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DETERMINING RESPONSE DIFFERENCES TO MICROGRAVITY IN MALE AND FEMALE
BIOENGINEERED CARTILAGE TISSUES**Abstract**

As humanity pushes further into the unknown, astronauts will be faced with heightened risks of physiological issues during missions of increasing duration. This is especially true with regards to the loss of bone mass seen in astronauts, which is proportional to the time spent in zero-gravity. This loss in mass increases the chance of osteoarthritis (OA) and already affects around 240 million earthlings worldwide. The condition occurs when the protective cartilage cushioning the joints degrade over time, and interestingly presents itself in women almost twice as much as in men. Knee osteoarthritis (KOA) is the most common form of OA and is used to study its pathogenesis. Several studies involving astronauts have already shown that prolonged periods of zero-gravity contribute directly to cartilage degradation in various measurable fashions. Others have investigated cartilage tissue behaviour inside artificial biological environments and centrifuges. The next step is to explore minute changes in cartilage tissue in microgravity, such as during a parabolic flight, to generate a deeper understanding of OA.

Flying aboard the Canadian Space Agency's Falcon-20 parabolic aircraft in summer 2020, this experiment will evaluate the molecular differences between female and male bioengineered cartilage samples when exposed to microgravity, while also for the first time specifically explore the role of metabolites (the intermediate products of metabolism) in KOA pathogenesis. Metabolite activity responds to gravitational changes on a per-second basis and will thus show exact variations in cartilage tissue metabolism and degradation over time more accurately than ever before. Such a focus on metabolites has, up to now, not been studied in this context. Samples will be subject to increasing parabola quantities to determine the effect of repeated microgravity exposures over time. Systems handling the transfer of nutrient solution (to maintain sample health) and reagent (to freeze the samples' molecular activity in time) will also be implemented. Upon return, all samples will be mRNA-sequenced and molecularly analyzed with OA markers.

This novel understanding of the metabolite role in cartilage degradation will help in the identification of drug-targetable pathways, leading to more robust and personalized OA treatment in astronauts and earthlings alike. Manned space missions will only get longer in the future; thus, the results of this study will be extremely beneficial in ensuring the long-term prevention, mitigation and treatment of OA in the hazardous and remote space environment. As a result, astronaut recovery time may be shortened, and mission readiness increased.