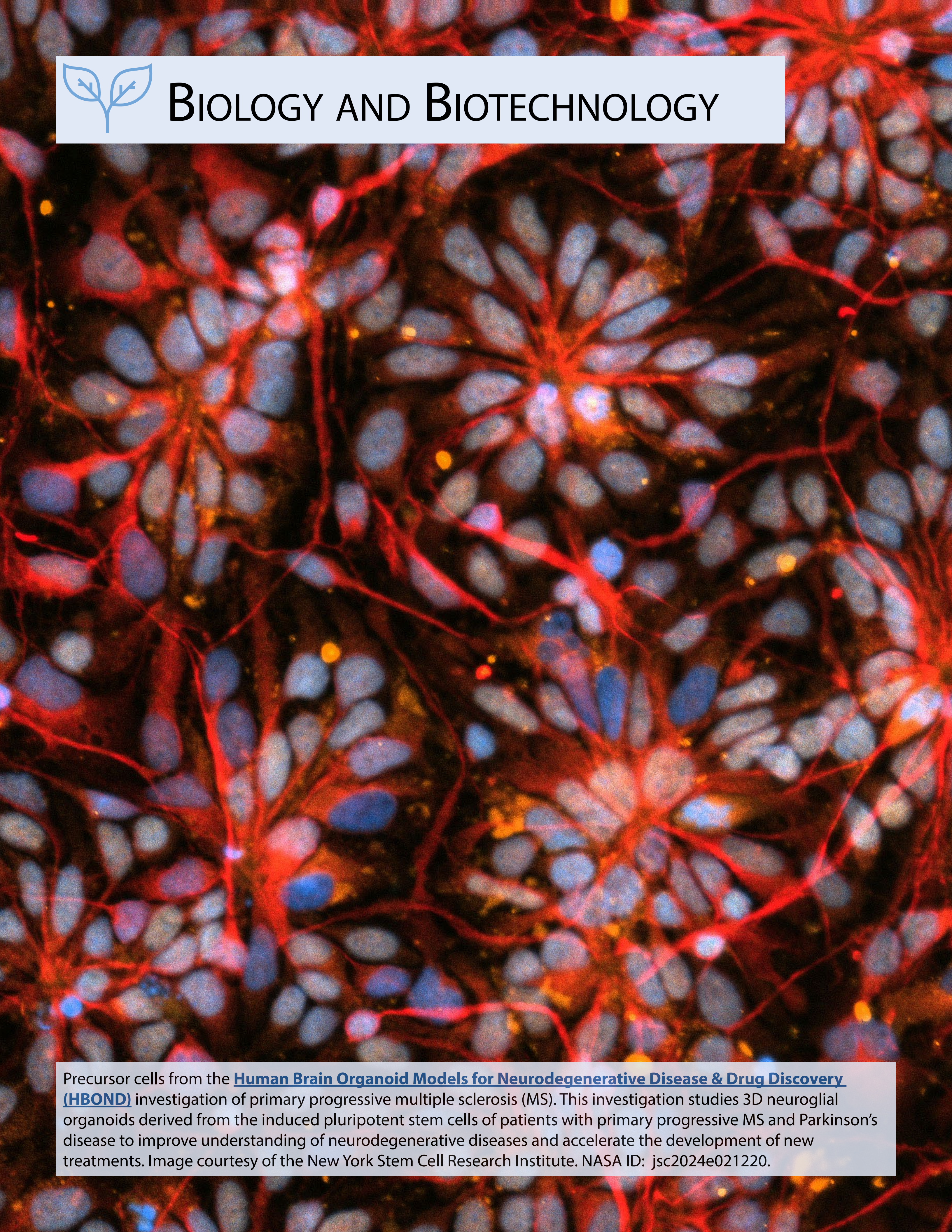
BIOLOGY AND BIOTECHNOLOGY



Precursor cells from the **Human Brain Organoid Models for Neurodegenerative Disease & Drug Discovery (HBOND)** investigation of primary progressive multiple sclerosis (MS). This investigation studies 3D neuroglial organoids derived from the induced pluripotent stem cells of patients with primary progressive MS and Parkinson's disease to improve understanding of neurodegenerative diseases and accelerate the development of new treatments. Image courtesy of the New York Stem Cell Research Institute. NASA ID: jsc2024e021220.

Highlights in Biology and Biotechnology

The space station laboratory provides a platform for investigations in the biological sciences that explore 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

Microgravity profoundly affects human physiology, causing conditions such as muscle atrophy and reduced bone density. The ESA investigation **Cytoskeleton**, which flew to station in March 2016, examined the molecular signals in mammalian cells sensitive to mechanical forces exerted in the environment to understand how proliferation, programmed cell death, gene expression, and cytoskeleton structure (i.e., interlinked protein filaments in the cell) react to microgravity.

In a new study published in *npj Microgravity*, researchers cultured a model of human bone cells (i.e., MG-63) for approximately 34 hours in the **BioLab incubator** along with control samples in 1g centrifuge[4]. Like primary human bone cells, MG-63 cells are responsive to mechanical loading, so they provide a suitable model for experimentation.

Researchers identified 24 regulatory pathways affected by microgravity. Among them were the cell proliferation and DNA repair pathways, which showed most genes downregulated. Other pathways associated with inflammation, cell stress, and iron-dependent cell-death showed most genes upregulated.

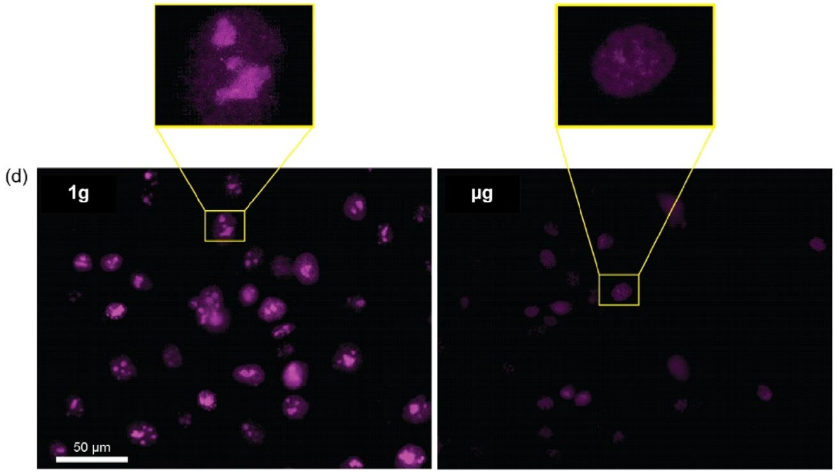


Figure 6. Immunoflourescent staining of cells in ground control (1g) and microgravity. Reduced proliferation is observed in microgravity cells. Reduced intensity of the stain indicates smaller nuclei size. *Image adopted from Garbacki, npj Microgravity.*

Complementary analyses showed a reduction in cell proliferation and nuclear size (Figure 6) as well as changes in chromatin organization and microtubule structure after exposure to microgravity. These alterations likely reflect cell cycle arrest that could lead to decreased DNA repair capacity and faster aging of the cell.

This new insight enhances the understanding of cell physiology and pathology and may assist the development of therapies to prevent Earth- and space-related health conditions affecting the musculoskeletal system, such as osteoporosis, skin atrophy, and excessive scar tissue in wound healing.

EXPLORATION

On long-term spaceflight missions, the risk to astronauts from space radiation increases. In the absence of Earth's atmosphere, protons and heavy ions from galactic cosmic rays increase the dose-equivalent rate of space radiation one hundred to three hundred times on station, potentially contributing to tumor progression in cancer, circulatory disease, and cognitive risks. The JAXA investigation **Study on the Effect of Space Environment to Embryonic Stem Cells to Their Development (Stem Cells)** examined how space radiation affects the development and DNA of embryonic mouse stem cells.

In a new study published in the *International Journal of Molecular Sciences,* researchers kept frozen wild-type and mutated embryonic stem cells missing the H2AX gene on station for over four years to measure the radiation doses absorbed and resulting biological effects [5] (Figure 7). The H2AX gene is known to play a role in DNA repair, so an H2AX-deficient stem cell is rendered unable to repair any DNA damage caused by radiation. Comparable ground control cells were irradiated with iron ion (Fe) particles using a medical accelerator. Upon return of the cells to Earth, researchers thawed and cultured the cells at different time intervals (0, 2, 8, 24, and 48 hours) to examine the expression profile over time. Then they conducted in-depth RNA-sequencing analyses to identify the genes that respond to DNA damage and those that regulate their expression.

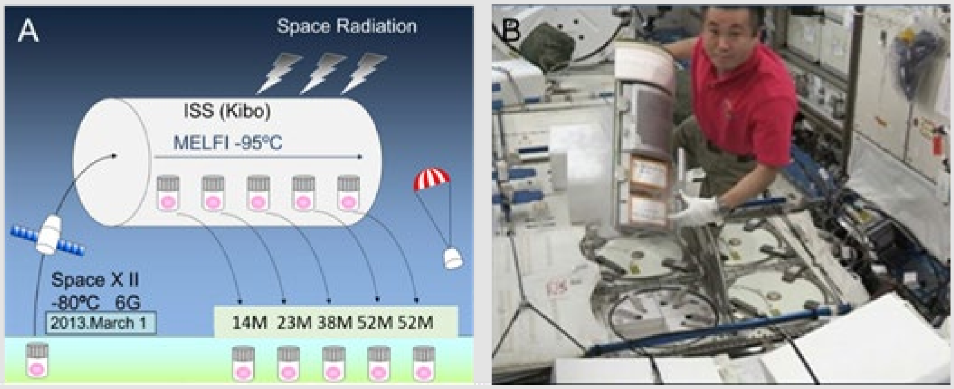


Figure 7. (A) The space experiment of "Stem cells". (B) Astronaut Koichi Wakata exchanging the dosimeter "PADLES", which was attached to the embryonic mouse stem cell package in the MELFI freezer. *Image provided by the Stem Cells research team.*

Researchers reported a total of 830 mSv of accumulated space radiation after four years and revealed more altered genes during longer incubation times (24 and 48 hours). Some of the genes increasingly expressed were involved in the degradation of the extracellular matrix and halting of early differentiation. The overall pattern of gene expression was similar across wild-type and H2AX-deficient cells, but the transcriptome profile of a few genes changed greatly in H2AX cells, and this alteration made them more sensitive to radiation.

Further analyses showed that space radiation enhances the expression of three genes (p21, Trp53inp1, and Mdm2) along with the activation of the protein p53. This protein appears to influence the expression of these genes by halting the erroneous proliferation of cells that form tumors. Researchers explained that the increased expression of these genes was not simply the result of being stored on station, but a direct consequence of space radiation as Fe ions.

This study demonstrates that longer exposure to radiation results in more modifications of repair proteins and the DNA damage caused by radiation has severe effects on the organism. This finding could help researchers identify the genes that respond to DNA damage and support development of ways to prevent cancers caused by radiation.

EXPLORATION

The NASA investigation [Advanced Plant Experiment-07 (APEX-07)](#) studies how multiple environmental differences associated with spaceflight affect the genetic expression of plants. Specifically, researchers are interested in investigating how processes controlled by RNA (e.g., turning genes on and off) are impacted by spaceflight in the roots and shoots of plants.

Previous research has shown that very short telomeres in humans can negatively impact health and longevity whereas hyper-long telomeres are a hallmark of cancer cells. Further study could help determine whether telomere length changes are reliable wellness indicators across different species.

In a study recently published in *Nature Communications*, researchers investigated the effects of spaceflight on plant telomeres, telomerase (the enzyme that synthesizes telomeres) and genome oxidation.[6] Arabidopsis thaliana, the model species for plant research, was grown on station for twelve days in the **Veggie** facility. Comparable Veggie conditions were used for the gravity control group on Earth, and a Random Positioning Machine (RPM) simulated microgravity on the ground.

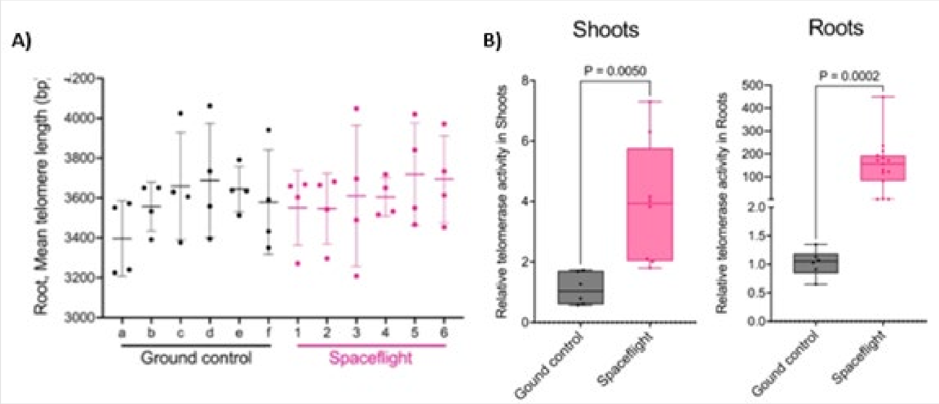


Figure 8. Charts showing average and unchanged telomere length during spaceflight (panel A) despite a significant increase in telomerase activity (panel B). *Charts adopted from Barcenilla, Nature Communications*.

After the samples were returned to Earth, biochemical analyses revealed that the shoots and roots of Arabidopsis seedlings grown in space retained their telomere length despite a significant increase in telomerase activity and genome oxidation. Similar findings in the ground control samples led researchers to conclude that the induction of telomerase activity was independent of telomere length (Figure 8). Notably, plants with increased telomerase activity exhibited decreased genome oxidation, suggesting a potential role for telomerase in redox biology.

These findings advance the understanding of plant survival mechanisms in space and may provide important clues for supporting food production on future exploration missions.

If you are interested in learning about plant growth facilities on station, how to execute plant experiments in space, and research sponsors, read our ***Researcher's Guide to: Plant Science****. This guide also includes a comprehensive review of plant science results detailing plant responses to environmental changes.*

Stem cells reproduce and differentiate into different cell types, and microgravity alters cell metabolism and function. The NASA investigation [Generation of Cardiomyocytes From Human Induced Pluripotent Stem Cell-derived Cardiac Progenitors Expanded in Microgravity (MVP Cell-03)], examined the effect of microgravity on the proliferation of cardiac progenitor cells, cells that originate from stem cells and await further specialization. Promising results in this fundamental research have direct impacts on drug development, disease modeling, and regenerative medicine applications.

DISCOVERY

In a recent study published in *npj Microgravity,* researchers cultured cardiac 3D human-induced pluripotent stem cells (HiPSC) on station for three weeks, and live cultures were returned to Earth for analysis.[7] A platform that included simulated Earth gravity on station allowed researchers to isolate gravity from radiation effects (Figure 9).

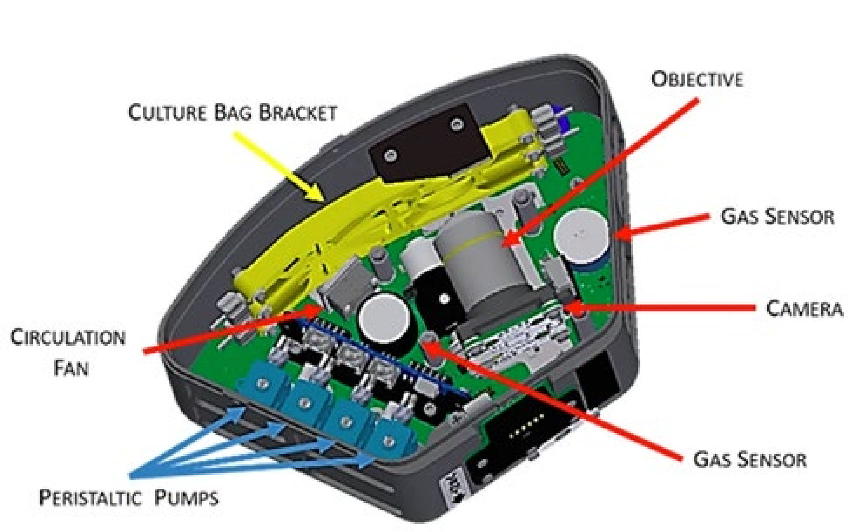


Figure 9. MVP Module on station. *Image adopted from Hwang, npj Microgravity.*

Initial RNA-sequencing analyses showed changes to gene expression, mostly upregulated genes associated with cell-division, differentiation, proliferation, as well as cardiac muscle tissue development and function. Additional analyses showed decreased expression of genes associated with extracellular matrix regulation, cardiac fibrosis, senescence, and apoptosis. Finally, comparing long-term exposure data to a previous study of cells exposed to microgravity for only three days,[8] researchers concluded that many of the improved properties and functions of cells are maintained in long-term cultures.

HiPSC-derived heart cells have potential for use in drug development and regenerative cell therapy, but such uses require large numbers of cells (heart repair, for example, requires an estimated 109 to 1010 cells per patient). Combining microgravity and tissue engineering could be a cost-effective way to increase the production of heart cells and may also generate cells with superior properties.

These findings of enhanced production of cardiac progenitor cells in space add to the research of cell proliferation in space that has been observed in bone marrow and adipose stem cells. Improvements to cell culture flight hardware, imaging systems, and other tools on station could help researchers test new hypotheses in the future.

DISCOVERY

The Roscosmos investigation **Studying the Features of the Growth and Development of Plants, and Technology for their Culturing in Spaceflight on the ISS RS (Rastenia-Pshenitsa (Plants-Wheat)** aims to understand the impact of spaceflight on plant growth and development. Uncovering genetic changes in plants after months of microgravity exposure informs the design and manufacturing of greenhouses for future space stations. Moreover, the production of high energy, low mass food sources in-flight reduces the need for continuous resupply and enhances crew members' independence in long distance space missions.

While extensive research has confirmed that leafy greens grown in space are equivalent to those grown on Earth, the quality of space-grown grain crops has not been determined. A new study published in *Plants* examines the quality of wheat grains grown in space, specifically super dwarf wheat species with a short life cycle.[9] Grain parameters included size, weight, and asymmetry of the kernels. Researchers hypothesized that increased asymmetry of the kernels could damage the composition of starch, impacting flour grade. Researchers used multiple imaging tools to measure the parameters of interest from wheat grains grown in space and on the ground. Some methods appeared more effective in assessing the asymmetry of the kernels.

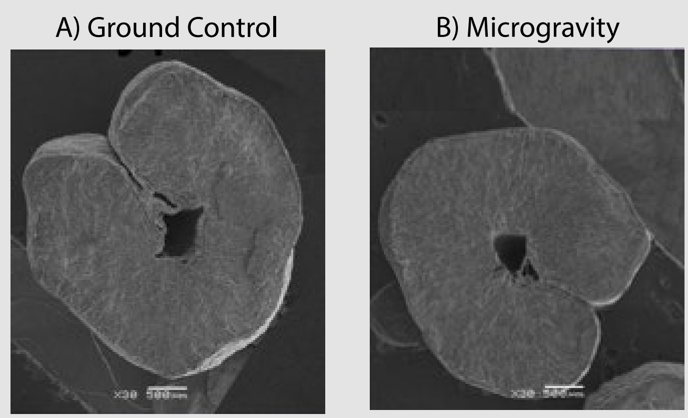


Figure 10. Kernel asymmetry compared between ground and space conditions. *Image adopted from Aniskina, Plants.*

Analyses conducted on Earth upon return of the samples showed that wheat grains produced in microgravity were smaller and had through-holes but were equally round as the kernels grown on Earth. Space-grown kernels also showed longer starch granules, which indicated low salt concentrations, changes in starch content, and inferior baking quality. Although small differences in asymmetry were identified within each separate group (i.e., changes between left/right or top/bottom parts of the kernels), there were no significant differences in asymmetry between wheat kernels grown in space and on the ground (Figure 10).

Researchers argue that if optimal conditions are artificially created in space (i.e., reduced water stress, hypoxia, gravity loss), then the quality of wheat grains and flour are likely to be the same as Earth grown wheat.

Growing plants on station serves as a source of food, in-situ production of pharmaceuticals, air regeneration, water recycling, and a haven for psychological well-being. These findings contribute to the advancement of space agriculture and the creation of sustainable closed-loop ecosystems.

References

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