



# EXPLORE

## Human Research Program

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***Committee on Biological and Physical Sciences in Space***

*National Academies of Sciences, Engineering, and Medicine*

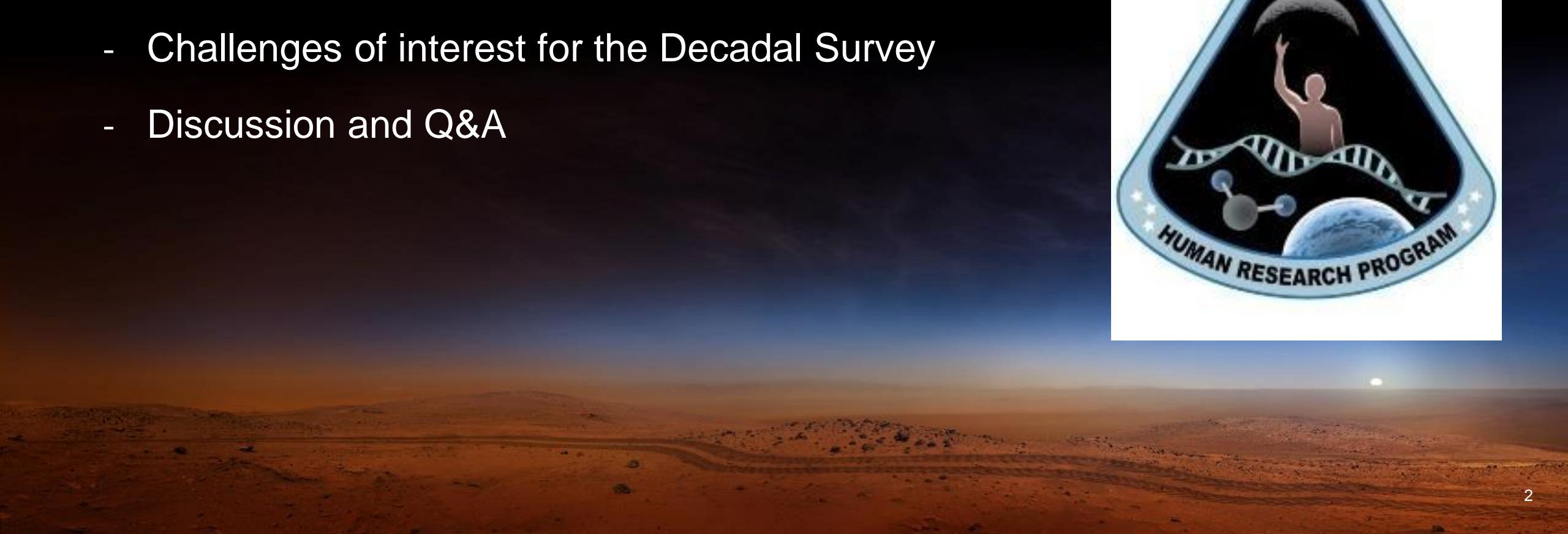
*Beckman Center, Irvine, CA*

*October 29, 2019*



# Agenda

- Status, Planning, Research Findings, Challenges
- Trends, forecasting science needs in HRP
- Challenges of interest for the Decadal Survey
- Discussion and Q&A





# Status, Planning, Research Findings, Challenges

# Human Research Program Mission

To enable space exploration beyond Low Earth Orbit by reducing the risks to human health & performance through a focused program of:

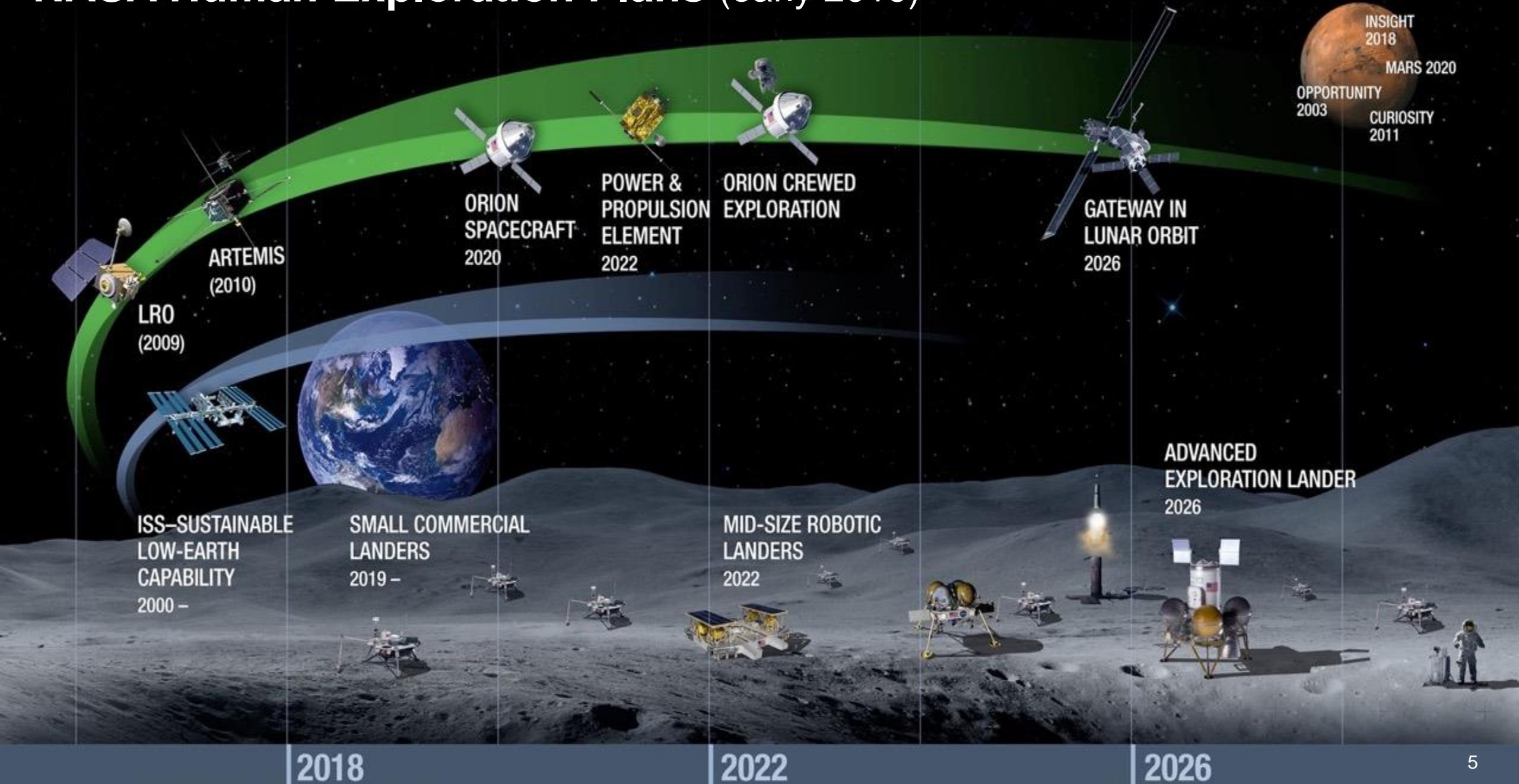
- **Basic, applied, and operational research**

leading to the development and delivery of:

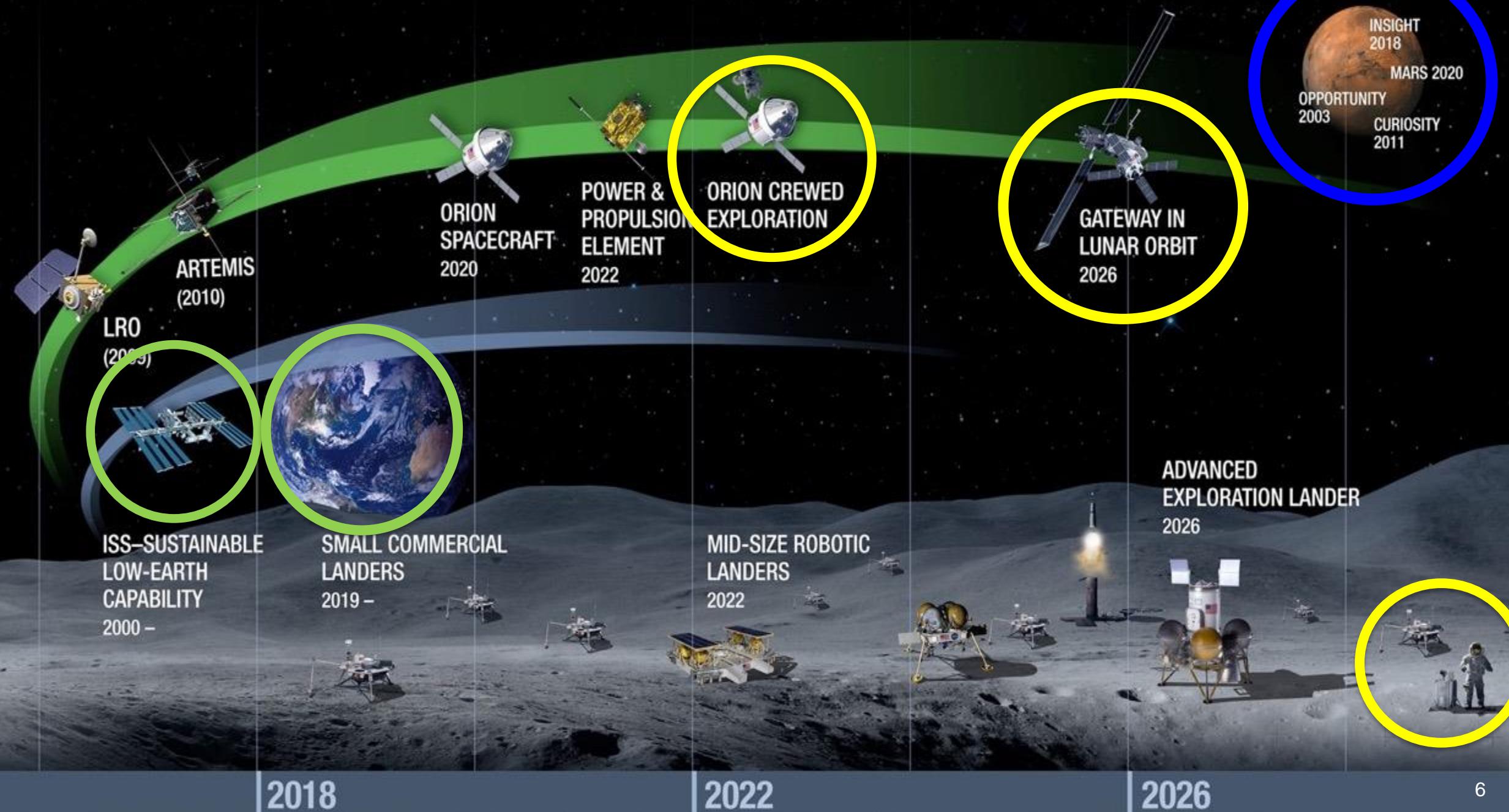
- **Human health, performance, and habitability standards**
- **Countermeasures and other risk mitigation solutions**
- **Advanced habitability and medical support technologies**



# NASA Human Exploration Plans (early 2019)



# HRP R&D VENUES/OPPORTUNITIES/TARGET



# Deep Space Stressors to Human Health & Performance



Earth

*Altered Gravity Fields*

*Hostile Closed Environment*

*Radiation*

*Isolation/Confinement*

*Distance from Earth*

# Exploration Health & Performance Risks – Mars DRM



## Altered Gravity Field

1. Spaceflight-Associated Neuro-ocular Syndrome (SANS)
2. Renal Stone Formation
3. Impaired Control of Spacecraft/Associated Systems and Decreased Mobility Due to Vestibular/Sensorimotor Alterations Associated with Space Flight
4. Bone Fracture due to spaceflight Induced changes to bone
5. Impaired Performance Due to Reduced Muscle Mass, Strength & Endurance
6. Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity
7. Adverse Health Effects Due to Host-Microorganism Interactions
8. Urinary Retention
9. Orthostatic Intolerance During Re-Exposure to Gravity

## Concerns

1. Concern of Clinically Relevant Unpredicted Effects of Medication
2. Concern of Intervertebral Disc Damage upon and immediately after re-exposure to Gravity

## Radiation

1. Risk of Space Radiation Exposure on Human Health:
  - Acute solar events
  - Cancer
  - CNS impairment
  - Tissue degeneration (cardio)

## Distance from Earth

1. Adverse Health Outcomes & Decrements in Performance due to inflight Medical Conditions
2. Ineffective or Toxic Medications due to Long Term Storage

## Isolation/Confinement

1. Adverse Cognitive or Behavioral Conditions & Psychiatric Disorders
2. Performance & Behavioral health Decrements Due to Inadequate Cooperation, Coordination, Communication, & Psychosocial Adaptation within a Team

## Hostile Closed Environment

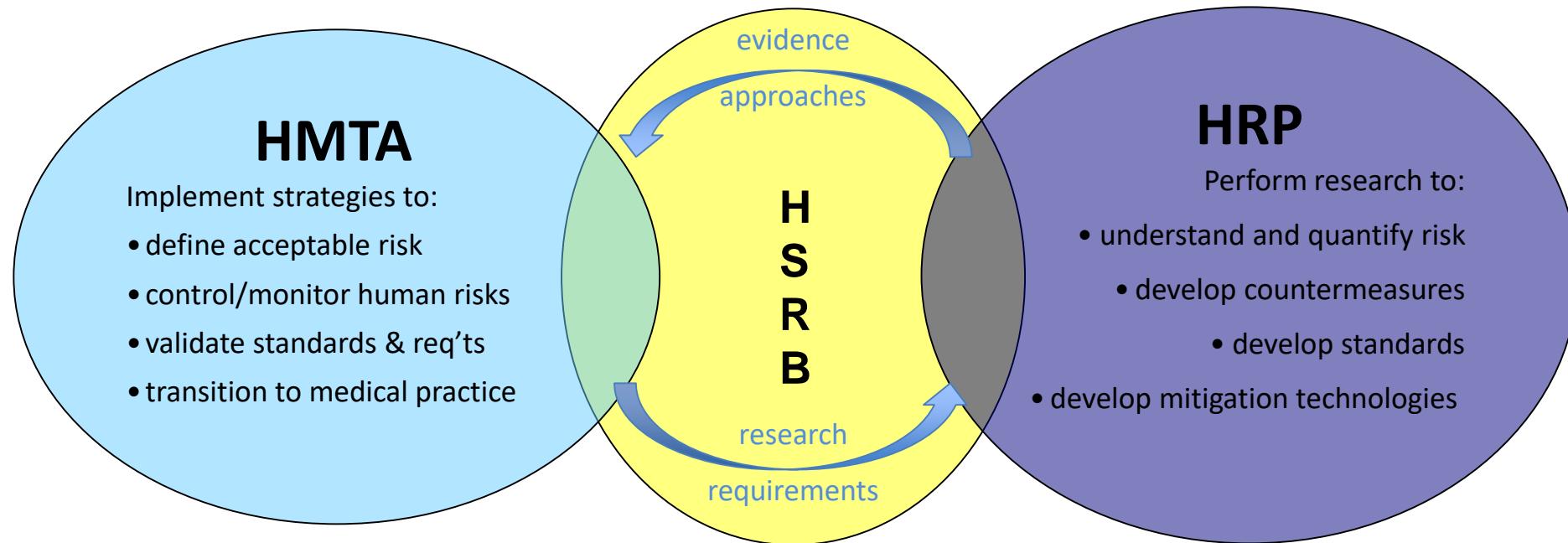
1. Acute and Chronic Carbon Dioxide Exposure
2. Performance decrement and crew illness due to inadequate food and nutrition
3. Injury from Dynamic Loads
4. Injury and Compromised Performance due to EVA Operations
5. Adverse Health & Performance Effects of Celestial Dust Exposure
6. Adverse Health Event Due to Altered Immune Response
7. Reduced Crew Performance Due to Hypobaric Hypoxia
8. Performance Decrements & Adverse Health Outcomes Resulting from Sleep Loss, Circadian Desynchronization, & Work Overload
9. Reduced Crew Performance Due to Inadequate Human-System Interaction Design
10. Decompression Sickness
11. Toxic Exposure
12. Hearing Loss Related to Spaceflight

Key: High LxC Medium LxC Low LxC TBD LxC

# Human System Risk Board



Provides independent assessment of crew health and performance risk status for various design reference missions of interest to NASA.



## ***Human System Risk Board***

- *HMTA/Space Medicine (chair)*
- *HRP/Human Research*
- *Environmental Science*
- *Human Factors Engineering*
- *Space Flight Operations*
- *Crew Office*

# Human System Risk Summary – Risks by Hazard

Last Updated: 24 October 2019

	LEO 6-12 months	Deep Space Sortie 1 month	Lunar Orbit Long 30d-1yr	Lunar Orbit +Surface Long 30d-1yr	Mars Preparatory ≤1 year	Mars Planetary 3 years
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## Radiation

Cancer
Degenerative Tissue Effects
Central Nervous System
Acute Radiation Syndrome

A	A	RM	RM	RM	RM
A	A	RM	RM	RM	RM
A	A	A	RM	RM	RM
A	A	A	A	A	A

## Distance from Earth

Adverse Outcomes Due to Inflight Medical Conditions
Renal Stone Formation
Inadequate Food and Nutrition
Injury from EVA Operations
Ineffective or Toxic Medications
Injury from Dynamic Loads
Hypobaric Hypoxia
Altered Immune Response
Decompression Sickness

A	A	RM	RM	RM	RM
A	A	A	A	RM	RM
A	A	RM	RM	RM	RM
A	A	A	RM	RM	RM
RM	A	RM	RM	RM	RM
A	A	A	A	A	RM
A	A	A	A	A	A

## Isolation & Confinement

Inadequate Human Systems Integration Architecture
Cognitive or Behavioral Conditions
Psychosocial Adaptation within a Team
Sleep Loss

A	RM	RM	RM	RM	RM
RM	A	RM	RM	RM	RM
A	A	A	A	A	RM
A	A	A	A	RM	RM

## Altered Gravity

Spaceflight Associated Neuro-ocular Syndrome
Cardiac Rhythm Problems
Sensorimotor Alterations
Reduced Muscle Mass, Strength
Reduced Aerobic Capacity
Bone Fracture
Orthostatic Intolerance

A	A	A	A	RM	RM
A	A	A	A	RM	RM
A	A	RM	RM	RM	RM
A	A	A	A	A	RM
A	A	A	A	A	A
A	A	A	A	A	A

## Hostile, Closed Environment

Host-Microorganism Interactions
Celestial Dust Exposure
Air, water, temperature, humidity control

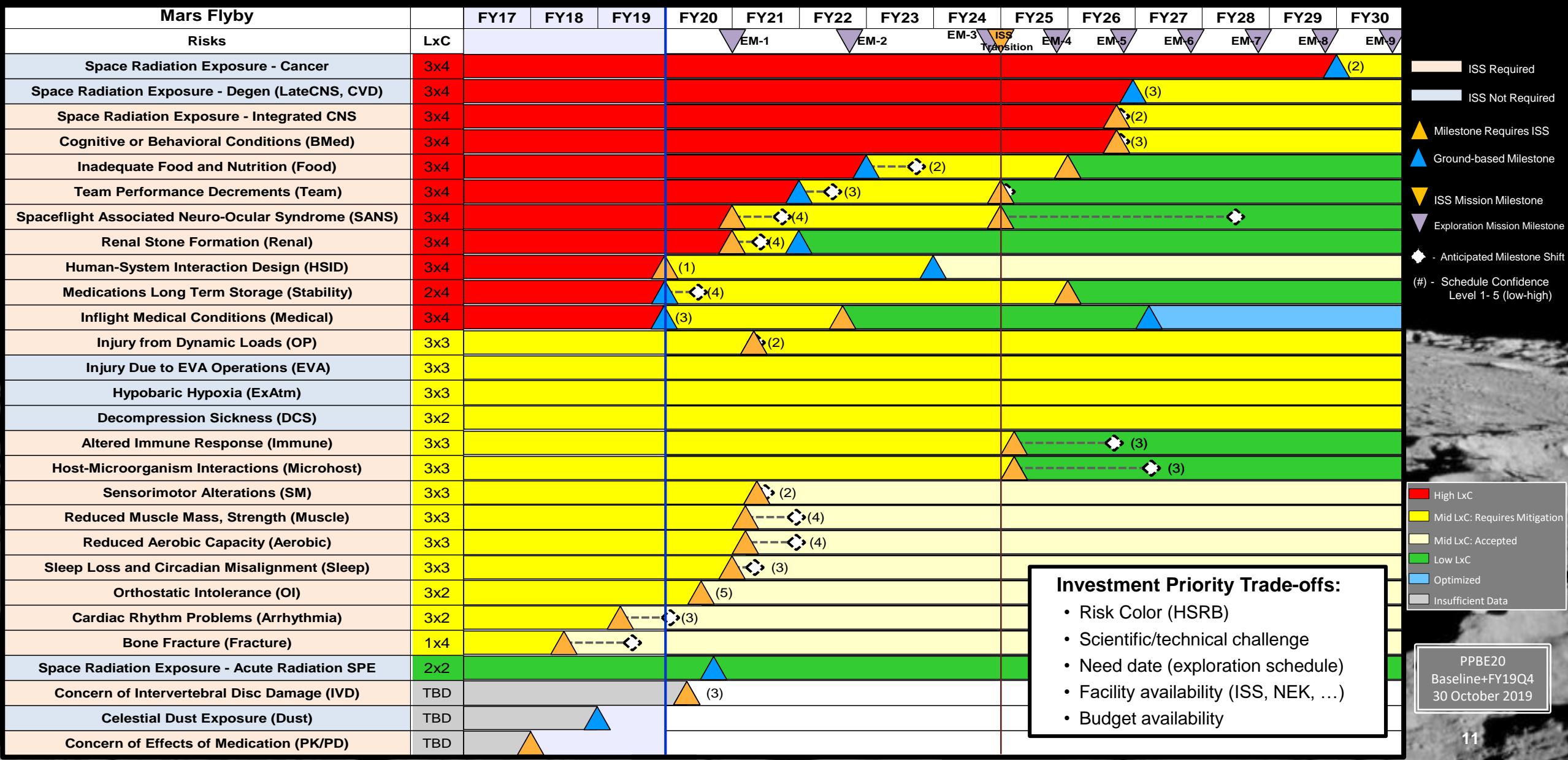
A	A	A	A	A	RM
N/A	N/A	N/A	A	N/A	TBD
not HRP					

Note: Lunar Orbit/Surface Long, Mars Preparatory DRM parameters under review by the HSRB.

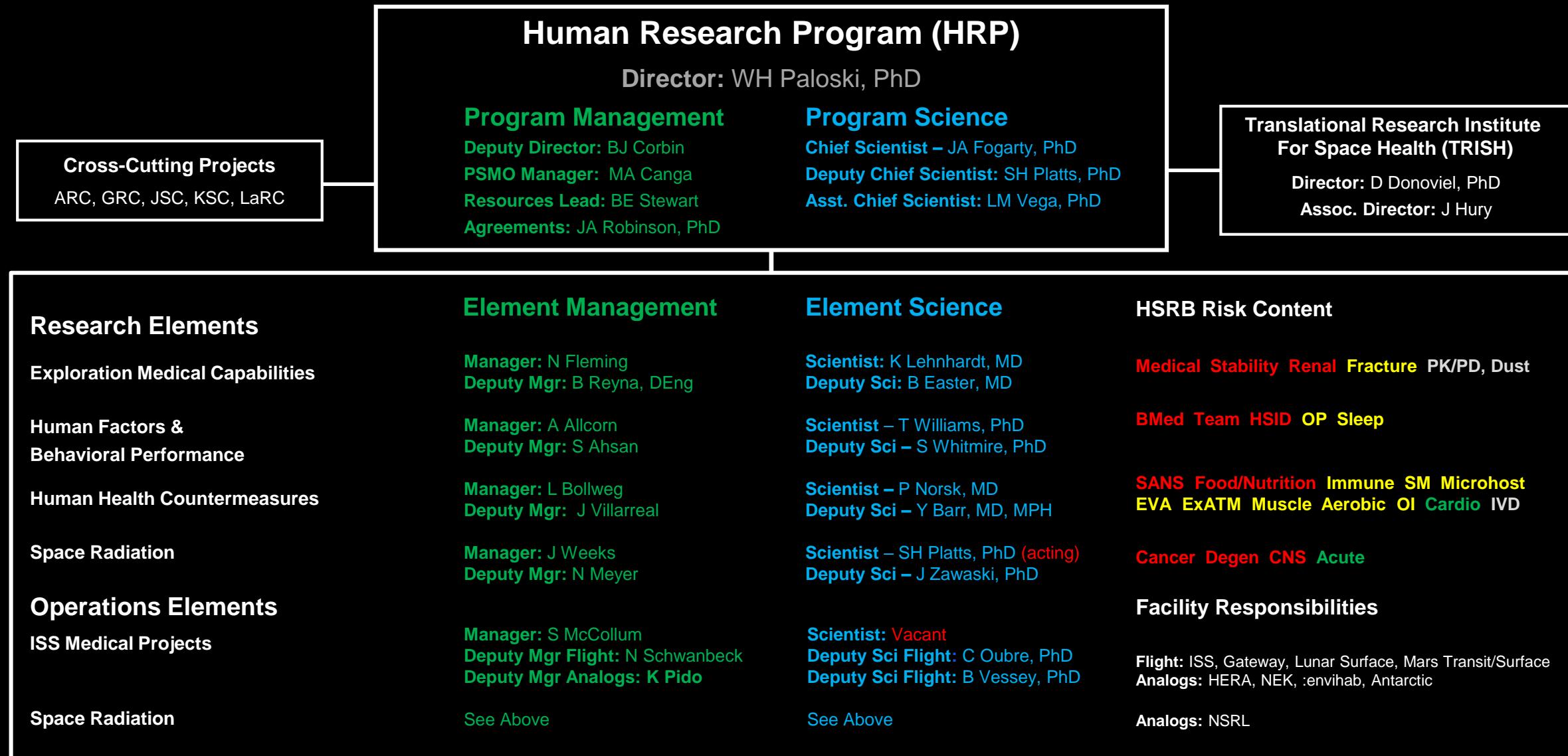
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<span style="background-color: red; width: 10px; height: 10px; display: inline-block;"></span>	High LxC

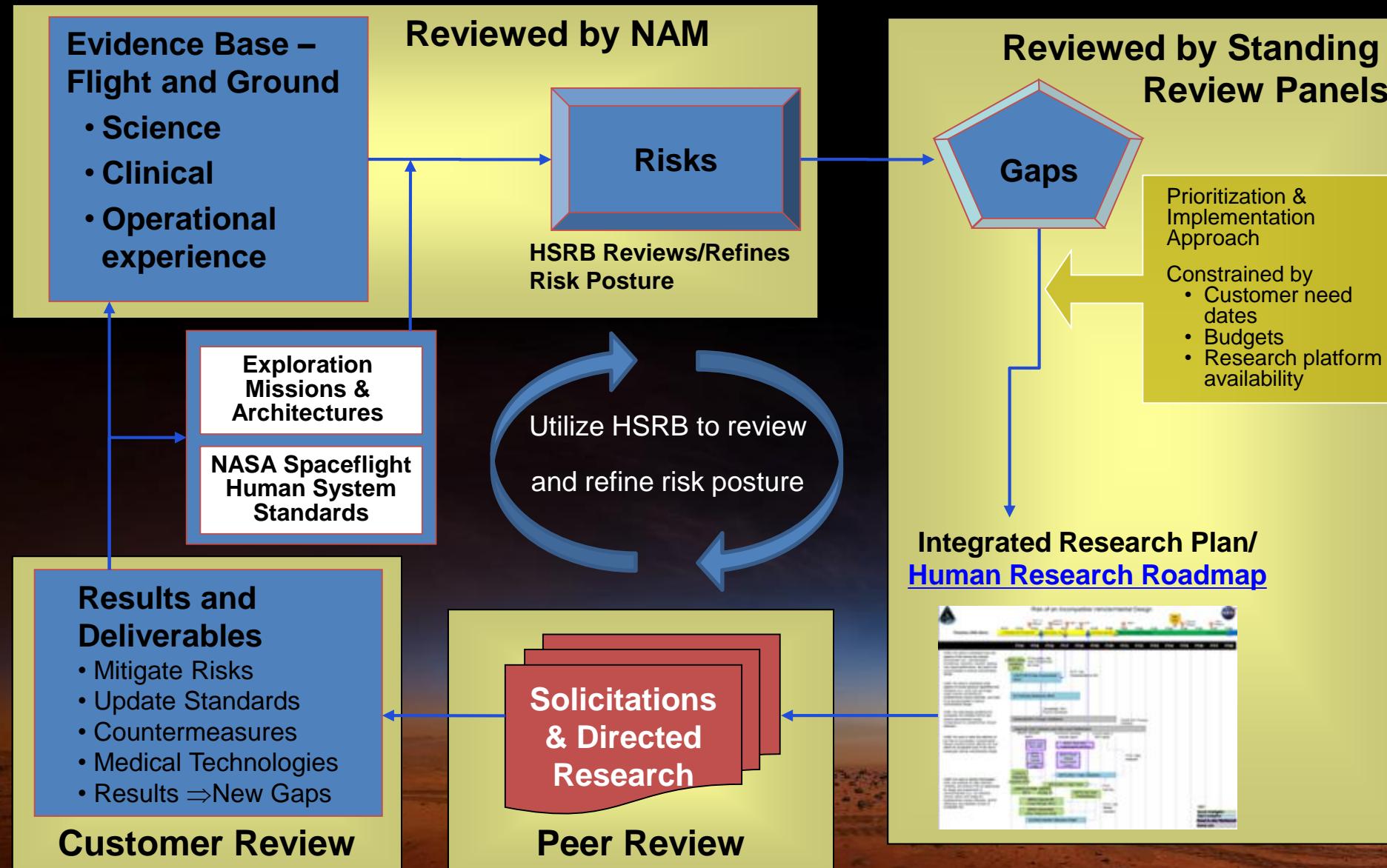
# HRP Integrated Path to Risk Reduction (Mars DRM)



# HRP Functional Organization



# Continuous Review & Evaluation of Priorities



# HRP MAJOR CHANGES 2019-2020



## Goal: position HRP to respond to changes in Exploration Planning (once solidified)

- Work *cross-element* and *cross-platform* to develop and validate strategic plans for each risk
- Consider how emerging exploration plans can best be used to:
  - relieve schedule for previously accelerated research areas
  - reinitiate delayed research with surface operations impacts
- Consider how emerging opportunities (e.g., Innovative use of ISS & CCP, ISS extension, Commercial LEO, lunar surface operations, etc.) can enhance risk reduction strategies. Incorporate new opportunities, as appropriate.
  - *LEO Transition Philosophy*: if it can be done in LEO, plan it in LEO, but do on ISS before 2024 if possible
- Assume 1-year Missions (1 year/6 months/6 week mission cadences) begin in 2021 and continue for 5 years.
- Update all ground analog needs to optimize risk mitigation outcomes
- Begin updating Gateway & Lunar Surface plans
  - Fold all required CTO's into baseline schedule and update tasks on Gateway that do not require "payload" capabilities
  - Identify as tasks on Gateway that would require "payload" capabilities (hardware or mass not part of the CHP system)



# HRP Guidance Regarding 2017 Risk Strategy Changes

## Accelerated Research areas from 2017 that are **eligible for schedule relief**:

- Radiation risks having potential in-mission consequences (CNS, Cardio)
- VIIP, Behavioral Health (BMED, Team), Food & Pharmaceutical Stability
- Autonomous medical operations (Inflight Medical Conditions)
- Integrated food/micro-host/immune system

## Delayed Research areas from 2017 that are **eligible to be re-initiated**:

- Research having surface operations impacts (EVA, DCS, Hypobaric Hypoxia, Sensorimotor)

## Delayed Research areas from 2017 that **should not be re-initiated at this time**:

- Long-term cancer risk (should continue to be delayed pending current research results in light of Potomac Institute Studies)

## Research Brought to Orderly Close During 2017, that **should not be re-initiated**:

- ~~Bone, Muscle and Aerobic research~~
- ~~Sleep Loss, Orthostatic Intolerance, Cardiac Rhythm~~
- ~~Concern of IVD Damage and Effects of Medication~~
- ~~Digital Astronaut~~
- ~~HZETRN/OLTARIS fine-tuning and/or future development~~

# ISS: Space Platform for HRP Studies





# ISS Utilization



## International Space Station

- ❖ Critical to understanding and mitigating 20 of the 25 exploration human risks/concerns
- ❖ Important test bed for space biomedical technology



## Standard Measures Project

- ❖ Implementation began with Increment 57/58
  - First in-flight sample return (55S)
  - Completed 57S inflight BDC, initiated 57S post-flight BDC
  - Completed 59S & 61S pre-flight BDC, initiated 62S pre-flight BDC
  - Enrolled UAE spaceflight participant, planned pre/post-flight BDC (direct return to GCTC)
  - Enrolled 58S 1YM crew (inflight re-pitch), initiated inflight BDC
  - Received approval to pitch remaining 2 Boeing CFT crewmembers
- ❖ Provides a consistent method to evaluate countermeasures
- ❖ Provides comparison between 6-month & 1-Year Missions



## Integrated One-Year Mission Project

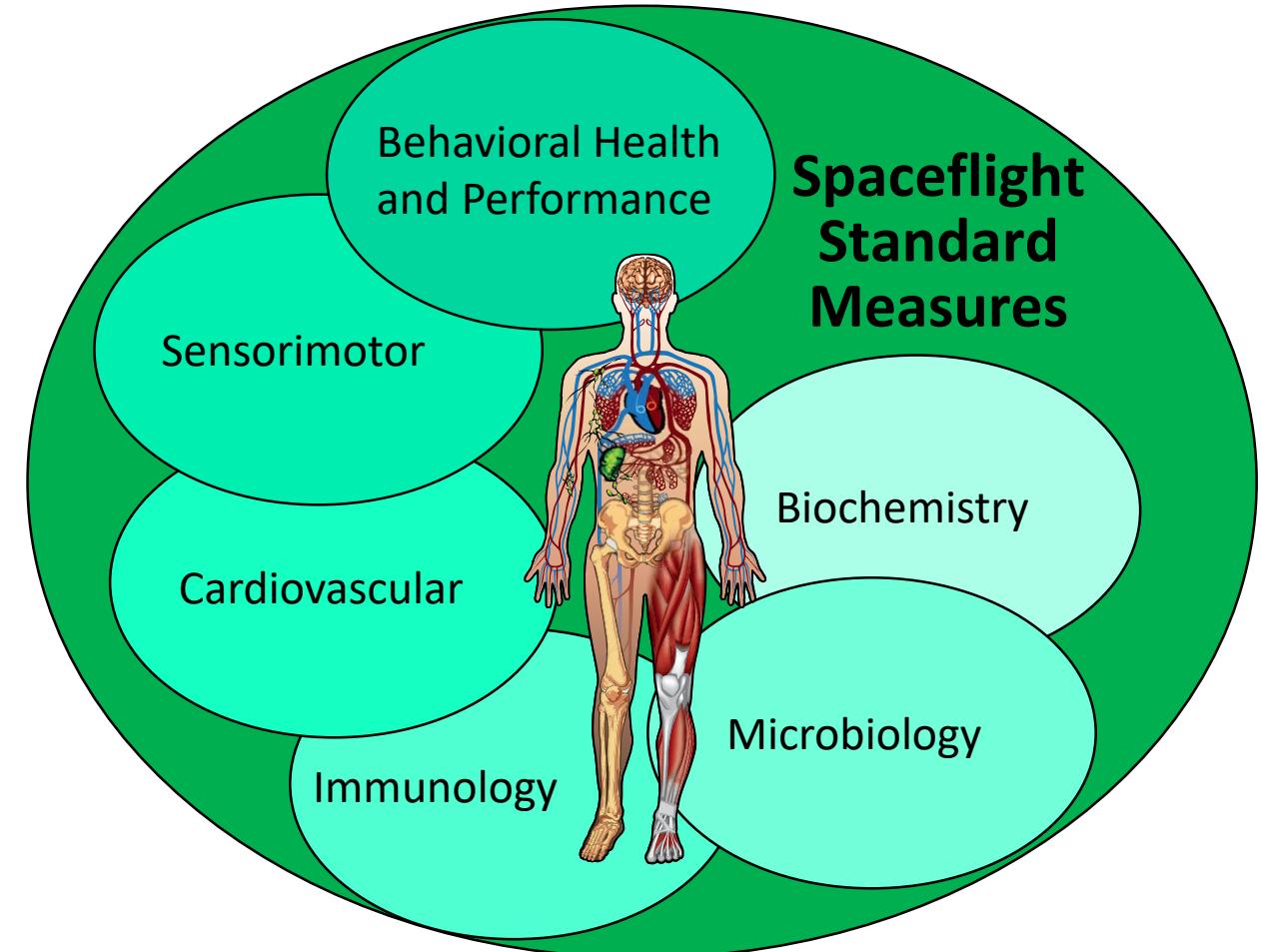
- ❖ In 2015, first 1YM mission with one cosmonaut and one astronaut
- ❖ Late 2020, HRP will begin testing 10 more 1-year mission participants
- ❖ IWG held July 2019

# Spaceflight Standard Measures



## Objectives

- To ensure that a minimal set of measures, relevant to human spaceflight risks, is consistently captured from crewmembers until the end of the ISS
- The data from these measures will be placed in an archive managed by HRP and can be made available to studies via data sharing agreements
- ***Spaceflight Standard Measures*** will constitute a database for:
  - Providing context for data acquired by concurrent experiments
  - Supporting or developing hypotheses
  - Evaluating the effectiveness of various in-flight countermeasure profiles
  - Comparing population responses to various mission durations (6 weeks, 6 months, 1 year)



# Spaceflight Standard Measures (ISS 6-month missions)



Pre-flight	In-flight	Post-flight
Actigraphy w/ sleep logs (2 weeks each) (L-270, L-180)	Actigraphy (continuous)	Actigraphy w/ sleep logs (2 weeks) (R+0)
Personality Survey (anytime preflight)	Sleep Quality/Team Questionnaire (monthly)	Cellular Profile Survey (R+15)
Cognition (L-120 fam, L-90)	Cognition (FD30 & R-30)	Cognition (R+10, R+30)
Cellular Profile (ambient blood, saliva) (L-270, L-90)	Cellular Profile (ambient blood, saliva) (Early mission vehicle return, R-0)	Cellular Profile (ambient blood, saliva) (R+30)
Biochemical Markers (blood, urine) (L-180)	Biochemical Markers (blood only) (FD30, R-30)	Biochemical Markers (blood, urine) (R+30)
Microbiome (body, saliva, fecal) (L-90)	Microbiome (body, saliva, fecal) (FD30, R-30)	Microbiome (body, saliva, fecal) (R+30)
Carotid Intima-Media Thickness (cIMT) (L-180)	N/A	Carotid Intima-Media Thickness (cIMT) (R+5, R+30)
Sensorimotor Measures (L-225 fam, L-90)	N/A	Sensorimotor Measures (R+0 at landing site, R+0 at JSC, R+9)

Crew time: 6.83 hrs

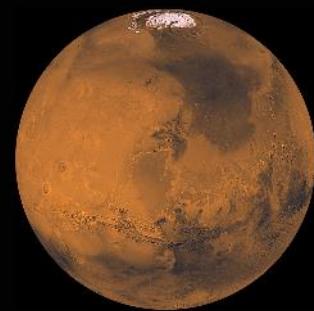
Crew time: 15.25 hrs

Crew time: 5.25 hrs



# THE INTEGRATED 1-YEAR MISSION PROJECT (i1YMP)

*i1YMP is a  
stepping stone to  
Mars.*



- Seeks to **bridge the gap** in knowledge and answer questions about the physiological and psychological adaptations of long-duration spaceflight
- Abundant data exists for two weeks and six months in space; little exists **beyond one year**
- We have **more to learn...**

# Spaceflight Standard Measures (SSM)



*i1YMP is built on the foundation of Standard Measures - a cross disciplinary approach to measuring the effects of spaceflight on the human body.*



- What's "normal" in space?
- **Battery of tests**, performed at consistent intervals, to monitor astronaut health and performance
- **Individuals adapt** to situations and environments at different rates.
  - Preflight, NASA takes SSM to obtain reliable benchmarks of an astronauts' "normal" health and performance
- Monitors the **effectiveness and interactions of countermeasures**
- **Provides a consistent understanding of how the human body changes in space.**

# Approach



- **NRA: HERO 80JSC017N0001-BPBA App C; Topic #1: Analyses of the Temporal Nature of Human Adaptation to Long-Duration Low-Earth Orbit Missions Virtual NASA Specialized Center of Research (VNSCOR)**
  - Proposals submitted April 2018, selection October 31, 2018
  - 10 NASA and 4 IP (CSA, DLR, and CNES ) experiments were selected for definition phase
- **NRA: HERO 80JSC017N0001-HCHFBP App D; Topic 1: Effects of Spaceflight Durations up to One Year in Low Earth Orbit on Cardiovascular Structure and Function in Astronauts**
  - Additional solicitation to complete intended interdisciplinary complement
  - Proposals submitted July 2019, selection anticipated December 2019
- **Complement will leverage Standard Measures sample collection and data**
- **Proposals will be integrated to become a single research complement collecting multi-disciplinary data targeting 10 one-year, 10 six-month missions and 10 short-duration missions**

# i1YMP Selected Studies



## Human Performance Integration

**Norcross** - Validation of Fitness for Duty Standards Using Pre- and Post-Flight Capsule Egress and Suited Functional Performance Tasks in Simulated Reduced Gravity

**Downs** - Temporal changes in astronauts muscle and cardiorespiratory physiology pre, during, and post spaceflight (CM efficiency and subsystem interrogation)

**Shelhamer** - Assessment of Otolith Function and Asymmetry as a Corollary to Critical Sensorimotor Performance in Missions of Various Durations

**Reschke** - Neuro-Vestibular Examination During and After Spaceflight (Vestibular Health)

**Bouxsein** - Time Course of Spaceflight-Induced Adaptations in Bone Morphology, Bone Strength and Muscle Quality

**Boyd** - *The effect of long-duration space flight on bone microarchitecture and strength using three-dimensional high-resolution imaging (CSA)*

**Romanillo** - Evaluating Resistive Exercise as a Long-term Countermeasure for Spaceflight-induced Bone Loss Using Calcium Isotopes

**Liphardt** - *Joint health during a 1-year mission to the ISS - an assessment of exploration relevance (DLR)*

**Hughson** - *Manifestations of spaceflight-induced sub-clinical cardiovascular disease as a long-term health risk (CSA Vascular)*

**Arbeille** - *Preventive Medical Ultrasound Investigation of Organs Potentially Affected by Prolonged Exposure to Microgravity (CNES)*

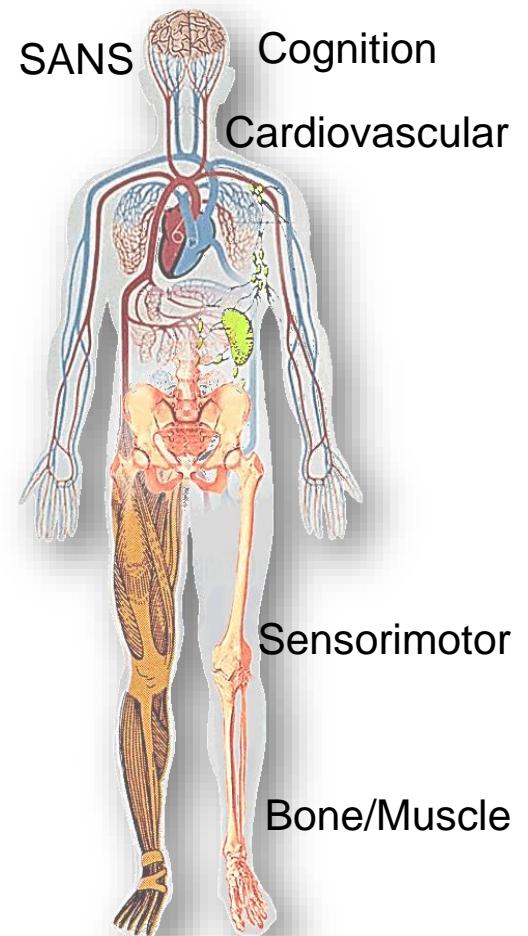
**Bailey** - *Telomeres and the One Year Mission Project*

## Cranial Optical Axis

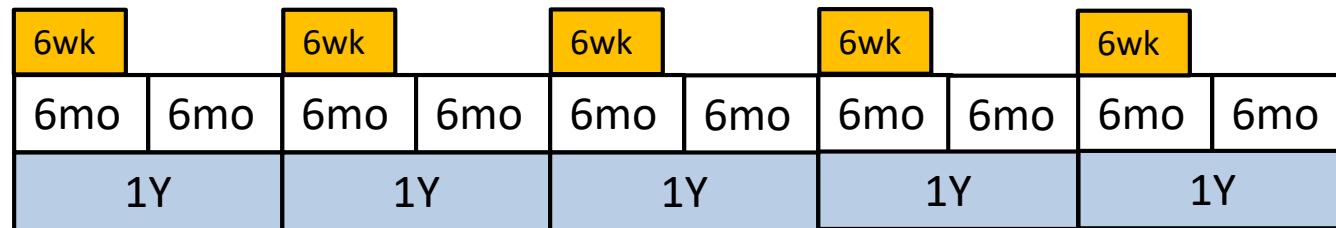
**Macias** - Investigating Structure and Function of the Eye (SANS)

**Basner** - Temporal Nature of Cognitive and Visuospatial Brain Domain Changes during Long-Duration Low-Earth Orbit Missions

**Zhang** - Characterizing the Baselines of Sleep Quality, Cognitive / Operational Performance, Immune Function, and Intracranial Fluids for Deep Space Expeditions (SANS/Immune)



# i1YMP Overview



Multi-disciplinary science measures will be combined into **one research complement** and all measures will be collected for each participating crew member

# ISS as a Deep Space Analog—ISS/HRP Accepted Use Cases FY19+

## Transit Durations (1-Year Missions):

- Science Selected and will begin in 2020, 10x
- Longer durations do not provide additional insights into performance after landing on Mars

## Sensorimotor performance for deconditioned landings of long-duration crew:

- Quick-start of crew tele-robotic performance capabilities and fine motor skills on Kazakhstan returns (started June 2019)
- 1-2 day landing simulation on Boeing CST-100 beginning on 3rd landing (2021), 4x

## Medical autonomy:

- Quick-start contingency operations without ground support (Spring 2020)
- 1-2 day medical simulation on orbit (2020), 4x

## Operations Autonomy with Comm Delay:

- Comm delay capability available beginning in September 2019
- 1-2 week simulation to follow in 2022, in existing volumes
- *30-day minimum and up to 1-year studies in smaller volumes desired but very operationally challenging for ISS with significant impacts on other users and partners; possible LEO Commercial module use*



# Simulating Exploration Stressors on Earth

Isolation & Confinement,  
Distance From Earth



Hostile Environment,  
Isolation & Confinement,  
Distance From Earth



Radiation



Altered Gravity,  
Hostile Environment





# Isolation Analogs



## HERA

### Campaign 5 (2019/20)

**Four 45-day missions with a crew of 4: 13 HRP studies + 1 RUS/NASA study**

- ❖ Mission 1: ingress Feb 16; egress Apr 1
- ❖ Mission 2: ingress May 24; egress Jul 8
- ❖ Mission 3: ingress Aug 16; egress Sep 30
- ❖ Mission 4: ingress Jan 25; egress Mar 9 (2020)

**Campaign 6 (2020)** – Four 45-day missions with a crew of 4; Human Capabilities Assessment for Autonomous Missions (HCAAM)

- ❖ Autonomy requirements and science implementation planning underway
- ❖ IWG – 15 May 2020



HERA

## Antarctica

### Partnership between NASA and the US National Science Foundation (NSF)

- ❖ Winter-over 2019: Subject recruitment and BDC complete; Scale and Crews study began 2 May
- ❖ Winter-over 2020: Joint planning and implementation of winter-over studies, including Palmer Station – Palmer Pilot study submitted for review; accepted for implementation



Palmer Station



Admumson-Scott Station

## NEK

### Partnership between NASA and IMBP

- ❖ SIRIUS-19 (4-month) mission ingress Mar 19; egress 17 July – COMPLETE
- ❖ SIRIUS-20 (8-month) mission planning initiated; draft schedule in work (mission start Fall 2020)





# :envihab and NSRL



## :envihab

### AGBRESA: 2x60-day AG Bedrest – Joint ESA/NASA

- ❖ 60-day bed rest studies using the :envihab centrifuge (:envifuge) to study physiological and behavioral responses in humans to intermittent artificial gravity during 60-days HDT Bed Rest
- ❖ 3 NASA studies, 7 ESA studies
- ❖ Additional measures added for SANS due to early VaPER results
  - First Campaign: ingress Mar 26; egress Jun 26
  - Second Campaign: Ingress 3 Sept – CO2 Dose Response and SANS CMs

### Un-named: 5x30-day Bedrest+CO<sub>2</sub>+Countermeasures– in Planning



## NSRL

### Summer Run (NSRL-19B)

- ❖ Began 14 May; ended 26 June. Final report received July.
- ❖ 241 hours of total beam time

### Fall Run (NSRL-19C)

- ❖ Began late Sept; will end early Jan 2020

### FY20 NSRL Planning (NSRL-20A/B/C)

- ❖ Call for proposals released 12 June; proposals received 18 July



# Flight & Flight Analog Research Plans



**Lunar Vicinity**

- Orion crew**: EM2, EM3 (ESPRIT UMM), EM4 (Hab), EM5, EM6 (US Hab), EM7 (AL), EM8, EM9.
- Gateway Uncrewed**: 10-11 m intervals between 2024-2030.
- Gateway Assembly/Cargo**: ~204 d intervals between 2024-2030.
- NHRO/Gateway Crewed**: 21-30d, 26-40d, 26-40d, 40-60d, 40-60d, 40-60d, 40-60d.
- Lunar Surface Crew**: 2-3d, tbd days, tbd day.

**LEO**

- ISS w/ Private Module**: 1YM2 intervals (10-11 m).
- LEO Commercial**: 1YM2 intervals.
- ISS ICE**: 2d med, 2d, 2d med, 2w ICE, 2w ICE, 30d ICE, 30d ICE, 30d ICE, 30d ICE \* in discussion with ISS.
- CST Surface Analog**: 6wk, 6wk.

**Radiation**

- NSRL (DoE)**: pink boxes.

**Isolation**

- HERA (NASA)**: blue boxes, C5, C6 intervals.
- NEK (IBMP)**: green boxes.

**Environment**

- Antarctica (NSF)**: yellow boxes for McMurdo, South Pole, and Palmer.
- AGBRESEA**: blue boxes.
- VaPER 2 + CO2 Dose Response**: blue boxes.
- envihab (DLR)**: blue boxes.

# HRP FY19/20 Research Acquisition Status



HERO	Appendix	Release Date	Step 1 Received	Step 2 Received	Peer Review Date	Selection Date	# Planned Awards	# Actual Awards	Notes		
2017	D	3/30/18	27	11	Oct-18	Feb-19	3	3	HHC and HFBP topics		
2018	A	7/31/18	44	26	Feb-19	Apr-19	4-5	5	Flagship – HFBP, HHC and Radiation topics		
	B	7/31/18	108	45	Feb-19	Apr-19	8-10	7	Omnibus		
	C	11/30/18	28	15	Jun-19	Aug-19	2-4	4	HHC/SANS (delayed due to Furlough)		
	D	3/29/19	32	23	Sep/Oct-19	Dec-19	2	TBD	Cardiovascular (i1YMP) and Team		
2019	A	7/31/19	56	TBD	Feb-20	Apr-20	4-5	TBD	Sensorimotor and SR Tissue Sharing		
	B	7/31/19	162	TBD	Feb-20	Apr-20	4-5	TBD	Omnibus		
TRANSNATIONAL RESEARCH INSTITUTE FOR SPACE HEALTH				Title	Release Date	Step 1	Step 2	Selection Date	# Planned Awards	# Actual Awards	Notes
2018	TRI-IND-1801 Industry Solicitation released via the Consortia for Improving Medicine with Innovation & Technology (CIMIT)				03/08/2018	16	8	07/06/18	4-5	3	Emerging point-of-care technology; Algorithms to diagnose in-flight conditions
	Biomedical Research Advances for Space Health (BRASH 1801)				03/16/2018	126	82	11/29/2018	6-12	15	Predictive algorithms of health, behavior & medical events; resilience through nucleotide therapy; shielding medications
	2018 TRISH Postdoctoral Fellowship Solicitation TRISH-RFA-1802-PD				5/21/18	N/A	11	11/1/2018	4	2	Postdoctoral Fellowships
	TRISH-FLEX-1801 – Human Factors Augmenting Research (HFAR)				09/28/18	N/A	11	01/31/19	5 (\$100K ea)	4	Synergy projects focusing on human center design; collaborations w/ TRISH PIs
2019	2019 TRISH Postdoctoral Fellowship Solicitation TRISH-RFA-1901-PD				10/30/18	N/A	25	July 2019	6	6	Postdoctoral Fellowships
	TRI-IND-1901 Industry Solicitation released via the Consortia for Improving Medicine with Innovation & Technology (CIMIT)				12/17/18	N/A	29	04/01/19	5 (\$50K ea) 5 (\$250K ea)	5 (\$100K ea) 4 (\$250K ea)	Ophthalmic imaging; physical health surveillance; gaming behavioral tools; advanced medical training; advanced human-computer interfaces; lab tests to go; AI-supported medical diagnostics; onboard manufacturing of medications
	Biomedical Research Advances for Space Health (BRASH 1901)				12/17/18	116	75	Oct.2019	~6 (\$400K/ea)	6	Ophthalmic imaging; physical health surveillance; enriched spaceflight environments; augmented medical knowledge; personalized detection of space radiation; just-in-time medications

# TRISH Project Example 1



## Multipurpose ultra-portable ultrasound imager with artificial intelligence (AI) capability

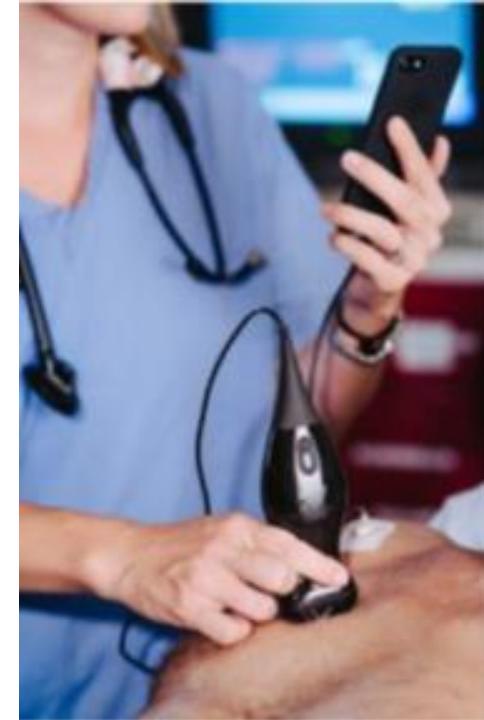
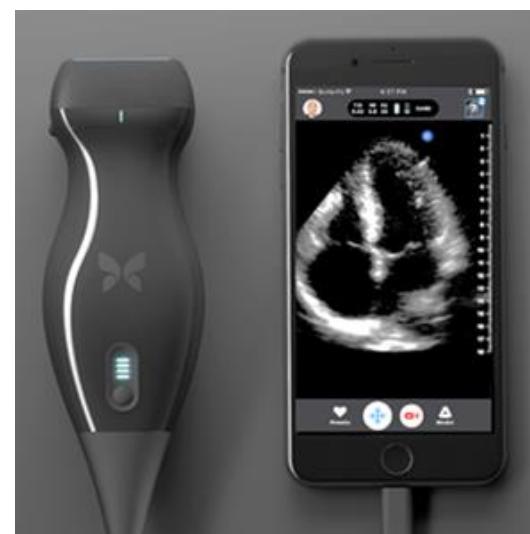
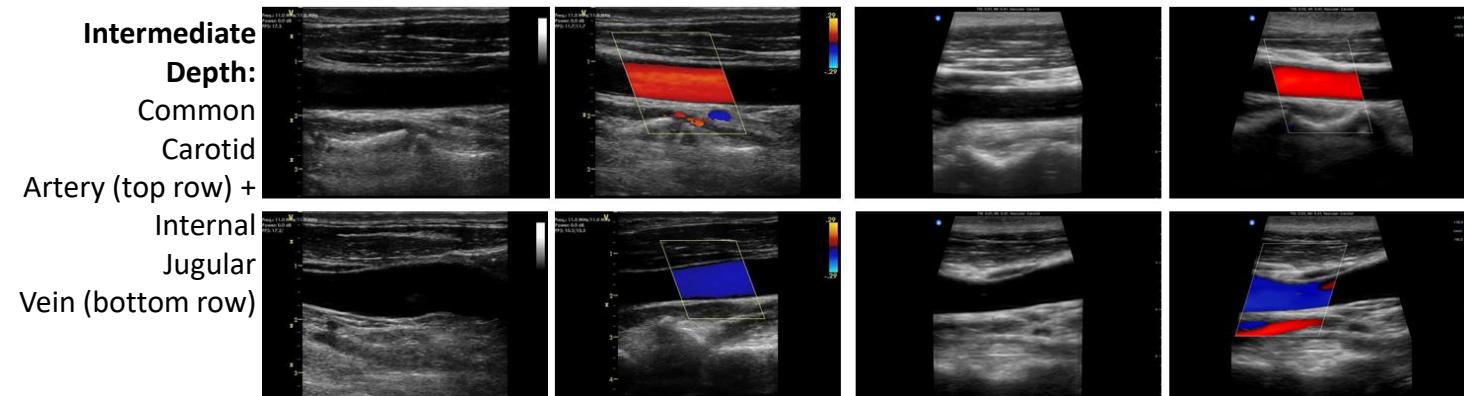
PI: Ashot Sargsyan, KBR, Inc.

### Butterfly iQ Ultrasound:

- Ground-based comparison against ISS Ultrasound2 (GE Vivid Q) showed comparable clinical performance but with significant reduction in mass, volume, power operational footprint
- Highly configurable all in one probe and device for multiple organ scans
- Demonstrated end-to-end data connectivity and integration with future planned data management infrastructure to enable artificial intelligence capabilities allowing for **in-real time user guidance in acquiring scans** and autonomous diagnosis
- Anticipated launch on SpX19 to support ISS medical operations

• GE Vivid-q

• Butterfly iQ



Breakthrough  
CMUT  
Technology

# TRISH Project Example 2



## Irradiated Mice with Humanized Hematopoietic System and Novel Bio-dosimetry Approach for Radiation Damage

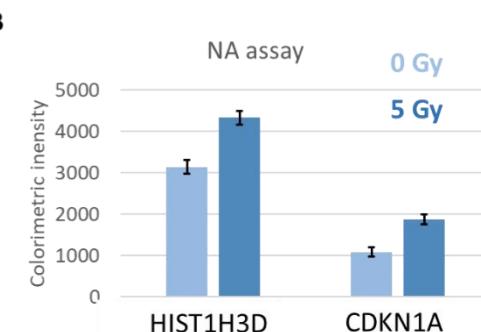
Dr. Fred Zenhausern (U. of Arizona) working together with Dr. Chris Porada (Wake Forrest)

### Innovation Through Synergy:

- TRISH is funding Dr. Porada to develop a mouse model with a “humanized” blood system and to identify biomarkers of radiation exposure.
- Dr. Zenhausern was supported by a **\$25K TRISH Synergy Grant** to test a technology that allows for a multiplexed detection of biomarkers - providing a nucleic acid-based radiation biodosimeter using small blood volumes.
  - Completed the development and miniaturization of a Vertical Flow paper-based Platform (VFP).
  - Tested data analytics software that detects gene expression changes after 5Gy-irradiation in real time.



The device is portable and can 1) connect to a mobile phone to perform blood analysis and 2) store data



Successful biomarkers detection after radiation exposure

# TRISH Project Example 3



## Novel Human Organs-on-a-Chip Models: Testing Space Radiation Effects and Countermeasures

### Impact of Radiation Exposure on a 3D *In-Vitro* Model of Human Bone Marrow

PI: Steven George, M.D., Ph.D., University of California, Davis

Develop a dose-response curve between ionizing radiation (proton) and normal biological function of human bone marrow (leukocyte production) as well as compare to known results from a number of *vivo* studies in different animal species

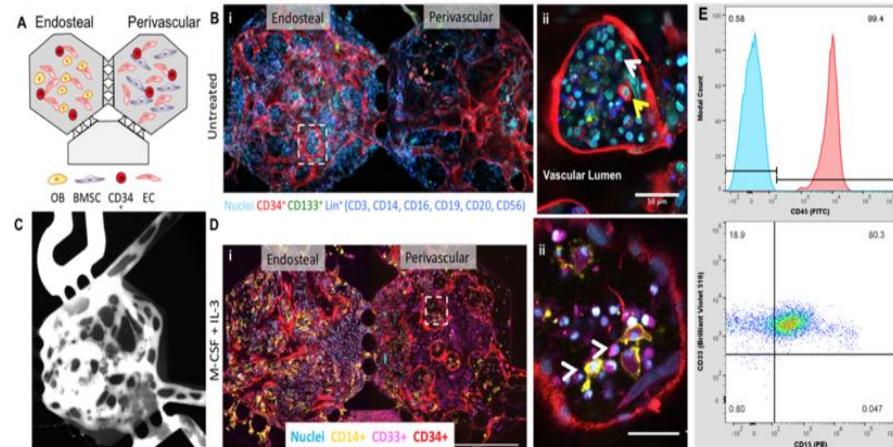
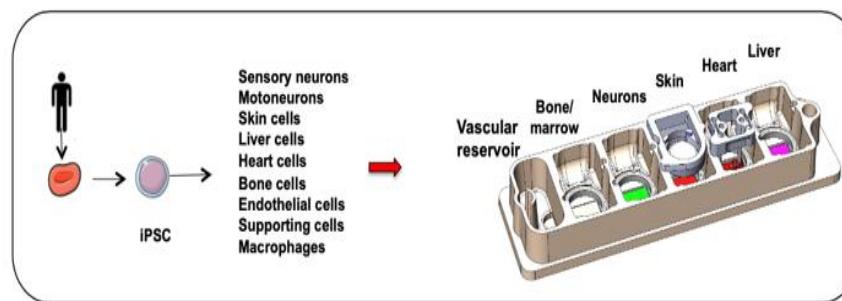


Figure 4. 3D *in vitro* model of human bone marrow including egress of mature neutrophils. A) conceptual design of

Figure 1: George, S (2019).



### Organs on a Chip Platform for Assessing Cosmic Radiation Damage

PI: Gordana Vunjak-Novakovic, Ph.D., Columbia University

This project will utilize a neutron radiation source to study the impact of exposure to the human heart, liver, bone, bone marrow, sensory neurons, and innervated skeletal muscle derived from a single human iPS cell line

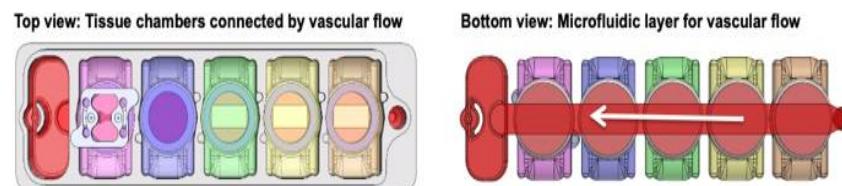


Figure 2: Vunjak-Novakovic, G (2019).

# TRISH Project Example 4



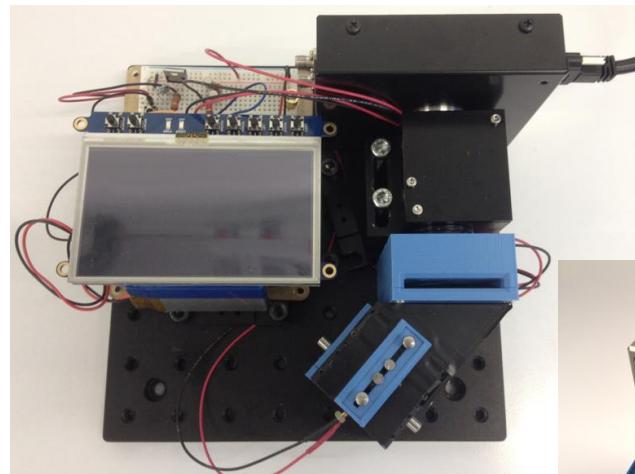
## Miniaturized Diagnostics Platform for Health Assessment

PI: Luc Gervais 1Drop Diagnostics, Inc.

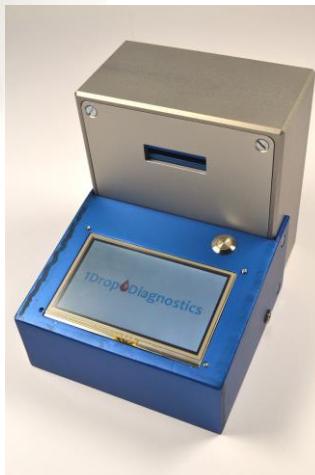
### Innovation Through Partnership with a Small Company:

1 drop of blood; 64 tests in one biochip; optimized biochip manufacturing; small device

Will be tested in extreme environment; secured a ISS National Lab flight opportunity



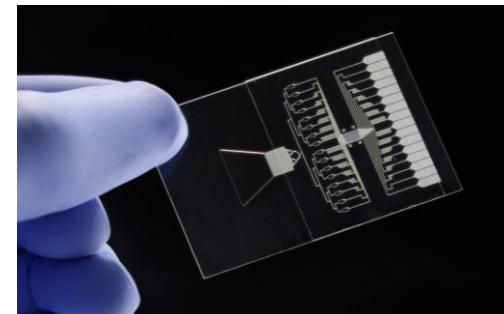
Original 1Drop prototype to measure CV ischemia markers



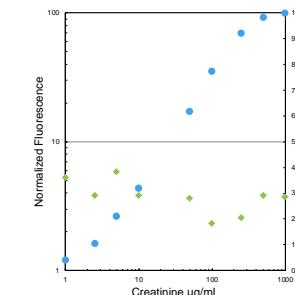
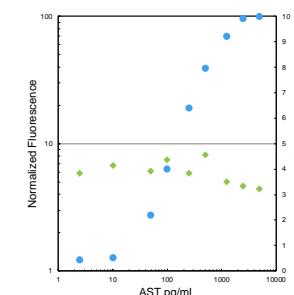
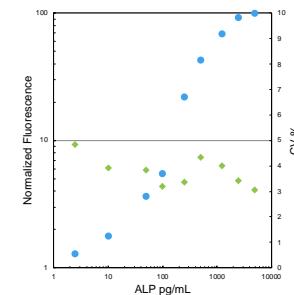
With TRISH funding



64-channel cartridge



Kidney and liver function markers added (AST, ALT, Creatinine)  
Titration curves below:



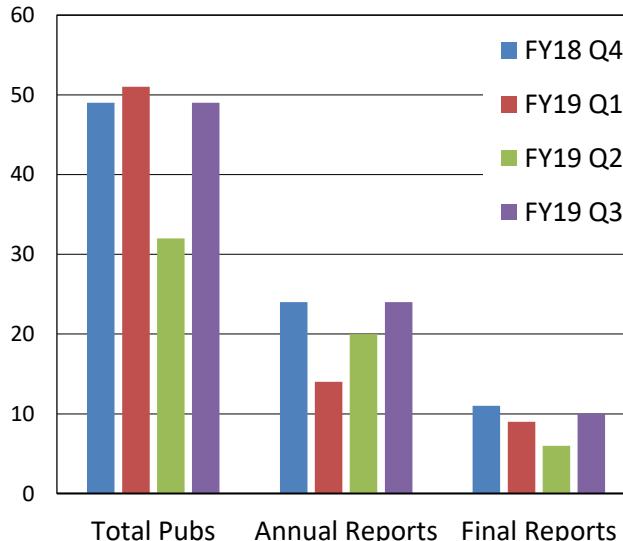
Miniaturized and refined device



# HRP Publication Metrics – (7/1/18- 6/30/19)



## Number of Publications



## HRP-funded research (FY19)

247 Research Grants

198 Principle Investigators

97 Institutions in 28 states

## High-Impact Factor Publications – JIF > 5

1. Garrett-Bakelman FE, Darshi M, Green SJ, Gur RC, Lin L, Macias BR, et al. The NASA Twins Study: A multidimensional analysis of a year-long human spaceflight. *Science*. 2019 Apr;364(6436).
2. Dionisio-Santos DA, Olschowka JA, O'Banion MK. Exploiting microglial and peripheral immune cell crosstalk to treat Alzheimer's disease. *J Neuroinflammation*. 2019 Apr;16(1):74.
3. Kumar S, Suman S, Fornace AJ, Datta K. Intestinal stem cells acquire premature senescence and senescence associated secretory phenotype concurrent with persistent DNA damage after heavy ion radiation in mice. *Aging (Albany NY)*. 2019 Jun;11(12):4145–58.
4. McHill AW, Hull JT, Cohen DA, Wang W, Czeisler CA, Klerman EB. Chronic Sleep Restriction Greatly Magnifies Performance Declements Immediately After Awakening. *Sleep*. 2019 May;42(5):zsz032.
5. Patel R, Zhang L, Desai A, Hoenerhoff MJ, Kennedy LH, Radivoyevitch T, et al. Mlh1 deficiency increases the risk of hematopoietic malignancy after simulated space radiation exposure. *Leukemia*. 2019 May;33(5):1135–47.
6. Scott JM, Tucker WJ, Martin D, Crowell JB, Goetchius E, Ozgur O, et al. Association of Exercise and Swimming Goggles With Modulation of Cerebro-ocular Hemodynamics and Pressures in a Model of Spaceflight-Associated Neuro-ocular Syndrome. *JAMA Ophthalmol*. 2019 Jun;137(6):652–9.
7. Pattison PM, Tsao JY, Brainard GC, Bugbee B. LEDs for photons, physiology and food. *Nature*. 2018 Nov;563(7732):493–500. St Hilaire MA, Anderson C, Anwar J, Sullivan JP, Cade BE, Flynn-Evans EE, et al. Brief (<4 hour) sleep episodes are insufficient for restoring performance in first-year resident physicians working overnight extended-duration work shifts. *Sleep*. 2019 May;42(5):zsz041.
8. Deymier AC, Schwartz AG, Cai Z, Daulton TL, Pasteris JD, Genin GM, et al. The multiscale structural and mechanical effects of mouse supraspinatus muscle unloading on the mature enthesis. *Acta Biomater*. 2019 Jan;83:302–13.
9. Graff RM, Kunz HE, Agha NH, Baker FL, Laughlin M, Bigley AB, et al.  $\beta$ 2-Adrenergic receptor signaling mediates the preferential mobilization of differentiated subsets of CD8+ T-cells, NK-cells and non-classical monocytes in response to acute exercise in humans. *Brain Behav Immun*. 2018 Nov;74:143–53.
10. Khera A, Budoff MJ, O'Donnell CJ, Ayers CA, Locke J, de Lemos JA, et al. Astronaut Cardiovascular Health and Risk Modification (Astro-CHARM) Coronary Calcium Atherosclerotic Cardiovascular Disease Risk Calculator. *Circulation*. 2018 Oct;138(17):1819–27.
11. Krukowski K, Grue K, Frias ES, Pietrykowski J, Jones T, Nelson G, et al. Female mice are protected from space radiation-induced maladaptive responses. *Brain Behav Immun*. 2018 Nov;74(106–120).
12. Kumar S, Suman S, Fornace AJ, Datta K. Space radiation triggers persistent stress response, increases senescent signaling, and decreases cell migration in mouse intestine. *Proc Natl Acad Sci USA*. 2018 Oct;115(42):E9832–41.

# Trends, Forecasting Science Needs in HRP



## Autonomous Medical Operations

- Severe mass, power, volume, communication delays/restrictions; no resupply; 4 crewmembers
- Health monitoring, diagnostic capabilities, therapeutic capabilities; in situ analysis, pharmaceuticals, medical disposables, ...

## Behavioral Health and Performance in a Distant, Austere Environment

- Monitoring techniques, intervention techniques
- Human/System Integration maturation; interfaces between humans and intelligent machines

## Radiation Effects

- Translation of results from rodents to humans
- Countermeasures—pharmaceuticals, nutraceuticals, synergies with other stress responses?

## Physiological Effects

- SANS, nutrition, immune function/interactions with microbiome, monitoring, intervention, atmospheric composition
- Countermeasures—exercise, fluid shifting capabilities, pharmaceuticals, nutraceuticals, synergies with other stress responses?

## Synergistic Effects of Multiple Stressors

## Unknown Unknowns

# Challenges of Interest for the Decadal Survey



## HRP R&T Investment Priority Drivers

- Risk Color (HSRB)
- Scientific/technical challenge
- Need date (exploration schedules)
- Facility availability (ISS, HERA, NEK, enviHab, NSRL, Antarctic Stations, Parabolic Flight...)
- Budget availability (OMB, Congress, HEOMD)

## Areas of direct focus for HRP by Decadal Survey

- Insight into novel approaches, analog populations, research communities, etc. would be welcomed and valued

## Space Biology is an important partner to HRP (fundamental science, mechanisms, maturation)

- Today: Microbiome (crew and environment), plants (crops, psychological support), gravity as a continuum
- Future possibilities: Genelab as a repository, Tissue Chip validation, pharmaceutical testing, ...
- This synergistic relationship could be bolstered by recommendations in the Decadal Survey

# Discussion and Q&A

