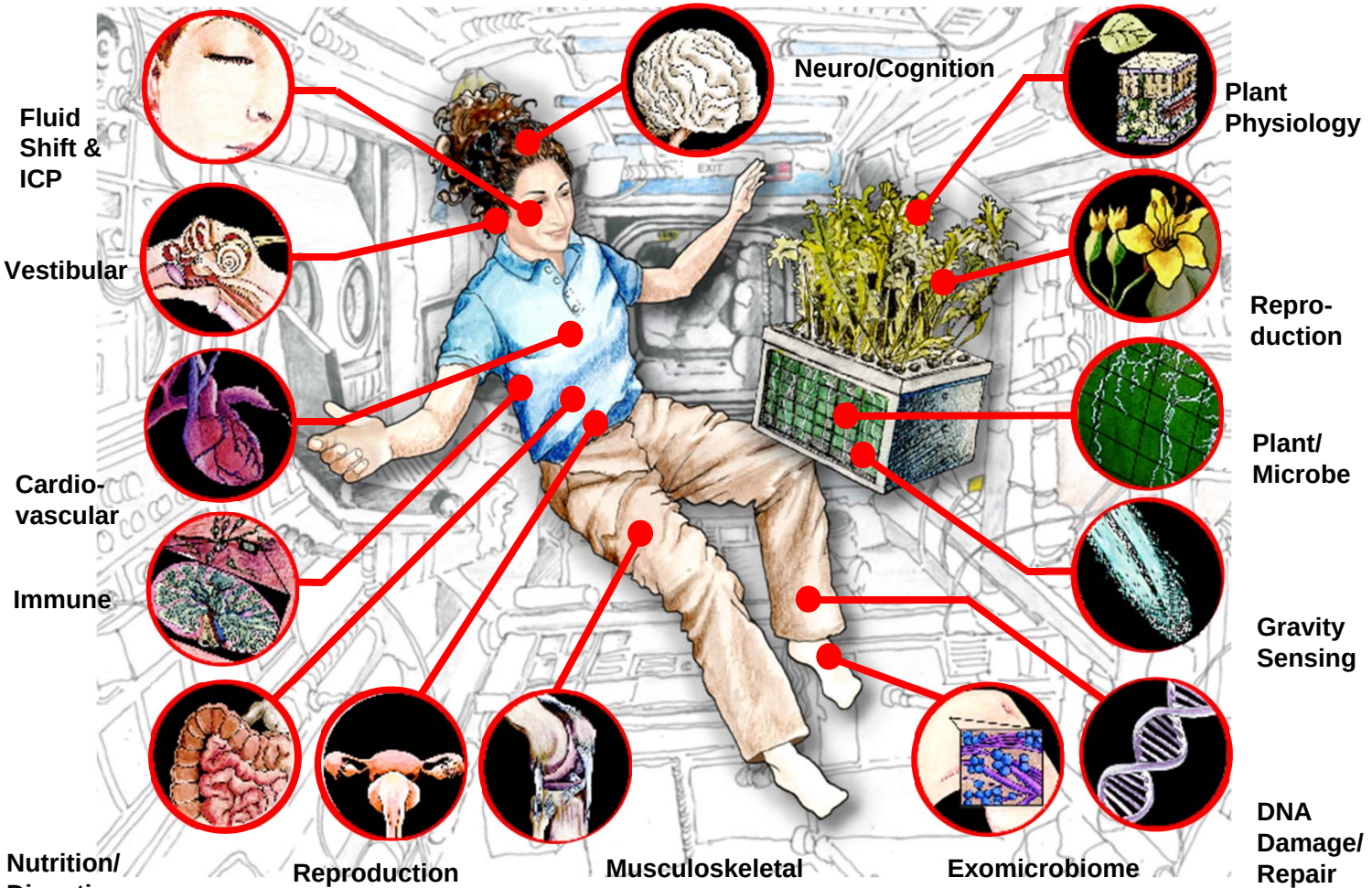
4. **Progress to improve astronaut health will be impeded without early (T0 & T1) translational research (FSB)**

5. **FSB isn't likely to fare well without a translational focus**



Inferences

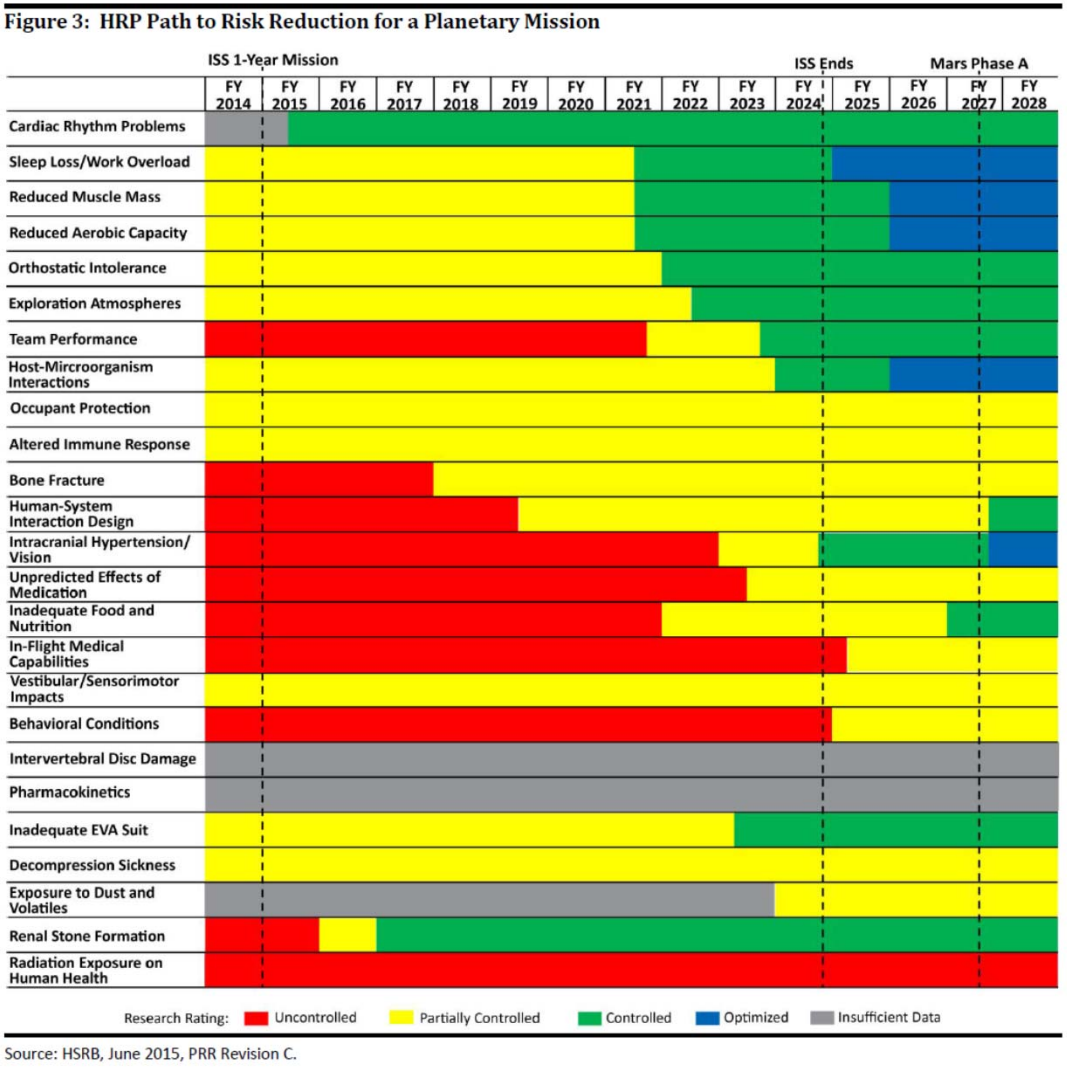
6. The life sciences research portfolio is diverse … Is this opportunity being translated to maximal effect?



David Tomko, NASA/HQ
ACTS meeting, 2016

NASA/HRP has its own translation gap

"According to the 2015 version of the [Pathway to Risk Reduction], the Agency will lack validated countermeasures for 11 of the 23 identified risks and both of the 2 concerns in time for a Mars mission in the 2030s." (p.7)



NIG Report 16-003
October, 2015

Summary
aka, things I worry about ….

1. Neither the phenotype nor expressome of space explorers (not just space sojourners) is known and understood
   - Focus on exploration scale … 30 months+
   - Systems biology will help; so will a larger operational envelope
2. Focus on exploration-centered outcomes
   - e.g., microbial evolution >> virulence >> disease
   - Biomarker validity and reliability
3. High energy radiation effects beyond the genome
   - e.g., CV disease, cognitive function
4. Implementation science
   - The need for “concierge” functions to translate research from C/TRL 1 to C/TRL 7+
   - Behavioral health


NIH NSF
PENNSTATE
1855

Earth is the cradle of humanity,
but one cannot remain in the cradle forever.

Konstantin Eduardovich Tsiolkovsky