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EXPOSURE OF CARTILAGE TISSUE MODELS TO GRAVITATIONAL TRANSITIONS ASSOCIATED WITH SPACEFLIGHT: IMPLICATIONS FOR INTERPLANETARY EXPLORATION

Abstract

Spaceflight is well known to detrimentally affect human musculoskeletal system by significant decrement of bone and muscle mass, implying short-term mobility impairments and long-term tissue alterations upon return to Earth (Burkhart 2019 DOI: 10.1097/BRS.0000000000002959, Stavnichuk 2020 DOI: 10.1038/s41526-020-0103-2, Gabel 2022 DOI: 10.1038/s41598-022-13461-1). As part of the musculoskeletal system, joint cartilage is also deemed to be target of deleterious spaceflight effects: pointing to acquisition of aging-related phenotype, evidence of (mal)adaptive responses of human cartilage to spaceflight is however far from being conclusive (Niehoff 2016 DOI: 10.1016/j.joca.2016.01.282, Liphardt 2022 NASA Human Research Program Investigators' Workshop ID: 20210022954, Liphardt 2024 DOI: 10.1016/j.joca.2023.11.007). To improve the comprehension of phenomena underlying cartilage remodelling under altered gravity conditions, different models for cartilage tissue have been proposed *in vitro* and *in vivo*, respectively resorting to human (healthy chondrocytes, tumour and stem cells) and to animal (mice, rats *etc.*) sources, either in the presence or absence of scaffolds supporting cell functions, and under real or simulated spaceflight conditions (Freed 1997 DOI: 10.1073/pnas.94.25.13885, Aleshcheva 2016 DOI: 10.1007/s12217-015-9479-0, Kwok 2022 DOI: 10.1038/s41598-021-90010-2, Ramachandran 2023 DOI: 10.21037/jss.2018.04.07, Steinwerth 2024 DOI: 10.3390/biom14010025). Among these models, bioengineered cartilage constructs obtained by seeding human bone marrow-derived mesenchymal stem cells on porous scaffolds were demonstrated to undergo sex-dependent transcriptome regulation during exposure to parabolic flight (*i.e.* to gravitational transitions), and upregulation of aging-related cartilage degeneration markers only in female cell donors (Aissiou 2023 DOI: 10.1038/s41526-023-00255-6). By

envisioning an increasing female participation to missions of space exploration on a long distance (since NASA Artemis program establishment), it becomes imperative obtaining of a wider comprehension of the effects of gravitational transitions on cartilage tissue *in vitro* with ground-based models (prior to testing in real spaceflight conditions). For this reason, this study aims at capturing information on post-transcriptional responses to gravitational transitions by cartilage constructs obtained with SW1353 cells (i.e. derived from a female donor), potentially shedding light onto the molecular bases useful to the treatment of aging-related cartilage alterations.