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SEEING CLEARLY NOW

PIONEERING STEPS IN SPACE TOWARD A CURE FOR BLINDNESS

ON PAGE 2

VOLUME 8 ISSUE 1

VIEW FROM THE CUPOLA
HEMA RAMKUMAR

MICROGRAVITY MANUFACTURING

CELESTIAL CELLS

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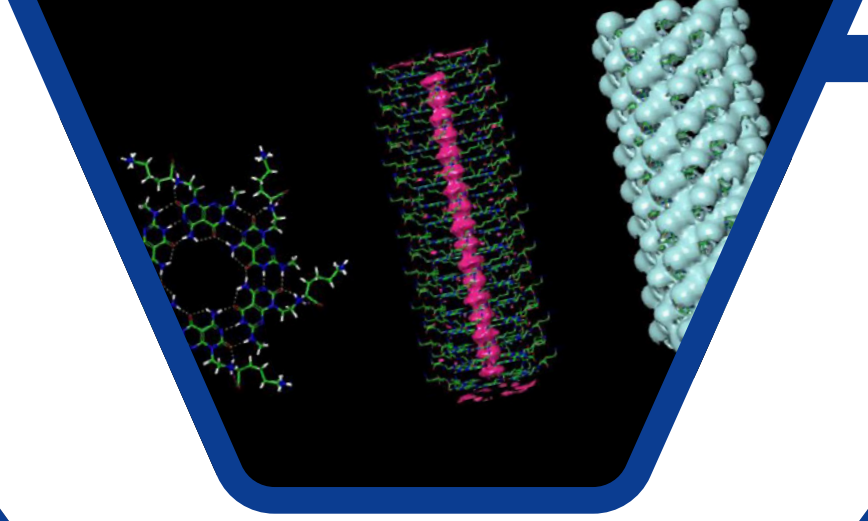

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VIEW FROM THE CUPOLA

By Hema Ramkumar | Oculogenex Founder and CEO

Hema Ramkumar is a retinal surgeon and the founder of Oculogenex, a Southern California-based research and development company specializing in innovative treatments for retinal diseases.

At age 11, I was crazy enough to declare my intent to cure blindness. Throughout my teens and twenties, I spent every minute after school, on weekends, and late nights in research laboratories learning how the eye works and how vision fails. This foundation shaped my future as a retinal surgeon. Over the last 10 years, I have found pride and joy in restoring my patients' eyesight in Southern California.

However, the leading cause of blindness in the U.S., dry age-related macular degeneration (AMD), remains daunting. We have no answers for patients with this debilitating disease, which leads to the loss of central vision. It's often the elephant in the room at eye clinics, the thing we can't fix—a disease that strips millions of their independence and ability to see the results of their life's endeavors, the faces of their loved ones, and the legacy they aim to leave.

The relentless progression of the disease and the absence of effective treatments deeply frustrates me. Witnessing the daily suffering of my patients often leaves me exhausted and nearly defeated. This feeling of defeat compelled me to return to my scientific roots in search of meaningful, long-term solutions where seemingly none existed.

Fueled by this determination, I established Oculogenex in 2020. We created a comprehensive facility that included a research and development lab, a retinal imaging center, and a surgical lab, all aimed at fighting retinal degeneration. Our team developed mouse models and tissue cultures that demonstrated our promising gene therapy could halt disease progression. Maybe it wasn't so crazy to think I could cure blindness after all.

Despite our progress, the limitations of our laboratory models on Earth prevented us from fully understanding our therapy's regenerative properties. To find a better model of macular degeneration, we looked for an environment that is as hostile to the eye as macular degeneration is to those with the disease. To explore this potential, we leveraged the International Space Station (ISS)—a unique environment that degrades the macula in a way that mimics macular degeneration. Our participation in the MassChallenge accelerator program led to a Technology in Space Prize in 2021, which affirmed our innovative approach and facilitated sponsorship by the ISS National Laboratory®. Collaborations with our Implementation Partner Leidos, NASA's Kennedy Space Center, and others further enabled us to send genetically treated mice to space onboard SpaceX's 30th Commercial Resupply Services (CRS) mission.

As you read through this issue's cover story, you will see how our journey into space-based research with the ISS National

Lab opened a revolutionary new path to treating macular degeneration. Our findings have validated our gene therapy's potential to address this challenging disease and paved the way for clinical trials that could change lives. This endeavor goes beyond scientific achievement—it's a collective step toward a future where the world's leading cause of blindness is nothing more than a memory.

This issue also highlights ISS National Lab-sponsored research on Janus base nanomaterials (JBN), which could provide innovative new treatments for osteoarthritis and cancer. By taking JBN production to space, where gravity-driven forces are eliminated, researchers from the University of Connecticut and Eascra Biotech significantly increased the quality of their nanomaterials. Manufacturing JBNs in microgravity could lead to better treatment outcomes for patients on Earth, and the team is partnering with Axiom Space to one day make this a reality.

The third feature in this issue tells the story of Emory University researchers utilizing space-based research to accelerate the development of cell replacement therapies to treat heart failure. Through a series of ISS National Lab-sponsored investigations, the team uncovered insights that could be applied on Earth to more efficiently generate the large numbers of heart muscle cells needed for cell replacement therapies. The findings could also enable scientists to develop cells that are more resilient post-transplantation, potentially improving outcomes for over 6.5 million Americans suffering from heart failure.

This research, conducted in the unique space environment, reflects our broader goal: to harness space-based science for the benefit of Earth. Each story in this issue expands on how these extraordinary efforts could soon offer real hope to millions. As I reflect on our progress and the potential of our discoveries, I'm filled with gratitude for every scientist, partner, and supporter joining us on this path. Together, we are turning once-distant dreams into tangible realities, proving that innovation and collaboration can overcome even the most formidable challenges.

Seeing Clearly Now

Pioneering Steps in Space Toward a Cure for Blindness

By Stephenie Livingston,
Staff Writer

Macular degeneration is a patient thief. It doesn't ransack your vision all at once but lifts details one by one—the fine print on a menu, the headlights on a wet road, the familiar contours of a loved one's face. Eventually, even basic tasks become guesswork. Is that a six or a nine? A friend or a stranger? A sidewalk or an especially aggressive shadow? For millions, this is reality. The leading cause of vision loss in older adults, age-related macular degeneration (AMD), is a slow-motion heist that too often steals its victim's independence.

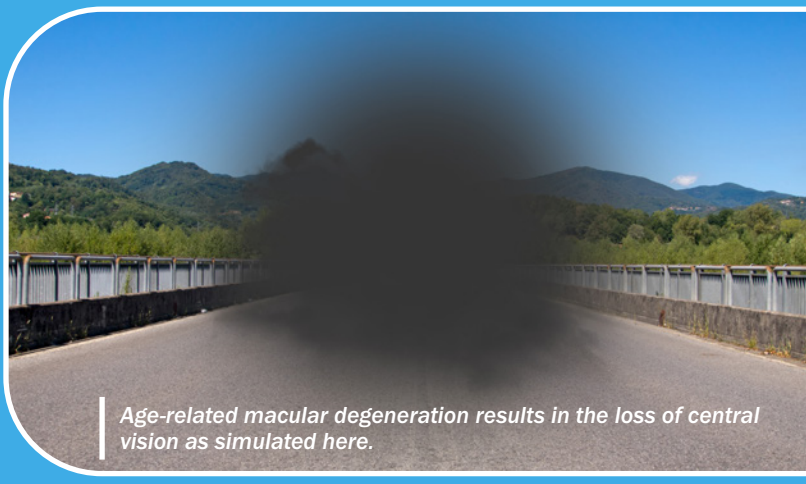
And, despite decades of research, treatments remain frustratingly reactive: slow the decline, cushion the fall.

"Macular degeneration is one of those diseases where you're constantly playing catch-up," said Hema Ramkumar, a retinal surgeon and founder of California-based startup Oculogenex. "Patients in the intermediate stages struggle to drive at night or read fine print. By the advanced stages, they're tethered to monthly eye injections just to keep the disease from getting worse. There's nothing preventative. There's no cure."

AMD, as the name suggests, is both age-related (most patients are over 50) and macula-related (the macula being the part of the retina responsible for sharp, central vision). It comes in two unappealing flavors: dry, which erodes vision slowly through damage from oxidative stress, and wet, which works fast and chaotically, thanks to rebellious blood vessels that bleed and scar. Wet AMD can be managed—if you count frequent, needle-to-the-eyeball injections. As for dry AMD? There's no treatment to improve vision, no magic eye drops. It's just a slow fade into a blurry new world.

Anatomy of the Eye

To understand macular degeneration, it helps to know a little about the eye's anatomy. The retina is the thin, light-sensitive layer of tissue at the back of the eye. It acts like the film in a camera, capturing images and sending them to the brain via the optic nerve. At the center of the retina is the macula, a small but critical area responsible for sharp, detailed vision. Tasks like reading, driving, and recognizing faces rely on the macula functioning properly.



Age-related macular degeneration results in the loss of central vision as simulated here.

Ramkumar grew weary of delivering the same bleak prognosis, offering patients little more than a slower descent. In 2020, she found herself at a crossroads at the height of the pandemic. The pause in routine gave her time to reevaluate her path, prompting the surgeon to revisit her lifelong passion for science that began with a promise to cure blindness made at age 11 after her first eye doctor's visit resulted in glasses. She founded Oculogenex with a bold goal: develop a gene therapy that does not just slow the disease but stops it cold—and maybe even reverses it.

"There's a huge unmet need for therapies that can prevent or even reverse the damage before it's too late," Ramkumar says.

But how do you test a therapy for a disease that takes years to wreak havoc? This is an especially critical problem when you see patients every day who don't have much time to spare. Ramkumar's solution was unexpected, even to her: space.

This forward-thinking approach earned her a ticket to conduct a scientific investigation through the International Space Station (ISS) National Laboratory. What she discovered could revolutionize our understanding of and approach to treating macular degeneration.

The Space Connection

Scientists found that the radiation and fluid shifts that occur during spaceflight create the same kind of oxidative stress in the retina that leads to macular degeneration. Oxidative stress, a damaging process caused by harmful molecules called free radicals, is the primary cause of dry AMD and is something no existing treatment effectively addresses. What's more, astronauts, it turns out, occasionally exhibit early signs of retinal aging—a coincidence that intrigued Ramkumar.

Her lightbulb moment arrived during a MassChallenge startup accelerator program competition when someone floated the idea of leveraging the ISS National Lab to accelerate her research. The clincher? A 2019 study showing that just 35 days in low Earth orbit (LEO) triggered retinal changes in mice that looked eerily like the early stages of macular degeneration in humans.

If Earth-based scientists are hindered by long waits for AMD to develop in animal models or by the costly methods needed to induce it, space might be the fast-forward button. After pitching her idea, Oculogenex was selected for the Technology in Space Prize, funded by Boeing and the Center for the Advancement of Science in Space®, which manages the ISS National Lab, in partnership with MassChallenge. The award recognized the potential of Ramkumar's innovative approach to gene therapy.

The therapy employs a simple yet bold method: it uses an adeno-associated virus (AAV), a common gene delivery system, to introduce the BMI1 gene directly into retinal cells. This gene is like a molecular bodyguard, shielding the retina from oxidative stress.

(Above) SpaceX CRS-30 launches from Cape Canaveral in March of 2024.

Ben Cooper

Hema Ramkumar and her team gather to watch the SpaceX CRS-30 launch at Kennedy Space Center.

Oculogenex

Cheryl Rowe-Rendleman, a clinical development expert guiding Oculogenex through the U.S. Food and Drug Administration (FDA) approval process, emphasized the unique potential of targeting BMI1. She explained that BMI1 therapy works by rejuvenating cells damaged by the disease's

progression. It specifically alters how these cells handle energy and waste, boosting their metabolic efficiency. This enhancement in cellular metabolism is key to strengthening the retina's cells, giving them a better chance to withstand the degenerative effects of AMD.

"Despite the myriad environmental and metabolic pressures these cells face, which could push them into an advanced stage of degeneration, BMI1 remains agnostic to these pressures," she said. "This crucial intervention allows the patient's cells to gain a resilience that is comprehensive and enduring."

Ramkumar further explained, "Our goal was to design a therapy that is more robust and durable, one that doesn't require frequent injections but instead offers long-term protection for the retina. We're aiming for a single injection that lasts years."

Yet, moving from theory to execution, especially in space, introduced a series of unexpected challenges. To Ramkumar's surprise, launching an experiment to the space station isn't as simple as slapping a FedEx label on it. After three years of meticulous planning and navigating complex regulatory requirements to test the therapy in space, Ramkumar's team spent five intensive months at Kennedy Space Center prepping for launch on SpaceX's 30th Commercial Resupply Services (CRS) mission for NASA.

The goal: send 40 female mice into orbit, half treated with the gene therapy, and the other half serving as controls. But getting those 40 mice flight-ready took work—more than 300 mice were screened on the ground to ensure only the healthiest, most retinally pristine candidates made the cut.

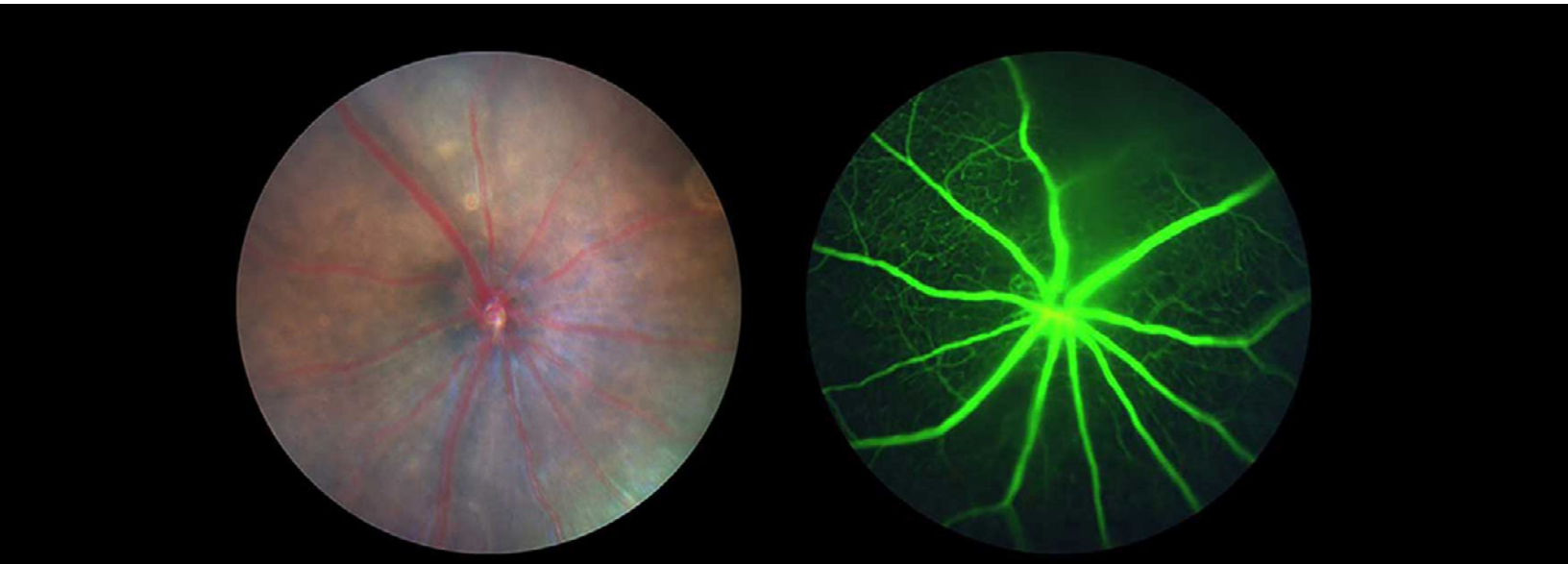
"We tested different devices and techniques for recording retinal function, performing injections, and ensuring that the mice were stable under anesthesia," said Zhongyang Lu, Oculogenex's senior scientist and lab director. "It was a lot of trial and error to make sure everything was precise and ready."

They also screened and selected 40 female mice for the ground control experiment housed at Kennedy Space Center in ISS environmental simulator chambers—miniature, ground-based replicas of the space station's temperature and humidity conditions.

"The team started measurements a month before launch, using electroretinography (ERG), which is basically an EKG for the retina, and optical coherence tomography (OCT), which provides detailed images of retinal layers," said Kristin Kopperud, science program director for the ISS National Lab, who worked closely with the team.

Taken with a specialized camera, images of a mouse retina before spaceflight (left) and a fluorescein angiogram, captured using a fluorescent dye, of the microvascular circulation of a mouse retina (right) are shown here.

Oculogenex



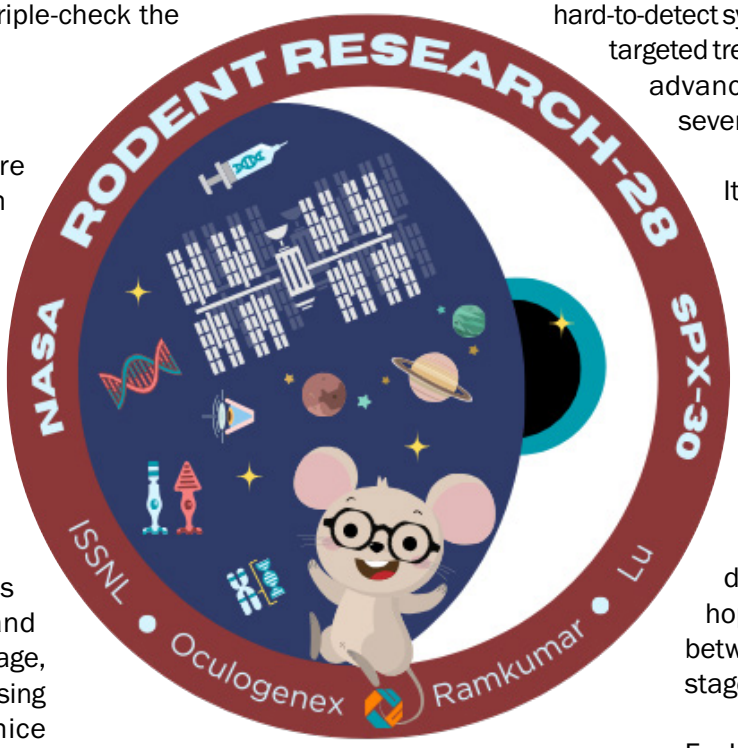
After a month in orbit, the mice returned safely to Earth for a battery of postflight tests—retinal imaging, electrophysiology, and tissue sampling. The data was, in a word, striking.

What did the team find? Let's just say it was enough to make them double- and triple-check the results.

Unlocking Vision

Because AMD affects more women than men, the team sent only female mice to space to test the gene therapy. What they found was unexpected: the retinas of the mice suffered little damage from the harsh space environment.

"We think estrogen is protective," Ramkumar said. "The hormone boosts antioxidants in the retina and mitigates stress-related damage, which might explain the surprising resilience of the female mice and offer evidence for why post-menopausal women lose eyesight to AMD."



Shown here is the mission patch for the team's investigation that launched on SpaceX CRS-30.

Oculogenex

While this resilience complicated the team's ability to test the damage-prevention aspect of the therapy, they did see signs of preservation compared with the control group, and it brought another revelation: improvement. "We saw a measurable improvement in retinal function after treatment," Ramkumar said. "Not just preservation—actual improvement in how the retina works."

That's a surprising finding in macular degeneration research, she says. The therapy appears to enhance the retina's bioenergetics, making cells more efficient at processing energy and oxygen. The treatment could potentially restore the cells' health and functionality by improving these cellular functions.

"We are optimistic that this therapy will eventually reverse vision loss from AMD, a milestone we could only approach by leveraging the microgravity environment provided by the ISS National Lab," Ramkumar said.

Oculogenex is conducting critical safety studies now, with plans to develop a device to deliver the drug before identifying patients for clinical trials, which are expected to begin within the next two years, said Rowe-Rendleman.

"I'm particularly moved by the focus on a patient population with intermediate AMD, a group that has historically been poorly identified and underserved in our field," she said. The challenge with intermediate AMD (between early and late-stage AMD) lies not only in its more subtle, sometimes hard-to-detect symptoms but also in the lack of targeted treatments, as most therapeutic advancements focus on the more severe, late stages of the disease.

It's also not out of the realm of possibilities for Ramkumar's research to influence how vision loss is treated beyond macular degeneration. "By educating physicians on the benefits of the BMI1 pathway," Rowe-Rendleman says, "we could fundamentally change the approach to treating macular degeneration, offering new hope to those caught in the gap between early detection and late-stage intervention."

For Kopperud, this study feels like an especially important one to be a part of, as it's not just advancing science—it has a clear pathway to improving lives. "When this therapy reaches patients, it'll be life-changing," she says.

And what of the mice themselves? Ramkumar reports that the treated group returned from space looking notably sprightlier than their saline-injected counterparts. "Our mice were alert and active," she said. "You could see the difference. Vision is so much more than eyesight; it's about engagement with your surroundings."

The team's postflight data provided invaluable insights into how their gene therapy interacts with the stresses of space. Ramkumar said that leveraging the ISS National Lab to explore gene therapy in ways not possible on Earth paved the way for what might be a significant breakthrough in retinal medicine.

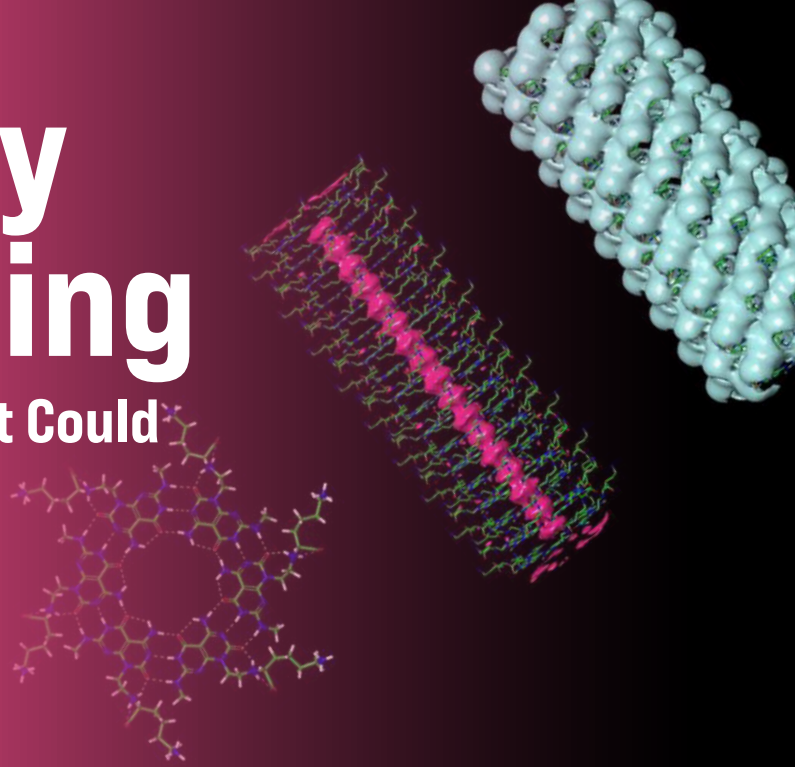
"This study gave me hope," she said. "It reminded me why I got into this field—to change lives."

For millions facing a slow fade to gray, it might just deliver a light switch.

Microgravity Manufacturing

Producting Nanomaterials That Could Revolutionize Medicine

By Amelia Williamson Smith,
Managing Editor



In Roman mythology, Janus is the god of endings and new beginnings. He is usually depicted as having two faces—one looking to the past and the other to the future. In his hand, Janus holds a key, symbolizing his power to unlock doors to new possibilities.

When Yupeng Chen and his team at the University of Connecticut developed synthetic molecules that self-assemble into nanomaterials that could revolutionize drug delivery and lead to new treatments for osteoarthritis and cancer, the Roman god immediately came to mind. Like Janus, the molecules have two faces, allowing them to bind together in a way that mimics DNA. To further develop Janus base nanomaterials (JBNs) as commercial products, Chen and his colleague Mari Anne Snow co-founded Eascra Biotech, a spinoff from his University of Connecticut lab.

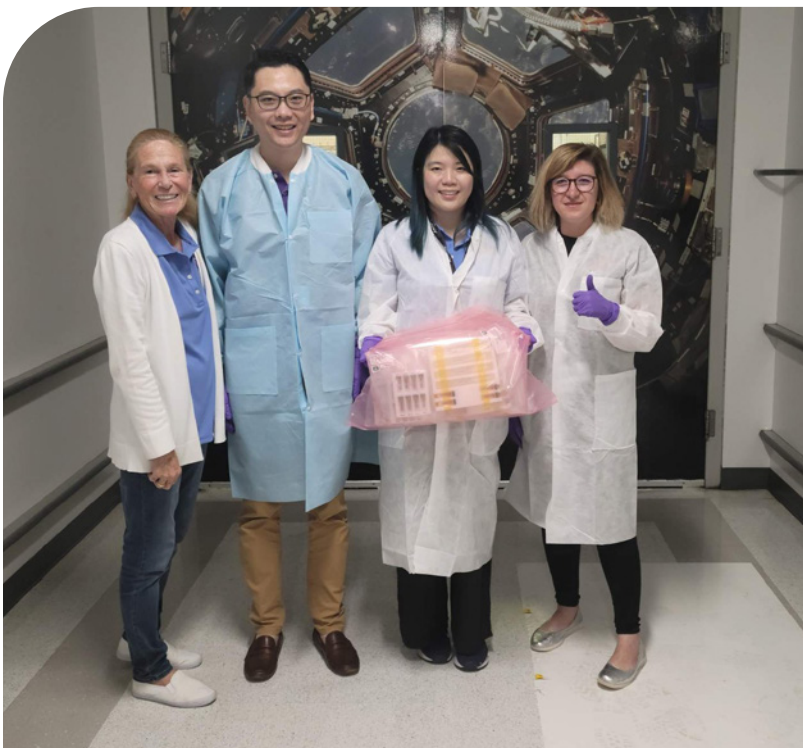
Eascra's JBN products performed well but had slight defects. Janus base molecules first self-assemble into rings that then stack like dinner plates to form nanotubes. Gravity-driven forces like convection cause the molecules to aggregate in some places as they assemble into the rings, which reduces the uniformity of the nanotubes. The imperfections frustrated the team, but they didn't know what to do.

Then, as if Janus stepped in with his key and opened the door to something they never imagined, Chen and Snow came upon a possible answer—manufacturing their nanomaterials in space.

They had read about others who leveraged microgravity on the International Space Station (ISS) to produce more uniform and well-ordered protein crystals than can be produced on Earth. They wondered: Could microgravity similarly improve nanomaterial assembly? To find out, Chen's lab and the Eascra team conducted a series of investigations sponsored by the ISS National Laboratory®.

Yupeng Chen (second from left) and Anne Yau (second from right) from the University of Connecticut work with the Axiom team to prepare the JBN in-space production investigation for launch on the Ax-2 mission.

University of Connecticut/Eascra Biotech



"We started thinking about how we could better form the nanomaterials, and producing them in microgravity could be a solution," Chen said. "If in-space production could give us nanomaterials with better structure, integrity, and uniformity, it may also give us better bioactivity and therapeutic outcomes."

Reconstructing Cartilage at the Nanoscale

The first project from Chen's team, funded by the U.S. National Science Foundation, launched on Northrop Grumman's 20th Commercial Resupply Services mission for NASA. The aim wasn't to manufacture JBNs but to test their effectiveness for cartilage regeneration.

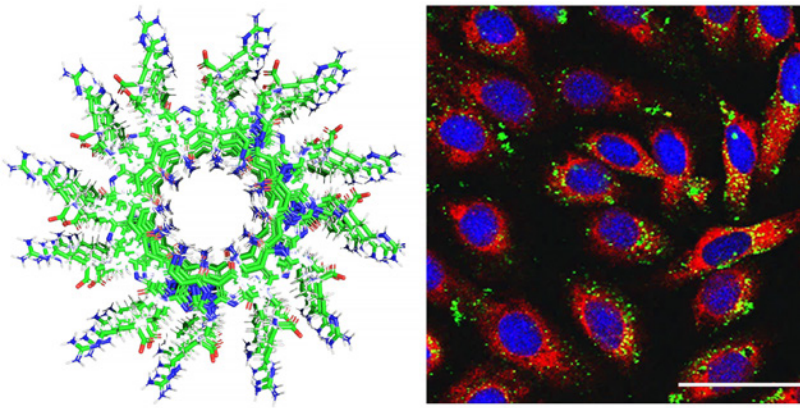
Cartilage is the tough, flexible tissue that pads joints. For people with osteoarthritis, which affects one in seven Americans, cartilage in joints like the knees and hips slowly breaks down over time, which causes pain and inflammation.

Yupeng Chen and graduate students Ian Sands and Anne Yau prepare their experiment for launch on NG-20.

University of Connecticut

Because cartilage has a limited blood supply, it does not regenerate well, so it isn't easy to restore once it is gone. Currently, the only long-term solution for osteoarthritis is expensive joint replacement surgery with a long and painful recovery. In the United States, nearly 800,000 knee replacements and more than 540,000 hip replacements are done every year. The JBNs developed by Chen and his team could be a game-changer by providing a way to rebuild lost or damaged cartilage.

The team's Janus base nanoparticles, which are 1,000 times smaller than a cell, can carry therapeutics into hard-to-penetrate tissues like cartilage. The nanoparticles can be loaded with an RNA-based drug that stops cartilage breakdown and stimulates cell formation. RNA drugs cannot pass through the cell membrane of cartilage cells, but the nanoparticles can, making them the perfect delivery vehicle.



(Left) A cross section of a Janus base nanotube with a diameter of 3.5 angstroms. (Right) Green-fluorescence-labeled RNA drugs were delivered into human cartilage cells by JBNs (scale bar is 100 micrometer).

Maxwell Landolina, Trystin Cote, and Jinhyung Lee, University of Connecticut

The team also developed a Janus base nano-matrix to support and maintain cartilage cell growth. You can think of the nano-matrix as scaffolding for building construction, said Max Landolina, a graduate student at Chen's lab. "When we put up the scaffold, all the workers, the cells, are attracted to it and go there to get set up," he explained. "Once they have that good foundation, they can start to rebuild and create new structures."

The nanoparticles and nano-matrix are both flexible and can be injected into affected joints. The JBNs' ability to fit into every corner of an irregularly shaped defect to regenerate cartilage results in a better repair outcome, Chen said. The JBNs are also stable at room temperature. This means they do not have to be kept at sub-zero temperatures like other RNA-based drugs that immediately degrade in ambient conditions. Because refrigeration is not required, it is much easier to ship the JBNs to different locations around the world and store them for use.

In microgravity, cartilage degeneration happens more quickly than on Earth. So, the space station provides a valuable platform to test how well JBNs work.

"By using disease models in microgravity, instead of waiting for years, we may just have to wait a couple weeks to see disease progression," Chen said.

Housed in Space Tango's CubeLab hardware, the team's tissue samples—half treated with the JBNs and half not—remained on the ISS for 14 days before returning to Earth for analysis. The results revealed that the nanoparticles successfully prevented cartilage degradation and supported cartilage cell formation. The team also found that the nano-matrix significantly promoted cartilage regeneration and maintenance.

When Yupeng Chen came to the U.S. to pursue his Ph.D. nearly 20 years ago, Mari Anne Snow served as his cultural mentor through the International House.

Yupeng Chen

Becoming a Space Company

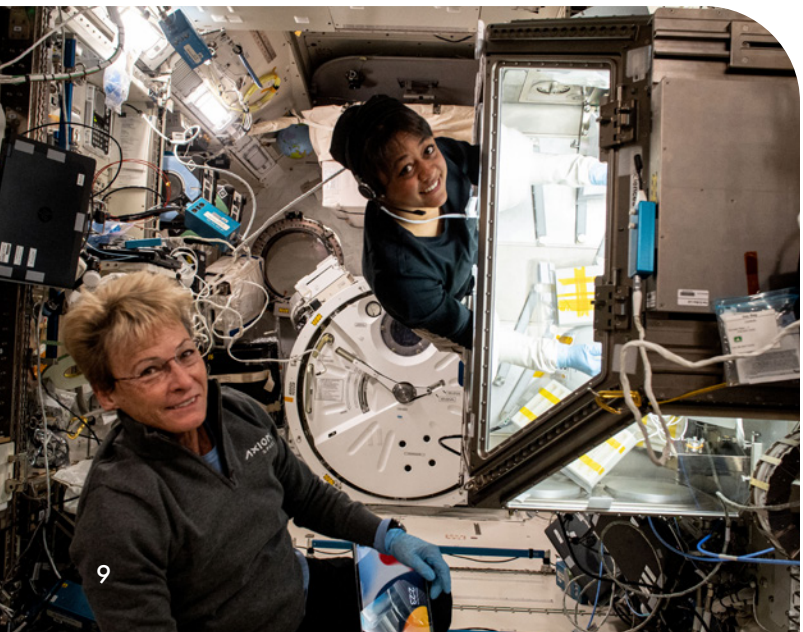
After the first successful project, the team's mindset shifted to using microgravity to improve JBN production. "While we didn't intend to be a space company, we're actually the perfect candidate," said Snow, CEO of Eascra Biotech.

Chen and Snow co-founded Eascra in November 2021, but the two have known each other for nearly 20 years. They met when Chen first came to the U.S. to pursue his Ph.D. at Brown University. Snow was part of a nonprofit called International House that provides cultural mentorship for international students pursuing graduate degrees in the U.S. and served as a mentor for Chen.

"We celebrated the holidays together and shared our different cultures," Chen recalls. "I had my first Thanksgiving and Christmas with Mari Anne and her husband, and even today, we always celebrate Thanksgiving together."

Axiom Space astronauts Peggy Whitson and Rayyanah Barnawi producing the Janus base nano-matrix for the first time on station.

NASA



Over the years, Chen and Snow talked about one day partnering on a biotechnology startup, Chen with his biomedical science expertise, and Snow with her background in business and finance. When Chen and his team created and patented JBNs, the time had come, and Eascra was born.

At the time, Chen and Snow never dreamed that Eascra's products would one day be manufactured in space. But after reading about other researchers' successes, they were anxious to see if microgravity would improve the quality of their nanomaterial products. The team partnered with Axiom Space on two investigations sponsored by the ISS National Lab.

"Axiom Space is all about expanding access so anyone anywhere can leverage the unique space environment," said Pinar Mesci, Axiom Space senior program manager and global head of regenerative medicine and disease modeling. "Microgravity research enables us to look at the same problem through a very different lens, and that's where innovation happens."

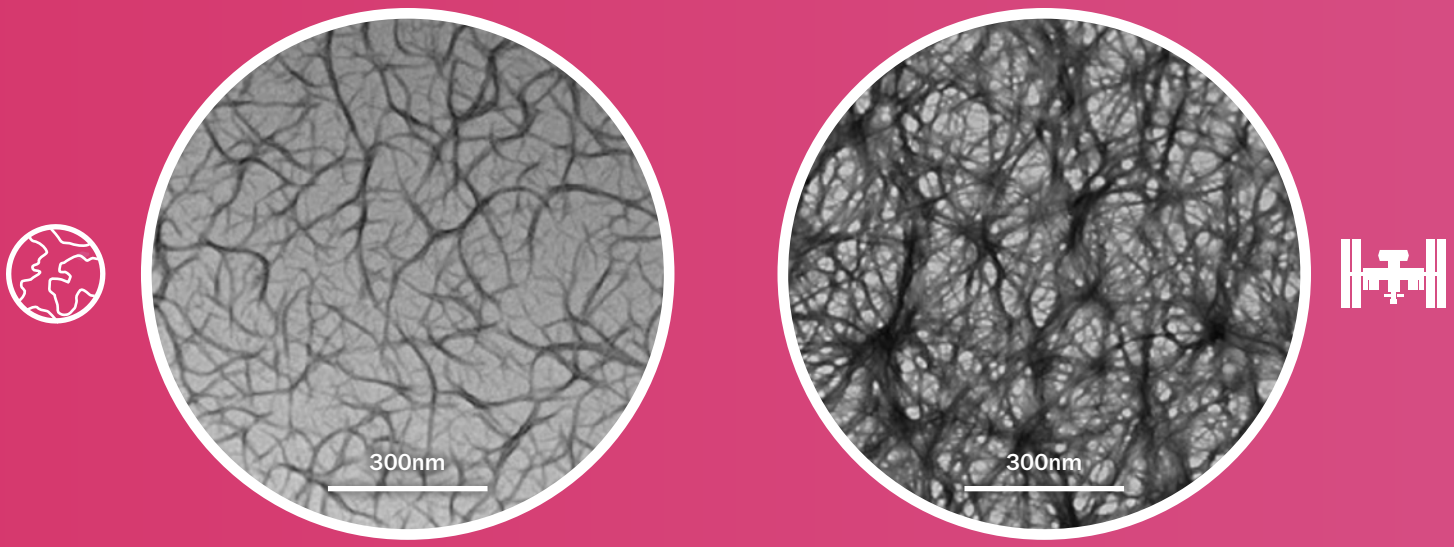
The first project, which was aimed at manufacturing Eascra's Janus base nano-matrix, flew on Axiom Mission 2 (Ax-2). The experiment was simple: First, the astronauts added water into reaction tubes filled with a powdered form of Janus base molecules. They then added a protein solution and waited for the nano-matrix to self-assemble.

The samples remained on the ISS for two weeks before being returned to Earth. When Chen and Snow compared the space-manufactured nano-matrix with what they produced on the ground using the same methods and procedures, they couldn't believe what they saw.

"We discovered that in space, we were able to achieve huge gains in uniformity and homogeneity, with up to 40-percent improvement in the structure of the nano-matrix scaffold," said Snow, beaming with excitement as she pulled up images from the investigation. "You can clearly see that the space-produced nano-matrix is structurally denser and stronger."

With these results, Eascra's future was clear. "That was the moment we became a space company," Snow said.

For the next ISS National Lab-sponsored project, which launched on SpaceX's 30th Commercial Resupply Services (CRS) mission for NASA, the team produced the nano-matrix and nanoparticles loaded with an RNA-based drug. The team also sent up a small UV spectrometer to characterize the JBNs in real time and a handheld sonicator, which uses sonic waves to agitate the nanomaterials and break them into smaller nanoparticles.



This image of the first Janus base nano-matrix produced in space (right) clearly shows the significant improvement in structure over the nano-matrix produced on the ground (left).

University of Connecticut/Eascra Biotech

While the project was on station, the team watched via livestream. "My favorite part was coming into the lab at 2 a.m. to communicate with the astronauts while they did our experiments," said Trystin Cote, a graduate student in Chen's lab. "We could give them tips on how to work with our samples and help them in any way needed to improve the science."

After two weeks in space, the JBNs were returned for analysis, and once again, the team was excited about the results. "In space, we were able to not only build nanoparticles with better structure but also encapsulate RNA, which is a very fragile cargo, in such a way that we can maintain its bioactivity at room temperature for months," Snow said.

University of Connecticut graduate students Max Landolina (far left) and Trystin Cote (far right) work with Alexis Rios and Pinar Mesci from Axiom Space to prepare the team's SpaceX CRS-30 investigation.

University of Connecticut/Eascra Biotech

The team also found that the space-produced nanoparticles result in better functional outcomes when compared with those produced in the ground control. "The benefit we get from assembling our nanomaterials in space is unparalleled to what we can do on the ground," Cote said. "Our Earth-made samples are already really good, so being able to advance them that much just by sending them into space is amazing."

Refining Production and Scaling Up

Following these successes, the team was awarded two additional ISS National Lab-sponsored investigations funded by NASA to continue working with Axiom Space on the in-space production of JBNs.

"We were doing foundational work to get everything in place so we could start to expand quickly," Snow said. "Our goal every single flight is to get closer to being production-ready and to optimize the formulation for commercialization."

In the first project, which launched on SpaceX CRS-31, the team increased from 30 or 40 samples to 140 samples and from two to four weeks on station. The second project will launch on the upcoming SpaceX CRS-32 mission with the same sample size but fewer variables.

"We have refined our production procedure and verified that our nanomaterials can be better produced in microgravity, and we achieve not only better uniformity but also better bioactivity," Chen said.

The team is now working to identify the best conditions for in-space production and develop an automated system to

(Above) Max Landolina, Maddie Picket, and Jared Lawrence (left to right) from the University of Connecticut prepare the team's investigation for launch on SpaceX CRS-31.

University of Connecticut/Eascra Biotech

Yupeng Chen (left) and Mari Anne Snow (middle) with Eascra Biotech science advisor Gary du Moulin (right) when the company was named 2024 MassBioDrive Startup of the Year.

Eascra Biotech

scale up. The ISS National Lab provides a critical platform to do this, Mesci said. "It's where we conduct all types of proof-of-concept research to generate the data we need to go to the next steps where we can scale up the manufacturing process."

The Eascra team is collaborating with Google to use machine learning and AI tools to better characterize JBNs and improve quality control. Chen said the team's goal is to standardize production and quality control processes to comply with the requirements from regulatory agencies such as the U.S. Food and Drug Administration.

"Commercial companies like Axiom Space coming into this arena is important," Mesci said. "We have to be able to meet commercial timelines to make products in a timely manner and make sure quality controls are still intact for regulatory approvals."

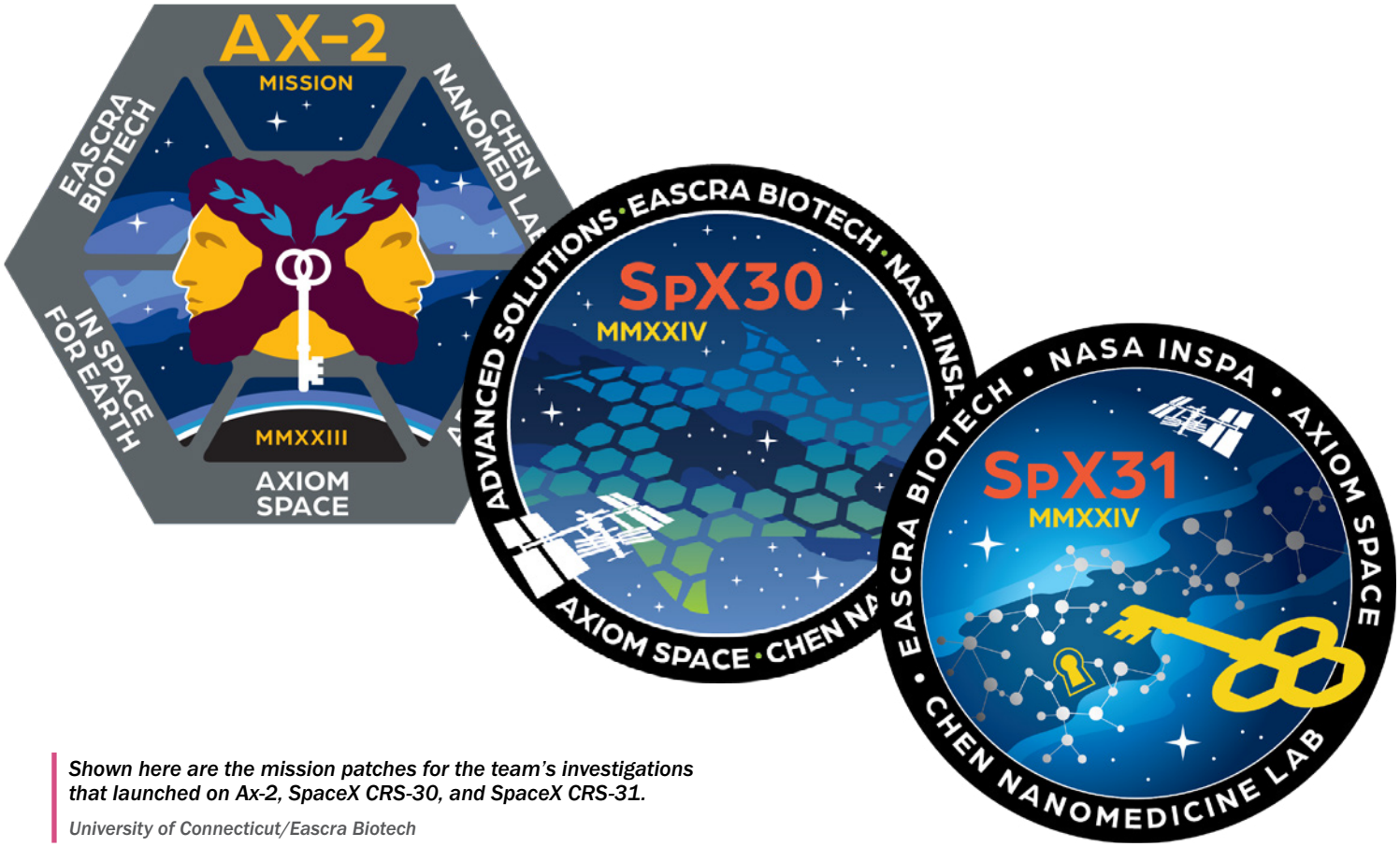
Eascra is also expanding beyond osteoarthritis to cancer treatment. The startup received grant funding through the inaugural ISS National Lab Igniting Innovation solicitation, in partnership with NASA's Biological and Physical Sciences Division, to produce Janus base nanoparticles for precision cancer treatment.

The nanoparticles can encapsulate cancer drugs and directly deliver them into dense solid tumors that are notoriously difficult to penetrate, Snow said. The nanoparticles also prevent the drugs from affecting other parts of the body, significantly reducing side effects. And because JBNs mimic DNA, the nanoparticles don't trigger the immune system, which allows the drugs to remain at the tumor site for longer.

"Drug discovery is not going to be effective if there's not a way to deliver the therapeutic to the treatment site," Snow said. "If you go to any major therapeutic conference, there's lamenting about the fact that there's not a good delivery system." Eascra's JBNs could be the solution for a wide range of therapeutics that need an effective delivery method.

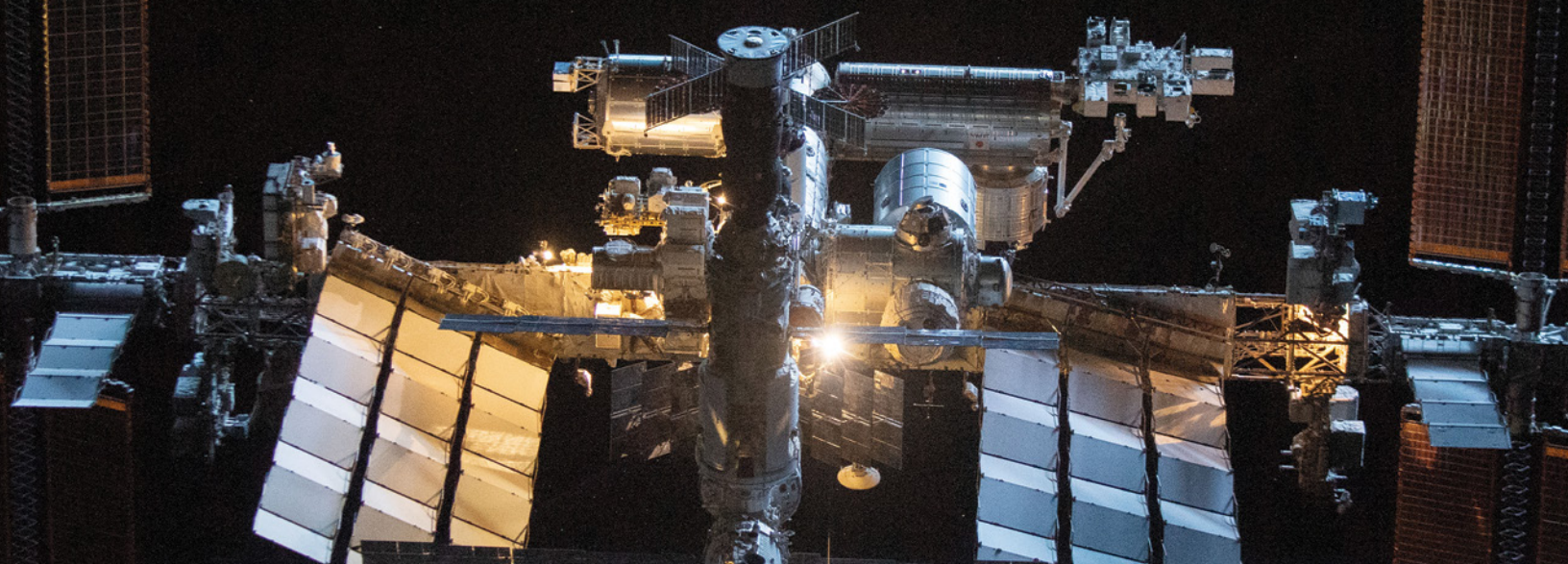
Like Janus, Snow looks both to the past and to the future. "We've had a lot of 'pinch me' moments," she said. "How many opportunities do you get in life to access one of the most extraordinary research environments that allows you to push the boundaries of what's possible?"

Reflecting on the team's space-based research, she describes the experience as incredible. Looking forward, she is excited about the future of Eascra and how manufacturing JBNs in space could one day help millions of people worldwide by providing more effective treatments for some of life's most difficult health challenges.



Shown here are the mission patches for the team's investigations that launched on Ax-2, SpaceX CRS-30, and SpaceX CRS-31.

University of Connecticut/Eascra Biotech



Celestial Cells

Advancing Regenerative Heart Therapies in Space

By Amelia Williamson Smith,
Managing Editor

Flight Engineer Jasmin Moghbeli works onboard the ISS in March 2024 to retrieve bags containing heart cells for the Emory team's experiment.
NASA

Even the darkest cloud has a silver lining, and the blackest night shines with stars. If you look closely, something good can come out of even the most destructive things.

Consider cancer cells: notorious for their ability to multiply and invade tissues, spreading through the body and wreaking havoc. But what if an observation about cancer cells in space could lead to life-saving treatments for heart failure on Earth?

Scientists have found that cancer cells proliferate—grow and divide to produce more cells—much more quickly in microgravity. Spaceflight also triggers cancer cell survival mechanisms, helping the cells better cope with the stressful environment.

Reading about these findings, Chunhui Xu, a professor in the department of pediatrics at Emory University, was struck with an idea. For cancer cells, increased proliferation and cell survival can be deadly. But in Xu's area of research—the production of cardiac cells to repair heart damage—increased proliferation and cell survival could help save lives. If cardiac cells respond to microgravity in the same way cancer cells do, space-based research could hold the key to accelerating the development of cell-based regenerative therapies for heart disease.

Xu was one of the earliest investigators to take advantage of research opportunities through the International Space Station (ISS) National Laboratory. Beginning in 2013 with a ground-based experiment using simulated microgravity, Xu and her team began exploring the effects of the space environment on stem cell-derived heart cells.

The team conducted two investigations on the ISS, looking first at stem cells as they differentiate into heart muscle cells and then at heart muscle cells as they mature into tissue-like structures. Findings from these ISS National Lab-sponsored projects led to multiple peer-reviewed publications, including two in the high-impact journal *Biomaterials*.

Chunhui Xu (second from right) and her team shortly after their investigation launched to the ISS on SpaceX CRS-20.
Rich Boling

"The space environment provides an amazing opportunity for us to study cells in new ways," Xu said. "Our research on the ISS could allow us to develop a new strategy to generate cardiac cells more efficiently with improved survival when transplanted into damaged heart tissue, which would greatly benefit patients on Earth."

Healing a Failing Heart

In the United States, one in five deaths is from heart disease, making it our nation's number one killer. The heart is a powerful muscle that pumps oxygen-rich blood throughout the body, but once heart muscle tissue is damaged, it becomes scarred and cannot regenerate. This makes it difficult for the heart to pump enough blood to meet the body's requirements. The only option for people with end-stage heart failure is a heart transplant, but the number of people in need of a transplant far outnumbers the donor hearts available.

"Not everyone can have a donor heart, so the research community has been looking for other ways to save patients by transplanting new heart cells into the damaged area," Xu said. "This is a very promising field, but there are also challenges."

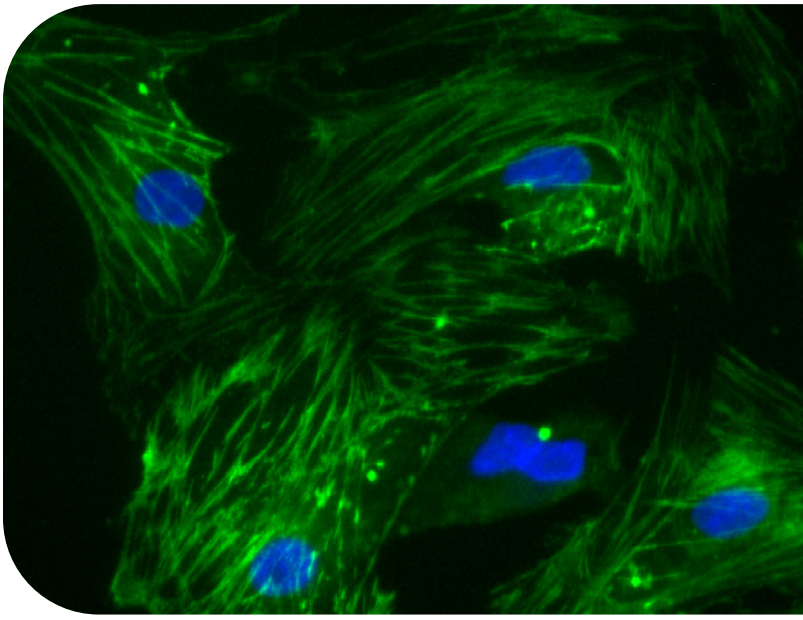
One problem is the number of cells needed. Treating a patient's heart requires about a billion heart cells, which is a lot to generate, so scientists need a way to produce the cells more efficiently.

A Pioneer on Earth and in Space

Xu has been studying stem-cell derived heart cells for a long time. In fact, she is a pioneer in the stem cell field. As a postdoctoral fellow at the Burnham Institute in San Diego, Xu identified a molecule critical for differentiating stem cells into heart cells. She also invented a feeder-free method for culturing human stem cells that is now widely used in the community and is viewed as a milestone in stem cell research. Her publications on stem cells have been cited more than 12,000 times.

To generate heart cells, researchers begin by reprogramming blood or skin cells into induced pluripotent stem cells (iPSCs). iPSCs can differentiate into many different types of cells that can then proliferate indefinitely. This makes iPSCs invaluable for producing specific cell types to model diseases, test new drugs, and develop regenerative therapies. For heart therapies, iPSCs are differentiated into cardiac progenitor cells that further differentiate into heart muscle cells, which can be transplanted into patients.

This brings us to another challenge: ensuring the heart muscle cells survive once transplanted. A damaged heart is a stressful environment for cells, which is why there's a lot of cell loss after transplantation, Xu explained.



Heart muscle cells stained for muscle proteins (green) and nuclei (blue).

Parvin Forghani, Cardiomyocyte Stem Cell Laboratory

"Even if you can generate a lot of cells, if they don't survive, you still can't repair the heart," she said. "So, finding ways to improve cells' ability to survive is a big step toward making cell replacement therapies a reality."

Xu believes the key to producing heart cells more efficiently and improving their survivability could lie beyond Earth's horizon—in space.

Improving Heart Cells With Microgravity

To explore microgravity's effects on stem cell-derived heart cells, Xu and her team first conducted a ground study using 3D cell growth techniques and simulated microgravity. The experiment revealed that the cells grown in simulated microgravity proliferated much more quickly—at a rate 1.5 times higher than a 3D culture in normal gravity and four times higher than a standard 2D culture.

The team also found that heart muscle cells generated in simulated microgravity were purer and more mature than those produced in normal gravity. Both characteristics are critical for cell replacement therapies.

With these encouraging results, the next step was to confirm the findings in actual microgravity. Xu's first investigation was launched to the space station on SpaceX's 20th Commercial Resupply Services mission for NASA. For this project, the team worked with ISS National Lab Commercial Service Provider Redwire Space Technologies Inc., formerly Techshot Inc. The experiment utilized the company's Multi-use Variable-gravity Platform (MVP), a facility that uses two centrifuges to provide artificial gravity for research on the space station.

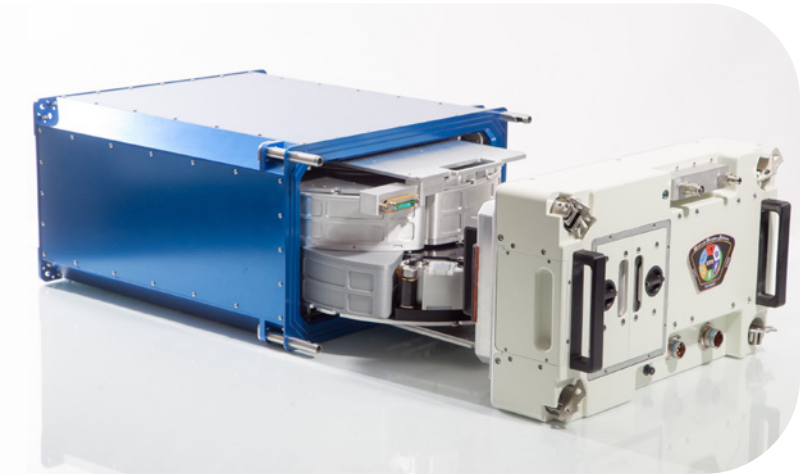
Finding Space

Xu first learned about microgravity research when the ISS National Lab and NASA held a Destination Station event at Emory in 2013. ISS National Lab representatives gave a talk at the Emory School of Medicine, and Xu was in the audience.

"If I had missed that seminar, I probably would have never ended up doing space research," she said. "Before that talk, I knew nothing about space, and it was so exciting to see their presentation about the value of science in microgravity."

Redwire's Multi-use Variable-gravity Platform (MVP), which uses two centrifuges to provide artificial gravity for research on the ISS.

Redwire



NASA astronaut Jessica Meir working on Xu's first investigation on the ISS.

NASA

Normally, a ground control experiment is done at the same time as a flight project to compare results from microgravity with those from normal Earth gravity (1g). However, with the MVP, scientists can have a 1g control on the ISS alongside the flight experiment, said Rich Boling, a VP at Redwire.

"The MVP's ability to provide a 1g control in space is important because gravity really is the only difference between the samples," he said. "They experience the same g-loads during launch and the same atmosphere on the space station—everything is exactly the same between the two experiment groups, and gravity is the only variable."

The road to space isn't always easy, and Xu and her team had to overcome several hurdles in preparing the flight project. On the ground, cell culture requires carefully controlled levels of carbon dioxide in the growth medium. However, at the time, the MVP hardware did not support the addition and monitoring of carbon dioxide, so the team had to develop a method to culture cells without it.

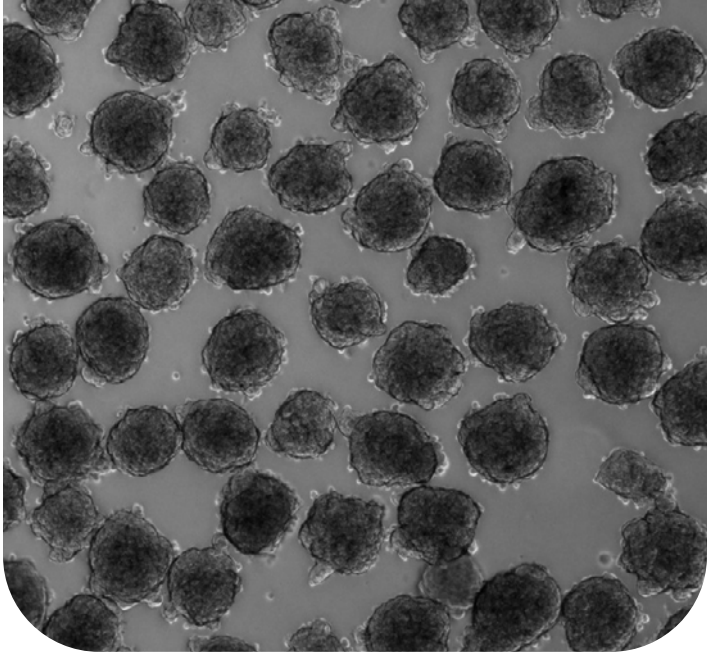
Another challenge was finding a way to keep the cells at a very specific stage of development until they reached space. To do this, the team needed to freeze the 3D cell cultures before transporting them to the ISS.

"Freezing 2D cells is a piece of cake—everybody's doing it, and it's very routine," Xu said. "But when you're dealing with 3D cells, it's not as easy, so we worked to develop a cryopreservation protocol that allows us to freeze them and have them survive."

With everything in place, the investigation launched to the space station in March of 2020, right as the COVID-19 pandemic began. "On Earth, everything was shut down," Xu remembers. "But in space, the astronauts were working on our experiment. Even with everything happening down on Earth, ISS science was still moving on."

The cells remained in space for 22 days, where they matured from cardiac progenitor cells into beating heart muscle cells. When the live cells were returned to Earth, Xu and her team were excited to find the cells had survived the trip, showing that functioning heart muscle cells could be generated in space and successfully returned to Earth.

Upon analysis, the team found several changes in gene expression in the microgravity-cultured cells when compared with the 1g control. Microgravity increased gene expression involved in cardiac cell development and proliferation, confirming the results from simulated microgravity. The team published three peer-reviewed papers on the investigation and then focused on the next step: looking more closely at microgravity's effects on cardiac cell survival.



Cardiac microtissues (spheroids) generated from human stem cells using microscale tissue engineering.

Parvin Forghani, Cardiomyocyte Stem Cell Laboratory

Space as a Steppingstone to Regenerative Therapies

Xu's second flight project examined stem cell-derived heart muscle cells as they matured into cardiac microtissues. These tiny three-dimensional spheroids mimic the structure and function of the human heart.

To culture the cells, the team used BioCell hardware from ISS National Lab Commercial Service Provider BioServe Space Technologies. "We worked with BioSeve to do very intensive testing with the BioCell to make sure the cells would be happy," Xu said. "We did a lot of testing to prepare for our space experiment because we know it's such a precious opportunity."

The team used its cryopreservation method and prepared the cells well before launch. This helped streamline the space experiment and allowed the team to characterize the cells ahead of time. "We wanted to make sure they differentiated nicely into beating cells and that they were the best quality to send to the ISS," Xu explained.

This time, the control experiment was done on the ground. Xu and her team used the same BioCell hardware and procedures to check and feed the cells that the astronauts used in space. The team even packaged the ground control cells like their spaceflight counterparts and mimicked shipping to eliminate as many variables as possible.

The investigation—Project EAGLE (engineering heart aggregates by leveraging microgravity)—launched on SpaceX's eighth rotational crew mission (Crew-8) contracted by NASA. While the astronauts worked on the project, the BioServe team, which included a large group

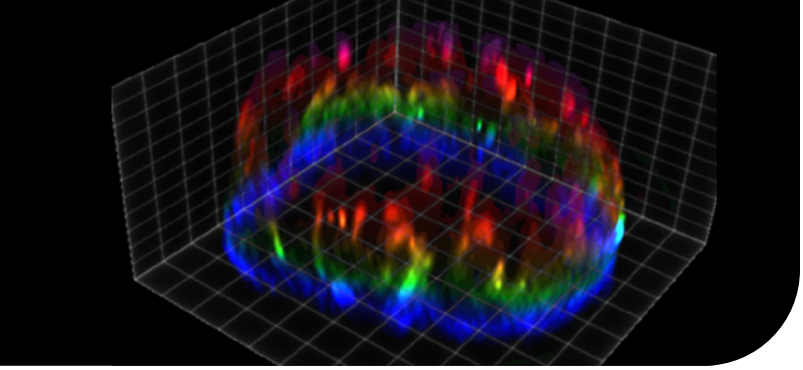
Cardiac muscle cell samples loaded into BioServe's BioCell hardware for Project Eagle.

Sheila Nielsen, BioServe

of undergraduate students, watched on a live video feed. Because BioServe is a research institute within the University of Colorado Boulder, students play a big role in spaceflight experiments, working on electronics, recording operations, and taking notes, said BioServe research associate Sheila Nielsen.

The payload patch for Project EAGLE (engineering heart aggregates by leveraging microgravity).

Emory University



3D imaging of beating cardiac microtissues from the spaceflight culture for functional assessments.

Zhi Ling, Shu Jia Laboratory, Georgia Institute of Technology

"During the microscopy, when the astronauts pulled up the cardiac tissues and we could see the cells beating through the microscope, the students were amazed," she said. "It's rewarding to mentor students and watch them experience things like that for the first time and see the impact it's having on them."

After eight days on the ISS, the microtissues were returned to Earth, and the team was anxious to start the analysis. First, a team of collaborators at Georgia Tech led by Shu Jia performed functional studies, looking at things like cell contraction and calcium signaling. They found that the space-grown microtissues displayed normal heart function.

Xu's lab then did molecular characterizations and found many differences between the spaceflight microtissues and ground control. Exposure to microgravity led to significant changes in protein levels and gene expression involved in cell stress response, survival, and metabolism.

"Metabolic pathways that we've seen in the proliferation and survival of cancer cells were also activated in the cardiac cells in space," Xu said. "In microgravity, the cells seem to conquer that stressful environment by trying to upregulate their molecular signals for survival, which was quite amazing to see."

These results, which were recently published in *Biomaterials*, are valuable because they provide a new avenue that has never been explored to improve the proliferation and survival of iPSC-derived cardiac cells. Insights gained through Xu's space-based research could lead to significant advances in the Earth-based production of cardiac cells for regenerative therapies to treat heart disease.

"Taking cells out of the gravity environment that they've evolved to survive in challenges them in a completely different way," Nielson said. "By seeing how the cells respond, we can learn an enormous amount and apply it to critical health advances on Earth."

More Answers Raise More Questions

While Xu is excited about the results achieved so far, there are still many questions to explore in future spaceflight studies. "How exactly is mitochondrial function changing? How are the metabolites changing? Additional studies will eventually put the pieces of the puzzle together and give us the details needed to find a new way to produce better heart cells," she said.

Xu stressed the critical role the ISS National Lab and Commercial Service Providers play in helping researchers like her take their science to space. "You want to lean on their resources and insights—it will help your experiment tremendously," she said. "They have rich expertise and experience and spend a lot of time working with us to help us understand every small aspect of space research."

She's also encouraged by how far science in low Earth orbit has come over the last decade. "Conducting research in space is a lot easier now than it was in the early days," she said, explaining that there's more expertise, research capabilities and facilities, funding opportunities, and publication of results. There are also more people aware of the benefits of space research.

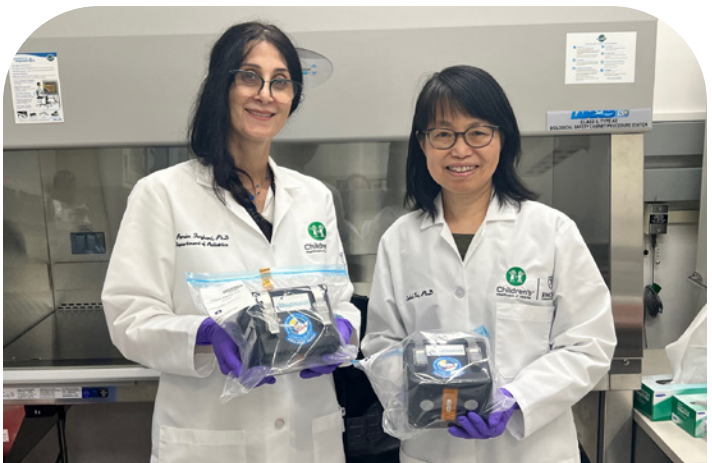
"Scientists are looking at all aspects of biology to see how microgravity can affect cells, tissues, animals, and disease models—so much can be done in space to help people on Earth," she said. "By continuing our space research, our goal is to get closer to developing products that could one day reverse heart damage."

At Kennedy Space Center preparing Project Eagle for launch on Crew-8 (left to right: Sheila Nielsen of BioServe, Chunhui Xu of Emory, John Catechis and Kristin Kopperud of the ISS National Lab, and Parvin Forghani Esfahani of Emory).

Sheila Nielsen

Parvin Forghani Esfahani (left) and Chunhui Xu (right) of Emory prepare their investigation that launched on Crew-8.

Sheila Nielsen



FORGING THE PATH

Ryan Reeves, Ph.D., is the Technical Director of Research and Innovation for the ISS National Lab, where he works with talented colleagues to identify promising science and technology that can leverage the unique space environment for the benefit of life on Earth.

By Ryan Reeves | Technical Director of Research and Innovation, ISS National Lab

Continuous Technical Innovation Requires Continuity of Fundamental Research

Humans have lived and worked in low Earth orbit (LEO) for decades—from Skylab to Mir to the space shuttle missions to more than 20 years on the International Space Station (ISS). Studies conducted in space have revealed new technological innovations and breakthroughs that benefit humans on Earth. Scientists are testing human cells in space as accelerated disease models to develop therapeutics for some of the most impactful diseases of our time, such as cancer. Investigators are leveraging the ISS to produce kilometers of specialty optical fibers that could potentially reduce optical losses tenfold. And researchers are manufacturing artificial retinas layer-by-layer in microgravity to improve their uniformity and, one day, provide sight-restoring treatment for macular degeneration and retinitis pigmentosa.

These breakthroughs are a direct result of sustained access to LEO through the ISS National Laboratory® and support for fundamental science in space that planted the seeds for technological innovation. We continue to reap the harvest of these seeds with discoveries from ISS research that improve human life through economic and technological advancement. However, if we want to continue to benefit from innovations in the decades to come, we must be diligent about planting new seeds by supporting fundamental research on the ISS now and on future commercial space stations.

Many examples of space-based investigations have led to improved products or processes in advanced manufacturing in LEO. NASA funded many early studies in microgravity focused on colloids and particles. Building on this research, the NASA Biological and Physical Sciences (BPS) program has funded several colloidal studies under the Advanced Colloids Experiments (ACE) program. The ISS National Lab has sponsored multiple ACE projects, including research from Procter & Gamble (P&G) that studied colloid gelation on the ISS. As a result of these experiments and others conducted with BPS, P&G developed the colloid stabilization technology that went into its Febreze Unstopables Touch Fabric Spray, released in 2021.

Another example is research to produce high-value optical fiber by harnessing the advantages of the microgravity environment. For decades, it has been known that fluoride glass optical fibers have the potential to transmit light and data with an order-of-magnitude reduction in losses compared with traditional silica fibers, resulting in significantly lower power requirements. However, these improvements have not materialized, in part, due to the propensity for the glass to develop crystalline defects during the transition from a liquid to an amorphous solid. NASA funded a series of early studies in the 1990s that demonstrated reduced crystallization when the fibers were drawn in microgravity. These early exploratory studies stimulated several companies to leverage the ISS National Lab for optical fiber manufacturing in LEO. Through ISS National Lab-sponsored research, Flawless Photonics reported producing kilometers of fluoride glass fiber on the

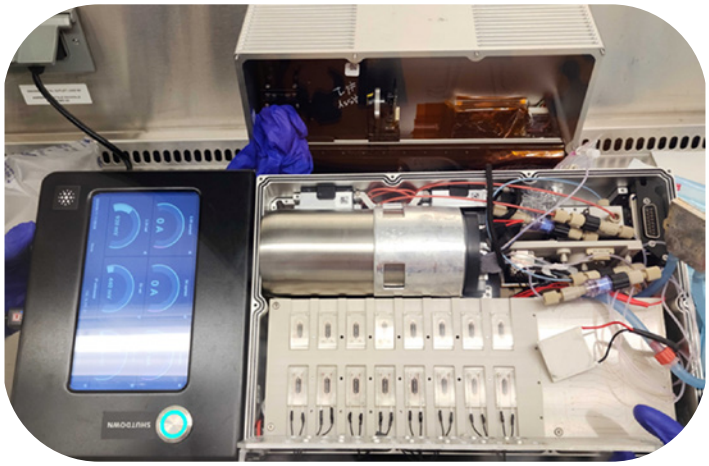
space station in the past year, including individual fiber draws more than a kilometer in length. This potentially revolutionary product manufactured in LEO directly results from the seeds planted by NASA nearly 30 years ago.

The ISS National Lab has long believed in the critical importance of fundamental research. We are proud to have partnered with the U.S. National Science Foundation (NSF) for nearly 10 years to leverage the unique microgravity environment of the ISS to explore fundamental science for groundbreaking discoveries. Through our long-running annual joint solicitations, we have sponsored space-based research in transport phenomena, such as combustion and fluid physics, as well as tissue engineering and mechanobiology.

This research has led to valuable discoveries. For example, insight gained on cool flame chemistry could one day help improve internal combustion engine efficiency and reduce the emission of harmful pollutants. Findings on the complex fluids of pharmaceuticals could lead to higher-quality therapeutics and improved pharmaceutical manufacturing processes. And results on the accelerated aging of cells in microgravity could enable the development of robust models to study age-related diseases and test potential new treatments.

The Ring Sheared Drop system on the ISS containing a concentrated solution of human serum albumin, the main protein constituent of blood. Small white dots are glass tracer particles that allow researchers to study fluid flow of biofluids in space.

Joe Adam



The 16 human skeletal muscle tissue cihps integrated into a CubeLab for an experiment on the ISS. Half of the tissue chips contain electrodes to deliver electrical stimulation to induce contraction in the myobundles.

University of Florida

In addition to our work with NSF, the ISS National Lab funded early stem cell research on the space station more than a decade ago. This work paved the way for a partnership with the National Institutes of Health (NIH) to study tissue chips, engineered systems containing human cells, which can serve as avatars for human organs during experiments in space. This collaboration led to a tissue chip program between NIH and NASA BPS, and the current NIH Tissue Chips in Space solicitation with the ISS National Lab.

Microgravity studies on stem cells and tissue chips are bearing critical innovations. Tissue chips in space have been validated as accelerated disease models to help researchers better understand disease progression and screen drugs for efficacy and toxicity. Results are also driving advancements in regenerative medicine technologies and the development of new therapeutics to treat cancer, neurodegenerative diseases, musculoskeletal diseases, and more.

The ISS National Lab will continue to support research that brings to fruition the innovations sown by decades of research in LEO. And even as we foster these innovations as they develop, we are cognizant of the importance of planting the next generation of seeds by continuing to sponsor fundamental research. As the LEO ecosystem enters a new era of commercial space stations, it is paramount that we as a nation continue to seed this fertile field of microgravity research without interruption. On future commercial LEO destinations, how will fundamental research be prioritized among competing interests such as applied R&D, manufacturing, and tourism? We must not lose sight of the value of fundamental science, as the seeds sown today grow to produce technological innovations of the future.

This piece is part of our Forging the Path series in which CASIS® experts share knowledge and insight from their experience managing a national lab in space.

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UPWARD

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