Space twins: Scott Kelly's one-year space mission could yield genetic bounty

Twins in space? For millennia, that was possible only in Greek mythology, when Zeus placed his sons Castor and Polydeuces in the sky, forming the constellation *Gemini*. Then, in the mid 1960s, NASA launched the *Gemini* program— the first time that American astronauts flew two at a time in the same space capsule.

NASA's astronaut corps now includes a pair of real-life, identical twins: Scott and Mark Kelly—and they are in space (one of them, at least). A Russian *Soyuz* spacecraft lifted off (UTC 19:42 March 27) from the Baikonur Cosmodrome, in Kazakistan, and delivered Scott Kelly, and his crewmate cosmonaut Mikhail Kornienko, to the International Space Station (ISS) where they will live for a full year.

During that time, Mark will remain on Earth and the genomes of the two brothers will be analyzed to assess how space travel affects different genes. Various medical studies will be conducted on both brothers. The results could tell us a lot about how the human body works in space, and how it responds to radiation and to other stresses anywhere, but that's only if the results are ever published. Should the genetic analysis reveal anything negative, or something that the family might want to keep private, either brother could veto release of the information.

Meet the twins

Scott Kelly is not new to long-duration space flight. From his experience on space shuttle, *Soyuz*, and especially ISS missions, he's already logged roughly a half a year in space. By sending astronauts to ISS for long periods, NASA, the Russian Federal Space Agency (Roscosmos), and other space agencies hope to learn enough about human physiology in space to keep space travelers healthy and productive during upcoming missions through deep space, including an eventual mission to Mars. But having a pair of twins to study is a bonus, since people react and adapt differently to the stresses that spaceflight puts on virtually all body systems. It's important to know how big a role genetics plays in how spaceflight affects the body. The best way to do this is to take people with same genome –in other words, identical twins– and look at them in and out of the spaceflight environment. During the one-year mission, this can be achieved by leaving Mark Kelly on Earth and carrying out the same scientific studies on him and his orbiting brother.

Mark Kelly retired from NASA in 2011 after his wife, Congresswoman Gabrielle Giffords, was shot in Arizona. Since that time, he has been helping with her recovery, while also advocating for gun control and for a strong space program. Now, functioning as the "ground control twin", he'll be almost as busy as his brother with medical tests. Pretty much everything that Scott will be doing in orbit, Mark will be doing on the ground. They'll duplicate one another's exercise, sleep cycles, and keep track of what they eat. Additionally, they both have provided numerous samples of just about everything that comes out of, or can be sampled from, the human body (blood, urine, saliva, feces, etc), and this will continue throughout the mission and after it.

The study

Some key questions that the medical and genetic studies of the one-year mission are designed to answer include the following:

1. How do weightlessness, space radiation, and other factors of spaceflight (such as living in an enclosed structure with just a few other people) affect the immune system? Evidence from astronauts on shorter missions and from studies on laboratory animals suggest that an immune function called T-cell response could be affected in a negative way, putting astronauts at risk for debilitating infectious diseases, such as tuberculosis.
2. How do those same factors affect the heart and blood vessels? In particular, scientists want to know if spending such a long time in space might increase the risk for atherosclerosis. That's a common blood vessel condition on Earth that leads to heart attacks and strokes.
3. How are the microorganisms of the gut affected? In each human being, bacteria cells that inhabit the body actually outnumber human cells ten to one. The intestinal bacteria (which live mostly in the large intestine) comprise just one of several microbial communities in the body, but it's the biggest community, and it has a major impact on the health of the human host. Thus, increasingly, gut microbiology has been a subject of space medicine research.
4. Which exercises are most helpful during space flight? Because of weightlessness, astronauts are prone to osteoporosis. Bones demineralize; they lose the mineral content (called hydroxyapatite: $Ca_{10}(PO_4)_6(OH)_2$) that keeps them hard. For each month in weightlessness, space travelers lose 1-2 percent of their bone mineral. Loss of the mineral from the bone puts the space travelers at risk for kidney stones, because the mineral concentrates in the urine. After a very long mission, the bone loss can have lasting effects for astronauts back on Earth, but the bigger concern is what would happen to astronauts arriving on Mars with weak bones. The worst part of the story is that certain bones lose more mineral than other bones. The hip bone in particular is at great risk. Should an astronaut fracture a hip while on Mars, it could have fatal consequences. For this reason, exercise must be optimized to keep strong the hip and other weight bearing bones. To keep bones strong, muscles also must be maintained. Like bone, muscles weaken in weightlessness, especially muscles that maintain posture on Earth. Finally, exercise also must be optimized to keep the heart in good health, since the heart too undergoes changes due to weightlessness.
5. How does spaceflight affect the eyes? You might not think of eyes as parts of the body vulnerable to spaceflight, but they are. That's because weightlessness changes the shape of the eye. Also, in space there is ultraviolet radiation from the sun, which puts astronauts at risk for cataracts.
6. How does very long duration spaceflight affect mental health? You probably did think of this one. But what you may not know is that NASA and Roscosmos are both extremely worried about it. On rare occasions, people working at science bases in Antarctica have broken down mentally and gotten violent with their peers. It's never happened on a spacecraft, but, considering the controls of a spacecraft and the vulnerability of the crew to the outside environment, it's obvious why it must be avoided.

Most of the studies related to the questions outlined above will make use of samples from blood and other body fluids. Along with the astronauts' samples come all of their genes. The entire genome of both

brothers is being sequenced. In addition to tracking physiologic changes in all body systems, scientists will compare changes in genes, such as which genes are turned on or off, before, after, and at different points during the mission.

“This study represents the most comprehensive molecular profile that has ever been made of any human being,” according to geneticist Christopher Mason of the Weill Cornell Medical College in New York. “And it’s twins.”

Comprehensive and expensive. With a price tag of $1.5 million, it’s a pretty costly study for just one set of twins. But, of course, that amount of money is small compared with the cost of the space mission. The cost is very justifiable, so long as the potential scientific value of the study is great. Is it?

Useful study or hype?

Back in 1998, NASA sent former astronaut Senator John Glenn on a space shuttle flight when he was 77 years old. The rationale was based on the fact that certain aspects of space flight –especially weightlessness, which promotes osteoporosis and is associated with shortened telomeres (the tips of the DNA strands of chromosomes)– mimic the aging process on human cells. By comparing Glenn’s test results during the 1998 mission with results from when he had flown in space at age 41, and with blood samples frozen since his early NASA days, the idea was that scientists could learn something about aging and disease.

But the rationale was criticized on two grounds. First, Glenn was in much better physical shape than the average 77 year-old. Second, there was only one of him and in science one subject alone does not usually provide much useful information. Glenn defended the rationale based on the idea that NASA would eventually send more older people into space, and this could still happen, but probably not for a very long time. Does similar criticism apply to the Kelly twins? Will the results of the one-year mission experiments be of limited use, until a few dozen or more sets of twins become astronauts?

According to Northwestern University neurobiologist Martha Vitaterna, the answer is no. With the one-year mission, even though it involves just one pair of twins, the potential to obtain useful data is enormous, because of the long-period of time in space. “That gives us a lot more power [than the the Glenn mission] ”, Vitaterna says, and she is not the only researcher who thinks this way.

“We’re going to look before, during and after flight,” says Susan Bailey of Colorado State University. She studies radiation effects, a major issue when it comes to humans in space, and her research team will be looking at telomere length in white blood cells. Telomeres are thought to shorten with aging, but non-human animal studies and cell culture studies conducted on earlier space missions suggest that spaceflight also shortens telomeres. Thus, Bailey predicts that Scott’s telomeres will shorten faster than Mark’s telomeres during the one-year mission. “In the end, we will have good enough numbers that we’ll be able to make some statistically significant conclusions.”

Because the studies will reveal how different genes affect health in spaceflight, it may have big implications for other astronauts. Suppose, for example, that having a certain gene makes an astronaut

particularly susceptible to space radiation. Such a finding could lead to screening for that gene in order to eliminate radiation-sensitive individuals from the astronaut corps, or from certain space missions. Or, it could lead to a system in which certain astronauts can fly only on a limited number of missions and then must retire. On the other hand, it's possible that genes could be discovered that make certain humans particularly robust to space radiation. Such individuals might be particularly good candidates for long space missions.

If you're wondering whether it's a problem that the ground subject, Mark, has been on space missions in the past, it's not. "In many ways [Mark's] experience in space is different than mine," Scott explains. While Mark flew on four space shuttle missions, they were fairly short, giving him a lifetime total of only 54 days in space compared with Scott's half year, which is now set to triple. "He's never been there long enough to adapt and feel close to normal, which I have," In other words, the twins will differ substantially in terms of long-duration space flight exposure, the very condition the researchers want to study.

Genetic privacy

Throughout the course of the study, both brothers are receiving genetic counseling and are learning about potential implications of the genetic findings. Only ten researchers will have access to the genomic information. However, no study using the genomic data can be published, unless both twins give their consent. Both brothers are highly motivated to contribute to medical advances on Earth and specifically to space medicine. Both are aware that future decisions to send a human crew on a Mars mission may depend on the success of this one-year study. But, as we've discussed previously on this blog, once available, genetic data may end up on-line for all to see, possibly affecting the families, and even the descendants, of those who supplied the samples. The genetic privacy article cited in the previous sentence is also being cited by space publications in connection with Kelly's one-year mission. So, while the one-year mission may reveal a lot about the effects of gravity on our cells and bodies, the gravity of the privacy issue cannot be ignored. Whatever the Kelly twins decide, the implications could be as long-lasting as the Greek story of the Gemini.

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