The Effects of Spaceflight on Cellular Aging in *Saccharomyces cerevisiae.*

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The conditions encountered during spaceflight place unique stresses on physiological processes that oftentimes lead to deleterious effects. Identifying these effects and better understanding their molecular mechanisms will be essential in enabling long-duration space travel by humans. Studies in *Saccharomyces cerevisiae* suggest an aging model that involves the accumulation of toxic components, such as excess extrachromosomal rDNA and damaged mitochondria. This build-up then limits the replicative lifespan (the number of times a mother cell can form a new daughter cell). Remarkably, each new daughter cell emerges completely renewed from the senescing mother cell through an asymmetric distribution of aging determinants *via* mechanisms that are intricately linked to the budding process. When exposed to simulated microgravity, *S. cerevisiae* undergoes an altered budding process characterized by a breakdown in bud scar polarity. Because the budding process is critical to replicative aging, we hypothesize that the replicative lifespan may be affected by microgravity as well. To measure relative replicative aging rates, we will construct a strain of yeast in which daughter cells are inviable. In this strain, the Cre recombinase will be expressed under the control of the daughter cell specific promoter, *pSCW11*, and LoxP sites will be inserted at both flanks of two essential genes involved in the cell cycle, *UBC9* and *CDC20*, using a CRISPR/Cas9 system. Thus, *UBC9* and *CDC20* will be excised from daughter cells, leading to cell-cycle arrest and eventual death. To mimic the low shear conditions encountered in microgravity, this strain will be grown in rotating wall vessels. The number of viable mother cells will be monitored over time, and this rate will be compared to cells growing in standard conditions. Because asymmetric division also occurs in mammalian cells (*e.g.* in neural stem cells), this study will provide insight into how cellular aging rates may change in mammals and will help empower humans to thrive in space for extended and even indefinite periods of time.

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