Space Research in the Age of Translational Science

Jim Pawelczyk, PhD

PennState

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?
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- 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
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

Abnormal place cell firing

29 citations to date

and facilitating a Nobel Prize

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.”
54 Years After Yuri Gagarin First Orbited the Earth …
we have rarely ventured far from Earth, and never for very long.

Suborbital & Ground Studies
ISS & free flyers in LEO
Moon
Near Earth Object

Known limits of life, and living beyond Earth

Beyond

Mars

Jeff Smith  NASA/ARC
Summary of human long-duration spaceflight

Concept attribution:
John Charles NASA/JSC

as of 30 Oct 2016

Flight Duration (months)

Number of Participants

Russia/USSR
USA/Other
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/confineoment, Sleep disorders*

- Hostile/closed environment
  *Vehicle Design, Environment (CO₂ 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

### Translation the NASA way

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

- Law of unintended consequences
- Framing the challenge
- 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.”

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
- Inhabited: 1991-1993
- Evacuated: Sept 1993
- Score: Soil microbes 1, Humans 0
## Artificial Gravity vs. Exercise

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

“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

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

The most expensive gym membership ever created!
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Inferences

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

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**Fundamental Science**

**Synergism Translational Research**

- Space Biology providing knowledge to help HRP identify risks and develop countermeasures
- HRP advising Space Biology in defining research goals and priorities
- Common areas:
  - Animal research
  - Cells & Tissues
  - Immunology
  - Wound healing & fracture repair
  - Bone and muscle
  - Radiation/micro-g interactions
  - Human Systems Integration

**Medical Operations**

- Identify, characterize, and mitigate the risks to human health and performance in space
- Exercise Countermeasures
- Physiological Countermeasures
- Space Radiation Biology
- Behavioral Health and Performance
- Space Human Factors and Habitability
- Exploration Medical Capability
- Environmental Monitoring

Science exploring the unknown

Science addressing the known risks

David Tomko, NASA/HQ
ACTS, 2016
Inferences

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

2000’s FSB funding Hx

- Frequency

- Categories: PI, Postdoc, PhD, MS, BS

- Years: 2000’s

- Colors: 2001 (black), 2002 (red), 2003 (green), 2004 (yellow), 2005 (blue), 2006 (pink), 2007 (cyan), 2008 (gray)
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)

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>ISS 1-Year Mission</th>
<th>ISS Ends</th>
<th>Mars Phase A</th>
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</thead>
<tbody>
<tr>
<td>Cardiac Rhythm Problems</td>
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<td>Sleep Loss/Work Overload</td>
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<td>Reduced Muscle Mass</td>
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<tr>
<td>Reduced Aerobic Capacity</td>
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<tr>
<td>Orthostatic Intolerance</td>
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<tr>
<td>Exploration Atmospheres</td>
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<tr>
<td>Team Performance</td>
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<tr>
<td>Host-Microorganism Interactions</td>
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<td>Occupant Protection</td>
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<td>Altered Immune Response</td>
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<td>Bone Fracture</td>
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<td>Human-System Interaction Design</td>
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<tr>
<td>Intracranial Hypertension/Vision</td>
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<tr>
<td>Unpredicted Effects of Medication</td>
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<tr>
<td>Inadequate Food and Nutrition</td>
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<td>In-Flight Medical Capabilities</td>
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<tr>
<td>Vestibular/Sensorimotor Impacts</td>
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<tr>
<td>Behavioral Conditions</td>
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<tr>
<td>Intervertebral Disc Damage</td>
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<tr>
<td>Pharmacokinetics</td>
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<tr>
<td>Inadequate EVA Suit</td>
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<tr>
<td>Decompression Sickness</td>
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<tr>
<td>Exposure to Dust and Volatiles</td>
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<tr>
<td>Renal Stone Formation</td>
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<tr>
<td>Radiation Exposure on Human Health</td>
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</tbody>
</table>

Research Rating: Uncontrolled, Partially Controlled, Controlled, Optimized, Insufficient Data

Source: HSRB, June 2015, PRR Revision C.
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
Earth is the cradle of humanity, but one cannot remain in the cradle forever.

Konstantin Eduardovich Tsiolkovsky