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Facilities and Operations of Microgravity Experiments (5)

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TRANSCRIPTOMIC RESPONSE OF BIOENGINEERED HUMAN CARTILAGE TO PARABOLIC  
FLIGHT MICROGRAVITY IS SEX-DEPENDENT**Abstract**

**INTRODUCTION:** Microgravity induces osteoarthritic-like alterations at the transcriptomic levels in articular and meniscal cartilages of rodents. However, little is known about the effects of microgravity on the transcriptome of tissue-engineered human cartilage cells. Furthermore, women have a worse prognosis with osteoarthritis than men and this is not well understood. We assessed the transcriptome response of engineered human cartilage tissue to short exposure to microgravity. We also assessed for sex-specific molecular changes in the cartilage tissue after exposure to microgravity. We hypothesize that the transcriptome profile of engineered human cartilage will respond to short-term microgravity via parabolic flight and some of these changes will be sex-specific.

**METHODS:** Human bone marrow aspirates from 3 male and 3 female age-matched donors were collected from the University of Alberta Hospital. The University of Alberta Health Research Ethics Board-Biomedical Panel waived the need for consent of donors, as specimens were intended for discard post-surgery. Mesenchymal stem cells were isolated from these aspirates and expanded in a humidified incubator for 7 days. Next, these cells underwent in vitro chondrogenic differentiation in type 1 collagen porous scaffolds for 21 days. The parabolic flight was conducted in the Falcon 20 shuttle at the National Research Council of Canada. Our samples cycled through 11 parabolas on the flight, exposing them to approximately 140 seconds of true microgravity. After levelling-off, the cartilage was terminated in RNA later. Post-experiment analysis included total RNA extraction, RT-qPCR and whole transcriptome next-generation sequencing.

**RESULTS:** We observed 30 differentially expressed genes of human cartilage tissue in response to short

term exposure to microgravity ( $p < 0.05$ ). Furthermore, 94 male specific genes and 74 female specific genes were differentially expressed in response to microgravity.

**DISCUSSION:** Our research shows microgravity specific molecular changes in human bioengineered cartilage are largely sex specific. This has wide reaching implications including in the identification of drug targetable pathways and development of countermeasure technologies for long duration spaceflight. This research also helps elucidate the sex specific differences in the pathology of human cartilage tissue.