ISS NATIONAL LABORATORY®

Biological and Physical Sciences
Advisory Committee Meeting (BPAC)

ISS National Lab Update

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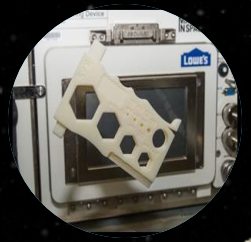
April 25, 2024

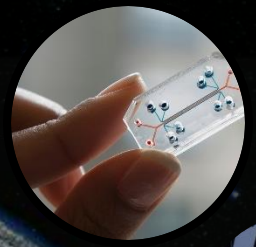
International Space Station: A Lab Off the Earth, For the Earth

A world-class laboratory in space enabling more than 4,400 researchers from 109 countries to conduct more than 3,000 experiments in the unique environment of low Earth orbit.

Educational Outreach (STEM) and Workforce Development

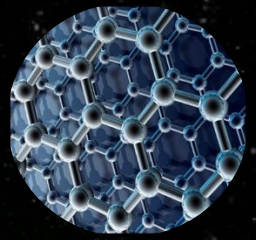
Human Research





Biology & Biotechnology

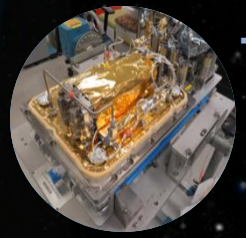
Combustion



Fluids & Materials

Earth & Space Observation

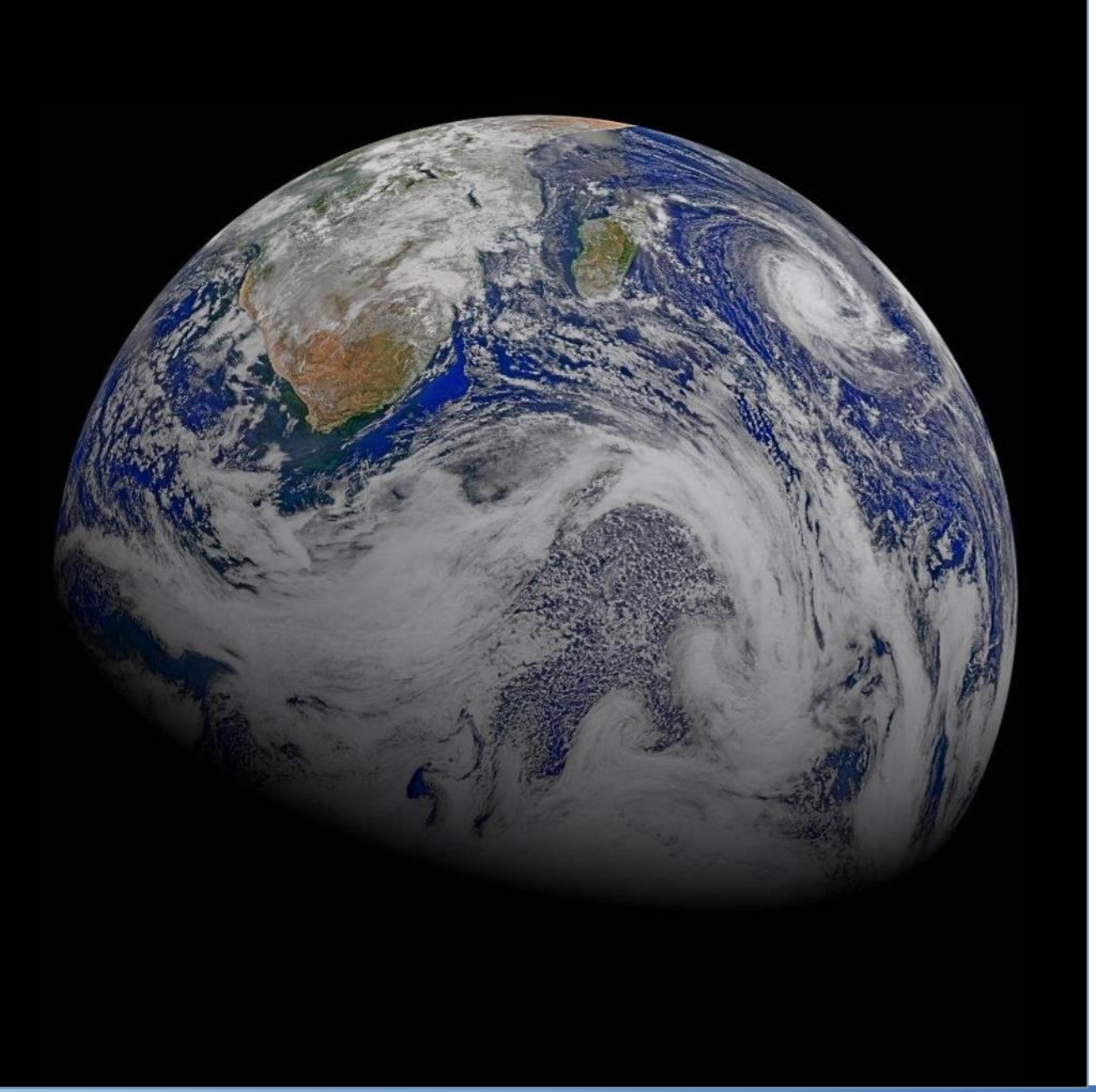
NASA ISS National Lab
Igniting Innovation Initiative



Technology Demonstration

In-Space Production Applications (InSPA)

Source: NASA.



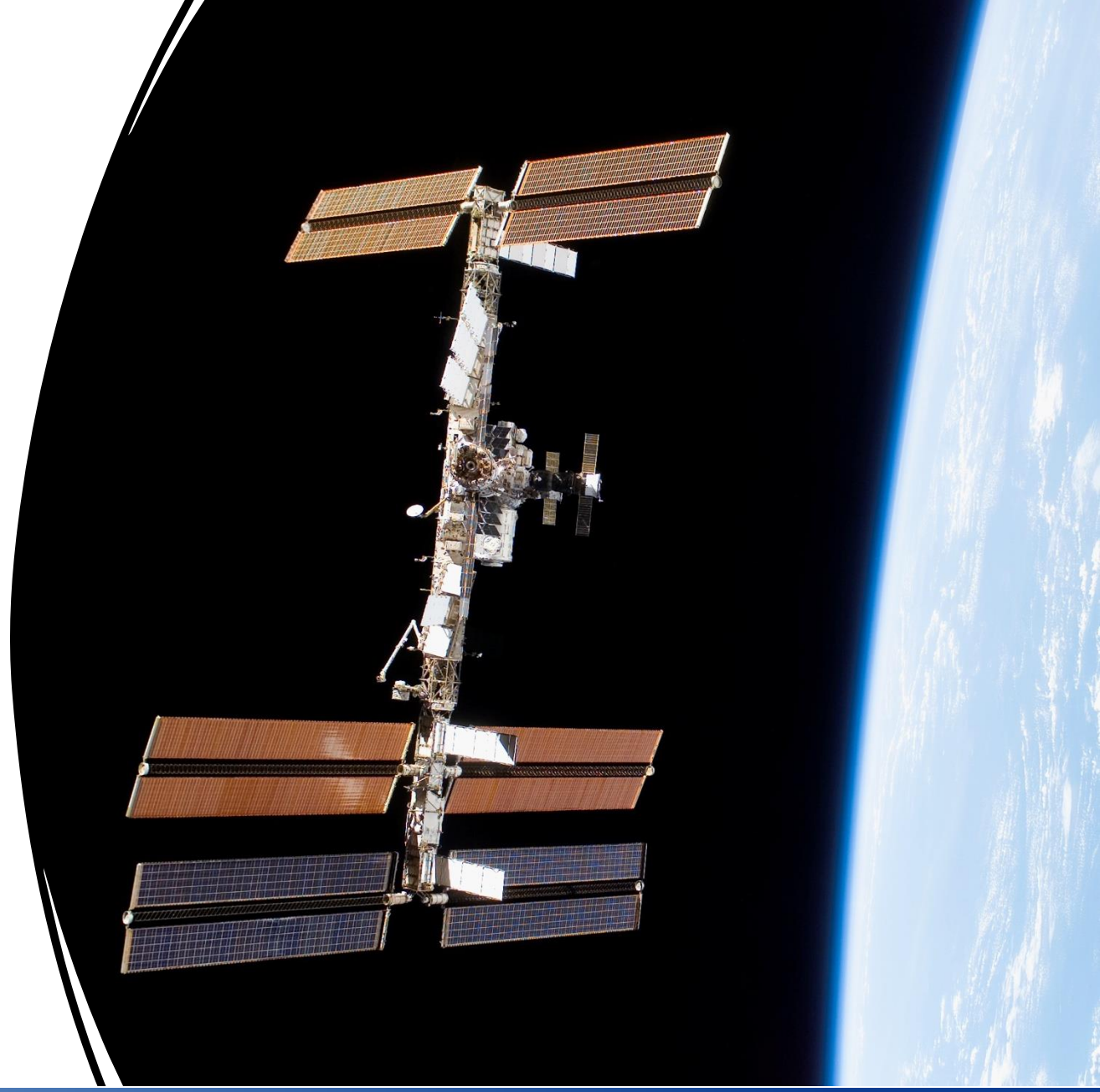
The Center for the Advancement Of Science In Space™ (CASIS™)

Awarded a Cooperative Agreement in 2011 to work in partnership with NASA to manage the ISS National Laboratory® on the International Space Station (ISS).

ISS National Laboratory

Offers a unique vantage point for scientific observation and technology development in low Earth orbit that extends beyond the horizon of NASA's exploration goals.

We leverage microgravity and look at our planet from the ISS to gain insight, identify challenges, understand human impacts on our surroundings, and improve lives here on Earth.



ISS National Lab Vision:

To be the leading source for innovation in space, enabling life-changing benefits for humanity.

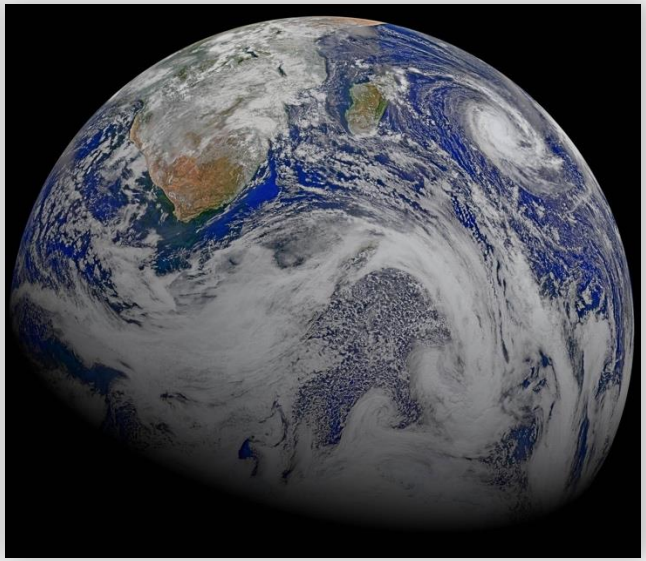
ISS National Lab Mission:

We manage the premier space laboratory, providing expertise, connection, and inspiration to visionaries.

Microgravity R&D accelerates scientific discovery for the translation of observations into applications for humans on Earth that improve health outcomes, fuel manufacturing innovation, and create economic value.

ISS National Lab Portfolio by Strategic Focus Area

- Fundamental Science
- Technology Development & Demonstration
- In-Space Production Applications (InSPA)
- Commercial Service Provider Utilization
- STEM Engagement & Workforce Development



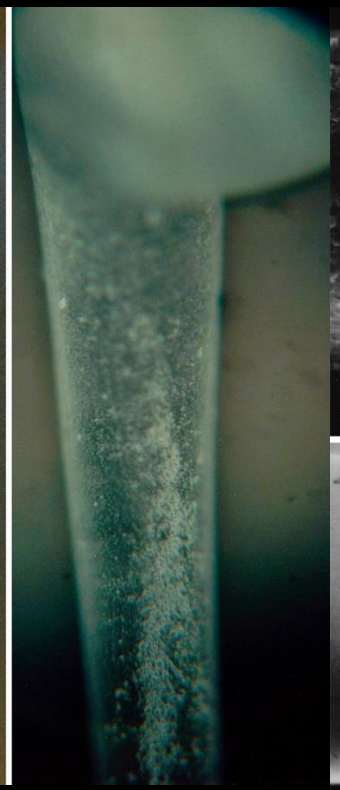
Microgravity affects the physical properties of materials and mechanisms of transport (that in turn have profound effects upon biological systems)

Microgravity removes gravity-dependent physical phenomena including:	**Resulting in fundamental changes in physical (and biological) systems:**
• Buoyancy-driven convection • Density-driven segregation • Matter-container interaction	• Heat and mass transport • Interfacial dynamics • Multiphase system dynamics • Solidification kinetics and thermodynamics • Fluid dynamics

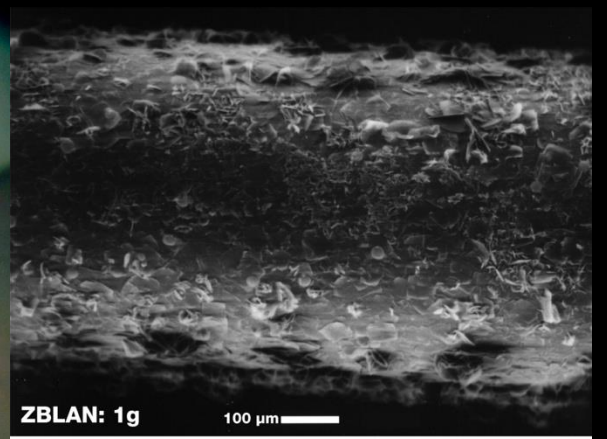
For example, microgravity reduces nucleation during solidification processes

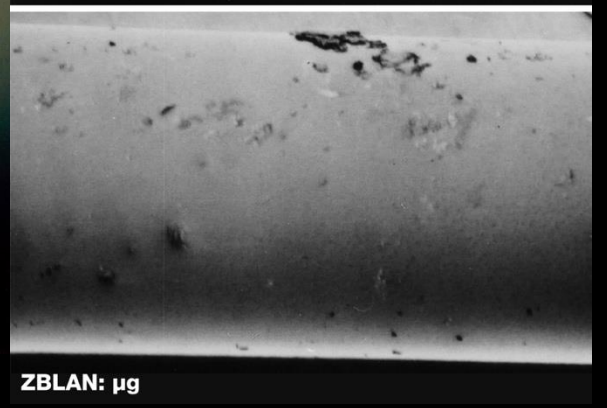
- ZBLAN has long been among the most promising of high-value, exotic optical fibers for optical signal transmission in the infrared range (IR to ~5 µm) for multiple applications without significant signal attenuation
- The intrinsic loss limit of ~0.001dB/km far exceeds doped silica and other materials, but imperfections introduced during melt and solidification on Earth remain a challenge
- Microgravity mitigates the driving force for compositional segregation and crystal nucleation in the melt during solidification
- In addition to metallic glass, other high-value, high-entropy, metal alloys and ceramics benefit from microgravity processing

Microgravity (µg)



Normal Gravity (1g)





ZBLAN Optical Fibers

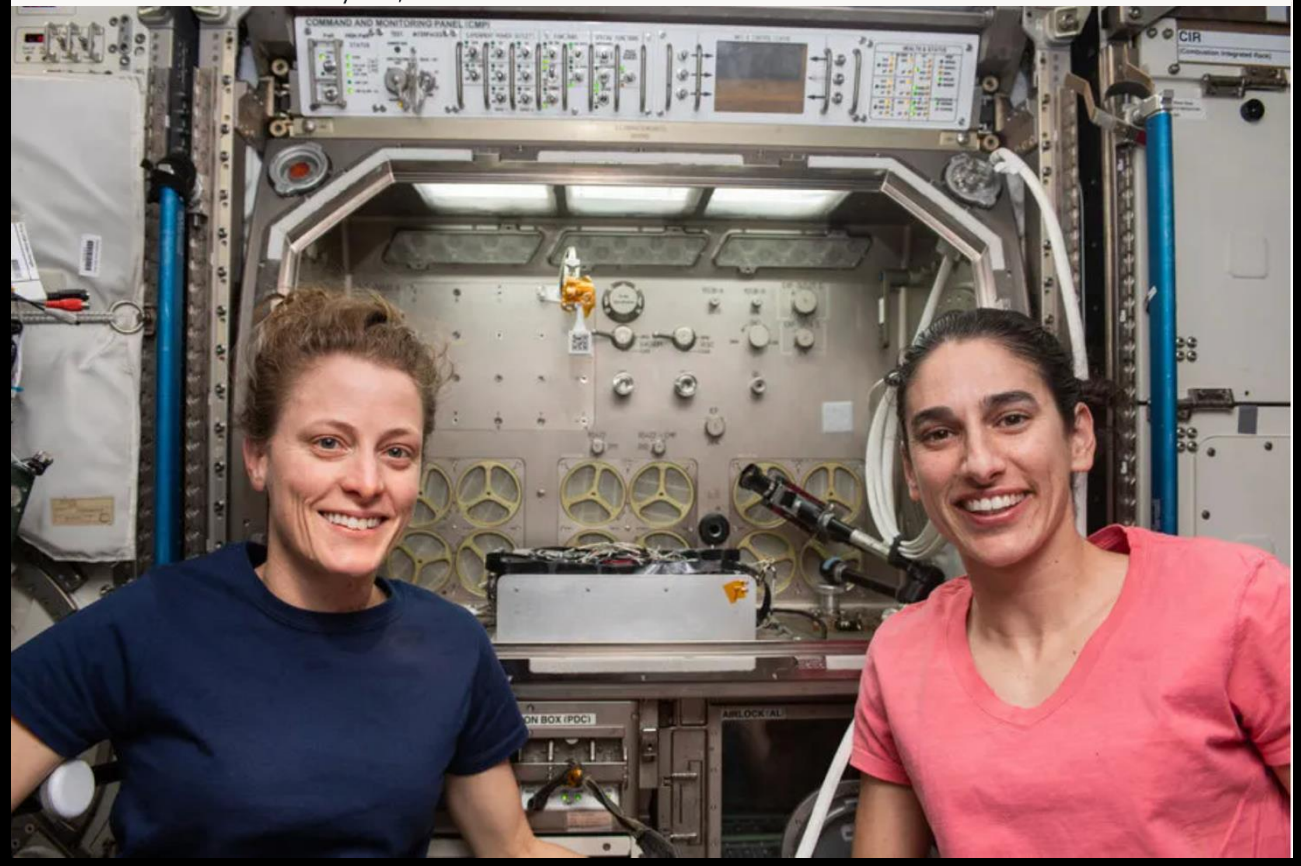
ZrF_4-BaF_2-LaF_3-AlF_3-NaF

And progress toward in-space manufacturing continues....

Flawless Photonics Kicking Glass

Silicon Valley startup produces more than 5 kilometers of ZBLAN in two weeks

Debra Werner February 23, 2024



SPACENEWS
BUSINESS | POLITICS | PERSPECTIVE

Astronauts Loral O'Hara and Jasmin Moghbeli (from left) are pictured in front of the Microgravity Science Glovebox, a research facility for conducting biology and physics experiments in the International Space Station's Destiny laboratory module. Moghbeli installed Flawless Photonics' machine for drawing optical fiber in space in the Microgravity Science Glovebox.

Source: https://spacenews.com/flawless-photonics-kicking-glass/

Unprecedented Technological Advancements in Crystallization

- Analysis of 50 years of crystallization experiments in space
- 90% of all published crystallization data demonstrate some improvement in one or more quantitative metrics
  - Size, structure, uniformity, resolution limit, mosaicity
- Near absence of gravity eliminates convection, eddy-currents, and sedimentation during crystallization
- This enables advances in drug discovery, drug development, pre-clinical testing, and manufacturing

pubs.acs.org/crystal

Communication

An Analysis of Publicly Available Microgravity Crystallization Data: Emergent Themes Across Crystal Types

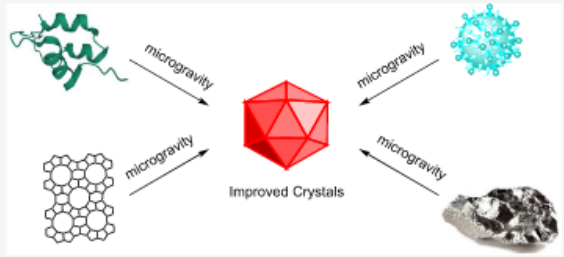
Hannah Wright, Amari Williams, Ashley Wilkinson, Lynn Harper, Ken Savin, and Anne M. Wilson*

Cite This: *Cryst. Growth Des.* 2022, 22, 6849–6851

Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: A retrospective analysis, curation, and organization into searchable databases of public domain data of crystals grown in microgravity was undertaken. The data were then analyzed and marked for improved results (size, structure, uniformity, resolution limit, and/or mosaicity). Overall, 90% of the crystals analyzed showed improvement in one or more of the metrics utilized for analysis.



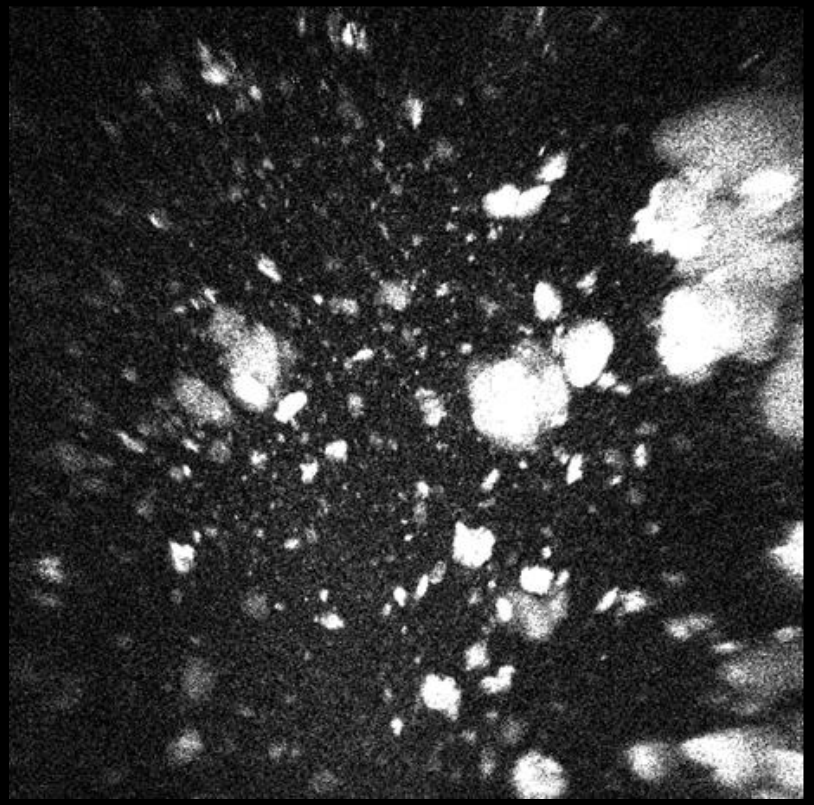
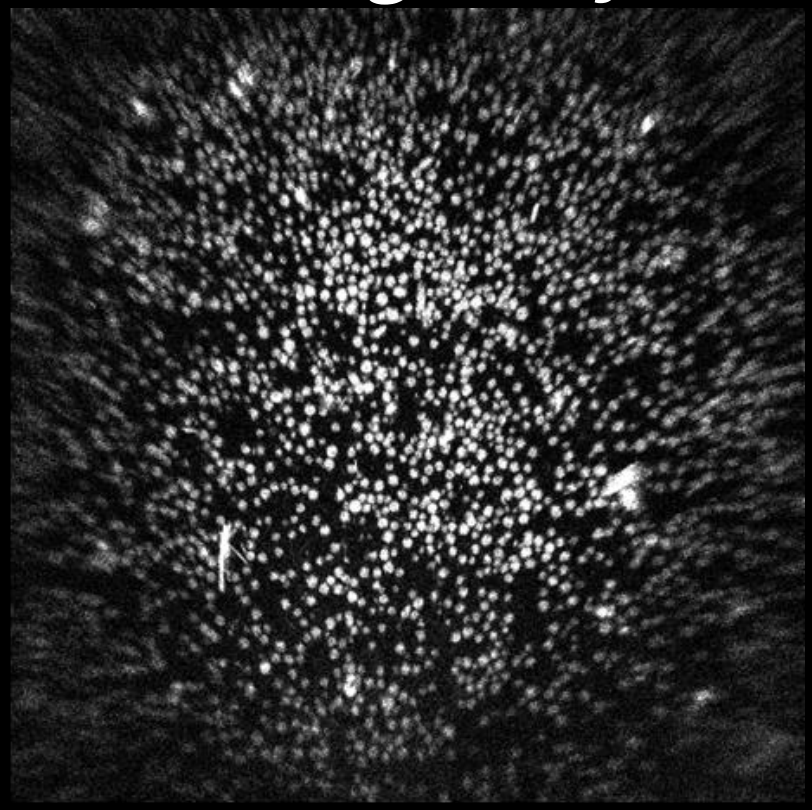
Microgravity crystallization efforts have been undertaken since 1973 with Apollo and Skylab, advanced with Mir, the Space Shuttle, and individual recovery satellites, and has continued with the International Space Station and Tiangong. Reviews of crystallization data have demonstrated some of the aspects of improvement to the crystals produced in microgravity.[1−6] There it is known that there have been numerous crystals produced in microgravity, especially proteins,[7] but the data for most of these crystals are proprietary. However, a searchable compendium of the public domain crystal data is still needed in order for researchers to evaluate the data, identify opportunities, and come to their own conclusions. In order to address this need, we developed such a searchable database and performed an initial meta-analysis.

Included in our database are the compounds by name, ground. With repeat experiments involving the same compounds removed, there are 187 unique compounds (130 macromolecules and 61 inorganics) that have been crystallized in space. This data set underwent an initial, more detailed analysis. The authors acknowledge a predisposition in the literature toward publishing results that are favorable (positive outcome bias).[8] Even with this caveat, a preliminary evaluation of the aggregated crystal data is warranted.

Improvements in crystals grown in microgravity versus ground experiments were evaluated using the following metrics: size, structurally better, more uniform, improved resolution limit, and improved mosaicity (see Table 1). Not all studies reported the same information as separate metrics are appropriate for different applications. For example, improved resolution limit and mosaicity are metrics that apply to

pubs.acs.org/doi/full/10.1021/acs.cgd.2c01056

Merck Keytruda® Study

	Ground	Microgravity
Merck Keytruda®		

Crystallization of the active pharmaceutical ingredient in Keytruda®, *pembrolizumab,* in microgravity achieved greatly improved homodispersity (shown on the right). This discovery promises to reduce manufacturing costs by limiting purification steps and to increase drug safety and efficacy to improve the quality of life for patients on Earth.

Paul Reichert et al. npj Microgravity 5, 28 (2019)

InSPA Biomanufacturing

Startup company LambdaVision, initially funded through an ISS National Lab and Boeing Technology in Space Prize, is working with Space Tango to improve the process of in-space manufacturing by **layer-by-layer, thin-layer deposition** of the protein bacteriohodopsin to manufacture artificial retinas with superior performance for the treatment of macular degeneration and retinitis pigmentosa on Earth.

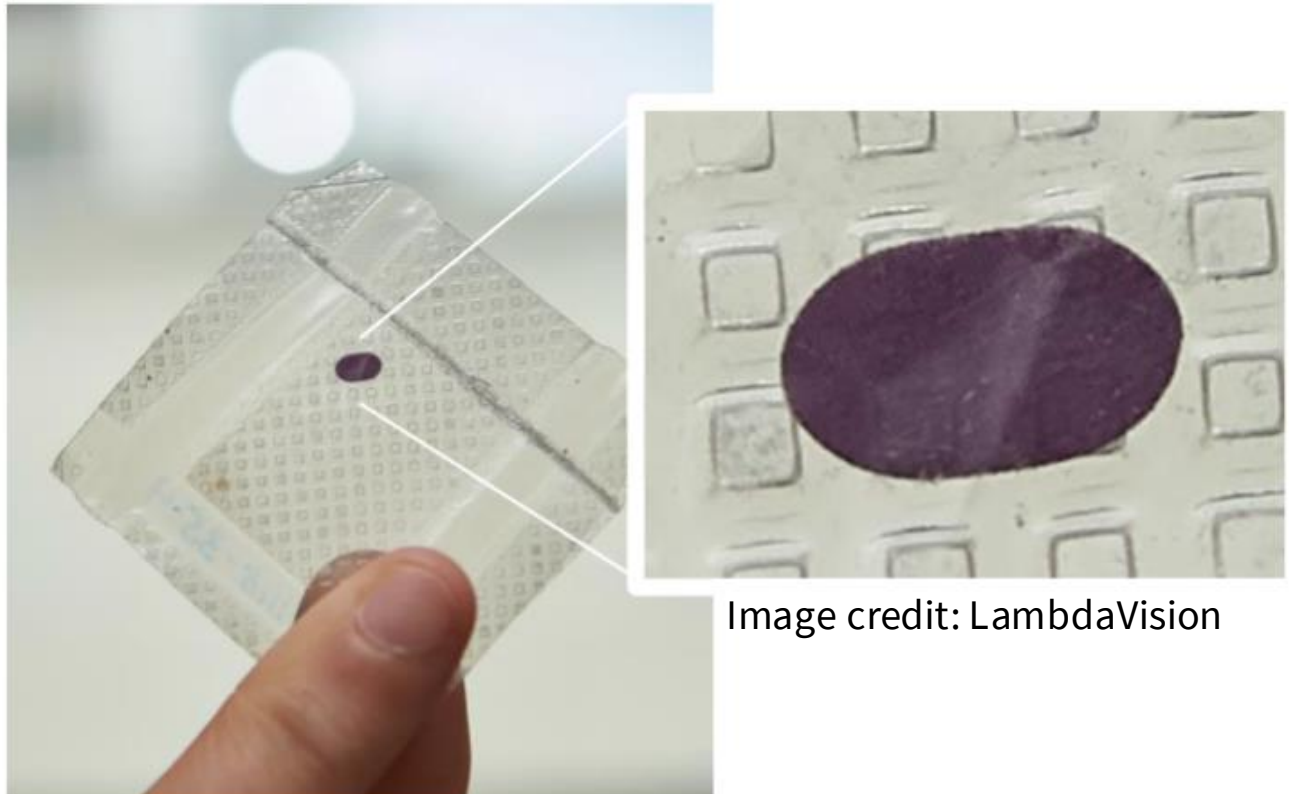
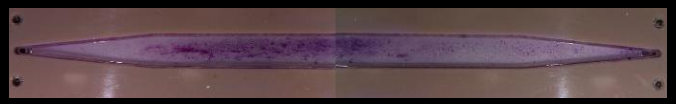


Image credit: LambdaVision

LambdaVision & Space Tango achieved their target of 200-layers of protein/polymer matrix with near perfect autonomous operations on their 5th flight.

Preflight

Demo 4 (200 layers)



Demo 5 (200 layers)

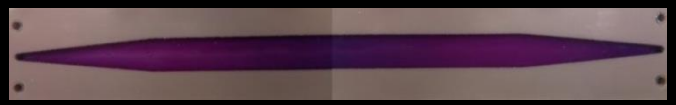


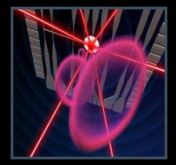
Image Credit: NASA and LambdaVision

Microgravity Works:

In-SPA builds on 50+ years of µg research in space to accelerate the application of new technologies on Earth that benefit humanity, from subatomic through global scale.

Medical Advances from Space for 50+ years

Quantum Subatomic



Cold Atom Lab

Manufacturing Bose-Einstein condensates in space near absolute zero since 2019

Molecular

Crystals
Pharma
Industrial
Semiconductors

90% of crystals manufactured in space since 1973 improved in structure, uniformity, size, or reduction of defects

Thin Films

Medical Devices
Artificial Retinas
Nerve Regen

Semiconductors

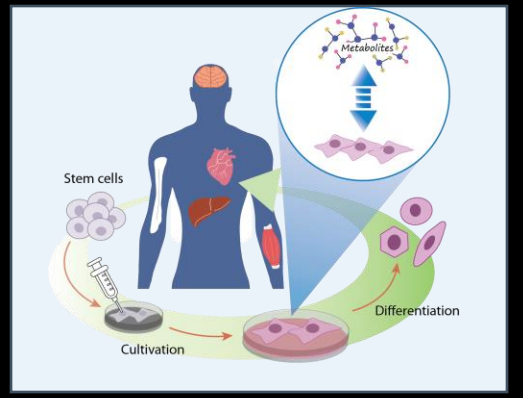
Space-manufactured artificial retinas ready for animal trials, Semiconductors in parabolic testing

Alloys and Photonics

ZBLAN Optical Fibers
Semiconductors

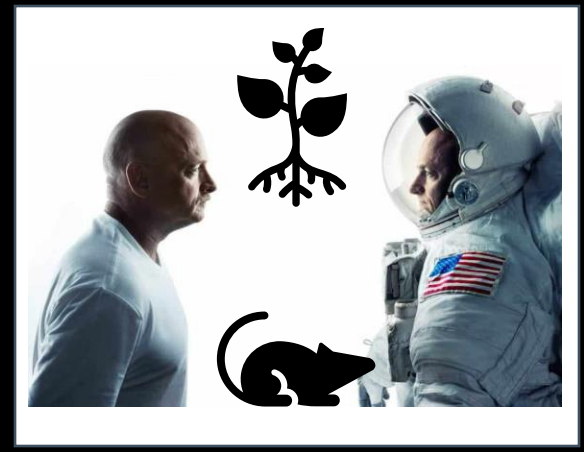
High-throughput 11.9 km optical fiber manufactured on the ISS to commercial lengths

Cells and Tissues



Cancer
Neurodegenerative
Stem Cells
3D Tissues
Artificial Organs

Whole Organisms

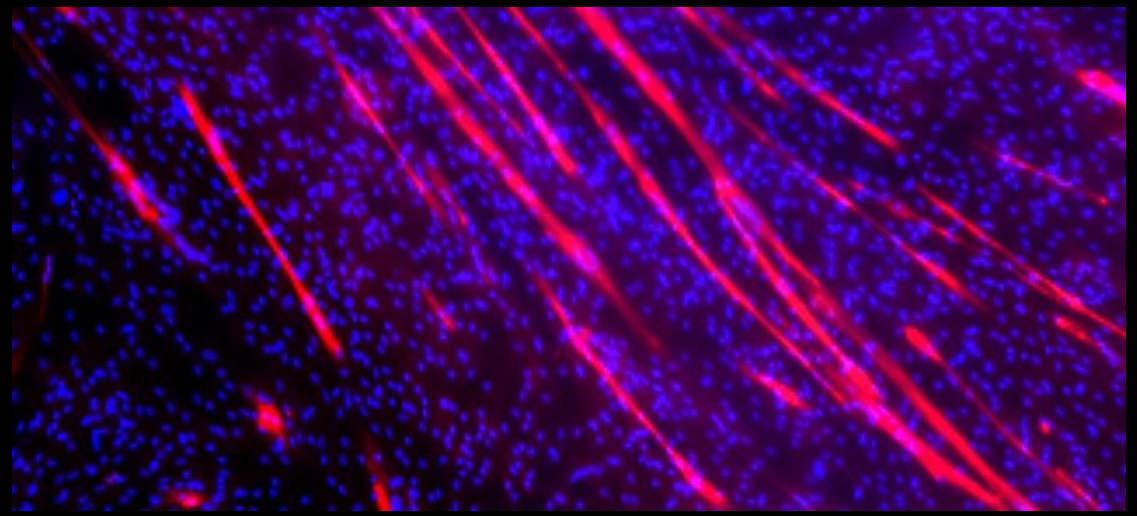


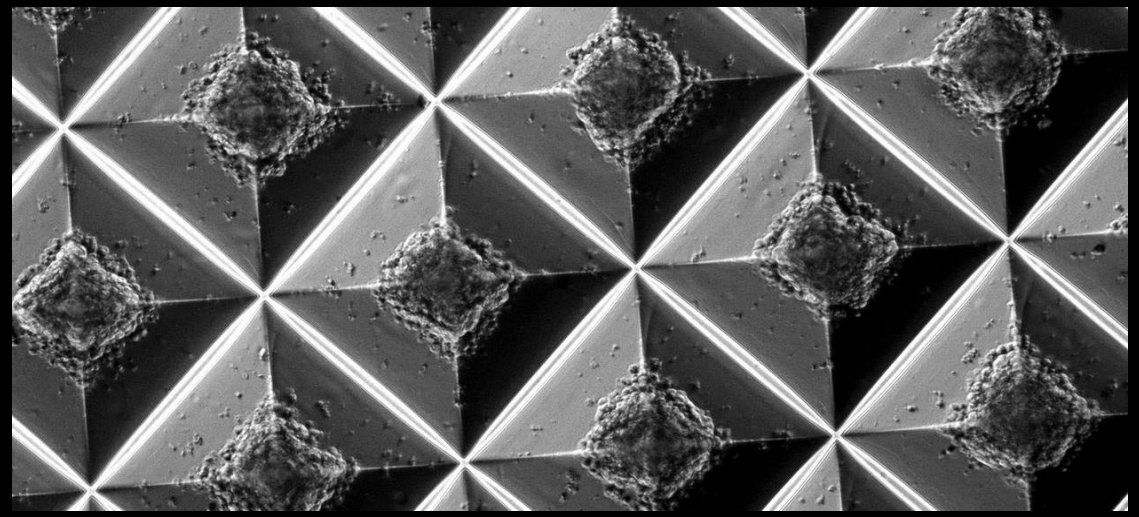
Microbes
Plants
Animals
Humans

Slide Credit: NASA, In-Space Production Applications (InSPA).

NSF/CASIS Tissue Engineering and Mechanobiology

- Partnered with NSF for 7 annual joint solicitations since 2018
- 17 flight projects sponsored, $6.9M in NSF funding
  - Cardiovascular disease
  - Muscle wasting
  - Vascular tissue grafts
  - 3D printed tissues





NIH-CASIS Tissue Chips in Space

National Center for Advancing Translational Sciences

Tissue chips are powerful organ system avatars on Earth, but in µg chips offer high-fidelity, high-throughput accelerated models of human disease. Tissue chip flight and ground research supported by collaborations with the National Institutes of Health (NIH), U.S. National Science Foundation (NSF), NASA, and the ISS National Lab accelerate translation.

https://ncats.nih.gov/news/releases/2023/as-flights-end-tissue-chips-in-space-projects-offer-glimpses-into-the-biology-of-aging?utm_source=Twitter&utm_medium=Social&utm_campaign=Tissue+Chips

NIH-NCATS and NIBIB Tissue Chips in Space

- 2016 - ISS National Lab Organ-on-a Chip solicitation
- 2017 & 2018 - CASIS partnered with NIH on tissue chip solicitations
    - Sponsored 9 multi-flight projects with $22.2M in NIH funding:
        - Cardiomyopathy
        - Immune dysfunction
        - Post-traumatic osteoarthritis
        - Kidney dysfunction

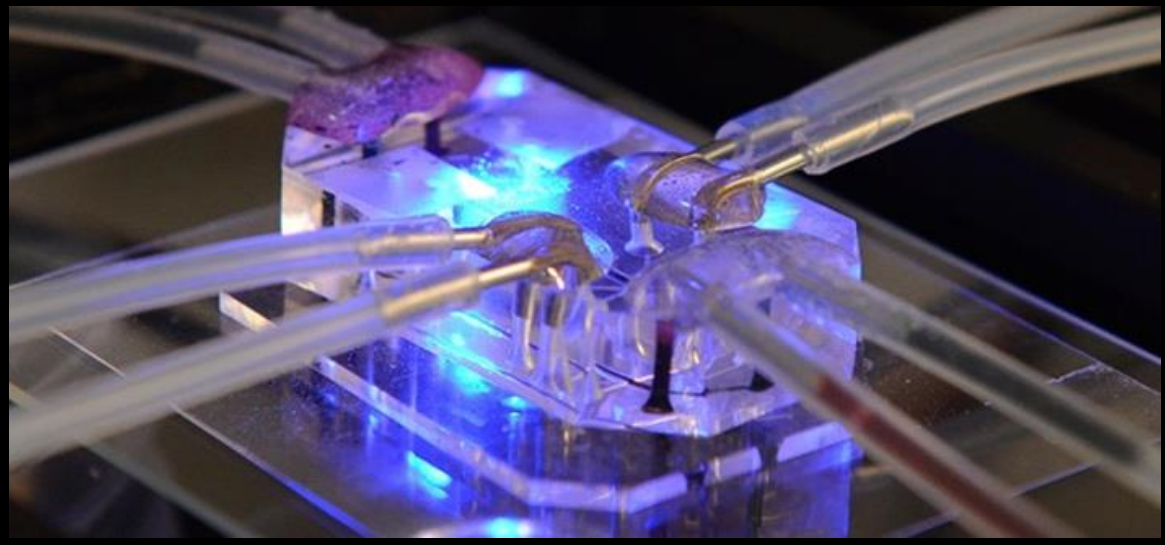


Image Courtesy of Wyss Institute for Biologically Inspired Engineering, Harvard University

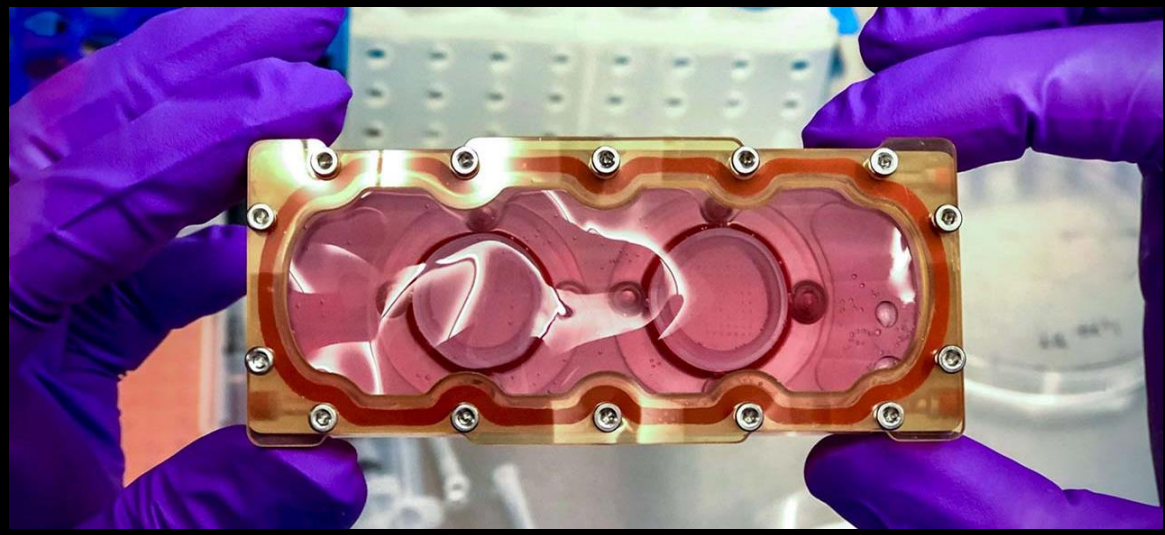
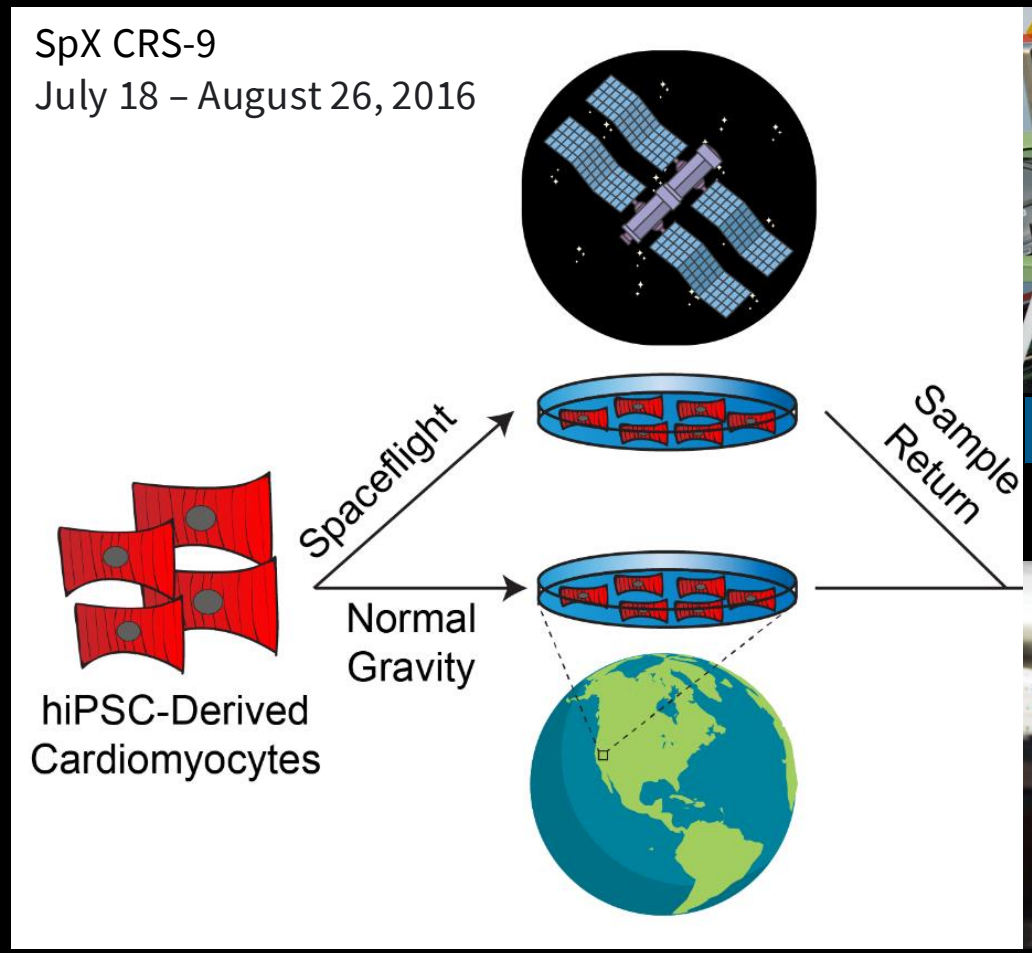


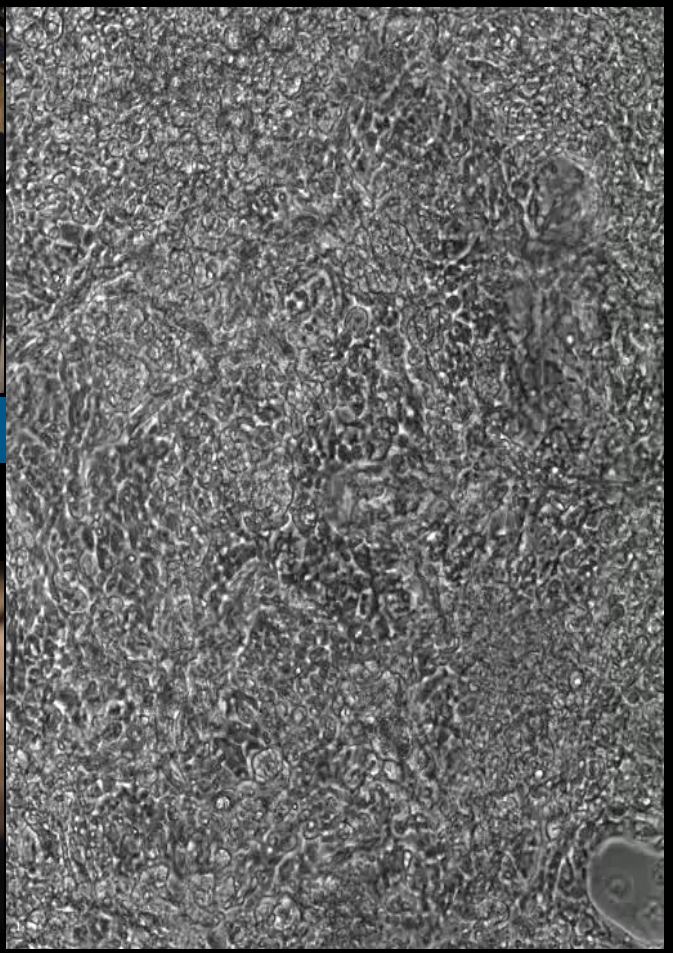
Image Courtesy of Drs. Joseph Wu, Dilip Thomas and Xu Cao, Stanford Cardiovascular Institute

Stem Cell-Derived Heart Cells (hiPSC-cardiomyocytes) Reveal Effects of Microgravity on Heart Cells During Spaceflight



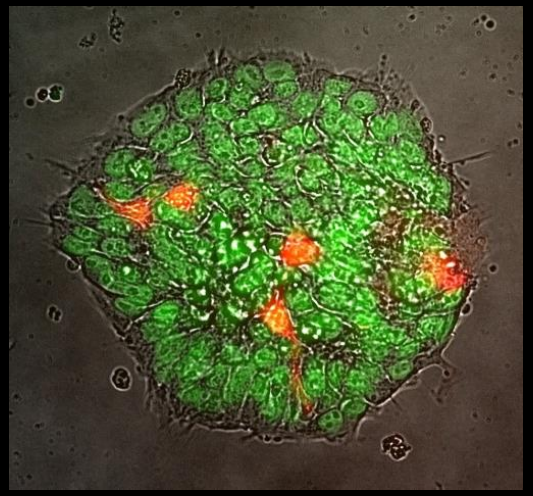
STEM CELL REPORTS ISSCR

Wnorowski and Sharma et al, 2019.
"Effects of spaceflight on hiPSC-derived cardiomyocyte structure and function"



Human Induced Pluripotent Stem Cells Manufactured in Space

- For the *Stellar Stem Cells* experiment, hiPSCs (human induced pluripotent stem cells) with a green fluorescent biomarker were launched to the ISS as part of the Axiom Space Ax-2 PAM (private astronaut mission) on May 21-31, 2023, led by Drs. Arun Sharma and Clive Svendsen of the Cedars-Sinai Medical Center.



- This is the first of a series of missions funded by NASA and sponsored by the ISS National Lab where, for the first time, iPSCs will be manufactured in space by astronauts.

Image credit: Cedars-Sinai

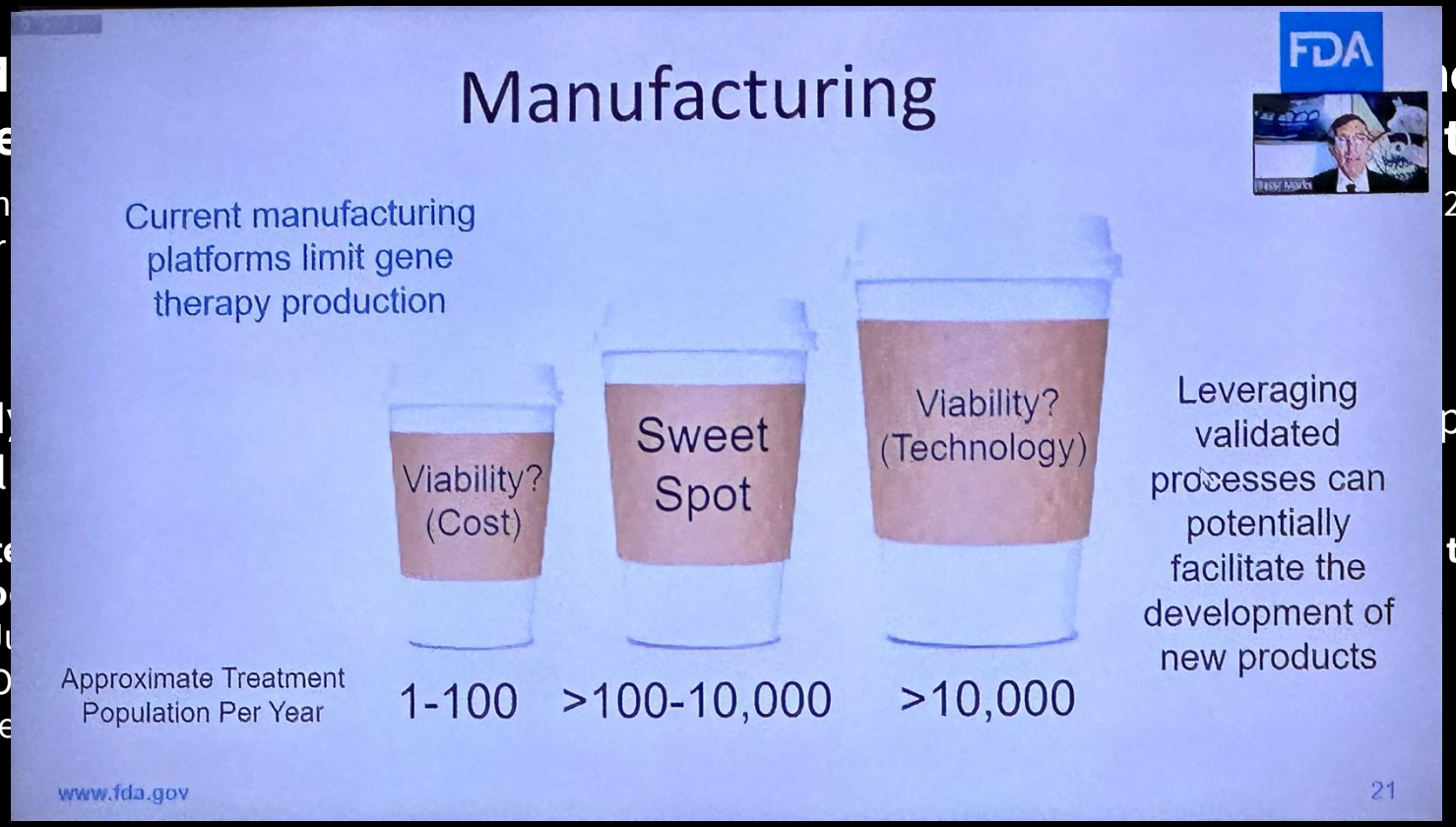
Biomanufacturing on Earth is Bound by R&D Innovation and the Cost of Production at Scale

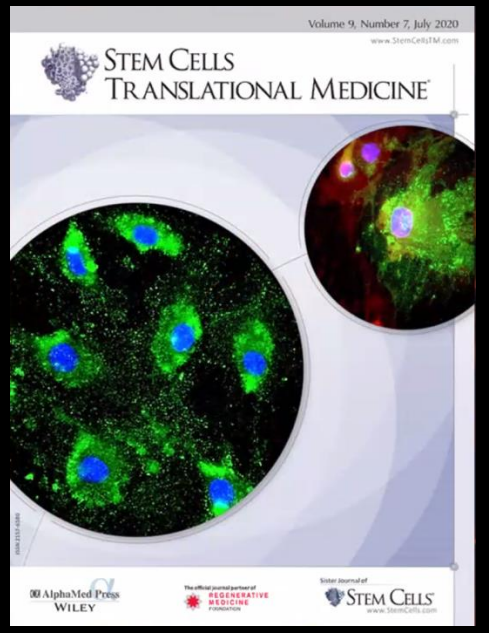
"M … erative me … t access."

Hun … 2020
Mar …

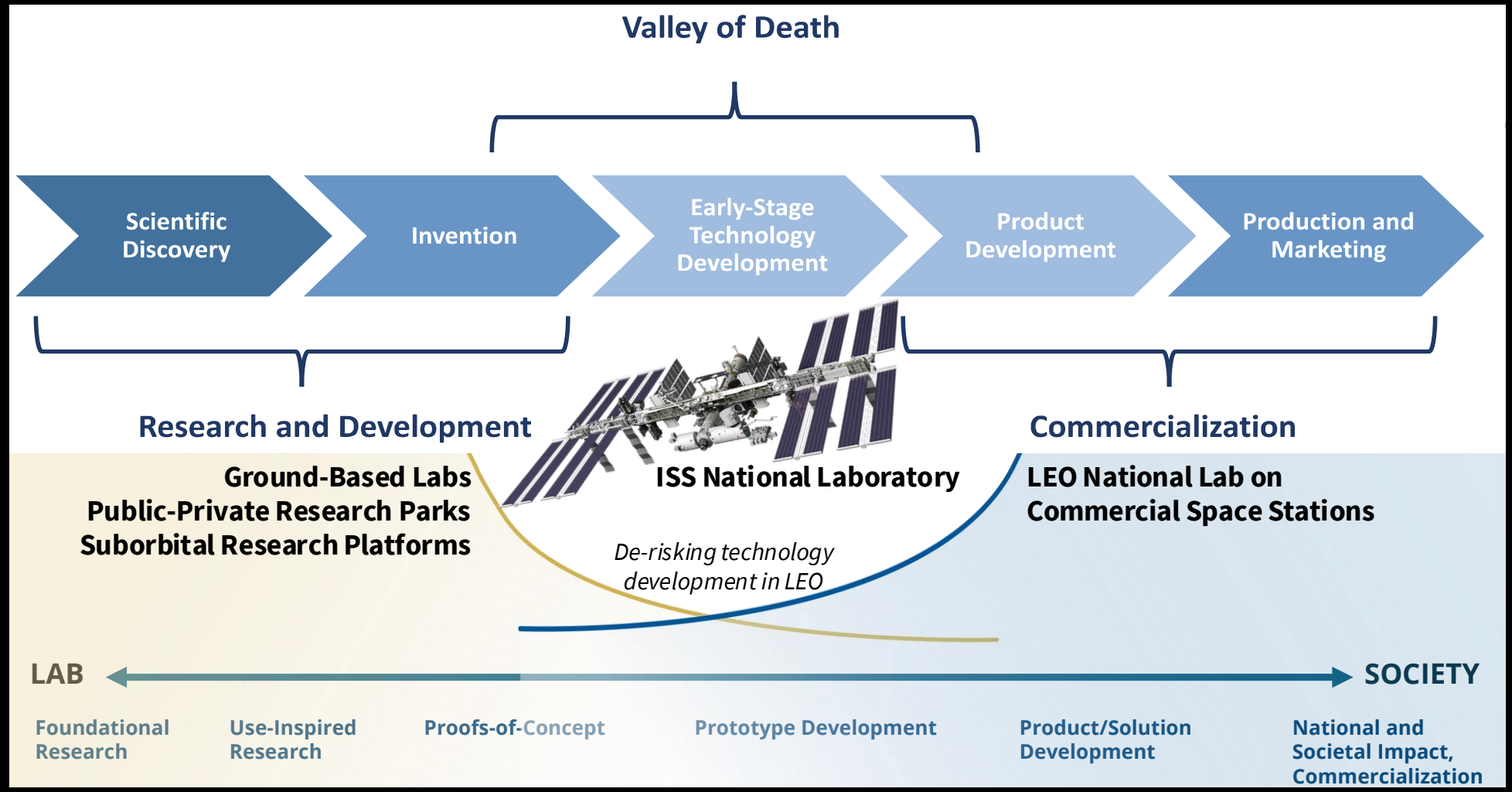
"My … panies wil …

Pete … the US Foo …
* Ju …
** O … re …





Space Enables Value Creation and Accelerates Innovation to Translation



Technology in Space Prize Award Information

- Funding awarded annually via the MassChallenge incubator program
- Funding Amount:
  - CASIS and Boeing combined, non-dilutive annual funding up to $500K
- Funding Uses:
  - Sponsorship of ISS National Lab resource utilization:
    - Payload launch to the ISS, in-orbit crew time, data and payload return, if required
- Period of Performance: No longer than three years from date of award

CASIS-Boeing Technology In Space Prize
Awarded annually at MassChallenge

Past Awards

2023
Flux Works
Symphony Biosciences

2022
MachineBio

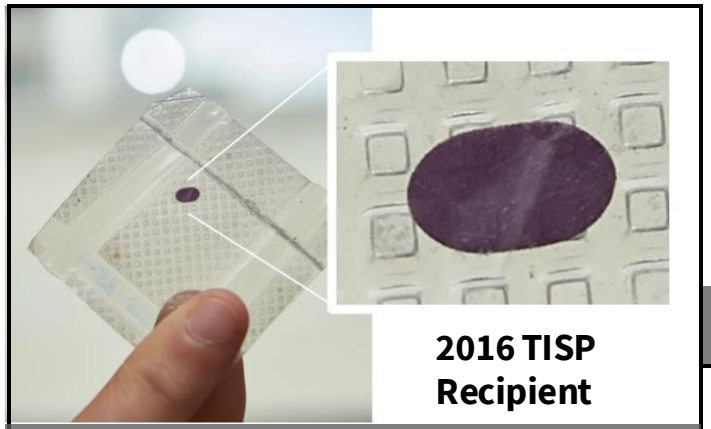
2021
Krtkl Inc.
Oculogenex

2019
Axonis Therapeutics
Encapsulate LLC

2018
Kernal Biologics, Inc.
MicroQuin

2017
Cellino Biotech, Inc.
Guardian Technologies
MakerHealth

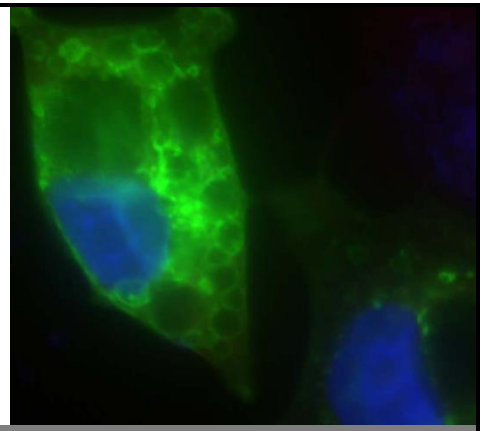
2016
Angiex, Inc.
Dover Lifesciences
LambdaVision, Inc.



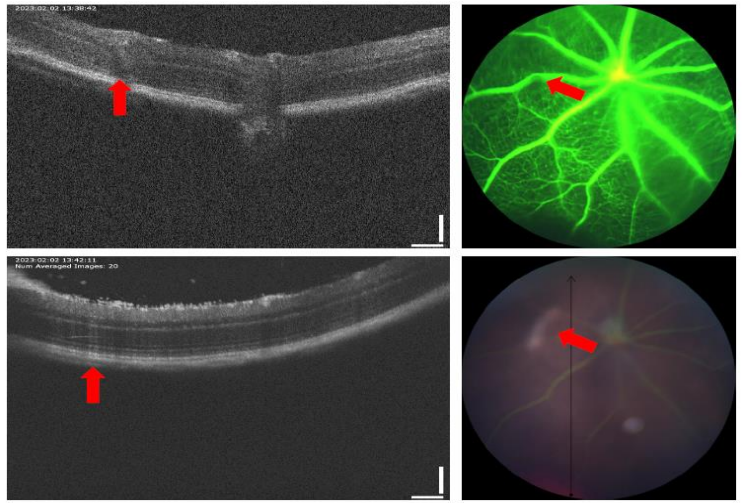
2016 TISP Recipient

LambdaVision

2018 TISP Recipient



MicroQuin

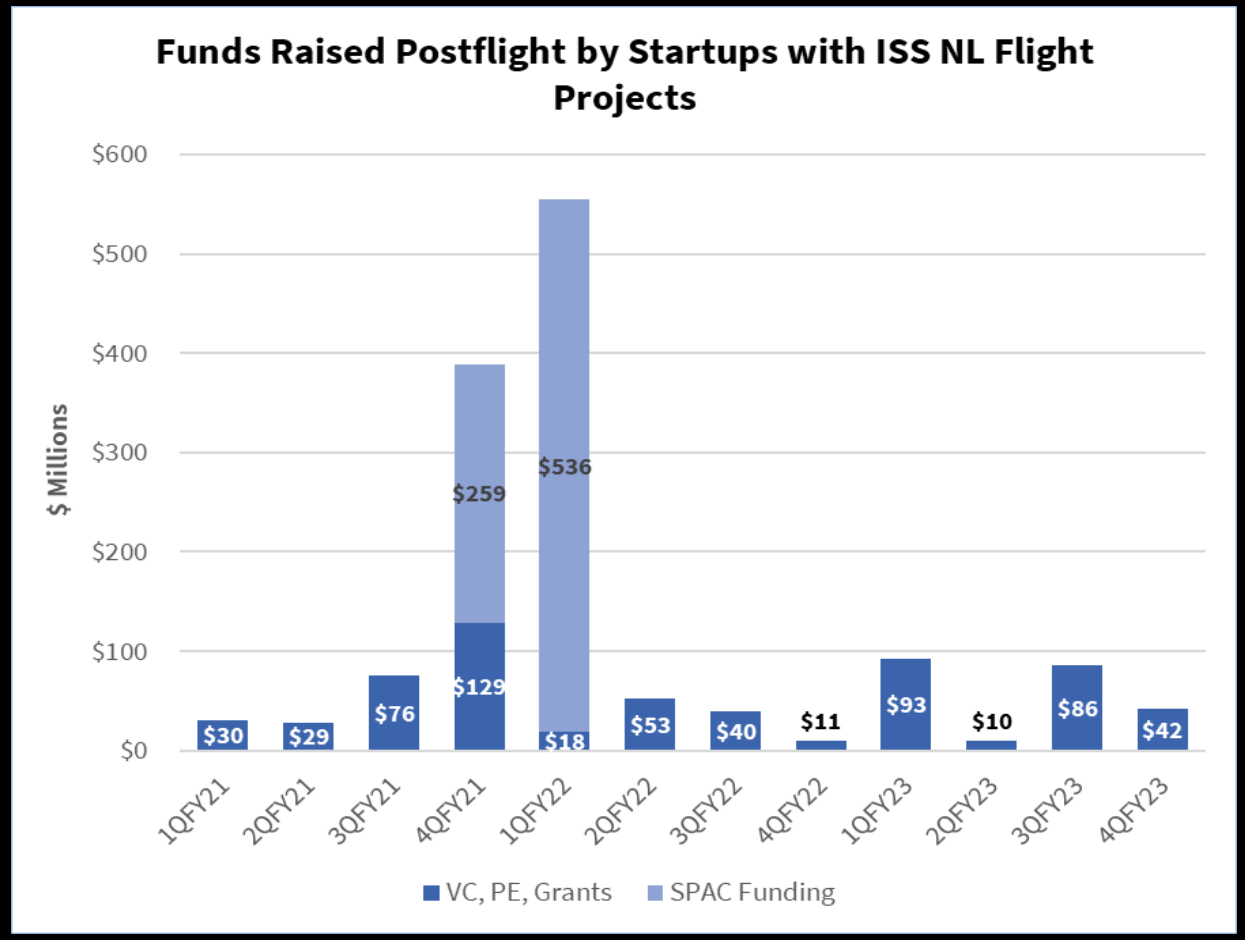


Oculogenex

2021 TISP Recipient

Oculogenex

Postflight Funding for ISS National Lab-Supported Startups



Note: 3QFY23 data as of 10/4/23 and may not accurately capture all capital raising activity in the quarter.

Postflight funding in FY23 **$231M**

- Startup interest remains strong, but lower capital availability continues to affect ISS National Lab post-award/postflight capital metrics.
- CLD realignment and NASA budget uncertainty highlights risks to emerging markets and customers' business models, particularly for those contemplating in-space manufacturing.

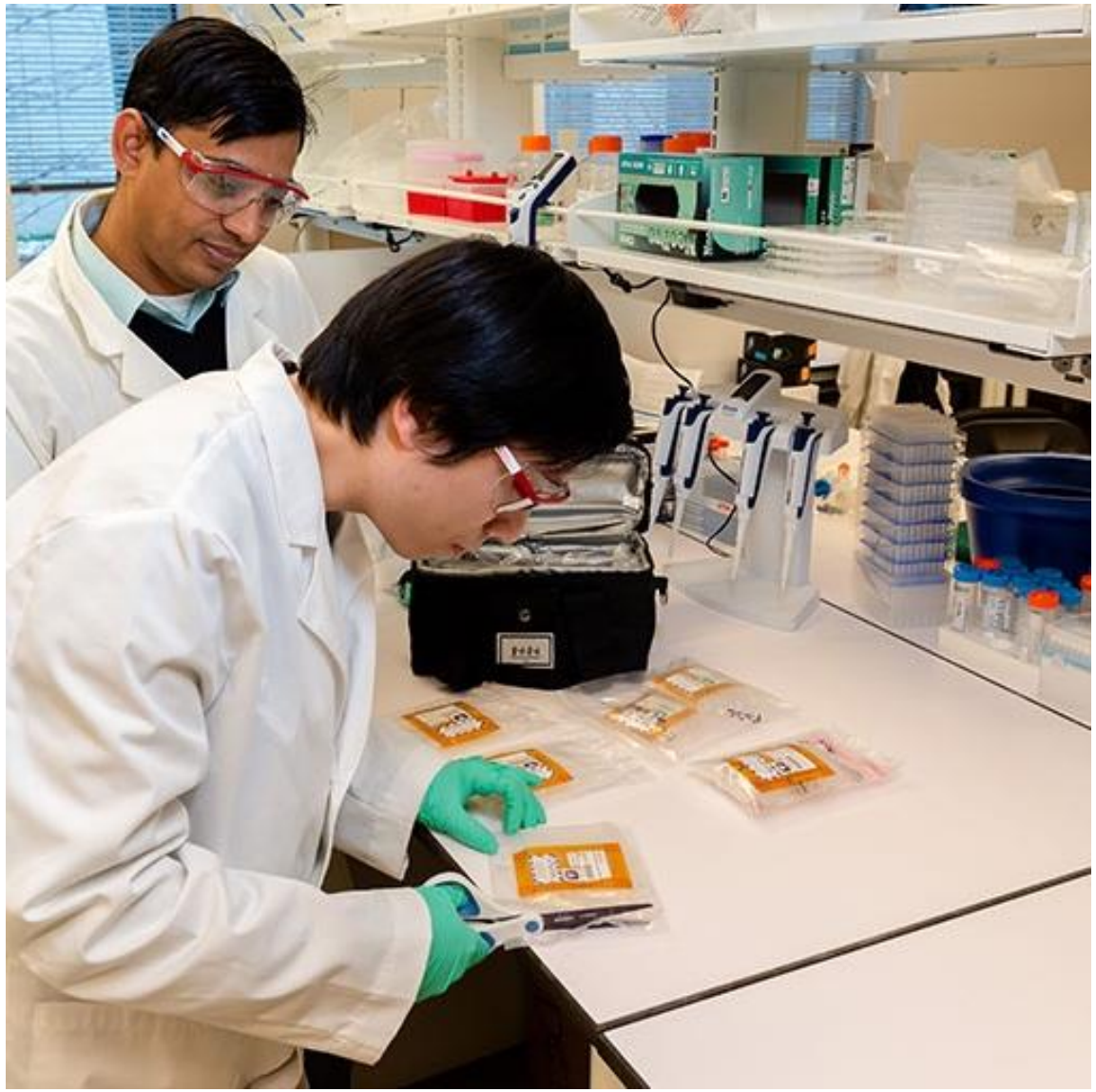
All-time postflight funding **$2.1B**

All-time external funding **$286M**

NASA's investment in CASIS **$192M**

- Has resulted in **$2.4B** in funding, a **12x multiplier.**

Data from October-2021 thru September-2023, FY21-23



Partnering with NASA and BPS to Address National Priorities like the Cancer Moonshot

Launched a new initiative in 2023 in partnership with NASA Biological and Physical Sciences program: **"*Igniting Innovation: Science in Space to Cure Disease on Earth*"**

- R&D moving us toward translational research and transformative applications to aid in the fight against cancer and other diseases that benefit from accelerated cell and tissue models in microgravity
- Expect to award 2-3 grants in July-2024 to support transformative technology development and in-space biomanufacturing R&D

Photo courtesy of Frederick National Laboratory for Cancer Research

After the ISS

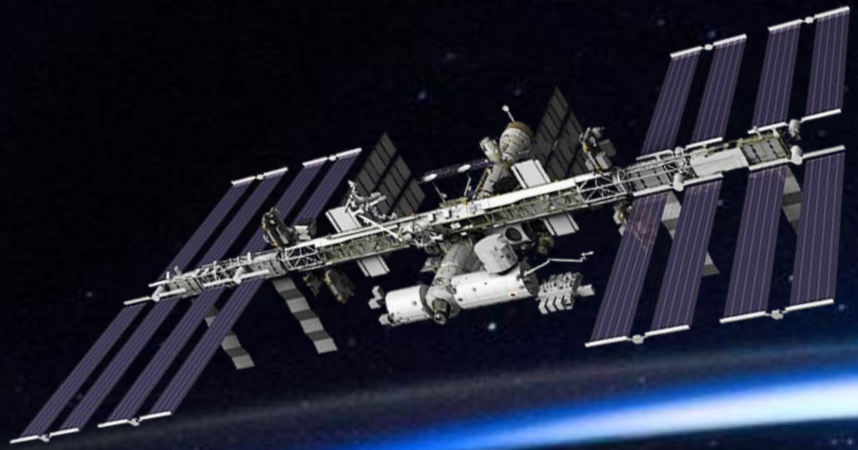
- The ISS will be deorbited around 2030.
- Commercial LEO Destinations (CLDs) will be operating in low Earth orbit before 2030.
- A planned transition from the ISS National Lab to a National Lab operating on multiple CLD platforms is under study.

2000 – 2030ish

2000-2010 DECADE OF ASSEMBLY

2010-2020 DECADE OF UTILIZATION

2020-2030 DECADE OF RESULTS



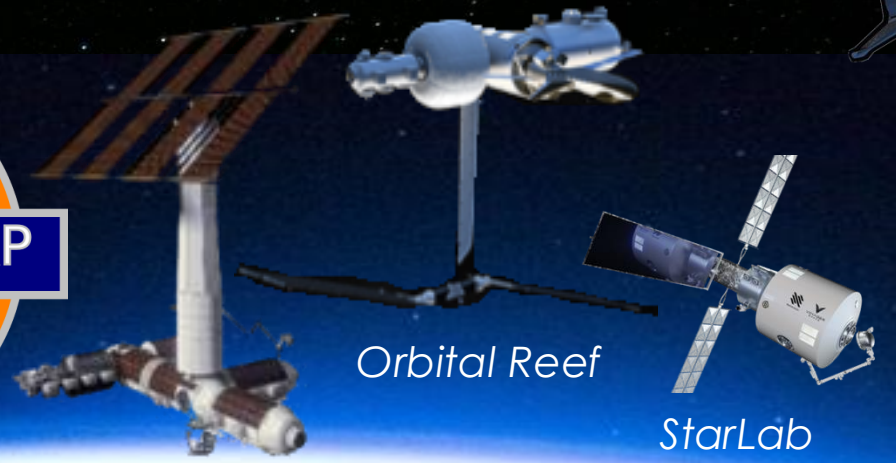
MIND THE GAP

International Space Station

2026ish – the future

TRANSITION TO COMMERCIAL LEO DESTINATIONS
& A NEW LEO NATIONAL LAB CONCEPT

SpaceX Starship

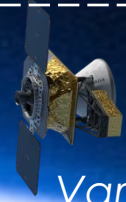


Orbital Reef

StarLab

Axiom Station

Vast Haven-1



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