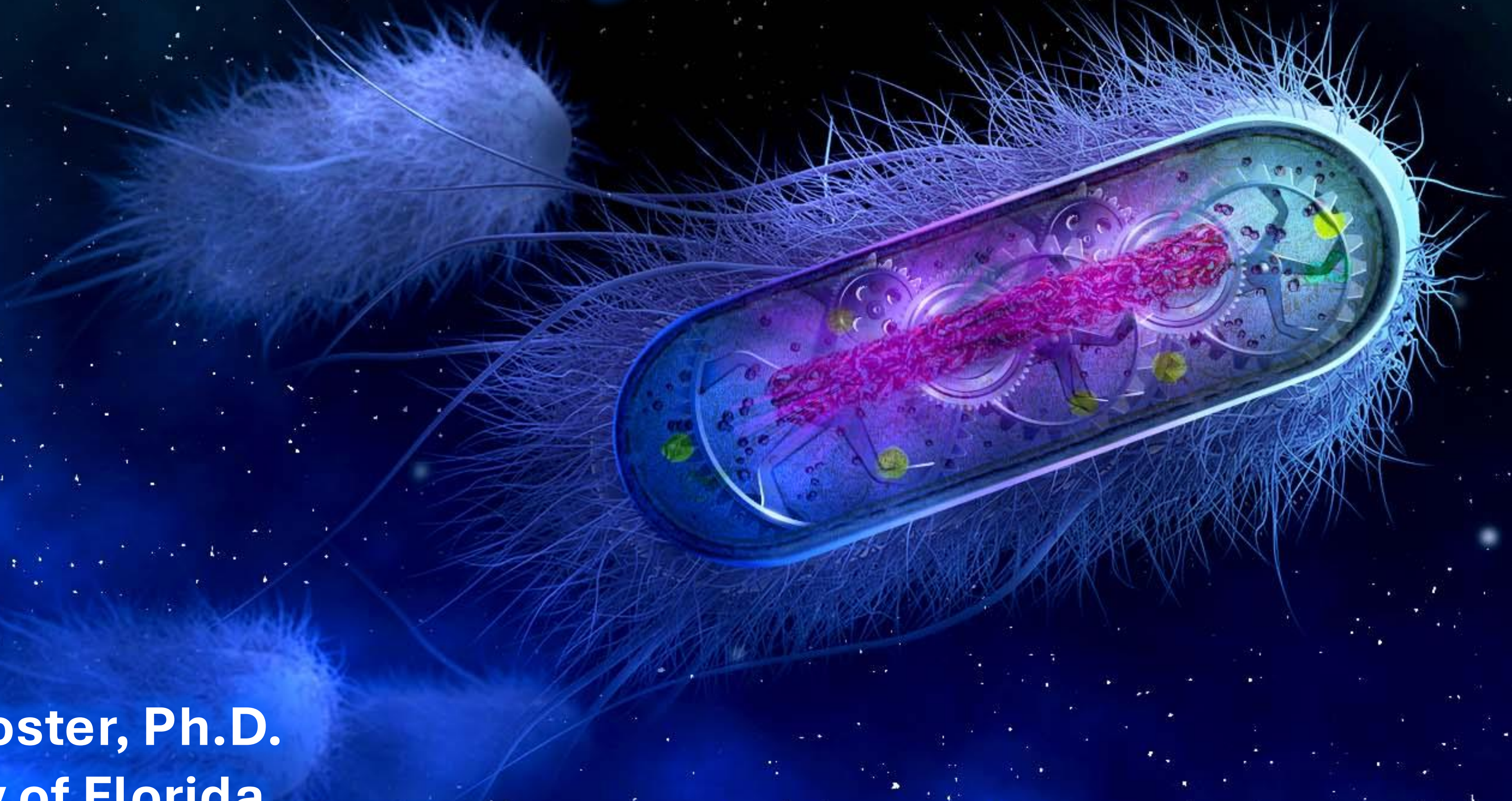
Biomanufacturing: Survival, Utility, and Reliability beyond Earth



Jamie S. Foster, Ph.D.
University of Florida
B-SURE Team Member
jfoster@ufl.edu

B-SURE

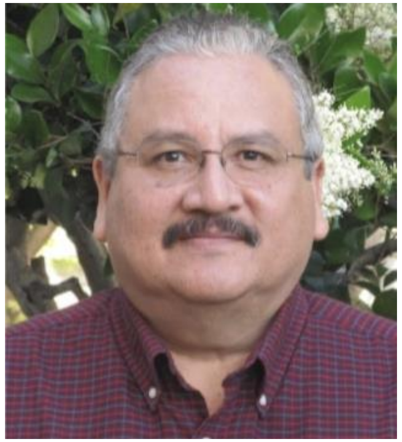
B-SURE Original Team – DARPA Biotechnologies Office

Anne Cheever, Ph.D.
DARPA BTO,
Program Manager

Lenny Tender, Ph.D.
DARPA BTO,
Program Manager

Andrew Younger, Ph.D.
Lead Systems Engineering & Technical Assistance (SETA)

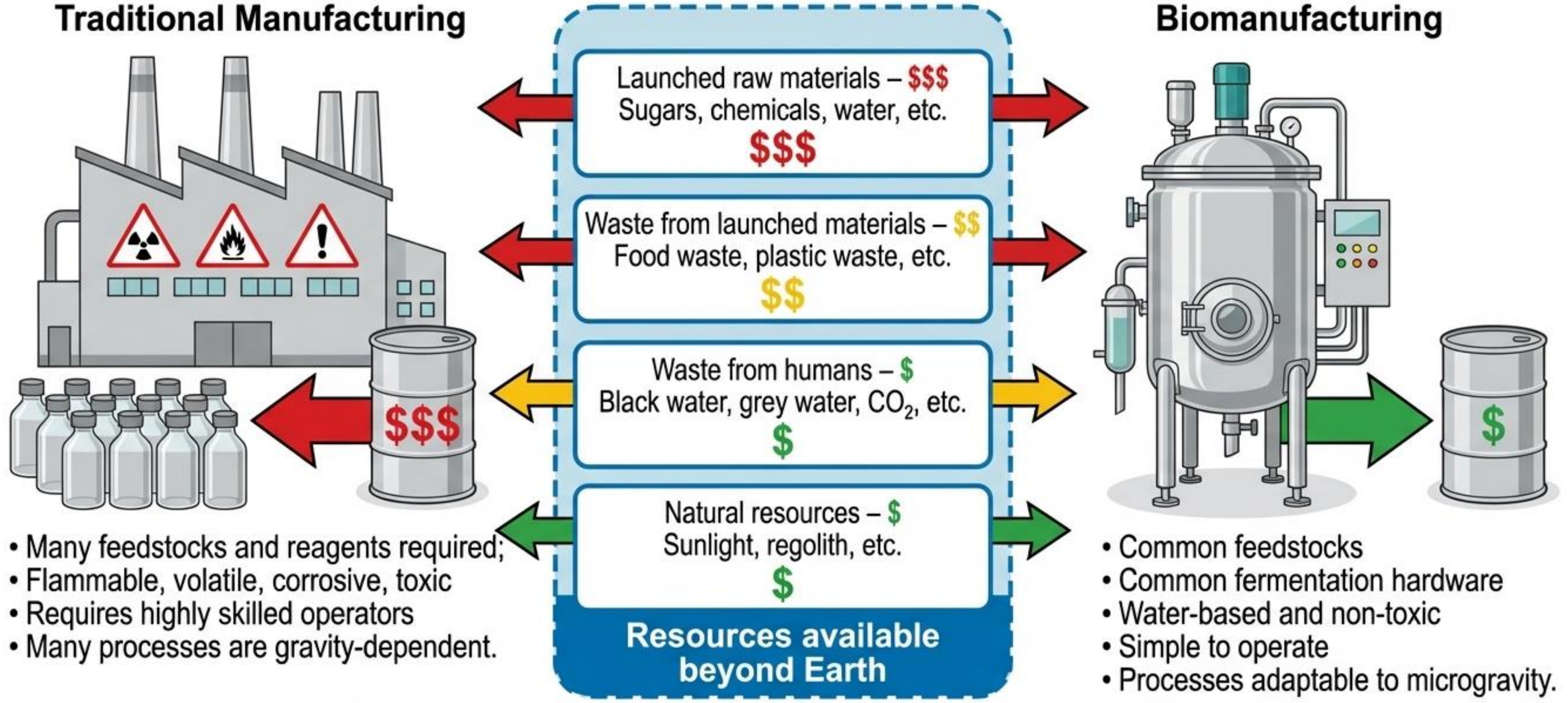
Lianne Parr
DARPA Programmatic & Ethical, Legal, Societal Implications SETA



Ernie Arias
Naval Information Warfare Center (NIWC) Contracting Officer's Representative

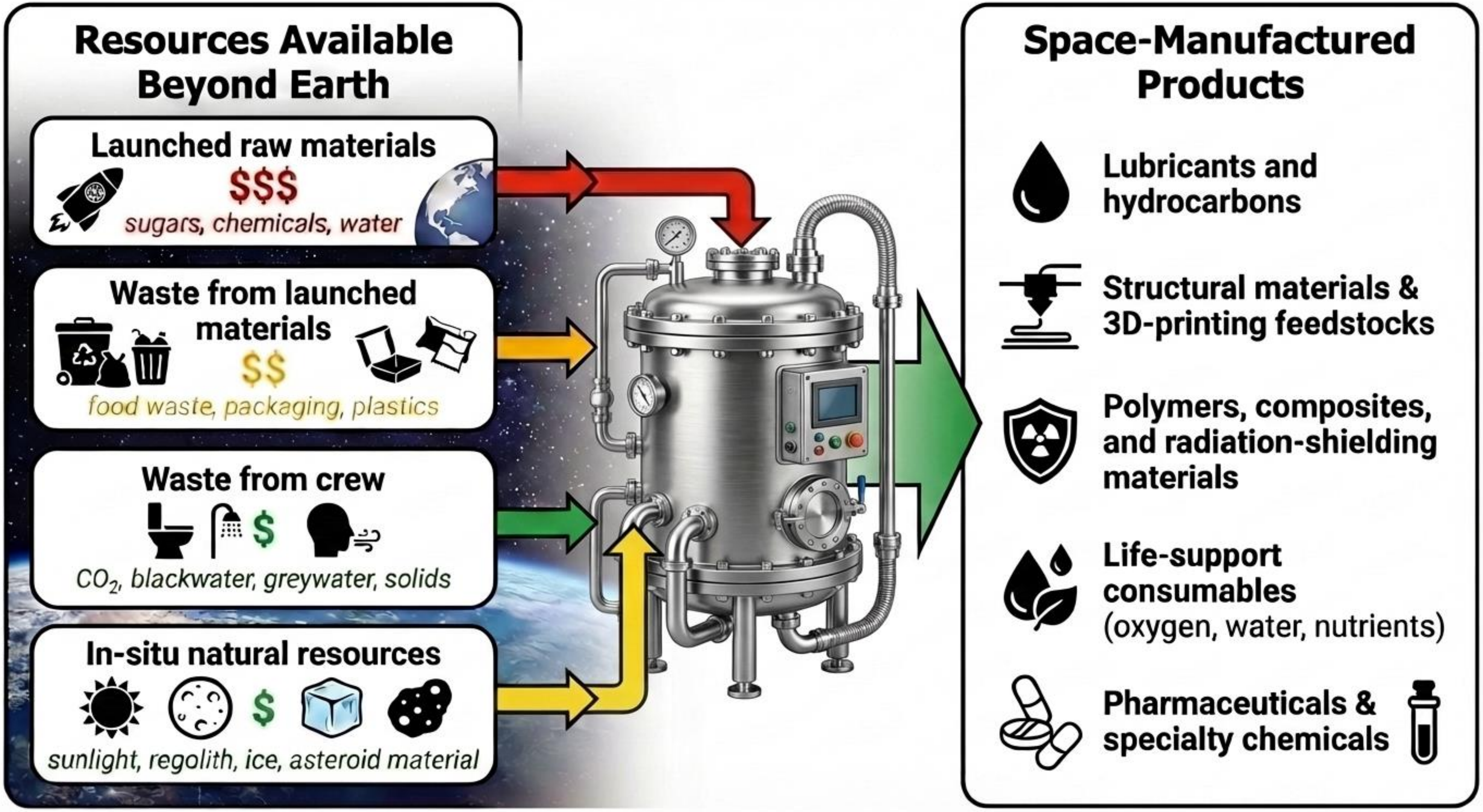
Jennifer Rollman
DARPA Budget & Finances SETA

Biomanufacturing can help meet DoD priorities of the future



Biomanufacturing offers a method by which low–cost in–situ resources can be transformed into DoD–relevant products beyond Earth.

Space biomanufacturing offers a method by which low cost *in-situ* resources can be transformed into relevant products beyond Earth



B-SURE Tracks and Foundational Research Questions

$8 million program for all three tracks

Track 1: Alternative Feedstocks

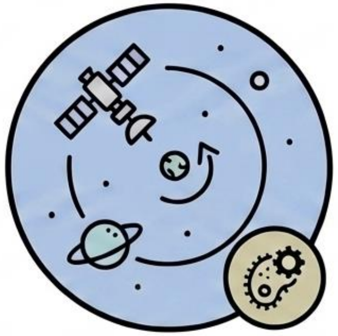
Foundational Science Questions

1. Quantify alternative feedstock(s) consumption & requirements
2. Quantify glucose replacement capability
3. Identify optimal *in situ* resources
4. Metabolic mechanisms of utilization
5. Purity requirements

Key Predictive Modeling Question

- Energy & time requirements

Track 2: Reduced Gravity



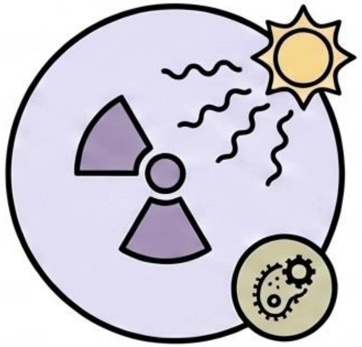
Foundational Science Questions

1. Quantify growth cost of engineering
2. Efficacy of microgravity simulators for production
3. Identify best host strains
4. Variable gravity effects on microbes

Key Predictive Modeling Question

- Genome engineering under simulated reduced gravity

Track 3: Variable Radiation



Foundational Science Questions

1. Temporal aspects of GCR resistance
2. Relevant timescales for production of molecules
3. Engineered resistance mechanisms
4. Cost of GCR resistance to lifespan, productivity, and population

Key Predictive Modeling Question

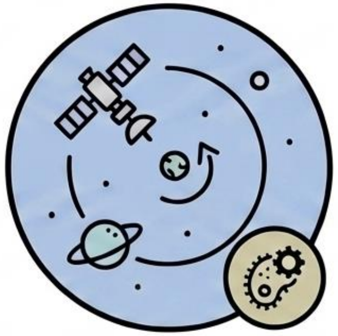
- Engineering hosts under radiation shielding

B-SURE Tracks and Foundational Research Questions

Track 1: Alternative Feedstocks

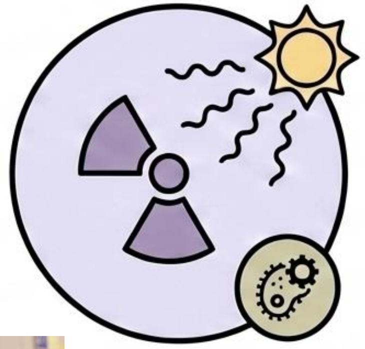
Yinjie Tang, Ph.D.
Washington University in St. Louis
PI, Track 1

Track 2: Reduced Gravity



Amor Menezes, Ph.D.
University of Florida
PI, Track 2

Track 3: Variable Radiation



Hal Alper, Ph.D.
University of Texas, Austin
PI, Track 3

Products & organisms investigated under B-SURE

THREE TEAMS

*Saccharomyces cerevisiae**
Ethanol, fuels, solvents, flavorings

*Escherichia coli**
Proteins, therapeutics, nutrients, amino acids

TWO TEAMS

Yarrowia lipolytica
Lipids, fatty acids, hydrocarbons

Pichia pastoris
Proteins, therapeutics

Pseudomonas putida
Biodegradable Plastics, natural products

ONE TEAM

Synechococcus elongatus S2973*
Photosynthetic, sugar production

Rhodococcus sp RPET
Can consume plastic and lignin, produce oils

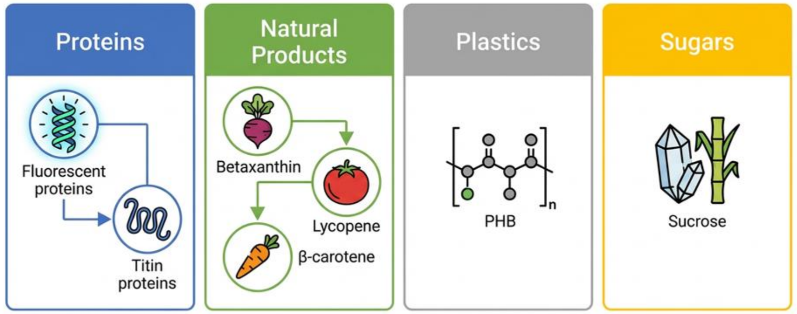
Cupriavidus basilensis
Biodegradable Plastics

Vibrio natriegens
Halophile, extreme growth rate

Deinococcus radiodurans
Extreme radiation tolerance

Vibrio fischeri
Forms beneficial interactions with animals

Products Produced in B-SURE



* Co-cultures of taxa were used

B-SURE Program Timeline: 18-month program

FY23				FY24			
Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4

Track 1: Alternative Feedstocks

March 2023 – Sept 2024

Tolerance Testing
Compare growth, production, and purity constraints for Alternate feedstock (AF) consumption

Optimize Feedstock Conversion
Engineering hosts for increase AF consumption

Generate LEO Space Station Model
Project optimal inputs and conversion efficiencies

Model Economic Impact of AF Consumption
Model mass/energy balance from microbial growth

Proof of concept wastewater bioreactor
Using biomanufacturing host taxa

Alternative feedstock testbed for final Engineered strains

Track 2: Reduced Gravity

Nov 2022 – May 2024

Characterize Microbial Growth & Biomanufacturing Activity
Simulated microgravity analog platforms across all taxa

Modeling Data from Simulated and Natural Spaceflight

Flight 1 Feb 2023

Flight 2 Aug 2023

Test Engineered Strains in µG
Assess impact µG on gene expression

Reengineer strains to increase bioproduction

Flight 3 Nov 2024

Track 3: Variable Radiation

March 2023 – Sept 2024

Characterize Microbial Physiology of Radiation Resistant Taxa
Test lifespan, productivity and quality of microbes

Test Engineered Strains Under High Radiation and Simulated Galactic Cosmic Radiation
Impact of radiation levels and tolerance on microbes – select optimized strains

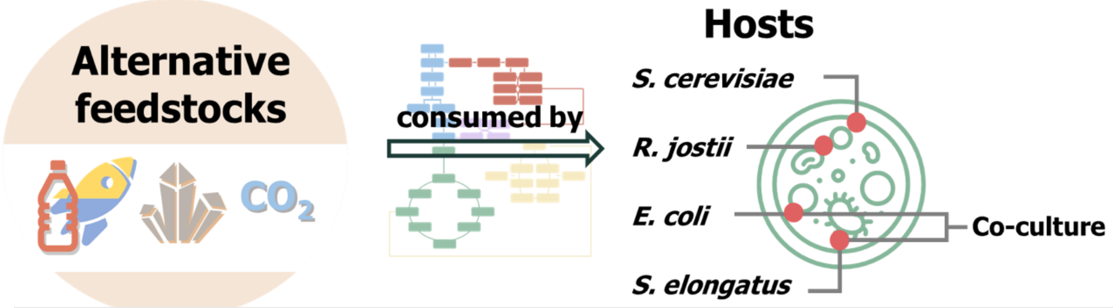
Validation aboard International Space Station
Exposure to space radiation environment – 223 days

Track 1: U-SAFEST: Utilization of Space-based Alternative Feedstock through Engineered Strains

Enabling Space biomanufacturing

- Hosts (phototroph vs. heterotroph)
- Products (polymer & nutrients)
- Space Resources (Regolith & CO_2)
- Modeling and TEA analysis

Project Period March 10, 2023~ Sept 9, 2024



Lee et al., Developing an alternative medium for in-space biomanufacturing. ***Nature communications*** *2025* 16 (1), 728

Achievement 1

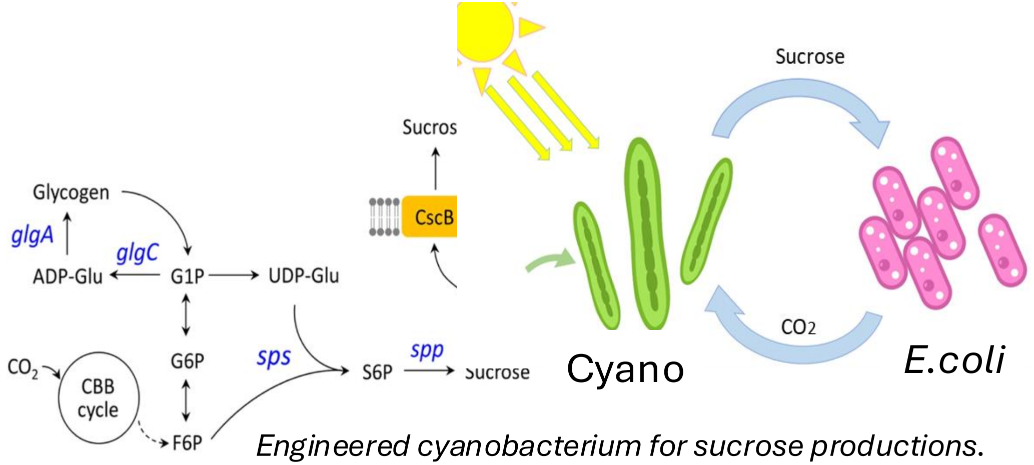
We have engineered plastic utilizing bacteria to convert PET, regolith and wastewater into lycopene.

Achievement 2

We developed phototrophic cocultures through genetic engineering and culture optimizations.

Muddana et al., Anabaena – A promising chassis for space exploration. ***npj Microgravity.*** *2026* In press.

Zhao et al., Development of Multimodal AI for Photobiorefineries via Knowledge Syntheses, Transfer Learning, and Techno-Economic Analysis. ***Bioresource Technology***. 2026, 133646.

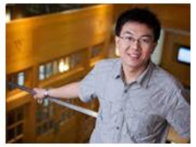


Engineered cyanobacterium for sucrose productions.

WashU

Yinjie Tang
Expertise: Metabolic analysis and modeling

Himadri Pakrasi
Expertise: Systems biology, Cyanobacterial engineering

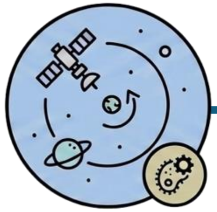


Fuzhong Zhang
Expertise: synthetic biology for manufacturing

Jinjin Diao
Expertise: Synthetic biology for plastic upcycling

Sunkyu Park
Expertise: Biomass engineering, TEA/LCA

NCSU



Track 2: Efficient and Resilient Biomanufacturing in Variable Gravity

Amor Menezes, PI

UF UNIVERSITY of FLORIDA

Team Members:

Yousong Ding, Jamie Foster, Sean Niemi, Mark Blenner, Ali Mesbah, Olivia Gámez Holzhaus, Heath Mills

Many Students!

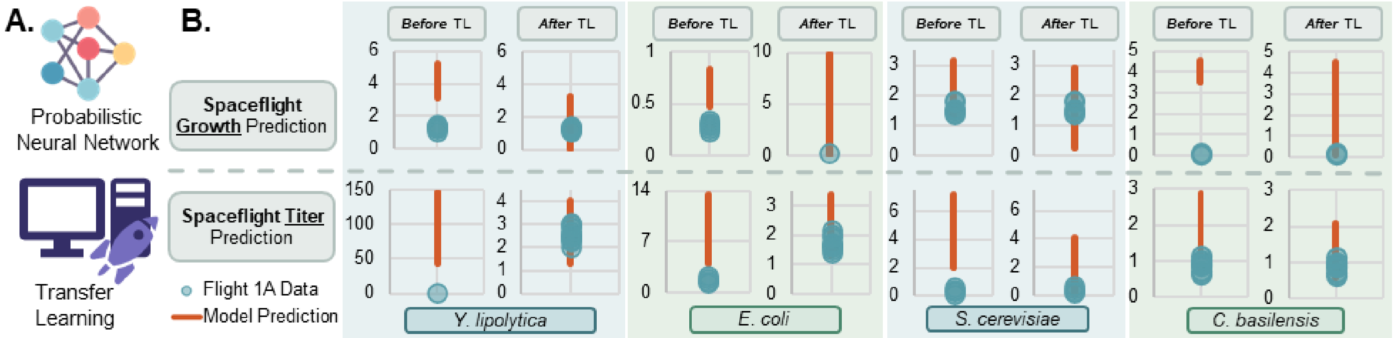
Project Overview & Workflow:

Multiple Hosts	Multiple Bioproducts	Multiple Gravities	Multiple Analogs and Spaceflights	Predictive Model
Yeast *S. cerevisiae* *P. pastoris* *Y. lipolytica* **Bacteria** *V. natriegens* *E. coli* *P. putida* *C. basilensis* *V. fischeri*	β-carotene EYFP PHB Host-Microbe Interactions	1 G 0.38 G Moon 0.16 G ISS 0.01 G	**Ground Analog** HARVs RPM **Spaceflight** SpX-27 Crew-7 SpX-31	Probabilistic Neural Network Transfer Learning

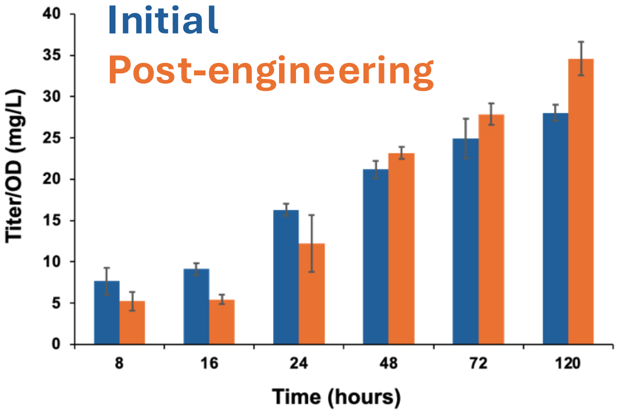
Major Findings & Results:

- Motility increases growth rate of strains under μG
- Examined variable gravity induced gene expression for all 8 taxa
- Strains could be reengineered on rapid timeline to improve product titer (3 flights in 18 months)
- New bioproducts made in space for first time titers increased (e.g., Poly(3-hydroxybutyrate))

- **Deliverable:** Machine Learning Computational Model Architecture for Biomanufacturing Predictive Ability



Example: increased titer of bioproduct



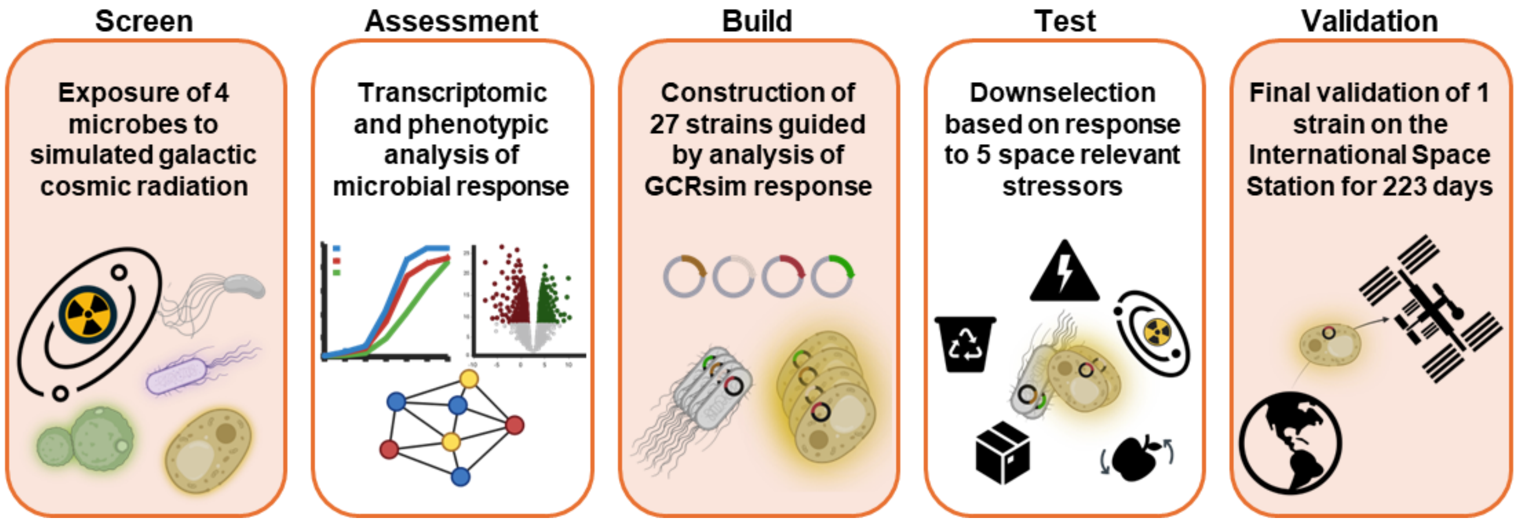
Yarrowia lipolytica

23% increase in β-carotene titer between flights

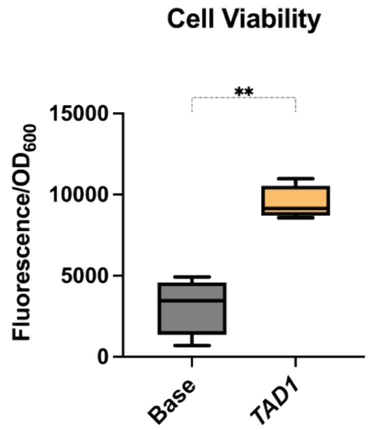
Track 3: Assessing and engineering microbes for bioproduction in conditions of variable radiation

PI: Hal Alper, The University of Texas at Austin

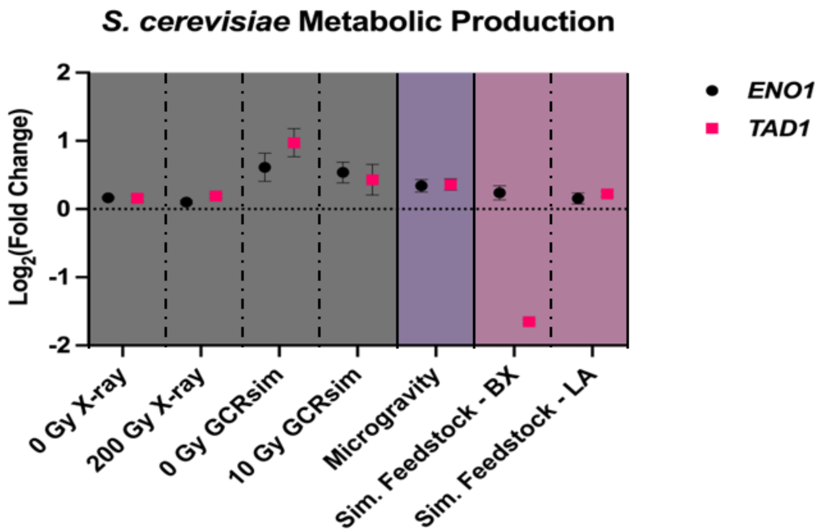
Project Workflow



Performance post-space flight



Robustness Improvement Metric



Major Findings/Results

- Identified mutations that can improve robustness to GCRsim, X-Ray, simulated microgravity, and simulated feedstock
- Mutations work in prokaryotic and eukaryotic hosts
- Resulted in 200% improvement in viability post-space flight
- Facilitated Equivalent System Mass analysis for TEA associated with biomanufacturing in space

After B-SURE: Next Steps in Space Biomanufacturing

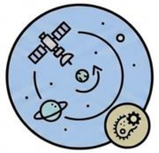
B-SURE Outcomes

Publications

Track 1

- Two published
- One in press
- Two in preparation
- Track 1& 2 collab.

Track 2



- One in revision
- One in review
- Six in preparation

Track 3

- Two in review
- Two in preparation

B-SURE has also led to Special Collection in *npj Microgravity*

Open until June 15, 2026

- Engage **government, academia,** and **industry** for coordinated partnerships and roadmaps
- Scale up long-duration biomanufacturing in LEO and cislunar space
- Optimize organisms and bioprocesses for space conditions (e.g., microgravity, radiation, limited resources)
- Increase flight cadence across multiple platforms: ISS, free-fliers, commercial stations, lunar vicinity
- Integrate biomanufacturing modules into mission architectures for in-situ resource use and sustainability
- Develop autonomous, closed loop-bioreactors with real-time quality control and AI monitoring
- Demonstrate practical products: therapeutics, diagnostics, biomaterials, food & life-support consumables for LEO, Lunar, and terrestrial applications

Broader Partnership & Applications

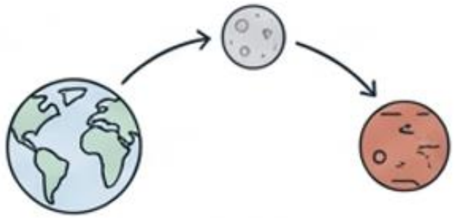
Gov agencies

Academia

Industry

Commercial space

International partners



LEO → Lunar → Mars-era applications