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Task Description:	The ultimate goal of the studies proposed here is to establish temporal profiles of human telomere length dynamics and DNA damage responses of importance for maintenance of human health and performance during long-duration deep space missions. We hypothesize that telomere length dynamics (changes over time) represent a particularly relevant and informative biomarker of health for the astronauts, as it reflects the combined experiences and exposures encountered during spaceflight. That is, an astronaut's individual genetic susceptibilities, unique lifestyle stresses encountered (e.g., nutritional, psychological, physical), and particular environmental exposures (e.g., altered atmospheres, microgravity, space radiations) are all integrated and captured as changes in telomere length. Thus, the rate at which telomeres shorten provides a general measure of health that can be linked to aging, as well as to risk of developing age-related pathologies, ranging from reduced immune function and dementia, to cardiovascular disease and cancer. Importantly, functional telomeres are also essential for maintaining genomic integrity and stability, as they protect chromosomal termini from inappropriate DNA damage responses (DDRs). To identify trends in adaptations to human health and performance during long-duration low-Earth orbit, we propose telomere length and DDR/cytogenetic measures pioneered and validated in the NASA Twins Study/first One Year Mission, across the Integrated One-Year Mission Project onboard the International Space Station and the concurrent ground analog (prolonged isolation) component.		
Rationale for HRP Directed Research:			
Research Impact/Earth Benefits:	Identifying interactive effects of genetic and nongenetic telomere length determinants and DDRs will improve understanding of aging and aging trajectories (disease risk), as well as guide future studies and development of potential strategies for improving health-span not only in astronauts on long-duration missions, but for those on Earth, too.		
	Complement of Integrated Protocols for Human Exploration Research (CIPHER) Selected for Flight (Oct 2020). First mission launch ~December 2021; first BDC ~April/May 2021. Working on details of sample collection before, during, and after spaceflight. Together with cell-by-cell analyses, approaches for more high throughput analyses (e.g., ddPCR) are being tested and optimized.		
Task Progress:	We are developing machine learning strategies for predicting telomere length outcomes, which will become more and more reliable/informative as the models see more data. We are also seeking ways to test mechanisms; e.g., to assess the influence of chronic oxidative stress on telomere length. We evaluated telomere length in blood samples from humans climbing Mt. Everest, and matched twin non-climbing controls.		
	Established Telomeres 2 stem/progenitor cell evaluation as part of Standard Measures; collaborating with Brian Crucian.		
	Established NASA and home institution (Colorado State University-CSU) Institutional Review Boards (IRBs) – continuing process. Awaiting crew selection and recruitment into the Telomeres 2 study.		
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