Use of Kidney MPS in Precision Health and Microgravity Research

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My background and microgravity research

Training:

PharmD, University of Michigan

PhD (Medicinal Chemistry), University of Washington

MPH (Epidemiology), University of Washington

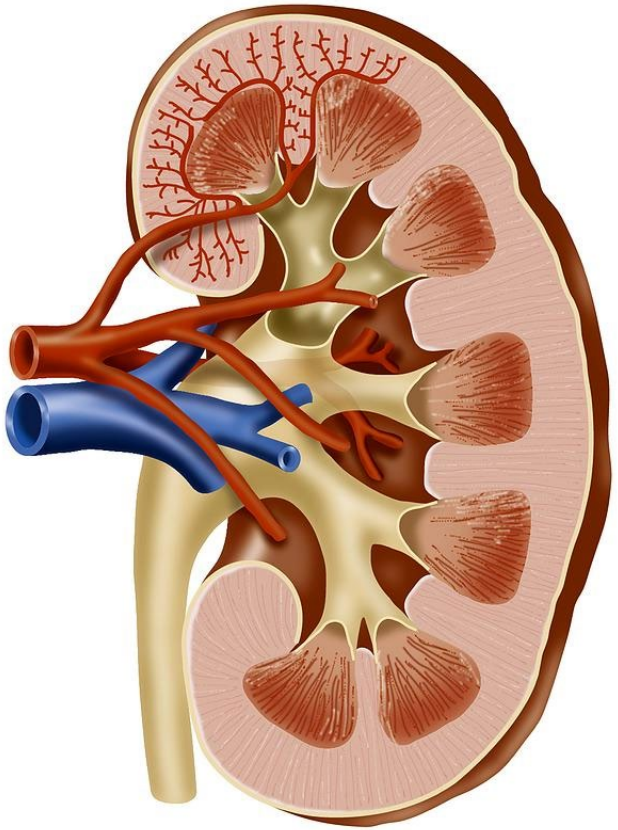
Fellowships:

Pharmaceutical Chemistry

Pharmacokinetics

Training in microgravity research:

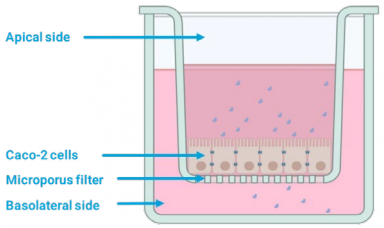
🔥 CRS-17 and CRS-22



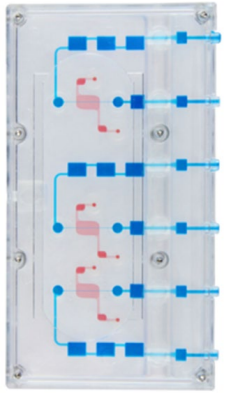
What is the currently accepted definition of NAMs?

It depends who you ask…

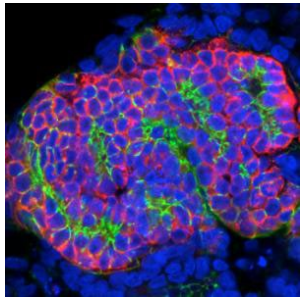
According to the NIH, NAMs (New Approach Methods) describe “any technology, methodology, approach, or combination thereof that can be used to provide information on chemical hazard and risk assessment that replaces, reduces, or refines the use of animals.”



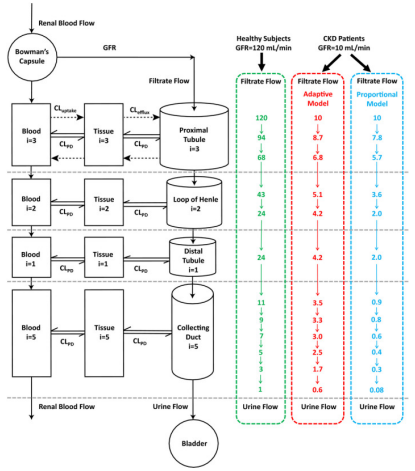
Cell-based models



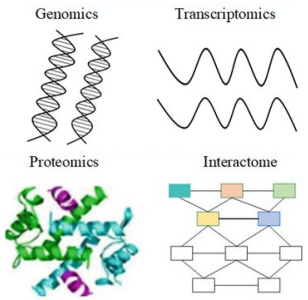
MPS



Organoids



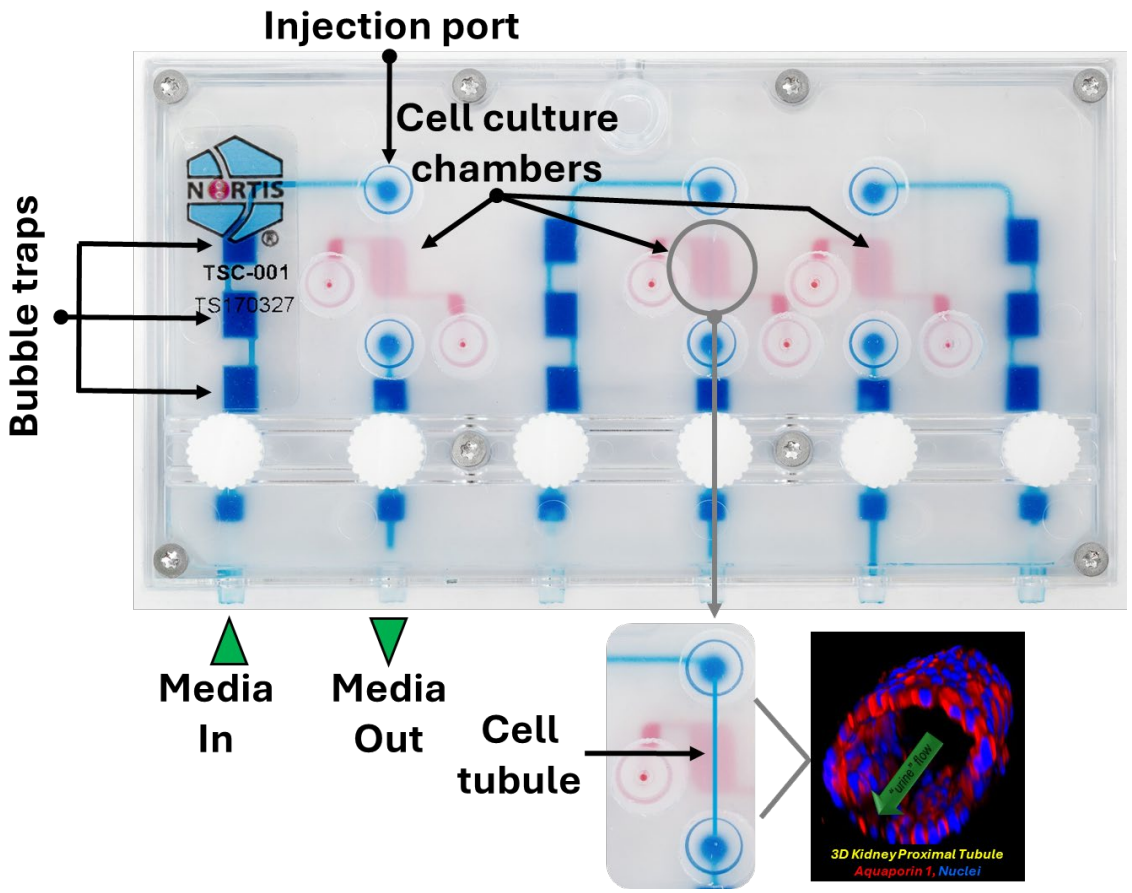
Computational models

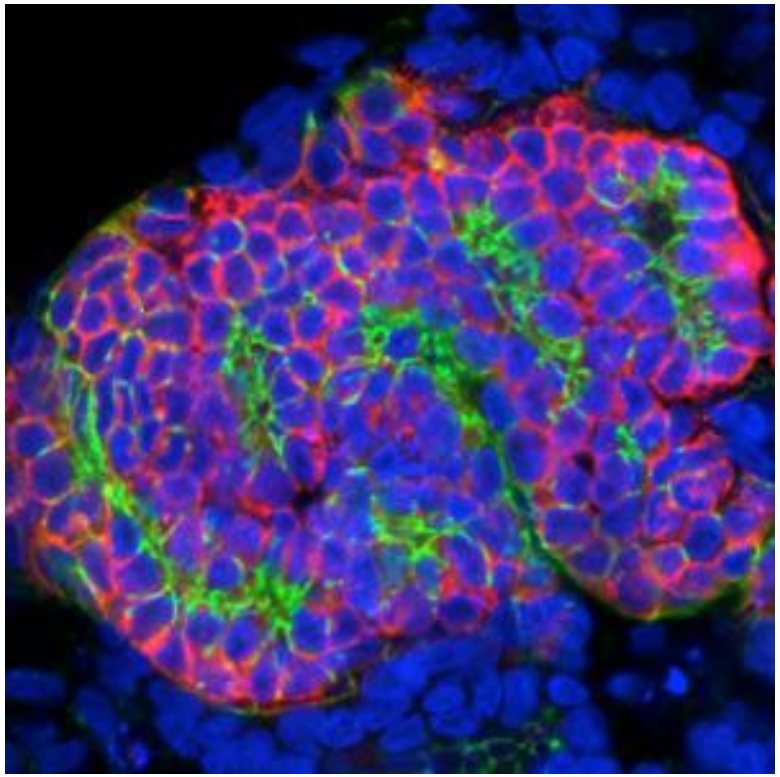


Multi-omics

Non-mammalian models

Kidney chips vs. kidney organoids





- Engineered microchips with primary adult human kidney cells in tubular geometry.
- Cellular components are encased in hydrogel extracellular matrix.
- Recapitulates fluid shear stress and mechanical strain observed in vivo.
- Media to cell ratios (flow rates) approximate physiological values.
- Inputs and outputs can be introduced from apical (lumenal) surface or basal (peritubular) surface of cells.

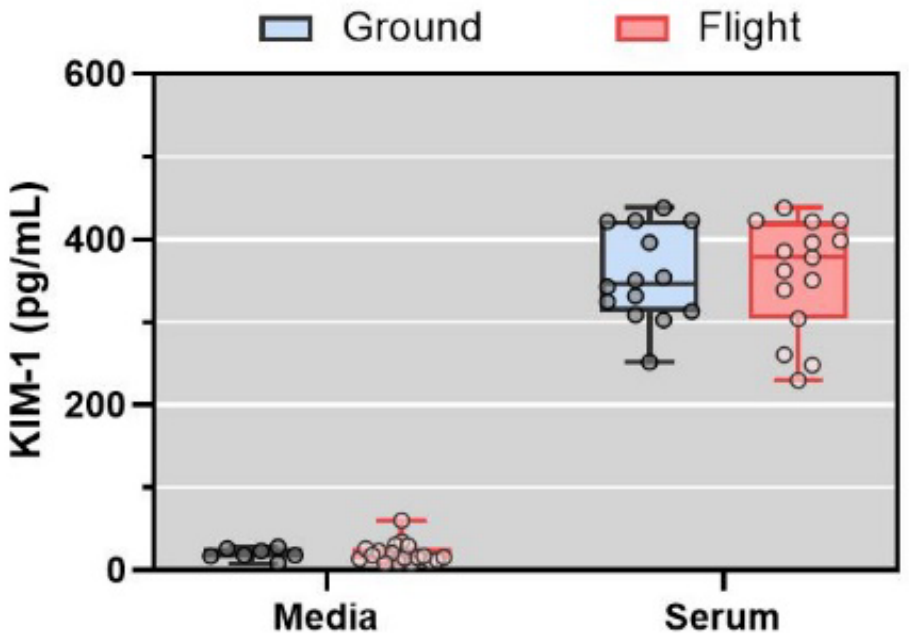
- Derived from human iPS cells which have the potential to form full complement of cells
- iPS cell lines are permanent & gene editable.
- Contiguous nephron segments enable interactions of diverse cell types
- Exhibit structural phenotypes of disease such as tubular cyst formation.
- Amenable to high-throughput formats (384-well) and automated production

Overview of uses of kidney chips in space

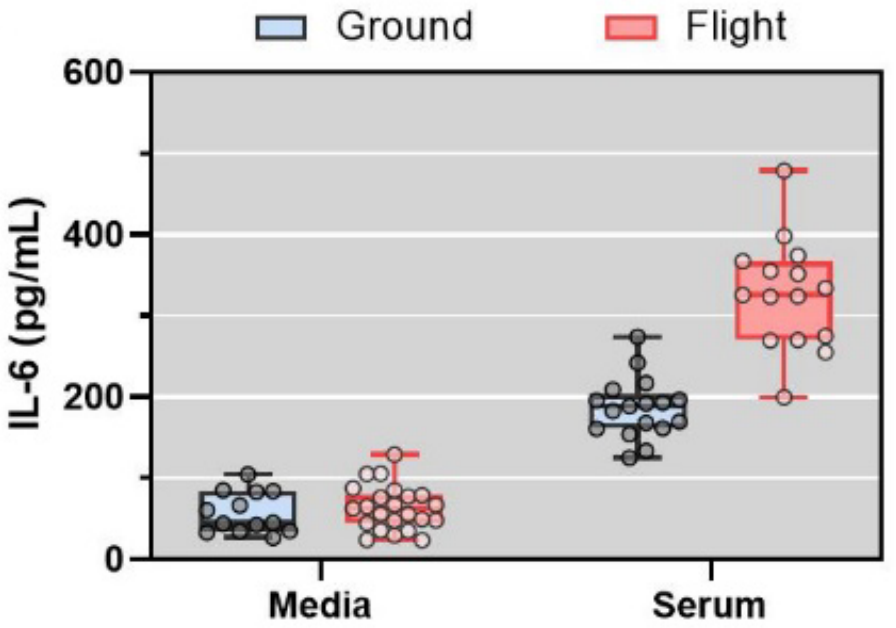
- Kidney health in space exploration
- Kidney stone prevention and treatment in microgravity
- Kidney aging and countermeasures
- Pharmacokinetics

Kidney health in microgravity: ↑ IL-6 with serum exposure

Injury Biomarker



Inflammation Biomarker



Kidney stone risk in microgravity

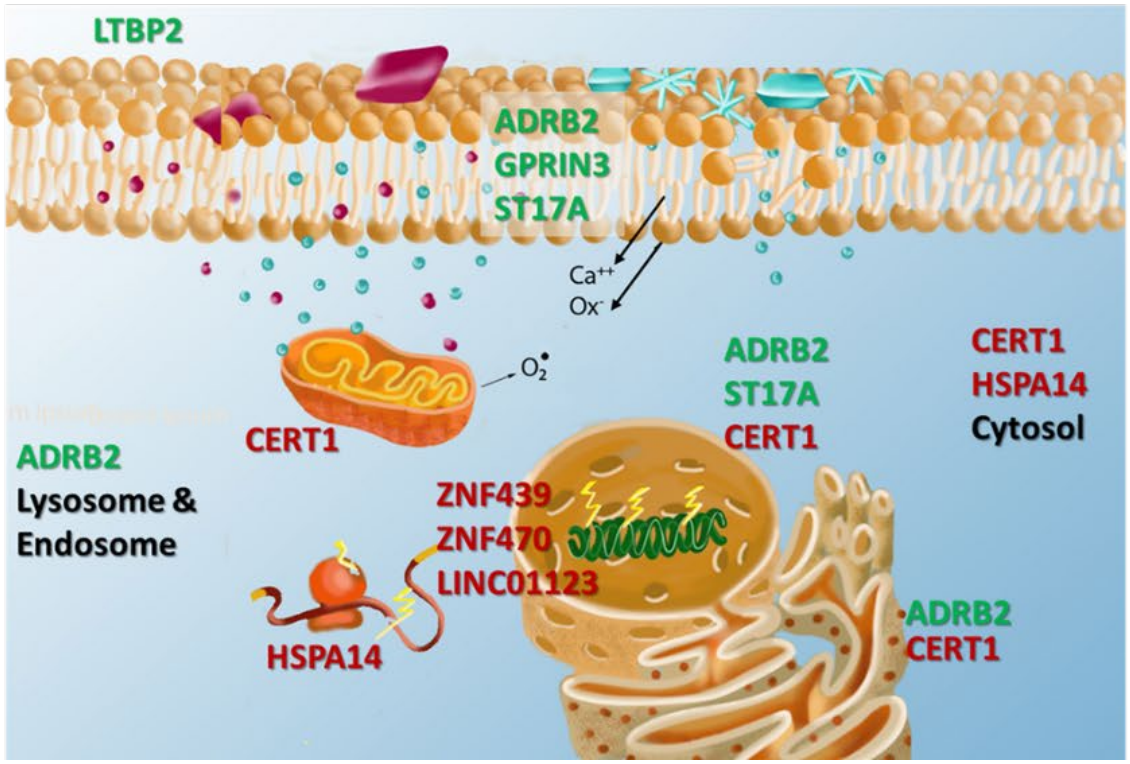
Factors that may ↑ risk:

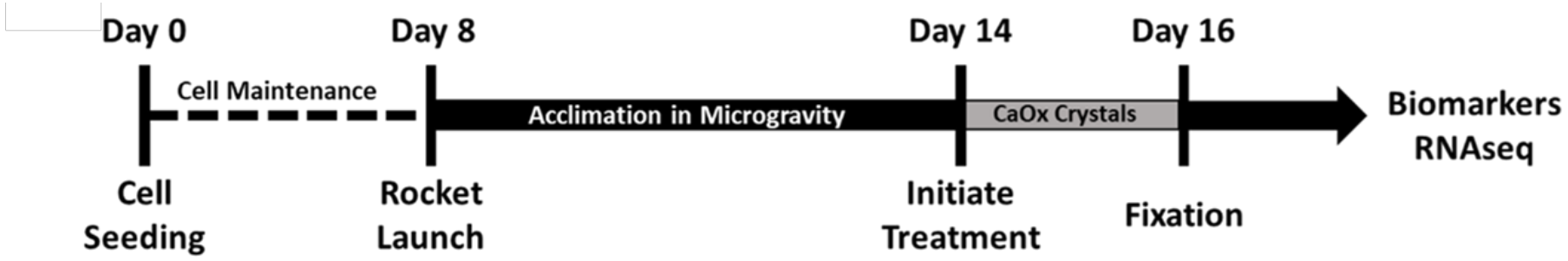
- Pseudo-dehydration
- Altered fluid distribution
- Bone resorption
- High protein diet
- High sodium diet

Kidney stone microcrystal response & countermeasures

Differentially expressed genes

	COM vs Control	KCit vs Control
ADRB2	1.34	-
GPRIN3	1.33	-
LTBP2	1.24	-
STK17A	1.13	-
CERT1	0.91	-
HSPA14.2	0.88	-
LINC01123	0.82	0.83
ZNF439	0.81	0.82
ZNF470	0.86	-





Kidney aging – does microgravity = ground aging?

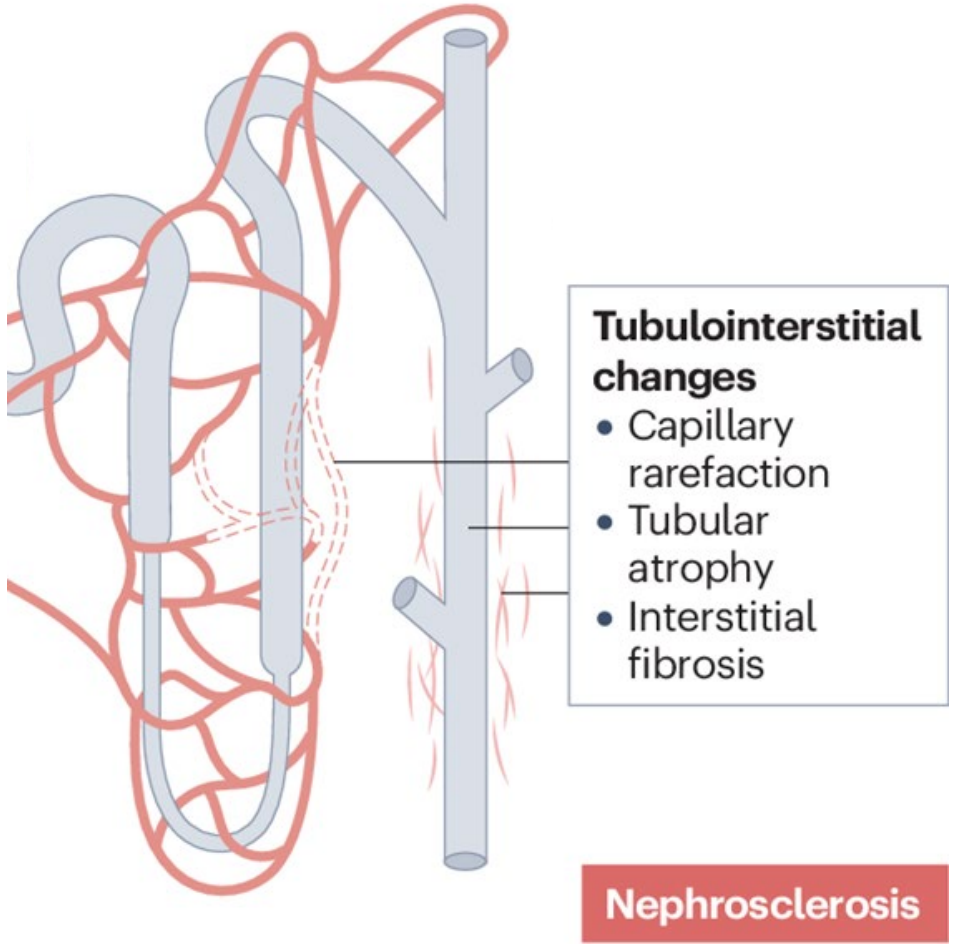


Figure adapted from PMID 38977884

Article https://doi.org/10.1038/s41467-024-49212-1

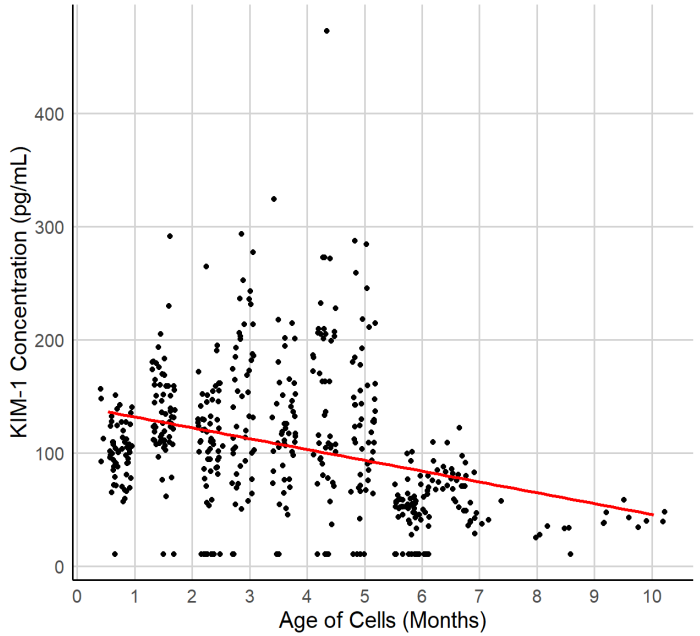
Cosmic kidney disease: an integrated pan-omic, physiological and morphological study into spaceflight-induced renal dysfunction

We found that spaceflight induces: 1) renal transporter dephosphorylation which may indicate astronauts' increased risk of nephrolithiasis is in part a primary renal phenomenon rather than solely a secondary consequence of bone loss; 2) remodelling of the nephron that results in expansion of distal convoluted tubule size but loss of overall tubule density; 3) renal damage and dysfunction when exposed to a Mars roundtrip dose-equivalent of simulated GCR.

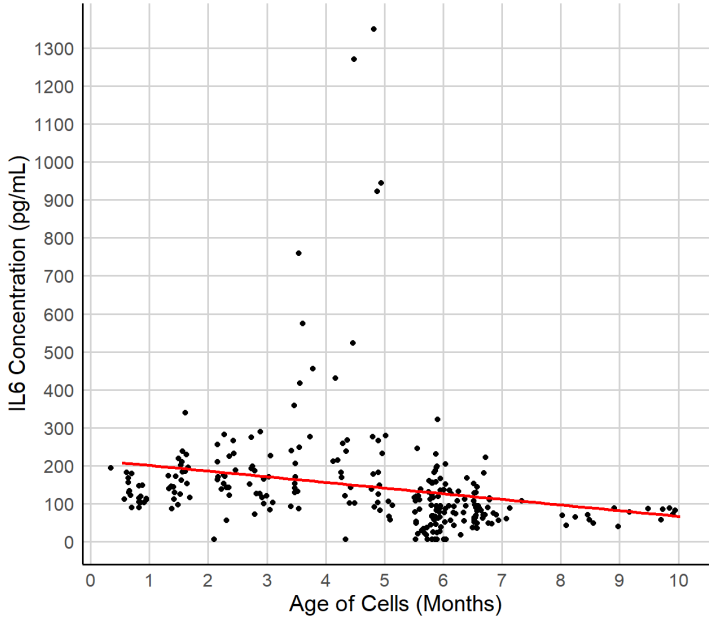
PMID 38862484

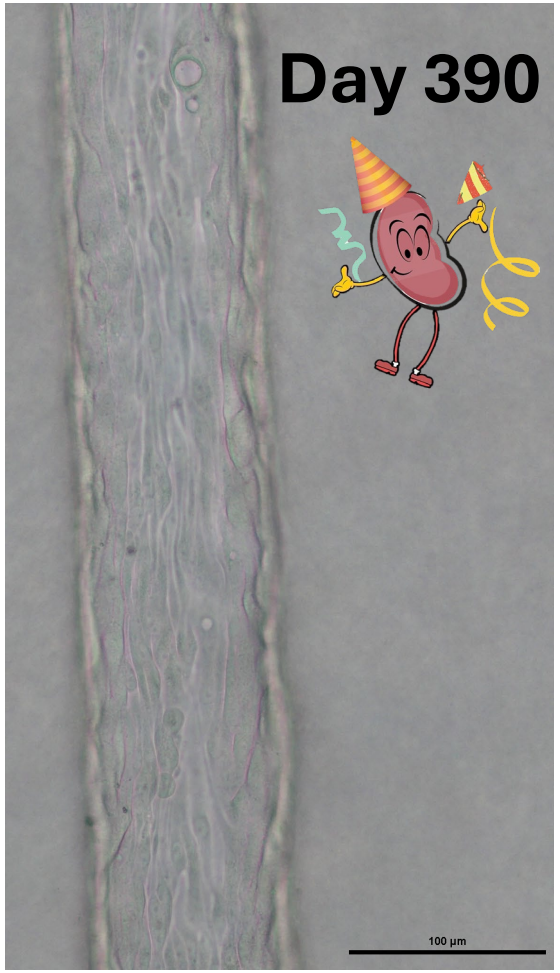
Do kidney MPS age (ground experiments)?

KIM-1 in effluent



IL-6 in effluent



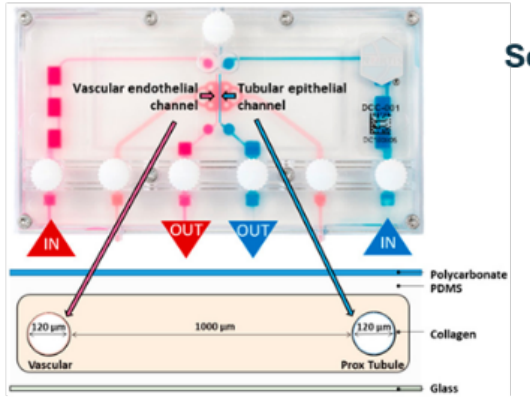


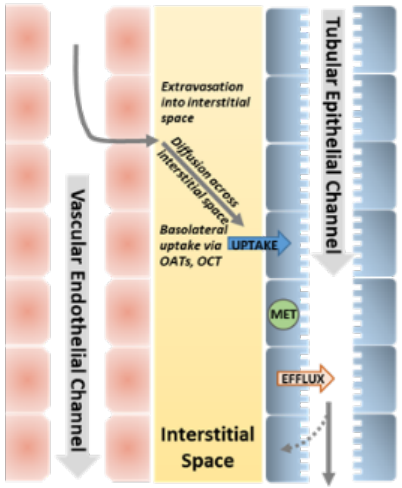
Do kidney cells in MPS undergo aging?

Can we use a microgravity accelerated aging model to understand kidney aging and test anti-aging drugs?

Pharmacokinetics- using MPS to model human exposure

MPS Platform → Scaling MPS to human CLrenal → PBPK Modeling





Scaling Results: PAH and Morphine/Morphine 6-Glucuronide

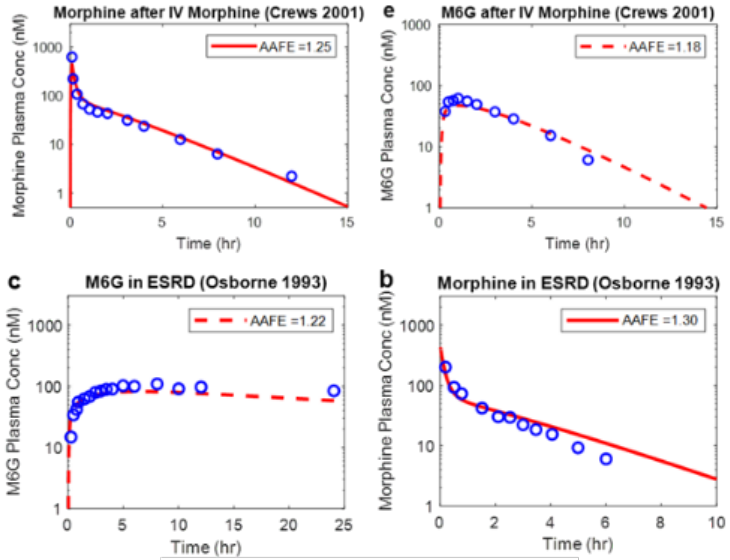
	PAH	Morphine	M6G
MPS	267.88 ± 77.51 mL/min	7.58 ± 2.53 L/h	9.45 ± 2.21 L/h
In Vivo	469 mL/min	6.8 – 9.6 L/h	9.20 – 14.3 L/h
Ratio	**1.93**	**1.08**	**1.24**

Scaling Parameters

$$CLsecretion = \frac{CL_{int,active\ secretion,MPS}}{5000\ (PTECs/MPS)} \times 60\ (Million\ prox\ tub\ cells/g\ kidney) \times 300\ (g\ kidney)$$

	VPT-MPS tubule	In vivo prox tubule
length (l)	6 mm	15 mm
diameter ($2r$)	120 µm	70 µm
surface area ($\pi \times 2r \times l$)	2.26 mm^2	3.29 mm^2
scaling factor	1.46	

Physiologically-Based Pharmacokinetic Simulation



Chapron A, Chapron BD, Hailey DW, Chang SY, Imaoka T, Thummel KE, Kelly EJ, Himmelfarb J, Shen DD, Yeung CK, An Improved Vascularized, Dual-Channel Microphysiological System Facilitates Modeling of Proximal Tubular Solute Secretion. ACS Pharmacol Transl Sci. 2020 Jan 28;3(3):496-508

Imaoka T, Huang W, Shum S, Hailey DW, Chang SY, Chapron A, Yeung CK, Himmelfarb J, Isoherranen N, Kelly EJ. Bridging the gap between in silico and in vivo by modeling opioid disposition in a kidney proximal tubule microphysiological system. Sci Rep. 2021 Nov 1;11(1):21356

Huang W, Isoherranen N, Development of a Dynamic Physiologically Based Mechanistic Kidney Model to Predict Renal Clearance. CPT Pharmacometrics Syst Pharmacol. 2018;7(9):593-602

Huang W, Isoherranen N. Novel Mechanistic PBPK Model to Predict Renal Clearance in Varying Stages of CKD by Incorporating Tubular Adaptation and Dynamic Passive Reabsorption. CPT Pharmacometrics Syst Pharmacol. 2020;9(10):571-583.

The future… where do we go from here?

- Extended duration experimentation to simulate effects of long-term space exploration
- Multi-system models (but only with good justification)
- Use of microgravity as a tool to study ground-based health conditions
- Strategic targeting of health conditions and countermeasures
- Integrate NAMs, computational tools, banked biosamples
- Standardization of lab facilities and opportunities for iterative experimentation

“The team, the team, the team” - Bo Schembechler

Team Members:

Jonathan Himmelfarb
Catherine K. Yeung
Edward J. Kelly
Benjamin Freedman
Kenneth E. Thummel
Nina Isoherranen
Brooke Chalker
Sophie Blackburn (UW PhD 2024, MD 2026)
Yousif Abuhamad (UW MS 2024)
Kevin Lidberg (UW PhD 2022)
Kendan Jones-Isaac (UW PhD 2023)
Jade Yang (UW BS 2020)
Jacelyn Bain (US BS 2021)
Paul Koenig (BioServe)
Stefanie Countryman (BioServe)

UNIVERSITY of WASHINGTON

BioServe SPACE TECHNOLOGIES

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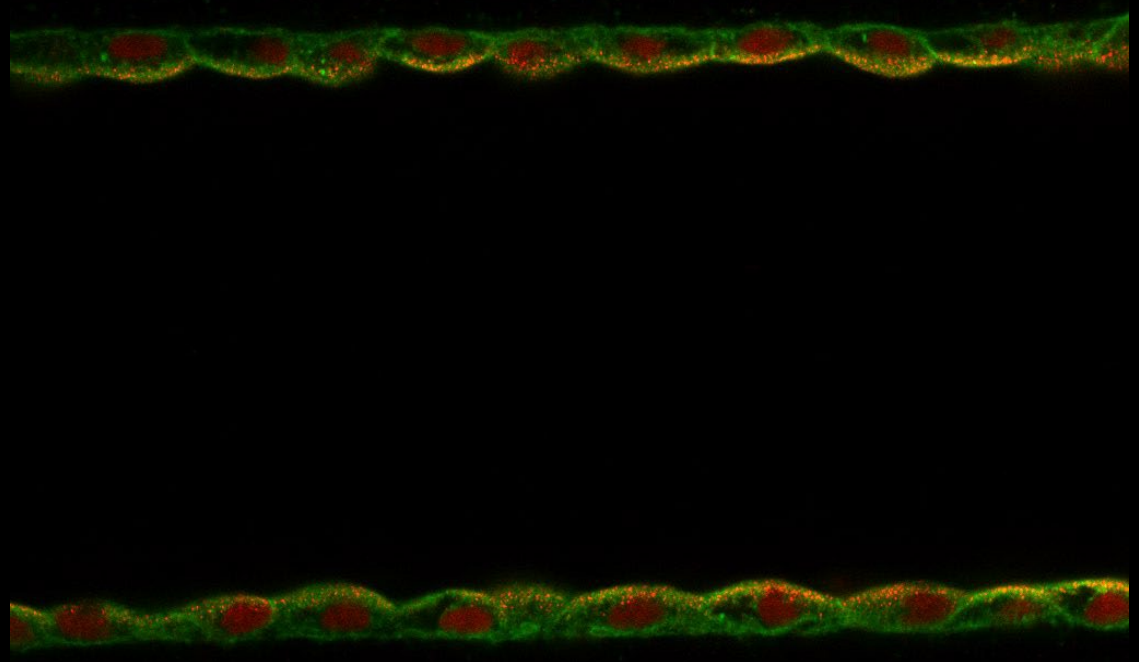
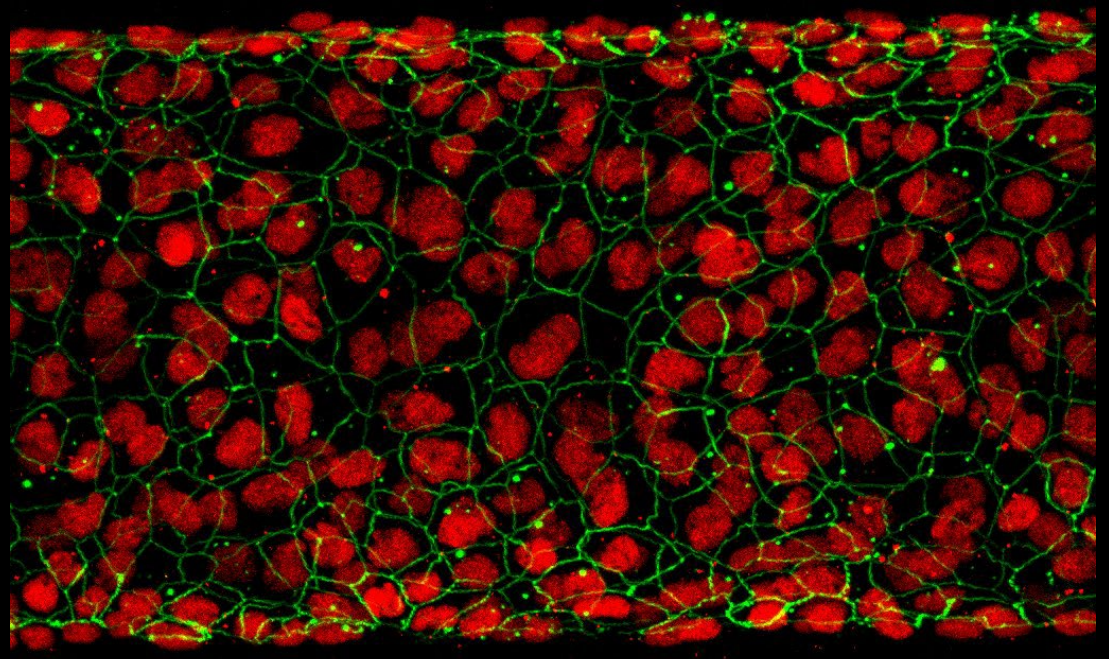
Questions?





Which system is “best”?

All systems have advantages and disadvantages

	Animal models	Organ Chip	Organoid
Advantages	Complex whole-body system Inexpensive High content data Regulatory acceptance	Easier to interpret findings Moderate content data Human cells and tissues Controllable system Reproducibility	Multiple cell types Inexpensive Can be easily gene edited Disease phenotype Stem cell derived
Disadvantages	Ethically challenging Not always translatable to humans Mechanism cannot always be determined	Low/moderate throughput Limited to few cell types Expensive Technically challenging Regulatory acceptance unclear	Cell disorganization, flow path Semi-differentiated cells (fetal) Variability in culture Regulatory acceptance unclear