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BUILDING BONES: TESTING A NEW OSTEOPOROSIS THERAPY

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DREAMUP LAUNCHES LEARNING INTO ORBIT STUDENT CONTEST WINNERS GROW CRYSTALS IN SPACE

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THE VIEW FROM THE CUPOLA

BY KATHLEEN FREDETTE. ILEAD SCHOOLS

Below, Kathleen Fredette, Director of STEAM Initiatives at iLEAD Schools, discusses how a partnership between iLEAD Schools, which has locations in several U.S. states, and DreamUp is helping to inspire students and engage them in science, technology, engineering, and mathematics topics. DreamUp, an educational spinoff company from commercial services provider NanoRacks, works with student groups to bring student-designed experiments to the International Space Station (ISS). DreamUp is also highlighted on pages 12–15 in this issue.

If you're reading this, you're the kind of person who enjoys the wonder of thir that sparkle in the night. If you've tried teaching, you also know that seeing t shining eyes of wonder is infinitely more meaningful than an educator shining before mesmerized kids. Conductor and author Ben Zander once said, "Look their eyes. If they are shining, you know you are doing it."

In the age of one-to-one learning, smartphones, and social media, teaching has become a bit more like conducting-amidst the distractions, we strive to draw students to that place of wonder that is harmonious with real learning. Last summer a partnership with DreamUp began an amazing journey for me few courageous teachers, and hundreds of students.

Not many teachers have the opportunity to develop an educational project that results in launching a student-designed experiment to the ISS. At iLEAD Schools (K-12 public charter schools), we use project-based learning and social emotional learning as educational delivery systems to develop not just good students but also lifelong learners. Although sending a student experiment to the ISS is exciting, it's tricky to develop and run a project that engages and inspires young people, who are often more interested in their smart devices than in school.

Science-related projects often appeal to a small group of students, leaving the rest stranded in boredom. Our task: How do we create a project that is engaging, rigorous, and accessible to all students and that invites each young person into the arena of authentic learning? How can we use the topic of space as an entry point to the imagination of students, whether they are interested in sports, music, gaming, or dance, or whether they seem altogether uninterested in learning?

We're now in the final phases of experimental It turns out that space is the perfect environment for a reentry into that place design selection, with a launch to the ISS of wonder, awe, and infinite questioning-one that opens our minds and hearts scheduled for next fall. Six finalist teams must to the engagement that real learning requires. Author Elizabeth Gilbert wrote, create a short video pitching their team's vision, "Curiosity only does one thing, and that is to give. And what it gives you is including how they will use this honor to reach clues to the incredible scavenger hunt that is your life." Real learning begins to more students and the iLEAD community if their take place when curiosity and wonder are sparked. experiment is selected to run on the ISS.

Effective educators start with the end result and work backwards. So, we asked the question, "What content knowledge and skills are needed for young people to design, run, and analyze a space-based experiment?" Because iLEAD Schools are public schools, the project also had to connect to Common Core and Next Generation Science Standards.

We knew kids needed to understand large concepts like gravity versus microgravity and the basics of astronomy, engineering, and the scientific UPWARD JUNE 2018



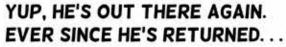


Kathleen Fredette iLEAD Schools.

ngs he S at	method, but we also wanted each student involved in the project to be able to answer the question, "Why do astronauts float in space?" Developing a space-based experiment also provides for
	other educational entry points, such as history, space travel, nutrition, rocketry, mathematics applications, technology, art, and geography.
a	Through DreamUp, our students were able to come up with their own experiment ideas and collaborate with subject matter experts. One of our teachers remarked, "The freedom to choose something that the kids were passionate about was a game
	changer. Because they could come up with an idea of their own, even some of the lowest-achieving kids were empowered to succeed." These are truly shining-eye moments!
	Our partnership with DreamUp involved five il FAD

School campuses spanning grades 5 through 10. Students presented their ideas at a culmination of learning, our Space and Innovation Expo held at a local college (think a science fair on steroids). Jacob Cohen, Chief Scientist at NASA's Ames Research Center, shared the vision of space exploration with our families, inspiring all present to find and use their unique gifts.

The future of education and the culture of science is not measured by the efficacy of repeating back memorized answers: it's in the potential of our children's ambitions and their desire not just to learn but also to explore, inspire, and create! That recipe begins with something tricky, yet brilliant, and it's our goal: wonder, awe, and the literal ability to reach for the stars and dare to dream.



UNEXPECTED PIONEERS OF DISCOVERY & COMMERCIAL SERVICES

BY EMILY TOMLIN, Staff Writer

hree years ago, a two-headed worm returned from the International Space Station (ISS), and in the summer of 2017, the worm achieved internet and popular media fame when researchers from Tufts University published a paper describing the worm and other results from their ISS U.S. National Laboratory experiment.

The story behind this mutant worm, however, is even more rich than its delightfully deformed morphology. The payload that carried the famous worm and 77 of its relatives to the ISS and back inspired researchers, payload specialists, and even FedEx to take the first steps toward new scientific discoveries and processes that now have their own successes to share, all of which was pioneered by these first worms-planarian flatworms, that is-in space.

THE WONDER OF WORMS

Planarian flatworms have been studied since the 1800s as a model for genetics, body patterning, and neuroscience. The flatworms have a "true brain," unlike earthworms and other species in which the nervous system is more spread out and less well-developed.

Because of their brain's bilateral symmetry, their genomes, and other factors, planarian flatworms are more similar to our human ancestors than some of the more derived model systems such as flies or Caenorhabditis elegans (nematodes), said Michael Levin, director of the Allen Discovery Center at Tufts. This model system is being used to understand regeneration, stem cell regulation, and behavior. The worms are also popular for drug addiction research because they have most of the same neurotransmitters as humans, so they exhibit symptoms of withdrawal and addiction to the same drugs.

Levin's lab, however, uses the worms to study how physical forces influence body patterning, the process through which an organism ensures that cell types and body structures are properly shaped and placed during development. Planarian flatworms are a unique model for such studies because they are incredibly robust regenerators and yet they are mixaploid-their cells accumulate a plethora of mutations from constant regeneration and non-sexual reproduction.

There's not even the same number of chromosomes in every cell of a single worm," said Levin. "How can your genome be such a mess and yet you retain this beautiful ability

> to create a perfect, correctly shaped planarian every time? Through our work over the last 15 years, the worms are telling us that patterning is controlled by very interesting biophysical dynamics."

> > lichael Levin, director of the Allen Discovery Center at Tufts

Planaria fragments in a Petri dish Space Tang



An amputated flatworm fragment sent to space regenerated into a double-headed worm, which is a rare spontaneous occurrence.

Allen Discovery Center at Tufts University

In other words, because the DNA of planarian flatworms can diverge widely and yet their anatomy remains intact, their cellular decisionmaking is revealing novel aspects of how genetics and physics cooperate to control dynamic anatomy. Levin and his team studies the role of bioelectric signals-electrical communication between individual cells-in determining anatomy. They created the firstever line of stable patterning mutants in planarians by editing their natural electrical signals, said Levin. In doing so, the team showed that it is possible to re-write electrical pattern memories to control anatomy.

Over the long term, understanding these processes may shed light on how biophysical dynamics are involved in the development, aging, and modification of body plans in higher organisms-and how we might use bioelectric and other signals to control cell behavior. Beyond myriad benefits in discovery science, the power to control cell fate with bioelectric signals could ultimately allow manipulation of regenerative or developmental processes involved in human health. For example, perhaps doctors could use this knowledge to accelerate wound healing, grow organs outside of the body for use in transplants, slow negative effects of aging, prevent certain birth defects, or improve treatments for neurodegenerative diseases.



WHY SPACE?

A notable player in biophysical dynamics is the geomagnetic field, or GMF. This natural characteristic of the Earth imposes a magnetic field of approximately 0.5 Gauss onto all living organisms. The GMF changes over only very large areas, so it may seem unintuitive that organisms sense and use it in their daily behaviors. However, experiments on plants, animals, and cells in culture show that they do sense and respond to changing magnetic fields, and some classic examples (such as migrating fish and birds) demonstrate ways in which organisms perceive and use Earth's magnetic field lines. Despite these data, it is unknown *how* and *why* embryonic cells (like the stem cells of a regenerating planarian) sense the GMF.

In laboratory model organisms that are shielded from the GMF by metals and other techniques, "all kinds of things go wrong," Levin said. "Cells are counting on this field for something, and we have no idea what." The unique GMF conditions onboard the ISS are what prompted Levin to seriously consider an unexpected opportunity to send worms to space.

The opportunity was borne of a search for innovation. The nonprofit Kentucky Space, LLC was seeking white papers from new-to-space investigators interested in using microgravity to tackle big research questions—to spark their imagination in the early stages of the nonprofit learning how to enable research onboard the ISS.

"We heard there was this group from Kentucky that was doing some space stuff, and they were interested in sending worms to space," said Junji Morokuma, who joined the Levin lab in late 2004 and subsequently worked on the space worms project. "I thought 'oh wow,' but we weren't sure what to do or what we would find." There was some research on worms in simulated microgravity that had shown a strong increase in regenerative capacity, he said, but there had been no planarian flatworms in space to shed light on what the team should expect.

So the team kept it simple, said Levin, and set out to determine how the combined components of space travel might affect regeneration in the worms. These components included takeoff, acceleration, splashdown, vibration, microgravity, and, of course, the altered geomagnetic field. These physical forces perturb how the cells talk to each other and thus can influence the pattern formation within cells of a regenerating worm. "It's not zero GMF," Levin said, as it is in ground-based shielding experiments, "but it's different, and we didn't have any clue what we might find."

A canister developed by Space Tango houses vials of flatworms for launch to the ISS National Lab. Space Tango



Space Tango CEO Twyman Clements cuts the flatworms into thirds prior to spaceflight. Space Tango

BREAKING NEW GROUND

As the first-ever space-faring planarian flatworms unknowingly prepared for their launch onboard commercial resupply services (CRS) vehicle SpaceX CRS-5, Kentucky Space and the Levin lab tackled a variety of their own firsts.

F Space business and research is exciting, but there's lots of money, paperwork, delays, and 'oops' involved," said Morokuma. "I've heard to launch a rocket, you need paperwork taller than the rocket," he laughed, "but luckily Kentucky Space handled all of that."

Kris Kimel, founder of Kentucky Space and co-founder of its for-profit spinoff Space Tango, acknowledged that early experiments like the space worms, while simple in design, played a critical role in allowing his team to "learn the ropes" with respect to payload integrations, interfacing with NASA, and dealing with customers.

"This experiment was a really important one for us," said Kimel. "We learned a lot technically from the payload as well as how to protect the end user from some challenging processes. This experience laid the philosophical bed for what became TangoLab and our successful business ventures as Space Tango."

Supported by CASIS sponsorship, the worms launched on January 10, 2015, spent several weeks onboard the ISS National Lab, and retuned exactly one month later.

Prior to return, Kentucky Space also worked with Levin and new partner FedEx Space Solutions to arrange delivery services for the worms back to the lab following splashdown. "The logistics were really interesting," said Levin. "I've never weighed a flatworm. I understand why they needed that data, but it was kind of wild."

David Drees, who managed the flatworm delivery process for FedEx, said his primary concern was returning the worms as rapidly as possible after splashdown so the team could analyze the worms before they readjusted too much to Earth's conditions. Some of this depended on temperature. "We needed to keep them not warm enough for cell division but not cold enough to kill them," said Drees.

The rest was timing. "We have a great infrastructure at FedEx, but we run on schedules," said Drees. "The capsule coming down from the ISS is not on a schedule we can predict months in advance. It could come down any time of day or night, and we'll get maybe three hours' notice." To adjust to this uncertainty, resources from several FedEx operating companies were activated, and a FedEx Express courier was on standby.

Adding to the lists of firsts on the space worms' resume, this was the first payload that FedEx executed as a "rapid return," in which they intercept returning experiments during the handoff from launch provider to NASA, in this case at an airport on the California coast.

"It was a new thing, so I actually went out there and personally worked with Kentucky Space as they took possession of the box with the worms from the NASA plane," said Drees. "I was a space geek growing up, so it was a really cool thing to be a part of." From there, the box was fitted with a "SenseAware" device that sends information on location, pressure, light, moisture, and temperature to a customer web portal and then, since it was 11 p.m., it went to a FedEx station for the night.

"Our operations folks really stepped up to handle a nontraditional shipping situation," said Drees. "Everyone was really proud to play a small part in the experiment." The worms' proof-of-concept "rapid return" helped FedEx develop this service as a new product offering to its customers, with an entire system now developed for this purpose. "Space worms was the prototype!" said Drees.

A DARK AND MURKY JOURNEY

Meanwhile, back in Boston, there was a blizzard as the Tufts team waited for the new FedEx delivery process to return their box of worms from the ISS (via Long Beach, California).

FedEx executes a "rapid return," ntercepting the experiment for mmediate delivery. Space Tango





UPWARD JUNE 2018

Postflight vial of flatworms Space Tango

For the weeks they were in space, we'd had no way of monitoring them, so we didn't have any clue what we would find," said Levin. "I mean, they were up there without any supervision. Our biggest concern was that when they got back they'd all be dead."

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Normally, the worms would routinely receive fresh water and air and would be exposed to light when they were fed and cleaned twice a week. But to keep the initial experiment as elegant and simple as possible, none of these elements were preserved in the spaceflight experiment or ground controls. Because the goal was to evaluate regeneration, the worms were merely cut into thirds, placed into the approved container and space-certified hardware, and loaded onto the SpaceX rocket.

"We basically shoved a lot of worms into a test tube, which went into a sealed coffee-can-sized container," said Morokuma. "Temperature was controlled to some degree, but that was it." As promised, the postflight box arrived, and the team gathered to see whether their planarian pioneers had successfully re-grown and survived—and what stories they had to tell. "We got this box that came from space, and we were all very excited to open this box," said Levin, "and sure enough, they were alive!'

Immediately, the team witnessed the first interesting behavior of the space worms. When they took the worms out of the dark, stagnant water from their long journey and placed them in normal water, the worms' bodies curled. Normally, this type of curling response indicates that worms are unhappy with their environment, said Levin. "It was amazing. We put them into this beautiful, fresh Poland Springs water they normally love, they all curled up like they didn't like it," he said, "like they had gotten used to the stinky water-which is really strange."



Worms returning from space curled up and were immobile when transferred to petri dishes containing fresh spring water. By contrast, stay-athome control worms moved rapidly and fully extended themselves. Allen Discovery Center at Tufts University

Then of course, as the team examined the individual worms more closely, they noticed the now-famous two-headed worm-which later garnered acclaim in mainstream media outlets including Gizmodo, CNET, CBS News, Fox News, Engadget, Yahoo, and Smithsonian Magazine.

Beyond being visually captivating to the public, this phenotype is statistically significant. "Planaria are robust, stable regenerators," said Levin. "You'd have to cut thousands of these kinds of worms on the ground to see two heads." This was the first indicator that something indeed was unique about the regenerative environment onboard the ISS.

Yet as unexpected and interesting as these early findings were, the most astounding results from the space worms study would not be seen for more than a year, when the team examined the worms' behavior 18 months after readjusting to normal Earth conditions.

MORE THAN JUST A BOX OF WORMS

At first look after 18 months of reacclimation, the worms remarkably had a different complement of bacteria than their relatives who had remained on Earth. As with the human microbiome, the population of microorganisms in a worm's gut, on its surface, and in its surroundings intimately influence bodily functions and behaviors.

According to Levin, until this point, no one had really studied planarian flatworm microbiomes-though some studies on their immune systems and response to infection may vield insights into the role of the microbiome. Inspired by the space worm results, however, Levin and collaborators are currently finalizing the first study of the native planarian microbiome, in terms of what the complement of bacteria typically looks like in standard populations and why it matters.

The second curious and remarkable behavior of the retired space worms suggested an atypical fear of the dark. "Normally, worms dislike the light," said Levin. "They're sort of photophobic and try to get into as dark a corner as they can." After 1.5 years of experiencing normal lab conditions on Earth. however, the space worms showed a notable and unusual preference for light.

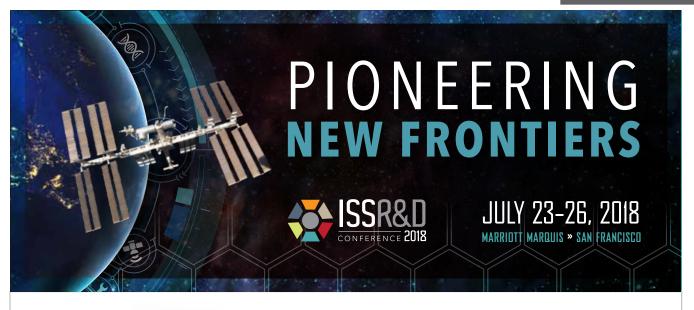
"Planarian flatworms are amazing in

that they are, in effect, immortal-they don't age," said Levin. "They have stem cells that continuously repopulate the animal as somatic cells age and die off." Within approximately one month, most of a worm's cells have to be renewed. Yet 1.5 years after spaceflight. after 18 such turnovers, the space worms still showed an imprint of their unique experience, moving toward and sitting in the light far more frequently than control worms.

"This is of course conjecture at this stage, but one possibility is that they remember that long," said Levin. "Another possibility is that it's related to the microbiome change." Evidence of the microbiome changing organism behavior and acting as a cognitive modulator has been seen in other animals and even humans, according to Levin.

However, more studies are needed to answer these and other questions about the influence of the ISS environment on planarians.

F The worms are telling us that the experience of going to space profoundly alters the mechanisms within the regenerative process-patterning, differentiation, and cell migration," said Levin. "But we need to understand how these effects are exerted if we are to work toward modulating regeneration for useful purposes on Earth."



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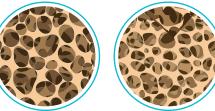
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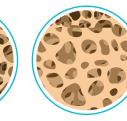


BUILDING **TESTING A NEW OSTEOPOROSIS** THERAPY WITH MICE IN MICROGRAVITY BY AMELIA WILLIAMSON SMITH, Staff Writer

The NELL-1-based osteoporosis therapy was pre-loaded in syringes prior to the launch of SpaceX CRS-11 and kept in a freezer until use onboard the ISS. RR-5 UCLA team

very three seconds, a person somewhere in the world breaks a bone due to osteoporosis—a progressive disease that decreases bone density, making bones weak and fragile. Osteoporotic fractures greatly reduce quality of life, and immobilization following a fracture can lead to further bone loss, which puts these patients at risk for breaking another bone.





When SpaceX CRS-11 launched to the space station last June, it carried 40 mice to the ISS National Lab for a mission aimed at improving treatment for the millions of people with osteoporosis back on Earth. The Rodent Research (RR)-5 mission successfully proved the robustness of a new potential osteoporosis therapy based on a naturally produced protein, NELL-1, and also led to significant improvements in the delivery of the therapy.

Most current osteoporosis drugs only work to slow bone breakdown, not form new bone. A therapeutic approach using NELL-1 being developed by a group of researchers at the University of California, Los Angeles (UCLA) works both ways. NELL-1 has been shown to not only help prevent further bone loss but also build new bone to replace what was lost. Such a therapy would be of tremendous benefit to patients with severe osteoporosis.



To further evaluate the effectiveness of NELL-1, the UCLA team, led by principal investigator Chia Soo, tested its therapeutic use in mice onboard the ISS National Lab. Microgravity has been shown to induce accelerated bone loss in

mice at rates that exceed those caused by either post-menopausal or disuse osteoporosis on Earth, making space an ideal environment to study osteoporosis therapies.

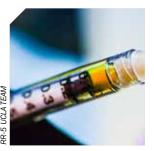
Testing in microgravity is a huge deal because it induces an extreme state of bone loss." said RR-5 co-investigator Jin Hee Kwak. "If NELL-1 was found to be successful in a microgravity model, then it may work for the most extreme cases of bone loss on Earth, and that would prove the rigorousness of our therapy."

Principal investigator Chia Soo assures data sync prior to RR-5 mission launch

LINKING NELL-1 AND BONE FORMATION

NELL-1 is a protein made by the body, and its bone-forming effects were originally discovered more than 20 years ago by craniofacial orthodontist and RR-5 co-investigator Kang Ting. He had been examining children with a condition that causes an overgrowth of bone in the skull and wondered whether looking at gene expression in these patients could reveal a protein involved in bone growth.

Ting said, "The question was, can we find a way to see what induces bone formation in patients with too much bone? Can we find the protein and use it to help people who need bone?"



After screening millions of genes. Ting found one protein-NELL-1-that was overexpressed in children with skull bone overgrowth, leading him to begin investigating

NELL-1 as a bone-forming agent. Following results from an independent research group that linked the underexpression of NELL-1 in patients to low bone density, Ting and his UCLA colleagues found that mice lacking NELL-1 exhibit symptoms of osteoporosis as they age.

In several animal models, the UCLA team was able to demonstrate the use of NELL-1 as a successful osteoporosis treatment; however, use of the protein as a therapy was possible only via local administration. In other words, the NELL-1 protein would have to be injected directly into a patient's affected bone during surgery.

> To make NELL-1 more useful for patients with osteoporosis, the team needed to modify NELL-1 to administer it systemically. This type of therapy could be given as a quick injection under the skin to build bone throughout the body.



Fluorochrome bone labels were injected in the mice three times throughout the study to measure the rate of bone formation. Because fluorochromes are susceptible to light, the pre-loaded syringes were stored in opaque protective bags. RR-5 UCLA team

As the UCLA researchers began working to modify NELL-1 for systemic use, they submitted a proposal to test the therapy in the microgravity environment on the ISS National Lab and were awarded a CASIS grant, which supported the RR-5 mission. Once modification of the molecule was complete, the team could launch their investigation to the space station.

MODIFYING THE MOLECULE

Developing NELL-1 into a systemic therapy that could be given as an injection every couple of weeks to build bone would greatly benefit patients; however, modifying the molecule to achieve this was no easy task. The team needed to find a way to keep the therapeutic protein molecules circulating in the blood long enough for NELL-1 to induce bone formation. The molecules also needed to be able to successfully and exclusively attach to bone tissue to be effective and safe.

Additionally, ISS crew members have typically accessed mice on the space station only once every 14 days, so the interval between injections had to be at least that long. Keeping NELL-1 in the bloodstream for such a long period was a tremendous challenge. Moreover, with such a long circulation time, the team needed to reduce any toxicity so that the therapy would be safe.

With the help of Benjamin Wu, RR-5 co-investigator and former chairman of the UCLA Department of Bioengineering, the team modified NELL-1 using a method called PEGylation, which slows the rate at which molecules are degraded by the liver. This would keep NELL-1 circulating in the bloodstream longer. Then, to help NELL-1 find bone tissue, the team attached the protein to an inactive form of a bone-seeking molecule called bisphosphonate.



We tried to modify the molecule so instead of just blindly circulating in the blood, it became kind of a targeted molecule that seeks bones and attaches to them," Ting said. "This increases efficacy in the bones and reduces toxicity in organs where we do not want the molecule."

The team tested the modified molecule, called BP-NELL-PEG, in a groundbased experiment using female mice whose ovaries had been surgically removed to induce osteoporosis. The team found that injection of the therapy into the abdomen of the mice once every 14 days was successful.

WHAT IS BISPHOSPHONATE?

Bisphosphonate used to be a common drug to treat osteoporosis; however, it is no longer used as often because of a serious potential side effect involving $0 = \dot{P} - C - P = C$ bone deterioration in the jaw. By inactivating bisphosphonate, the molecule no longer has a therapeutic effect (nor does it cause side effects). but it retains its bone-seeking function.

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Developing the therapy with a 14-day injection interval was one of the greatest technical challenges the team faced, but successfully extending the dosing interval will also be a substantial benefit to patients. Kwak said. Patients would need fewer injections of **BP-NELL-PEG** compared with most current osteoporosis drugs. This would not only save extra trips to the doctor's office but also make the therapy more affordable.

"Our work on the RR-5 mission really helped us make the delivery more effective and targeted, and it significantly increased the eventual clinical feasibility of the therapy," said RR-5 principal investigator Chia Soo. "If you have an easier way to deliver the therapy and if you don't have to deliver it as frequently, it has a much greater human application."



Grip strength testing was done to measure the muscle strength of the mice. RR-5 UCLA team

Having successfully optimized the molecule and achieved the 14-day injection interval necessary for rodent research on the space station, the team was now ready to test the systemic therapy in the extreme case of microgravity-induced bone loss.

SENDING MICE TO THE SPACE STATION

SpaceX CRS-11 launched to the space station last June with the RR-5 mission, carrying 40 female mice aged to 8 months, which is when they reach skeletal maturity. An additional 40 mice remained on the ground at NASA's Kennedy Space Center as a control group. In both the flight and ground groups, half the mice received BP-NELL-PEG treatment and the other half did not.



Rodent habitat onboard the ISS National Lab NASA

The RR-5 mission was unique in that halfway through the nine-week investigation. 20 mice in the flight group (10 receiving treatment and 10 not) were returned to Earth alive to complete the rest of the experiment on the ground at UCLA. The other

20 mice remained on the space station until the end of the investigation when they were sacrificed, and the frozen specimens were returned on SpaceX CRS-12.

Many analyses can only be performed on live tissues and cells, so live return was important to the RR-5 team. When the SpaceX Dragon capsule splashed into the Pacific Ocean last July with the RR-5 live-return mice, the team was elated to find that all 20 mice were alive and healthy. The team also noticed that the fur of the mice was shiny within a day of live return to UCLA, meaning they had been grooming-an indication of contentment.

"Our live return involved full survival of the animals, and they were safe, healthy, and happy," Kwak said. "This is a huge milestone, and the exciting part for our science team is that all of our data will be very reliable."

ANALYZING DATA AND LOOKING TO THE FUTURE

The RR-5 team is still in the process of analyzing all the data, but preliminary results indicate the investigation was a success. Data from the hind limbs and vertebrae of the spaceflight mice showed significant bone loss from microgravity and a remarkable recovery by BP-NELL-PEG treatment.

We can unequivocally say that NELL-1 increases bone density in microgravity conditions, which is very exciting," Soo said. "This success demonstrates the robustness of the therapy to treat extreme bone loss."

From here, the team plans to probe deeper into the molecular biology of the NELL-1 protein to gain a more detailed understanding of how the molecule works, while continuing to focus on the practical translational aspects of the therapy.

"We want to look at how we can make this a better osteoporosis treatment for eventual clinical application," Soo said. "Not only for the millions of osteoporosis patients on Earth but also, in thinking



The RR-5 team: Benjamin Wu, Chia Soo, Kang Ting, and Jin Hee Kwak

RR-5 UCLA team

about future space travel and a mission to Mars, we want to see how we can prevent the detrimental effects of microgravity on bones during spaceflight."

Although modification and use of NELL-1 as a therapy has come far since its discovery more than 20 years ago. there's still a long journey ahead before this treatment approach can be applied to humans, Ting said.

COLLABORATION FOR DATA COLLECTION Bone scans and behavioral tests were done on all the mice before launch. at the time of live return. and again at the experiment's conclusion. Blood tests were also done before launch and at the conclusion.

Collecting these data on the ground and in orbit would not have been possible without close collaboration among the science teams from CASIS. NASA's Ames Research Center. UCLA. and implementation partner BioServe Space Technologies, as well as NASA crew members onboard the ISS. During the mission, the teams collaborated in three distant locations: NASA's Kennedy Space Center, where the ground control mice were housed; the ISS National Lab, where the flight groups were housed; and UCLA, where the live-return mice were housed.

"Everything had to be done at the same time point, with the same exact methodology, using the same type of injections and animal care, and doing the same analyses—it was a tremendous effort to make that happen," Kwak said. "I was always on standby and always had my phone on next to me when I was asleep because anyone could call me at any time to ask questions about the experiment."

Additional testing included oral swabs to analyze changes in the oral microbiome of the mice. Fecal samples were also analyzed to correlate oral microbiome changes with changes in the digestive tract microbiome.

RR-5 UCLA team



"But that's what research is about—you have persistence and tenacity, and you never give up," he said. "Everyone involved in the RR-5 mission was so devoted and committed to making the project successful, and it shows that if we all have the same goal and push forward, we can achieve anything. The sky is not the limit anymore!"

DreamUp Launches Learning INTO ORBIT

BY JULIA SABLE, Staff Writer

Inspired youth stand in Kennedy Space Center's rocket garden on SpaceX CRS-14 launch day.

he mood is festive as students shuffle onto the bleachers next to the Saturn V building at the NASA Kennedy Space Center Visitor Complex. They have had

a busy day exploring exhibits and explaining their science projects to visitors during a stage presentation and a poster session. The jitters from public speaking have passed, but the students still feel a bit nervous as they take their seats at the launch viewing area. The SpaceX Falcon 9 rocket is expertly engineered and thoroughly tested, but there's still a small chance it could fail. One group of students on these bleachers had to rebuild an experiment after the rocket carrying their original one exploded two minutes into flight.

Four miles away, the rocket bearing the Dragon capsule is barely visible. It looks tiny, but the students know it holds thousands of pounds of supplies and science experiments including their own payloads!

Hundreds of voices chant the final countdown and cheer as smoke billows along the ground and the rocket streaks into the sky. The engines' orange glow dazzles the students' eyes. A few seconds later, a delightful deep rumble reaches their ears. At last, after months of work, their experiments are on the way to the ISS! They are now true space researchers!



This scene describes the launch of SpaceX CRS-11 last June, which carried 24 student experiments to the ISS National Lab. These experiments were supported by DreamUp, an educational spinoff company from commercial services provider NanoRacks. DreamUp cofounder and CEO Carie Lemack has shared the students' exhilaration at this and many other launches. The upcoming SpaceX CRS-15 mission will carry 40 DreamUp-supported experiments to the space station.

DreamUp uses the wonder of spaceflight to ignite young people's interest in science, technology, engineering, and mathematics (STEM). Through competitions, flight opportunities, and curricular support materials, the company empowers educators and students to use space to enhance education. However, DreamUp's mission extends beyond the classroom.

DreamUp is a partner in the Space Station Explorers Consortium, a growing community of partner organizations managed by CASIS that aims to engage learners in meaningful STEM education experiences centered on the ISS National Lab. DreamUp provides multiple pathways for students in elementary school through college to design and launch experiments to the space station. For example, some initiatives challenge students to create their own experimental apparatus for use on the ISS. Such projects showcase students' inventiveness and perseverance.

STUDENTS



SpaceX CRS-14 carried dozens of student experiments to the ISS. Nathan Adams

Ultimately, we look at our organization as focusing on workforce development," said Lemack. Participating in authentic space-based research helps inspire students to become scientists, engineers, and innovators who will thrive in the globalized, technology-driven 21st century.

PATHWAYS TO STUDENT SCIENCE IN SPACE

85.000+ More than 85,000 students have participated in such initiatives, spending hundreds of hours inside and outside of class. The students and their teachers and mentors agree that these intensive engineering-focused projects are worth the work. The many rewards include new skills, career connections, and strong friendships with their teammates-not to mention the chance



idents from iLEAD nd Innovatior Expo, 2018.

to see the fruits of their labors soar into space! But building and flying a customdesigned apparatus can be expensive and time-consuming, which can put these projects out of reach for some communities.

DreamUp has long recognized the need for alternate, lower-cost ways to send science to space, partnering with a variety of organizations, such as iLEAD Schools, the Ramon Foundation, Blue Origin, and CraftED to lower the barriers to entry for students and educators inspired by space. "It's about more than simply payloads," said Lemack. "It's about increasing access to space for all learners and educators, regardless of background, resources, or current state of knowledge."

For example, since 2010, DreamUp has partnered with the Student Spaceflight Experiments Program (SSEP), run by the National Center for Earth and Space Science Education, as one path to accomplish this goal. Through SSEP, instead of building custom hardware. students design experiments using well-established modular hardware and write research proposals describing their idea. SSEP has engaged more than 82,000 American students in community-scale competitions-and each year, one proposal from each participating SSEP community is selected for development into an ISS flight project.

In another partnership to inspire tomorrow's innovators. DreamUp collaborated with a program called Überflieger, in which university teams across Germany competed for the opportunity to launch an experiment to space. After an initial down-selection process, eight university teams from all over Germany qualified for the final selection round of the competition. During a two-day selection workshop, students presented their experiment proposals and took questions from an expert board of evaluators. The three teams selected are investigating questions such as how planets form and how propulsion technology works in microgravity-with two of these projects launching on SpaceX CRS-15!

> Even more recently, DreamUp worked together with CASIS, who partnered with Marvel Entertainment for a challenge inviting students ages 13 through 18 to propose experiments to be conducted onboard the ISS National Lab. The contest focused on Rocket and Groot, characters from the Guardians of the Galaxy comic book franchise. Students were encouraged to develop innovative concepts to be tested in space based on the attributes of these superheroes. The two selected flight concepts will become official ISS investigations, intending to launch to the space station in 2018.

As part of the "Guardians of the Galaxy Space Station Challenge," students with an interest in technology and engineering were encouraged to submit flight concepts through Team Rocket—a superhero with strong ties to technological innovation and engineering. Students interested in fundamental biological concepts were encouraged



STUDENT DEVELOPMENT OF FLIGHT APPARATUS

Chicagoland Boy Scouts and high schoolers Connor Gregg and Merrick Jakelski competed in the National Design Challenge with support from CASIS. For their experiment on the folding of proteins related to Alzheimer's disease, they built a miniaturized fluorescence spectrometer with 3D-printed parts of their own design! Gregg and Jakelski were thrilled to see their project launch to the ISS on the SpaceX **CRS-14** resupply mission after two and a half years of work. The experience strengthened their interest in pursuing science and engineering after high school. Jakelski hopes to study electrical engineering or robotics at Purdue University. Gregg is interested in engineering and entrepreneurship and is considering Georgetown University or the U.S. Military Academy.

to submit flight proposals under Team Groot—a member of the Guardians of the Galaxy who is the embodiment of genetics and plant biology.

The winning students from Team Rocket will work alongside DreamUp (with team member NanoRacks) to help transform their ideas into research questions to be tested on the ISS National Lab. In the coming months, students will work with these commercial partners and be exposed to space station facilities, hardware development, and the engineering required to ensure successful projects on the orbiting laboratory.



Adia Bulawa holds Rocket, the Guardians of the Galaxy Character that inspired her winning idea to test a UV-activated dental glue on the ISS. Adia Bulawa



DreamUp will specifically sponsor the Team Rocket winners of the Guardians of the Galaxy Space Station Challenge, led by Adia Bulawa of Greeneville, Tennessee, for a project titled "Staying Healthy in Space."

The winners for Team Groot, led by Sarina Kopf of Golden, Colorado, for a project titled "Aeroponic Farming in Microgravity." will work alongside hardware partner Space Tango, Inc. However, this student team is familiar with DreamUp, having worked together on a plant biology project through NASA's HUNCH program that recently evolved into a patent application!

"It's the first students we're aware of that have a patent application resulting from their ISS work," said Lemack.

THE NEXT CHALLENGE: REACHING MORE STUDENTS

Through its programs and partnerships with a variety of organizations such as SSEP. Überflieger. NASA HUNCH (High schools United with NASA to Create Hardware), Uniphi Space Agency, and dozens of schools and universities around the world, DreamUp has sent more than 400 student research payloads to the ISS National Lab. Moreover, today DreamUp is expanding its reach through new approaches.

400 +For example, the team has expanded its professional **PAYLOADS** development offerings for educators.

We're trying to be holistic in how we're developing tomorrow's workforce," said Lemack. "Getting educators engaged and empowered is really important. If you have empowered educators, you'll have excited learners."

The team is also planning to release a set of new educational kits in late 2018. The kits enable students to replicate specific experiments that have previously been performed on the ISS. Each low-cost kit includes materials for student investigators and access to an online portal that lets students compare their results with the original space-based experiment. Two kits currently in production will engage students in ground-based versions of experiments that grow sugar crystals and culture microbes.

These kits bring real ISS research into the classroom in a way that is authentic yet affordable-and unlike flight projects, the kits do not require out-of-school time. The activities are brief, self-contained, and will align with Next Generation Science Standards, making them easy to integrate into existing lesson plans. DreamUp also has free curricular support materials on its website to further engage educators and reach more students with the excitement of science in space.

Another new program is a U.S. extension of an existing partnership with the Australian startup Cuberider. DreamUp has a programmable experiment unit on the ISS with data loggers, cameras, and sensors to monitor acceleration, radiation, and other aspects of the environment. Students learn simple programming and design experiments for the automated unit to perform. The students' code is uploaded, and the flight unit carries out the experiment, sending data to the classroom in near-real time. Students pose research questions, analyze data, and communicate results to their peers and community.

DreamUp is preparing to bring an 8- to 12-week version of this program to American students in fall 2018. Standards-aligned curricular support materials will introduce engineering design practices and rudimentary coding in Python. This program will be affordable and accessible to educators in many settings, because uploading code to the ISS is much faster and cheaper than launching hardware on a rocket.

DreamUp's efforts to expand its reach through these and other new pathways of engagement are helping maximize use of the ISS for innovation and educational outreach. Opportunities to do classroom versions of ISS experiments and program computer code for upload to the ISS National Lab are cost-effective, fun, and effective in cultivating STEM literacy. Moreover, DreamUp continues to reimagine ways to make their space-based student research programs even more accessible. After all, it's hard to match the excitement of watching one's own experiment launch into space. The lasting impact of programs like these inspire students long after their experiments are complete, helping our next generation of leaders envision themselves in STEM careers and continue to reach for the stars.

BEYOND STEM: BUILDING 21ST CENTURY SKILLS

Beyond the excitement of competing for a flight project, SSEP and other DreamUp programs help students develop STEM literacy and essential skills for their future careers. The National Education Association suggests that the four most important 21st century skills—known as the "Four Cs"—are critical thinking, communication, collaboration, and creativity. All of these skills are practiced as part of DreamUp programs.

Katrina Whipple, an enrichment teacher and instructional coach at Carter Middle School in Knoxville, Tennessee, says that SSEP gave her students extensive practice with teamwork and communication, which are vital in the workforce yet sometimes underemphasized in traditional classroom activities. Through nine weeks of intense teamwork developing a research proposal (just like professional researchers!), the team's communication skills were put to the test. Before this project, the students had never even seen—let alone written—a document in this style. "It was a real challenge for them to get a feel for professional scientific writing: how it looks and how it sounds," said Whipple.

Whipple noticed that the program's most transformative impact on the students was not that it introduced them to new aspects of STEM but rather that it introduced STEM into other aspects of their education. Traditional middle school curriculum is not very interdisciplinary, she said. "They do all their writing in language arts class. They do math in math class. They do science in science class. This was the first time they'd really had to synthesize what they'd learned across all these areas—combining science, math, and language arts to write this proposal." This early engagement in crossdisciplinary thinking will give these students an advantage as they progress through their academic and professional lives.

Randolph Middle School Science Club students in Huntsville, Alabama, test a prototype of DreamUp's educational kits.

Penny Pettigrew

DREAMUP LAUNCHES LEARNIN

Student Contest Winners Grow Crystals in Space BY AMELIA WILLIAMSON SMITH, Staff Writer

C tudents in Wisconsin eagerly awaited the return of the SpaceX CRS-14 Dragon capsule last month, which Carried their space-grown crystals back to Earth. The students, winners of the 2017 Wisconsin Crystal Growing Contest, had sent their investigation to the ISS National Lab to test their optimized conditions for Earthbased crystallization against microgravity-based crystallization. Although the students are still in the process of comparing their space-grown crystals with ground controls, they were excited to find crystals in each of the space station sample bags.



The contest, held by the Molecular Structure Laboratory of the University of Wisconsin–Madison Chemistry Department, invited Wisconsin students ages 11 to 18 to try to grow the biggest and highest-quality single crystal on the ground. The winning students then had the opportunity to adapt their Earth-based crystallization methods for a flight project

to the ISS National Lab.

Crew checks sample bags for crystal growth onboard the ISS National Lab NASA

"The Wisconsin Space Crystal Mission experience motivated the student participants to apply themselves in new areas and grow as scientists," said Ilia Guzei, director of crystallography at the University of Wisconsin–Madison. "They learned to work with scientific literature, plan and execute experiments in a laboratory setting, and keep a laboratory journal. Importantly, they learned to communicate and collaborate with fellow students because this project united students from different geographical locations in Wisconsin."

Through their experience, the students learned that the ISS is an optimal platform for molecular crystal growth because crystals grown in microgravity are often larger and more well-ordered than Earth-grown crystals. Space-based crystallization of organic and inorganic molecules has the potential to significantly

The 2017 Wisconsin Crystal Growing Contest winners

and their families at Kennedy Space Center in April

benefit life on Earth through numerous applications, and several companies are already taking advantage of the ISS National Lab to advance their crystal growth research and development.

As a first step in developing a long-term crystallization program onboard the ISS National Lab and to discuss how to inspire the next generation through crystallization educational opportunities. CASIS held a workshop in 2015 to gather input from experts in the field of protein crystallography. Based on recommendations from the workshop, CASIS established an ISS National Lab Microgravity Molecular Crystal Growth (MMCG) Program.

On July 19, CASIS will hold a second MMCG workshop at the Hauptman-Woodward Medical Research Institute in Buffalo, New York, just prior to the 2018 American Crystallographic



preparing samples CASIS

Students on the ground

Association's annual meeting in Toronto, Canada, At this workshop, participants will discuss progress made toward the goals outlined in the 2015 meeting, review new opportunities, and identify forward plans for both streamlined commercial use and continued educational programming. For more information on the upcoming MMCG workshop, visit www.iss-casis.org/ workshops/2018-mmcg.

Materials Science Space Station Investigations: Where Are They Now? **BY HAYLIE KASAP.** Contributing Author

esearch performed on the ISS National Lab isn't one and done—it keeps moving forward. Upward has Relative deveral ISS National Lab materials science experiments, including research on Ras Labs' Synthetic Muscle, Proctor & Gamble's colloid development, and the synthesis of semiconductor crystals using the hightemperature SUBSA furnace. These researchers have continued to make progress based on the results of their ISS investigations, as highlighted below.



Ras Labs Synthetic Muscle

Ras Labs has made several advancements since testing their Synthetic Muscle™ on the ISS. Results from that testing led Ras Labs to develop shapemorphing technology that allows a prosthetic to expand and contract with the body for an improved fit throughout the day. This pressure-sensing technology in the socket of the prosthetic

Ras Labs' custom polymers created as Synthetic Muscle™ Ras Labs

helps to auto-control the fit, reducing the need for manual adjustment. Such pressure sensors have also been used in robotic applications to enable dynamic movements and grippers in automated systems, as well as in products that fit within the ear such as ear buds. Ras Labs' Synthetic Muscle is currently in customer testing, with product development expected within one to two years. The company's eventual goal is to develop a streamlined way to mimic tactile touch, which is still missing in the field of prosthetics. With funding from Breakout Labs and a National Science Foundation Small Business Innovation Research Phase I grant, Ras Labs is continuing to make strides toward advancing their product to market.





principal scientist at P&G, there are Confocal image stack showing currently three patent applications 3D colloidal structure related to product development

and shelf life resulting from their ISS National Lab research and development (R&D). Much of P&G's current research pertains to the stability and dispensability of their products, such as cleaning sprays, for their billions of users worldwide. P&G expects that products featuring their new advancements might be released as soon as this year.



Devices, Inc.

impurities. Ostrogorsky's flight experiment, currently on the ISS and using the refurbished SUBSA furnace, also uses vapor diffusion, with the added benefit of microgravity crystallization conditions. He expects even better results in microgravity than on the ground, which could lead to important insights about these crystals, which are used to detect radiation in a variety of safety and security applications here on Earth.

To keep up with how investigators are using the ISS National Lab to advance materials science R&D, join CASIS and the National Science Foundation at a Materials in Space Workshop on July 22 in San Francisco, California, held in conjunction with this year's ISS R&D Conference. Network with a broad community of materials scientists and engineers who have space-related R&D experience and those who are new to space. The workshop will focus on advanced materials R&D on the ISS, where the unique environment of low Earth orbit enables investigations that are not possible or practical to perform on Earth. Learn more at www.cvent.com/d/kgg15j.





Radiation Monitoring

Synthesis of Semiconductor **Crystals Using SUBSA**

Aleksandar Ostrogorsky has continued his research on the crystallization of indium iodide, a type of semiconductor material that can be used to detect nuclear radiation. Ostrogorsky's ground controls produced positive data, with samples responding well to use of the vapor diffusion crystal growth method, producing large crystals with few





WHAT IS SUBSA?

Solidification Using a Baffle in Sealed Ampoules (SUBSA) is a hightemperature furnace onboard the ISS. The original SUBSA hardware was launched to the ISS in 2002 and returned to Earth following the completion of initial studies. Because

of increasing demand for capabilities provided by SUBSA, NASA refurbished the hardware and worked with CASIS to identify payloads that could use the renovated furnace.



TIONA

News & Notes from the ISS NATIONAL LAB

DESTINATION STATION: SALT LAKE CITY

In May, Destination Station, a NASA-led outreach effort to educate the public about the ISS, traveled to Salt Lake City, Utah. CASIS and the NASA Program Science Office, along with NASA Astronaut Randy Bresnik, met with representatives from the state of Utah and local companies to discuss and promote ISS capabilities. CASIS and NASA representatives also participated in the Governor's Energy Summit, a conference focused on new paths for responsible global energy-sector growth.

EXPANDING HORIZONS SALON

CASIS held an event in Silicon Valley in May as part of the Expanding Horizons salon series. Attendees learned about commercial innovation opportunities available on the ISS and how space-related ventures are advancing research and development in health, engineering, consumer products, and other markets. Featured guest Dan Lopez, founder and CEO of

Orbitmuse and chief technologist of space data analytics institution Radiant.Earth, joined CASIS staff to discuss the global innovation platform for space entrepreneurship.

MISSION PATCH

Earlier this month, CASIS unveiled its latest mission patch collaboration, with a patch designed by iconic filmmaker Sir Ridley Scott. The patch represents all ISS National Lab payloads for 2018 and features the night sky with a female astronaut looking toward the ISS.

DESTINATION IMAGINATION

Destination Imagination, a global leader in teaching the creative process from imagination to innovation, held global finals in May in Knoxville, Tennessee, with the goal of inspiring and equipping the next generation of innovators and leaders. CASIS participated in the event, which was attended by more than 17,000 students, parents, and volunteers and highlighted achievements across seven different challenges in science, technology, engineering, arts, and mathematics.

LAUNCHING TO THE ISS

The Orbital ATK CRS-9 mission successfully launched to the ISS in May, carrying payloads focused on technology development as well as the physical, materials, and life sciences. The mission also included several small satellites and validation of new facilities that will contribute to greater research capabilities in the future. SpaceX CRS-15 is anticipated to launch in late June.

FORGING UNIQUE MEDIA COLLABORATIONS TO FURTHER STATION RESEARCH

In May, science content publisher Seeker announced the launch of its new digital platform, "Seeker Universe," dedicated to covering all things space. Seeker and CASIS have forged a collaboration to provide Seeker's vast audience with meaningful content about the ISS, and Seeker has already posted multiple videos and articles on ISS National Lab facilities and CubeSats that have reached millions of viewers through Seeker's social media platforms. Seeker is also featuring ISS National Lab articles on their website to connect its readers with research taking place on the orbiting laboratory.

Read UPWARD online at upward.iss-casis.org



