

# Characterization of Metabolomic Profiles of Encapsulated Chondrocytes Exposed to Short-Term Simulated Microgravity: A Pilot Study

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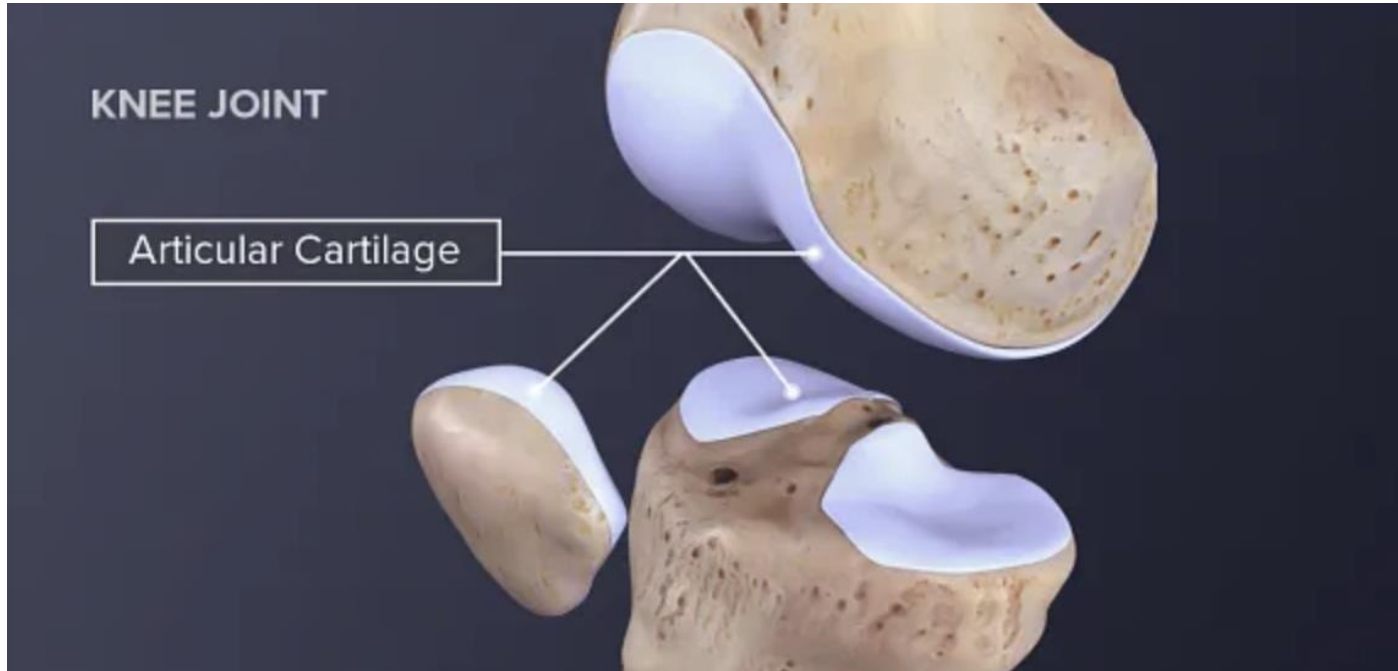
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*Disclosure:* the authors have no conflicts of interest for this work.



# Articular Cartilage



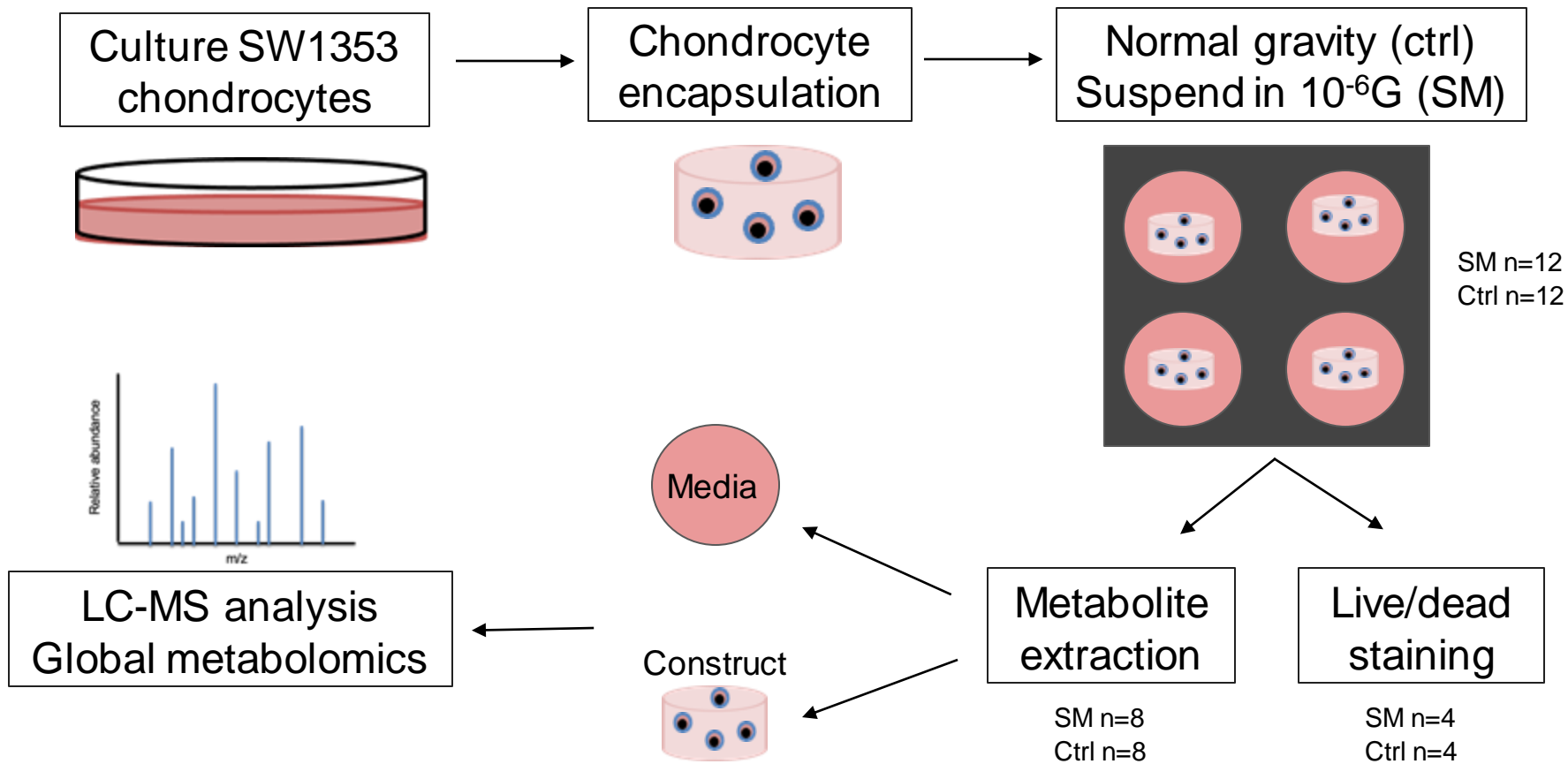
# Microgravity → Metabolic Perturbations → Osteoarthritis

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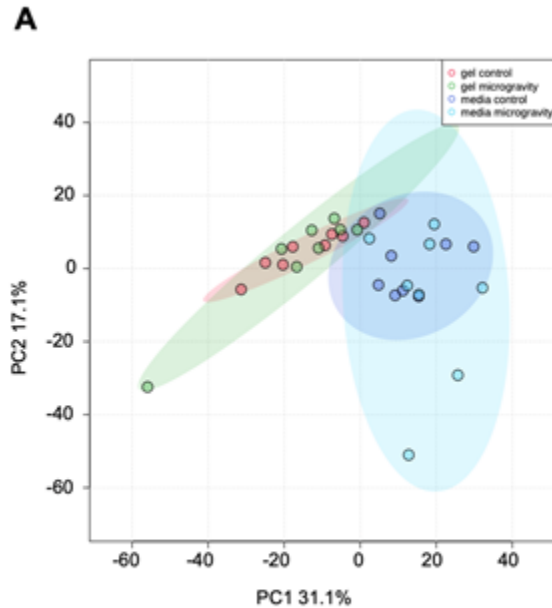
**Objective:** Expand our understanding of the risk of developing OA post-spaceflight by analyzing metabolic shifts induced by simulated microgravity (SM)

# Experimental Design

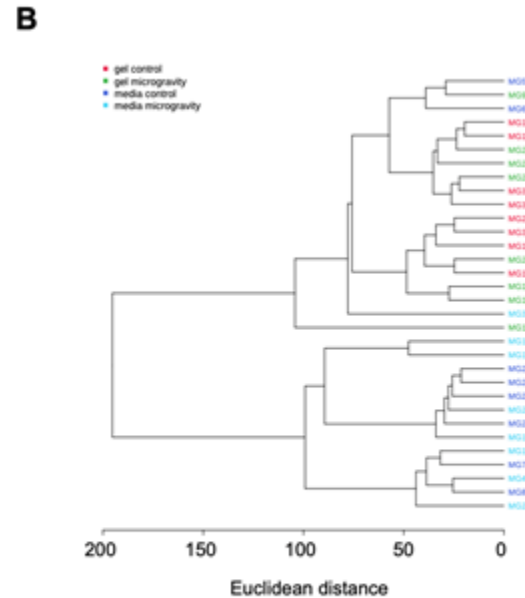


# Results: Minimal separation of SM and control cohorts in unsupervised statistical analyses

## Principal component analysis (PCA)



## Hierarchical cluster analysis (HCA)

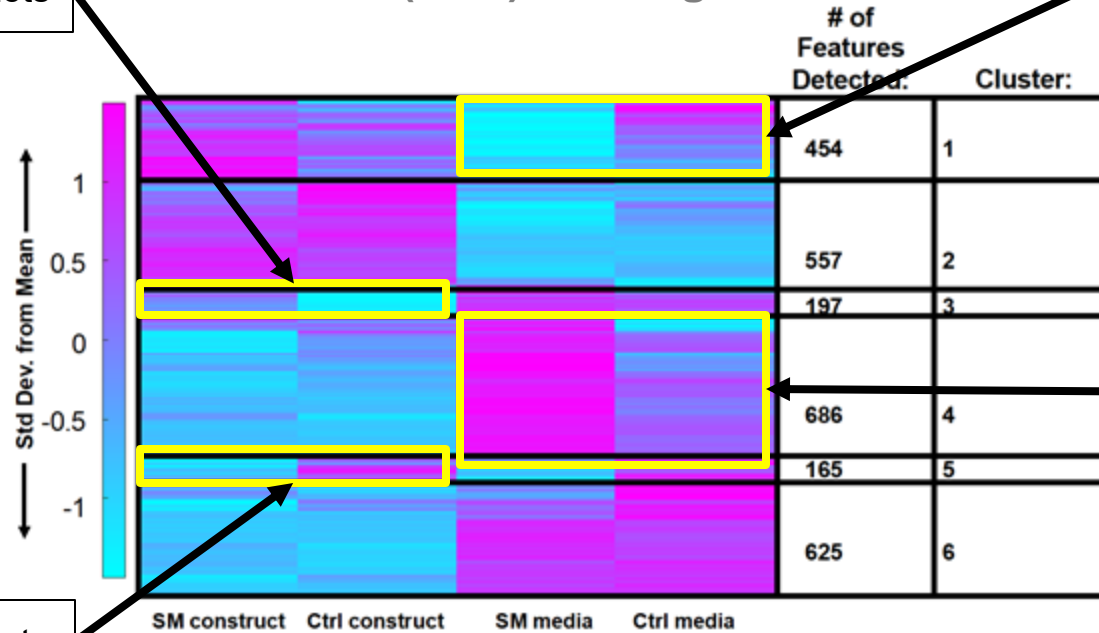


■ gel control   ■ gel microgravity   ■ media control   ■ media microgravity

**Conclusion 1:** Short-term exposure to simulated microgravity did not induce large-scale shifts in chondrocyte metabolism.

# Results: Simulated microgravity-induced metabolic shifts

Hierarchical cluster analysis  
(HCA) Clustergram



↑ SM ↓ Ctrl Constructs

↑ Ctrl ↓ SM Media

↑ SM ↓ Ctrl Media

↑ Ctrl ↓ SM Constructs

# Results: Simulated microgravity-induced metabolic shifts

Cluster 1: ↑ Ctrl ↓ SM Media	Cluster 4: ↑ SM ↓ Ctrl Media	Cluster 3: ↑ SM ↓ Ctrl Constructs	Cluster 5: ↑ Ctrl ↓ SM Constructs
Aminoacyl tRNA biosynthesis	Amino acid metabolism (valine, leucine, isoleucine degradation, metabolism of glycine, serine, threonine, histidine, cysteine, and methionine)	Amino sugar and nucleotide metabolism	Vitamin B6 metabolism
Glutathione metabolism	Pantothenate and CoA biosynthesis	Valine, leucine and isoleucine metabolism	Tyrosine metabolism
Amino acid metabolism (arginine, tyrosine, glutamine/glutamate, phenylalanine, tryptophan)	Propanoate metabolism		Porphyrim metabolism
Glyoxylate and dicarboxylate metabolism	Porphyrim metabolism		Phenylalanine metabolism
Pyrimidine metabolism	Aminoacyl-tRNA biosynthesis		
Nitrogen metabolism			

Pathways listed have an FDR corrected significance level < 0.05.

**Conclusion 2:** Simulated microgravity induced shifts in metabolism of amino acids, nucleotides, nitrogen, vitamin B6, glutathione, porphyrin, propanoate, pantothenate and CoA biosynthesis, and glyoxylate and dicarboxylate.

# Discussion: Simulated microgravity-induced similar metabolic shifts as detected in human OA synovial fluid

## Osteoarthritis and Cartilage



Characterization of synovial fluid metabolomic phenotypes of cartilage morphological changes associated with osteoarthritis

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Glutathione metabolism

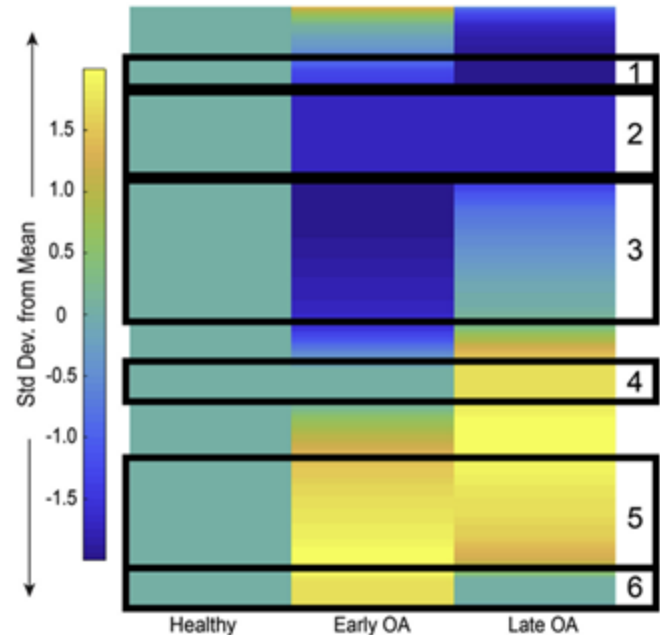
Amino acid metabolism (glycine, serine, threonine, lysine, valine, leucine, isoleucine, tyrosine, phenylalanine, histidine, cysteine, methionine, tryptophan, glutamine, glutamate, arginine)

Porphyrin metabolism

Vitamin B6 metabolism

Nitrogen metabolism

Pyrimidine metabolism



**Conclusion 3:** Short-term simulated microgravity exposure induced metabolic shifts consistent with early OA.

# Conclusions

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**Conclusion 1:** Short-term exposure to simulated microgravity did not induce large-scale changes in metabolism in encapsulated chondrocytes.

**Conclusion 2:** Simulated microgravity-induced shifts in metabolism of amino acids, nucleotides, vitamin B6, glutathione, porphyrin, propanoate, pantothenate and coA biosynthesis, and glyoxylate and dicarboxylate.

**Conclusion 3:** Short-term simulated microgravity exposure induced metabolic shifts consistent with early OA.

**Significance:** Short-term exposure to microgravity, or other reduced mechanical loading environments, may lead to the development of OA.

**Limitations:** small sample size, SW1353 cells, short duration of exposure

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# Questions?

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