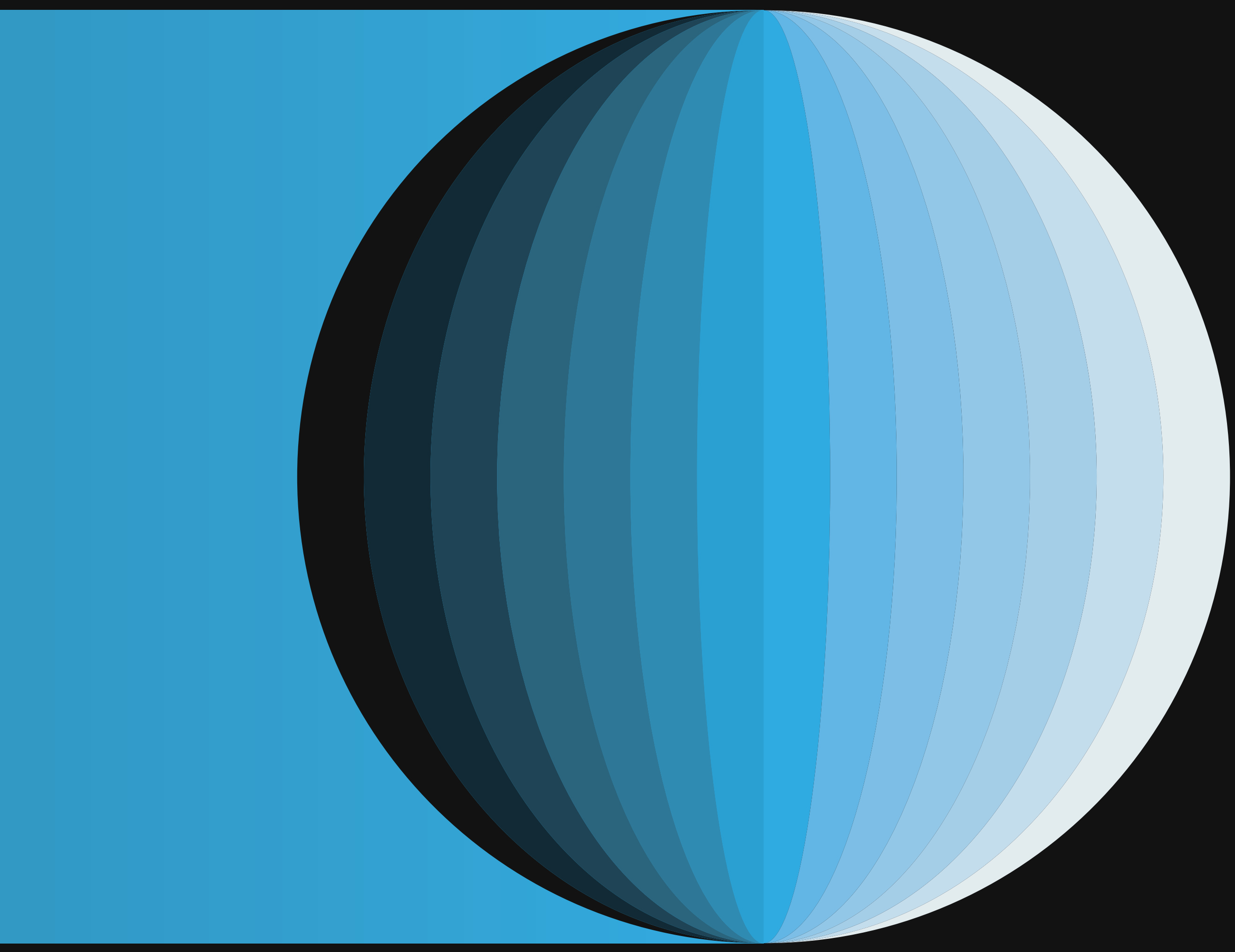
National Aeronautics and
Space Administration

ANNUAL HIGHLIGHTS of RESULTS from the INTERNATIONAL SPACE STATION

October 1, 2020 - October 1, 2021



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Product of the International Space Station Program Science Forum

This report was developed collaboratively by the members of the Canadian Space Agency (CSA), ESA (European Space Agency), Japan Aerospace Exploration Agency (JAXA), National Aeronautics and Space Administration (NASA), and the State Space Corporation Roscosmos (Roscosmos). The highlights and citations in this report, as well as all the International Space Station (ISS) results and citations collected to date, can be found at www.nasa.gov/stationresults.

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Introduction

The International Space Station (ISS) is an orbiting platform that astronauts and researchers use to understand the effects of space on human health and to develop technologies to mitigate those effects that are a barrier to future human exploration missions. The unique microgravity environment enables scientific investigation of physical, chemical, and biological processes in an environment very different from Earth.

November 2, 2020 marked the 20th anniversary of continuous human presence in space aboard ISS. In marking that milestone, it's important to acknowledge the successful cooperation between member nations. These collaborations have sustained more than 20 years of continuous research and technology development activities, nurturing the evolution of the ISS from an outpost in space to a dynamic laboratory hosting an increasing variety of government and privately-owned science facilities, external testbeds, and observatory sites. ISS research activities have impacted scientific fields from particle physics to plant biology, while inspiring the next generation of scientists and engineers and facilitating efforts to expand commercial use of low-Earth orbit (LEO).

As the third decade of continuous human presence onboard the International Space Station (ISS) begins, the impact of scientific research conducted aboard this orbiting laboratory continues to grow. In this year's Annual Research Highlights, we report ISS scientific results from a wide range of fields, from investigating ways to sustain human life in space, such as plant seedling growth and early detection of osteoporosis in space to better understanding the electrostatic levitation processes and Bose-Einstein condensate bubble dynamics.

The ISS Program Research Office (PRO) collected 410 scientific publications between October 1, 2020 and October 1, 2021. Of these, 355 were articles published in peer-reviewed journals, 39 were conference papers and 16 were gray literature publications such as technical reports or books. Out of the 410 items

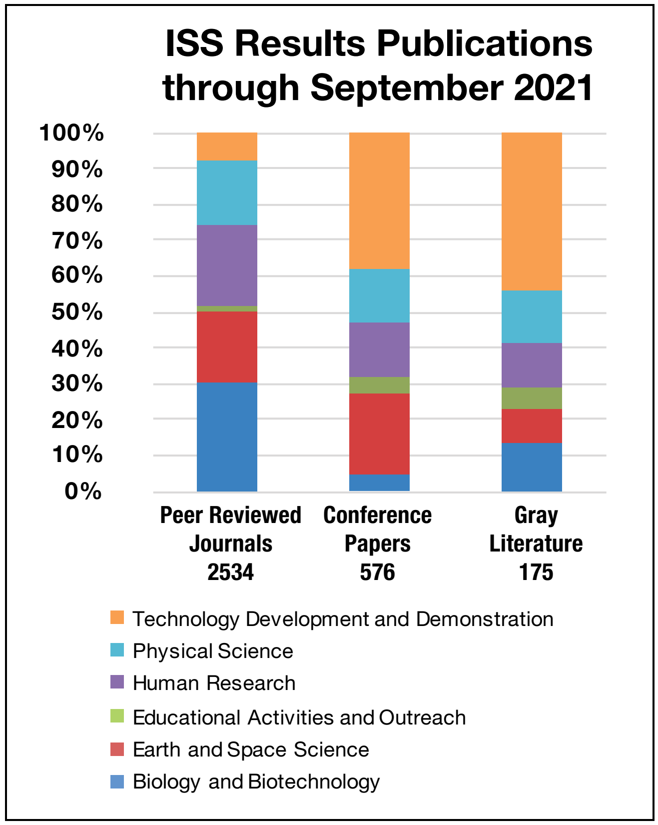


Figure 1: A total of 3285 publications (through October 1, 2021) represent scientists worldwide. This chart illustrates the percentages for each research discipline by publication type.

collected, 31 were published prior to October 1, 2020, but not identified until after October 1, 2020.

These results represent research activities sponsored by the National Aeronautics and Space Administration (NASA), the State Space Corporation Roscosmos (Roscosmos), the Japanese Aerospace Exploration Agency (JAXA), ESA (European Space Agency), the Canadian Space Agency (CSA), and the Italian Space Agency (ASI). This report includes highlights of collected ISS results as well as a complete listing of the year's collected publications on ISS results that benefit humanity, contribute to scientific knowledge, and advance the goals of space exploration for the world.

As of October 1, 2021, the ISS PRO has identified a total of 3285 results publications since 1999, with sources in peer-reviewed journals, conferences, and gray literature, representing the work of more than 5000 scientists worldwide (Figure 1). Overall, this number of result publications represents a 22% increase from a year ago.

The ISS PRO has a team of professionals dedicated to continuously collecting and archiving research results from all utilization activities across the ISS partnership. The archive can be accessed at www.nasa.gov/iss-science. The database captures ISS investigations summaries and results, providing citations to the publications and patents as they become available at www.nasa.gov/stationresults.

MEASURING SPACE STATION IMPACTS

Because of the unique microgravity environment of the ISS laboratory, the multidisciplinary and international nature of the research, and the rigorous selection process, much of the research generated from ISS has significant impact.

Currently, the PRO Research Results Management team tracks research articles that report ISS findings by scientists from the space agencies associated with the ISS to archive all science done on station and evaluate their scientific significance. The journals in which these articles are published are annually ranked by Eigenfactor score. Since different disciplines have different standards for citations and different time spans during which citations occur, Eigenfactor applies an algorithm that uses the entire Web of Science citation network from Clarivate Analytics® spanning the previous five years.[1] This algorithm creates a metric that reflects the relative importance of each journal. Using Eigenfactor counts citations to journals in the physical and social sciences, eliminates self-citations of journals, and is intended to reflect the amount of time researchers spend reading the journal. From October 1, 2020, to October 1, 2021, 74 ISS articles were published in the top 100 journals based on Eigenfactor. Twenty-seven of those ISS articles were in the top 10 journals as shown in Table 1. Relative to last year's counts, 17 more articles were published in the top 10 global journals in the last 12 months.

	Clarivate Analytics® Rank	Source (Number of Publications)
ISS Publications In Top 100 Sources	1	Nature Communications (2)
	2	Scientific Reports (8)
	3	Nature (3)
	4	PLOS ONE (7)
	5	Science (2)
	6	PNAS (4)
	8	Cell (1)
	12	Advanced Materials (1)
	13	Physical Review Letters (5)
	14	ACS Applied Materials & Interfaces (1)
	26	Monthly Notices of the Royal Astronomical Society (11)
	27	Science Advances (2)
	32	Circulation (1)
	34	International Journal of Molecular Sciences (10)
	40	Physical Review D (4)
	44	Frontiers in Microbiology (5)
	55	Geophysical Research Letters (1)
	62	Astronomy and Astrophysics (4)
	81	Applied Physics Letters (2)

Table 1: 2019-2020 ISS Publications collected in the Top 100 Global Journals, by Eigenfactor. From October 1, 2019, to October 1, 2020, as reported by 2019 Journal Citation Reports, Clarivate Analytics®.

The completion of ISS investigations has contributed to the growth of top tier publications seen today. As shown in Figure 2, many more ISS studies are now being published in high-ranking journals compared to previous years. Figure 2 also shows that all space agencies show top tier publication growth in Biology and Biotechnology and stable contribution in Human Research. From our earliest record of top tier ISS science in 2007 to October 1, 2021, there have been **377 articles** published in Top 100 journals.

While 377 articles may seem like a small number compared to the total of 3,285 publications, a bibliometric network analysis (Figure 3, panel A) shows that even a small number of publications in high-ranking journals can have a significant impact in how

1. West JD, Bergstrom TC, Bergstrom CT. The Eigenfactor Metrics™: A Network approach to assessing scholarly journals. College and Research Libraries. 2010;71(3). DOI: 10.5860/0710236.

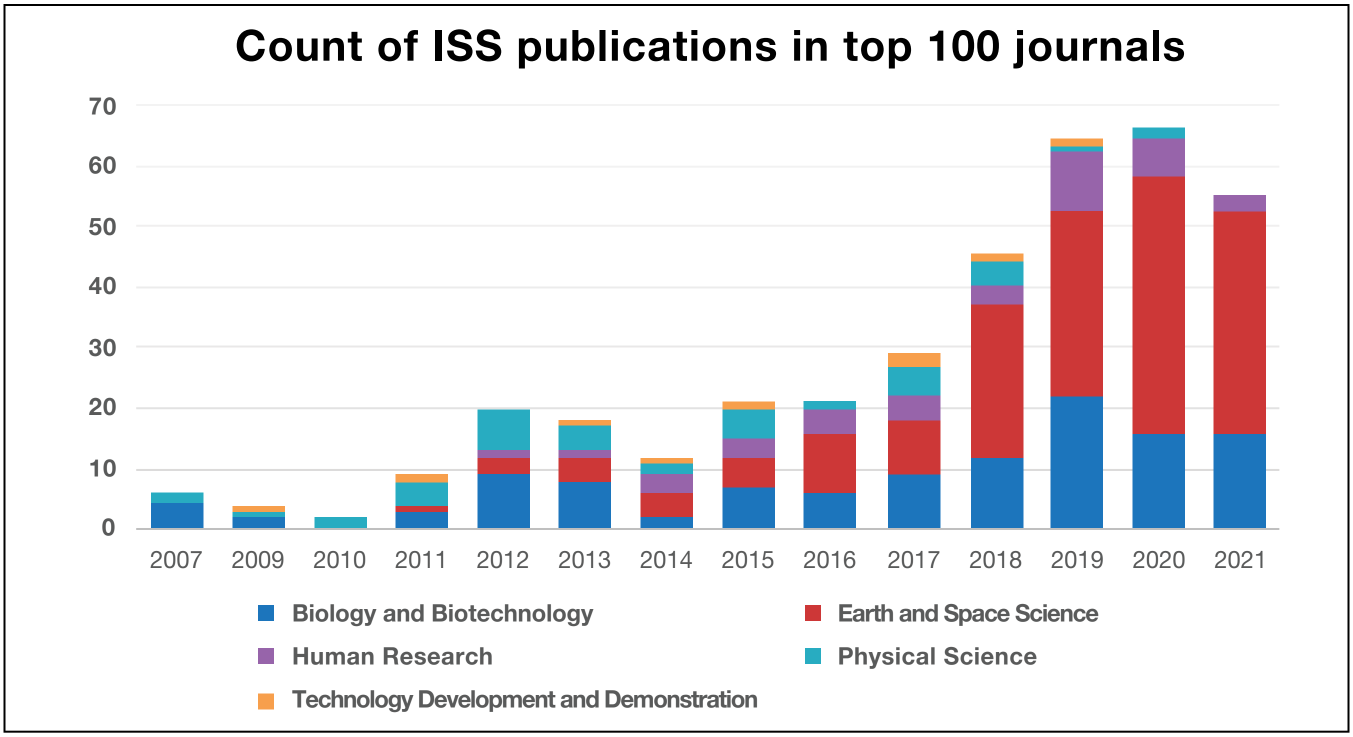


Figure 2. ISS articles published in Top 100 journals according to Clarivate's Eigenfactor ranking. Data are displayed by year, space agency, ISS research category, and ranking. Larger dots represent more distinguished journals based on Eigenfactor score.

the research study is received by others and how the knowledge is disseminated through citations in other journals. For example, six ISS studies have been published in *Nature,* represented as a small node in the graph. Network analysis shows that findings published in *Nature* are likely to be cited by other similar leading journals such as *Science* and *Astrophysical Journal Letters* (represented in bright yellow links) as well as specialized journals such as *Physical Review D and New Journal of Physics* (represented in a yellow-green link). Six publications in *Nature* led to 512 citations according to VOSviewer's network map (version 1.6.11), an increase of over 8,000% from publication to citation.

For comparison purposes, 6 publications in a small journal like *American Journal of Botany* led to 185 citations and 107 publications in *Acta Astronautica*, a popular journal among ISS scientists, led to 1,050 citations (Figure 3, panel B). This count of 1,050 citations represents an approximate 900% increase from publication to citation. It is additionally worth noting that the publications from *Acta Astronautica* were primarily cited by other mid-ranking journals. Therefore, ISS research studies that go through the rigorous peer-review of high-quality journals are likely to have the greatest impact in the scientific community through citations in other respected journals. Based on this knowledge, the 377 ISS articles published in top tier journals have had a significant impact on multiple areas of science. These discoveries, and their influence in the direction of future research, sets the ISS apart from other large-scale research efforts.

Bibliometric analyses measure the impact of space station research by quantifying and visualizing networks of journals, citations, subject areas, and collaboration between authors, countries, or organizations[2]. Using bibliometrics, a broad range of challenges in research management, and research evaluation can be addressed. The network visualizations presented here demonstrate how journal ranking influences citations of ISS research and how NASA's collaboration network has evolved.

[2] *Van Eck NJ, Waltman L. Software survey:VOSviewer, a computer program for bibliometric mapping. Scientometrics. 2010;84(2):523-538. DOI: 10.1007/s11192-009-0146-3.*

INTERNATIONAL SPACE STATION TOP TIER SCIENCE

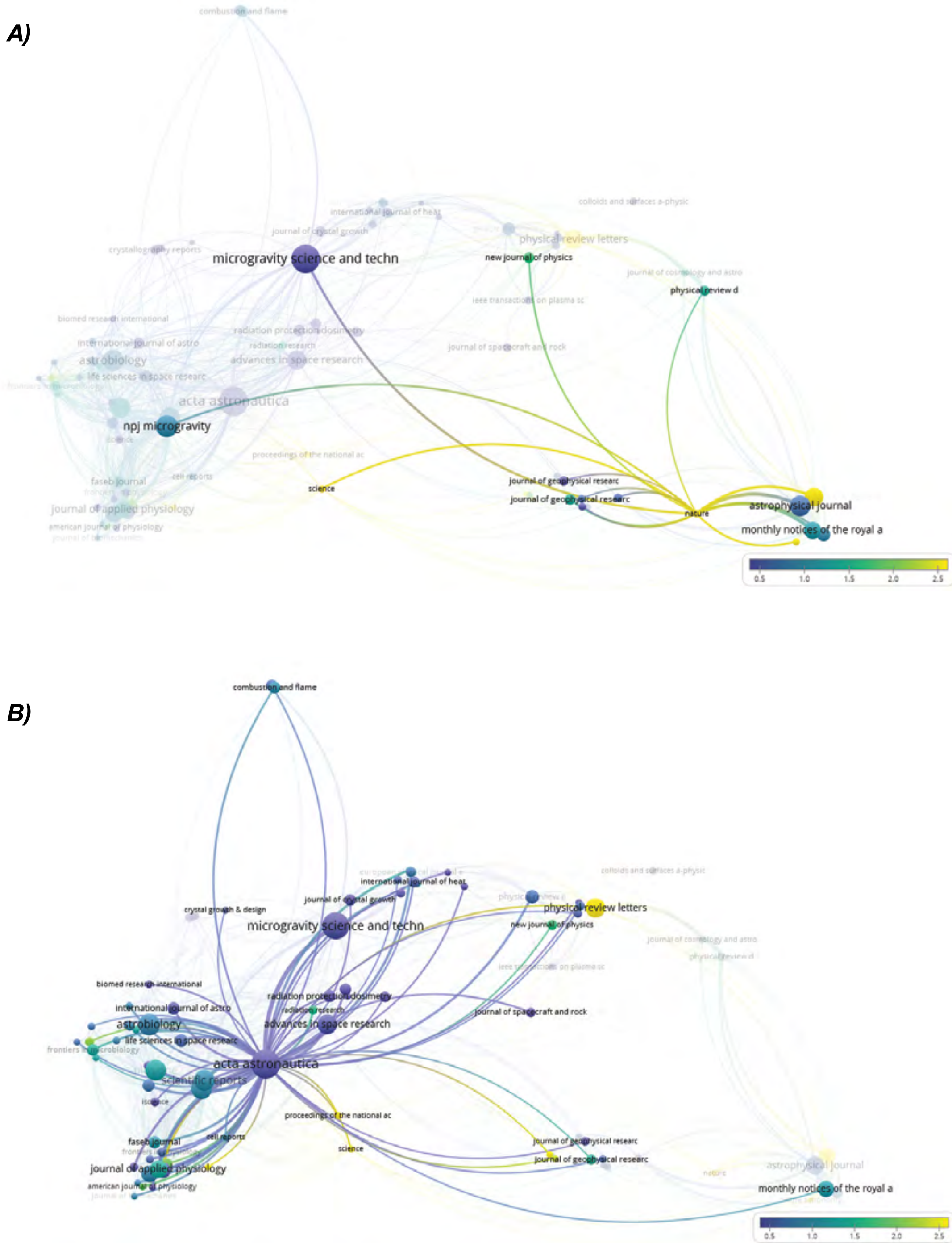


Figure 3. Top Tier ISS journals and citation overlay network. Node size represents the number of articles published in each journal (small node = few publications, large node = many publications). Distance between nodes represent the topic similarity between journals (closer nodes = similar journals, distant nodes = dissimilar journals). The color scale represents the average normalized number of citations received by the articles published in each journal (bright green and yellow indicate more citations. Purple indicates fewer citations). A) Network of a top-tier journal, Nature. B) Network of a popular mid-tier journal, Acta Astronautica.

EVOLUTION OF SPACE STATION RESULTS

The archive of the ISS investigations went online in 2004. Since that time, the PRO team has implemented several changes to how investigations are tracked. The team has split and added new research disciplines as more investigations become active, and many fields have been redefined since the roll out of the archive. Currently, the following publication types are included in the Program Science Database (PSDB):

- ISS Results - publications that provide information about the performance and results of the investigation, facility, or project as a direct implementation on ISS or on a vehicle to ISS
- Patents - applications filed based on the performance and results of the investigation, facility or project on ISS or on a vehicle to ISS
- Related - publications that lead to the development of the investigation, facility, or project.

Through continual analysis of the database, the team has determined the need for two new types of results publications to track: ISS Flight Preparation Results and Derived Results.

ISS Flight Preparation Results are articles about the development work performed for the investigation, facility, or project prior to operation on the ISS. Derived Results are articles that use data from an investigation that operated on ISS, but the authors of the article are not members of the original investigation team. Derived Results articles have emerged as a direct outcome of the open data initiative, which provides access to raw data to researchers from outside the investigation, enabling them to analyze and publish results, providing wider scientific benefits and expanding global knowledge. As of October 1, 2021, the PRO Research Results Management team identified 148 publications as ISS Flight Preparation Results and 157 publications as Derived Results. Although the Annual Highlights of Results spotlights ISS Results publications, recognition of these additional publication types in the database will contribute to the spread of scientific knowledge from the ISS.

LINKING SPACE STATION BENEFITS

ISS research results lead to benefits for human exploration of space, benefits to humanity, and the advancement of scientific discovery. This year's Annual Highlights of Results from the International Space Station includes descriptions of just a few of the results that were published from across the ISS partnership during the past year.

EXPLORATION

ISS investigation results have yielded updated insights into how to live and work more effectively in space by addressing such topics as understanding radiation effects on crew health, combating bone and muscle loss, improving designs of systems that handle fluids in microgravity, and determining how to maintain environmental control efficiently.

DISCOVERY

Results from the ISS provide new contributions to the body of scientific knowledge in the physical sciences, life sciences, and Earth and space sciences to advance scientific discoveries in multi-disciplinary ways.

BENEFITS FOR HUMANITY

ISS science results have Earth-based applications, including understanding our climate, contributing to the treatment of disease, improving existing materials, and inspiring the future generation of scientists, clinicians, technologists, engineers, mathematicians, artists and explorers.

NASA crew member Nicole Stott transferring ASI's investigation Mice Drawer System (MDS) from STS-128 to the ISS. (s128e007083)

PUBLICATION HIGHLIGHTS:
BIOLOGY AND BIOTECHNOLOGY

The ISS laboratory provides a platform for investigations in the biological sciences that explores the complex responses of living organisms to the microgravity environment. Lab facilities support the exploration of biological systems, from microorganisms and cellular biology to the integrated functions of multicellular plants and animals.

DISCOVERY

The NASA investigation **Functional Effects of Spaceflight on Cardiovascular Stem Cells (Cardiac Stem Cells)**, launched to the Space Station in early 2017, set out to investigate the effect of spaceflight on heart progenitor cell stages of migration, proliferation, differentiation, and aging. The new knowledge gained is expected to elucidate the role of stem cell development on cardiac structure and tissue regeneration for the design of therapies to treat heart conditions.

A new study drew comparisons between adult and neonatal cardiovascular progenitor cells (CPCs) cultured in a space environment aboard the International Space Station (ISS) for 30 days. Upon return to Earth, microRNA sequencing and transcriptomic analyses were conducted to examine their genetic profiles.

Compared to ground controls, results showed that spaceflight induces "stemness" (i.e., the maintenance of an early unspecialized appearence in the cell regardless of age) in adult and neonatal CPCs. This finding suggests that microgravity could be used as a tool to activate select transcripts associated with stemness in adult CPCs.

To further investigate cell aging, transcripts activated in spaceflight were compared to a list of 279 genes that either induced or inhibited cellular aging according to the CellAge database. Sixteen percent of the transcripts activated in space were found to match genes listed on CellAge, including transcripts that induced and inhibited aging. Since several of the transcripts known to induce aging have dual roles in proliferation and stemness, the overall impact of spaceflight on aging is unclear. However, the transcript analysis revealed an effect of spaceflight on specific molecular signaling pathways associated with cell cycle progression, cell differentiation, heart development and oxidative stress. This effect of spaceflight may improve regeneration, survival, and proliferation of CPCs. Understanding how to trigger developmental cycle re-entry in specific organ progenitor cells could benefit the field of regenerative medicine.

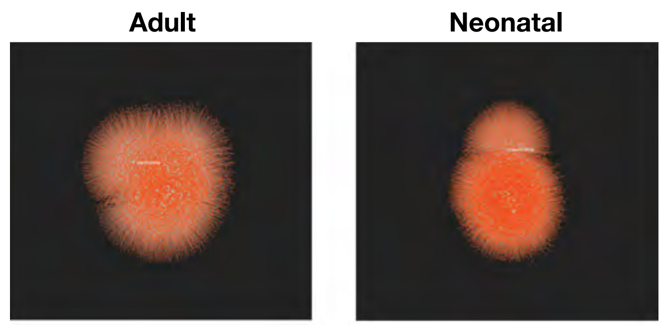


Figure 5. Live adult and neonatal stem cells flown to the ISS. Clonically identical cells were cultured on Earth as controls. Image adapted from Camberos, International Journal of Molecular Sciences.

Camberos V, Baio J, Mandujano A, Martinez AF, Bailey L, et al. The impact of spaceflight and microgravity on the human Islet-1+ cardiovascular progenitor cell transcriptome. International Journal of Molecular Sciences. 2021 March 30; 22(7): 18pp. DOI: 10.3390/ijms22073577.

The JAXA investigation **Transcriptome Analysis and Germ-cell Development Analysis of Mice in Space (Mouse Habitat Unit-1/Mouse Epigenetics)** examined spaceflight-elicited changes to DNA and gene expression in several organs of male mice and their offspring. Previous findings have demonstrated that artificial Earth gravity (AG) aboard the ISS prevents retinal cell death. In a new study, researchers followed up on this notion that AG may counteract human health concerns, such as muscle loss, by flying a dozen mice to space and investigating if AG conditions prevents skeletal muscle deterioration at the cellular level.

Once aboard the ISS, half of the mice were exposed to microgravity (MG) and the other half were centrifuged to simulate AG conditions. Creating an AG group aboard the ISS allowed equal exposure to potential confounding factors that could influence the results such as space radiation, microbial environments, lack of circulating air flow, and shock during launch and return. After roughly 35 days on station, the mice were returned to Earth for analysis.

Researchers measured the muscle mass of 5 different hindlimb musles (i.e., soleus, grastrocnemius, plantaris, tibialis anterior, and extensor digitorum longus). Relative to microgravity, researchers found that all muscles retained their weight in AG. A staining procedure was conducted to examine muscle fiber composition of the soleus muscle in depth. This analysis showed that the decrease of type-IIa fibers (i.e., fast twitching oxidative) and an increase of type-IIb fibers (i.e., fast-twitching glycolytic) observed in microgravity, were absent in AG. Cross-sectional areas of myofibers also retained their structure under AG. Therefore, exposure to AG aboard the ISS is sufficient to maintain muscle fiber type composition and overall muscle mass during spaceflight. Additional transcriptome analyses showed that AG prevented gene expression changes, confirming that the negative impact of spaceflight on muscle deterioration is explained by reduced gravity and not other factors. Atrophy-related genes, which were significantly changed in MG, appeared blocked in AG.

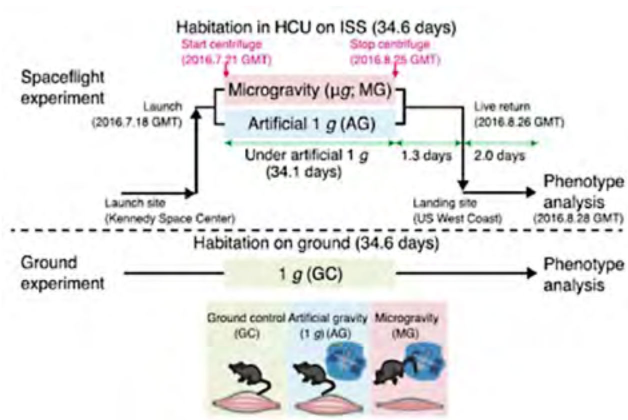


Figure 6. Schematic overview of the study timeline, experimental conditions, and procedures. Image adapted from Okada, Scientific Reports.

Finally, based on computer simulation analysis, the gene *Cacng1* was identified as being associated with muscle atrophy. Expression of this gene was upregulated in MG relative to AG. While ground *in vitro* and *in vivo* analyses showed that *Cacng1* induces a reduction in muscle fiber size, more studies are required to understand its role during spaceflight. These results are expected to assist in the diagnosis and treatment of muscle disorders, and it positions AG as a potentially effective tool for long-term habitation in MG.

Okada R, Fujita S, Suzuki R, Hayashi T, Tsubouchi H, et al. Transcriptome analysis of gravitational effects on mouse skeletal muscles under microgravity and artificial 1 g onboard environment. Scientific Reports. 2021 April 28; 11(1): 9168. DOI: 10.1038/s41598-021-88392-4.

The ESA investigation **Biorock** was designed to study the interaction between microbes and the minerals of basalt igneous rocks in microgravity and Martian environments to uncover the impact of gravity changes on the microbe's ability to naturally mine the rocks. Investigators initially expected altered gravity to reduce the mixing of liquids and gases, thereby affecting 1) the food supply to the microbes, 2) the structure of biofilms (i.e., bacterial colonies), and 3) gene expression.

Microorganisms naturally contribute to the weathering of rocks into soils and the cycling of elements in our ecosystem. They are also purposefully used in the manufacturing process of electronics and alloy production, and in the accelerated extraction of gold,

Figure 7. ESA astronaut Luca Parmitano at the BioRock Experimental Unit aboard the ISS. An experiment container is being inserted into the KUBIK incubator for sample processing. Image adapted from Cockell, Nature Communications.

copper, and other economically valuable rare earth elements (REEs) for high-tech devices such as cell phones and computer screens. This artificial and deliberate process is known as biomining.

In a new study, researchers examined the ability of three species of bacteria to extract REEs from basaltic rock, commonly found on the surface of the Moon and Mars. The hardware, BioRock Experimental Unit, contained basalt slabs with a known composition of 14 REEs. Media containing either *Sphingomonas desiccabilis*, *Bacillus subtilis*, or *Cupriavidus metallidurans* were injected into separate chambers, which were set to different gravity conditions: microgravity, simulated Earth, and simulated Mars. Non-biological samples without microorganisms and ground controls were also conducted to draw comparisons.

Contrary to the researchers' hypotheses, there was a main effect of organism but not gravity condition; that is, some bacteria (i.e., *S. desiccabilis*) enhanced biomined concentrations of REEs in all gravity conditions, particularly in Mars and Earth simulated gravities. Other bacteria, (i.e., *B. subtilis*) biomined less across all gravity conditions, and some other bacteria (*C. metallidurans*) did not enhance biomining at all. Between biological samples with microorganisms, there were no significant differences across gravity conditions. These results suggest that biomining on the Moon and Mars can be equally effective as on Earth. It was additionally demonstrated that S. desiccabilis biomined heavy REEs more than light REEs. Enhancing our understanding of microbe-mineral interactions can lead to applications in geology, closed-loop life support systems, as well as the production of raw and construction materials for sustainable microbial living and human habitation in settings beyond Earth.

Cockell CS, Santomartino R, Finster KW, Waajen AC, Eades LJ, et al. Space station biomining experiment demonstrates rare earth element extraction in microgravity and Mars gravity. Nature Communications. 2020 November 10; 11(1): 5523. DOI: 10.1038/s41467-020-19276-w.

BENEFITS FOR HUMANITY

The NASA investigation **NanoRacks-CellBox-Effect of Microgravity on Human Thyroid Carcinoma Cells (NanoRacks-CellBox-Thyroid Cancer)** studied the effect of microgravity on human thyroid carcinoma cells with the goal of identifying biomarkers in the DNA or in the cellular proteins expressed or secreted. The unique three-dimensional spheres formed in microgravity are expected to facilitate the identification of such biomarkers for improved diagnosis, treatment, and pharmaceutical innovations.

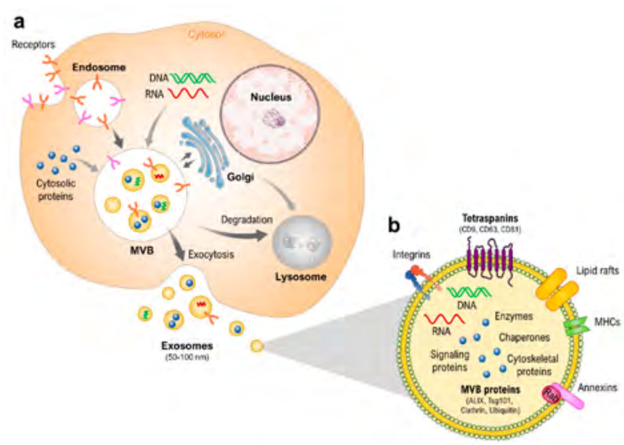


Figure 8. Schematic overview of exosome genesis, cargo-loading, and release to extracellular fluid. Image adapted from Wise, International Journal of Molecular Sciences.

In this new study, researchers analyzed changes in growth, gene, and protein expressions, as well as protein interactions in cultured follicular thyroid cancer cells (FTC-133) along with their supernatants after prolonged exposure to microgravity. Three samples incubated in space for 12 days were compared to three control samples on Earth.

Extracellular vesicles (EVs), a family of cytoplasmic sacs enclosed by a membrane and secreted outside the cell, mediate cell to cell communication and hold potential as biomarkers for disease. Exosomes, a type of EV, were examined to understand their role in tumorigenesis. To overcome previous methodological limitations, researchers employed a new technique called single-particle interferometric reflectance imaging sensor (SP-IRIS) that allowed multiple-signal phenotyping and digital counting of different populations of exosomes obtained from biofluids. To assess the type, amount, and population distribution of exosomes in the cell supernatants, a test kit was used to inspect specific transmembrane surface markers (i.e., tetraspanins: CD9, CD63, CD81) known to bind to specific antibodies printed on the microarray chip where they were counterstained with fluorescent antibodies to reveal their protein expression.

Results showed a 74% increase in exosome counts in flight module (FM) samples compared to ground module (GM) samples. Tetraspanin CD63 captured a significant number of these exosomes. Particle size distribution was similar across FM and GM samples, potentially indicating that the content of exosomes depends on intracellular and extracellular conditions. Flourescent analysis also showed a significant increase in particle count for all tetraspanis in FM samples, with CD63 showing the highest count. These results point to an adaptation of the cells in the microgravity environment. Previous studies have linked increased expression of CD63 and CD81 to tumor growth and metastasis, but researchers recommend further exploration of the subject to understand the tumorigenic behavior of FTC-133 cells.

Wise P, Neviani P, Riwaldt S, Corydon TJ, Wehland M, et al. Changes in exosome release in thyroid cancer cells after prolonged exposure to real microgravity in space. International Journal of Molecular Sciences. 2021 January; 22(4): 2132. DOI: 10.3390/ijms22042132.

ESA crew member Thomas Pesquet performing the Human Research experiment GRIP. The investigation examines astronauts' grip force while manipulating objects in space using different types of movements. The knowledge gained will contribute to the development of intelligent haptic systems.

PUBLICATION HIGHLIGHTS:

HUMAN RESEARCH

ISS research includes the study of risks to human health that are inherent in space exploration. Many research investigations address the mechanisms of these risks, such as the relationship to the microgravity and radiation environments as well as other aspects of living in space, including nutrition, sleep and interpersonal relationships. Other investigations are designed to develop and test countermeasures to reduce these risks. Results from this body of research are critical to enabling missions to the lunar surface and future Mars exploration missions.

BENEFITS FOR HUMANITY

The ROSCOSMOS investigation **Cardiovector** was designed to measure body movements along multiple linear and rotational directions, and various heart activity parameters to assess cardiac health. Small and regular variations of blood displacement from the heart to the arteries were examined in microgravity using a method called ballistocardiography.

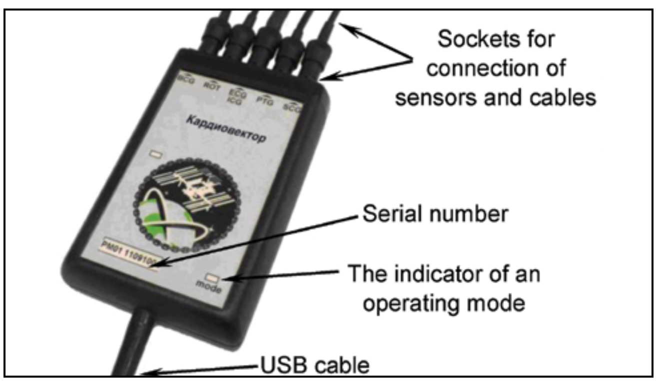


Figure 9. Cardiovector device worn by cosmonauts on ISS to measure cardiac activity. Image adapted from Baevsky, Acta Astronautica.

Ballistocardiography measures the body motion generated by blood pulses at every cardiac cycle. In a new study, researchers used a cardiovector device to record multiple physiological signals from the heart including 1) ballistocardiogram along 3 transverse and 3 rotation axes, 2) electrocardiogram, 3) impedance cardiogram, 4) seismocardiogram, and 5) pneumotachogram. In addition to these cardiac function measurements, crew members were asked to breath in, breath out, and hold their breaths at regular intervals. Cardiac and breathing measurements obtained twice before flight, every month during flights, and twice after flight, enabled researchers to examine heart contractility in relation to breathing. Typically on Earth, ballistocardiographic waves rise with inhalation and subside with exhalation.

Results from ISS showed that amplitude waves during quiet breathing are disrupted in microgravity, with higher amplitude waves during exhalation and relative to pre and postflight control data. This effect may have been observed because the already taxed systolic volume of the right ventricle cannot be further expanded during inhalation while the left ventricle diastolic is filling and systolic volume increases during exhalation. These results suggest that early cardiovascular changes in microgravity cause more intense activity of the left ventricle.

Baevsky RM, Funtova II, Luchitskaya ES. Role of the Right and Left Parts of the Heart in Mechanisms of Body Adaptation to the Conditions of Long-Term Space Flight According to Longitudinal Ballistocardiography. Acta Astronautica. 2020 October 6; 178: 894-899. DOI: 10.1016/j.actaastro.2020.10.001

EXPLORATION

The ROSCOSMOS investigation **Comprehensive Study of the Pattern of Main Indicators of Cardiac Activity and Blood Circulation (Cardio-ODNT)** assesses the relationship between circulation and unloading adaptation of the human body in microgravity, applying negative pressure to the legs as countermeasure for orthostatic intolerance.

Reduced blood pressure in microgravity affects the cardiovascular system, the veins in particular. Previous studies have demonstrated changes in vein structure soon upon arrival to the ISS. The changes appear to be more prominent in the lower extremities. In a new study, researchers examined leg vein health in astronauts who participated in two 6-month spaceflight missions.

Figure 10. ROSCOSMOS Plethysmograph Unit used during expedition 60. Image iss060e022611.

A plethysmograph, an instrument that detects organ or whole-body volume changes caused by blood flow, was used to obtain and compare preflight and in-flight (first and second mission) measurements of leg volume, capacity, compliance (i.e., vein distensibility), and vein filling rate. In-flight data was acquired two months and five months into each of the spaceflight missions, and the period between spaceflight missions ranged from three to five years.

Results showed that leg volume increased from preflight to the second spaceflight mission, but this change was partly explained by enhanced muscular volume acquired because of exercise regimens carried out between missions on Earth. Additionally, venous capacity increased in microgravity relative to Earth, but there were no significant differences in venous compliance or vein filling rate. The individual leg vein health characteristics of the astronauts remained largely unchanged across missions. In all, these results reveal that participation in two spaceflight missions do not worsen leg vein health if a substantial interval exists between flights and adequate leg muscle to support the cardiovascular system is present. These findings suggest that good muscular health (i.e., high elasticity) in lower extremities support vein structure and function, consequently demonstrating that physical exercise is a promising countermeasure to mitigate orthostatic intolerance.

Kotovskaya AR, Fomina GA, Salnikov VA. Investigations of leg veins in cosmonauts after repeated 6-month missions to the RS of the ISS. Human Physiology. 2020 December 1; 46(7): 776-779. DOI: 10.1134/S0362119720070087.

Studies of resistive exercise countermeasures designed to combat spaceflight-induced bone atrophy have shown that not all astronauts benefit from exercise to the same degree. CSA **TBone** researchers in collaboration with NASA's **Biochemical Profile** investigators used high-resolution peripheral quantitative CT (HR-pQCT) imaging before and after flight, biochemical data shared by other investigations, and an exercise history questionnaire to study: 1) bone changes in microarchitecture, density, and strength of the bilateral tibia and radius in response to long-duration spaceflight, and 2) the relationships among mission duration, biochemical markers associated with bone resorption and formation, and exercise.

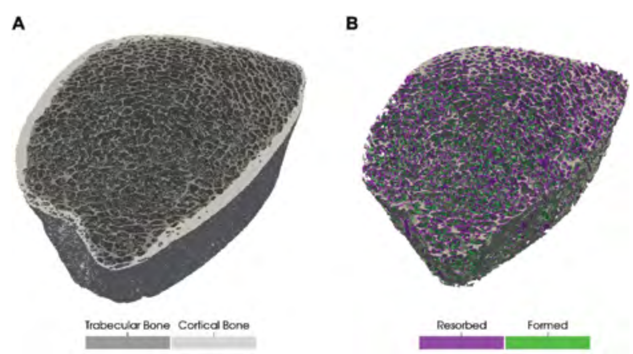


Figure 11. Representative image of crewmember before (A) and after (B) spaceflight showing trabecular bone changes. Image adapted from Gabel, British Journal of Sports Medicine.

Results revealed that the bilateral tibia underwent significant changes from preflight to postflight, proportional to mission duration. The bilateral radius did not appear to change significantly in cortical thickness, porosity, density, or failure load. Bone breakdown (aka resorption) markers CTx and NTx were elevated throughout flight and postflight compared to preflight. These markers appeared to correlate negatively with tibia bone density and strength. Finally, it was also found that greater running volume before flight predicted greater trabecular bone loss of the tibia during flight. This likely occurred because astronauts who ran more before flight decreased their running volume during flight. Researchers explain that the bone loss observed in space is equivalent to bone loss during a 20-year period on Earth and six times faster than the rate observed in post-menopausal women.

Consistent with previous literature, lower extremity bones experienced atrophy in microgravity due to their reduced weight bearing function and reduced use while onboard the ISS. Data suggest that bone loss experienced in some astronauts in space could be predicted by elevated biomarkers preflight. Changes in these markers precede visible anatomical changes after flight. These findings suggest that bone biomarkers and exercise history can help identify astronauts at greater risk for bone loss. Researchers recommend in-flight resistance training to mitigate bone atrophy and further examination of this phenomenon with astronauts participating in longer missions.

Gabel L, Liphardt A, Hulme PA, Heer MA, Zwart SR, et al. Pre-flight exercise and bone metabolism predict unloading-induced bone loss due to spaceflight. British Journal of Sports Medicine. 2021 February 17; epub: 9pp. DOI: 10.1136/bjsports-2020-103602.

The ROSCOSMOS investigation **Development of a System of Supervisory Control Over the Internet of the Robotic Manipulator in the Russian Segment of ISS (Kontur)** studied different ways to improve autonomous control of the robotic arm on the Russian segment of the ISS through the internet.

Future space exploration missions to the moon and Mars require the use of robotic systems teleoperated from orbital spacecraft to avoid communication delays. A new study examined how compromised task performance in space due to sensorimotor impairment during spaceflight impacts the teleoperation of robotic systems aboard the ISS. Because task performance in space varies between crew members depending on adaptation, task demands, and individual cognitive resources, this study used a joystick with different haptic settings (i.e., technology that applies forces to the user) to improve sensorimotor performance.

Figure 12. Experimental setup of Kontur aboard the ISS. Image adapated from Weber, Experimental Brain Research.

Using a force feedback joystick connected to a laptop and with a strap to measure arm position, crew members and a control group on Earth performed vertical and horizontal stability tracking tasks in which the cursor manipulated by the joystick was required to match a moving target on the computer screen. The experiment was completed once before, three times during, and once after spaceflight. Experimental conditions varied the haptic settings for stiffness, damping, and mass. An additional isotonic condition with no haptics was included. A test of sensorimotor coordination was completed at the end of the study. Time on task was used as a measure of sensorimotor coordination ability.

Results showed that the control group benefited from higher stiffness and damping to reduce tracking error in the horizontal tracking task. Cosmonauts' standardized test results for sensorimotor abilities (measured in terrestrial trials) were average or above average. During spaceflight, they were able to stabilize horizontal and vertical tracking motions, i.e., tracking error did not increase compared to their terrestrial baseline. However, tracking smoothness was impacted considerably in the early phase of spaceflight, and the magnitude of this effect depended on the cosmonaut's sensorimotor abilities. Researchers concluded that while individual cognitive sensorimotor ability can help overcome difficulties with task performance, distorted proprioception impacts motion stability in the early stage of adaptation to microgravity. Therefore, enhanced robotic haptic technology ought to be used to improve teleoperations.

Weber B, Riecke C, Stulp F. Sensorimotor impairment and haptic support in microgravity. Experimental Brain Research. 2021 March 1; 239(3): 967-981. DOI: 10.1007/s00221-020-06024-1.

DISCOVERY

The ROSCOSMOS investigation **Spatial Orientation and Interaction of Eisodic Systems Under Conditions of Weightlessness (VIRTUAL)** studied the impact of microgravity on vestibular function along with multisensory interactions involved in visual tracking.

The microgravity environment affects vestibular function mechanisms, leading to space adaptation syndrome and space motion sickness. Multisensory areas of the brain that converge visual, vestibular, and motor signals to understand the position of the body receive conflicting information in microgravity. A new study examined a vestibular-ocular reflex in real and simulated microgravity by analyzing two routes of the incoming reflex signal (i.e., afferentation): a direct route from otolith to ocular (OOR) and an indirect route from otolith to cervical to ocular (OCOR). Both reflex routes were studied in static torsional methods, and the direct route was additionally examined in centrifugal acceleration (OORCF).

Using video oculography in a virtual environment, the reflex afferentations were investigated before, during, and after spaceflight. The simulation, also in a virtual environment, was conducted with participants exposed to dry immersion and bed rest. In the static torsional

Figure 13. Assessment of ocular reflexes aboard the ISS. Image adapted from Naumov, Human Physiology.

condition, participants were instructed to tilt their heads to a 30-degree angle. In the centrifugal acceleration condition, participants were rotated vertically 0.5 m from the axis of rotation. During testing, participants' eye movements were tracked while wearing a helmet equipped with velocity sensors, accelometers, and infrared video cameras. The ratio between angles and amplitude of compensatory torsional ocular counter-rolling were measured.

Researchers found that crew members displayed atypical and reduced reflexes (i.e., absence or inversion of reflex) in spaceflight and simulated microgravity when compared to baseline measures. No significant differences between the afferentation routes (OOR and OCOR) were identified after spaceflight. However, the vestibular-ocular reflex was significantly different when studied under static torsional or centrifugal acceleration conditions. Typical reflexes were observed about a week after return to Earth. These results demonstrate that microgravity compromises direct and indirect afferentations involved in the support of the vestibular system.

Naumov IA, Kornilova LN, Glukhikh DO, Ekimovskiy GA, Kozlovskaya IB, et al. The effect of afferentation of various sensory systems on the otolith-ocular reflex in a real and simulated weightlessness. Human Physiology. 2021 January 1; 47(1): 70-78. DOI: 10.1134/S0362119720060080.

JAXA crew member Norishige Kanai in the Japanese Experiment Module aboard the ISS while working with the Two-Phase Flow experiment. Two-Phase Flow examines the behavior of bubbles, liquid-vapor flow, and heat transfer in microgravity. iss055e098144.

PUBLICATION HIGHLIGHTS:
PHYSICAL SCIENCE

The presence of gravity greatly influences our understanding of physics and the development of fundamental mathematical models that reflect how matter behaves. The ISS provides the only laboratory where scientists can study long-term physical effects in the absence of gravity without the complications of gravity-related processes such as convection and sedimentation. This unique microgravity environment allows different physical properties to dominate systems, and scientists are harnessing these properties for a wide variety of investigations in the physical sciences.

BENEFITS FOR HUMANITY

The ROSCOSMOS-ASI investigation **Multiwavelength Imaging New Instrument for the Extreme Universe Space Observatory (Mini-EUSO – UV-Atmosphere)**, classified as Physical as well as Earth and Space Science, is a state-of-the-art multipurpose telescope designed to operate during nighttime. It is part of a larger program (i.e., JEM-EUSO) with about 300 scientists from 16 countries whose overall goal is to enhance the observations of cosmic rays in the ultraviolet range of various atmospheric phenomena. Mini-EUSO, launched to the ISS in August 2019, is mounted on the Russian Zvezda module and is expected to operate for three years. The focal surface system contains 36 multianode photomultiplier tubes capable of detecting single photons. This system allows Mini-EUSO to detect different levels of brightness, from a few pixels in cosmic ray showers to many more pixels in ELVES and lightning.

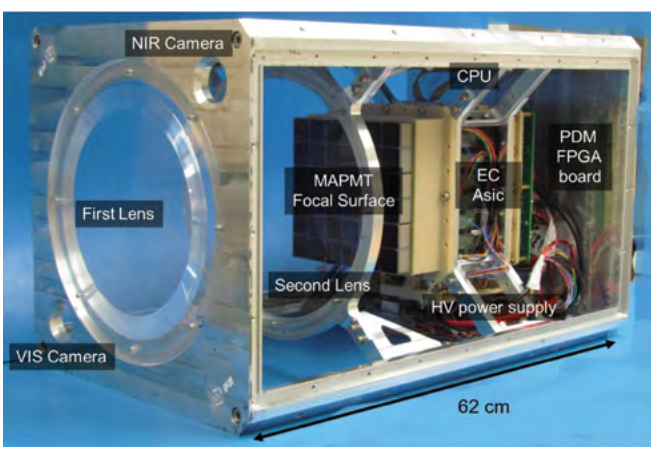


Figure 14. Mini-EUSO mock-up displaying three main compartments (optics, focal surface, and data acquisition). Image adapted from Bacholle, The Astrophysical Journal Supplement Series.

Air showers, a cascade of ionized particles and electromagnetic radiation that produce a streak of fluorescent light when ultrahigh-energy cosmic rays enter the Earth's atmosphere, have been studied by ground telescopes located in the Northern and Southern hemispheres. Observing the fluorescent light from space with a telescope such as Mini-EUSO allows researchers to determine the energy of the cosmic rays, the arrival direction, and the position of the shower.

Six months of operations indicate correct functionality of the instrument, including its ability to measure variations in airglow and ultraviolet emissions from Earth, track space debris, estimate meteor hazards, study strange quark matter, observe transient luminous events, and track ultrahigh-energy cosmic rays. Operation of the Mini-EUSO is expected to provide data on climate effects, marine pollution, geomagnetic disturbances, space debris removal, and possibly predict the three-dimensional path of meteors.

Bacholle S, Barrillon P, Battisti M, Belov A, Bertaina M, et al. Mini-EUSO Mission to Study Earth UV Emissions on Board the ISS. The Astrophysical Journal Supplement Series. 2021 March 17; 253(2): 36. DOI: 10.3847/1538-4365/abd93d

DISCOVERY

The ESA investigation **Electromagnetic Levitator Batch 2 - Non-equilibrium Multi-Phase Transformation: Eutectic Solidification, Spinodal Decomposition and Glass Formation (EML Batch 2 – MULTIPHAS)** studied alloy phase transformations in microgravity to manipulate chemical and thermal properties.

The quality of a metallic microstructure as the end product of the manufacturing process depends on the initial arrangement of particles during crystallization (i.e., nucleation) and subsequent crystal growth, both of which are influenced by temperature and fluid flow. While the intrinsic properties of a liquid and the amount of supercooling can lead to clean and pure nucleation, undissolved impurities can lead to flawed nucleation. Previous studies have examined the effects of pressure, electric, and magnetic fields on nucleation, but this study is the first to investigate the effect of stirring (fluid flow) on the nucleation rate of solids from supercooled liquid metals.

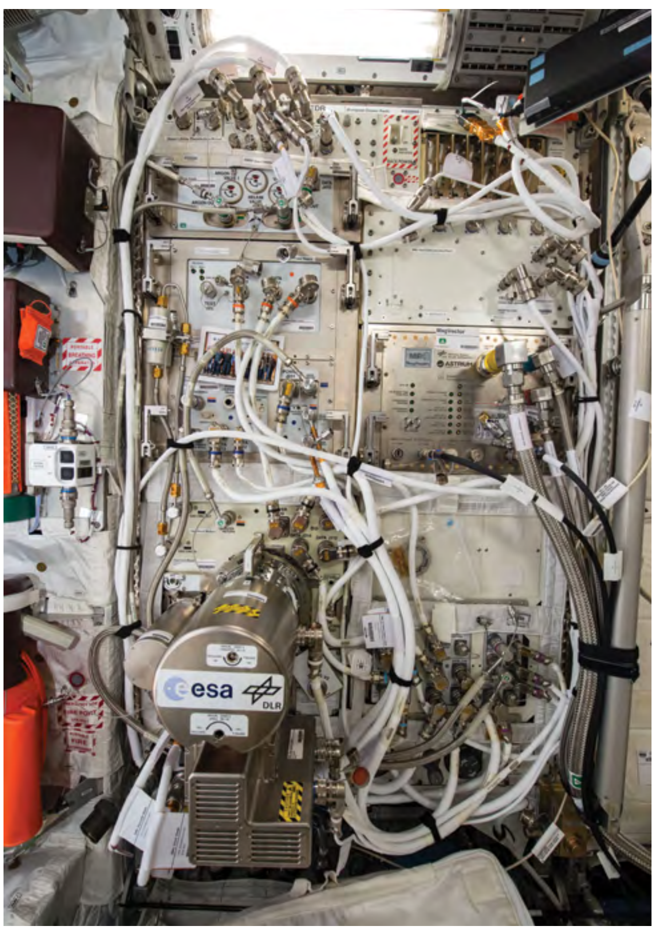


Figure 15. Electromagnetic Levitator in the Columbus module of ISS. NASA image: iss041e096097.

To overcome density and surface tension driven convection limitations known to occur under terrestrial conditions, a new study used the Electromagnetic Levitator aboard the ISS to examine how fast three different types of metal mixes nucleated under uniform heating and constant electromagnetic stirring. One of the liquid metals (Ti39.5 Zr39.5 Ni21) is known to form a quasicrystal upon nucleation, whereas the other two liquid metals (Cu50Zr50 and Vit106) are known to form a bulk metallic glass. Several melting and solidification cycles performed under a vacuum atmosphere in quiescent conditions (i.e., minimum positioner voltage and heater off), and fluid flow parameters (velocity and shear) were indirectly measured through model calculations.

Irrespective of pure or flawed nucleation, researchers discovered that increased stirring accelerated the nucleation rate of one of the liquid metals (i.e., Vit106). This faster nucleation led to increased temperature due to the heat release during solidification. However, increased stirring did not accelerate nucleation for the other two liquid metals. These results are consistent with the coupled-flux model, which states that stirring should have a large effect on nucleation when compositional changes occur during solidification.

This new observation contributes to the fundamental understanding of nucleation mechanisms in partitioning systems, the processing of high-performing materials in space, and manufacturing under extra-terrestrial conditions.

Gangopadhyay A, Sellers M, Bracker GP, Holland-Mortiz D, Van Hoesen D, et al. Demonstration of the effect of stirring on nucleation from experiments on the International Space Station using the ISS-EML facility. npj Microgravity. 2021 August 6; 7(1): 31. DOI: 10.1038/s41526-021-00161-9.

DISCOVERY

NASA's Flame Design, one of several investigations included in the Advanced Combustion via Microgravity Experiments (ACME) project, examined the starting point and propagation of soot to improve oxygen-enriched combustion for the design of soot-free flames that are more efficient and less polluting.

Diffusion flames (i.e., flames in which the fuel and oxidizer are not mixed prior to combustion) are

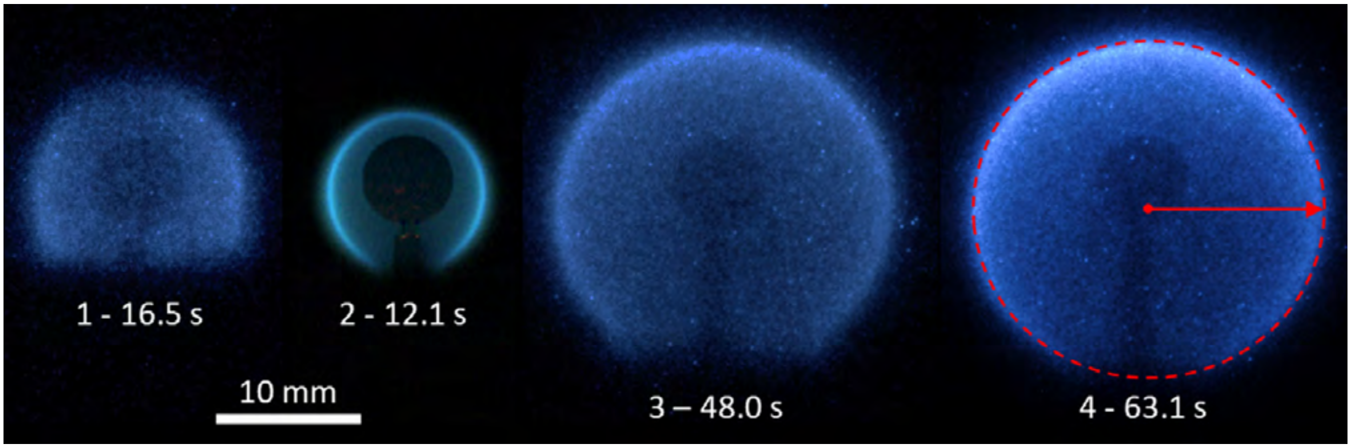


Figure 16. Samples of four flames exposed to varying experimental conditions: X_{O2} Ambient, X_{C2H4} Burner, m_{C2H4}, and m_{N2}. Note differences in flame radius. Image adapted from Irace, Combustion and Flame.

commonly used in practical combustion applications. Microgravity diffusion flames supported on a porous spherical burner enable researchers to study spherical gaseous diffusion flames while controlling the reactant flow rate, the concentration of the fuel, and the direction of convection across the flame. This analysis is not possible in the presence of gravity, where buoyancy exists. The absence of buoyancy in microgravity leads to a much longer period of time for the flame to fully develop and researchers are still unsure if a steady state flame can exist. While several configurations of diffusion flames have been previously studied in microgravity, this new study is the first to investigate the dynamics of gaseous spherical diffusion flames in long-duration spaceflight.

The experiment aboard the ISS, which was compared to a numerical simulation, was conducted in the Combustion Integrated Rack (CIR) using ethylene as the fuel, nitrogen as a diluent, and a mix of nitrogen and oxygen as the oxidizer. The burner was a small porous stainless steel sphere. A fuel and diluent mixture were supplied to the burner through a support tube. Color images and video recordings of the flames were used to measure flame size. Further processing of the images using thin filament pyrometry allowed researchers to measure the temperature of the flames. Other diagnostics aboard the ISS allowed researchers to measure the flame intensity and burner temperature.

Researchers observed that spherical diffusion flames grow steadily after ignition. The burner temperature is associated with the flame size (i.e., the smaller the flame, the hotter the burner) and gas flow rate. It was also observed that the burner temperature may decrease as the flame grows away from the burner. At large flame size, the flame is unstable and oscillates between partial flame extinguishment and reformation, eventually leading to total extinction of the flame. These observations enhance the understanding of fire behavior in spacecraft and on Earth.

Irace PH, Lee HJ, Waddell K, Tan L, Stocker DP, et al. Observations of long duration microgravity spherical diffusion flames aboard the International Space Station. Combustion and Flame. 2021 July 1; 229: 111373. DOI: [10.1016/j.combustflame.2021.02.019](https://doi.org/10.1016/j.combustflame.2021.02.019).

The JAXA investigation **Interfacial behaviors and Heat transfer characteristics in Boiling Two-Phase Flow (Two-Phase Flow)** examines heat transfer in flow boiling on the ISS. Thermal systems in space require an understanding of liquid-vapor two-phase flow, boiling, and condensation. Advanced boiling and two-phase flow thermal management systems can be used as cooling technologies for high performance computers, servers in data centers, automotive electronics, avionics, and satellite systems.

A new study examined the effect of microgravity on flow boiling and two-phase behaviors and compared them to results of experiments on Earth under the strictly same flow and heating conditions. Prior to analysis on gravity effects, heat loss analysis was performed for the sections of test loop concerned. To account for avionics air flowing inside the facility, researchers calculated heat loss in detail and developed a model from experiments with subcooled liquid single-phase flow at the entry of a metal heated test tube.

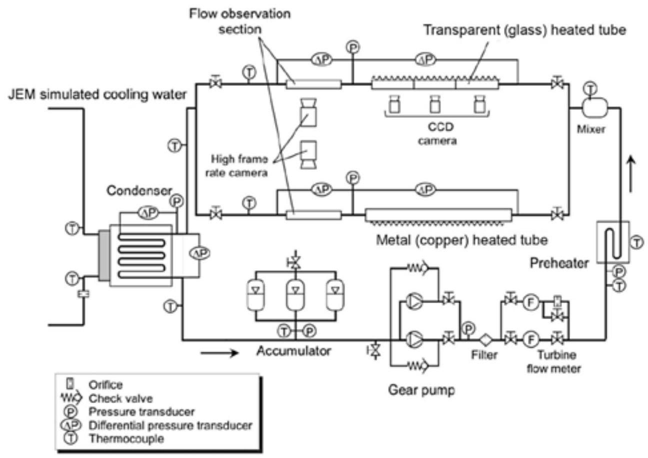


Figure 17. Diagram of test loop of Two-Phase Flow. Image adapted from Inoue, Microgravity Science and Technology.

Researchers used microgravity as a stable environment to improve upon past experimental shortcomings. The equipment inside the Two-Phase Flow facility consisted of a condenser, a gear pump, a preheater, heating test sections (metal and glass heated tubes), and accumulators. Because avionics air constantly flows through the equipment to ensure safe temperature levels and because heat loss cannot be replicated on the ground, the experiments on ISS were directly used to estimate heat loss of a fluid in the equipment. More exactly, researchers calculated heat loss of a fluid with a moderate boiling point that facilitated cooling and heating as it ran through different sections of insulated thermal material in the equipment. The test fluid as a subcooled single-phase liquid was heated in the preheater and then flowed to the metal heated test tube.

Results showed that thermal resistance evaluations improved heat loss calculations. Corrections also improved the evaluation of heat transfer coefficient and allowed accurate analysis of gravity effects on it. Finally, researchers confirmed that estimated single-phase local heat transfer coefficients obtained through the proposed heat loss model were similar to calculated heat transfer correlations. These results make it possible to remove the effect of heat loss from the measured data in ISS and elucidate flow boiling heat transfer characteristics under microgravity conditions.

Inoue K, Ohta H, Toyoshima Y, Asano H, Kawanami O, et al. Heat loss analysis of flow boiling experiments onboard International Space Station with unclear thermal environmental conditions (1st Report: Subcooled liquid flow conditions at test section inlet). Microgravity Science and Technology. 2021 March 27; 33(2): 28. DOI: 10.1007/s12217-021-09869-5.

NASA crew member Serena Auñón-Chancellor working in the Microgravity Investigation of Cement Solidification (MICS) inside a portable govebag. Results may impact construction processes and designs for space habitats on the surface of the Moon and Mars.

PUBLICATION HIGHLIGHTS:

TECHNOLOGY DEVELOPMENT AND DEMONSTRATION

Future exploration — the return to the moon and human exploration of Mars — presents many technological challenges. Studies on the ISS can test a variety of technologies, systems, and materials that are needed for future exploration missions. Some technology development investigations have been so successful that the test hardware has been transitioned to operational status. Other results feed new technology development.

DISCOVERY

The ESA investigation **Microbial Aerosol Tethering on Innovative Surfaces in the International Space Station (MATISS)** studied how bacteria settle and grow on the surfaces of different high-tech materials made from polymers and water-repellent hybrid silica. The materials are meant to prevent the adhesion of bacteria resulting in more hygienic surfaces. The optimization of antibacterial coatings is expected to enhance the design of spacecraft equipment for long-duration missions to the Moon and Mars.

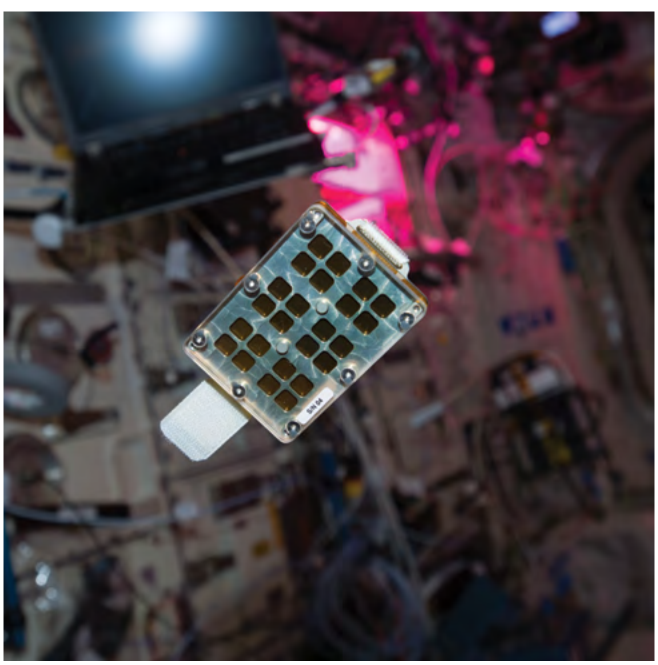


Figure 18. MATISS sample holder. NASA image iss050e010908.

Microbial pathogens that contaminate water, food, air, and equipment surfaces aboard the ISS are routinely disinfected by crew members. To reduce microbial growth, researchers typically design payloads using materials that mitigate pollution. In this new study, three types of surface hydrophobic coatings (i.e., FDTS, SiOCH, and Parylene) and an untreated surface mounted on glass were exposed to microgravity for 6 months to investigate bio-contamination diversity. Upon return of the samples, optical microscopy on the sealed MATISS holder and image analysis at low and high magnification showed large and fine particles on different surfaces.

The analysis revealed that, on average, large particles accumulated twice as much on the FDTS surface than on the SiOCH or Parylene surfaces, whereas fine particles tended to accumulate on the Parylene surface only. Researchers presume that higher hydrophobicity of the FDTS and SiOCH surfaces prevented small particle contamination carried by water droplets. In addition to examining particle concentrations, this study served to demonstrate the usability of the MATISS sample holder. Results presented in this study are expected to assist in the design of new microbial monitoring devices.

Lemelle L, Campagnolo L, Mottin E, Le Tourneau D, Garre E, Marcoux P, Thevenot C, Maillet A, Barde S, Teisseire J, Nonglaton G, Place C. Towards a passive limitation of particle surface contamination in the Columbus module (ISS) during the MATISS experiment of the Proxima Mission. npj Microgravity. 2020 October 20; 6(1): 1-7. DOI: 10.1038/s41526-020-00120-w.

The JAXA investigation **ExHAM-Radiation Shielding** studied the effect of cosmic radiation on the mechanical and chemical properties of high-tech polymer materials with the goal of examing their potential for future space exploration applications.

Exposure of ISS equipment to space radiation in low-Earth orbit can be detrimental to equipment's component materials. In this new study, researchers examined the effect of open space radiation (i.e., ionizing beta particles) on a newly developed material, a mix of the polymer methyl methacrylate and the mineral colemanite, a calcium borate. The level of energy absorbed by the new material was measured to determine whether the irradiated samples improved shielding against beta rays. Researchers expected that an acrylic glass containing calcium and boron would reduce the transmission of beta rays.

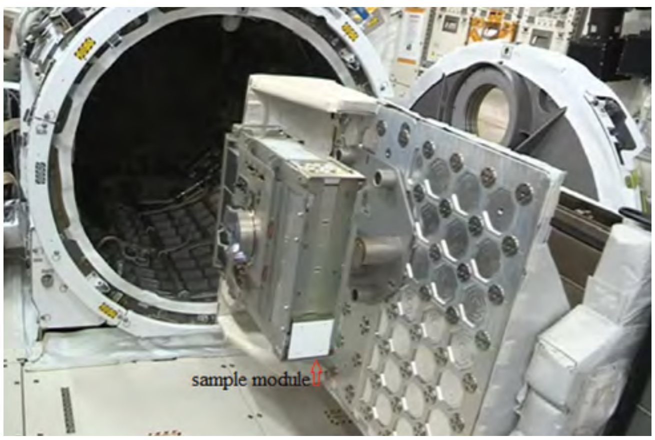


Figure 19. ExHAM sample module irradiated with trapped high-energy electrons. Image adapted from Bel, Journal of Applied Polymer Science.

Using an Atom Transfer Radical Polymerization (ATRP) technique, researchers were able to improve the molecular weight and structure of the mixed sample by manipulating the polydispersity index through the controlled addition of particles. The newly developed material was installed on the Experiment Handrail Attachment Mechanism (ExHAM) facility outside the Japanese module Kibo and exposed to space radiation for 363 days. The attenuation of beta rays was evaluated by using an experimental setup that measured beta transmission (i.e., Strontium-90 radionuclei as beta source and different sample thicknesses as destination). Comparisons of control non-mixed polymers and mixed polymer/colemanite showed that beta rays were less likely to pass through treated samples. Thicker mixed samples were particularly resistant to the beta rays. Further postflight gamma spectroscopy analysis of the composite samples showed no significant differences between beta irradiated and unirradiated samples, suggesting that the treated mixed samples improved shielding against beta rays. Therefore, researchers discovered that by modifying the polymer with the addition of colemanite, spaceflight equipment absorbs less radiation and can be better protected. Potential applications of this compound include the protection of satellite technology, low-earth orbit stations, and high-altitude planes.

Bel T, Mehranpour S, Sengul AV, Camtakan Z, Baydogan N. Electron beam penetration of poly (methyl methacrylate)/colemanite composite irradiated at low earth orbit space radiation environment. Journal of Applied Polymer Science. 2021 July 6; epub: 51337. DOI: 10.1002/app.51337.

The NASA investigation **Microgravity Investigation of Cement Solidification (MICS)** examined the cement solidification process in space.

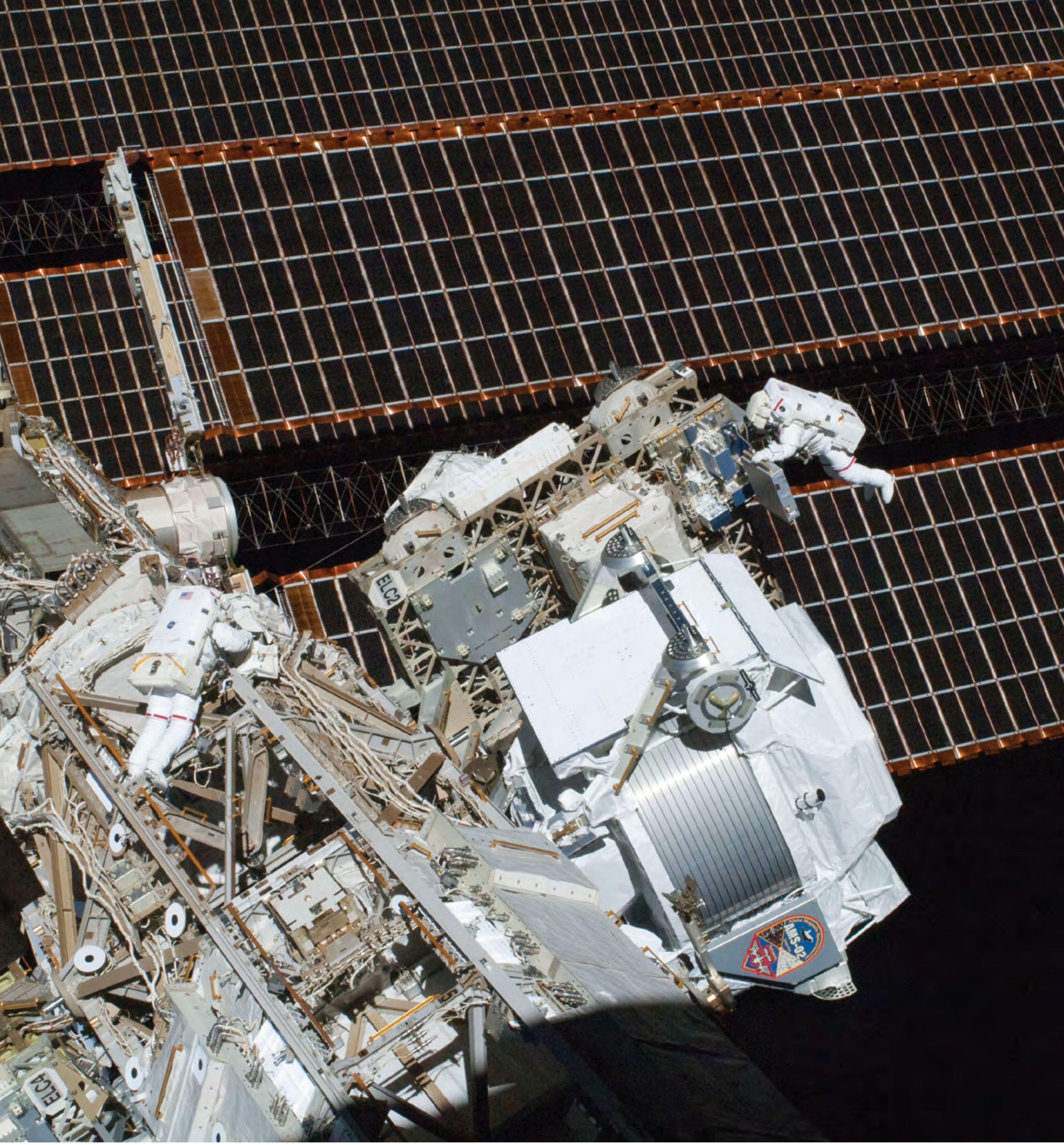
Due to the growing interest in building new habitats on the Moon and Mars, microgravity must now be examined as a potential confounding variable to the hydration process of cement. Crystal growth experiments in space have shown that reduced convection and fluid flow in microgravity leads to diffusion-controlled hydration processes. This study investigated the effect of microgravity on the hydration of cement (i.e., a mix of tricalcium aluminate (C3A) with gypsum) and its microstructural development.

Researchers ran two series of experiments. The samples, which were carefully packed in multi-compartment pouches, contained 80% C3A / 20% gypsum for series 1 and 90% C3A / 10% gypsum for series 2. Distilled water was added to the cement mix when it was time to create a homogeneous paste, and isopropanol was used a few hours after mixing to stop the hydration process. Two samples were left to hydrate for the entire duration of the flight. Scanning Electron Microscopy was used to examine the surfaces of the hardened samples to identify morphological and microstructural differences compared to control samples on Earth.

Figure 20. On the left, a pouch containing the cement and gypsum mix along with alcohol to stop the hydration reaction when needed. On the right, a pouch containing the cement and gypsum mix left to hydrate for the duration of the flight. Image adapted from Collins, Construction and Building Materials.

The analysis showed that microgravity samples (series 1) had striated microstructures high in porosity and trapped air a few hours into hydration. Longer hydration time revealed dense clusters and grains as well as increased pore distribution. The microgravity samples with half the gypsum (series 2) promoted a faster chemical reaction that resulted in fewer gypsum crystals and a ring around the gypsum. This ring may serve as a barrier to internal sulfate diffusion. The Earth samples showed more developed microstructure with a higher degree of hydration. These results contribute to the improvement of materials on Earth and the development of new materials in space for the construction of extraterrestrial habitats.

Collins PJ, Grugel RN, Radlinska A. Hydration of tricalcium aluminate and gypsum pastes on the International Space Station. Construction and Building Materials. 2021 May 24; 285: 122919. DOI: 10.1016/j.conbuildmat.2021.122919.



NASA crew members Andrew Feustel (right) and Greg Chamitoff (left), during an installation and repair spacewalk. The newly-installed Alpha Magnetic Spectrometer-2 (AMS) is at center frame.

PUBLICATION HIGHLIGHTS:

EARTH AND SPACE SCIENCE

The position of the space station in low-Earth orbit provides a unique vantage point for collecting Earth and space science data. From an average altitude of about 400 km, details in such features as glaciers, agricultural fields, cities, and coral reefs in images taken from the ISS can be combined with data from orbiting satellites and other sources to compile the most comprehensive information available. Even with the many satellites now orbiting in space, the ISS continues to provide unique views of our planet and the universe.

DISCOVERY

The JAXA investigation **CALorimetric Electron Telescope (CALET)** is a charge detector able to distinguish between different chemical elements with high resolution. It includes an imaging and a total absorption calorimeter, and two hodoscopes for observing the paths of high-energy cosmic ray nuclei. It was launched to the ISS in 2015 and is installed on the Japanese Experiment Module Exposure Facility. Analysis of CALET data will provide new insight into the source of cosmic rays, the nature of astrophysical energetic particle acceleration mechanisms, and characteristics of the interstellar space in our galaxy.

A new study measuring the energy spectra of carbon and oxygen in cosmic rays from the greater tera electron-volts (TeV) energy range reveal, for the first time, a unique local source of astrophysical energetic particles. The results, which include a detailed assessment of systematic uncertainties (i.e., error bars plotted in Figure 20), indicate that carbon and oxygen fluxes harden in a similar way above a few hundred Giga electron-volts (GeV). The carbon to oxygen flux ratio is well fitted to a constant value of 0.911 above 25 GeV=n, indicating that the two fluxes have the same energy dependence. These results are consistent with those reported by AMS-02.

Increased data collection of cosmic nuclei is expected to improve statistical and spectral analyses, thereby enhancing researchers' understanding of the origin of carbon and oxygen flux hardening.

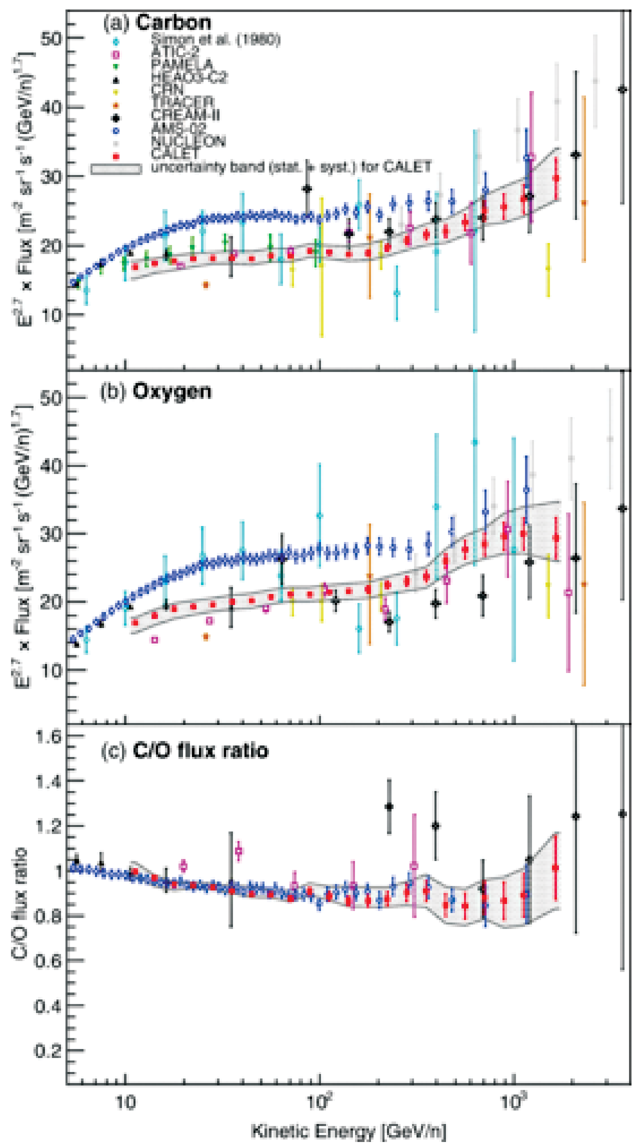


Figure 21. Plot of direct measurements of carbon flux, oxygen flux, and ratio of carbon/oxygen flux in relation to kinetic energy. Image adapted from Adriani, Physical Review Letters.

Adriani O, Akaike Y, Asano K, Asaoka Y, Bagliesi MG, Berti E, Bigongiari G, Binns WR. Direct measurement of the cosmic-ray carbon and oxygen spectra from 10 GeV/n to 2.2 TeV/n with the Calorimetric Electron Telescope on the International Space Station. Physical Review Letters. 2020 December 18; 125(25): 251102. DOI: 10.1103/PhysRevLett.125.251102.

DISCOVERY

ESA's investigation **Atmosphere-Space Interactions Monitor (ASIM)** aboard the ISS, with two state-of-the-art cameras and three photometers to measure light intensity with incredible spatial and temporal resolution, was designed to study thunderstorms and their impact on Earth's climate and atmosphere.

A new study examined the physical properties of blue jets, the electric discharges generated by disturbances of positively and negatively charged regions in the upper levels of the clouds. Blue jets arise from the tops of thunderclouds and propagate upwards into the stratosphere, reaching the stratopause at ~50 km altitude.

ASIM detected five intense blue flashes of 10-20 microsecond duration in the top of a thunderstorm cloud over the South Pacific. One of the flashes appeared to generate a blue jet. Four of the flashes occurred within 10 seconds of lighting activity, and the last flash appeared 48 seconds after. Some of the blue flashes were accompanied by UV pulses interpreted as ELVES, the expanding rings in the lower ionosphere excited by radio waves from lightning currents.

The measurements by ASIM shows that blue jets may originate with a "blue bang" in a cloud top. Further, this study shows that both the explosive onset and the jet itself primarily are made of streamer ionization waves, with only faint signatures of leader activity, as expected for normal lightning. Researchers suggest that blue flashes are the optical equivalent of "negative narrow bipolar events" observed in radio waves. While narrow bipolar events have been observed at the onset of lightning within the clouds, the ASIM observations show that they may also mark the onset of "blue lightning" into the stratosphere.

Figure 22. View of ASIM attached externally to the ISS. NASA image iss057e055409.

Neubert T, Chanrion O, Heumesser M, Dimitriadou K, Husbjerg L, Rasmussen IL, Ostgaard N, Reglero V. Observation of the onset of a blue jet into the stratosphere. Nature. 2021 January 21; 589(7842): 371-375. DOI: 10.1038/s41586-020-03122-6.

EXPLORATION

The NASA investigation **Alpha Magnetic Spectrometer (AMS-02)** is an ultramodern particle detector designed to collect high-energy cosmic nuclei from deep space. Examination of high-energy radiation is expected to reveal new findings about the nature of our universe and assist with the improvement of radiation shielding for crew members in long-duration spaceflight.

Previous measurements of Nitrogen (N) fluctuations in the cosmos conducted with AMS-02 have revealed that nitrogen, over the entire rigidity range (i.e., an energy range set to measure the resistance of a charged particle to deflection by a magnetic field), is the sum of primary and secondary components. More recent AMS studies have revealed that there are two classes of primary cosmic rays – He-C-O and Ne-Mg-Si, particles that

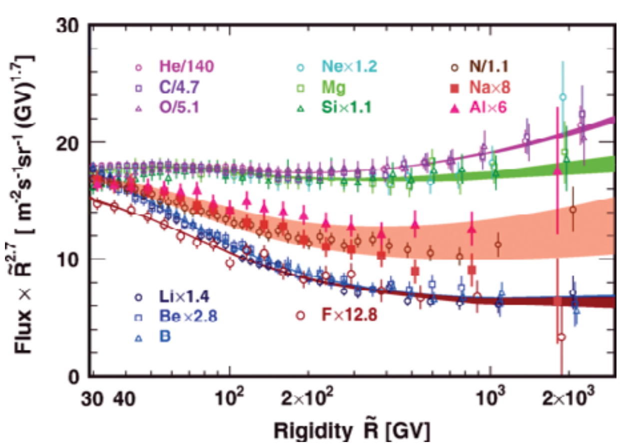


Figure 23. Graph of three cosmic ray groups. Nitrogen, sodium, and Aluminum show as a new distict group of cosmic rays in the middle orange band. Image adapted from Aguilar-Benitez, Physical Review Letters.

originate from massive star explosions – and two classes of secondary cosmic rays – Li-Be-B and F, particles that are produced in the collisions of primary cosmic rays with the interstellar medium.

This study presents new and precise measurements of Sodium (Na) and Aluminum (Al) compared with over 50% measurement error in previous studies. Advanced parameters in the AMS-02 allowed researchers to measure cosmic nuclei fluctuations as a function of rigidity in a wide energy range with millions of atoms collected over a period of 8 years. Results showed that the contributions of the primary component in the sodium and the aluminum flux increase with energy, whereas the contributions of the secondary component decrease with energy. This led researchers to discover that Na and Al nuclei, like N nuclei, belong to a distinct cosmic ray group. This new group of cosmic rays is the combination of primary and secondary cosmic rays; that is, Na, Al, and N are produced both by astrophysical sources (i.e., supernova explosions) and by the collisions of nuclei with other particles in the interstellar medium. These are new and unexpected properties of cosmic rays.

Precise measurement of the rigidity of N, Na, and Al reveals new insights into cosmic ray origin and propagation. Increased understanding of cosmic ray production and dissemination can help mitigate health risks associated with radiation in crew members.

Aguilar-Benitez M, Cavasonza LA, Alpat B, Ambrosi G, Arruda MF, Attig N, Barao F, Barrin L, Bartoloni, Basegmez-du Pree S, Battiston R, Behlmann M, Beranek B, Berdugo J, Bertucci B, Bindi V, Bollweg KJ. Properties of a new group of cosmic nuclei: Results from the Alpha Magnetic Spectrometer on sodium, aluminum, and nitrogen. Physical Review Letters. 2021 July 7; 127(2): 021101. DOI: 10.1103/PhysRevLett.127.021101.

Multilingual word cloud of key ISS terms.

ISS Research Results Publications

October 1, 2020 – October 1, 2021

(Listed by category and alphabetically by investigation.)

BIOLOGY AND BIOTECHNOLOGY

Advanced Plant Habitat (Plant Habitat) — Morrow RC, Richter RC, Tellez G, Monje OA, Wheeler RM, Massa GD, Dufour NF, Onate BG. A new plant habitat facility for the ISS. *46th International Conference on Environmental Systems*, Vienna, Austria; 2016 July 10-14. 14pp.*

Animal Enclosure Module / GeneLAB / Transcriptome Analysis and Germ-cell Development Analysis of Mice in Space/ Rodent Research-6 (AEM/GeneLAB/Mouse Habitat Unit -1 (MHU-1/Mouse Epigenetics)/RR-6) — Nelson CA, Acuna AU, Paul AM, Scott RT, Butte AJ, et al. Knowledge network embedding of transcriptomic data from spaceflown mice uncovers signs and symptoms associated with terrestrial diseases. *Life*. 2021 January; 11(1): 42. DOI: 10.3390/life11010042.

Arthrospira sp. Gene Expression and Mathematical Modelling on Cultures Grown in the International Space Station (**Arthrospira B**) — Poughon L, Creuly C, Godia F, Leys N, Dussap C. Photobioreactor Limnospira indica growth model: Application from the MELiSSA plant pilot scale to ISS flight experiment. *Frontiers in Astronomy and Space Sciences*. 2021; 8: 128. DOI: 10.3389/fspas.2021.700277.

Biological Research In Canisters - 16: Investigations of the Plant Cytoskeleton in Microgravity with Gene Profiling and Cytochemistry (BRIC-16-Cytoskeleton) — Johnson CM, Subramanian A, Pattathil S, Correll MJ, Kiss JZ. Comparative transcriptomics indicate changes in cell wall organization and stress response in seedlings during spaceflight. *American Journal of Botany*. 2018 August; 104(8): 1219-1231. DOI: 10.3732/ajb.1700079.*

Biological Research in Canisters-20 (BRIC-20) — Hutchinson S, Basu P, Wyatt SE, Luesse DR. Methods for on-orbit germination of Arabidopsis thaliana for proteomic analysis. *Gravitational and Space Research*. 2016 December 19; 4(2): 20-27. DOI: 10.2478/gsr-2016-0009.*

Biological Research in Canisters-20 (BRIC-20) — Kruse CP, Basu P, Luesse DR, Wyatt SE. Transcriptome and proteome responses in RNAlater preserved tissue of Arabidopsis thaliana. *PLOS ONE*. 2017 April 19; 12(4): e0175943. DOI: 10.1371/journal.pone.0175943.*

Biological Research in Canisters-21 and 23 (BRIC-21/BRIC-23) — Morrison MD, Nicholson WL. Comparisons of transcriptome profiles from Bacillus subtilis cells grown in space versus High Aspect Ratio Vessel (HARV) clinostats reveal a low degree of concordance. *Astrobiology*. 2020 October 19; 20(12): 12 pp. DOI: 10.1089/ast.2020.2235.

Biomass Production System / Photosynthesis Experiment and System Testing and Operation (BPS/PESTO) — Monje OA, Stutte GW, Wang HT, Kelly CJ. NDS water pressures affect growth rate by changing leaf area, not single leaf photosynthesis. *SAE Technical Paper*. 2001 July; 2001-01-2277: 7pp. DOI: 10.4271/2001-01-2277.*

Biomolecule Extraction and Sequencing Technology (BEST) — Stahl-Rommel SE, Jain M, Nguyen HN, Arnold RR, Aunon-Chancellor SM, et al. Real-time culture-independent microbial profiling onboard the International Space Station using nanopore sequencing. *Genes*. 2021 January 16; 12(1): 106. DOI: 10.3390/genes12010106.

Biorock — Cockell CS, Santomartino R, Finster KW, Waajen AC, Nicholson N, et al. Microbially-enhanced vanadium mining and bioremediation under micro- and Mars gravity on the International Space Station. *Frontiers in Microbiology*. 2021 April 1; 12: 641387. DOI: 10.3389/fmicb.2021.641387.

BioScience-4 (STaARS BioScience-4) — Shaka S, Carpo N, Tran V, Espinosa-Jeffrey A. Behavior of astrocytes derived from human neural stem cells flown onto space and their progenies. *Applied Sciences*. 2021 January; 11(1): 41. DOI: 10.3390/app11010041.

BioScience-4 (STaARS BioScience-4) — Shaka S, Carpo N, Tran V, Ma Y, Karouia F, et al. Human neural stem cells in space proliferate more than ground control cells: Implications for long-term space travel. *Journal of Stem Cells Research, Development & Therapy*. 2021 April 27; 7(2): 69. DOI: 10.24966/SRDT-2060/100069.

Characterizing the Effects of Spaceflight on the Candida albicans Adaptation Responses (Micro-14) — Nielsen-Preiss S, White KR, Preiss K, Peart D, Gianoulias K, et al. Growth and antifungal resistance of the pathogenic yeast, Candida albicans, in the microgravity environment of the International Space Station: An aggregate of multiple flight experiences. *Life*. 2021 March 27; 11(4): 24pp. DOI: 10.3390/life11040283.

Commercial Biomedical Test Module - 2 (CBTM-2) — Coulombe JC, Sarazin BA, Ortega AM, Livingston EW, Bateman TA, et al. Microgravity-induced alterations of mouse bones are compartment- and site-specific and vary with age. *Bone*. 2021 June 2; 116021. DOI: 10.1016/j.bone.2021.116021.

Commercial Biomedical Testing Module-3: Assessment of Sclerostin Antibody as a Novel Bone Forming Agent for Prevention of Spaceflight-induced Skeletal Fragility in Mice / STS-135 Space Flight's Affects on Vascular Atrophy in the Hind Limbs of Mice / GeneLAB (CBTM-3-Sclerostin Antibody/CBTM-3-Vascular Atrophy/ GeneLAB) — Berrios DC, Weitz E, Grigorev K, Costes SV, Gebre SG, et al. Visualizing omics data from apaceflight samples using the NASA GeneLab platform. *Proceedings of the 12th International Conference on Bioinformatics and Computational Biology*; 2020 March 11. 89-98. DOI: 10.29007/rh7n.

Crystallizing Biological Macromolecules and Obtaining Biocrystalline Films in Microgravity Conditions (Kristallizator) — Timofeev VI, Slutskaya E, Gorbacheva M, Boyko KM, Rakitina T, et al. Structure of recombinant prolidase from Thermococcus sibiricus in space group P21221. Acta Crystallographica Section F: *Structural Biology and Crystallization Communications*. 2015 August 1; 71(8): 951-957. DOI: 10.1107/S2053230X15009498.*

Crystallizing Biological Macromolecules and Obtaining Biocrystalline Films in Microgravity Conditions -Modul-1-KPB (Kristallizator-Modul-1-KPB /Crystallizer-Modul-1-CPB) — Akparov VK, Grishin AM, Timofeev VI, Kuranova IP. Preparation, crystallization, and preliminary X-ray diffraction study of mutant carboxypeptidase T containing the primary specificity pocket of carboxypeptidase B. *Crystallography Reports*. 2010 September; 55(5): 802-805. DOI: 10.1134/S1063774510050147.*

Crystallizing Biological Macromolecules and Obtaining Biocrystalline Films in Microgravity Conditions -PCG-CPT (Kristallizator PCG-CPT / Crystallizer PCG-CPT) — Akparov VK, Timofeev VI, Kuranova IP, Khaliullin IG. Study of the interaction of sorption and catalytic centers in carboxypeptidase T by X-ray analysis. *Crystals*. 2021 September; 11(9): 1088. DOI: 10.3390/cryst11091088.

Crystallizing Biological Macromolecules and Obtaining Biocrystalline Films in Microgravity Conditions -PCG-PPAT-1 (Kristallizator PCG-PPAT-1 /(Crystallizer PCG-PPAT-1) — Timofeev VI, Chupova LA, Esipov RS, Kuranova IP. Crystallization and preliminary X-ray diffraction study of phosphopantetheine adenylyltransferase from M. tuberculosis crystallizing in space group P32. *Crystallography Reports*. 2015 September; 60(5): 682-684. DOI: 10.1134/S106377451505017X. *

Determining Muscle Strength in Space-flown Caenorhabditis elegans (Micro-16) — Bilbao A, Patel A, Rahman M, Vanapalli SA, Blawzdziewicz J. Roll maneuvers are essential for active reorientation of Caenorhabditis elegans in 3D media. *Proceedings of the National Academy of Sciences of the United States of America*. 2018 April 17; 115(16): E3616-E3625. DOI: 10.1073/pnas.1706754115.*

Determining Muscle Strength in Space-flown Caenorhabditis elegans (Micro-16) — Hewitt JE, Pollard AK, Lesanpezeshki L, Deane CS, Gaffney CJ, et al. Muscle strength deficiency and mitochondrial dysfunction in a muscular dystrophy model of Caenorhabditis elegans and its functional response to drugs. *Disease Models & Mechanisms*. 2018 December 1; 11(12): dmm036137. DOI: 10.1242/dmm.036137.*

Determining Muscle Strength in Space-flown Caenorhabditis elegans (Micro-16) — Laranjeiro R, Harinath G, Hewitt JE, Hartman JH, Royal MA, et al. Swim exercise in Caenorhabditis elegans extends neuromuscular and gut healthspan, enhances learning ability, and protects against neurodegeneration. *Proceedings of the National Academy of Sciences of the United States of America*. 2019 November 19; 116(47): 23829-23839. DOI: 10.1073/pnas.1909210116.*

Determining Muscle Strength in Space-flown Caenorhabditis elegans (Micro-16) — Lesanpezeshki L, Hewitt JE, Laranjeiro R, Antebi A, Driscoll M, et al. Pluronic gel-based burrowing assay for rapid assessment of neuromuscular health in C. elegans. *Scientific Reports*. 2019 October 23; 9(1): 15246. DOI: 10.1038/s41598-019-51608-9.*

Determining Muscle Strength in Space-flown Caenorhabditis elegans (Micro-16) — Rahman M, Hewitt JE, Van-Bussel F, Edwards H, Blawzdziewicz J, et al. NemaFlex: a microfluidics-based technology for standardized measurement of muscular strength of C. elegans. *Lab on a Chip*. 2018 July 24; 18(15): 2187-2201. DOI: 10.1039/C8LC00103K.*

Effect of Microgravity on Osteoclasts and the Analysis of the Gravity Sensing System in Medaka (Medaka Osteoclast/Medaka Osteoclast 2) — Chatani M, Kudo A. Fish in space shedding light on gravitational biology. Zebrafish, Medaka, and Other Small Fishes: *New Model Animals in Biology, Medicine, and Beyond*; 2018. DOI: 10.1007/978-981-13-1879-5_5. *

Effect of Space Environment on Mammalian Reproduction (Space Pup) — Wakayama S, Ito D, Kamada Y, Shimazu T, Suzuki T, et al. Evaluating the long-term effect of space radiation on the reproductive normality of mammalian sperm preserved on the International Space Station. *Science Advances*. 2021 June; 7(24): eabg5554. DOI: 10.1126/sciadv.abg5554.

Effect of Space Flight on Innate Immunity to Respiratory Viral Infections (Mouse Immunology-2) — Dagdeviren D, Kalajzic Z, Adams DJ, Kalajzic I, Lurie A, et al. Responses to spaceflight of mouse mandibular bone and teeth. *Archives of Oral Biology*. 2018 September 1; 93: 163-176. DOI: 10.1016/j.archoralbio.2018.06.008.*

Effect of Space Flight on Innate Immunity to Respiratory Viral Infections (Mouse Immunology-2) — Hand AR, Dagdeviren D, Larson NA, Haxhi C, Mednieks MI. Effects of spaceflight on the mouse submandibular gland. *Archives of Oral Biology*. 2019 November 18; 110: 104621. DOI: 10.1016/j.archoralbio.2019.104621.*

Effect of Space Flight on Innate Immunity to Respiratory Viral Infections (Mouse Immunology-2) — Mednieks MI, Hand AR. Oral tissue responses to travel in space. *Beyond LEO - Human Health Issues for Deep Space Exploration*; 2019. DOI: 10.5772/intechopen.86728.*

Effect of Space Flight on Innate Immunity to Respiratory Viral Infections (Mouse Immunology-2) — Shen H, Lim C, Schwartz AG, Andreev-Andrievskiy A, Deymier AC, et al. Effects of spaceflight on the muscles of the murine shoulder. *FASEB: Federation of American Societies for Experimental Biology Journal*. 2017 December; 31(12): 5466-5477. DOI: 10.1096/fj.201700320R.*

Effects of Spaceflight on Endothelial Function: Molecular and Cellular Characterization of Interactions Between Genome Transcription, DNA Damage and Induction of Cell Senescence (Endothelial Cells) — Cazzaniga A, Locatelli L, Castiglioni S, Maier JA. The dynamic adaptation of primary human endothelial cells to simulated microgravity. *FASEB: Federation of American Societies for Experimental Biology Journal*. 2019 May; 33(5): 5957-5966. DOI: 10.1096/fj.201801586RR.*

Effects of Spaceflight on Endothelial Function: Molecular and Cellular Characterization of Interactions Between Genome Transcription, DNA Damage and Induction of Cell Senescence (Endothelial Cells) — Cazzaniga A, Moscheni C, Maier JA, Castiglioni S. Culture of human cells in experimental units for spaceflight impacts on their behavior. *Experimental Biology and Medicine*. 2017 May; 242(10): 1072-1078. DOI: 10.1177/1535370216684039.*

Environmental Response and Utilization of Mosses in Space - Space Moss (Space Moss) — Kume A, Kamachi H, Onoda Y, Hanba YT, Hiwatashi Y, et al. How plants grow under gravity conditions besides 1 g: perspectives from hypergravity and space experiments that employ bryophytes as a model organism. *Plant Molecular Biology*. 2021 April 14; epub: 13pp. DOI: 10.1007/s11103-021-01146-8.

Epigenetics in Spaceflown C. elegans (Epigenetics) — Higashitani A, Hashizume T, Takiura M, Higashitani N, Teranishi M, et al. Histone deacetylase HDA-4-mediated epigenetic regulation in space-flown *C. elegans. npj Microgravity*. 2021 September 1; 7(1): 33. DOI: 10.1038/s41526-021-00163-7.

EuTEF-Expose-Life — Onofri S, Selbmann L, Pacelli C, de Vera JP, Horneck G, Hallsworth J, Zucconi L. Integrity of the DNA and cellular ultrastructure of cryptoendolithic fungi in space or Mars conditions: A 1.5-year study at the International Space Station. *Life*. 2018 June 19; 8(2): 23. DOI: 10.3390/life8020023.*

Exercise Countermeasures for Knee and Hip Joint Degeneration During Spaceflight (Willey Gait) — Kwok AT, Mohamed NS, Plate JF, Yammani RR, Rosas S, et al. Spaceflight and hind limb unloading induces an arthritic phenotype in knee articular cartilage and menisci of rodents. *Scientific Reports*. 2021 May 18; 11(1): 10469. DOI: 10.1038/s41598-021-90010-2.

Functional Effects of Spaceflight on Cardiovascular Stem Cells (Cardiac Stem Cells) — Camberos V, Baio J, Mandujano A, Martinez AF, Bailey L, et al. The impact of spaceflight and microgravity on the human Islet-1+ cardiovascular progenitor cell transcriptome. *International Journal of Molecular Sciences*. 2021 March 30; 22(7): 18pp. DOI: 10.3390/ijms22073577.

Functional Effects of Spaceflight on Cardiovascular Stem Cells (Cardiac Stem Cells) — Fuentes TI, Appleby N, Raya M, Bailey L, Hasaniya N, et al. Simulated microgravity exerts an age-dependent effect on the differentiation of cardiovascular progenitors isolated from the human heart. *PLOS ONE*. 2015 July 10; 10(7): e0132378. DOI: 10.1371/journal.pone.0132378.*

GeneLAB / Rodent Research Hardware and Operations Validation (GeneLAB/Rodent Research-1) — Cahill T, Cope H, Bass JJ, Overbey EG, Gilbert R, et al. Mammalian and invertebrate models as complementary tools for gaining mechanistic insight on muscle responses to spaceflight. *International Journal of Molecular Sciences*. 2021 August 31; 22(17): 9470. DOI: 10.3390/ijms22179470.

GeneLAB / Rodent Research Hardware and Operations Validation / Assessment of Myostatin Inhibition to Prevent Skeletal Muscle Atrophy and Weakness in Mice Exposed to Long-duration Spaceflight / Exercise Countermeasures for Knee and Hip Joint Degeneration During Spaceflight (GeneLAB/Rodent Research-1/Rodent Research-3-Eli Lilly/Willey Gait) — da Silveira WA, Fazelinia H, Rosenthal SB, Laiakis EC, Kim MS, et al. Comprehensive multi-omics analysis reveals mitochondrial stress as a central biological hub for spaceflight impact. *Cell.* 2020 November 25; 183(5): 1185-1201.e20. DOI: 10.1016/j.cell.2020.11.002.

Generation of Cardiomyocytes from Human Induced Pluripotent Stem Cell-derived Cardiac Progenitors Expanded in Microgravity (MVP Cell-03) — Rampoldi A, Jha R, Fite J, Boland ED, Xu C. Cryopreservation and CO2-independent culture of 3D cardiac progenitors for spaceflight experiments. *Biomaterials*. 2021 February; 269: 120673. DOI: 10.1016/j.biomaterials.2021.120673.

Identifying the Genetic Features Determining Individual differences in the Resilience of Biological Objects to Long-term Spaceflight Factors Studies with the Fruit Fly Drosophila melanogaster - Poligen (Polygene) — Ogneva IV, Belyakin SN, Sarantseva SV. The development of Drosophila melanogaster under different duration space flight and subsequent adaptation to Earth gravity. *PLOS ONE*. 2016 November 18; 11(11): e0166885. DOI: 10.1371/journal.pone.0166885.*

International Space Station Internal Environments (ISS Internal Environments) — Blachowicz A, Venkateswaran KJ, Wang CC. Chapter 3 - Persistence of fungi in atypical, closed environments: Cultivation to omics. *Methods in Microbiology*; 2018. DOI: 10.1016/bs.mim.2018.07.006.*

International Space Station Internal Environments (ISS Internal Environments) — Bryan NC, Lebreton F, Gilmore M, Ruvkun G, Zuber MT, et al Genomic and functional characterization of Enterococcus faecalis isolates recovered from the International Space Station and their potential for pathogenicity. *Frontiers in Microbiology*. 2021 January 11; 11: 515319. DOI: 10.3389/fmicb.2020.515319.

International Space Station Internal Environments (ISS Internal Environments) — Khodadad CL, Oubre CM, Castro VA, Flint SM, Roman MC, et al. A microbial monitoring system demonstrated on the International Space Station provides a successful platform for detection of targeted microorganisms. *Life*. 2021 June; 11(6): 492. DOI: 10.3390/life11060492.

International Space Station Internal Environments (ISS Internal Environments) — Pourbavarsad MS, Jalalieh BJ, Harkins C, Sevanthi R, Jackson WA. Nitrogen oxidation and carbon removal from high strength nitrogen habitation wastewater with nitrification in membrane aerated biological reactors. *Journal of Environmental Chemical Engineering*. 2021 October 1; 9(5): 106271. DOI: 10.1016/j.jece.2021.106271.

International Space Station Internal Environments (ISS Internal Environments) — Rybalchenko OV, Orlova OG, Vishnevskaya ON, Kapustina VV, Potokin IL, et al. [Features of formation of bacterial biofilms in conditions of spaceflight]. *Zhurnal Mikrobiologii Epidemiologii I Immunobiologii*. 2016 November; (6): 3-10.*

International Space Station Internal Environments (ISS Internal Environments) — Van Houdt R, Provoost A, Van Assche A, Leys N, Lievens B, et al. Cupriavidus metallidurans strains with different mobilomes and from distinct environments have comparable phenomes. *Genes*. 2018 October 18; 9(10): 507. DOI: 10.3390/genes9100507.*

International Space Station Internal Environments (ISS Internal Environments) — Yang J, Barrila J, Ott CM, King O, Bruce RJ, et al. Longitudinal characterization of multispecies microbial populations recovered from spaceflight potable water. *npj Biofilms and Microbiomes*. 2021 September 6; 7(1): 70. DOI: 10.1038/s41522-021-00240-5.

International Space Station Internal Environments (ISS Internal Environments) – Yang J, Thornhill S, Barrila J, Nickerson CA, Ott CM, et al. Chapter 1 - Microbiology of the built environment in spacecraft used for human flight. *Methods in Microbiology*; 2018. DOI: 10.1016/bs.mim.2018.07.002.*

International Space Station-Microbial Observatory of Pathogenic Viruses, Bacteria, and Fungi (ISS-MOP) Project (Microbial Tracking-2) — Morrison MD, Thissen J, Karouia F, Mehta SK, Urbaniak C, et al. Investigation of spaceflight induced changes to astronaut microbiomes. *Frontiers in Microbiology.* 2021; 12: 659179. DOI: 10.3389/fmicb.2021.659179.

International Space Station-Microbial Observatory of Pathogenic Viruses, Bacteria, and Fungi (ISS-MOP) Project (Microbial Tracking-2) — Simpson AC, Urbaniak C, Singh NK, Wood JM, Debieu M, et al. Draft genome sequences of various bacterial phyla isolated from the International Space Station. *Microbiology Resource Announcements*. 2021 April 29; 10(17): e00214-21. DOI: 10.1128/MRA.00214-21.

Japan Aerospace Exploration Agency Protein Crystallization Growth (JAXA PCG) — Kinoshita T, Hashimoto T, Murakawa Y, Sogabe Y, Matsumoto T, et al. A microgravity environment improves structural resolution and endows cues for specific inhibition of mitogen-activated protein kinase kinase 7. *International Journal of Microgravity Science and Application*. 2019; 36(1): 360102. DOI: 10.15011//jasma.36.360102.*

Japan Aerospace Exploration Agency Protein Crystallization Growth (JAXA PCG) — Komatsu T, Kihira K, Yamada K, Yokomaku K, Akiyama M, et al. Physicochemical properties and crystal structures of recombinant canine and feline serum albumins. *International Journal of Microgravity Science and Application*. 2019; 36(1): 360104. DOI: 10.15011//jasma.36.360104.*

Japan Aerospace Exploration Agency Protein Crystallization Growth (JAXA PCG) — Nakae S, Shionyu M, Ogawa T, Shirai T. Crystallization of pearl biomineralization protein in microgravity environments. *International Journal of Microgravity Science and Application*. 2019 January 31; 36(1): 360105. DOI: 10.15011//jasma.36.360105.*

Japan Aerospace Exploration Agency Protein Crystallization Growth (JAXA PCG) — Nakamura T, Hirata K, Fujimiya K, Chirifu M, Arimori T, et al. X-ray structure analysis of human oxidized nucleotide hydrolase MTH1 using crystals obtained under microgravity. *International Journal of Microgravity Science and Application*. 2019; 36(1): 360103. DOI: 10.15011//jasma.36.360103.*

Japan Aerospace Exploration Agency Protein Crystallization Growth (JAXA PCG) — Takahashi S, Koga M, Yan B, Furubayashi N, Kamo M, et al. JCB-SGT crystallization devices applicable to PCG experiments and their crystallization conditions. *International Journal of Microgravity Science and Application*. 2019 January 31; 36(1): 360107. DOI: 10.15011//jasma.36.360107.*

Japan Aerospace Exploration Agency Protein Crystallization Growth (JAXA PCG) — Yamada M, Kihira K, Iwata M, Takahashi S, Inaka K, et al. Protein crystallization in space and its contribution to drug development. *Handbook of Space Pharmaceuticals*; 2021. DOI: 10.1007/978-3-319-50909-9_40-1.

Japan Aerospace Exploration Agency Protein Crystallization Growth (JAXA PCG) — Yoshizaki I, Yamada M, Iwata M, Kato M, Kihira K, et al. Recent advance in High Quality Protein Crystal Growth experiment on the International Space Station by JAXA. *International Journal of Microgravity Science and Application*. 2019 January 31; 36(1): 360101. DOI: 10.15011//jasma.36.360101.*

Life Cycles of Higher Plants Under Microgravity Conditions (SpaceSeed) — Kurogane T, Tamaoki D, Yano S, Tanigaki F, Shimazu T, et al. Visualization of Arabidopsis root system architecture in 3D by refraction-contrast X-Ray micro-computed tomography. *Microscopy*. 2021 July 15; epub: dfab027. DOI: 10.1093/jmicro/dfab027.

MELiSSA ON Board Danish Utilisation Flight (MELONDAU) — De Pascale S, Arena C, Aronne G, De Micco V, Pannico A, et al. Biology and crop production in space environments: Challenges and opportunities. *Life Sciences in Space Research*. 2021 March 2; 29: 30-37. DOI: 10.1016/j.lssr.2021.02.005.

Mice Drawer System (MDS) — Boyle RD, Varelas J. Otoconia structure after short- and long-duration exposure to altered gravity. *JARO-Journal of the Association for Research in Otolaryngology*. 2021 May 18; epub: 17pp. DOI: 10.1007/s10162-021-00791-6.

Microbial Dynamics (Microbe-I/Microbe-II/Microbe-III/Microbe-IV) — Satoh K, Alshahni MM, Umeda Y, Komori A, Tamura T, et al. Seven years of progress in determining fungal diversity and characterization of fungi isolated from the Japanese Experiment Module KIBO, International Space Station. *Microbiology and Immunology*. 2021 july 12; epub: 31pp. DOI: 10.1111/1348-0421.12931.

Microbial Tracking Payload Series (Microbial Observatory-1) — Bijlani S, Singh NK, Eedara VV, Podile AR, Mason CE, et al. Methylobacterium ajmalii sp. nov., isolated from the International Space Station. *Frontiers in Microbiology*. 2021 March 15; 12: 639396. DOI: 10.3389/fmicb.2021.639396.

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Microbial Tracking Payload Series (Microbial Observatory-1) — Daudu R, Singh NK, Wood JM, Debieu M, O'Hara NB, et al. Draft genome sequences of Bacillaceae strains isolated from the International Space Station. *Microbiology Resource Announcements*. 2020 October 29; 9(44): e00701-20. DOI: 10.1128/MRA.00701-20.

Microbial Tracking Payload Series (Microbial Observatory-1) — Solomon SA, Bharadwaj AR, Singh NK, Wood JM, Debieu M, et al. Draft genome sequences of Klebsiella species isolated from the International Space Station. *Microbiology Resource Announcements*. 2020 October 15; 9(42): e00923-20. DOI: 10.1128/MRA.00923-20.

Molecular Muscle (Molecular Muscle) — Gaffney CJ, Pollard AK, Deane CS, Cooke M, Balsamo M, et al. Worms in space for outreach on Earth: Space life science activities for the classroom. *Gravitational and Space Research*. 2018; 6(2): 74-82.*

Molecular Muscle (Molecular Muscle) — Laranjeiro R, Harinath G, Pollard AK, Gaffney CJ, Deane CS, et al. Spaceflight affects neuronal morphology and alters transcellular degradation of neuronal debris in adult Caenorhabditis elegans. *iScience*. 2021 February 19; 24(2): 102105. DOI: 10.1016/j.isci.2021.102105.

Mouse Antigen-Specific CD4+ T Cell Priming and Memory Response during Spaceflight (Mouse Immunology) — Kumar A, Tahimic CG, Almeida EA, Globus RK. Spaceflight modulates the expression of key oxidative stress and cell cycle related genes in heart. *International Journal of Molecular Sciences*. 2021 August 23; 22(16): 9088. DOI: 10.3390/ijms22169088.

Muscle Atrophy of Muscle Sparing in Transgenic Mice (Rodent Research-1 (CASIS)) — Wong CP, Iwaniec UT, Turner RT. Evidence for increased thermogenesis in female C57BL/6J mice housed aboard the International Space Station. *npj Microgravity*. 2021 June 18; 7(1): 1-4. DOI: 10.1038/s41526-021-00150-y.

Mycological Evaluation of Crew Exposure to ISS Ambient Air (Myco) — Satoh K, Yamazaki TQ, Furukawa S, Mukai C, Makimura K. Identification of fungi isolated from astronaut nasal and pharyngeal smears and saliva under operations nomenclature, Myco. *Microbiology and Immunology*. 2021 January 4; epub: 20pp. DOI: 10.1111/1348-0421.12872.

NanoRacks-CellBox-Effect of Microgravity on Human Thyroid Carcinoma Cells (NanoRacks-CellBox-Thyroid Cancer) — Melnik D, Kruger M, Schulz H, Kopp S, Wehland M, et al. The CellBox-2 mission to the International Space Station: Thyroid cancer cells in space. *International Journal of Molecular Sciences*. 2021 August 16; 22(16): 8777. DOI: 10.3390/ijms22168777.

NanoRacks-CellBox-Effect of Microgravity on Human Thyroid Carcinoma Cells (NanoRacks-CellBox-Thyroid Cancer) — Wise P, Neviani P, Riwaldt S, Corydon TJ, Wehland M, et al. Changes in exosome release in thyroid cancer cells after prolonged exposure to real microgravity in space. *International Journal of Molecular Sciences*. 2021 January; 22(4): 2132. DOI: 10.3390/ijms22042132.

NanoRacks-CellBox-Primary Human Macrophages in Microgravity Environment (NanoRacks-CellBox-PRIME) — Thiel CS, Vahlensieck C, Bradley T, Tauber S, Lehmann M, et al. Metabolic dynamics in short- and long-term microgravity in human primary macrophages. *International Journal of Molecular Sciences*. 2021 June 23; 22(13): 6752. DOI: 10.3390/ijms22136752.

Nanotechnology Solutions Against Oxidative Stress in Muscle Tissue During Long-term Microgravity Exposure (NANOROS) — Genchi GG, Degl'Innocenti A, Martinelli C, Battaglini M, de Pasquale D, et al. Cerium oxide nanoparticle administration to

skeletal muscle cells under different gravity and radiation conditions. *ACS Applied Materials & Interfaces*. 2021 August 19; epub: DOI: 10.1021/acsami.1c14176.

Osteocytes and Mechano-transduction (Osteo-4) — Uda Y, Spatz JM, Hussein A, Garcia JH, Lai F, et al. Global transcriptomic analysis of a murine osteocytic cell line subjected to spaceflight. *FASEB: Federation of American Societies for Experimental Biology Journal*. 2021 May; 35(5): e21578. DOI: 10.1096/fj.202100059R.

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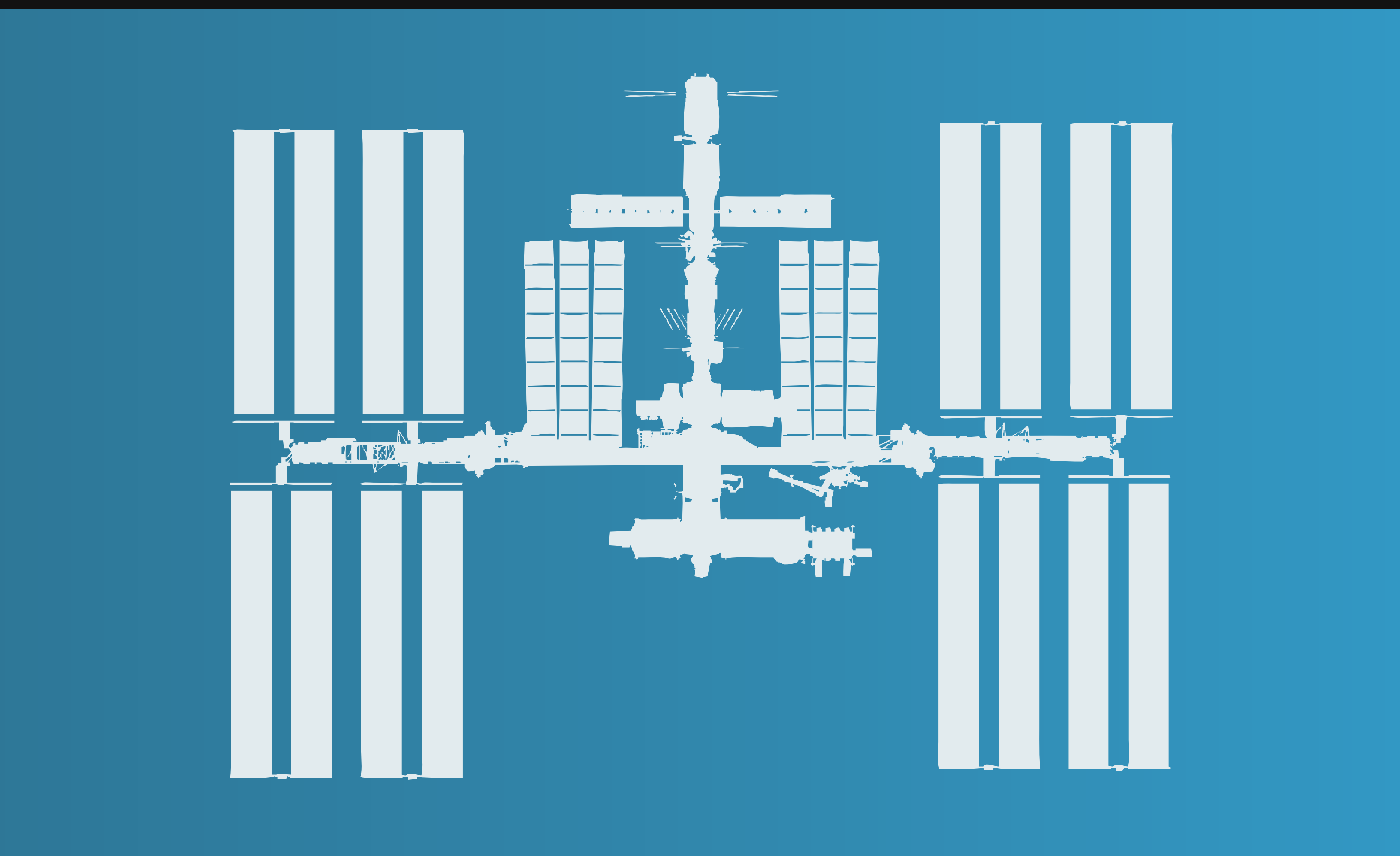

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