Differential effects on Telomeres and Telomerase in Twin astronauts associated with spaceflight

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Specific Aims

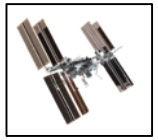
The rate at which telomeres shorten provides an informative biomarker of aging and age-related pathologies (e.g., cardiovascular disease and cancer) that captures the interplay between genetics and lifestyle factors.

We propose that for the astronauts telomere maintenance is particularly relevant, as it reflects the combined exposures (e.g., radiation) and experiences (nutritional, psychological and physical stressors) encountered during space travel.

The Twins study provides the extraordinary opportunity to control variables of individual genetic differences, susceptibilities and lifestyle factors, making differential effects observed between the twins space-flight specific.

Comparisons with unrelated astronauts (separate study), will allow evaluating role of genetics/individual susceptibilities.

Implications of Research for Space & Earth



Space: This twins study will identify space-flight specific factors that influence telomere length and telomerase activity, informative biological indicators of aging and age-related degenerative diseases (e.g., cardiovascular disease and cancer). Our mechanistic investigations will begin to establish relevant relationships and suggest potential mitigation strategies for future study and to improve astronaut overall health.

Earth: Aging and age-related diseases like cardiovascular disease and cancer are an everyday concern on earth as well, therefore this study also seeks to make comparisons with unrelated astronauts (and controls) that will serve to identify individual susceptibility factors that influence telomere length and telomerase activity. Taken together with our mechanistic studies, mitigation strategies will be improved and applicable to all.

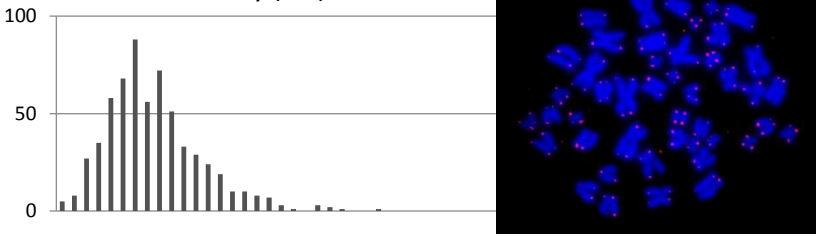
***Our goal* is to assess changes in telomere length and telomerase activity associated with the upcoming yearlong ISS mission in the space- and earth-bound twin astronauts.**

***We hypothesize* that accelerated telomere shortening and elevated telomerase activity will be associated with space flight** as compared to ground based control, in a duration and severity dependent manner.

- Blood samples will be taken ***pre-flight*** (to establish baseline), ***in-flight*** (to evaluate short-term/temporary changes) and ***post-flight*** (to evaluate long-term/permanent changes)
- Data sharing for other endpoints will also inform this effort
- *In vitro* studies will investigate potential mechanisms (e.g., oxidative stress) and mitigation strategies (e.g., antioxidants)

Telomere length will be assessed using TELO-FISH

Florescence *in situ* Hybridization (FISH) with telomere probe on chromosomes (and interphase nuclei) is evaluated as Relative Fluorescence Intensity (RFI) distributions.



Telomerase activity will be assessed using qRT-PCR TRAP

quantitative Real Time-PCR Telomere Repeat Amplification Protocol