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Author: Dr. Luis Zea

University of Colorado Boulder, United States, Luis.Zea@Colorado.edu

Mr. Tobias Niederwieser

University of Colorado Boulder, United States, tobias.niederwieser@colorado.edu

Dr. Louis Stodieck

University of Colorado Boulder, United States, Stodieck@Colorado.edu

Dr. Christopher Carr

Massachusetts Institute of Technology (MIT), United States, chris@mit.edu

Dr. Ralf Moeller

Deutsches Zentrum für Luft- und Raumfahrt e.V. (DLR), Germany, ralf.moeller@dlr.de

Prof. Corey Nislow

University of British Columbia, Canada, corey.nislow@ubc.ca

EXPERIMENT DESIGN FOR A GENOME-WIDE YEAST FITNESS PROFILING EXPERIMENT ON  
BOARD ORION'S ARTEMIS 1 MISSION**Abstract**

As human space exploration expands beyond lower Earth orbit, the environmental challenges that all living systems face must be understood so that robust mitigation measures can be developed. Towards this end, it is essential to characterize the effects of space radiation, microgravity, and the combination thereof on cells and organisms. Because it is prohibitive to study most organisms with a sufficiently large sample size, especially for humans, model organisms can be used to understand such fundamental gene environment questions. By selecting a model organism that shares many of the key, conserved aspects being studied, one can use large populations of model organisms, with well characterized genomes, to refine human tests which can be addressed with small, focused studies. In this case, we will use yeast, because 70% of its essential genes have a human homolog, and over half of these homologs can functionally replace their human counterpart. More specifically, this project will use a molecularly barcoded yeast genome-wide knockdown collection that will enable the systematic interrogation of the effect of microgravity, space radiation, and a combination thereof in each gene. To differentiate the effects of microgravity and space radiation on each strain, an experimental set will be flown beyond the van Allen belts on Orion's Exploration Mission 1 (EM-1) (considered in microgravity and irradiated by space radiation) and equivalent sets will be cultured asynchronously on board the International Space Station (ISS) (considered in microgravity but mostly – although not completely – protected of space radiation by the van Allen Belts) and on Earth. The experiment is designed to have a controlled start via rehydration of the lyophilized deletion and overexpression series after Orion is past the van Allen belts, and grown for 5-6 generations, having a natural self-termination by carbon depletion, for post-flight analyses. This is achievable through our battery-operated hardware - Peristaltic Laboratory for Automated Science with Multigenerations (PLASM) - that fits inside the BRIC-100VC canister and that is based on a spaceflight-proven system we have used for similar research on ISS on the past. To identify essential biological processes required to resist the effects of both microgravity and cosmic radiation, these data will be compared to our database of experiments collected on the ISS and over 3000 terrestrial genome-wide screens.

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