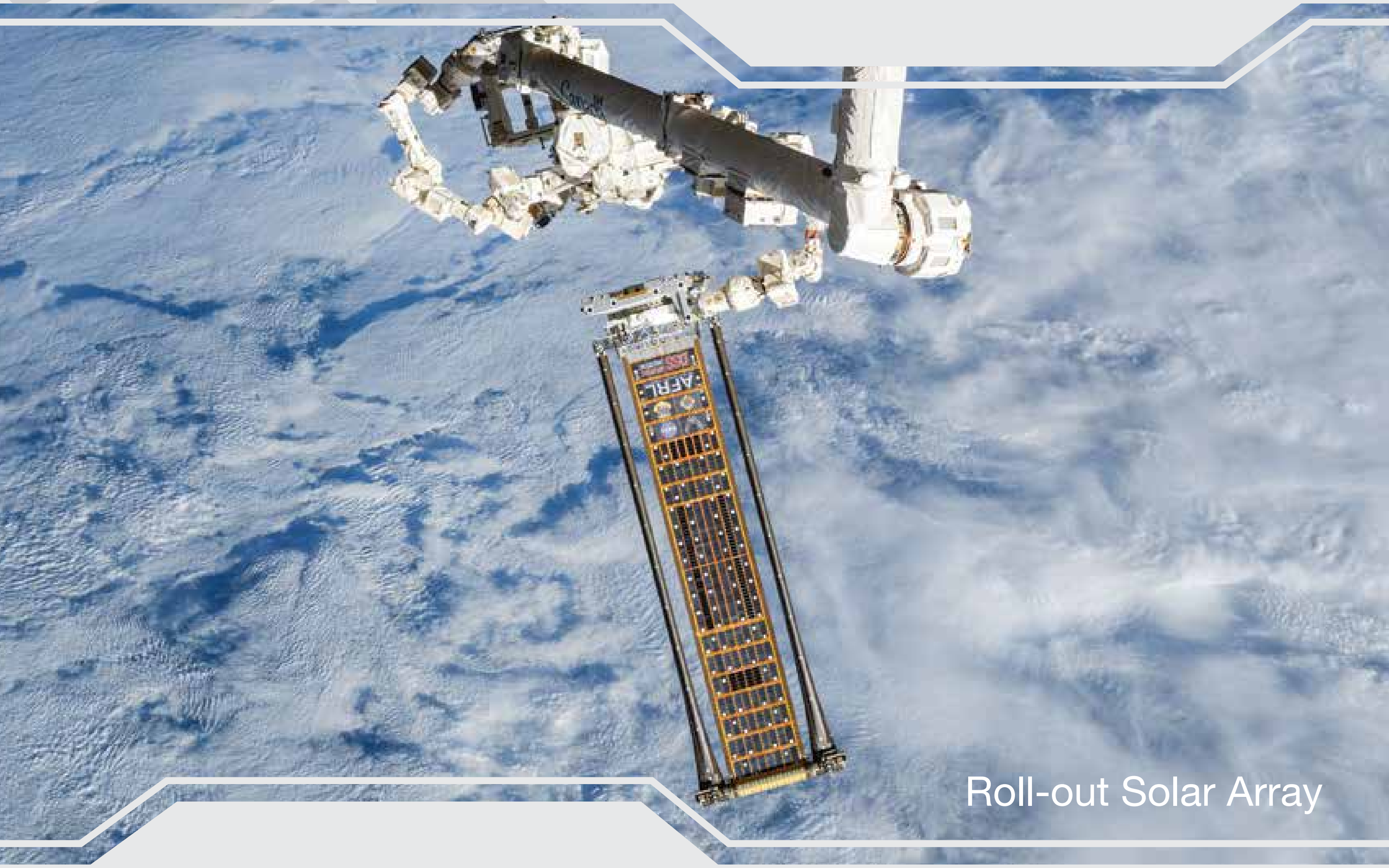
National Aeronautics and Space Administration

ANNUAL HIGHLIGHTS of RESULTS from the INTERNATIONAL SPACE STATION

October 1, 2018 – October 1, 2019



Roll-out Solar Array

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October 1, 2018 – October 1, 2019

Product of the International Space Station Program Science Forum

This report was developed collaboratively by the members of the Canadian Space Agency (CSA), European Space Agency (ESA), 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 https://www.nasa.gov/stationresults.

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Cover:

Image of the Space Station Remote Manipulator System (SSRMS) with the Roll-Out Solar Array (ROSA) attached and the Earth in the background (ISS052E086056).

NP-2019-11-010-JSC

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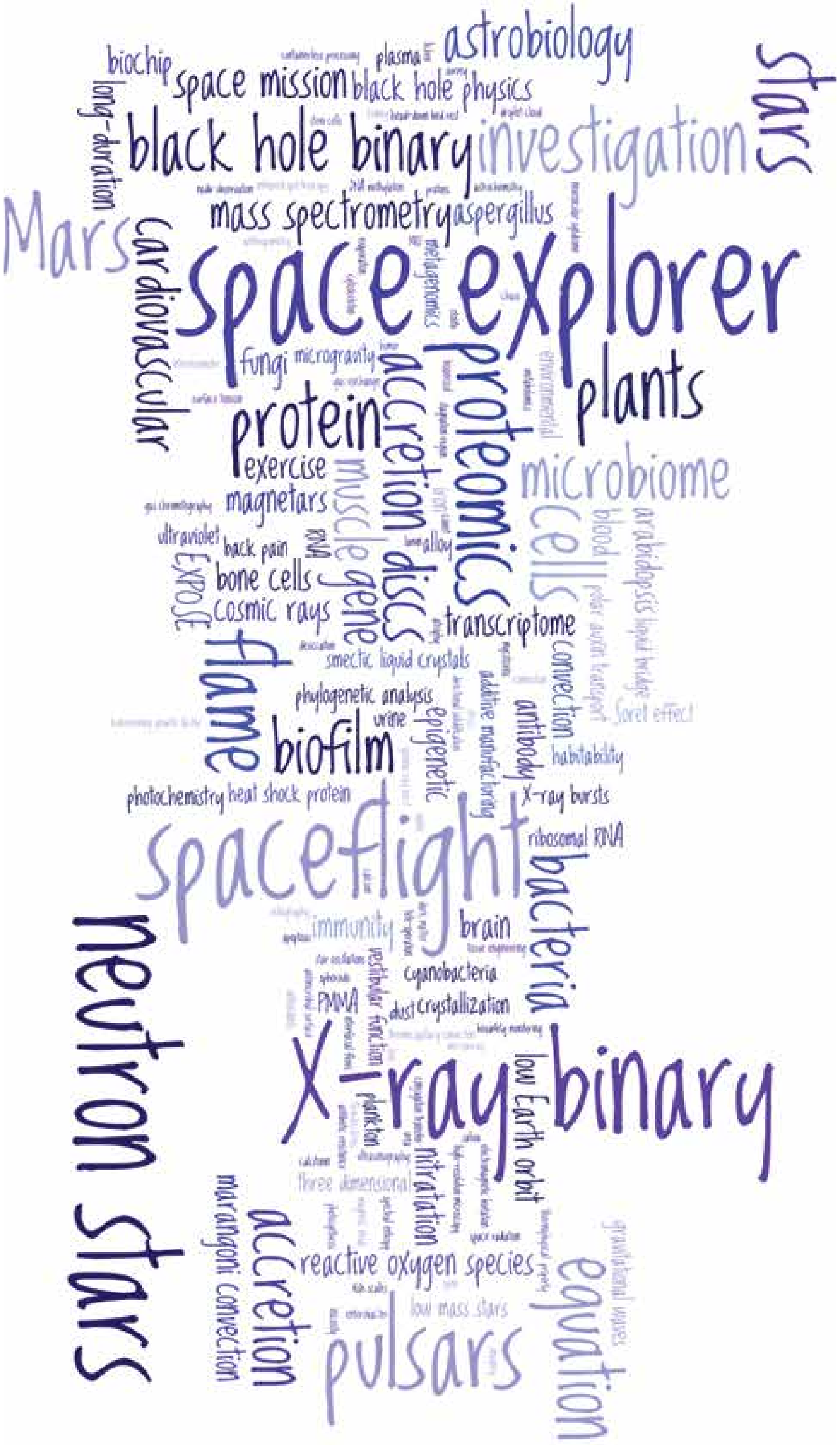

Word cloud of keywords identified in ISS results publications collected from October 1, 2018 - October 1, 2019.

Introduction

As we approach the milestone of humans living and working on the International Space Station (ISS) for 20 years, the scientific and cultural impact of the orbiting laboratory cannot be overstated. The ISS is far more than a symbol of human innovation: it has become a proving ground for scientific breakthroughs, international cooperation, cutting-edge technologies and business models that are preparing us for future missions to the moon – this time to stay – and eventually to Mars with the Artemis and Gateway programs. The knowledge gained has prepared us not only to survive in the harsh microgravity environment, but also to thrive while improving the opportunities for the success of future exploration missions beyond low-Earth orbit.

The ISS is a stepping-stone for exploration beyond low-Earth orbit. As the only location available to conduct long-duration research on how living in microgravity affects organisms, especially humans, as well as to test technologies that allow humans to work in microgravity, the space station serves as a unique asset in the effort to establish a sustainable presence beyond low-Earth orbit. The ISS facilitates research that benefits human lives on Earth and serves as the primary testing ground for technology development to sustain life in the extreme environment of space. ISS research is assigned to the following disciplines: biology and biotechnology, Earth and space science, human research, physical science, educational activities and technology development and demonstrations.

This year, ISS scientists and engineers published a wide range of ISS research results, from studying the long-term impacts of living in space on the human genome to better understanding how fire behaves in the absence of gravity. The ISS Program Science Office (PSO) collected 205 scientific publications between October 1, 2018, and October 1, 2019. Of these publications, 189 were articles published in peer-reviewed journals, 14 were conference papers and 2 were gray literature publications such as technical reports or books. Of the items collected, 34 were published prior to October 1, 2018, but not identified until after October 1, 2018.

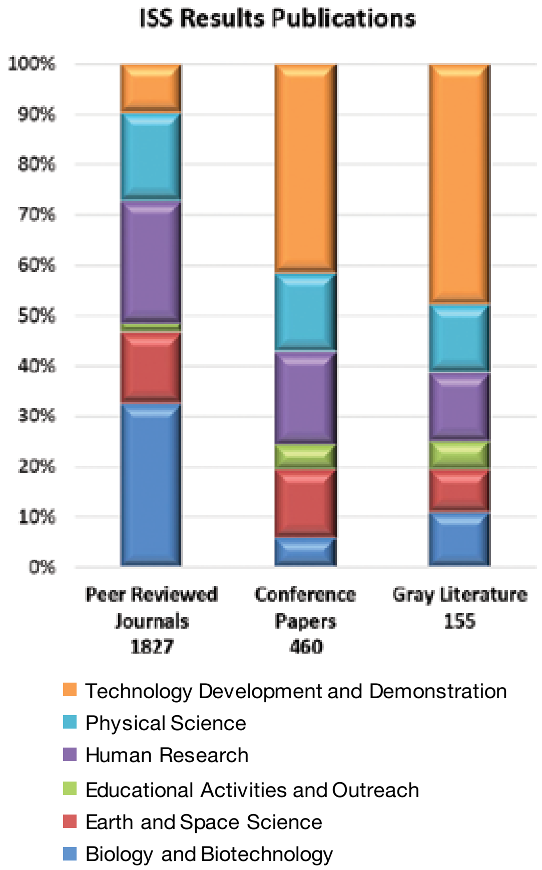

Figure 1: A total of 2442 publications (through October 1, 2019) represent scientists worldwide. This chart illustrates the percentages for each research discipline by publication type.

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

As of October 1, 2019, the ISS PSO has identified a total of 2442 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).

The ISS PSO 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. This database captures the 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 significance of the investment in its development, analyzing ISS scientific impacts is an exceptional challenge. As a result, the ISS PSO uses different methods to describe the impacts of ISS research activities.

One method used to evaluate the significance of scientific output from the ISS is to track article citations and the journal's Eigenfactor ranking across the ISS partnership. Since different disciplines have different standards for citations and different time spans across 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. Eigenfactor counts citations to journals in both the sciences and social sciences, eliminates self-citations of journals, and is intended to reflect the amount of time researchers spend reading the journal. For the period from October 1, 2018, to October 1, 2019, 52 ISS articles were published in the top 100 journals based on Eigenfactor. Twenty-five of those ISS articles were in the top 10 journals based on Eigenfactor, as reported by Clarivate Analytics® (Table 1).

Table 1: 2018-2019 ISS Publications collected in the Top 100 Global Journals, by Eigenfactor. From October 1, 2018, to October 1, 2019, as reported by 2018 Journal Citation Reports, Clarivate Analytics®.

	(Clarivate Analytics®) Ranks	**Source (# of ISS articles)**
ISS Publications In Top 100 Sources	1	PLOS ONE (3)
	2	Nature (1)
	3	Nature Communications (1)
	4	Science (1)
	5	Scientific Reports (16)
	6	Proceedings of the National Academy of Sciences of the United States of America (1)
	9	Physical Review Letters (3)
	17	The Astrophysical Journal (8)
	25	Monthly Notices of the Royal Astronomical Society (3)
	42	Astronomy and Astrophysics (1)
	45	Geophysical Research Letters (1)
	73	The Journal of Chemical Physics (1)
	88	Physical Review E (1)
	93	Frontiers in Microbiology (2)
	98	International Journal of Molecular Sciences (7)
	99	The Astrophysical Journal Letters (3)

The ISS PSO has implemented the use of bibliometrics as an additional method to measure the impact of space station research. Bibliometrics is the quantitative analysis of written documents. It is frequently used to analyze scientific and scholarly publications. Researchers may use bibliometrics to get an overview of their research field and of the connections with neighboring research areas. Bibliometrics can be used to address a broad range of challenges in research management and research evaluation. For instance, bibliometrics can be applied to support strategic decision making by the management of a research institution and

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[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.

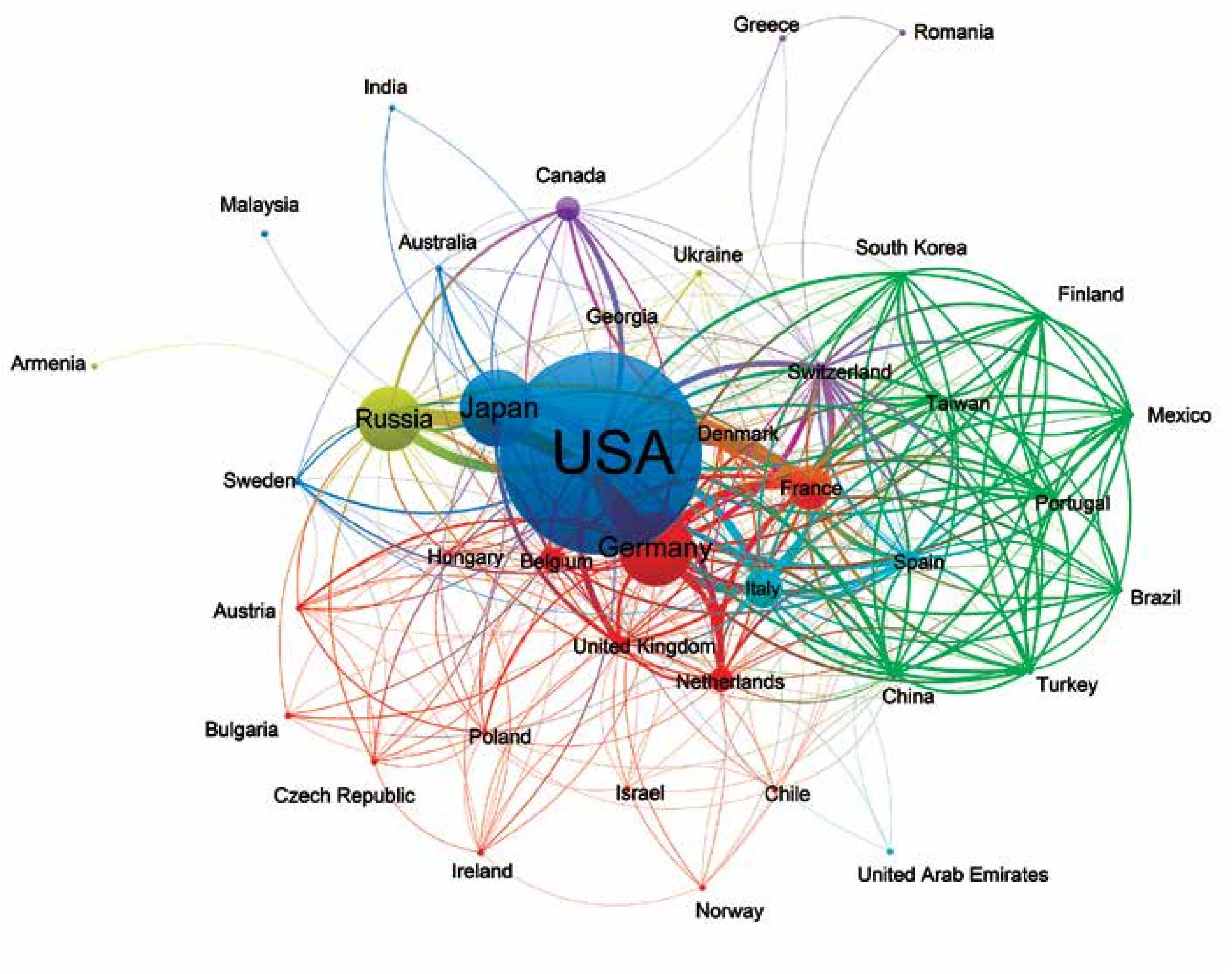

Figure 2. VOSviewer visualization of co-authorship by country. The size of the circle indicates the number of publications of the country. Lines indicate co-authorship links between countries.

to support the evaluation of research institutes and research groups.[2]

Bibliometric visualizations offer a powerful way to present detailed information in a way that improves understanding of the data. Visualizations can provide a network perspective; e.g., co-authorship networks or citation networks. When dealing with large numbers of publications, an overview of the global reach of the publications can be obtained by presenting a visualization of the authors. Using the ISS research results articles collected as of October 1, 2019, Figure 2 presents a VOSviewer visualization of a co-authorship by country network. The size of the circle indicates the number of publications of the country. Lines indicate co-authorship links between countries; this illustrates the wide impact of ISS research globally.

Evolution of Space Station Results

The archive of the ISS investigations went online in 2004. Since that time, the PSO team has implemented many changes to how they track investigations. The team has separated research disciplines and added new research disciplines as more investigations have become active. The team has added or redefined many fields since the rollout of the archive. Initially, the PSO

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[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.*

Research Results team collected only publications that were either related to an investigation or presented direct results from an investigation via a publication or patent. More recently, the Program Science Database (PSDB) included the following publication types:

- 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, we have determined that it is time to expand the types of publications. We have implemented two of these 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. 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.

As of October 1, 2019, the PSO Research Results team identified 137 Alpha Magnetic Spectrometer - 02 (AMS-02) publications: 101 were identified as Derived Results and 36 as ISS Flight Preparation Results. Due to our ongoing efforts to add these articles and new publication types to the PSDB, these data were not included in the final counts of publications collected since October 1, 2018. These new publication types and publications will be available in Space Station Research Explorer on NASA.gov later in 2020, and currently can be viewed at INSPIRE.

Linking Space Station Benefits

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

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.

ISS crew member Reid Wiseman performing the Biological Research In Canisters-19 actuation during Expedition 41 (ISS041E054879).

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.

EXPLORATION

New materials are needed to counteract the growth and spread of bacteria resistant to antibiotics and silver coatings. ROSCOSMOS' investigation, **Influence of Factors of the Space Environment on the Condition of the System of Microorganisms-Hosts Relating to the Problem of Environmental Safety of Flight Techniques and Planetary Quarantine (Biorisk-KM-Metally)**, tested the AGXX® antimicrobial coating and compared it to silver and stainless steel coatings. Crew members placed 12 plaques on the ISS bathroom door, one for each tested material, with samples to be collected at 6, 12 and 19 months. Human-pathogenic bacteria species recovered from the samples were characterized in terms of biofilm formation and antibiotic resistance.

ISS crew member Alexander Samokutyaev works with a Biorisk-MSN experiment container in the Zvezda Service Module of the ISS (ISS028E018265).

For AGXX® surface samples, there was no bacterial growth at 6 months. However, at 12 months, six bacterial strains were observed, and two bacterial strains were observed at 19 months. At all time periods, the AGXX® coating had significantly less bacteria than the surfaces with silver and stainless steel coatings. Of the human-pathogenic bacteria isolated from all surface samples, 32% were resistant to only one or two antibiotics, and 68% were resistant to three or more antibiotics, with the most resistant showing immunity to nine antibiotics. Genetic analysis suggested *ermC* and *tetK* are the most prevalent genes for antibiotic resistance. No serious human pathogens were observed, so infection risk to crew members was low. In addition, novel antimicrobial coatings such as AGXX® may further diminish the proliferation and spread of bacteria resistant to antibiotics.

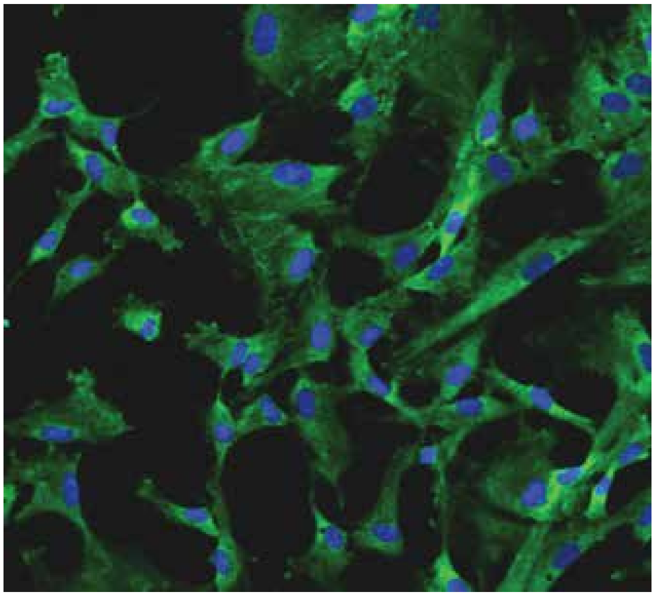
Sobisch L, Rogowski KM, Fuchs J, Schmieder W, Vaishampayan A, et al. Biofilm Forming Antibiotic Resistant Gram-Positive Pathogens Isolated From Surfaces on the International Space Station. Frontiers in Microbiology. *2019 March 19; 10(543): 1-16. DOI: 10.3389/fmicb.2019.00543.*

DISCOVERY

NASA's **Functional Effects of Spaceflight on Cardiovascular Stem Cells (Cardiac Stem Cells)** investigation determined that spaceflight alters many processes of the human body, including cardiac function and cardiac progenitor cell (CPC) behavior. The mechanism behind these changes remains largely unknown; however, clinostats – devices that simulate microgravity on the ground – are making it easier for researchers to isolate the effects of microgravity from the combined microgravity and radiation exposure experienced in flight. To study the changes that take place in cardiac progenitor cells in microgravity environments, adult cardiac progenitor cells with the ability to differentiate into all cardiovascular lineages were cultured aboard the ISS as well as in a clinostat. These cells were examined for changes in Hippo signaling, a pathway known to regulate cardiac development. Adult CPCs cultured under microgravity conditions, spaceflight-induced or simulated, displayed higher levels of transcripts encoding for the Yes Associated Protein 1 (YAP1). This finding is important because YAP1 expression improves functional outcomes following cell-based repair. Finding ways to induce YAP1 production through microgravity or cell conditioning may improve therapies designed to treat cardiac-related diseases.

The sheep myocardial infarction model described in this manuscript emphasizes the role of YAP1 in cardiac repair. Based on similarities to the human cardiovascular system, sheep are considered to be relevant preclinical models. Using this model, functional and safety implications of microgravity-mediated CPC conditioning *in vivo* can be identified. This study provides information that is relevant for human health on Earth and during space exploration missions beyond low-Earth orbit.

Camberos V, Baio J, Bailey L, Hasaniya N, Lopez LV, Kearns-Jonker M. Effects of Spaceflight and Simulated Microgravity on YAP1 Expression in Cardiovascular Progenitors: Implications for Cell-Based Repair. International Journal of Molecular Sciences*. 2019 June 4; 20(11): 2742. DOI: 10.3390/ijms20112742.*



CPCs cultured for the Cardiac Stem Cell investigation aboard the ISS. Image courtesy of Loma Linda University.

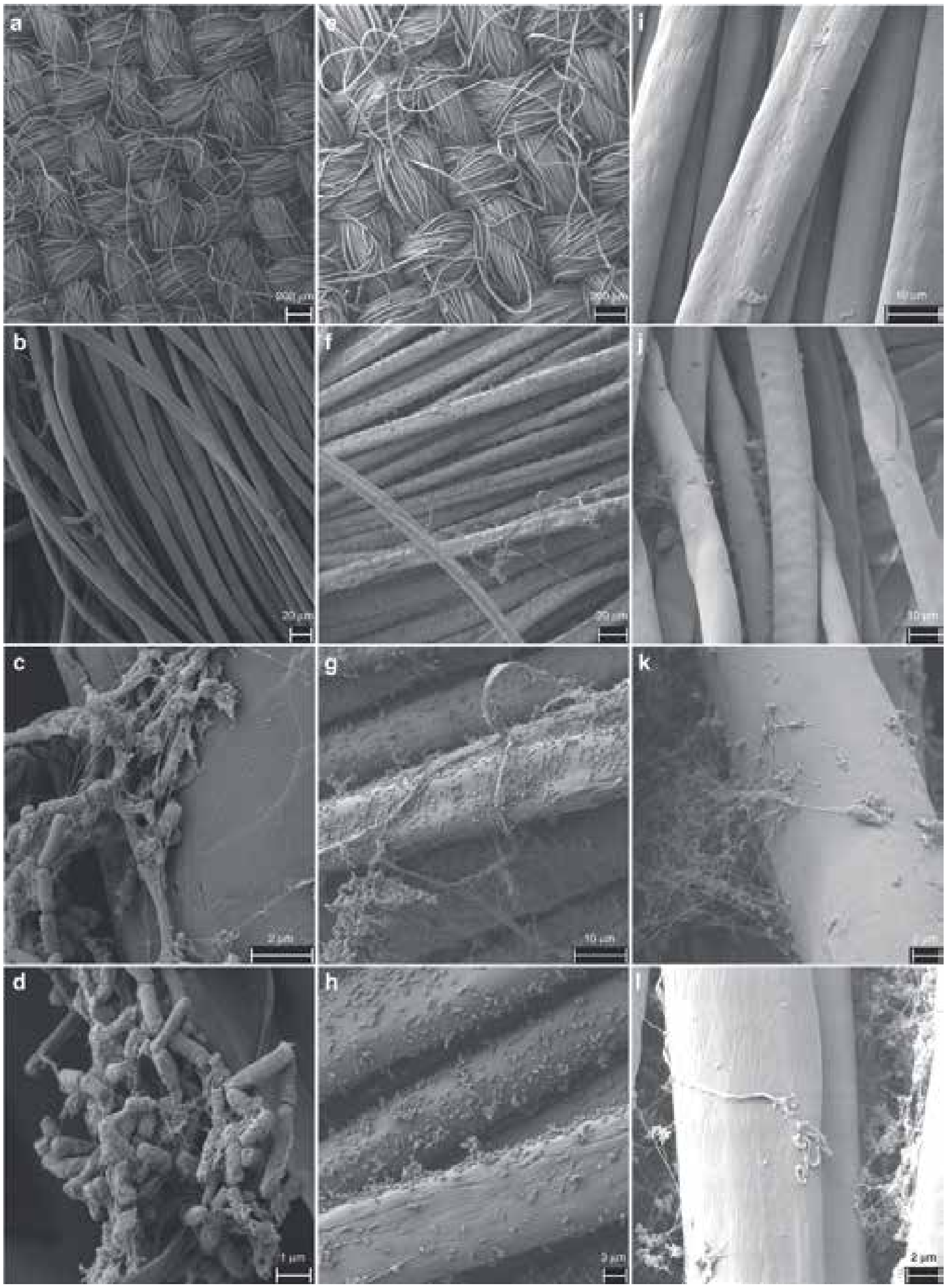
EXPLORATION

ESA's **Extremophiles** investigation required a crew member to wipe various locations aboard the ISS at three different times with 72 days between the first and last sessions. Contents from the wipes were extracted and the bacteria cultivated for diversity and distribution analysis. Researchers studied tolerances to the extreme space environment and antibiotics.

The majority of the bacteria found aboard the ISS were human-associated, particularly those found on skin, such as *Staphylococcus*, *Corynebacterium*, and *Streptococcus*. Although the ISS microbiome fluctuates in composition and diversity, a core microbiome has existed over time and independent of location. These core bacteria have remained consistent over the years, regardless of crew members, suggesting that the ISS has an established microbiome independent of the microbiome of individual crew.

The study did not support the hypothesis that bacteria become more extremophilic or antibiotic resistant in space. Instead, investigators hypothesize that only the best-adapted organisms survive in the space environment. Overall, out of the 76 bacterial isolates, 11 had opportunistic pathogenic potential. Investigators noted that the presence of these pathogens is not alarming; however, the presence of these microbes warrants continual monitoring.

Mora M, Wink L, Kogler I, Mahnert A, Rettberg P, et al. Space Station conditions are selective but do not alter microbial characteristics relevant to human health. Nature Communications*. 2019 September 5;10(3990). DOI: 10.1038/s41467-019-11682-z.*



Scanning electron micrographs of NOMEX® fabric. The fabric was co-incubated for 6 weeks with bacteria isolated from the ISS: a–d Co-incubation with Bacillus paralicheniformis; e–h Co-incubation with Cupriavidus metallidurans; i–l Negative control of NOMEX® fabric kept in sterile medium for 6 weeks (Image courtesy of Mora M, et al, Nature Communications, 2019).

DISCOVERY

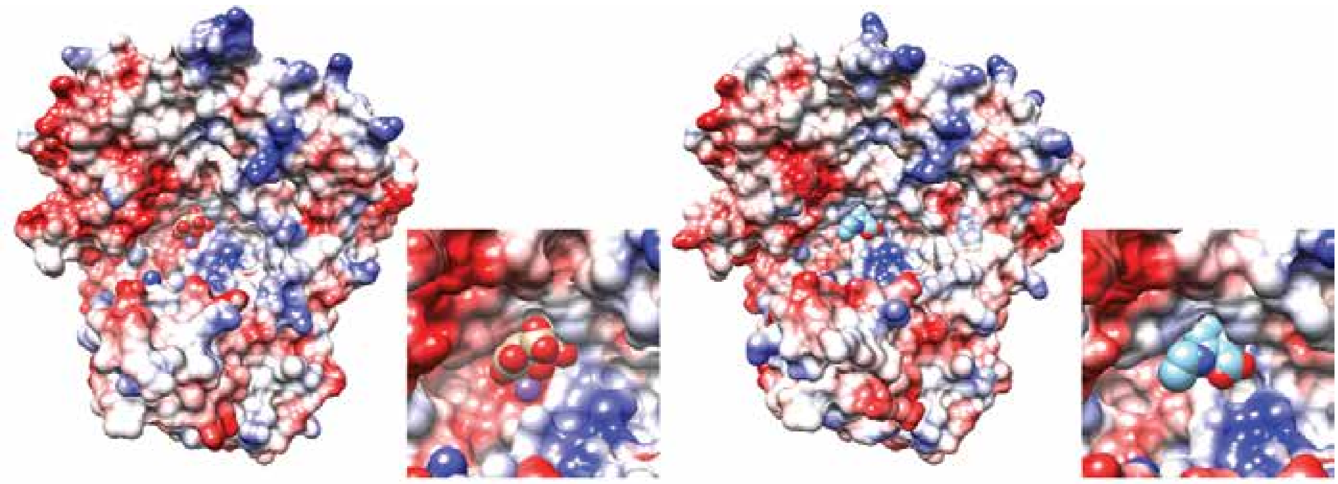
Periodontal disease, which destroys tooth-supporting tissues and leads to tooth loss, is one of the most widespread infectious diseases among human beings. This disease is caused by *Porphyromonas gingivalis* (*P. gingivalis*), a non-fermenting gram-negative rod (NFGNR) bacterium that uses amino acids as nutrients instead of carbohydrates. *P. gingivalis* creates PgDPP11, a known essential enzyme that contributes to bacterial growth and pathogenicity. Therefore, the substances that inhibit the activity of PgDPP11 may be candidates for antibiotics to fight periodontal disease.

In JAXA's **Protein Crystal Growth (JAXA PCG)** investigation, high-quality crystals of PgDPP11 were grown on board *Kibo*, the Japanese Experiment Module of the ISS. Crystallization and X-ray diffraction techniques are used to determine protein structures. Understanding the structure of proteins can lead to improvements in medical treatments and pharmaceuticals for numerous conditions. The microgravity environment removes the effects of sedimentation and convection seen on Earth and provides an exceptional environment for crystal growth. High-quality crystals are key for determining the structure of proteins.

Based on the ISS-grown PgDPP11 crystals, scientists were able to infer the molecular structure around the PgDPP11 active site required for the search and design of potential inhibitors. Scientists performed multiple screenings and computer docking simulation studies to discover potential inhibitors of PgDPP11. Thirteen candidate compounds were selected from 4 million options; of these candidates, the compound SH-5 showed a significant inhibitory effect against the growth of *P. gingivalis*. PgDPP11 and SH-5 were co-crystallized in microgravity, and SH-5 was clearly shown to bind to the active site of PgDPP11. The discovery of SH-5 is a good starting point for designing antibiotics for *P. gingivalis* and other NFGNRs.

This result provides a good example of the usefulness of high-resolution crystal structures that can be grown in microgravity, providing new insights into structure-based drug design.

Sakamoto Y, Suzuki Y, Nakamura A, Watanabe Y, Sekiya M, et al. Fragment-based discovery of the first nonpeptidyl inhibitor of an S46 family peptidase. Scientific Reports. *2019 September 19; 9:13587. DOI: 10.1038/s41598-019-49984-3.*



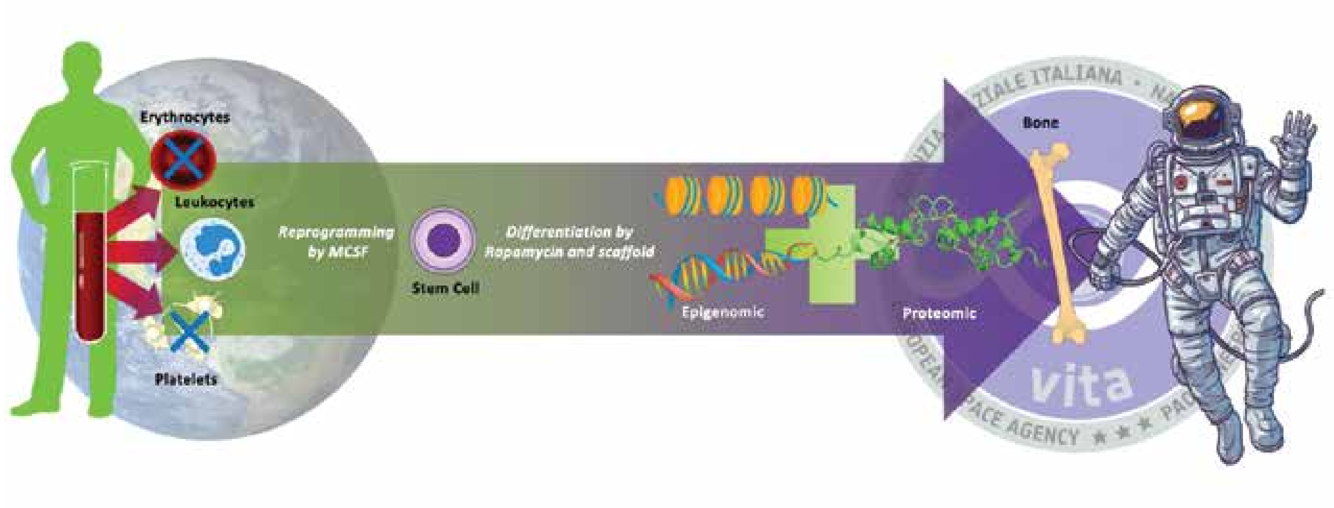
Mode of Citrate ion and Potassium ion binding in the S1 subsite of PgDPP11 (left). The bound citrate (cream and red) and potassium ions (purple) are shown in sphere models, respectively Mode of SH-5 binding in the S1 subsite of PgDPP11 (right). The bound SH-5 (cyan, red and blue) is shown in sphere model. The surface of PgDPP11 is colored by coulombic surface coloring (blue: positive, red: negative). Image courtesy of Sakamoto Y.

BENEFITS FOR HUMANITY

To better understand the formation of bone cells in space, the Italian Space Agency's (ASI) **Role of the Edocannabinoid System in Pluripotent Human Stem Cell Reprogramming under Microgravity Conditions (SERiSM)** investigation treated blood-derived stem cells (BDSCs) with rapamycin to induce the differentiation or formation of bone cells. Sixteen samples were flown to the ISS to study BDSC protein and epigenetic changes at 0, 48 and 72 hours after arrival. All samples were contained in the SERiSM experiment unit where autonomous growing and fixing of cell cultures occurred.

Fifteen protein markers were used to track key osteogenic changes such as pluripotency, commitment, and differentiation. Results showed that almost all proteins analyzed, including controls, increased aboard the ISS compared to those on Earth, suggesting that ascent to the ISS may affect gene expression. Overall, rapamycin is shown to induce increases in GATA4 and Sox17, proteins that modulate the transcription factor crucial for osteogenic differentiation. With differentiation, cells become mature and undergo epigenetic rearrangements that prevent the cell from returning to its undifferentiated state. Key histone proteins were observed to undergo this cellular reprogramming process. These proteins effectively control gene expression. The insight provided by this study contributes to the identification of new markers and therapeutic targets to treat osteoporosis in humans.

Gambacurta A, Merlini G, Ruggiero C, Diedenhofen G, Battista N, et al. Human osteogenic differentiation in Space: proteomic and epigenetic clues to better understand osteoporosis. Scientific Reports. *2019 June 6; 9(1): 8343. DOI: 10.1038/s41598-019-44593-6.*



Rapamycin-driven osteogenesis of human blood-derived stem cells on board the ISS (Image courtesy of Gambacurta A, et al, Scientific Reports, 2019).

ISS crew member Andre Kuipers performs his second orbital Neurospat session during ISS Expedition 30 (ISS030E022627).

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.

EXPLORATION

Numerous complex effects on the physiology of different organisms suggest a slowdown of aging in space. JAXA's **Biological Rhythms 48 hrs** examined the potential effect of geomagnetic space weather on human cardiac activity to explain physiological changes in the human body associated with longevity.

Electrocardiographic data obtained from ISS crew members before, during and after spaceflight assessed heart rate variability (HRV) while geomagnetic data obtained remotely from the Auroral Observatory of the University of Tromso, Norway, measured the Earth's magnetic field. ISS crew members' HRV was compared between magnetically quiet and disturbed days.

Results showed that changes in the magnetosphere can affect and enhance HRV indices associated with anti-aging biomarkers. Specifically, the SDNNIDX (mean of the standard deviations to normal sinus interbeat intervals in all 5-minute segments) and very low frequency components of HRV were higher on magnetically disturbed days. Investigators also found increased HRV bands associated with the brain's default mode network on disturbed days.

These findings suggest that spaceflight can have anti-aging effects as a result of the effects of Earth's magnetic field on human HRV indices associated with longevity.

Otsuka K, Cornelissen G, Kubo Y, Shibata K, Mizuno K, et al. Anti-aging effects of long-term space missions, estimated by heart rate variability. Scientific Reports. *2019 June 20; 9(1): 8995. DOI: 10.1038/s41598-019-45387-6.*

ISS crew member Koichi Wakata strapped into his sleeping bag in his sleep station located in the Node 2 (ISS038E024951).

EXPLORATION

Space explorers experience orthostatic intolerance – feelings of dizziness and nausea when standing upright upon return from space. This condition may result from a rapid decline in blood pressure (BP). CSA's study, **A Simple In-flight Method to Test the Risk of Fainting on Return to Earth After Long-Duration Spaceflights (BP Reg)**, employed pulse arrival time (PAT) as a potential surrogate for blood pressure when measurements of finger arterial pressure are not possible under postflight conditions.

ISS crew member blood pressure was measured before spaceflight and 1 day after return while completing a physical task that required them to change position from lying down to sitting to standing. Results showed that PAT was correlated with a change in systolic blood pressure during position changes.

These results demonstrate that arterial pulse arrival time could be a sensitive indicator of significant changes in blood pressure. The use of this non-invasive and accessible approach is expected to improve the monitoring of blood pressure in future space explorers.

Wood KN, Greaves DK, Hughson RL. Inter-relationships between pulse arrival time and arterial blood pressure during postural transitions before and after spaceflight. Journal of Applied Physiology. *2019 August 15; epub: 22 pp. DOI: 10.1152/japplphysiol.00317.2019.*

ISS crew member Chris Hadfield is photographed during BP Reg operations. He is wearing the Leg/Arm Cuff System on his thighs, and the Continuous Blood Pressure Device on his left hand. (ISS035E022360).

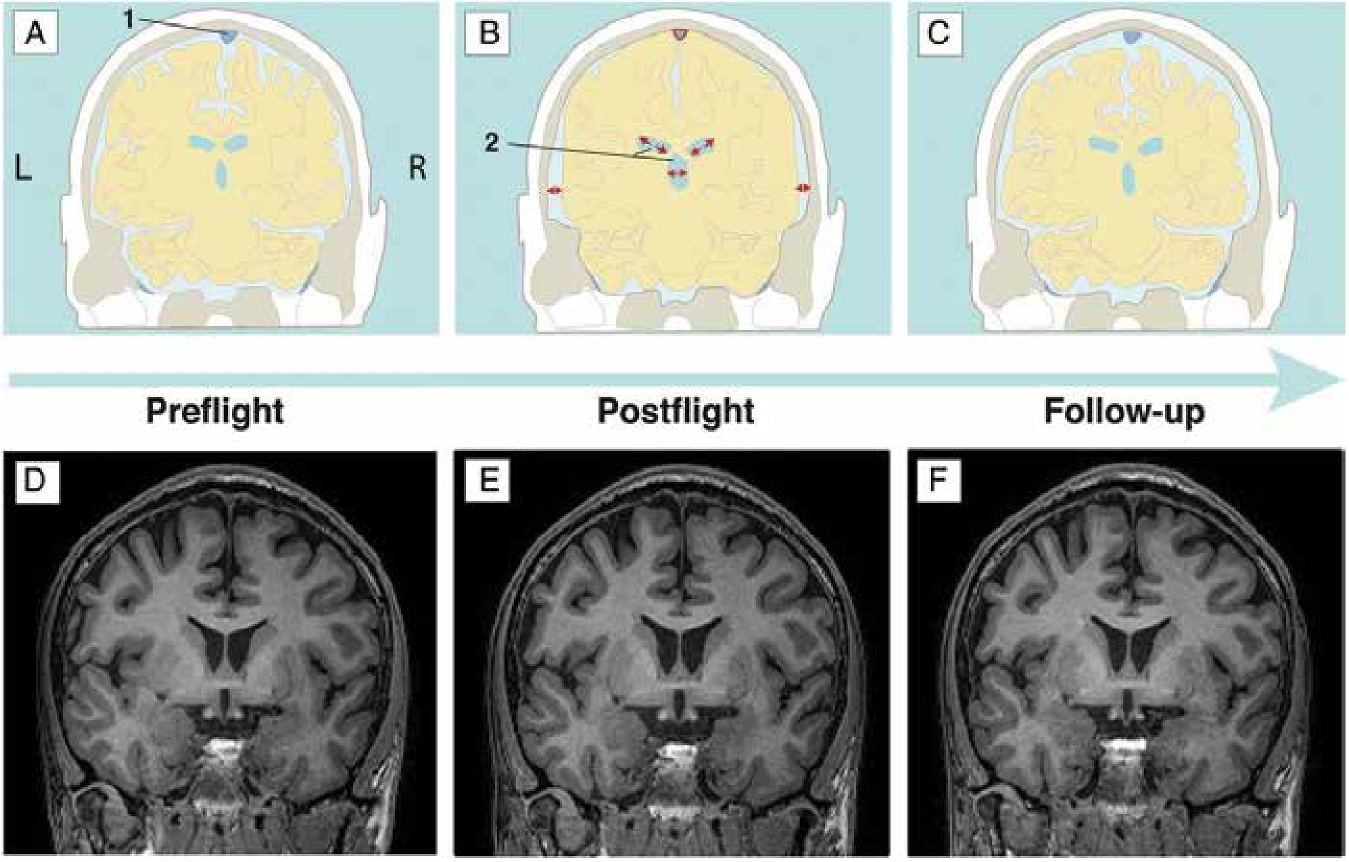
EXPLORATION

The brain activity of ISS crew members was investigated before and after spaceflight for the first time. The goal of ESA's **Brain-Diffusion Tensor Imaging (Brain-DTI)** study was to examine the mechanisms of sensorimotor processing by using a plantar stimulation functional magnetic resonance imaging (fMRI) task to stimulate the soles of space explorer feet.

Initial exploratory results showed activity in the expected areas of the somatosensory cortex, operculum, and cerebellum. Further analyses showed changes in connectivity in additional regions outside the sensorimotor network, including regions associated with vestibular system function, visuospatial processing, and proprioception. Although some increased connectivity was observed between the right supramarginal gyrus and the rest of the brain, there was reduced connectivity between regions involved in body position perception, visceral sensations and equilibrium (i.e., the anterior lobe of the cerebellum, vestibular nuclei, right inferior parietal cortex and insula bilaterally). Importantly, there was a significant correlation between connectivity in two areas of the brain, the right supramarginal gyrus and insula, and the severity of space motion sickness.

The functional connectivity changes observed may relate to adaptation in space and readaptation to Earth's gravity. This research generates new hypotheses in the study of sensorimotor adaptation.

van Ombergen A, Jillings S, Jeurissen B, Tomilovskaya ES, Rumshiskaya A, et al. Brain ventricular volume changes induced by long-duration spaceflight. Proceedings of the National Academy of Sciences of the United States of America. *2019 May 6; epub. DOI: 10.1073/pnas.1820354116.*



Overview of the changes occurring in the subarachnoid and intracerebral cerebrospinal fluid spaces, including the superior sagittal sinus (area 1) and the ventricles (area 2) of space explorers across the different time points (Image courtesy of van Ombergen A, et al, Proceedings of the National Academy of Sciences of the United States, 2019).

EXPLORATION

The ROSCOSMOS investigation **Study of Vegetative Regulation of the Cardio-respiratory System in Weightlessness (Puls)** used a novel non-invasive, easily operated oscillometric device to measure blood pressure with the goal of assessing vascular health before and after long-duration spaceflight.

Results showed that two important vascular aging biomarkers, pulse wave velocity and central blood pressure, did not increase during or after spaceflight. Researchers concluded that 6 months in space do not lead to clinically significant changes in vascular health.

These results demonstrate that space explorers do not experience signs or symptoms of cardiovascular disease during space travel, immediately after return, or a few days later. However, radiation-induced cardiovascular disease may develop many years after radiation exposure. Researchers recommend that the scientific community develop precise technologies that differentiate vascular adaption from preclinical vascular disease.

Hoffmann F, Mostl S, Luchitskaya ES, Funtova II, Jordan J, et al. An oscillometric approach in assessing early vascular ageing biomarkers following long-term space flights. International Journal of Cardiology Hypertension*. 2019 August 1;2: 100013. DOI: 10.1016/j.ijchy.2019.100013.*

ISS crew member Dmitry Kondratyev takes blood pressure measurements and electrocardiogram recording (ISS026E031635).

EXPLORATION

DISCOVERY

NASA's **Twins Study** demonstrated on the molecular level the resilience and robustness of how one human body adapted to the spaceflight environment compared to the Earth-bound twin. This study was a stepping-stone to future biological space research focusing on molecular changes and how they may predict health and performance of space explorers.

Results from the Twins Study noted several spaceflight-specific effects, including decreased body mass, changes in chromosomes (telomere dynamics, gene expression and genome instability), carotid artery distension and a thickening of artery walls, alterations in eye structure (ocular structure), impacts to metabolism, changes in DNA activity (DNA methylation), alterations in gut bacteria (gastrointestinal microbiome) and impacts to cognitive processing. Several changes returned to baseline levels within 6 months after returning to Earth. The persistent changes observed after 6 months on Earth included a subset (8.7%) of changes in gene expression, increased DNA damage from chromosomal inversions, increased numbers of short telomeres, and attenuated cognitive function.

As the Twins Study investigators note, it is difficult to draw conclusions for all humans from a single test subject in the spaceflight environment. Scientists recognize that there is more to learn. NASA's Human Research Program continues to gather experience with long-duration spaceflight to better identify health impacts and anticipate risks that future space explorers may encounter as they travel beyond low-Earth orbit.

Garrett-Bakelman FE, Darshi M, Green SJ, Gur R, Lin L, et al. The NASA Twins Study: A multidimensional analysis of a year-long human spaceflight. Science. *2019 April 11; 364: 20 pp.*

ISS crew member Scott Kelly (right) along with his twin brother, former astronaut Mark Kelly (left), prior to the 1-year mission aboard the ISS (JSC2015E004212).

ISS crew member Shane Kimbrough during Capillary Flow Experiment with the Interior Corner Flow hardware during ISS Expedition 50 (ISS050E014941).

PUBLICATION HIGHLIGHTS:
PHYSICAL SCIENCES

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 and 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.

DISCOVERY

Aluminum alloys are often used in cast metal applications for a number of automotive and transportation purposes, allowing manufacturers to reduce vehicle weight, increase the strength of components and improve emission controls. One of the most challenging problems associated with aluminum casting is the influence of convection during all stages of solidification. The strength of fluid flow changes the “as cast” internal structure (microstructure) such that the yield, fracture and fatigue strengths of the cast ingot can vary considerably. Although the importance of fluid flow has been recognized for decades, no model has been developed to predict the effect of microgravity on microstructure. ESA’s **Columnar-to-Equiaxed Transition in Solidification Processing (CETSOL)** investigation examines different crystal growth patterns and the evolution of microstructures during crystallization of metallic alloys in microgravity.

Columnar-to-equiaxed transition (CET) occurs during columnar growth when new grains grow ahead of the columnar front in the undercooled liquid. Under certain conditions, these grains can stop the columnar growth and then the solidification microstructure becomes equiaxed, or having axes of approximately the same length. Two solidification runs of CETSOL silicone and aluminum alloys were successfully completed in the Material Science Laboratory (MSL) on the ISS using the Solidification Quenching Furnace on board the ISS.

ISS crew member Frank De Winne removes a CETSOL sample cartridge assembly from its MSL mechanical protection container tube during MSL commissioning activities on board ISS (ISS021E023149).

A progressive CET was obtained in both ISS and Earth-based samples, implying the existence of an intermediate region after the inception position of CET defined as the end of growth of the columnar dendrites. However, a more progressive CET and longer dendrites aligned with the applied temperature gradient were observed in presence of gravity. This difference is attributed to the convective flow on Earth. On the one hand, this flow carries the grains that nucleate ahead of the columnar front away into the bulk liquid phase. On the other hand, it sweeps the solute away from the dendrite tip zone. Consequently, the blocking effect is diminished, allowing extended continuous growth of the elongated dendrites.

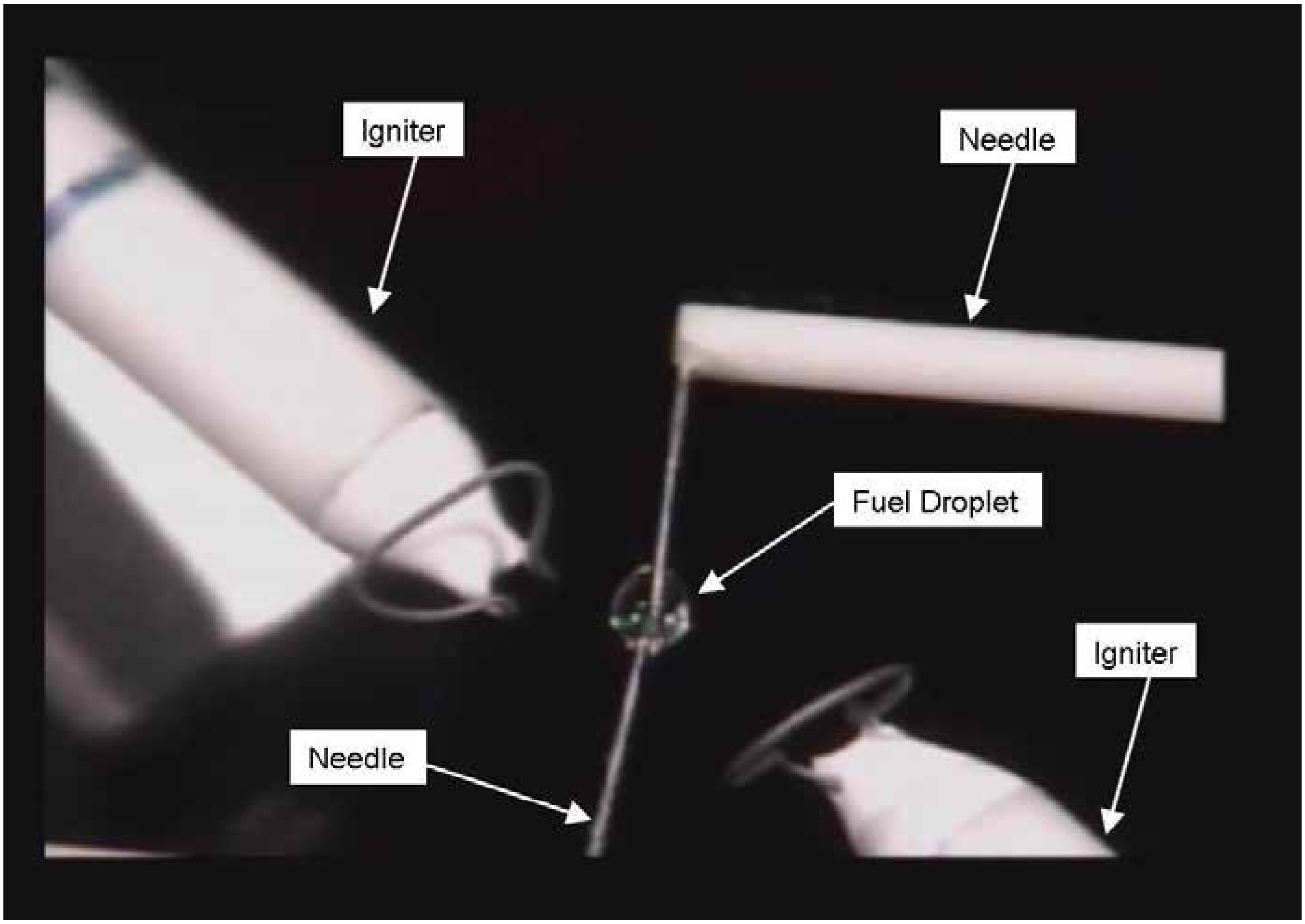
The results from this study will guide future development and understanding of material processes in a microgravity environment. CETSOL aims to provide science teams and industrial partners confidence in the reliability of the numerical tools introduced in their integrated numerical models of metallic alloy casting.

Li YZ, Mangelinck-Noel N, Zimmermann G, Sturz L, Nguyen-Thi H. Comparative study of directional solidification of Al-7wt.% Si alloys in space and on Earth: Effects of gravity on dendrite growth and columnar-to-equiaxed transition. Journal of Crystal Growth. *2019 May 1; 513: 20-29. DOI: 10.1016/j.jcrysgro.2019.02.050.*

DISCOVERY

The ROSCOSMOS study **Flame Extinguishment Experiment – ROSCOSMOS (FLEX-ROSCOSMOS)** confirmed the existence of two high and low n-heptane burning regimes. The extinction of visible flame around a droplet resulted in a cool flame that continued to burn while invisible to the visualization system. Quasi-steady burning after visible flame extinction confirmed the continued combustion. After radiative extinction of high-temperature droplet burning, the transition to low temperature stage with constant burning rate took place. In this second stage, the droplet continued to burn and evaporate without the presence of a visible flame, ultimately leading to a diffusive extinction at a finite droplet size. The low temperature diffusion combustion for an isolated droplet has never been proposed or suggested before the FLEX-ROSCOSMOS investigation. The FLEX-ROSCOSMOS investigation analyzed data provided by NASA from NASA's FLEX experiment.

Tyurenkova V. Two regimes of a single n-heptane droplet combustion. Acta Astronautica*. 2019 February 2; epub. DOI: 10.1016/j.actaastro.2019.01.045.*



Video screen shot of Multi-user Droplet Combustion Apparatus Flame Extinguishment Experiment Ignition 1 on March 5, 2009 (GMT 64/17:21). Igniters continue to cool. Combustion event continues (Image courtesy of NASA).

DISCOVERY

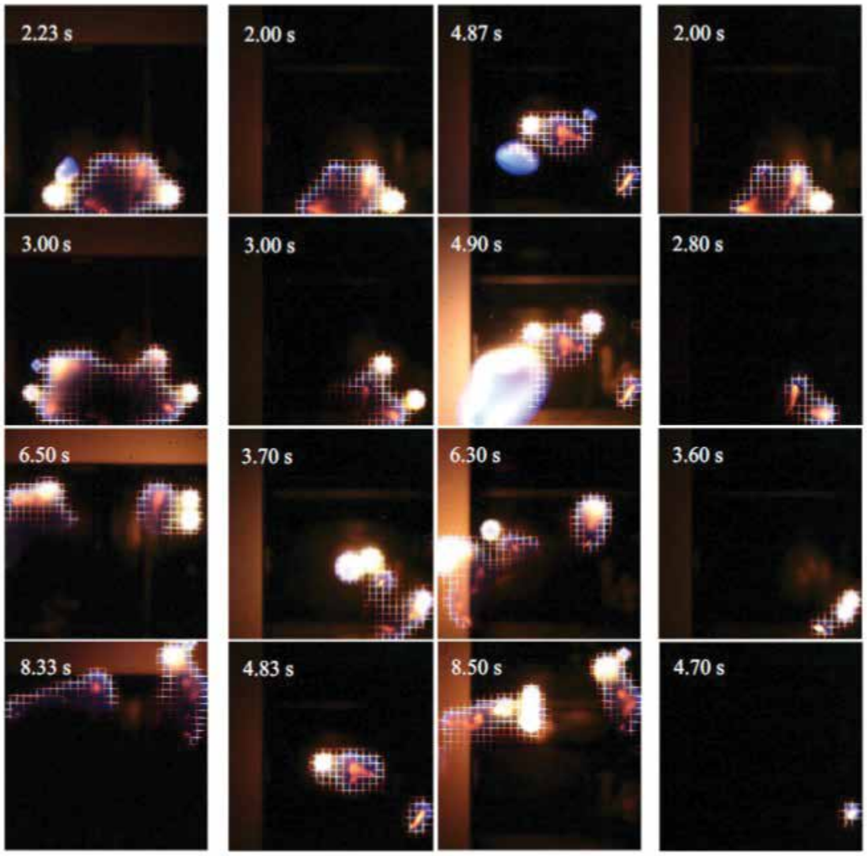
For JAXA's **Elucidation of Flame Spread and Group Combustion Excitation Mechanism of Randomly-distributed Droplet Clouds (Group Combustion)** investigation, researchers conducted microgravity experiments aboard the ISS and performed temperature-field analysis using the Thin Filament Pyrometry method based on visible light emissions to study the effects of droplet interaction on flame spread characteristics. Results show that the positions of the interactive droplets affect the flame spread around the droplets, and the flame-spread limit is extended by the interactive effect. If a burning droplet preheats a droplet existing outside the flame-spread limit, the pre-vaporization also extends the flame-spread limit around two interactive droplets.

Results also show that in the case with strong interaction by two or three interactive droplets, the high-temperature region is enlarged by the droplet interaction and the center of mass of the interactive droplets, playing an important role in the flame-spread-limit distribution. The flame-spread-limit distance from the center of mass of the interactive droplets increases with the burning lifetime. The behavior of combustion in a microgravity environment is critical to learning to control such events in spacecraft propulsion as well as prevention in locations where such combustion is not desired, such as a spacecraft cabin.

Yoshida Y, Iwai K, Nagata K, Seo T, Mikami M, et al. Flame-spread limit from interactive burning droplets in microgravity. Proceedings of the Combustion Institute*. 2019; 37(3): 3409-3416. DOI: 10.1016/j.proci.2018.07.106.*

Yoshida Y, Seo T, Mikami M, Kikuchi M. Temperature-Field Analysis of Flame Spread over Droplet-Cloud Elements with Interactive Droplets in Microgravity aboard Kibo on ISS. International Journal of Microgravity Science and Application*. 2019; 36(3): 360303.*

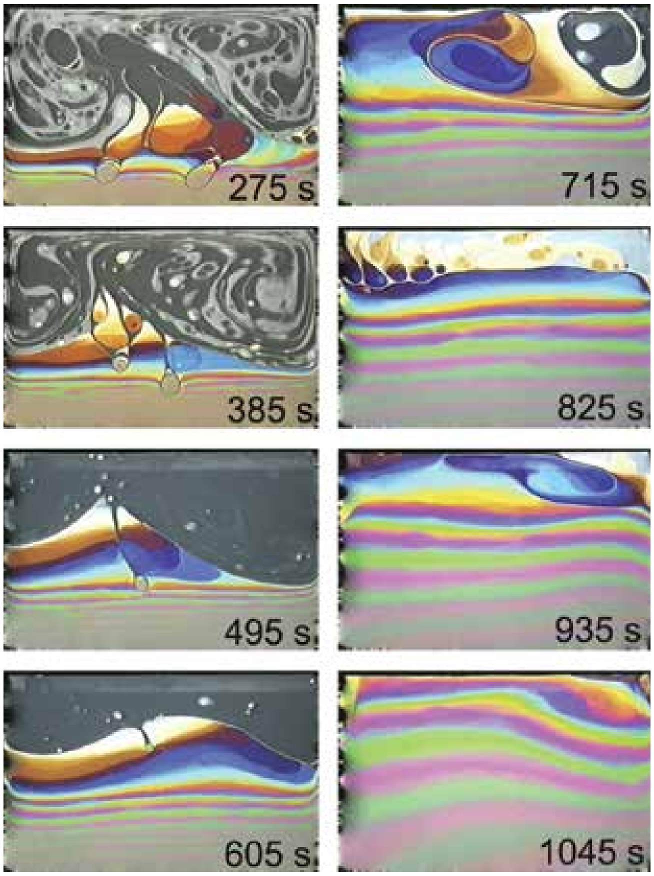
Nomura H, Suganuma Y, Mikami M, Kikuchi M. Observation of Interaction between a Spreading Flame and Movable Droplets using Microgravity Environment of "KIBO". International Journal of Microgravity Science and Application*. 2019; 36(3): 360304.*



Flame-spread behavior near the group-combustion-excitation limit for different mean initial droplet diameter d0 of a droplet cloud with the same droplet arrangement of M = 67 (Image courtesy of Masato M, et al. Microgravity Science and Technology, 2018).

NASA's **Observation and Analysis of Smectic Islands in Space (OASIS)** demonstrates that Marangoni flow of liquid crystal film can transport inclusions, a mechanism that could be used in practical applications such as droplets of reactants for chemical reactions or microprobes in chemical sensors. OASIS demonstrates that when the film is heated in a region far from a meniscus, material is transported against the temperature gradient as long as the film is homogeneously thick in the region far from the meniscus. Then, the hot region can grow by an expansion of existing holes or by the shrinkage of islands. Further growth of a homogeneous film region would require the creation of new holes by thermocapillary forces. This finding will help scientists understand the properties of material flow in microgravity.

Stannarius R, Trittel T, Klopp C, Eremin A, Harth K, et al. Freely suspended smectic films with in-plane temperature gradients. New Journal of Physics*. 2019 June 3;21(6):063033.*
DOI: 10.1088/1367-2630/ab2673.



Climbing of smectic layers in a vertically suspended film under the influence of a vertical temperature gradient. A thermostated block at the lower frame edge was set to a temperature of Th = 70°C. The top of the frame was not heated; it remained approximately at room temperature (25°C). During the first 10 minutes, hot air flowing upward induces a pair of convection rolls in the upper thin film region (thickness ≈80 nm). The thicker regions that climb up are less sensitive to air flow, thus the convection ceases (Image courtesy of Stannarius R, et al. New Journal of Physics, 2019).

ISS crew member Serena Auñón-Chancellor pauses for a photo during operations to insert a Microgravity Investigation of Cement Solidification Module into the Multi-use Variable-g Platform facility during ISS expedition 57 (ISS057E106264).

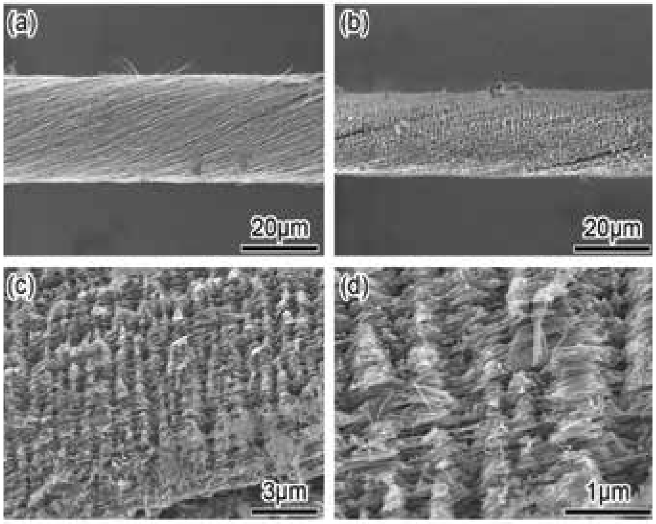
PUBLICATION HIGHLIGHTS:

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

JAXA's **Space Environment Exposure Experiment of CNT Material for Space Application (Carbon Nanotube)** tests an advanced carbon-based material for its ability to withstand erosion from the radiation of space. Carbon nanotubes (CNTs) are extraordinarily light, strong and conductive materials that can help make spacecraft lighter, stronger and more energy efficient, but their reliability and space readiness has not been fully established. Two ways to test material properties are ground-based simulations and space-based studies. For the space-based portion of the testing, CNT yarns were exposed to the space environment. The results of ground-based and on-orbit studies are summarized as follows: (1) The CNT yarns were damaged on the surface, mainly from exposure to Atomic Oxygen (AO), while Electron Beam irradiation and ultraviolet light exposure had almost no impact. (2) Tensile strength decreased by 40%–65% after exposure to the space environment. (3) Defects were generated during 395-day exposure in the wake direction, coinciding with the results for the tensile strength. In terms of tensile strength, the CNT yarn does not appear to be a reliable structural material for use on the ISS because of the space station's very high speed, which causes the relative kinetic energy of AO to be high, resulting in serious damage to CNT yarns without proper protective coatings.



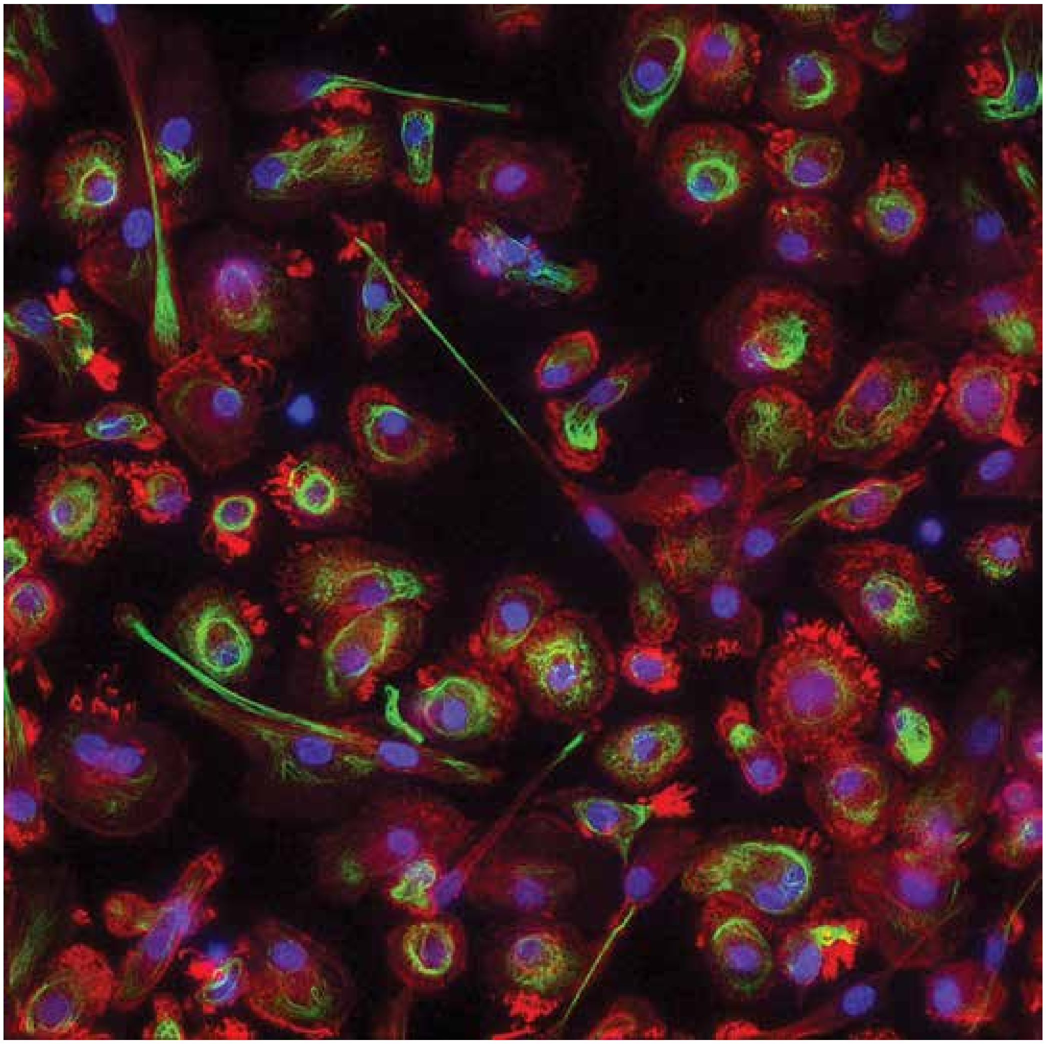
Scanning electron micrographs of a thin yarn sample (484-day exposure, ram direction): (a) a part shielded by a metal cover and (b)-(d) a part exposed to space (Image courtesy of Ishikawa Y et al. Acta Astronautica, 2019).

Ishikawa Y, Fuchita Y, Hitomi T, Inoue Y, Karita M, et al. Survivability of carbon nanotubes in space. Acta Astronautica*. 2019 August 22; 165:129-138. DOI: 10.1016/j.actaastro.2019.07.024.*

EXPLORATION

The ISS crew successfully demonstrated the ability of the three-dimensional high-resolution fluorescence microscope to generate digital images of human T-cell samples during NASA's **FLUMIAS-DEA** investigation. This microscope can be used for real-time analysis of cell behavior during long-duration spaceflight. This fast imaging capability is needed to monitor cellular and molecular reactions that can occur more quickly in altered gravity environments. The implementation of real-time analysis methods on the ISS dramatically extends our knowledge about the dynamics of cellular reactions and adaptations to the space environment, a requirement for evidence-based medical risk assessment, abnormal cell monitoring and countermeasure development against diseases for exploration-class missions.

Thiel CS, Tauber S, Seebacher C, Schropp M, Uhl R, et al. Real-time 3D high-resolution microscopy of human cells on the International Space Station. International Journal of Molecular Sciences. *2019 April 25; 20(8). DOI: 10.3390/ijms20082033.*



Fixed macrophages using three chromophores created by the FLUMIAS-DEA miniaturized fluorescence microscope during Science Verification Test. Image courtesy of Airbus (JSC2019E051831).

The Multi-mission Consolidated Equipment investigation consists of five small unique instruments that are located at Equipment Exchange Unit site 8 on the Japanese Experiment Module - Exposed Facility. (ISS020E042298)

PUBLICATION HIGHLIGHTS:

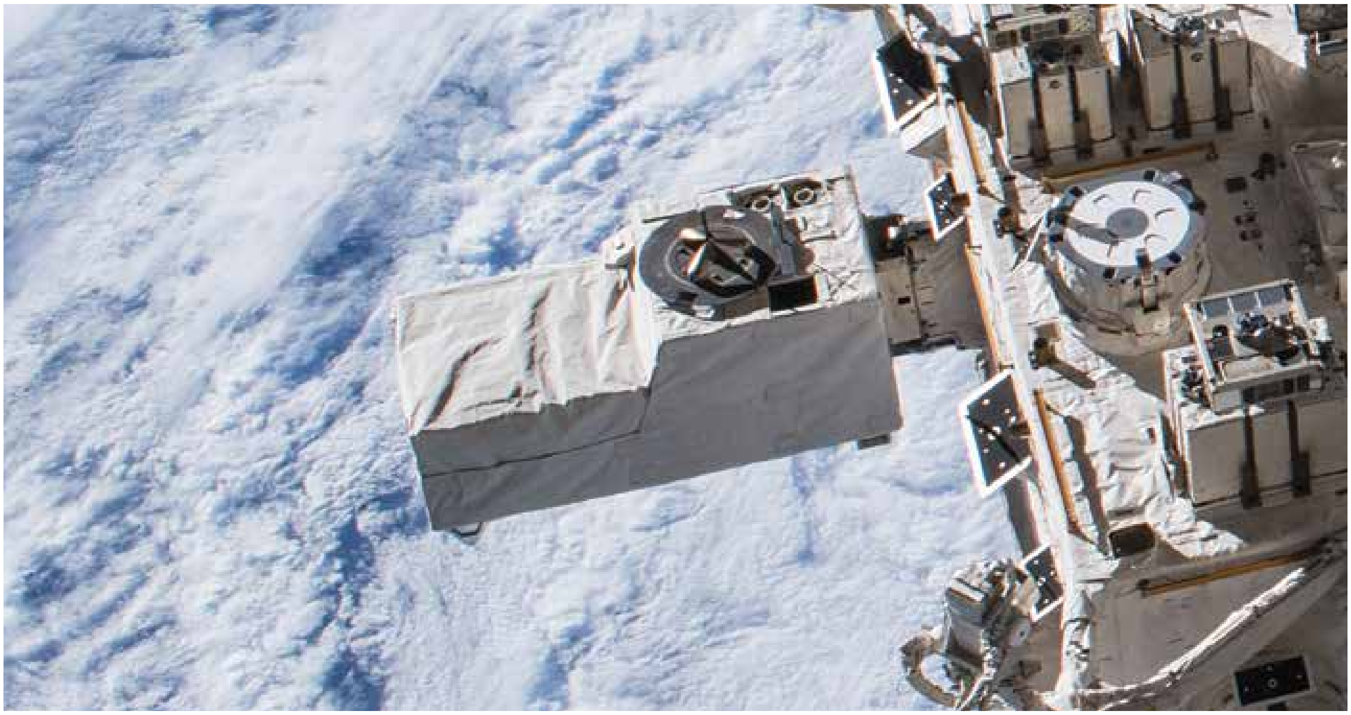
EARTH AND SPACE SCIENCE

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

During the observation period of October 13, 2015, to August 31, 2018, JAXA's **CALorimetric Electron Telescope (CALET)** recorded a wide range of measurements for cosmic proton spectrum from 50 GeV to 10 TeV. The instrument is the first to cover this wide range of proton spectrum, previously only covered by multiple detectors. The data will help astronomers shed light on the origin of spectral hardening, contradicting conventional single power-law spectrum predictions. Improved statistics and a better understanding of the instrument based on the analysis of additional flight data during the ongoing years of observations will help to confirm a charge-dependent energy cutoff, possibly due to the acceleration limit in supernova remnants in proton and helium spectra. The data are also expected to inform development of updated constraints on acceleration models.

Adriani O, Akaike Y, Asano K, Asaoka Y, Bagliesi MG, et al. Direct Measurement of the Cosmic-Ray Proton Spectrum from 50 GeV to 10 TeV with the Calorimetric Electron Telescope on the International Space Station. Physical Review Letters. *2019 May 10; 122(18): 181102. DOI: 10.1103/PhysRevLett.122.181102.*



Close-up view of CALET from the truss of the ISS (ISS055E006398).

BENEFITS FOR HUMANITY

The ISS provides a unique opportunity to capture a variety of sites on Earth by providing repeated overflight passes with different lighting and viewing angles. Through NASA's **Crew Earth Observations (CEO)**, ISS crew members share their views of the Earth with the public and take pictures of some of the most dramatic examples of change on the Earth's surface.

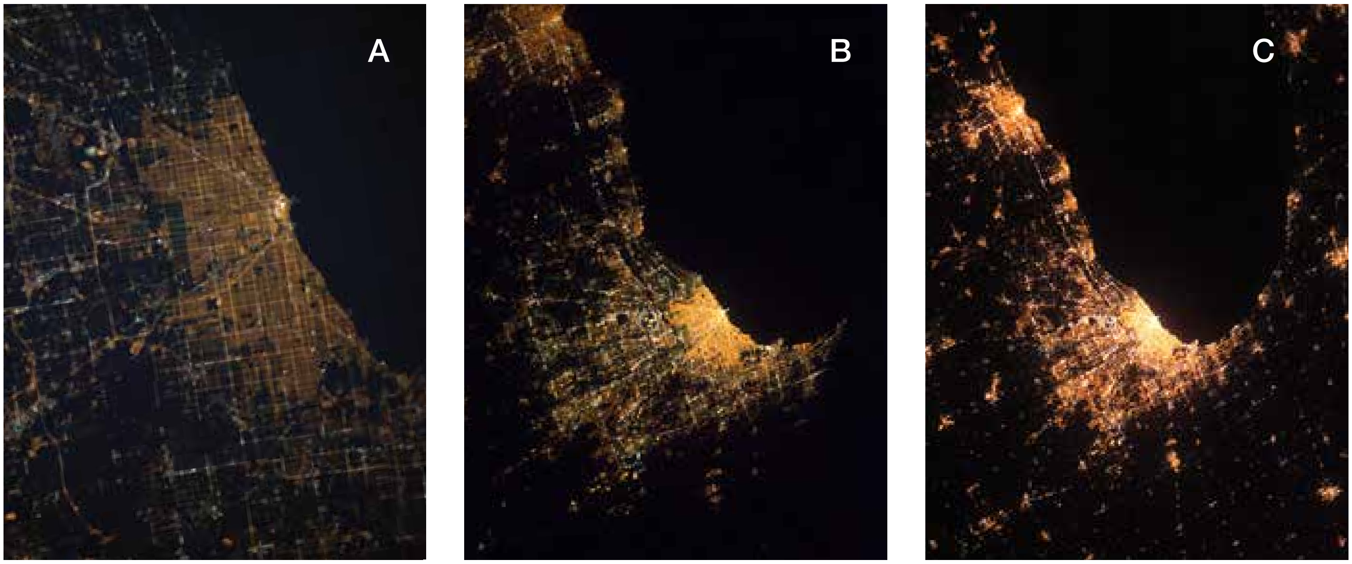
From Expedition 1 through the present, ISS crew members have taken more than 3 million images of Earth, almost 10 times more images than taken from orbit by explorers from the first Mercury mission to the last Space Shuttle mission. Scientists and the public around the world have access to CEO images captured by crew members on the ISS through the Gateway to Astronaut Photography of Earth website (http://eol.jsc.nasa.gov). Between 1,000,000 and 11,000,000 digital photographs of Earth taken from the CEO collection were downloaded by the public each month during 2018. Analyses using CEO data have been published in scientific journals in a wide variety of disciplines.

Images of the Earth at night are an exceptional source of human geographical data because artificial light highlights human activity. Since ISS imagery provides some spectral information as well as street-level resolution, nighttime imagery reveals "cultural footprints" and is of greater use than daytime photography in a variety of studies.

Earth imagery from the ISS provided critical data on the impacts of artificial nighttime lighting with the concurrence of studies of behavioral impacts and ecological effects on wildlife. The combination of laboratory and field techniques along with lighting values mapped out using ISS imagery provided significant evidence of the impacts from lighting patterns in urban areas. The area of focus was the city of Chicago. Area wildlife monitoring data were combined with illumination levels from artificial light along with several algorithms to isolate other factors not related to lighting to determine how lighting patterns may influence wildlife behavior on a broad scale.

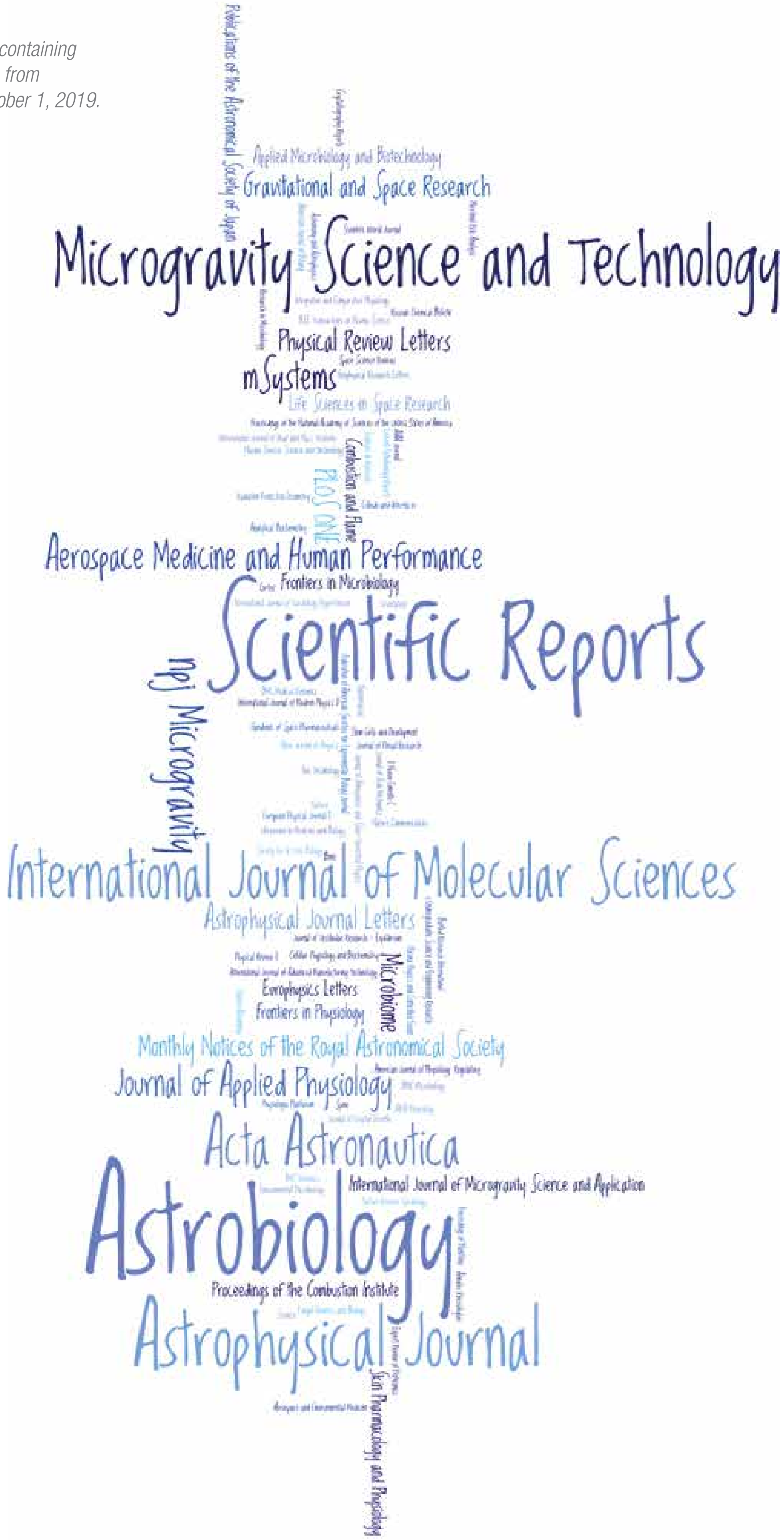
Because of how we understand habitat in urban environments, findings not only provide further information about the potential behavioral effects of nocturnal illumination, they also present important implications for urban design and policy, supporting calls to include analysis of artificial lighting in landscape ecology studies. Planners should consider not only the physical network of patches and corridors defining urban greenspace but also the "nocturnal network" formed by relatively dark areas in order to best support urban wildlife.

Schirmer AE, Gallemore C, Liu T, Magle S, DiNello E, Ahmed H, Gilday T. Mapping behaviorally relevant light pollution levels to improve urban habitat planning. Scientific Reports. *2019 August 15; 9(1): 11925. DOI: 10.1038/s41598-019-48118-z.*



CEO images of Chicago, IL, USA at night on (A) January 19, 2008, (B) January 31, 2012 and (C) October 9, 2013 (ISS16E024220, ISS30E061820, ISSE037E008303).

Word cloud of sources containing ISS results publications from October 1, 2018 – October 1, 2019.



ISS Research Results Publications

October 1, 2018 - October 1, 2019

(Listed by category and alphabetically by investigation.)

BIOLOGY AND BIOTECHNOLOGY

Advanced Plant Experiment -03 Transgenic Arabidopsis Gene Expression System Intracellular Signaling Architecture (APEX-03-2 TAGES-ISA) — Beisel NS, Noble J, Barbazuk WB, Paul AL, Ferl RJ. Spaceflight-induced alternative splicing during seedling development in *Arabidopsis thaliana*. *npj Microgravity.* 2019 3 April;5(9):5 pp. DOI: 10.1038/s41526-019-0070-7.

Advanced Plant Experiment -03 Transgenic Arabidopsis Gene Expression System Intracellular Signaling Architecture (APEX-03-2 TAGES-ISA) — Zhou M, Sng NJ, LeFrois CE, Paul AL, Ferl RJ. Epigenomics in an extraterrestrial environment: Organ-specific alteration of DNA methylation and gene expression elicited by spaceflight in *Arabidopsis thaliana*. *BMC Genomics*. 2019 March 12; 20(1): 205. DOI: 10.1186/s12864-019-5554-z.

Studies on gravity-controlled growth and development in plants using true microgravity conditions (Auxin Transport) — Kamada M, Oka M, Inoue R, Fujitaka Y, Miyamoto K, et al. Gravity-regulated localization of PsPIN1 is important for polar auxin transport in etiolated pea seedlings: Relevance to the International Space Station experiment. *Life Sciences in Space Research.* 2019 August; 22:29-37. DOI: 10.1016/j.lssr.2019.07.001.

Studies on gravity-controlled growth and development in plants using true microgravity conditions (Auxin Transport) — Miyamoto K, Inui A, Uheda E, Oka M, Kamada M, et al. Polar auxin transport is essential to maintain growth and development of etiolated pea and maize seedlings grown under 1 *g* conditions: Relevance to the international space station experiment. *Life Sciences in Space Research*. 2019 February;20:11 pp. DOI: 10.1016/j.lssr. 2018.11.001.

Biological Research In Canisters-17-1: Undifferentiated Cell development in Arabidopsis plants in Microgravity (BRIC-17-1) — Zupanska AK, LeFrois CE, Ferl RJ, Paul AL. HSFA2 functions in the physiological adaptation of undifferentiated plant cells to spaceflight. *International Journal of Molecular Sciences*. 2019 January;20(2):320. DOI: 10.3390/ijms20020390.

Biological Research In Canisters - 19 (BRIC-19) — Choi W, Barker RJ, Kim S, Swanson SJ, Gilroy S. Variation in the transcriptome of different ecotypes of *Arabidopsis thaliana* reveals signatures of oxidative stress in plant responses to spaceflight. *American Journal of Botany.* 2019 January;106(1):123-136. DOI: 10.1002/ajb2.1223.

Biological Research In Canisters - 21/ Biological Research In Canisters - 23 (BRIC-21/BRIC-23) — Morrison MD, Fajardo-Cavazos P, Nicholson WL. Comparison of *Bacillus subtilis* transcriptome profiles from two separate missions to the International Space Station. *npj Microgravity*. 2019 January 7;5(1):11 pp. DOI: 10.1038/s41526-018-0061-0.

Biological Research In Canisters - Natural Product under Microgravity (BRIC-NP) — Romsdahl J, Blachowicz A, Chiang AJ, Chiang Y, Masonjones S, et al. International Space Station conditions alter genomics, proteomics, and metabolomics in *Aspergillus nidulans*. *Applied Microbiology and Biotechnology*. 2018 December 12;103(3):1363-1377. DOI: 10.1007/s00253-018-9525-0.

Biological Research In Canisters - Natural Product under Microgravity (BRIC-NP) — Romsdahl J, Blachowicz A, Chiang AJ, Singh NK, Stajich JE, et al. Characterization of *Aspergillus niger* Isolated from the International Space Station. mSystems. 2018 October 30;3(5):e00112-18. DOI: 10.1128/mSystems.00112-18.

Influence of Factors of the Space Environment on the Condition of the System of Microorganisms-Hosts Relating to the Problem of Environmental Safety of Flight Techniques and Planetary Quarantine (Biorisk-KM-Metally and Biorisk-KM-Polimery) — Sobisch L, Rogowski KM, Fuchs J, Schmieder W, Vaishampayan A, et al. Biofilm Forming Antibiotic Resistant Gram-Positive Pathogens Isolated From Surfaces on the International Space Station. *Frontiers in Microbiology*. 2019 March 19;10(543):1-16. DOI: 10.3389/fmicb.2019.00543.

Functional Effects of Spaceflight on Cardiovascular Stem Cells (Cardiac Stem Cells) — Camberos V, Baio J, Bailey L, Hasaniya N, Lopez LV, Kearns-Jonker M. Effects of Spaceflight and Simulated Microgravity on YAP1 Expression in Cardiovascular Progenitors: Implications for Cell-Based Repair. *International Journal of Molecular Sciences*. 2019 June 4;20(11):2742.

Commercial Biomedical Testing Module: Effects of Osteoprotegerin on Bone Maintenance in Microgravity (CBTM) — Hammond TG, Allen PL, Birdsall HH. Effects of space flight on mouse liver versus kidney: Gene pathway analyses. *International Journal of Molecular Sciences*. 2018 December 18;19(12):12 pp. DOI: 10.3390/ijms19124106.

Commercial Biomedical Testing Module-3: Assessment of sclerostin antibody as a novel bone forming agent for prevention of spaceflight-induced skeletal fragility in mice/Commercial Biomedical Testing Module-3: STS-135 space flight's affects on vascular atrophy in the hind limbs of mice (CBTM-3-Sclerostin Antibody/CBTM-3-Vascular Atrophy) — Pecaut MJ, Mao XW, Bellinger DL, Jonscher KR, Stodieck LS, et al. Is spaceflight-induced immune dysfunction linked to systemic changes in metabolism? *PLOS ONE*. 2017 May 24;12(5):e0174174. DOI: 10.1371/journal.pone.0174174.*

Commercial Biomedical Testing Module-3: Assessment of sclerostin antibody as a novel bone forming agent for prevention of spaceflight-induced skeletal fragility in mice/Commercial Biomedical Testing Module-3: STS-135 space flight's affects on vascular atrophy in the hind limbs of mice (CBTM-3-Sclerostin Antibody/CBTM-3-Vascular Atrophy) — Mao XW, Sandberg LB, Gridley DS, Herrmann EC, Zhang G, et al. Proteomic analysis of mouse brain subjected to spaceflight. *International Journal of Molecular Sciences*. 2018 December 20; 20(1): 16 pp. DOI: 10.3390/ijms20010007.

European Technology Exposure Facility-Expose-Protect (EuTEF-Expose-Protect) — Chiang AJ, Mohan GB, Singh NK, Vaishampayan PA, Kalkum M, Venkateswaran K. Alteration of Proteomes in First-Generation Cultures of *Bacillus pumilus* Spores Exposed to Outer Space. *mSystems*. 2019 August 27; 4(4):e00195-19. DOI: 10.1128/mSystems.00195-19.

EXPOSE-R2-Biofilm Organisms Surfing Space (EXPOSE-R2-BOSS) — Panitz C, Frosler J, Wingender J, Flemming H, Rettberg P. Tolerances of *Deinococcus geothermalis* Biofilms and Planktonic Cells Exposed to Space and Simulated Martian Conditions in Low Earth Orbit for Almost Two Years. *Astrobiology*. 2019 March 29; 19(7):16 pp. DOI: 10.1089/ast.2018.1913.

Extremophiles — Mora M, Wink L, Kögler I, Mahnert A, Rettberg P, et al. Space Station conditions are selective but do not alter microbial characteristics relevant to human health. *Nature Communications*. 2019 September;10(1):3990. DOI: 10.1038/s41467-019-11682-z.

Investigation of the Osteoclastic and Osteoblastic Responses to Microgravity Using Goldfish Scales (Fish Scales) — Ikegame M, Hattori A, Tabata MJ, Kitamura K, Tabuchi Y, et al. Melatonin is a potential drug for the prevention of bone loss during space flight. *Journal of Pineal Research*. 2019 October;67(3):13 pp. DOI: 10.1111/jpi.12594.

Genes in Space-4 — Montague TG, Almansoori A, Gleason EJ, Copeland DS, Foley KD, et al. Gene expression studies using a miniaturized thermal cycler system on board the International Space Station. *PLOS ONE*. 2018 October 31;13(10):e0205852. DOI: 10.1371/journal.pone.0205852.

ISS Non-invasive Sample Investigation and results Transmission to ground with the Utmost easiness (In SITU) — Zangheri M, Mirasoli M, Guardigli M, Di Nardo F, Anfossi L, et al. Chemiluminescence-based biosensor for monitoring astronauts' health status during space missions: results from the International Space Station. *Biosensors and Bioelectronics*. 2019 March 15; 129:260-268. DOI: 10.1016/j.bios.2018.09.059.

International Space Station Internal Environments — Blaustein RA, McFarland AG, Maamar SB, Lopez A, Castro-Wallace SL, Hartmann EM. Pangenomic approach to understanding microbial adaptations within a model built environment, the International Space Station, relative to human hosts and soil. *mSystems*. 2019 February 26;4(1):e00281-18. DOI: 10.1128/mSystems.00281-18.

International Space Station Internal Environments — Singh NK, Bezdan D, Checinska Sielaff A, Wheeler K, Mason CE, Venkateswaran KJ. Multi-drug resistant *Enterobacter bugandensis* species isolated from the International Space Station and comparative genomic analyses with human pathogenic strains. *BMC Microbiology*. 2018 November 23;18(1):175. DOI: 10.1186/s12866-018-1325-2.

International Space Station Internal Environments — Boyajian B, Meyer ME. Characterization and analysis of aerosol particle retention and re-aerosolization from hook-and-loop fasteners on the International Space Station. *NASA Technical Memorandum*. 2018 October.

International Space Station Summary of Research Performed — Vaishampayan A, Grohmann E. Multi-resistant biofilm-forming pathogens on the International Space Station. *Journal of Biosciences*. 2019 September 21;44(5):125. DOI: 10.1007/s12038-019-9929-8.

International Space Station Summary of Research Performed — De Middeleer G, Leys N, Sas B, De Saeger S. Fungi and Mycotoxins in Space—A Review. *Astrobiology*. 2019 April 11;19(7):1-12. DOI: 10.1089/ast.2018.1854.

International Space Station Summary of Research Performed — Talburt ED, French AJ, Lopez DK, Polo SL, Boyko V, et al. Temporal RNA integrity analysis of archived spaceflight biological samples. *Gravitational and Space Research*. 2018 December 17;6(2):10 pp.

International Space Station Summary of Research Performed — Imura T, Nakagawa K, Kawahara Y, Yuge L. Stem Cell Culture in Microgravity and Its Application in Cell-Based Therapy. *Stem Cells and Development*. 2018 September 15; 27(18):1298-1302. DOI: 10.1089/scd.2017.0298.*

JAXA Mouse Habitat Unit (JAXA MHU) — Matsumura T, Noda T, Muratani M, Okada R, Yamane M, et al. Male mice, caged in the International Space Station for 35 days, sire healthy offspring. *Scientific Reports*. 2019 September 24;9(1):1-8. DOI: 10.1038/s41598-019-50128-w.

JAXA Mouse Habitat Unit (JAXA MHU) — Matsuda C, Kato T, Inoue-Suzuki S, Kikuchi J, Ohta T, et al. Dietary intervention of mice using an improved Multiple Artificial-gravity Research System (MARS) under artificial 1 *g*. *npj Microgravity*. 2019 July 8; 5(1): 16 pp. DOI: 10.1038/s41526-019-0077-0.

JAXA Mouse Habitat Unit (JAXA MHU)/Mouse Epigenetics — Horie K, Sasanuma H, Kudo T, Fujita S, Miyauchi M, et al. Down-regulation of GATA1-dependent erythrocyte-related genes in the spleens of mice exposed to a space travel. *Scientific Reports*. 2019 May 21; 9(1):7654. DOI: 10.1038/s41598-019-44067-9.

JAXA Mouse Habitat Unit (JAXA MHU) — Tominari T, Ichimaru R, Taniguchi K, Yumoto A, Shirakawa M, et al. Hypergravity and microgravity exhibited reversal effects on the bone and muscle mass in mice. *Scientific Reports*. 2019 April 29;9(1):6614. DOI: 10.1038/s41598-019-42829-z.

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State Space Corporation ROSCOSMOS (ROSCOSMOS)

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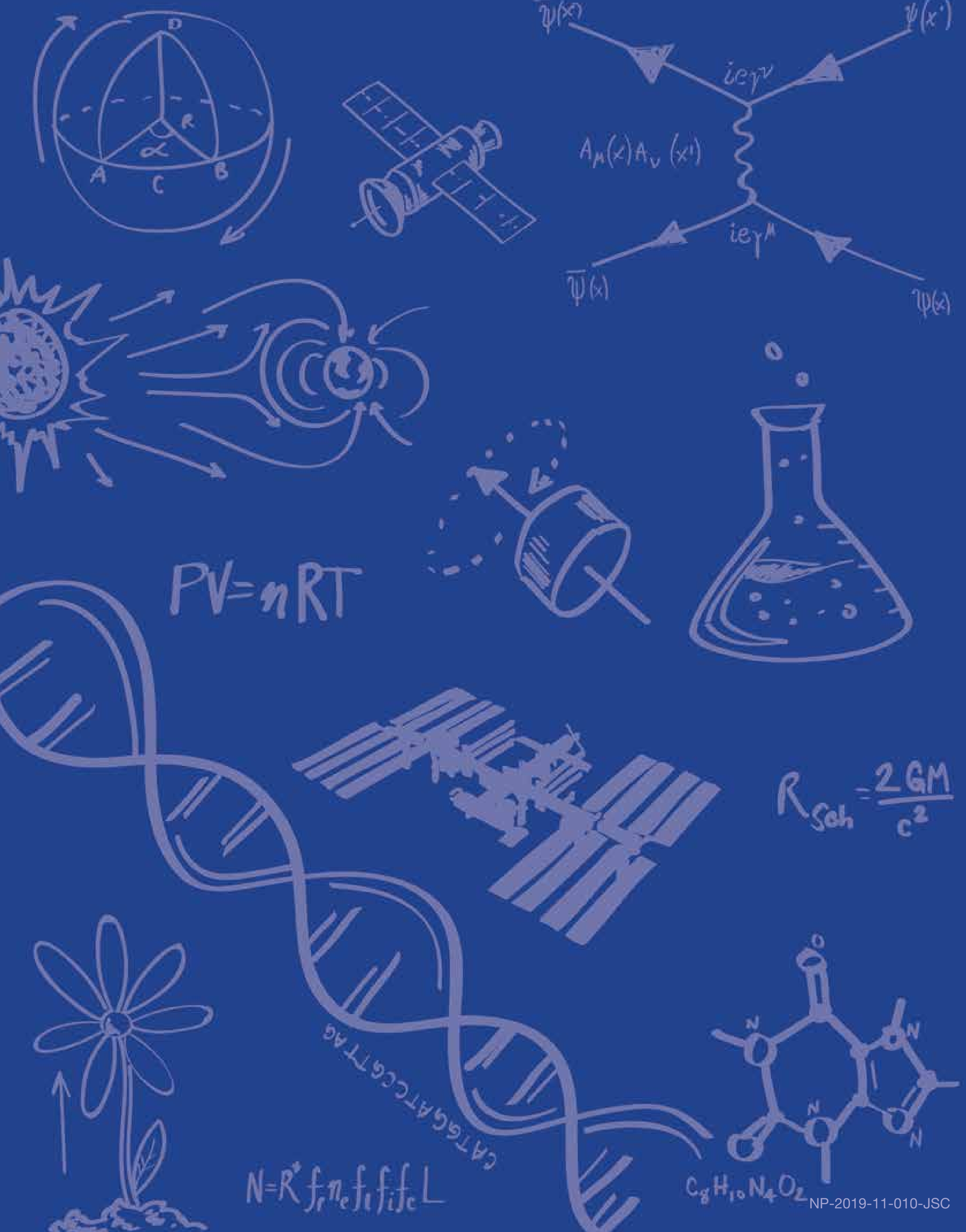

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