Virtual ILAR Roundtable Workshop National Academy of Sciences

Microphysiological Systems: Bridging Human and Animal Research

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The National Academies of SCIENCES ENGINEERING MEDICINE

Learning from Tissue Chips in Space: Development and Commercialization of Next-generation MPS Platforms

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CEO, Nortis Inc.

TISSUE CHIPS IN SPACE

A program supported by the:

- **National Center for Advancing Translational Sciences (NCATS)**
- **National Institute of Biomedical Imaging and Bioengineering (NIBIB)**
- **International Space Station U.S. National Laboratory (ISS U.S. National Lab)**

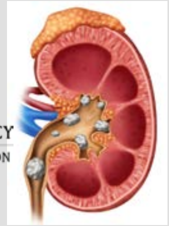
in partnership with **NASA**

Objective:

Collaborate on refining tissue chip technology for biomedical research use on the space station with the ultimate goal to improve human health on earth.

TISSUE CHIPS IN SPACE: 2016-2024 MISSIONS

Proteinuria and kidney stone formation



NORTIS
W SCHOOL OF PHARMACY UNIVERSITY of WASHINGTON
BIOSERVE SPACE TECHNOLOGIES

PI: Jonathan Himmelfarb

Immunosenescence

NORTIS
UCSF
BIOSERVE SPACE TECHNOLOGIES

PI: Sonja Schrepfer

Drugs across blood-brain barrier

emulate
Space Tango

PI: Christopher Hinojosa

Lung infection

Penn University of Pennsylvania
BIOSERVE SPACE TECHNOLOGIES
Space Tango

PI: Scott Worthen

Muscle wasting (sarcopenia)

UF UNIVERSITY of FLORIDA
Space Tango

PI: Siobhan Malany

Gut inflammation

emulate
Space Tango

PI: Christopher Hinojosa

Cardiac dysfunction & engineered heart tissues

W UNIVERSITY of WASHINGTON
THE OHIO STATE UNIVERSITY
BIOSERVE SPACE TECHNOLOGIES

PI: Deok-Ho Kim

Stanford University
UCSB
BIOSERVE SPACE TECHNOLOGIES

PI: Joseph Wu

Post-traumatic osteoarthritis

MIT
techshot

PI: Al Grodzinsky

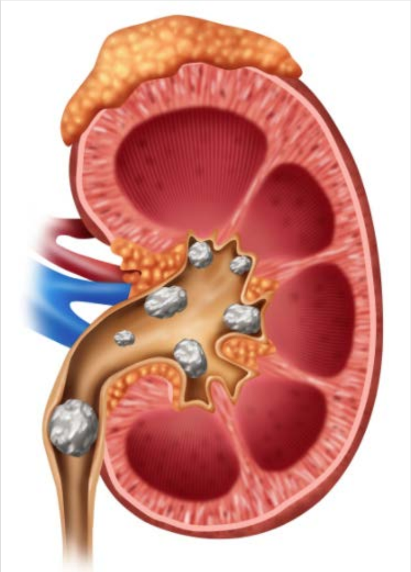
Images courtesy of
Dr. Lucie Low, NCATS

TISSUE CHIPS IN SPACE: 2016-2024 MISSIONS

Proteinuria and kidney stone formation

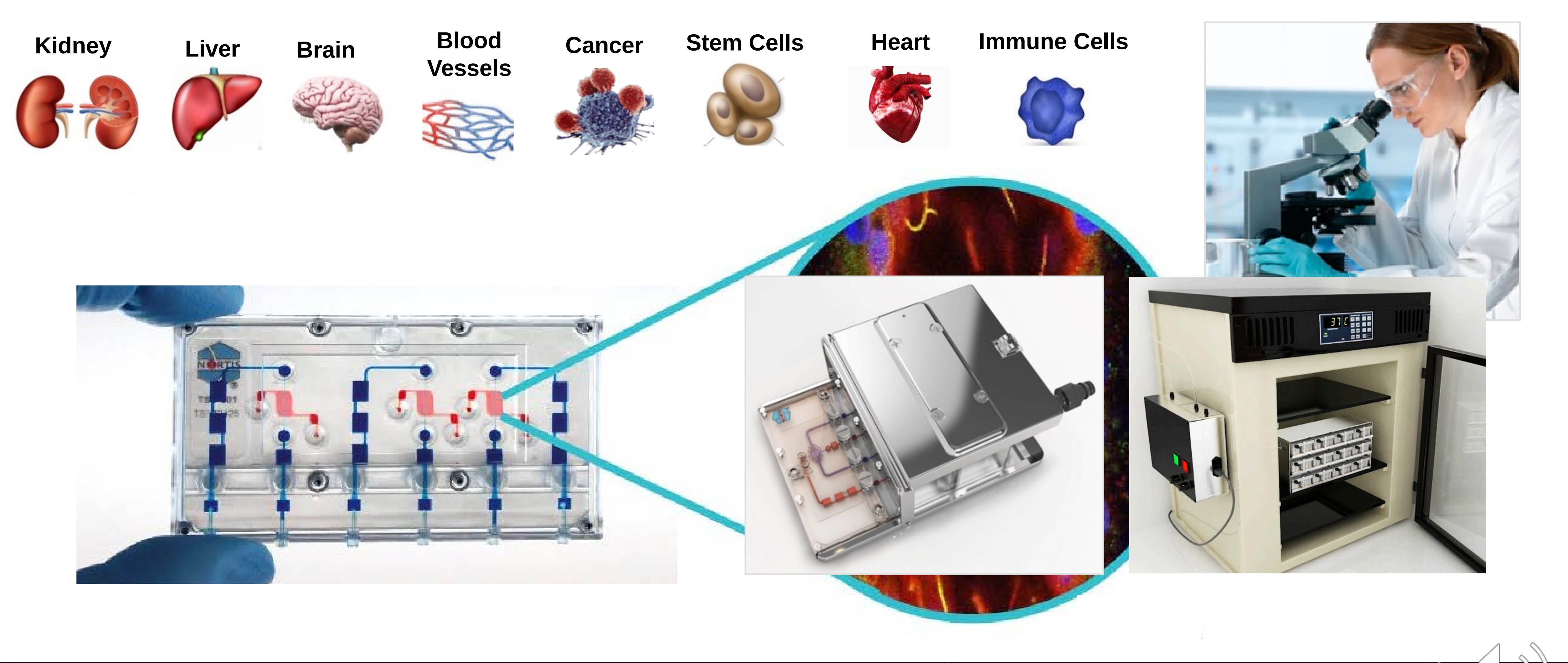
SCHOOL OF PHARMACY
UNIVERSITY of WASHINGTON

BIOSERVE
SPACE TECHNOLOGIES

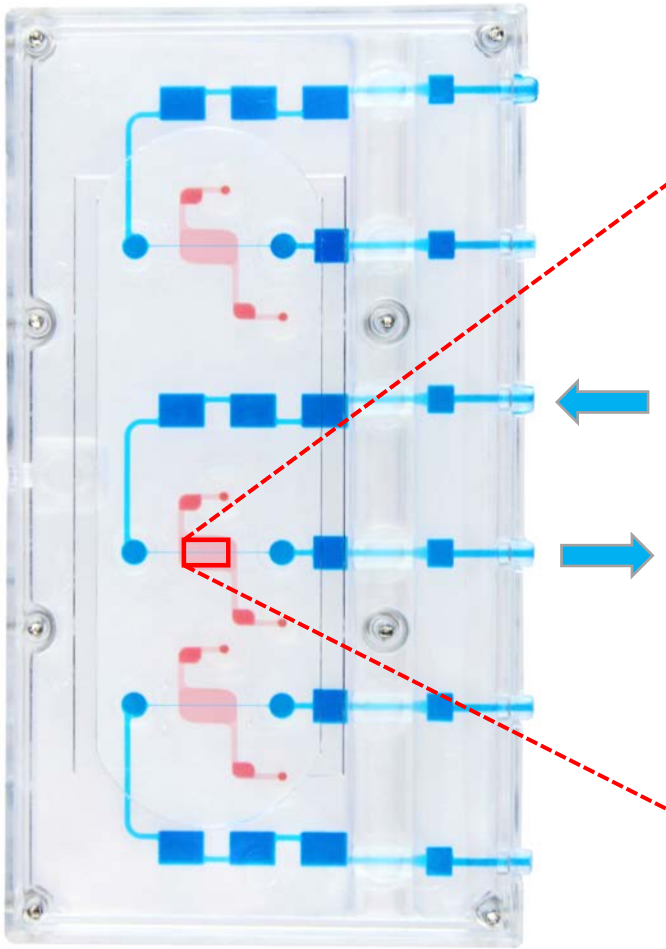


PI: Jonathan Himmelfarb

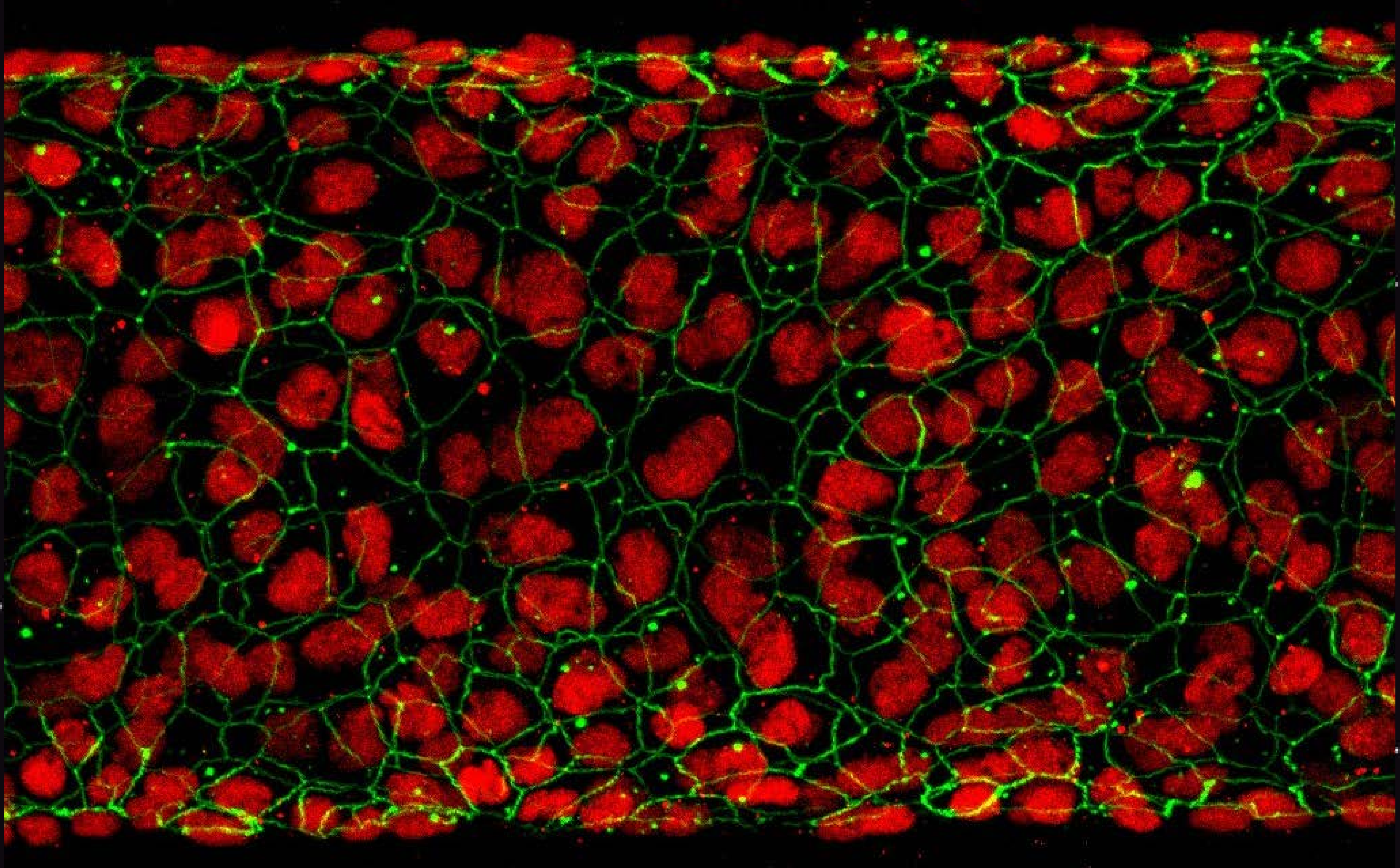
KEY ELEMENTS OF NORTIS' MPS TECHNOLOGY



CREATING KIDNEY TUBULES IN THE CHIP



STRUCTURAL INTEGRITY



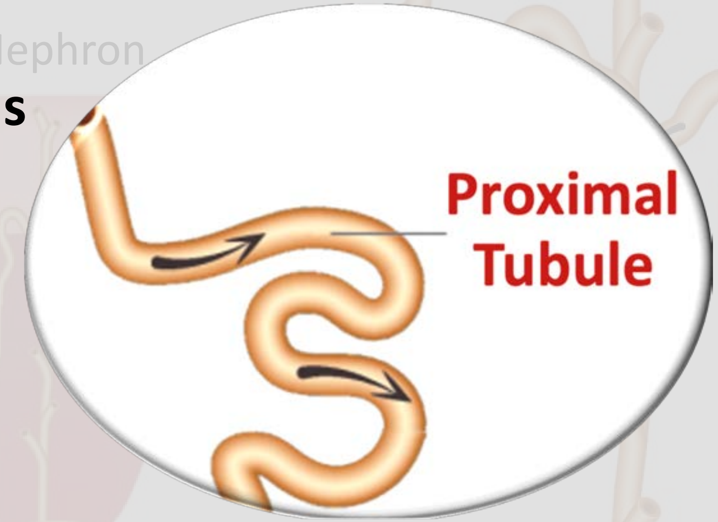
Kidney tubule; nuclei red, ZO-1 green

PROXIMAL TUBULE

MICROANATOMY, -PHYSIOLOGY, -PATHOLOGY

Functions

- Reabsorption of salts and water
- Intrinsic immune functions
- Glucose reabsorption
- Vitamin D synthesis
- Secretion of xenobiotics
- Erythropoietin synthesis



Pathologies

- Immunologic, ischemic or toxic injury
- Chronic kidney injury
- Reduced resilience
- Tubulointerstitial inflammation and fibrosis
- Mineral bone disorder
- Nephrolithiasis
- Anemia

https://www.corelaboratory.abbott/sal/learningGuide/ADD-00061641_Kidney_Learning_Guide.pdf

RENAL TRANSPORTERS

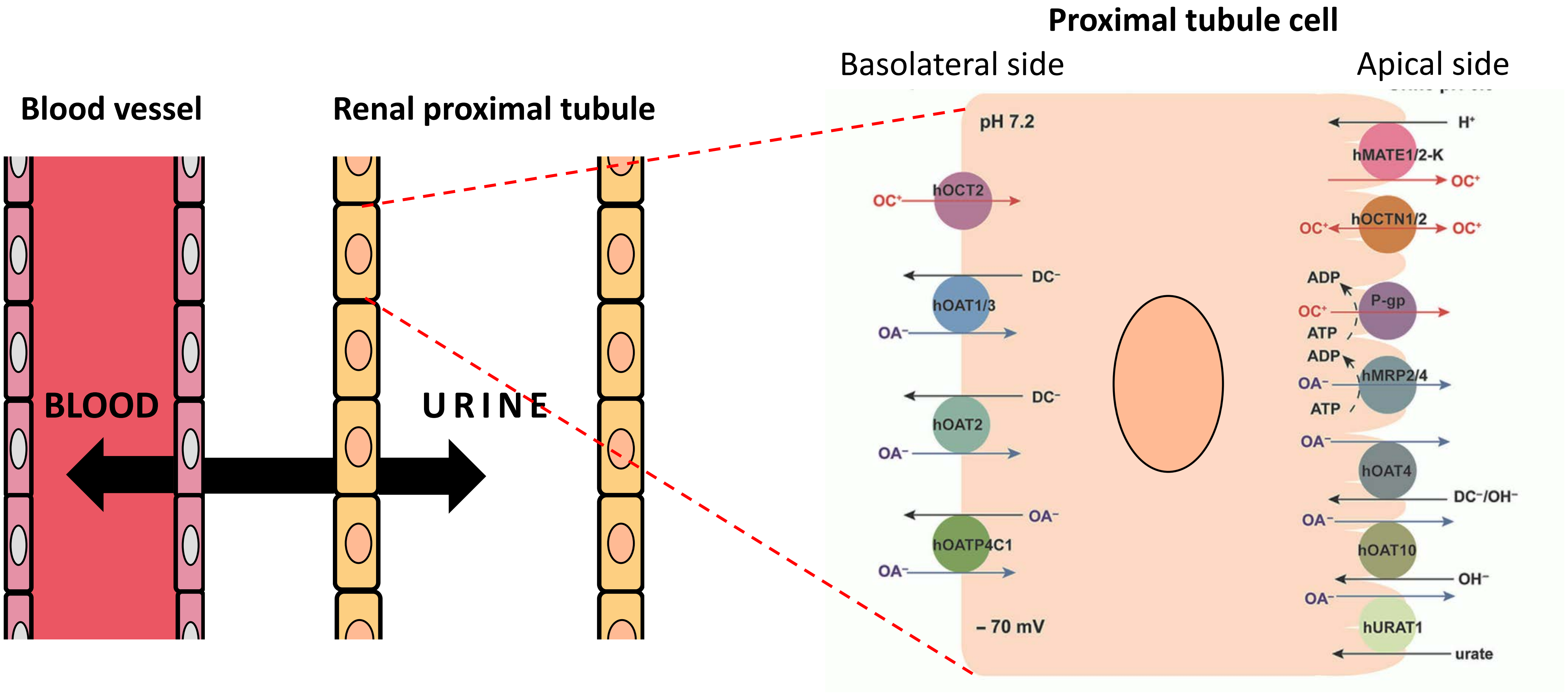
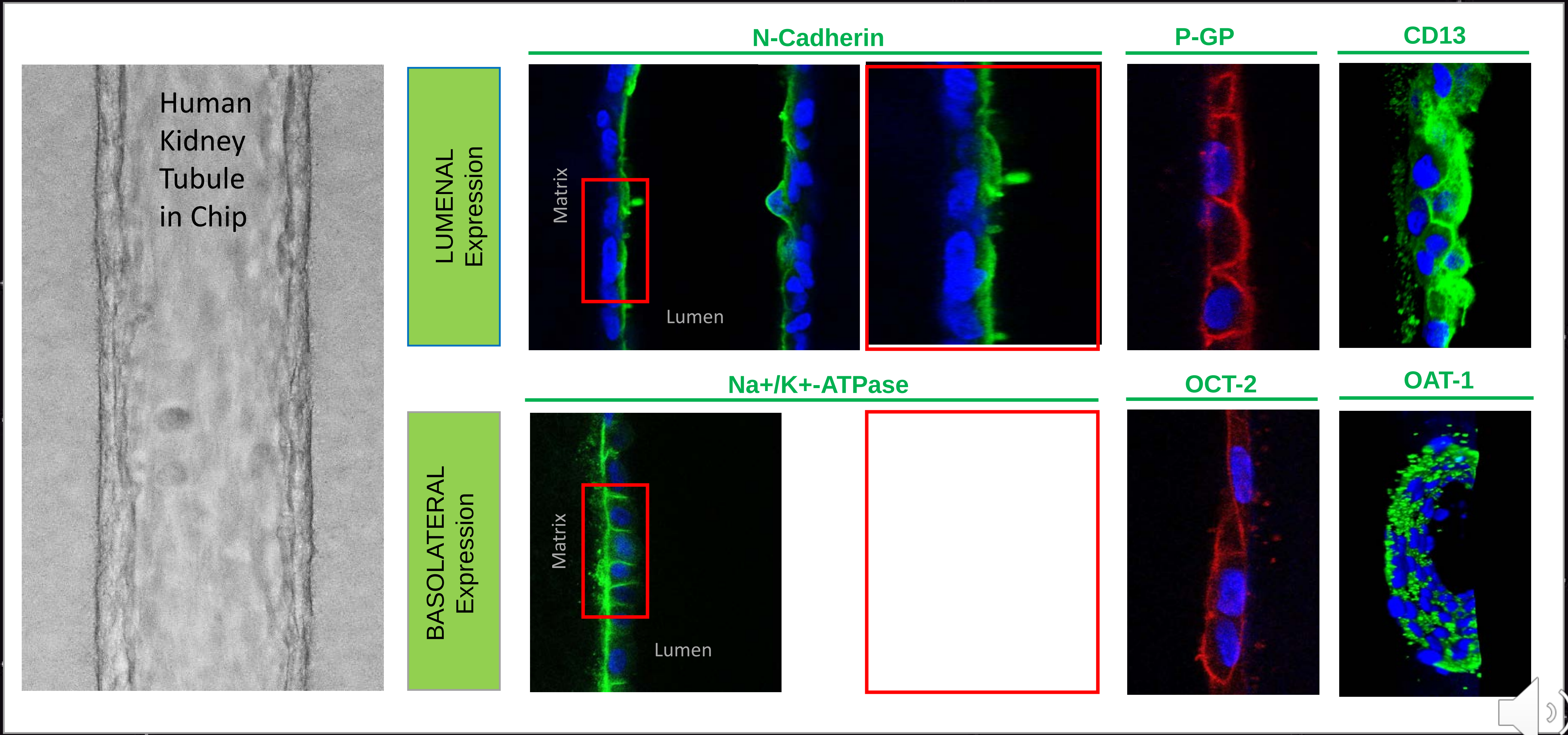


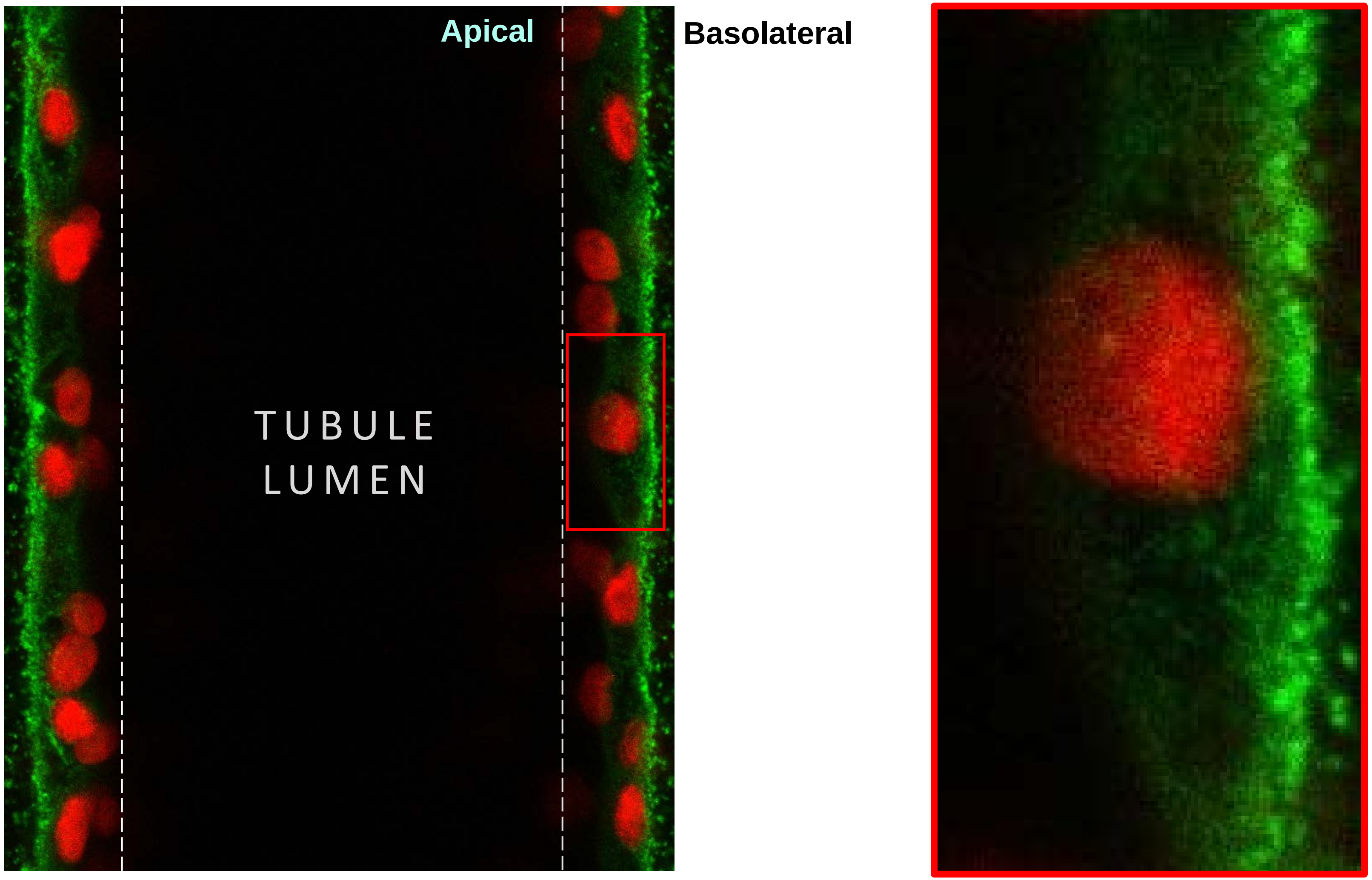
Image source: Yin and Wang, Acta Pharmaceutica Sinica, 2016

REPLICATING TUBULE POLARITY IN VITRO



REPLICATING TUBULE POLARITY IN VITRO

Basolateral Expression of Organic Anion Transporter 3 (OAT 3)

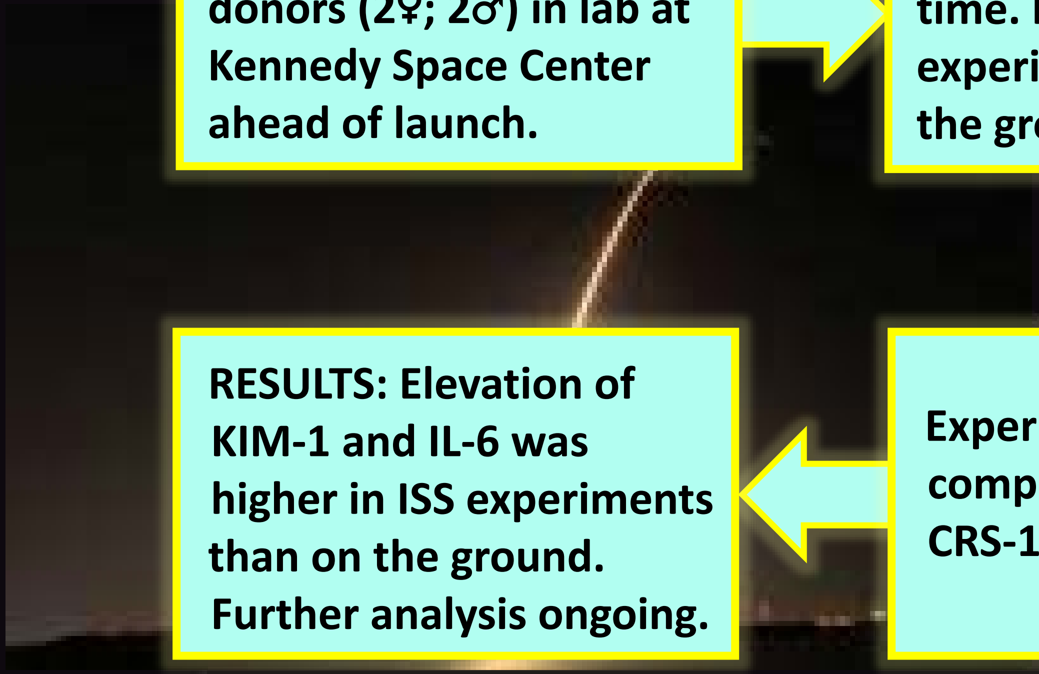


KIDNEY CHIP MISSION ON THE ISS

LAUNCH 1: CRS-17 | MAY 4TH, 2019 – RETURN JUNE 3RD 2019

Project 1: Role of proteinuria in the progression of chronic kidney disease

Project 2: Bioactivation of vitamin D3 in the kidney under microgravity



Kidney chips were seeded with cells from 4 human donors (2♀; 2♂) in lab at Kennedy Space Center ahead of launch.

→ Launch, installation on ISS and 6 days equilibration time. Matched experimental setup on the ground.

→ 48h perfusion with test articles (human serum, Vitamin D) via the lumen of the kidney tubules in the chips.

↓ Effluent from all chips collected and frozen for later RNAseq analysis on the ground. Chips were fixed in formalin.

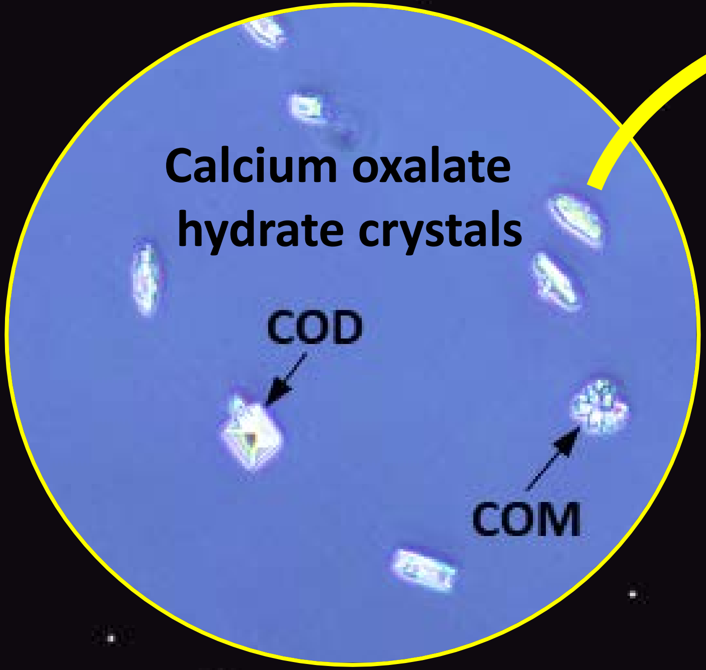
← Experiments were completed successfully. CRS-17 returned to earth.

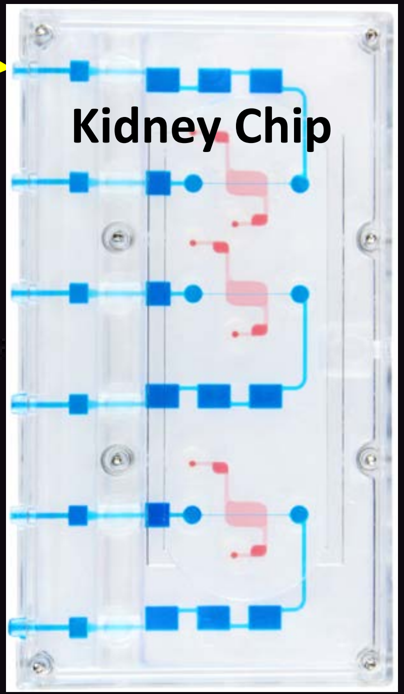
← RESULTS: Elevation of KIM-1 and IL-6 was higher in ISS experiments than on the ground. Further analysis ongoing.

...coming up

LAUNCH 2: CRS-22 | CURRENTLY SCHEDULED MAY/JUNE 2021

Project: Understanding the mechanisms of kidney stone formation in space





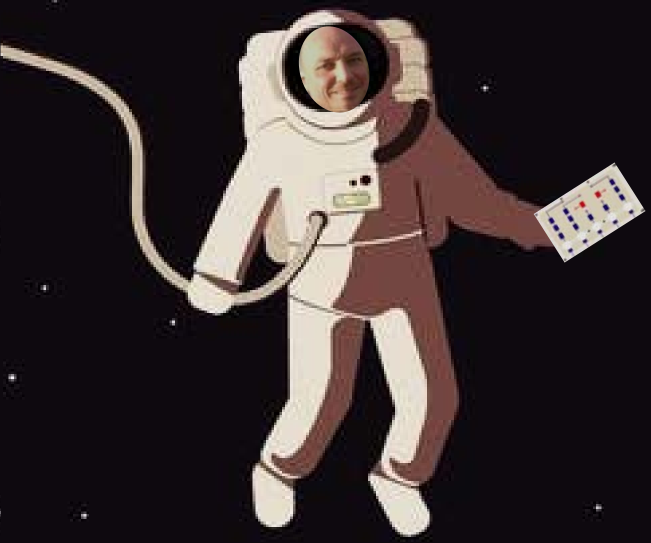
Astronauts have an increased risk for developing kidney stones

Monitor crystal growth and its effect on cell behavior in kidney chip under microgravity and on the ground

COM = Calcium oxalate monohydrate
COD = Calcium oxalate dihydrate

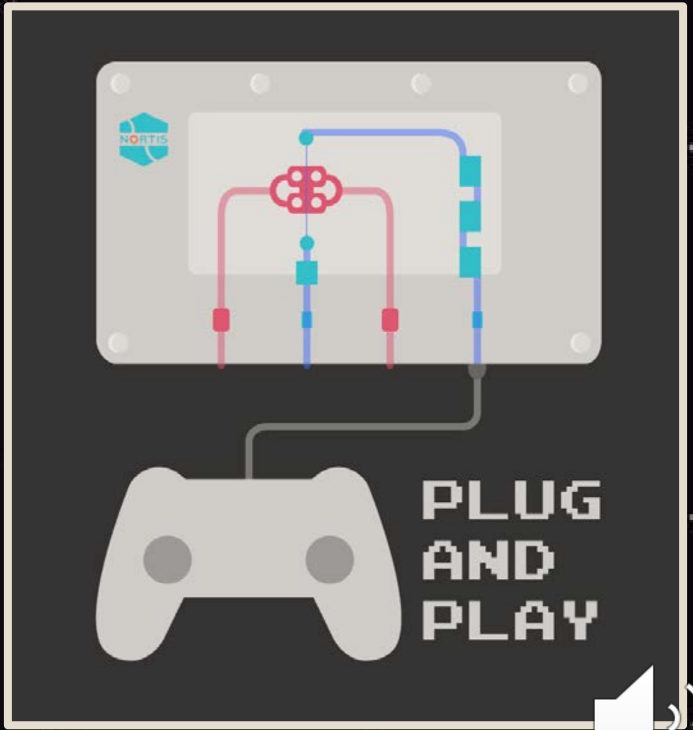
LESSONS LEARNED FROM TISSUE CHIPS IN SPACE

NEED FOR PLUG & PLAY



Many MPS users are like astronauts.

- High experimental success rate is a must
- Don't have the time to spend weeks on growing the tissue before using it
- Limited personnel, equipment, time and space



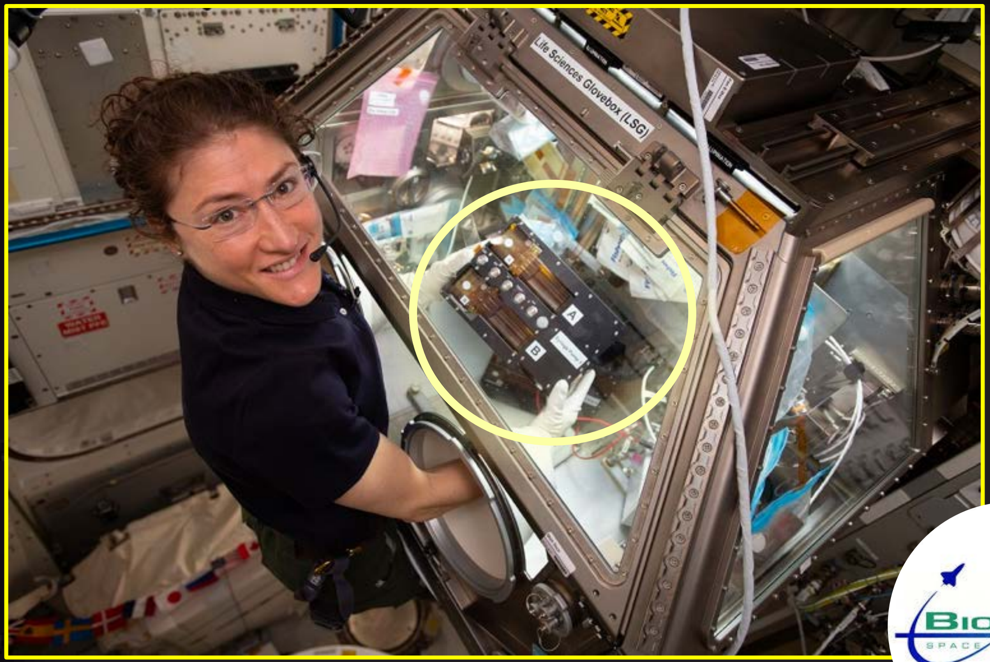
LESSONS LEARNED FROM TISSUE CHIPS IN SPACE

NEED FOR MINITURIZATION AND AUTOMATION

Ground

72 Experiments
24 chips
24 perfusion modules a 1 chip
1 incubator

ISS

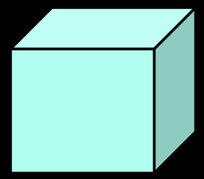


72 Experiments
24 chips
4 perfusion modules a 6 chips

LESSONS LEARNED FROM CHIPS IN SPACE

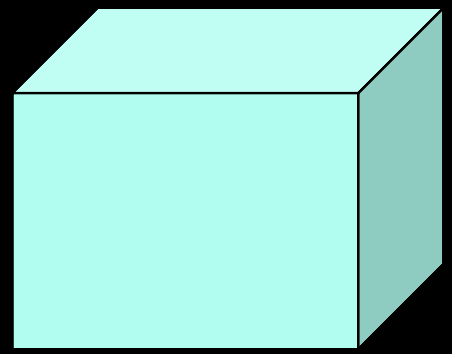
CONCEPT OF NEXT GENERATION MPS PLATFORM

Hardware System for Research Settings



- Small
- Modular
- Compatible with lab equipment
- High experimental freedom
- Empty or pre-seeded chips

Hardware System for Large-scale Routine Use



- Standalone unit
- Automated, integrated platform (imaging, fluid handling, software, reagents, protocols)
- Increased throughput
- Pre-seeded chips

Disposables

- Chips
- Reagents
- Cells

ACKNOWLEDGMENTS

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