Fruit flies reveal new insights into space travel's effect on the heart

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Scientist holds fruit fly vial next to box sent to ISS. Credit: Sanford Burnham Prebys Medical Discovery Institute

Scientists at Sanford Burnham Prebys Medical Discovery Institute have shown that fruit flies that spent several weeks on the International Space Station (ISS)—about half of their lives—experienced profound structural and biochemical changes to their hearts. The study, published today in *Cell Reports*, suggests that astronauts who spend a lengthy

amount of time in space—which would be required for formation of a moon colony or travel to distant Mars—could suffer similar effects and may benefit from protective measures to keep their hearts healthy. The research also revealed new insights that could one day help people on Earth who are on long-term bed rest or living with heart disease.

"For the first time, we can see the cellular and molecular changes that may underlie the heart conditions seen in astronaut studies," says Karen Ocorr, Ph.D., assistant professor in the Development, Aging and Regeneration Program at Sanford Burnham Prebys and co-senior author of the study. "We initiated this study to understand the effects of microgravity on the heart, and now we have a roadmap we can use to start to develop strategies to keep astronaut hearts strong and healthy."

Past studies have shown that under microgravity conditions, the human heart shifts from an oval to a more spherical shape. Space flight also causes the heart muscle to weaken (atrophy), reducing its ability to pump blood throughout the body. However, until now, human heart studies—completed using ultrasounds performed on the ISS—have been limited to a relatively small number of astronauts. While important, these studies didn't reveal the cellular and molecular changes that drive these transformations—information needed to develop countermeasures that will keep astronauts safe on prolonged flights.

"As we continue our work to establish a colony on the moon and send the first astronauts to Mars, understanding the effects of extended time in microgravity on the human body is imperative," says Sharmila Bhattacharya, Ph.D., senior scientist at NASA and a study author. "Today's results show that microgravity can have dramatic effects on the heart, suggesting that medical intervention may be needed for long-duration space travel, and point to several directions for therapeutic development."

Fruit flies are surprisingly good models for studying the human heart. The insects share nearly 75% of disease-causing genes found in humans, and their tube-shaped hearts mirror an early version of ours—which begins as a tube when we're in the womb and later folds into the four chambers with which we're familiar. Fortunately, fruit flies are also largely self-sustaining. All the food the flies needed for the duration of the trip were contained in special boxes designed for this study—allowing busy astronauts to focus on other tasks.

Journey to space

In the study, the scientists sent the special "vented fly boxes" containing vials filled with a few female and male fruit flies to the ISS for a one-month-long orbit. While in space, these flies produced hundreds of babies that experienced three weeks of microgravity—the human equivalent of three decades. The fruit flies that were born in space returned to Earth via a splashdown off the coast of Baja California. A member of the scientific team retrieved the flies from the Port of Long Beach and—very carefully—drove the specimens to Sanford Burnham Prebys' campus in La Jolla, California.

Once the flies arrived at the lab, the scientists sprang into action. Tests of heart function had to be taken within 24 hours of the return to Earth so gravity wouldn't interfere with the results. The researchers worked around the clock to measure the flies'

ability to climb up a test tube; to capture videos of the beating hearts to measure contractility and heart rate; and to preserve tissue for future genetic and biochemical assays, including mapping gene expression changes that occurred in the heart.

Extensive tissue remodeling

This work revealed that the space flies had smaller hearts that were less contractile—reducing their ability to pump blood and mirroring symptoms seen in astronauts. The heart tissue also underwent extensive remodeling. For example, the normally parallel muscle fibers became misaligned and lost contact with the surrounding fibrous structures that permit the heart to generate force—resulting in impaired pumping.

"In the normal fly heart, the muscle fibers work like your fingers when they squeeze a tube of toothpaste. In the space flies, the contraction was like trying to get toothpaste out by pressing down instead of squeezing," explains Ocorr. "For humans, this could become a big problem."

To the scientists' surprise, the fibrous extracellular matrix (ECM) surrounding the heart of the space flies was significantly reduced. After a heart injury such as a heart attack, this supportive tissue is often overproduced and interferes with heart function. For this reason, the interplay between the ECM and the heart is an active area of research for heart scientists.

"We were very excited to find several ECM-interacting proteins that were dysregulated in the space flies," says Rolf Bodmer, Ph.D., director and professor in the Development, Aging and Regeneration Program at Sanford Burnham Prebys and co-senior author of the study. "These proteins weren't previously on the radar of heart researchers, so this could accelerate the development of therapies that improve heart function by reducing fibrosis."

The tip of the iceberg

Ocorr and Bodmer are still busy analyzing genetic and molecular data from this study and believe these insights are the "tip of the iceberg" for this type of research. Vision problems are common in astronauts, so the scientists are also analyzing eye tissue from the space flies. Another area

of interest relates to the babies of the flies that were born in space, which would help reveal any inherited effects of space flight. While astronaut health is the primary goal, people on Earth may ultimately be the greatest beneficiaries of this pioneering work.

"I am confident that heart disease research is going to benefit from the insights we're gaining from these flights," says Ocorr. "Understanding how the heart functions in space is also going to teach us more about how the heart works and can break on Earth."

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