Is telomere shortening reversible? A clue from NASA's twins mission

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INTRODUCTION

Humans have been traveling to space since 1961 and the number is continuously increasing (https://www.nasa.gov/mission_pages/shuttle/sts1/gagarin_anniversary.html). Human space programs are recorded in a huge number (326), but the long duration space missions (>300 days) can be counted on fingers. Most developed space agencies or private bodies are in the queue of taking humans into deep space, so they are continuously sending their astronauts to study the duration impacts on the human body. Space environmental studies point out several factors that can be harsh on the human body; for example, the confinement, isolation, and environmental stressors such as microgravity, radiation, and noise (https://www.nasa.gov/sites/default/files/files/NP-2015-03-015-JSC_Space_Environment-ISS-Mini-Book-2015-508.pdf).

In such a key study, monozygotic twins, astronauts Mark and Scott participated in NASA's human space program which lasted more than 300 days (Fig. 1). Mark is on observation on the Earth and Scott has been sent to the International Space Station onboard. This study revealed multiple dynamic impacts on the human body and some surprising facts about the body adaptability and recovery from the extreme space conditions. This study included findings related to gene expression changes, immune system response, and telomere dynamics. Other changes included broken chromosomes rearranging themselves in chromosomal inversions and a change in the cognitive function. This study was recently published in Science (Garrett-Bakelman et al., 2019).

The study on Scott had been divided into three different sample collection steps that were preflight, in-flight and post-flight.

It has been found that Scott's leukocytes telomeres were unexpectedly longer in space, then shorter after his return to Earth with the average telomere length returning to normal six months later, while his brother Mark's telomeres remained as usual throughout the study period. Similar results were also recorded in a 2017 study according to the NASA press release, but these conclusions were verified in twins study after several advanced genomics studies (Garrett-Bakelman et al., 2019) (Fig. 2).

The second major finding was recorded in the sense of their immune response. There was no such difference in their immune response recorded in space. This was calibrated after flu vaccination on Mark in space and the immune system responded appropriately as for his brother Mike on the Earth. The flu vaccine responded the same as it did on the Earth. Cytokines data for inflammation signatures have been reviewed and not any of the cytokines assays were significantly different. This study has been a critical part of the long duration manned mission in space.

Figure 1. NASA study twins, Scott and Mark Kelly.

For a few events, constant changes were observed even after 6 months on Earth, including some genes' expression levels, increased DNA damage from chromosomal inversions, increased numbers of short telomeres and attenuated cognitive function.

Principal components analysis (PCA) revealed a distinction in global DNA methylation between the two cell types and between the subjects for the CD4 samples. The subtle difference in methylation has been recorded in inflight and return to baseline post-flight.

Metabolomic study showed an increase in the lactic/pyruvic acid ratio, demonstrating a change from aerobic to anaerobic metabolism.

The most significant result was the variability in gene expression in space, researchers observed changes in the expression of Scott's genes, which returned to normal after six months on Earth. However, a small percentage of genes related to the immune system and DNA repair did not return to the baseline after his return to Earth. A number of biomedical checkups were performed on Scott, for elucidating the adjustment of the body from harsh conditions such as weightlessness and space radiation. His brother Mark, is continuously on the observation on Earth to compare the effects of space on a body down to the cellular level (Garrett-Bakelman et al., 2019).

Telomeres are the cap at every chromosomal terminus just like the shoe laces have their protective ends. Telomeres have the repetitive essential DNA elements that help in maintaining the chromosomal length, prevent physical degradation and inappropriate DNA damage response (Greider, 1991). We know that our telomeres get shorter every time the cell divides. NASA's twins study on the telomere dynamics during the space flight and landing on Earth gives us a strong possible clue that telomere length can be reversible. We are more curious about the telomere length due to its dominant role in the the process of ageing. In 1986 for the first time, Cooke and Smith stated the relation between telomere length and ageing (Cooke and Smith, 1986). Consecutive findings further revealed that telomere shortening is the key factor for the senescence in the somatic cells (Harley et al., 1990; Counter et al., 1992). Apart from NASA study, evidence from observational studies on individuals participating in physical activity/exercise show longer telomere length in the skeletal muscles and leukocytes (Rae et al., 2010; Osthus et al., 2012 Cherkas et al., 2008; Werner et al., 2009; Borghini et al., 2015).

Telomere dynamics studies reveal that the longer telomeres provide a longer life span and shorter telomeres contribute to senescence, but in space, it could have another definition due to unknown reasons. Twins study helped establish an outline of widespread research that serves as a model for future biomedical research in the context of aging science.

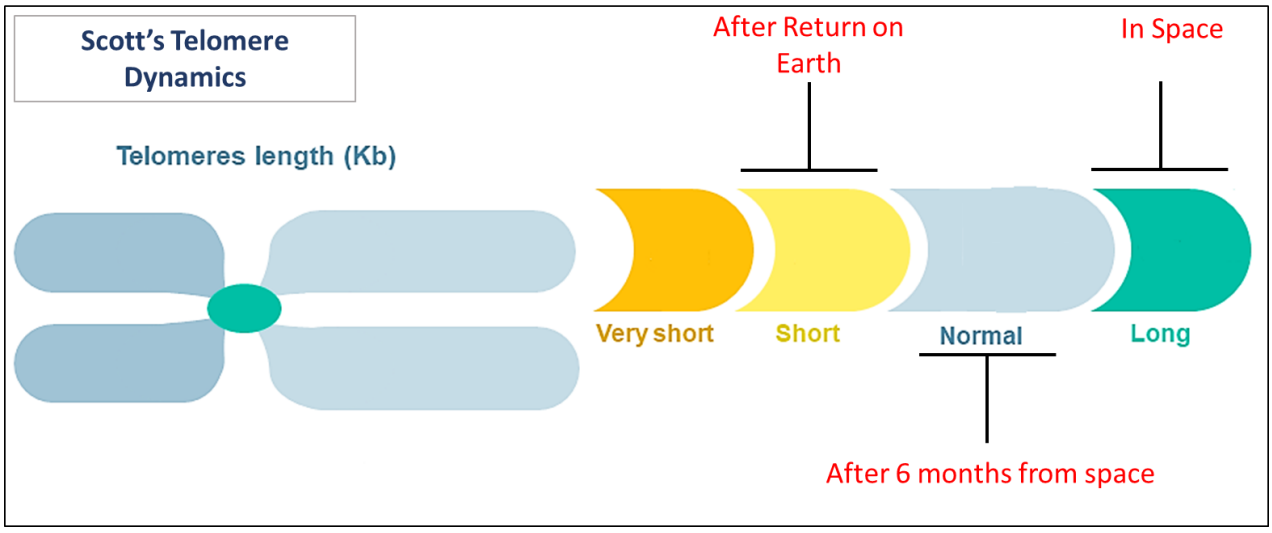

Figure 1. Telomere dynamics in space and Earth.

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