Commercial astronauts shed light on flights' health impacts and create spaceflight atlas

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Crew members of the Inspiration4 mission, from left: Chris Sembroski, Sian Proctor, Jared Isaacman, and Haley Arseneaux. Credit: Inspiration4 crew

Short-term space travel causes many of the same molecular and physiologic changes as long-term space missions, but most reverse within months of returning to Earth. Yet, those changes that are longer-lasting and distinct between crew members reveal new targets for aerospace medicine and can guide new missions, according to the results of a massive international research endeavor by investigators at Weill Cornell Medicine, SpaceX, and other organizations.

Dr. Christopher Mason, the WorldQuant Professor of Genomics and Computational Biomedicine at Weill Cornell Medicine, led the Space Omics and Medical Atlas (SOMA) project with Dr. Afshin Beheshti of the Broad Institute and NASA. In total, more than 100 investigators from institutions in more than two dozen countries contributed to the project. Together, the collaborators increased the amount of human spaceflight data by 10-fold, including analyses of changes in gene expression, gene regulation, protein production, metabolism, and the microbes in the human body.

The results were published on June 11 as a 40-article collection in *Nature* journals and summarized in an overview paper.

The SOMA team, including co-corresponding author Dr. Cem Meydan, an assistant professor of computational biology research in medicine at Weill Cornell Medicine, also has compiled more than 75 billion genetic sequences in an interactive atlas accessible to other researchers, and Weill Cornell Medicine will host a repository for nearly 3,000 biological samples from the studies. Dr. Mason's team has already begun collecting samples from other missions and forged several new international collaborations to harmonize efforts for spaceflight research.

"This is the largest treasure trove of data from astronauts and space biology ever released," Dr. said Mason, who is also a professor of physiology and biophysics, a professor of neuroscience in the Feil Family Brain and Mind Research Institute, member of the Sandra and Edward Meyer Cancer Center, and director of the WorldQuant Initiative for Quantitative Prediction at Weill Cornell Medicine. "We hope that sharing the data will help accelerate discoveries on the health impacts of space flight and yield fundamental discoveries on human health overall."

Commercial astronauts

When the Inspiration4 mission launched on September 16, 2021, with the first all-civilian, four-person crew for a three-day flight to low-Earth orbit, it provided an unprecedented opportunity for science. Before the mission, most data on the health impacts of space travel had been collected by government-sponsored space agencies from carefully selected and highly trained astronauts, but it was unclear if such data collected from the astronauts would apply more widely to the public; the Inspiration4 mission provided an opportunity to find out.

Dr. Mason served as the principal investigator for the Inspiration4 mission's work on clinical profiles of the crew, multi-omics research and biobanking. Crew members collected biological samples before, during, and after the flight and gave researchers full access to study and share their data. They also conducted a battery of experiments midflight, including the first-ever direct RNA sequencing and biopsied skin from astronauts. Drs. David Lyden, Richard Granstein, and Ari Melnick at Weill Cornell Medicine, and Dr. Iwijn De Vlaminck, at Cornell's Ithaca campus, also contributed to the project.

The new data was compared with that collected from previous flights, in particular, the NASA Twins Study, for which Dr. Mason was also a principal investigator. That endeavor analyzed data from astronaut Scott Kelly during and after his one-year mission on the International Space Station in 2015-2016 and found that longer space flights contribute to significant changes in gene expression in the blood, particularly in the immune system and DNA repair systems. New data from Dr. Jiwoon Park showed these differences also appeared in the skin.

The Inspiration4 data showed that many of the same changes also occurred in short-term space travelers. For example, Dr. Mason published a study with Dr. Susan Bailey showing that the telomeres, which cap the ends of chromosomes, began lengthening even during the 3-day Inspiration4 mission. They also saw similar immune system changes, with a spike in anti-inflammatory proteins called cytokines in the astronauts after their return to gravity.

Immune system alterations

The cytokine spike after reentry was one of several immune system changes documented by Weill Cornell Medicine investigators. Single-cell genetic sequencing, led by Dr. JangKeun Kim and Dr. Braden Tierney, research associates in the Mason lab, helped the scientists identify immune cells called T cells and CD16 monocytes as the cells most responsive to the stresses of spaceflight. These immune first responders undergo dramatic changes in gene expression and changes in chromatin that regulate gene expression.

"The immune system is primed for a fight, but it doesn't yet know what it is fighting," Dr. Mason said. He noted that the space travelers' exposure to low-dose radiation may trigger this immune response, as well as the telomere changes.

While some parts of the immune system ramp up, others ramp down. For example, travelers experience reduced expression of genes that encode immune system proteins called human leukocyte antigens, which help the body identify viruses and other invaders. This discovery may explain why about half of space travelers and astronauts experienced reactivation of old viral infections like the herpes simplex virus-1, a primarily benign virus that causes cold sores.

Another study, led by Nadia Houerbi and Irina Matei, a graduate student in the Mason lab and postdoctoral fellow in the Lyden lab, respectively, found evidence of brain proteins in the blood of the Inspiration4 space travelers as well as the blood of six Japanese astronauts and Scott Kelly. The discovery suggests some disruption in the blood-brain barrier, which protects the brain from invasion by immune cells. Samples from mouse studies from Xiao (Vivian) Mao at Loma Linda University confirmed that spaceflight perturbed the blood-brain barrier function.

"It is nothing worrisome, but it was surprising, and worth keeping an eye on in future missions," Dr. Mason said.

Though the Inspiration4 crew experienced many of the same changes as longer-term space travelers, they recovered quickly after the flight. Dr. Mason noted that within six months, the crew's biology had returned to its preflight state for more than 95% of the proteins, chromatin states and genes, including RNA modifications measured by Kirill Grigorev and Theodore Nelson, researchers in the Mason Lab.

'Second Space Age' and Aerospace Medicine Biobank

The findings provide much fodder for future studies. Despite having data on a small number of space travelers, the SOMA researchers detected a few differences in men and women, leveraging data from Dr. Min Yu at University of Maryland. For example, female space travelers return to their preflight states more quickly after returning to Earth, yet some cytokines stayed elevated in the women longer than men and were confirmed across 64 other astronauts. Individual physiologic responses to space travel also varied, and genes related to drug processing (called pharmacogenomics) were also distinct.

"We might have to personalize medications and other countermeasures for different crew members based on their individual responses to space flight," said lead and co-corresponding author of the SOMA study overview Dr. Eliah Overbey, a research associate in Dr. Mason's lab during the study, who is now starting her own lab on Bioastronautics at the University of Austin.

Making the atlas and biobank accessible to more scientists may help accelerate the pace of discovery on the impacts of spaceflight and its parallels with aging, chronic diseases and immune system disorders, according to Dr. Overbey. She noted that space travel mimics some of the effects of aging, such as bone and muscle loss, and may provide a way to test medications to counteract these changes.

"Opening up the data to the whole scientific community increases our ability to make connections between space-related changes and human health more generally," she said.

Dr. Overbey also suggested that the growing number of commercial spaceflights and crews may help expand the dataset and increase its power to detect smaller differences.

"We are entering a new space age," Dr. Mason said. "We have more data and more space launches than ever before, and we will need all possible biomedical data to make precision medicine for future crews a reality and to prepare for longer missions to the moon and Mars."

Participating institutions included the Japanese Aerospace Exploration Agency (JAXA); the European Space Agency; the National Aeronautics and Space Administration (NASA); and SpaceX, a company offering commercial spaceflight missions.

More information: Eliah G. Overbey et al, The Space Omics and Medical Atlas (SOMA) and international astronaut biobank, *Nature* (2024). DOI: 10.1038/s41586-024-07639-y