OVERVIEW OF TRANSLATIONAL PHYSIOLOGY IN THE HUMAN RESEARCH PROGRAM

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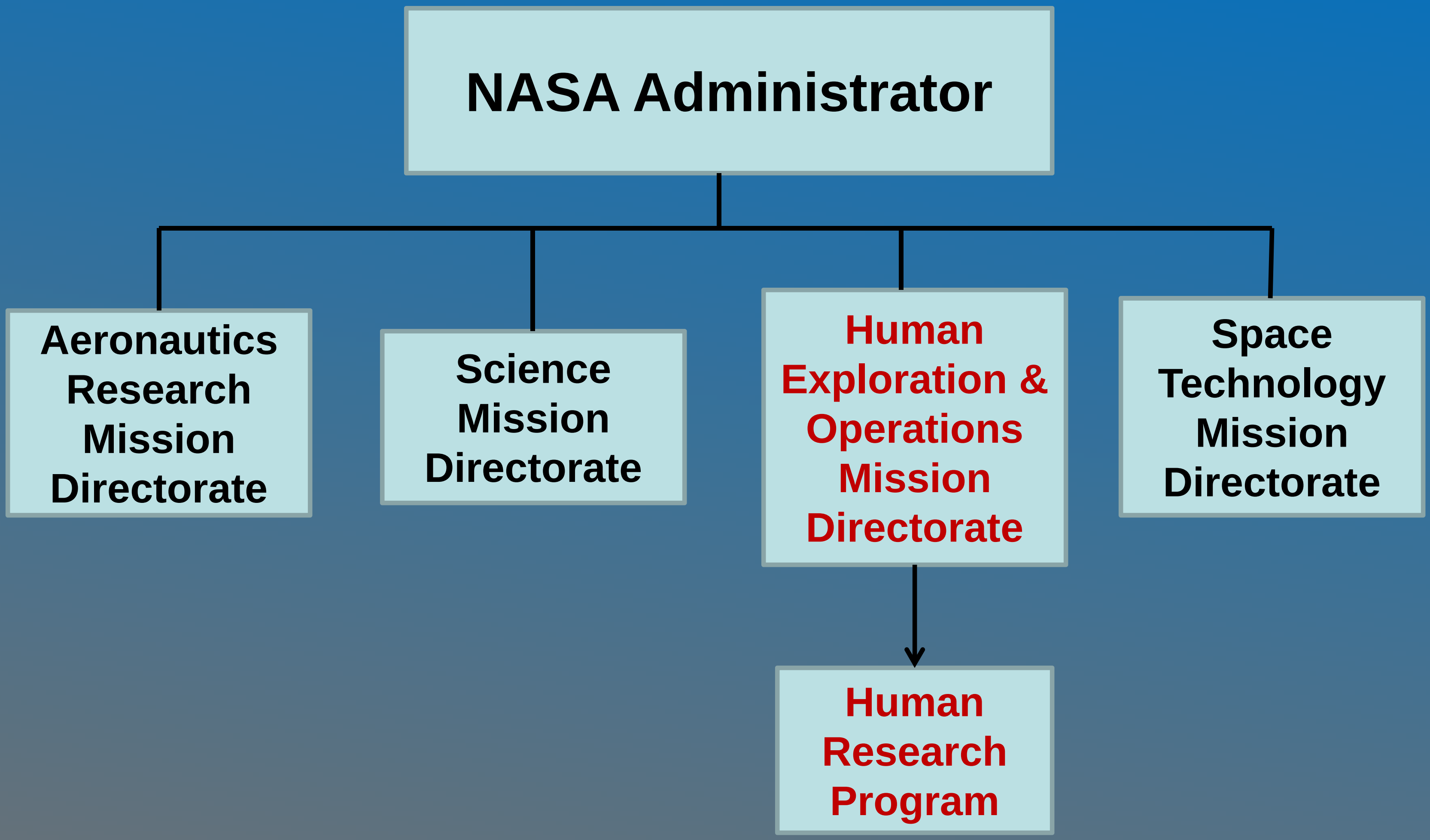
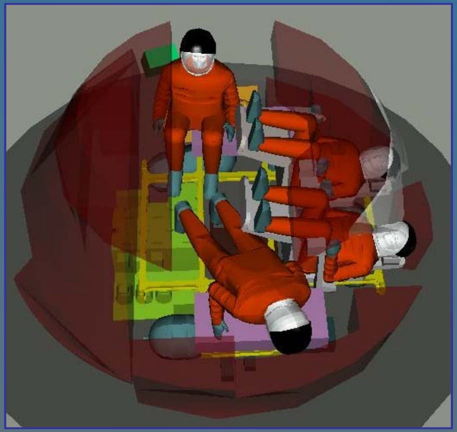
HRP Mandate within NASA



NASA Human Research Program

- Program goals
  - Perform research necessary to understand and reduce spaceflight human health and performance risks in support of exploration
  - Enable development of human spaceflight medical and human performance standards
  - Develop and validate technologies that serve to characterize and reduce medical risks associated with human spaceflight

Clay Anderson centrifuges Nutrition blood samples during Increment 15

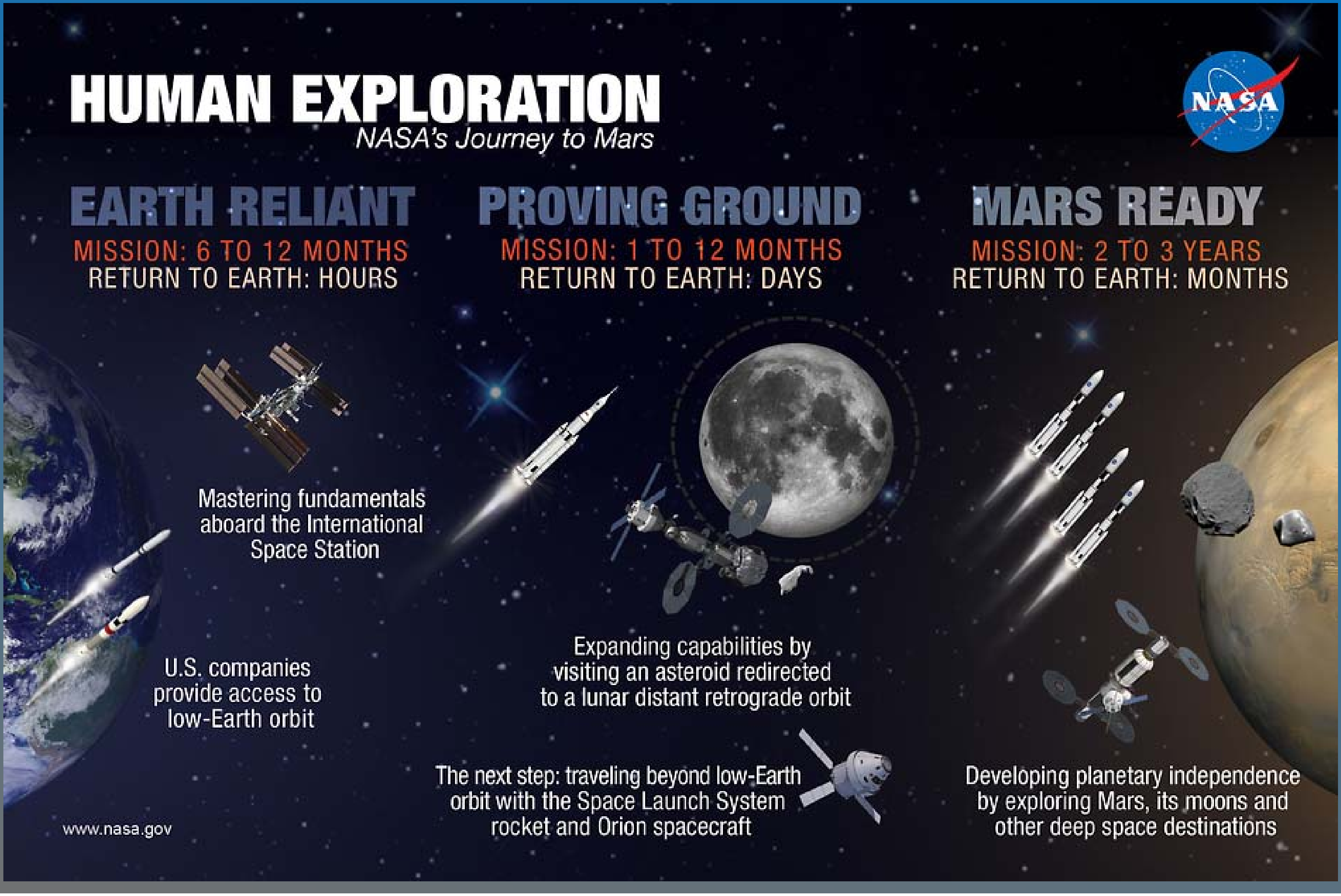


Seat layout for contingency EVA

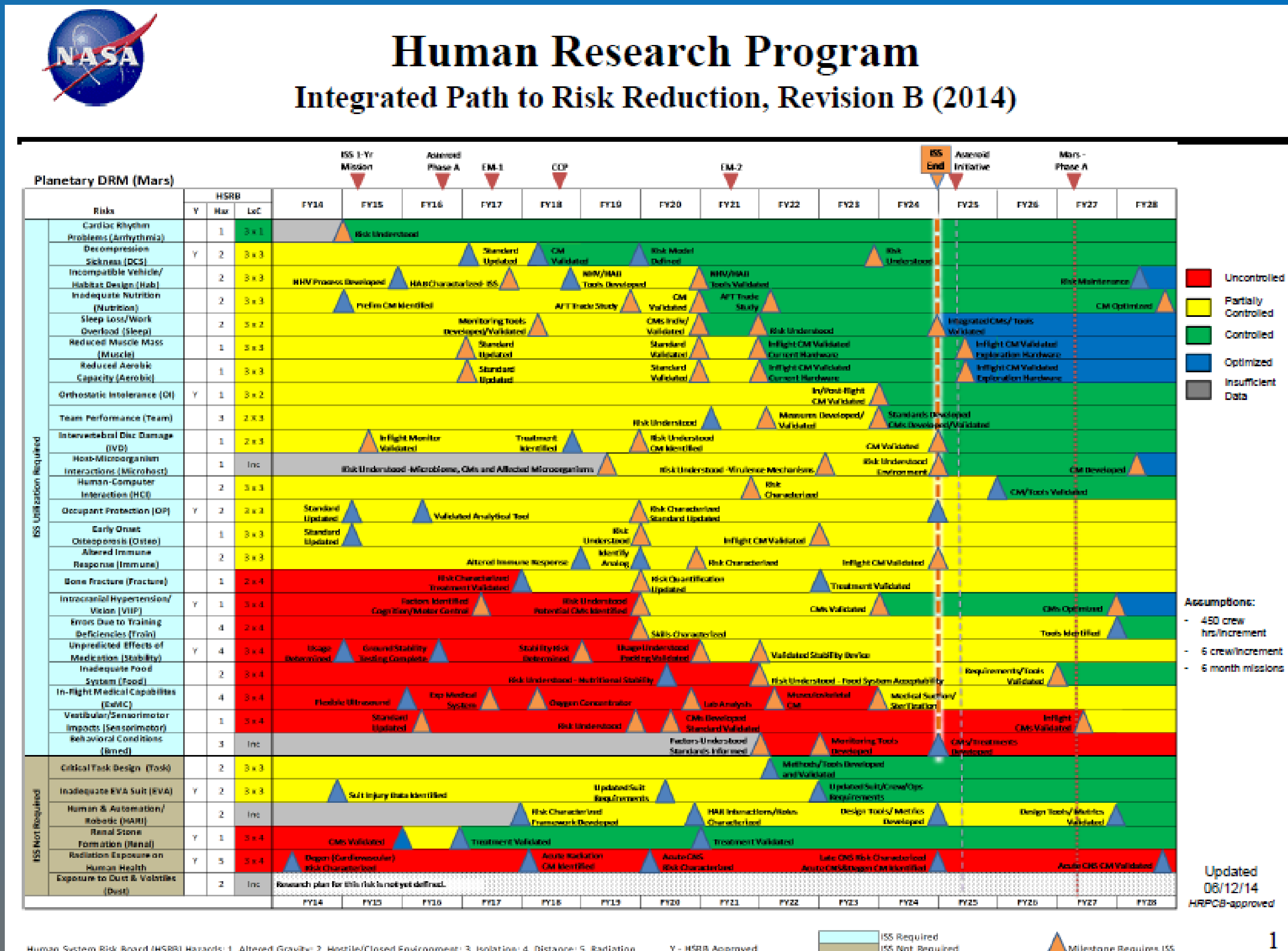
Example of a study on the effects of center of gravity on performance

An Applied Research Program

Destination - MARS



Integrated Path to Risk Reduction



HRP Integrated Science Plan

- Risks amenable to translational approach
  - Immune
  - Cancer
  - Bone (Osteo/Fracture)
  - Oxidative Stress & Damage
  - VIIP
  - Nutrition
  - Artificial Gravity

SPACE BIOLOGY PROGRAM GOALS

- To effectively use microgravity and other characteristics of the space environment to enhance our understanding of fundamental biological processes
- To develop the scientific and technological foundations for a safe, productive human presence in space for extended periods and in preparation for exploration
- To apply this knowledge and technology to improve our nation's competitiveness, education, and the quality of life on Earth

Decadal Survey Recommendations

- Elevate the priority of research in the agenda for space exploration
- Select research likely to provide value to an optimal range of future mission designs
- Develop a comprehensive database that is accessible to the scientific community
- Implement a translational science component to ensure bidirectional interactions between basic science and the development of new mission options
- Encourage and accommodate team science approaches to what are inherently complex multidisciplinary challenges

Source: *Life and Physical Sciences Research for a New Era of Space Exploration: An Interim Report*, National Research Council, 2010

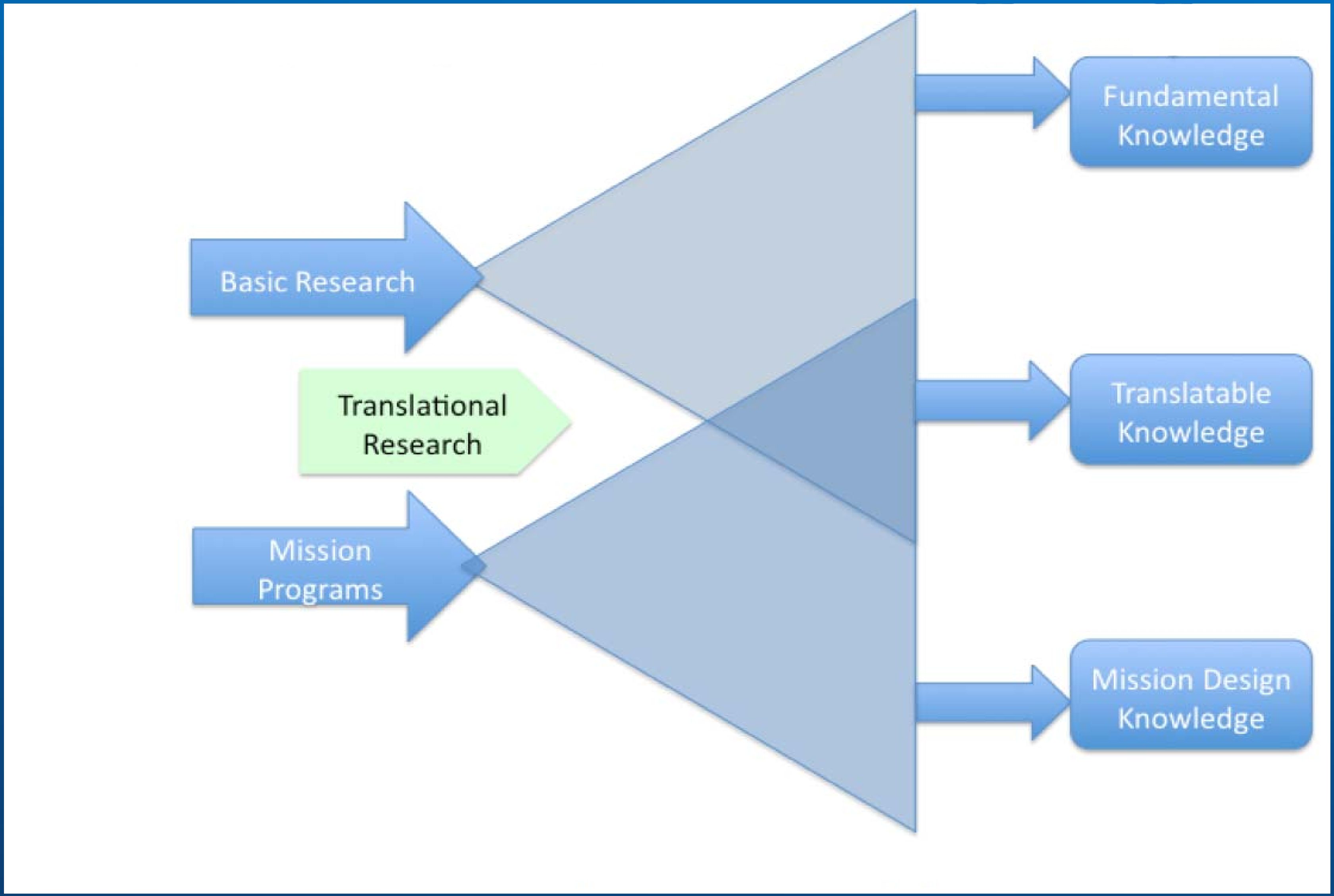
SYNTHETIC BIOLOGY PROGRAM GOALS

- Harness biology in reliable, robust, engineered systems to support NASA's exploration and science missions, to improve life on Earth, and to help shape NASA's future.

Astrobiology Institute Goals

- To study the origins, evolution, distribution, and future of life in the universe.
- To answer:
  - How does life begin and evolve?
  - Is there life elsewhere in the Universe?
  - What is the future of life on Earth and beyond?

Translational Research: Key Component of an Active Research Program



Source: *Life and Physical Sciences Research for a New Era of Space Exploration: An Interim Report*, National Research Council, 2010

HUMAN RESEARCH PROGRAM AND SPACE BIOLOGY INTERSECTIONS

Basic Research | Medical Operations

Space Biology

Study how life responds, adapts, develops, interacts and evolves in the space environment and across the gravitational spectrum

- Cell, Microbial and Molecular Biology
- Organismal & Comparative Biology
- Developmental Biology

Science exploring the unknown

Synergism

Translational Research

- SB provides knowledge to help HRP identify risks and develop countermeasures
- HRP advises SB in defining research goals and priorities
- **Common areas**:
  - **Animal research**
  - **Cells & Tissues Research**
  - **Immunology**
  - **Wound healing & fracture repair**
  - **Bone and muscle**
  - **Radiation/micro-g interactions**
  - **Oxidative Stress and Damage (OSaD)**

Human Research Program

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

Science addressing the known risks

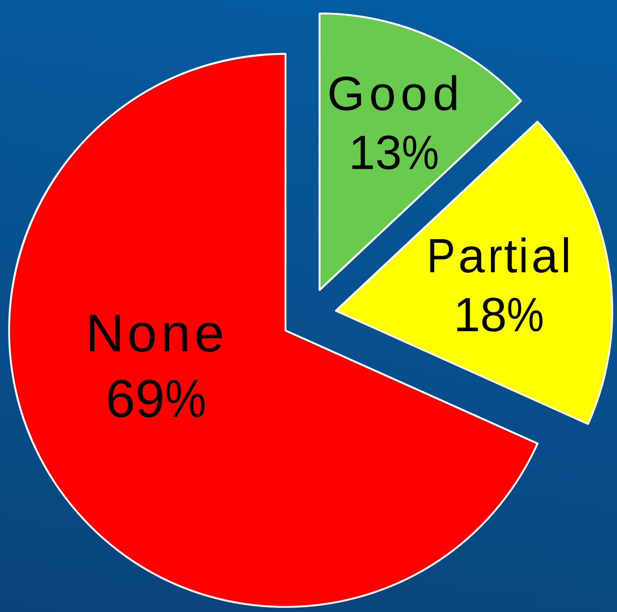
Synergistic Avenues Being Considered

- Translational Science at NASA
  - Synergy between Space Biology and HRP**
  - Basic Research helps close HRP Gaps and Risks**
  - Examples of Translational Research at NASA**
  - Synergies with Synthetic and Astrobiology (Ex: OSaD and there are others)
  - Synergies with other programs (Gov./ Commercial/ Academic)
  - Potential Products & Strategies**
  - Analogs
  - Standard Model Organisms
  - Teams

** Indicates Already In Progress

Goodness of Fit: HRP and SB

ANALYSIS OF HRP-SB OVERLAP



Total good+partial
31%
78 Gaps

Most Overlap
Immune
Cancer
CNS
Osteo/Fracture

Highest Priorities by HRP
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HRP Risk ShortTitle	#Gaps	Relevant Gaps (TG)		
		Good	Partial	None
Aerobic	4			4
Arrhythmia	4	1		3
ARS	8	1	3	5
Bmed	8		1	7
Cancer	15	5	6	4
CNS	8	3	5	
Degen	8	1	4	3
Dust	6			6
EVA	8	0	2	6
ExMC	32	0	4	28
Food	4			4
Fracture	11	3	2	6
Hab	6			6
HARI	4			4
HCI	7		1	6
Immune	10	7	2	1
IVD	1			1
Microhost	4	3	1	
Muscle	13	1	2	10

Good
Partial
None

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Translational Activities

- Integrated HERO solicitation
  - HRP annual major release plus periodic appendices
  - To include Space Biology in overview
- AG synergy
  - New HRP research portfolio
  - Includes animal and cell components
- Grants with animal/human transition
- Omics
  - Integrated/personalized countermeasures
  - CASIS interaction

IMMUNE RISK EXEMPLAR

HRP Gap Title	SpaceBio Guiding Question
IM1: Does spaceflight alter immune function? IM5: What is the time course and etiology of immune changes?	OCB-4: Are the normal defense systems of organisms compromised at fractional or hyper- gravity, e.g. mammalian immune system, wound healing, including fracture repair?
IM3: Are there suitable analogs for immune dysregulation?	
IM4: Can in-flight hardware to evaluate hematology/infection/immunity be developed?	OCB-4 CMM-4: Does the enhanced virulence observed with Salmonella typhimurium cultures flown in space occur in other species?
IM6: What are the cumulative effects of chronic immune dysfunction on missions greater than six months?	OCB-4 DEV-3: Do organisms that are raised in altered gravity environments develop normally, i.e., structurally, physiologically, behaviorally? Are reproduction, lifespan and the aging processes affected? Are changes expressed in altered g environment reversible when returned to 1g?

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BONE--OSTEO / FRACTURE RISKS EXEMPLAR

HRP Gap Title	SpaceBio Guiding Question
Bone 1: a) Is there an increased lifetime risk of fragility fractures/osteoporosis in astronauts; b) is bone strength completely recovered post-flight, and does BMD reflect it; c) what are the risk factors for poor recovery of BMD/bone strength?	OCB-4: Are the normal defense systems of organisms compromised at fractional or hyper- gravity, e.g. mammalian immune system, wound healing, including fracture repair? DEV-3: Do organisms that are raised in altered gravity environments develop normally, i.e., structurally, physiologically, behaviorally? Are reproduction, lifespan and the aging processes affected? Are changes expressed in altered g environment reversible when returned to 1g?
Bone 10: How can skeletal adaptation be monitored during flight to a) reflect changes in bone turnover/calcium kinetics, b) to determine whether there is a plateau in bone loss and c) to evaluate gender effects? Osteo 7: We need to identify options for mitigating early onset osteoporosis before, during and after spaceflight.	OCB-2: How do changes in gravity affect the regulatory mechanisms that govern alterations in the musculoskeletal system in animals and lignin formation in plants?

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NASA TRANSLATIONAL RESEARCH EXEMPLAR: BONE PHYSIOLOGY

Effects on Cells and/or Animals

- Loss of bone density
- Impaired bone healing
- Cell and molecular mechanisms of bone loss emerging
- Drug countermeasures to flight bone loss in mice appear effective

Implications for Astronaut Health

- Increased risk of fracture
- An anti-bone resorption drug and a pro-bone forming treatment tested in flight mice minimized bone loss also tested in humans
- Centrifugation in rats prevented negative effects of spaceflight on long-bone mechanical properties

Related Potential Countermeasures in Space

- Weight bearing activity essential to maintain bone density
- Artificial gravity options under study
- Drug treatment (Amgen) for lessening bone resorption and promoting formation received FDA approval in 2010 for treatment of osteoporosis.
- A 2nd drug developed, FDA approval anticipated 2017

Earth Benefits

- More comprehensive understanding of bone formation, growth, maintenance, healing
- Optimize treatment of osteoporosis and disuse arthritis in women and men
- Potential adjunct cancer treatments