Getting humans to Mars may rely on space twins, astronaut roundworms, and epigenetics

> By the mid-2030s, I believe we can send humans to orbit Mars and return them safely to Earth. And a landing on Mars will follow. And I expect to be around to see it.

This President Obama line from a 2010 speech was reminiscent of President Kennedy's bold commitment in 1961 that America should commit itself to putting a man on the moon by the end of the decade. Although JFK would not live to see it, the US did famously achieved his dream when Neil Armstrong walked onto the moon on July 20, 1969.

But putting an American on Mars during Obama's lifetime may require an even bigger technological leap forward for mankind. Mainly because the journey to Mars will require a human to be in space a lot longer than the 8 days of the Apollo 11 team. Mars One, which is working to put a human settlement on Mars, estimates a one way the trip to the red planet would take 6-8 months. Which begs the question: could a human survive a trip in outer space lasting as long as 2 years?

For decades, NASA has been studying the impact of long term exposure to outer space on the human body and identified a number of likely detrimental affects on the human body—muscle and bone loss, immune disfunction, depression. To send someone to space for a trip to Mars, NASA will need to know not only what these affects are, but how they occur and hopefully how to reverse or prevent them. One idea that has received a great deal of attention from scientists is that studying epigenetics may be the key to understanding how our physiology changes in response to space. To this end, two new projects have put epigenetics at the forefront of space research.

Epigenetics is not a new field of study; its origins go back to at least the 1930's. But in the last decade it has received renewed attention. Scientists have found that environmental triggers—like diet and stress or in this case possibly space travel—could induce physical, heritable changes to our DNA that lead to alterations in the way genes behave without actually changing the DNA sequence (a change in sequence is a mutation). These epigenetic changes might help explain why identical twins, accumulate small difference over time in the way they look despite having the same genome.

NASA has chosen to study the differences in epigenetics between a set of space twins: Mark and Scott Kelly. The Kelly brothers are the only siblings to have been to space, although Mark retired after a flight in 2011. For this study, Scott was sent to the International Space Station (ISS) for almost a year—from March 27, 2015 to March 3, 2016, while Mark stayed earthbound.

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> Nasas-twin-astronauts-Sco-009
> Scott (left) and Mark (right)

Before he left though, NASA chose ten studies for the twins to participate in, using Scott as the 'experimental human' and Mark as the control. Two of the ten studies are directly looking at epigenetic processes, while an additional four fall under the broader category of gene behavior. The studies on the Kelly brothers will provide scientists with a first look at how Scott's body responded to the environmental pressures that affect a body in space—e.g., zero gravity, higher levels of radiation—and compare those changes to Mark's earthly physiology. While these studies will only have a sample size of one, they will provide scientists an important insight on how the environment of space influences a person's physiology and their epigenetics, independent of genetics.

In the year, they spent 220 miles apart, Scott and Mark, with identical genes, were exposed to entirely different environments. Scientists believe any changes they find in Scott might be due to epigenetic changes that his cells made in response to being in space. The experiments will help address epigenetics questions such as how aging is affected by epigenetics and space, what effect radiation has on the epigenome (the collection of all epigenetic marks on the genome), and how epigenetics might affect circadian rhythms in space.

But NASA's twin study isn't the only recent project to look at epigenetics in the final frontier. In July of 2015, the first winner of the contest *Genes in Space* was announced as 16 year-old Anna-Sophia Boguraev for her proposal to study the epigenetic changes in response to space of the immune system. The contest, sponsored by Boeing, Math for America, The Center for the Advancement of Science in Space, miniPCR and New England Bio Labs, Inc., is, "for students in grades 7 through 12 to design an experiment to solve a real-life space exploration problem through DNA analysis."

Boguraev's project launched to ISS on April 8, 2016 and it will study methylation in immune cells, which is a process by which small molecules are added to the DNA double-helix that silences, or even shuts off, the activity of a gene. The experiment will look at the methylation of genes important for the activity and signaling of helper T cells (Th). She said of her project:

> Given that methylation is affected in space, and these genes are controlled by methylation, aberrant methylation could be related to the immune defects that we often see in astronauts in space, such as a suppressed immune system and a shift toward Th2 dominance.

Part of her project is also to assess the viability of DNA and methylation detection kits that were engineered to work specifically in space. If these kits do work, they could be used as important diagnostic tools to monitor astronauts health on the long journey to Mars. If a relationship between methylation (or epigenetics in general) and immune system deterioration can be established, these kits would could be used to pinpoint when an astronaut's immune system is in danger.

One small step for roundworms…

This is not the first time epigenetic changes will be studied on organisms in space. The roundworm preceded humans. The effects of space flight on the soil dwelling, non-parastic nematode *Caenorhabditis elegans* have been studied a few times over the past decade. During the course of these studies, scientists got their first indication that space flight can induce changes in gene activity, particularly in genes that are involved with muscle protein and metabolism. Scientists also found that epigenetic enzymes involved with the silencing of genes were hyperactive during space flight.

C. elegans is a model organism for molecular and developmental biology

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C. elegans is a model organism for molecular and developmental biology

Taken together, these results could indicate that microgravity causes cells to make epigenetic changes. In humans this could explain things like why astronauts experience difficulty in maintaining muscle and bone mass in space. Scott and Mark will also be examined for these type of changes.

But studying epigenetics in space is not just about advancing the possibility of sending humans to Mars. These studies, much like most NASA studies, have important implications for terrestrial humans too. Bone and muscle weakness and/or loss is a significant problem in human health, particularly for our elderly population. We are faced with a health crisis further exacerbated by the fact that humans are living longer lives than ever before. We are in need of new strategies and therapies to help an ever-expanding population of centenarians; studying the epigenetics of muscle loss in space could allow scientists to gain new insights into how muscle damage or weakness progresses and how to treat it.

It may take some time before we get the data from the experiments on Scott and Mark and the work by Boguraev, but roundworm studies suggest there are many epigenetic changes that occur in response to space travel. This means we may soon be learning a lot more about how our genes behave, both on planet earth and when we are traveling a little closer to the stars.

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