



# Organ-on-chip technologies as an integrative hub for biomedical research: toward a connected core facility

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# Organ-on-chip: definition

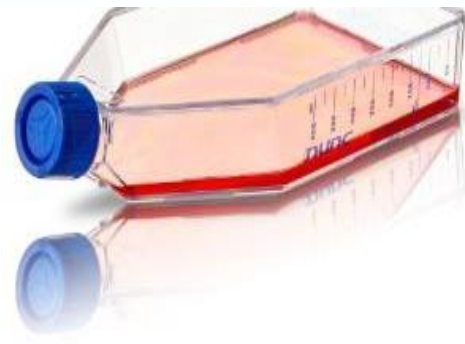
**Bioengineered microfluidics devices that recapitulate key functional aspects of organs and tissues (and body !)**



- **integration of multiple cell types** to reflect a more physiological balance of cells  
*(i.e. parenchymal, stromal, vascular and immune cells and/or microbiome)*
- **presence of biomechanical forces** relevant to the tissue being modelled  
*(i.e. stretch forces for lung tissues or haemodynamic shear forces for vascular tissues)*

# Why using organ-on-chip?

*In vitro*

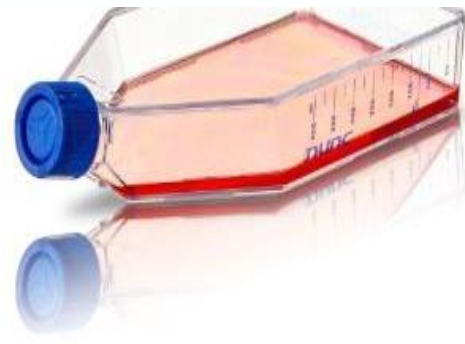


*In vivo*



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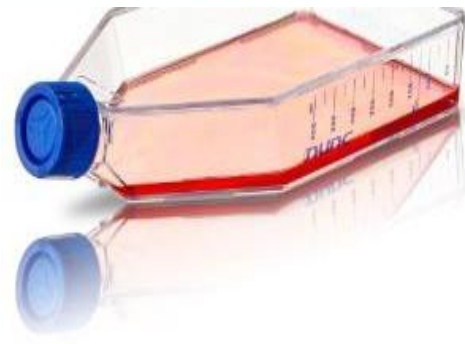
- Simple
- Human cells
- Controlled environment
- Reproducibility
- Low costs
- High-throughput (fast)
- Monolayer
- Few cell-cell and cell-matrix interactions
- Static environment
- Adhesion to high stiffness substrate (cellular morphology alteration)

## *In vivo*



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## *In vivo*



- Multicellular environment
- Hydrodynamic and mechanical cues
- 3D organization
- Not (human) physiologically relevant
- Confounding variables
- Expensive
- Strict regulations and compliance standards
- Ethical problems

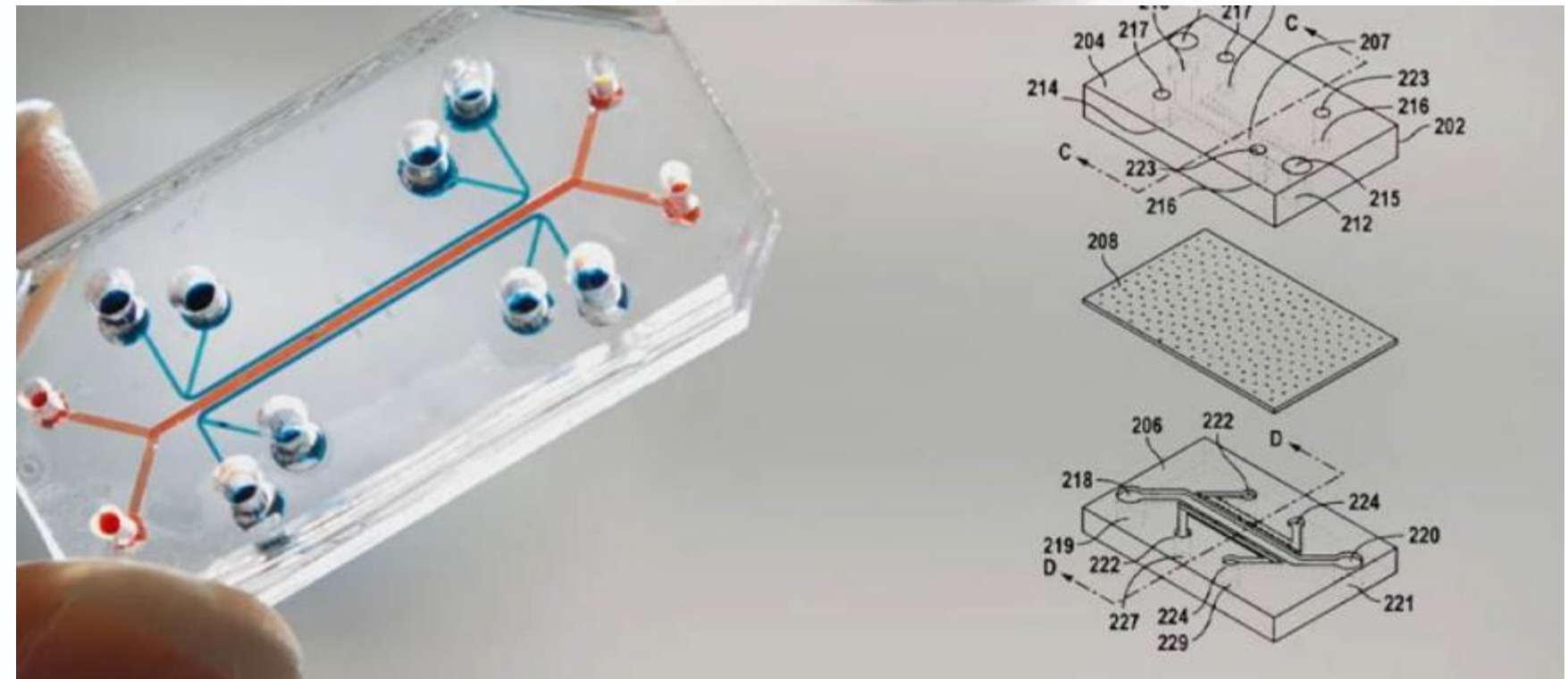
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# HuMiX

## Gut-on-chip

ARTICLE

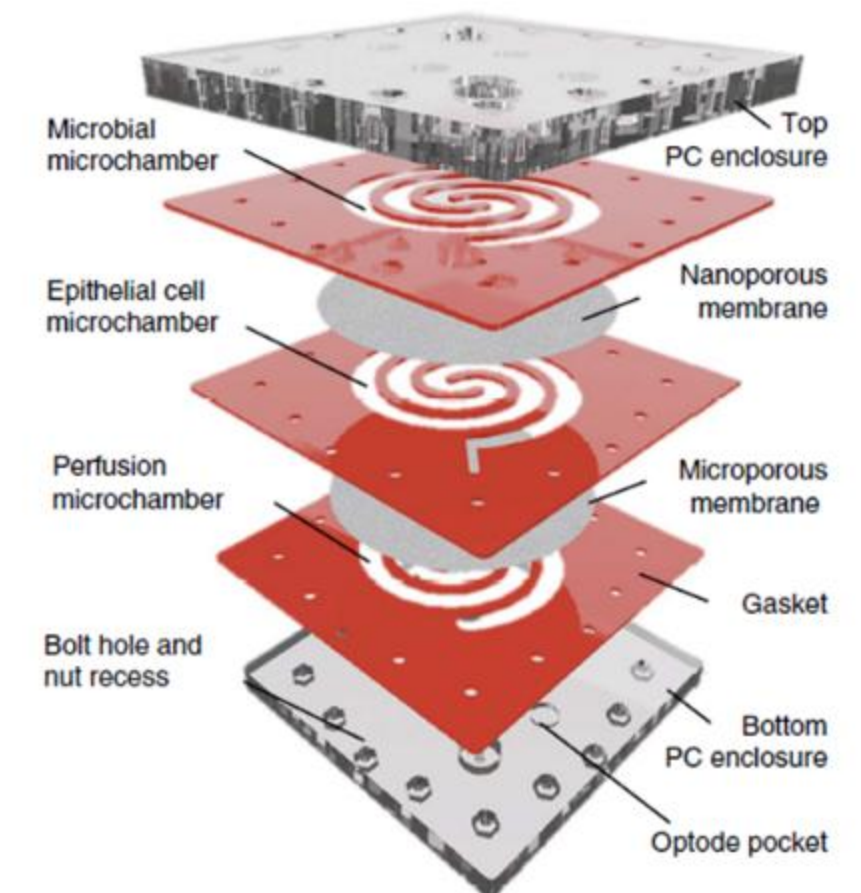
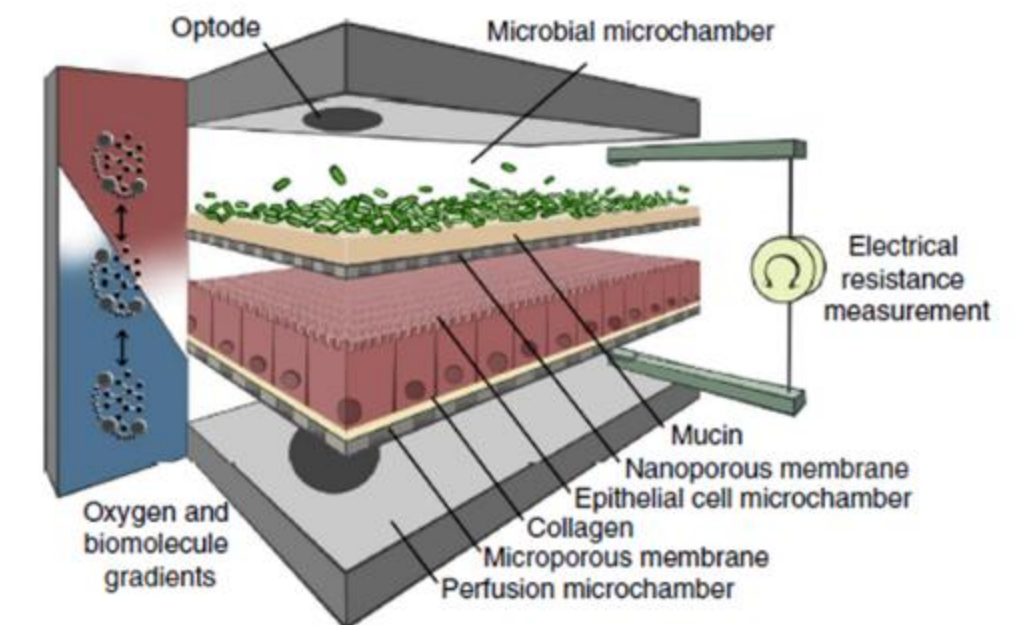
Received 31 Jan 2016 | Accepted 6 Apr 2016 | Published 11 May 2016

DOI: 10.1038/ncomms11535

OPEN

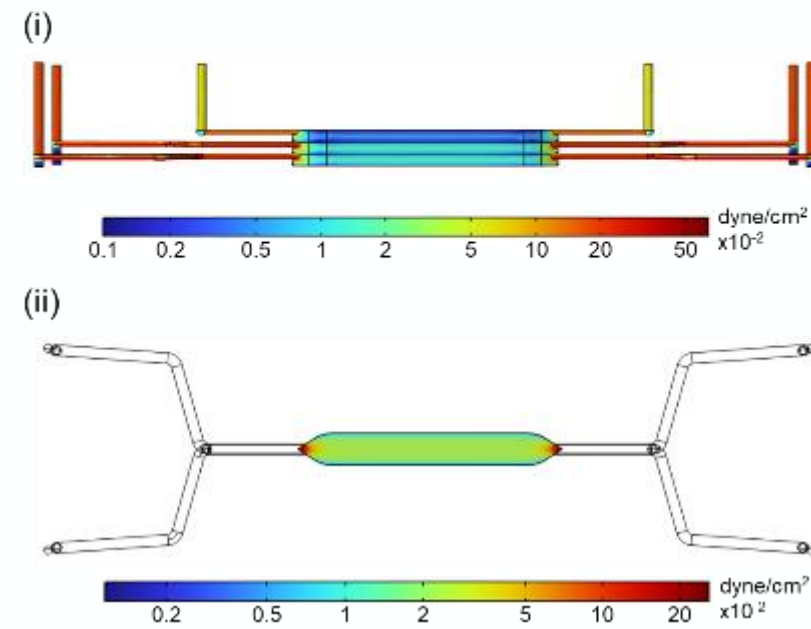
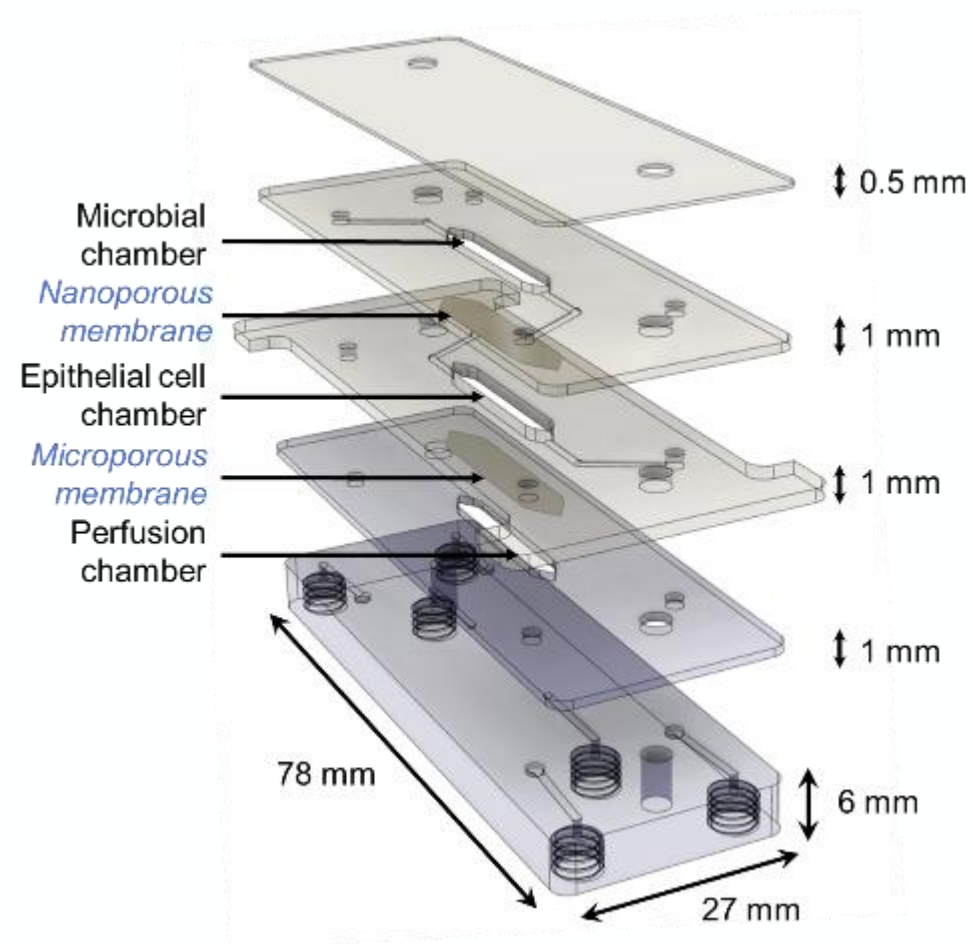
## A microfluidics-based *in vitro* model of the gastrointestinal human-microbe interface

Pranjul Shah<sup>1</sup>, Joëlle V. Fritz<sup>1</sup>, Enrico Glaab<sup>1</sup>, Mahesh S. Desai<sup>1,†</sup>, Kacy Greenhalgh<sup>1</sup>, Audrey Frachet<sup>1</sup>, Magdalena Niegowska<sup>1</sup>, Matthew Estes<sup>2</sup>, Christian Jäger<sup>1</sup>, Carole Seguin-Devaux<sup>3</sup>, Frederic Zenhausern<sup>2,4</sup> & Paul Wilmes<sup>1</sup>



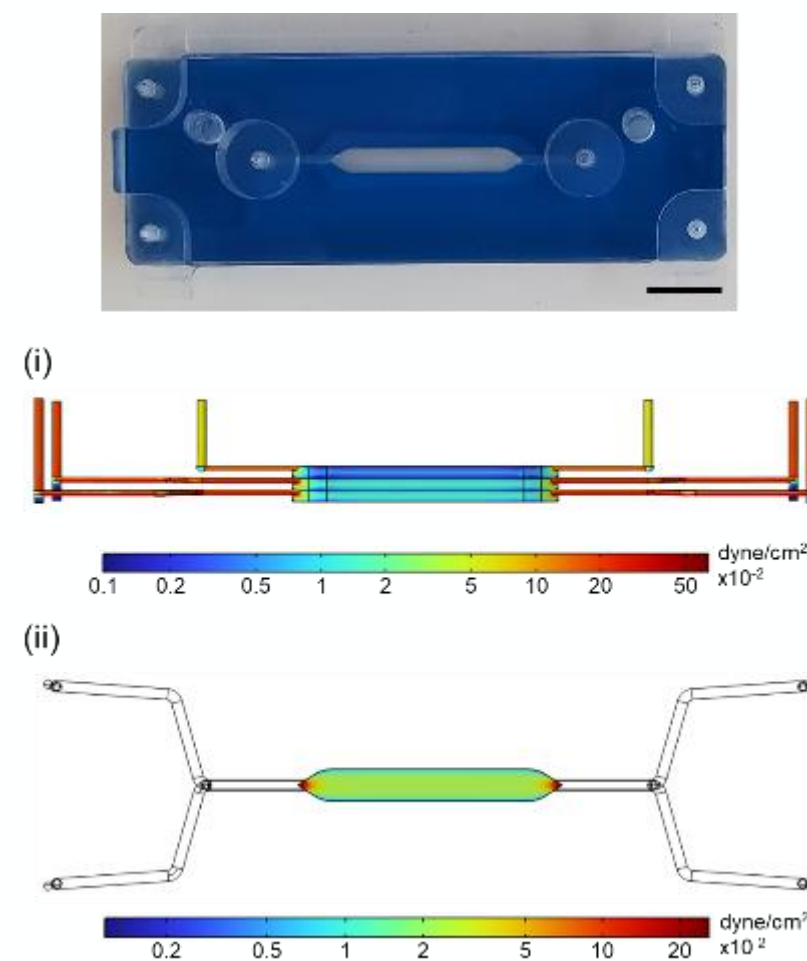
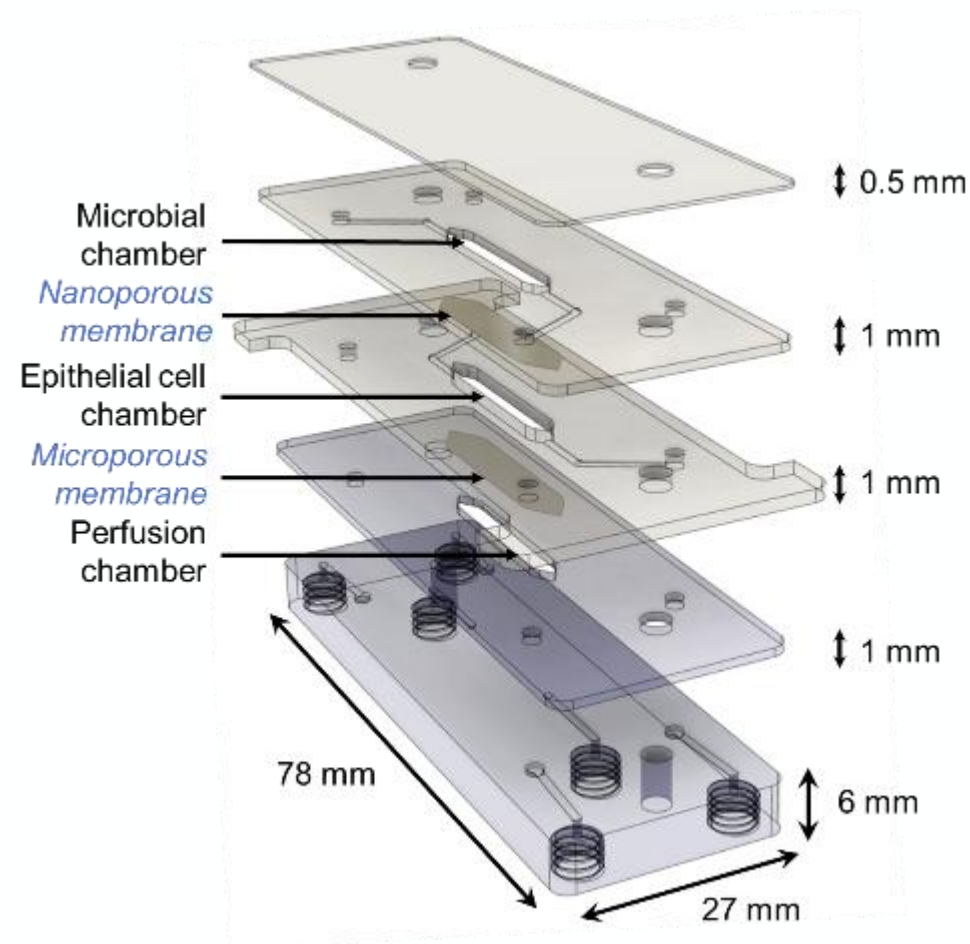
# HuMiX (Human-Microbial Crosstalk): Gut-on-chip

## HuMiX platform model



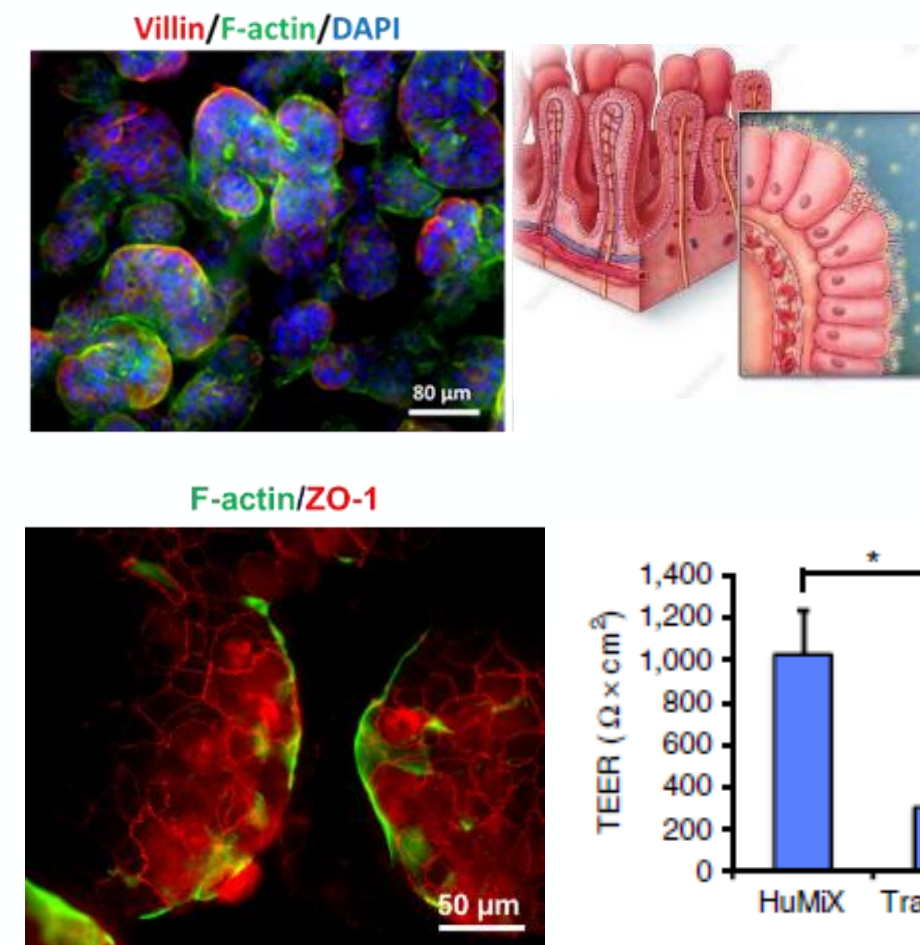
# HuMiX (Human-Microbial Crosstalk): Gut-on-chip

## HuMiX platform model

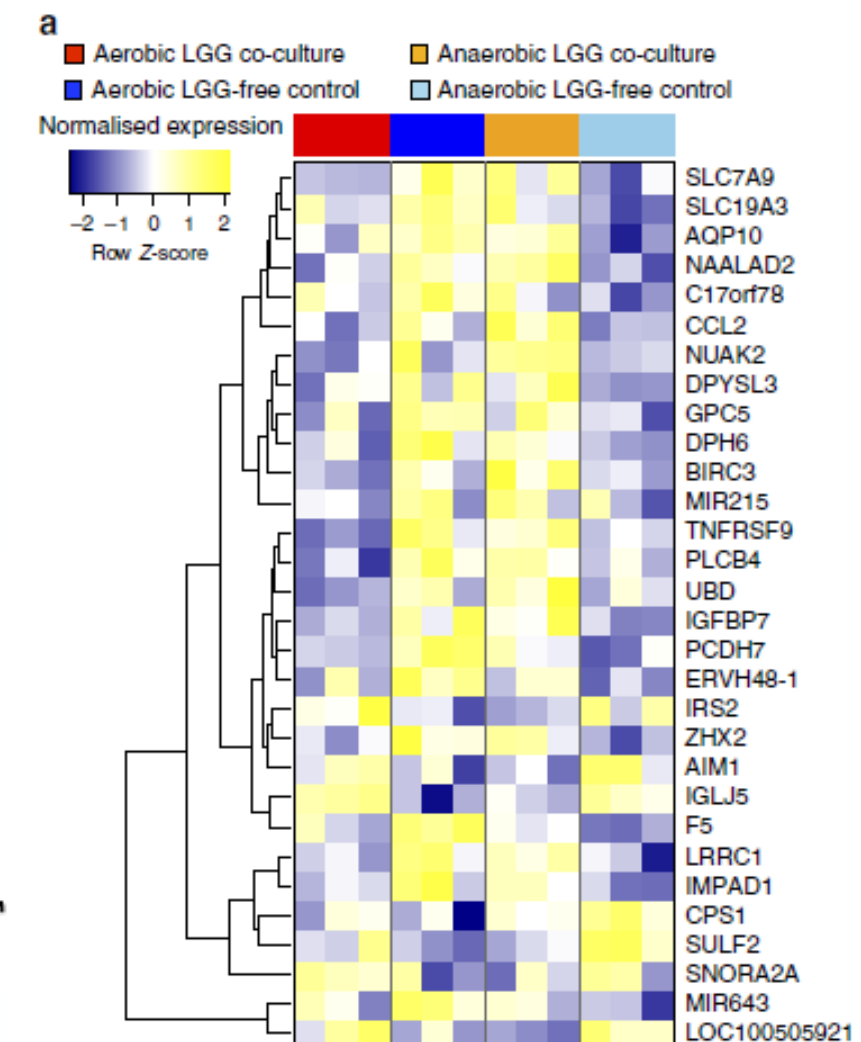


HuMiX recapitulates intestinal barrier

### Formation of intestinal villi



Anaerobic or aerobic bacterial culture differentially affects human transcriptional responses



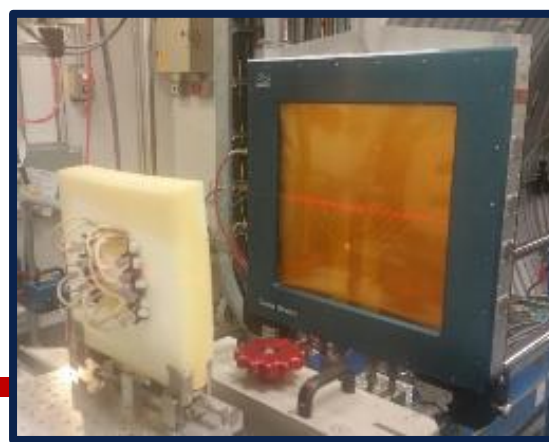
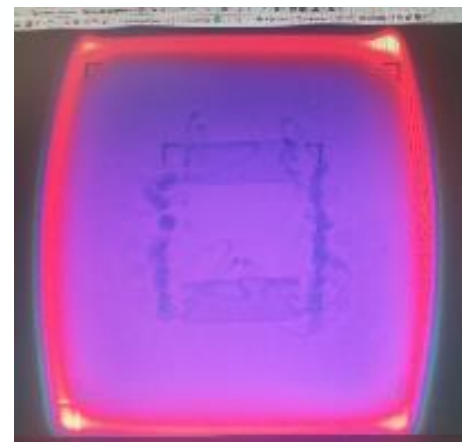
# HuMiX to study the effects of space radiation on human gut microbiome and intestinal cells

## Irradiation at Brookhaven National Laboratory (BNL)

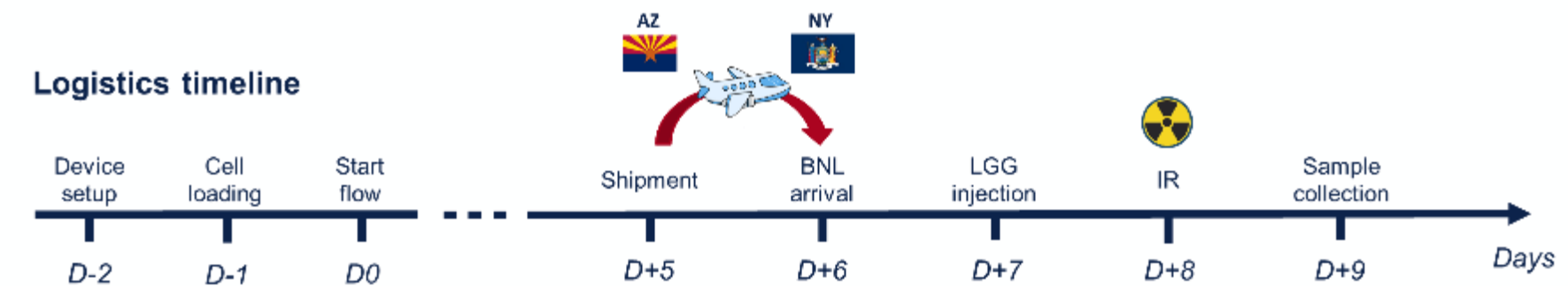
NASA Space Research Laboratory (NSRL)



*HuMiX device in NSRL beam*



### Logistics timeline

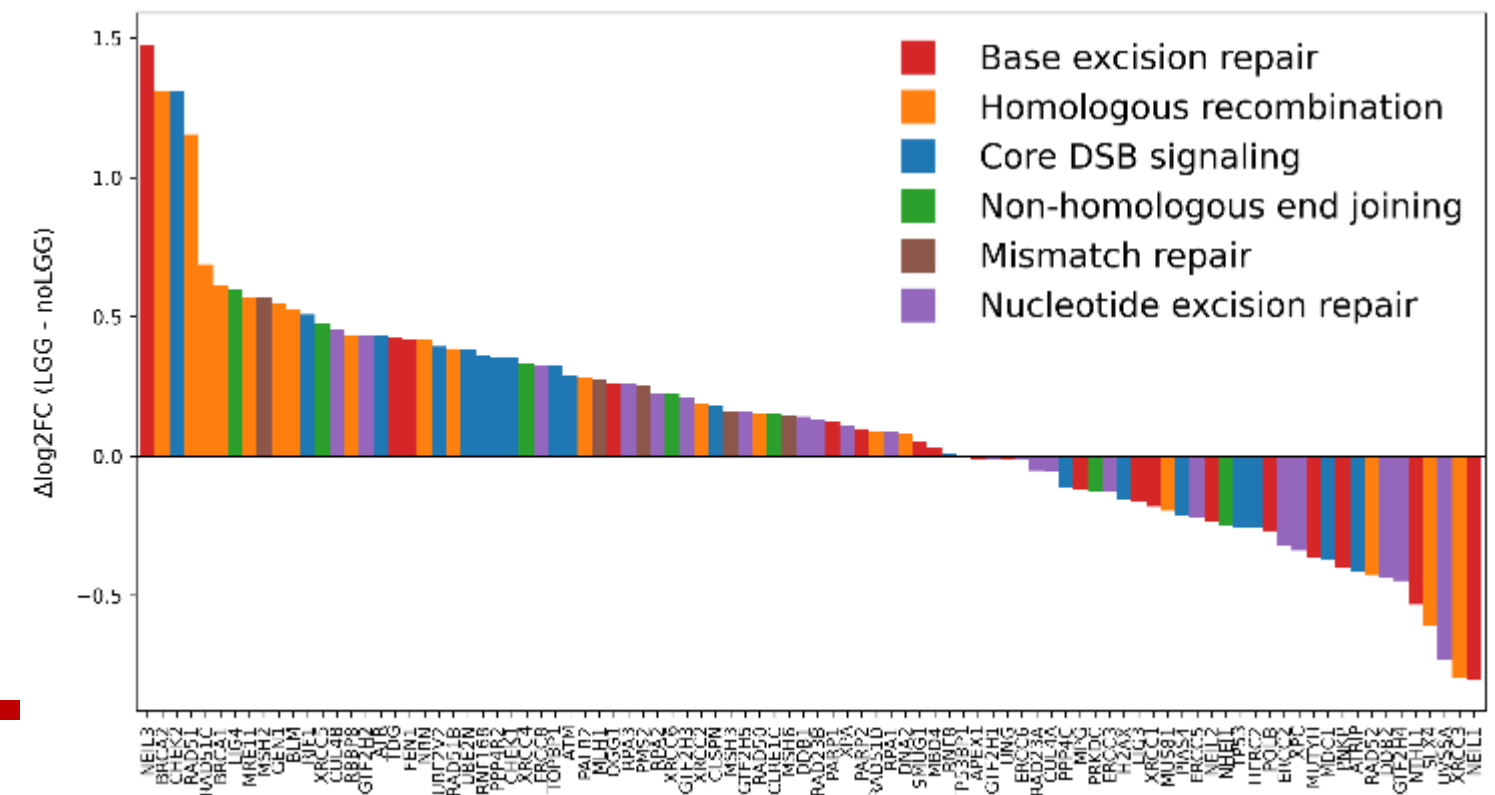
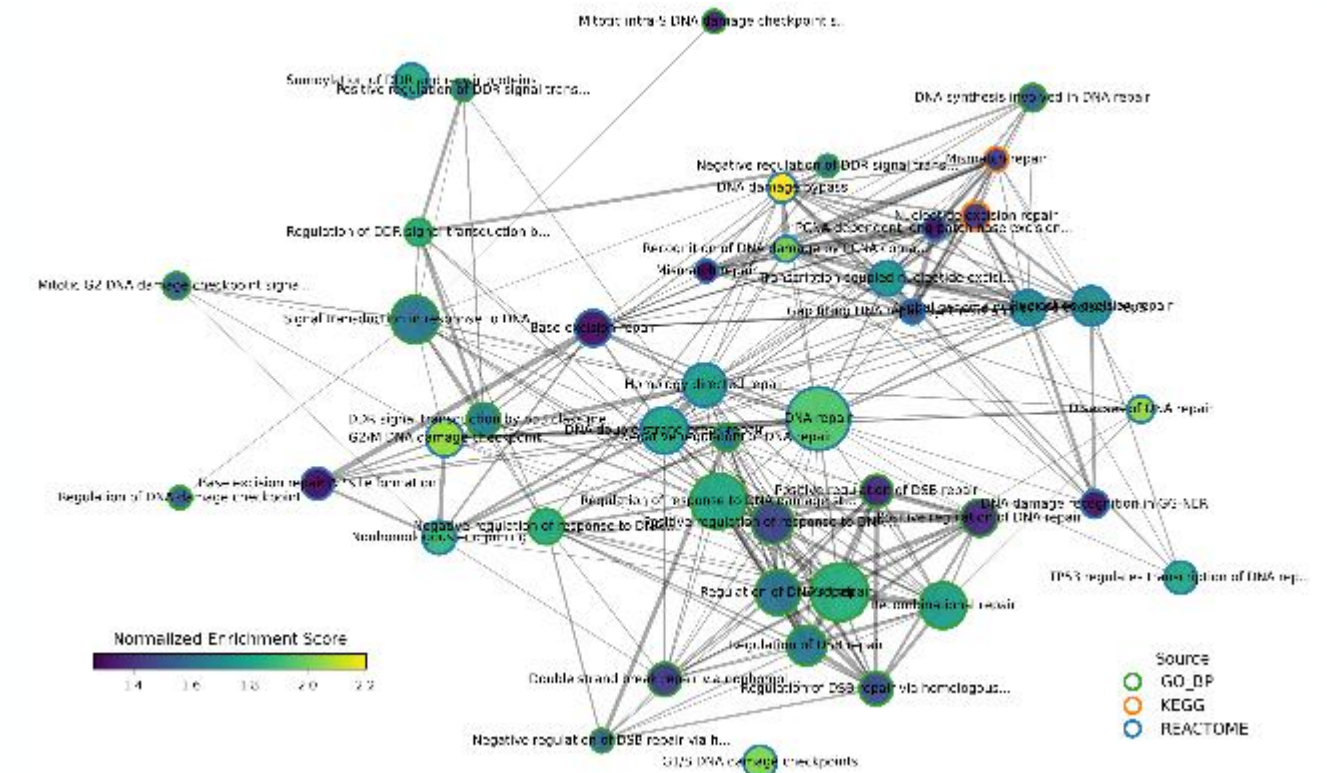
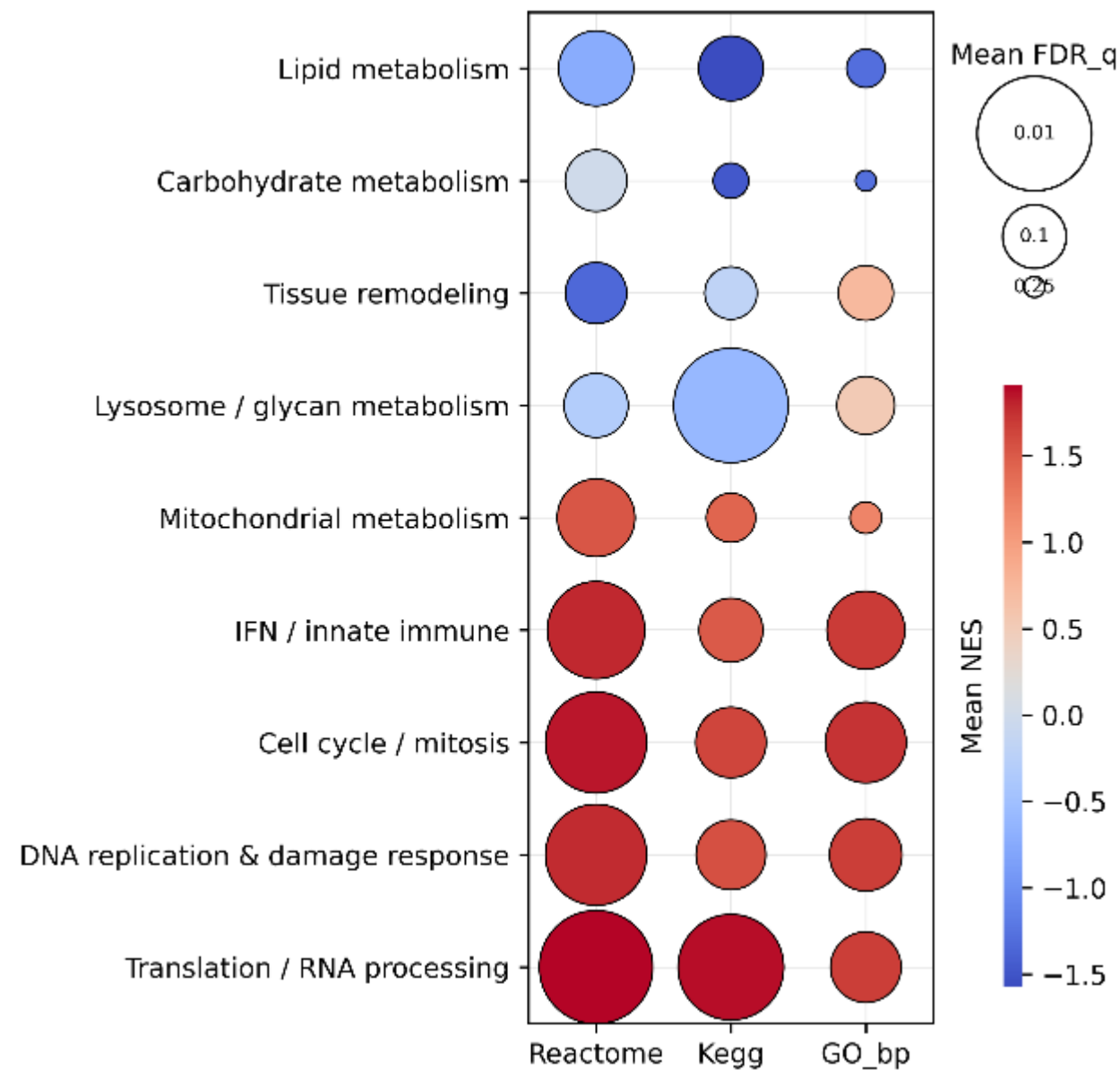


### Sampling and experimental design:

- Radiation types:  $^{28}\text{Si}$ ,  $^{56}\text{Fe}$ ,
- Space-relevant radiation doses: 0.75 Gy for  $^{28}\text{Si}$ ,  $^{56}\text{Fe}$
- LGG vs. no LGG
- RNA sequencing, functional assays

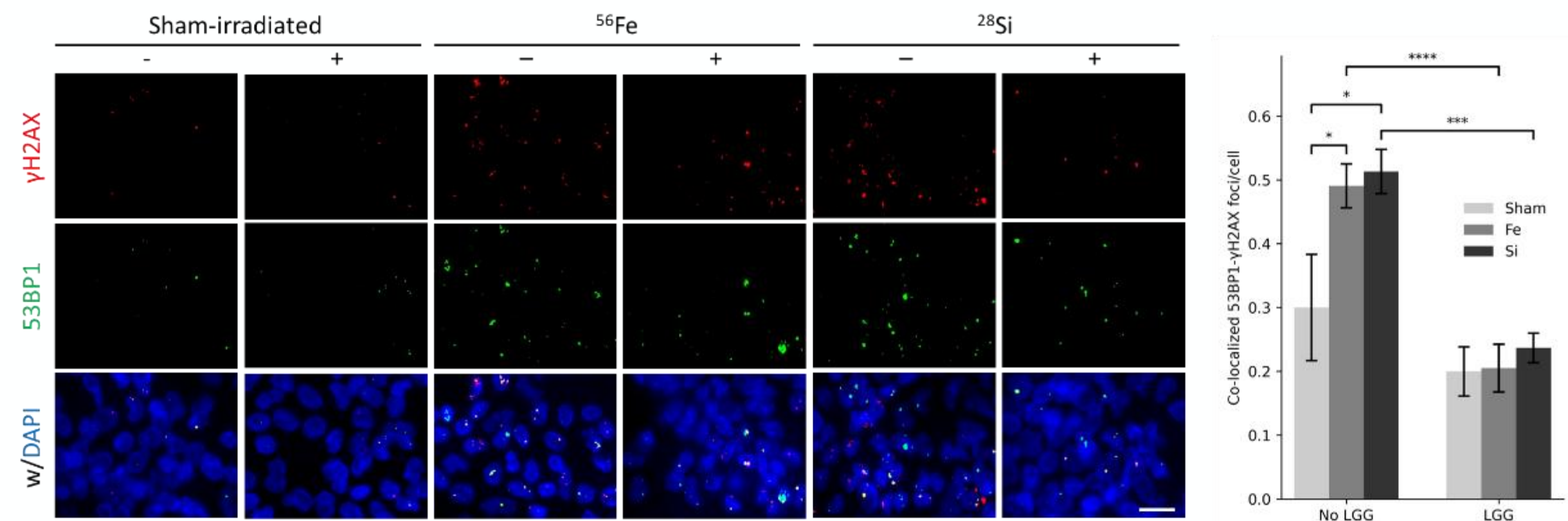
# HuMiX to study the effects of space radiation on human gut microbiome and intestinal cells

At the transcriptomic level, LGG-exposed cells respond differently to both  $^{56}\text{Fe}$  and  $^{28}\text{Si}$  radiation compared with cells not co-cultured with LGG



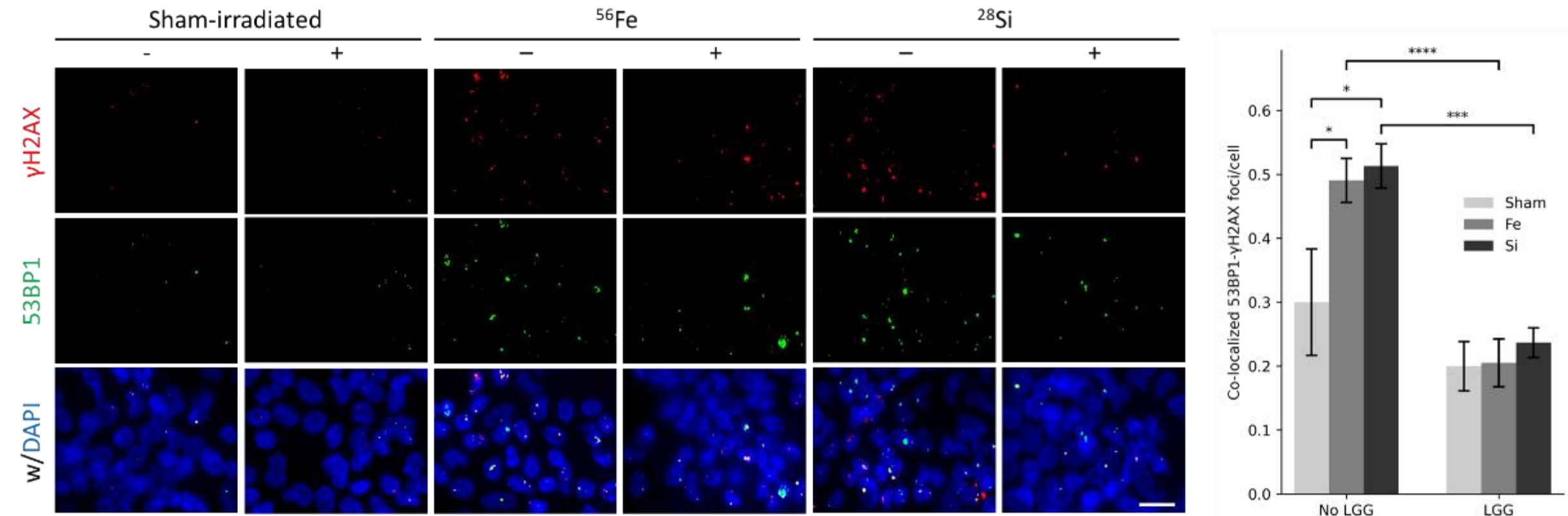
# HuMiX to study the effects of space radiation on human gut microbiome and intestinal cells

LGG decreased DNA damage in human intestinal cells after  $^{56}\text{Fe}$  and  $^{28}\text{Si}$  exposure



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LGG decreased DNA damage in human intestinal cells after  $^{56}\text{Fe}$  and  $^{28}\text{Si}$  exposure



*Lactobacillus rhamnosus* GG alleviates radiation-induced intestinal injury by modulating intestinal immunity and remodeling gut microbiota

Li-Li Zhang<sup>a</sup>, Jia-Ying Xu<sup>b</sup>, Yifei Xing<sup>a</sup>, Pengcheng Wu<sup>c</sup>, Yi-Wen Jin<sup>a</sup>, Wei Wei<sup>b</sup>, Lin Zhao<sup>b</sup>, Jing Yang<sup>d</sup>, Guo-Chong Chen<sup>a</sup>, Li-Qiang Qin<sup>a,\*</sup>

Zhang et al. *Microbiol Res.* 2024;286:127821.

*Lactobacillus rhamnosus* GG protects the intestinal epithelium from radiation injury through release of lipoteichoic acid, macrophage activation and the migration of mesenchymal stem cells

Terrence E Riehl,<sup>1</sup> David Alvarado,<sup>1</sup> Xueping Ee,<sup>1</sup> Aaron Zuckerman,<sup>1</sup> Lynn Foster,<sup>1</sup> Vaishali Kapoor,<sup>2</sup> Dinesh Thotala,<sup>2</sup> Matthew A Ciorba,<sup>1</sup> William F Stenson<sup>1</sup>

Riehl et al. *Gut.* 2019;68(6):1003-1013.

*Lactobacillus* probiotic protects intestinal epithelium from radiation injury in a TLR-2/cyclo-oxygenase-2-dependent manner

Matthew A Ciorba,<sup>1</sup> Terrence E Riehl,<sup>1</sup> M Suprada Rao,<sup>1</sup> Clara Moon,<sup>2</sup> Xueping Ee,<sup>1</sup> Gerardo M Nava,<sup>2</sup> Monica R Walker,<sup>2</sup> Jeffrey M Marinshaw,<sup>1</sup> Thaddeus S Stappenbeck,<sup>2</sup> William F Stenson<sup>1</sup>

Ciorba et al. *Gut.* 2012;61(6):829-38

# Combining organ-on-chip and 3D cell culture

nature reviews bioengineering

<https://doi.org/10.1038/s44222-024-00207-z>

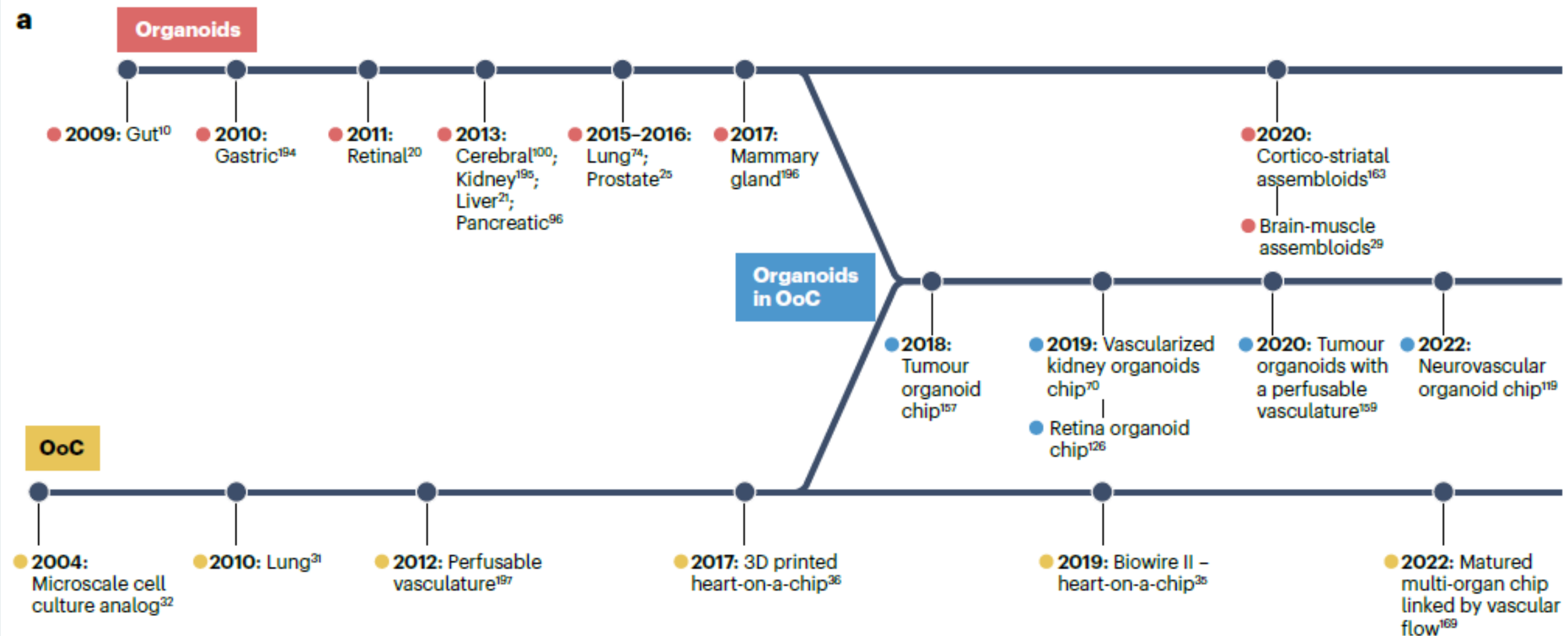
Review article

 Check for updates

## Integrating organoids and organ-on-a-chip devices

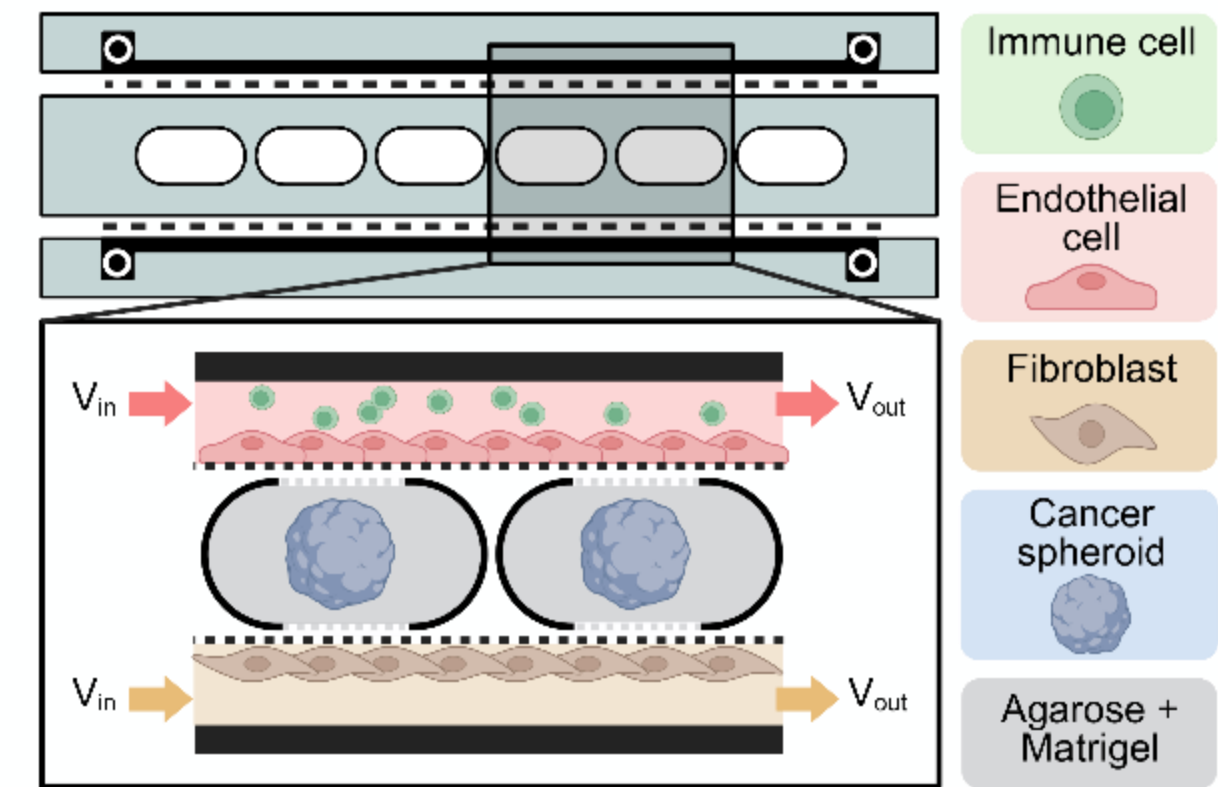
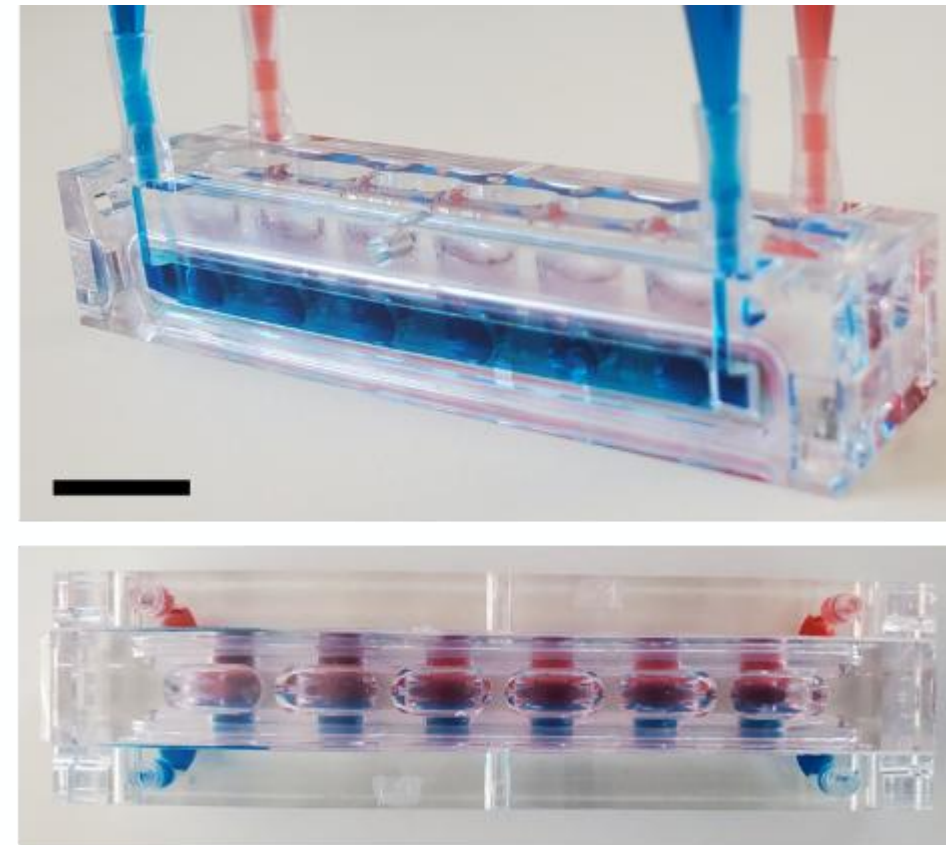
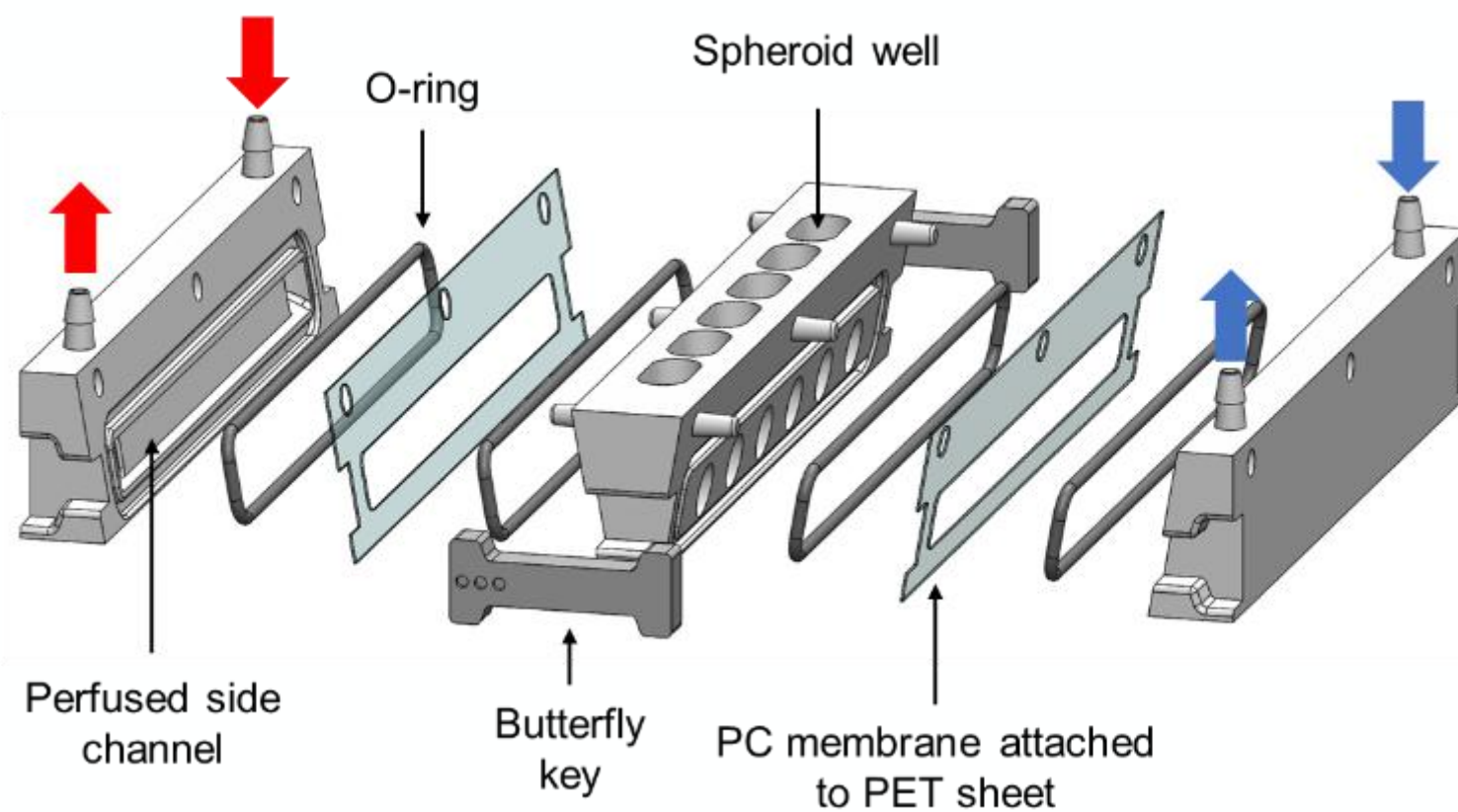
Yimu Zhao<sup>1,2,7</sup>, Shira Landau<sup>1,2,7</sup>, Sargol Okhovatian<sup>1,2</sup>, Chuan Liu<sup>1,2</sup>, Rick Xing Ze Lu<sup>1</sup>, Benjamin Fook Lun Lai<sup>1</sup>, Qinghua Wu<sup>1,2</sup>, Jennifer Kieda<sup>1</sup>, Krisco Cheung<sup>3</sup>, Shravanthi Rajasekar<sup>4</sup>, Kimia Jozani<sup>5</sup>, Boyang Zhang<sup>4,5</sup> & Milica Radisic<sup>1,2,3,6</sup>✉

Takebe et al. *Cell Stem Cell*. 2017. 7;21(3):297-300.



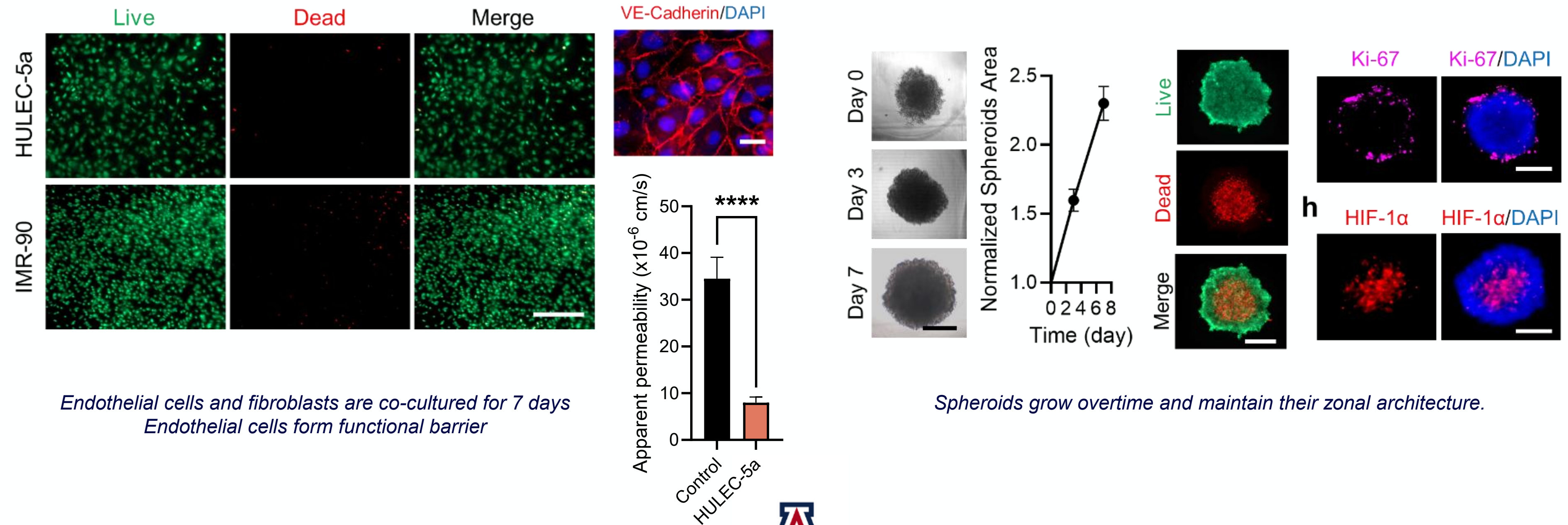
# ASTEROIDS: combination of 3D cell culture with organ-on-chip

**ASTEROIDS**: Apparatus to Simulate Tumor Environment and Reproduce Organs using an Interactive and Dynamic System

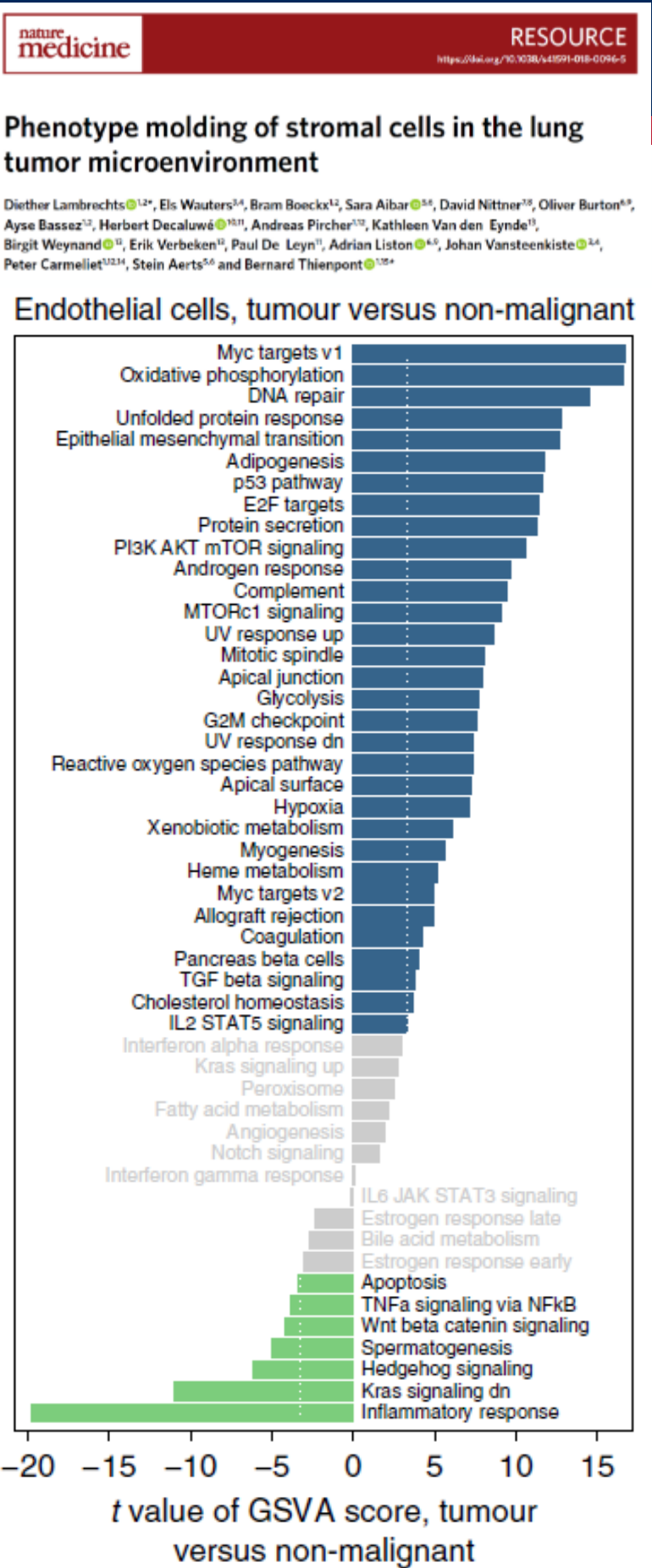


# ASTEROIDS: combination of 3D cell culture with organ-on-chip

ASTEROIDS maintains cell viability and tissue morphology after 7-day culture



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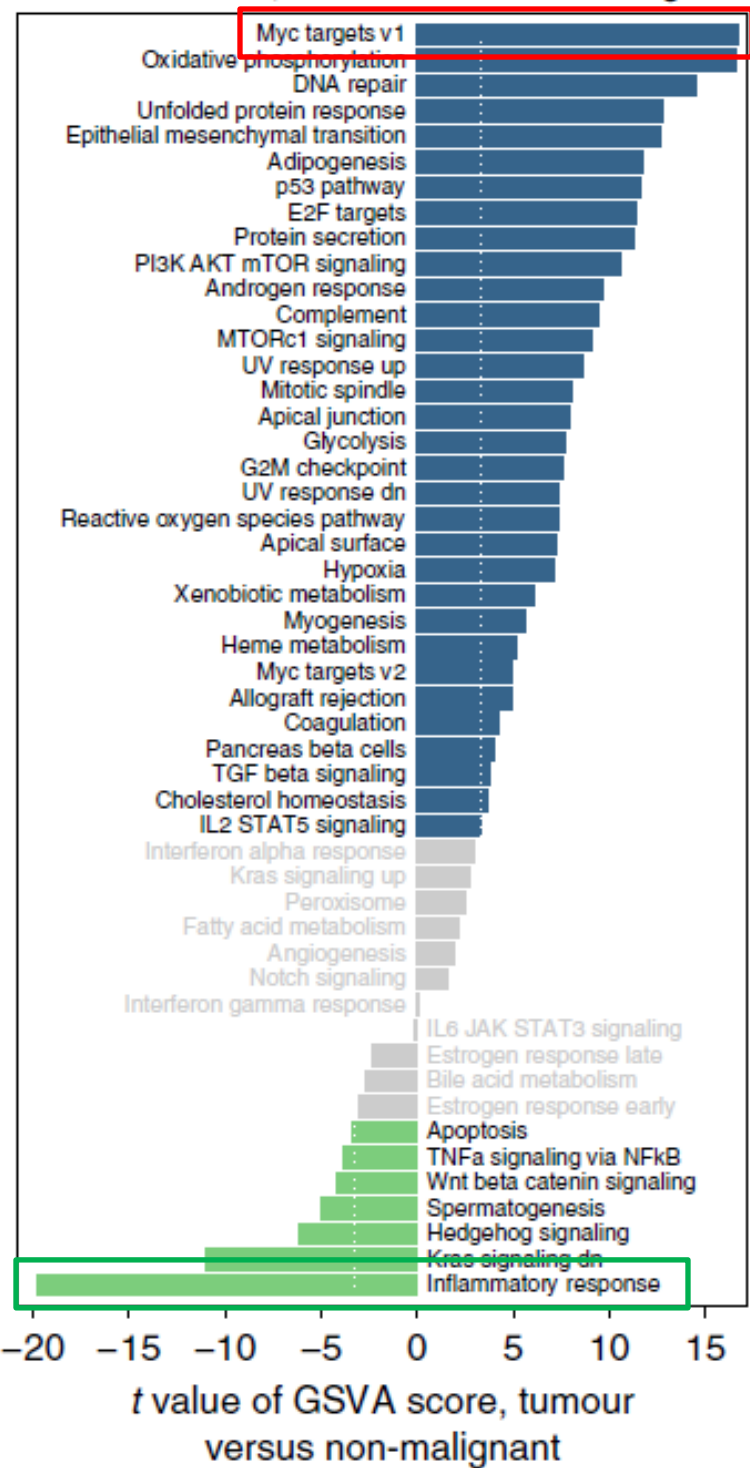


# ASTEROIDS: combination of 3D cell culture with organ-on-chip

## Phenotype molding of stromal cells in the lung tumor microenvironment

Diether Lambrechts<sup>1,2\*</sup>, Els Wauters<sup>3,4</sup>, Bram Boeckx<sup>1,2</sup>, Sara Aibar<sup>5,6</sup>, David Nittner<sup>7,8</sup>, Oliver Burton<sup>6,9</sup>, Ayse Bassez<sup>1,2</sup>, Herbert Decaluwé<sup>10,11</sup>, Andreas Pircher<sup>12</sup>, Kathleen Van den Eynde<sup>13</sup>, Birgit Weynand<sup>14</sup>, Erik Verbeke<sup>15</sup>, Paul De Leyn<sup>16</sup>, Adrian Liston<sup>17,18</sup>, Johan Vansteenkiste<sup>19,20</sup>, Peter Carmeliet<sup>21,22</sup>, Stein Aerts<sup>23</sup> and Bernard Thienpont<sup>1,22\*</sup>

### Endothelial cells, tumour versus non-malignant

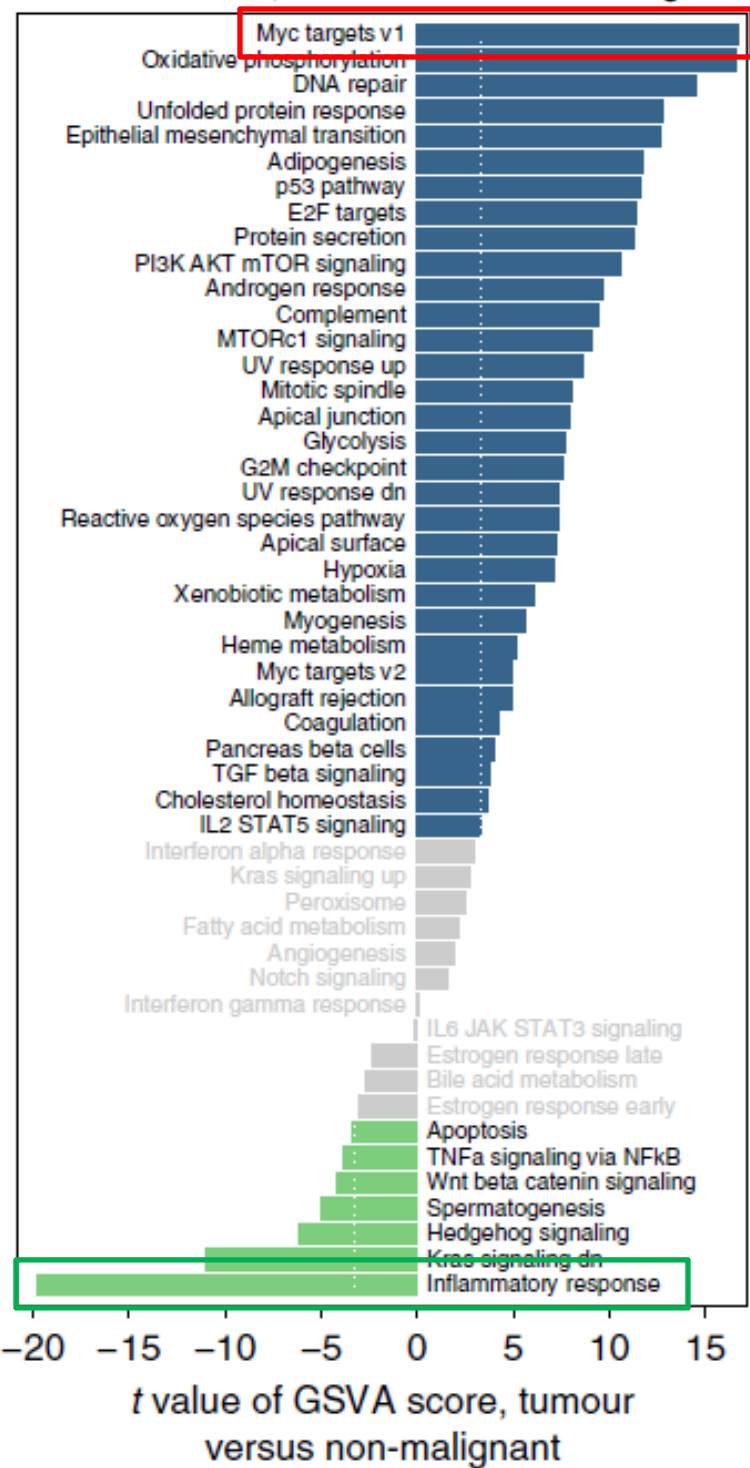


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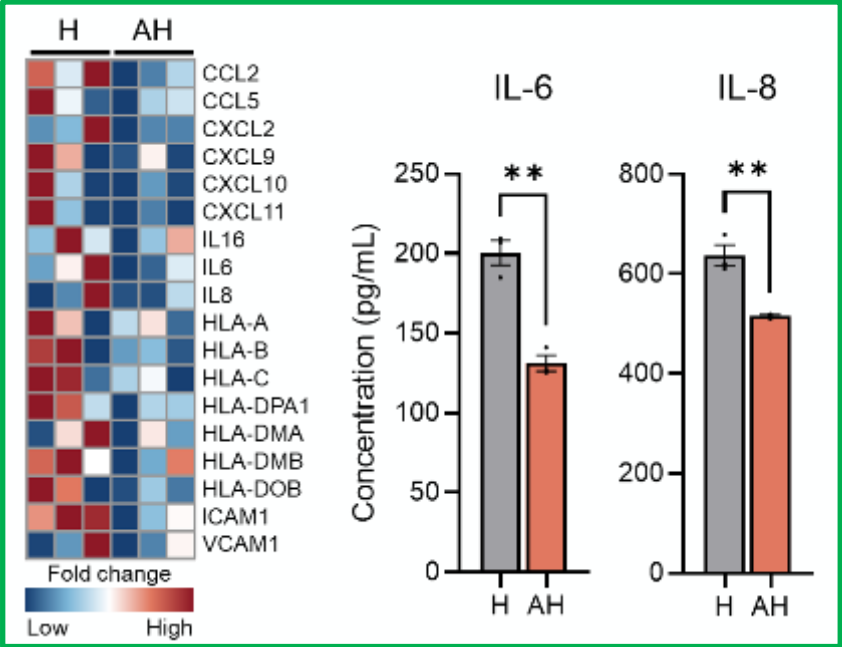
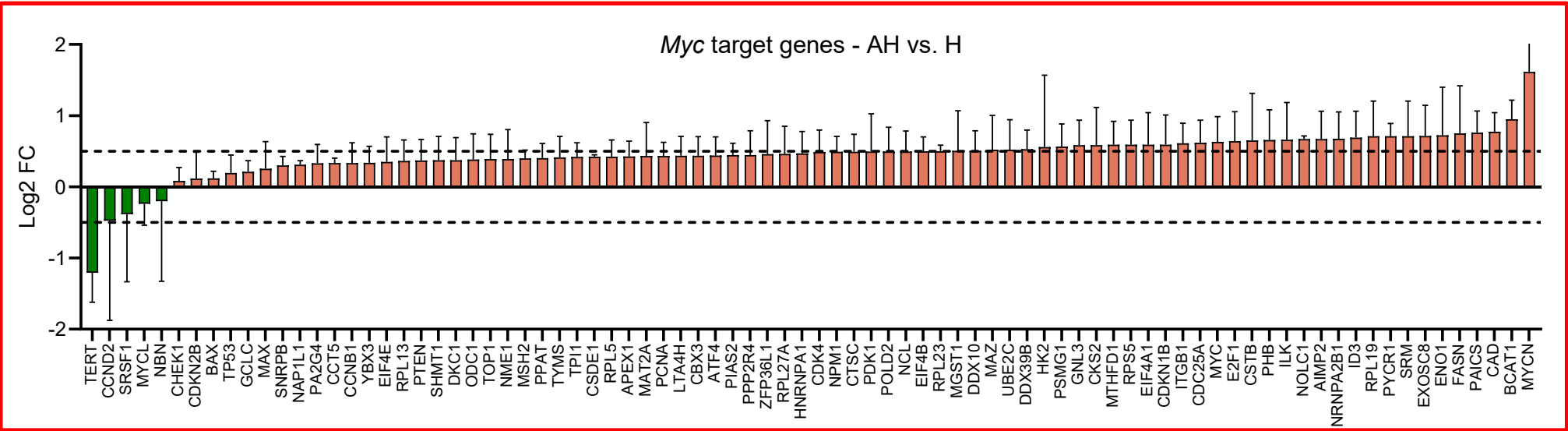
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### Endothelial cells, tumour versus non-malignant



## ASTEROIDS allows biochemical communication and reproduces in vivo cellular interactions

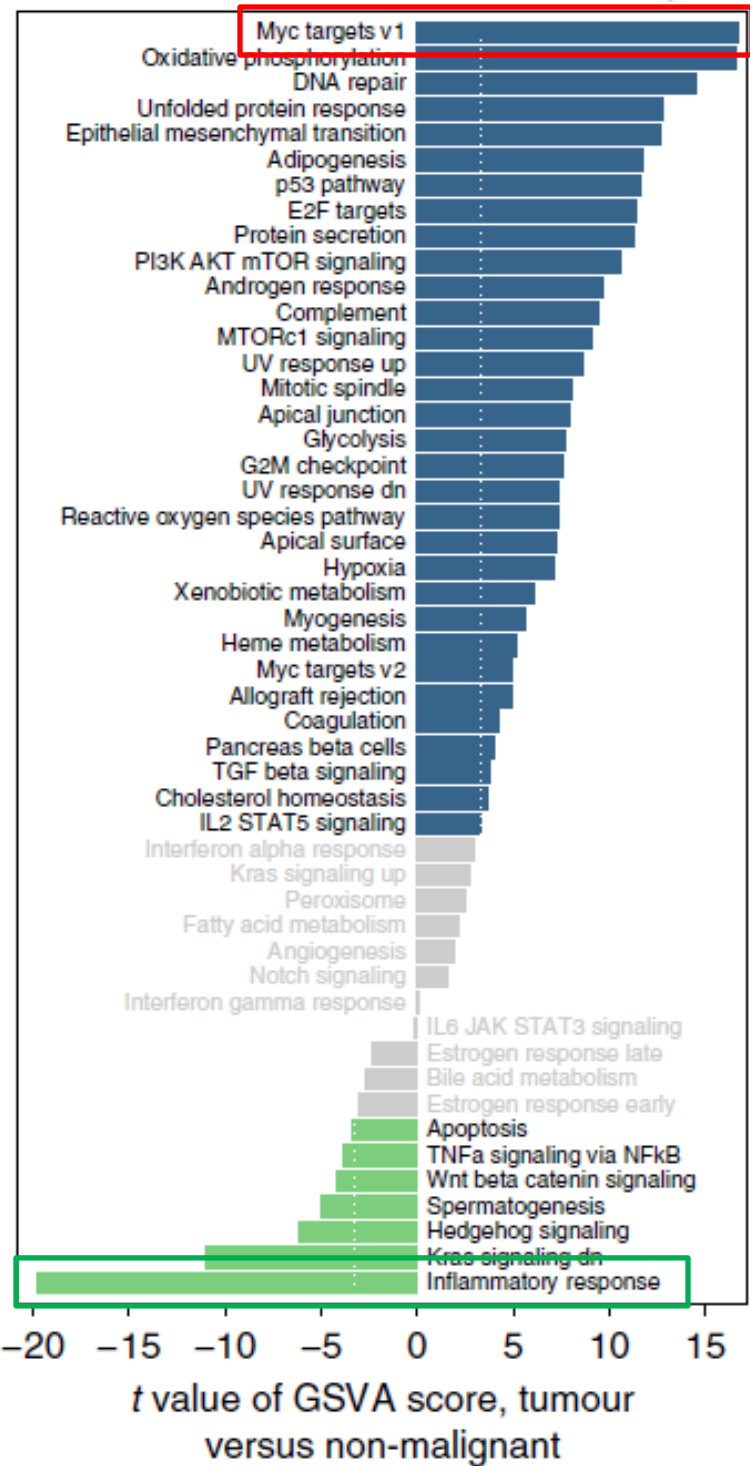


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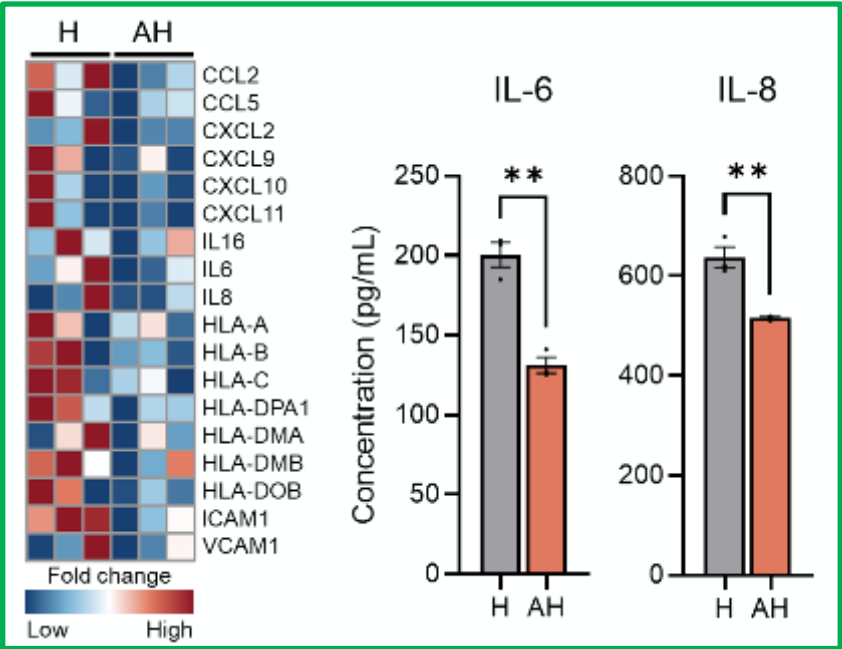
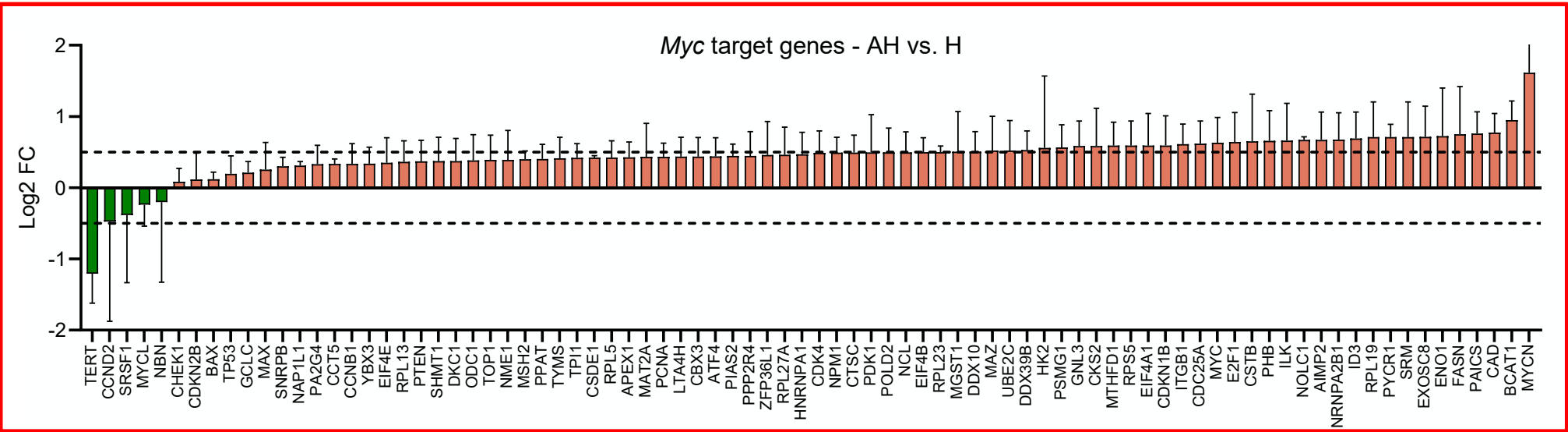
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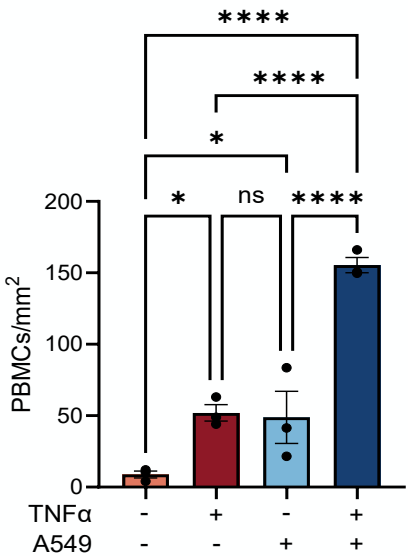
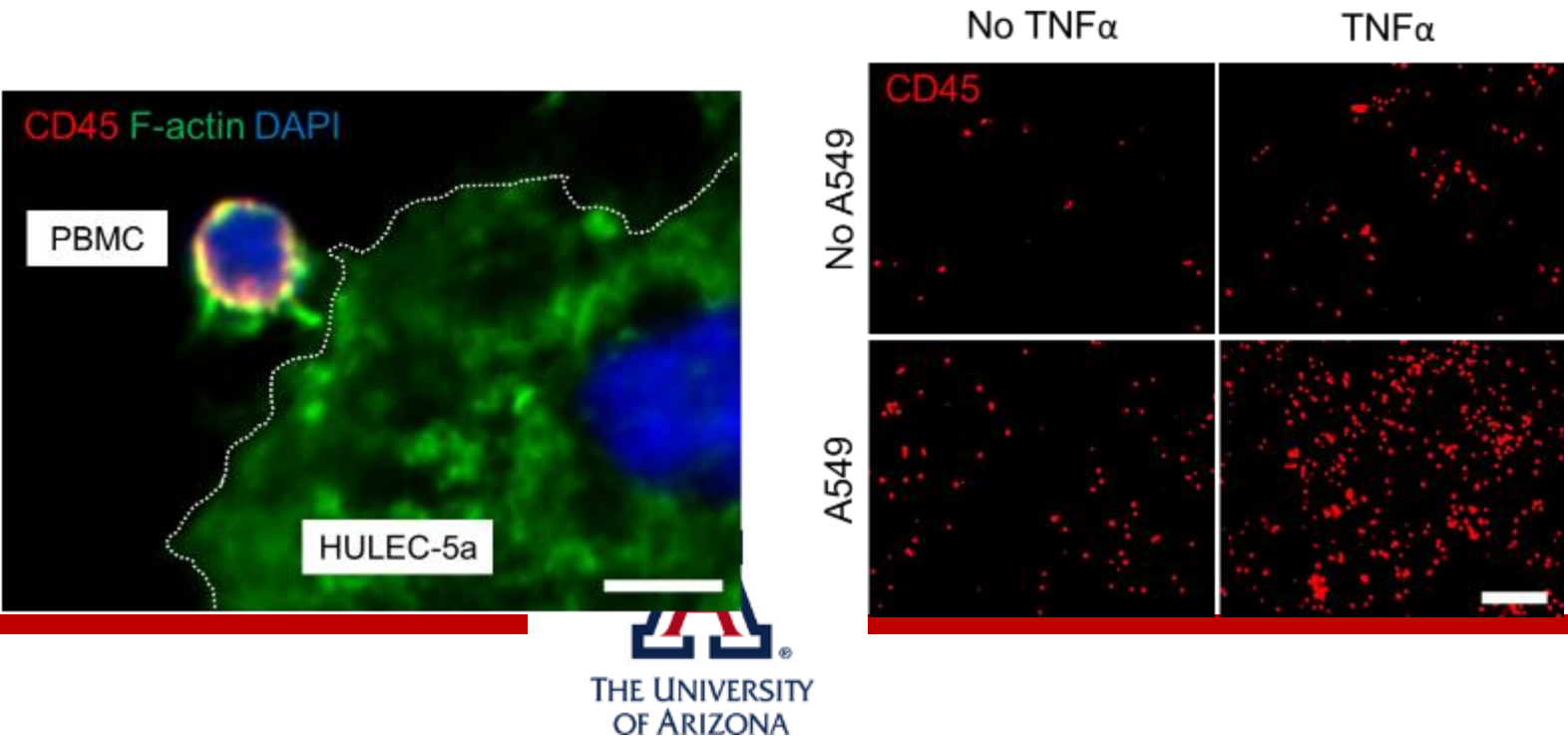
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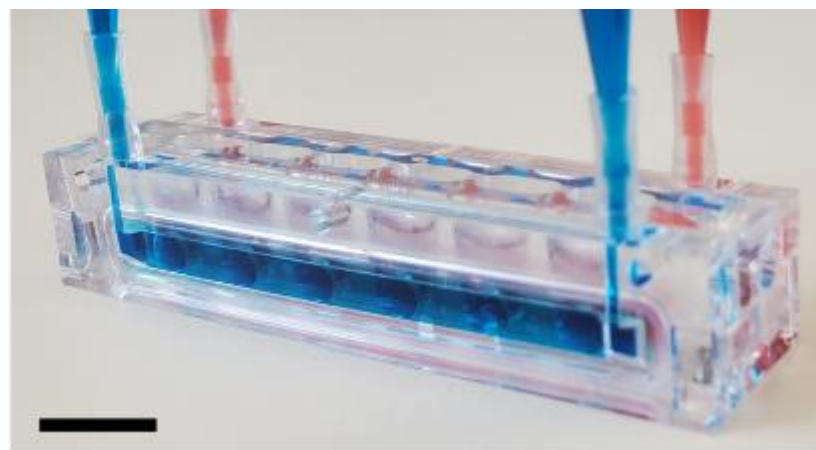
## ASTEROIDS allows biochemical communication and reproduces in vivo cellular interactions



## Immune cells flow in ASTEROIDS, interact and communicate with cancer and stromal cells



# Organ-on-chip studies interface with many core facilities



Bioimaging core



Sequencing core



Flow cytometry core



Radiation facilities



Molecular discovery core



Tissue biobanks



iPSCs core



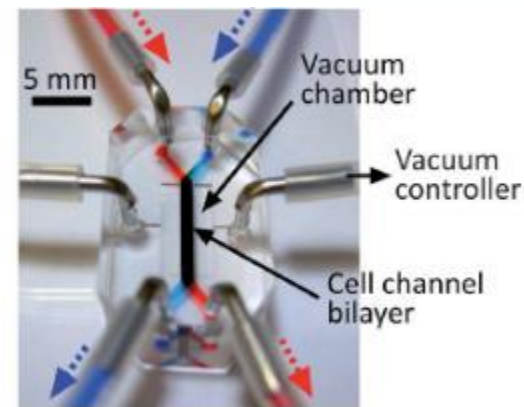
Bioinformatics core

# Organ-on-chip technology as a core facility

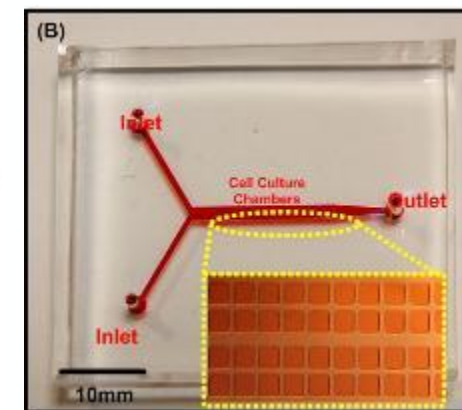
# Organ-on-chip technology as a core facility

## A wide range of OoC architecture...

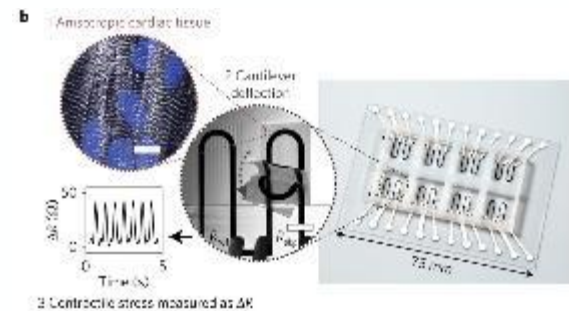
*Two-channels PDMS OoC*



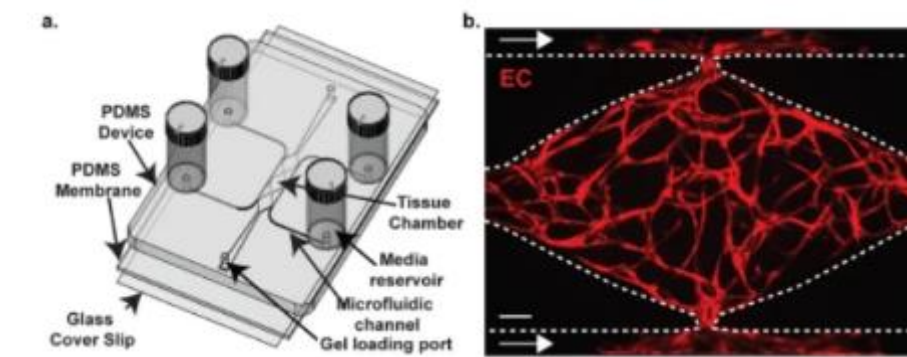
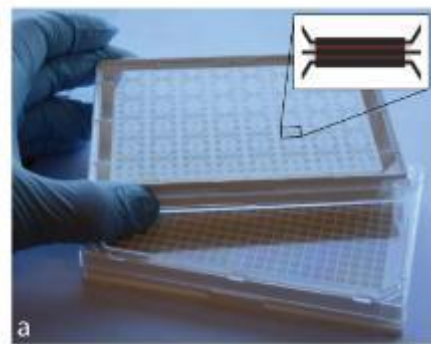
*Spheroid-on-chip*



*Mechanically compliant OoC*

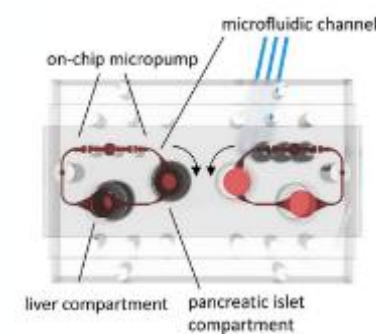


*Multiplexed array*



*Functional, perfusable 3D microvascular chambers*

*Membrane-free 3 compartments device*



*Multi-organ device*

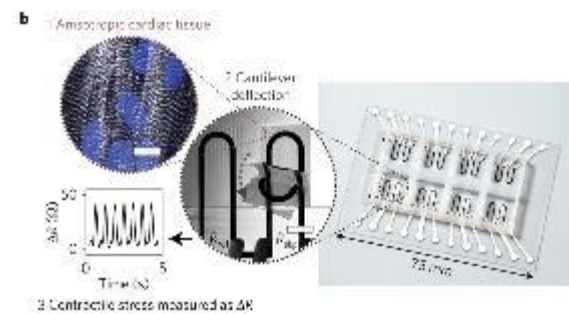


*Hanging-drop microfluidic network*

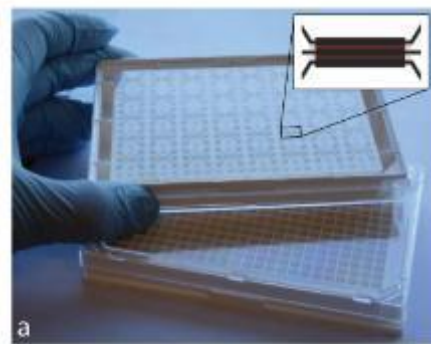
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## A wide range of OoC architecture...

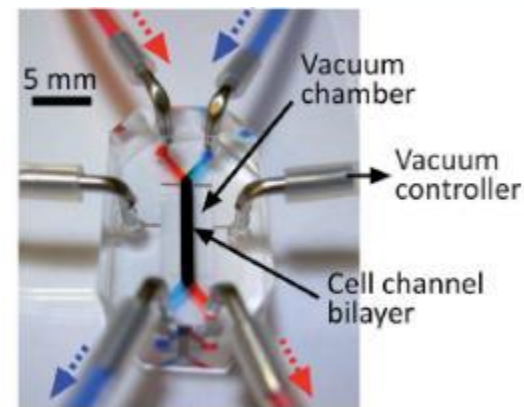
### Mechanically compliant OoC



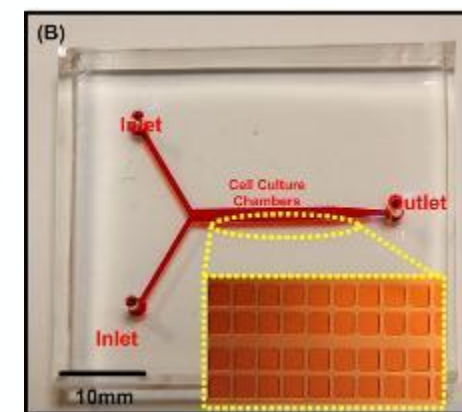
### Multiplexed array



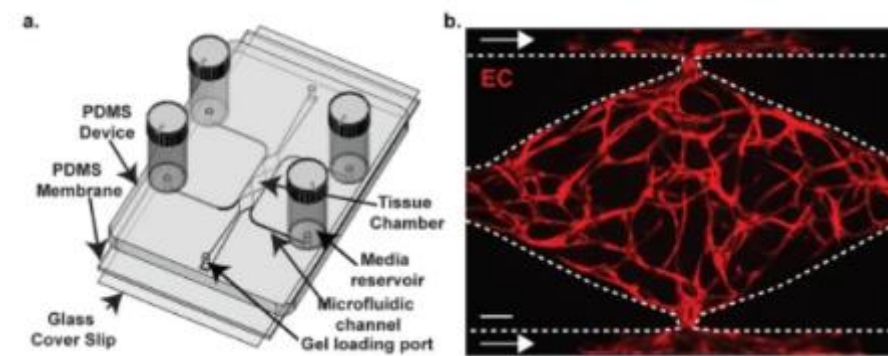
### Two-channels PDMS OoC



### Spheroid-on-chip



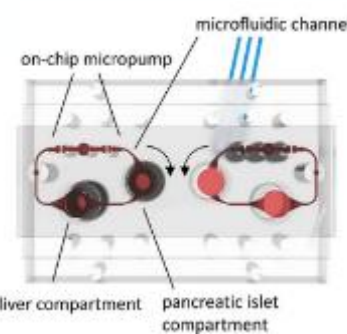
### Functional, perfusable 3D microvascular chambers



### Membrane-free 3 compartments device



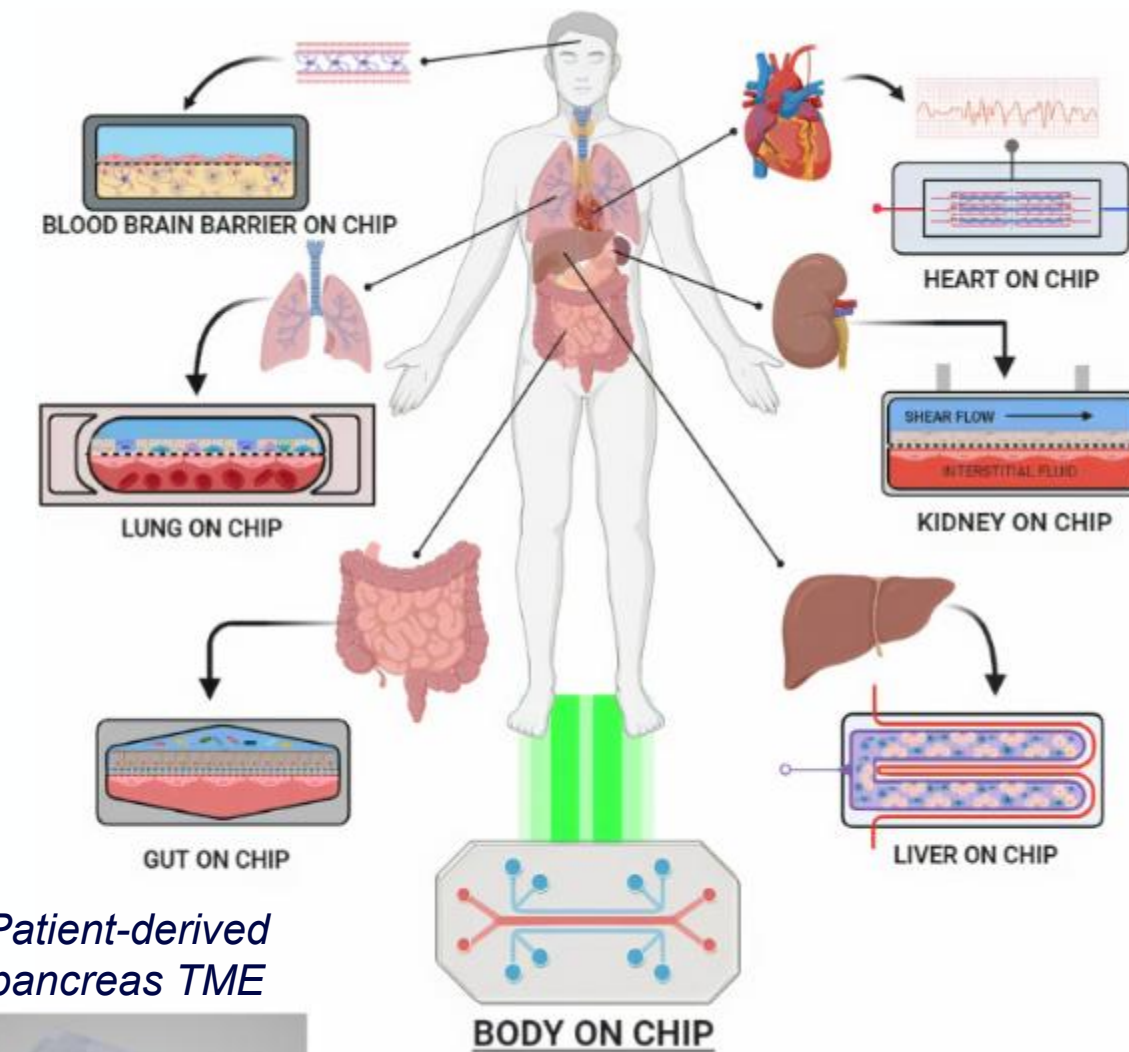
### Multi-organ device



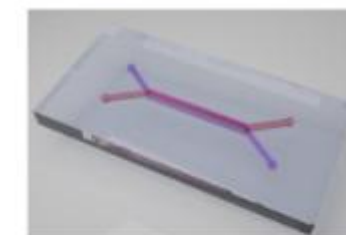
### Hanging-drop microfluidic network



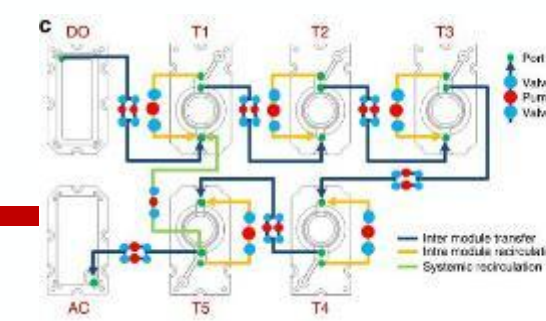
## ... reproducing multiple tissues/organs/functions...



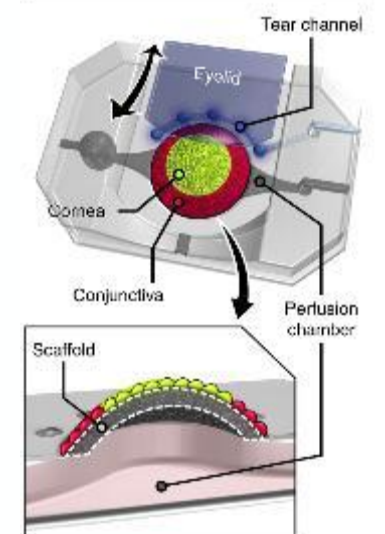
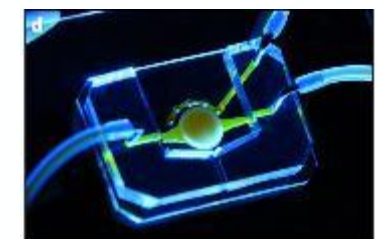
### Patient-derived pancreas TME



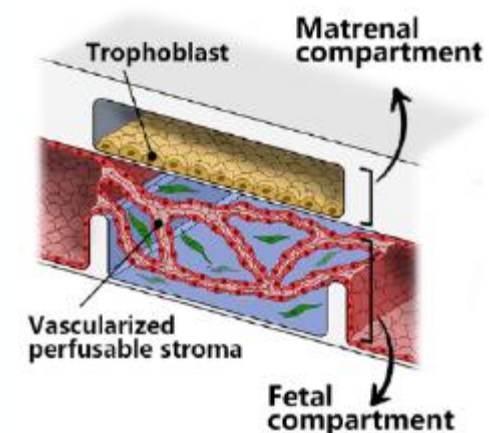
### Reproductive tract and 28-day menstrual cycle



### Eye mechanobiology



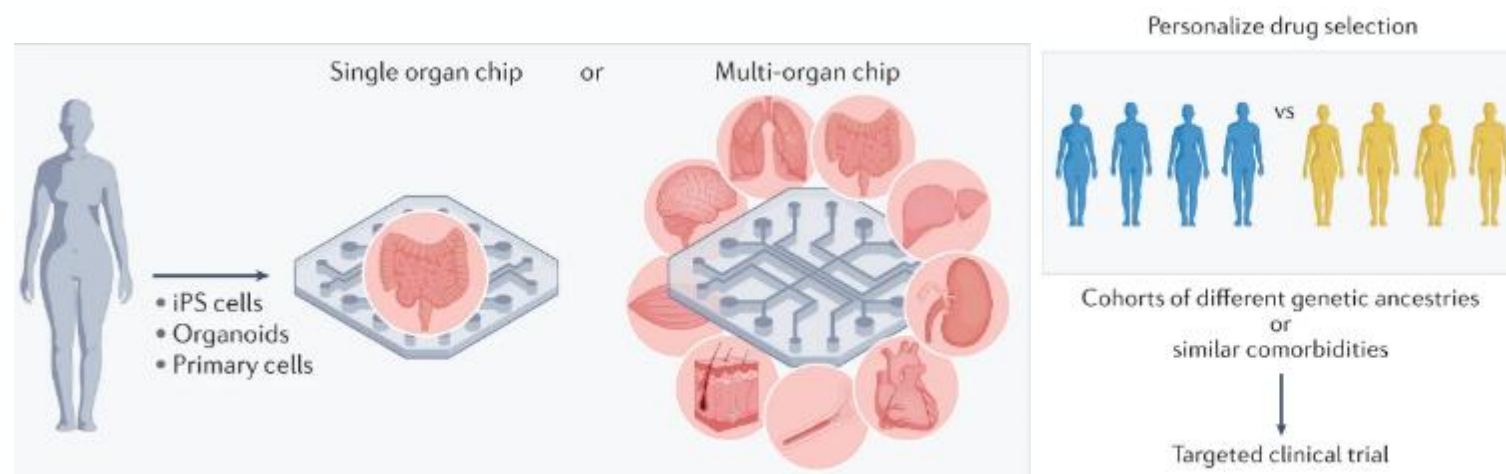
### Maternal-fetal interface in the human placenta



# Organ-on-chip technology as a core facility

... for a wide range of applications...

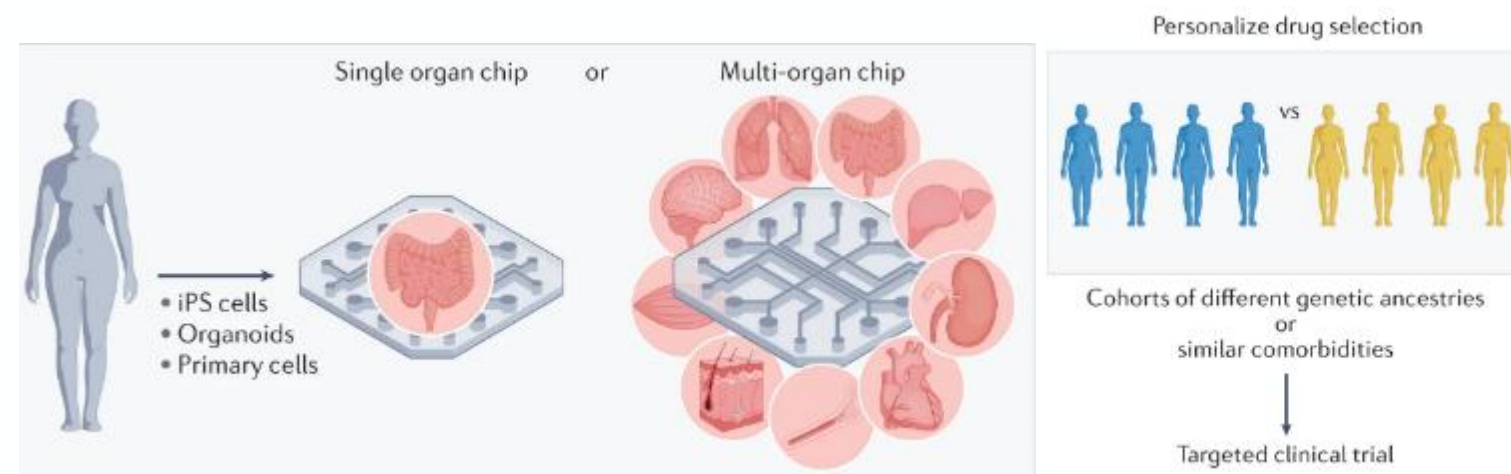
- **Disease Modelling**  
Investigation of both inherited and acquired disease in a human setting
- **Probing and mimicking the cell microenvironment**  
Effect of different environmental factors (such as shear stress, autocrine/paracrine soluble factors, cell–cell and cell–ECM interactions, etc.)
- **Single-organ tissue function**
- **Drug screening/Multi-organ functions in ADME-Tox**  
Predicting efficacy and toxicity of pharmacological compounds
- **Personalized Medicine**



# Organ-on-chip technology as a core facility

## ... for a wide range of applications...

- **Disease Modelling**  
Investigation of both inherited and acquired disease in a human setting
- **Probing and mimicking the cell microenvironment**  
Effect of different environmental factors (such as shear stress, autocrine/paracrine soluble factors, cell–cell and cell–ECM interactions, etc.)
- **Single-organ tissue function**
- **Drug screening/Multi-organ functions in ADME-Tox**  
Predicting efficacy and toxicity of pharmacological compounds
- **Personalized Medicine**



## ...with different needs

- **High physiological fidelity**  
Reproduce relevant tissue architecture, cellular diversity, extracellular matrix, and biochemical and mechanical cues
- **Long-term stability**  
Maintain tissue viability and function throughout extended culture and repeated exposures
- **High throughput**  
Support many conditions and replicates in parallel, with efficient handling and readouts
- **Reproducibility**  
Deliver consistent device performance and biological responses across chips, batches, operators, and laboratories
- **Human and patient relevance**  
Accommodate primary cells, patient-derived tissues, or iPSC-derived cells while preserving relevant characteristics

# Organ-on-chip technology as a core facility

**An organ-on-chip core could bridge diverse research needs with appropriate models, shared expertise, and reliable experimental workflows.**

- **Access:** OoC technology available to labs without specialized engineering expertise
- **Fit-for-purpose models:** large choice of platforms to align complexity and capabilities with the desired application
- **Reliability:** standardized methods, quality control
- **Efficiency:** cost-effective, possibility to have multiple chips for high throughput

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## New Approach Methodologies (NAMs)

- Organ-on-chip
- Organoids
- In Silico (AI, ML, Digital twins, etc.)

## Organoid and Organ-Chip Shared Resources Laboratory

We enhance basic research in stem cell biology by providing tools and training to analyze organoids and organ-chips.



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- Microfluidic chip design and fabrication
- Photolithography, wet etching, soft lithography, and hot pressing
- Plasma-activated and thermal bonding of glass and polymeric elements
- Testing of microfluidic chip performance

# Organ-on-chip technology as a core

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## Organ-on-a-Chip Facility

**Short Name:** Cellular Pump



### Facility Description

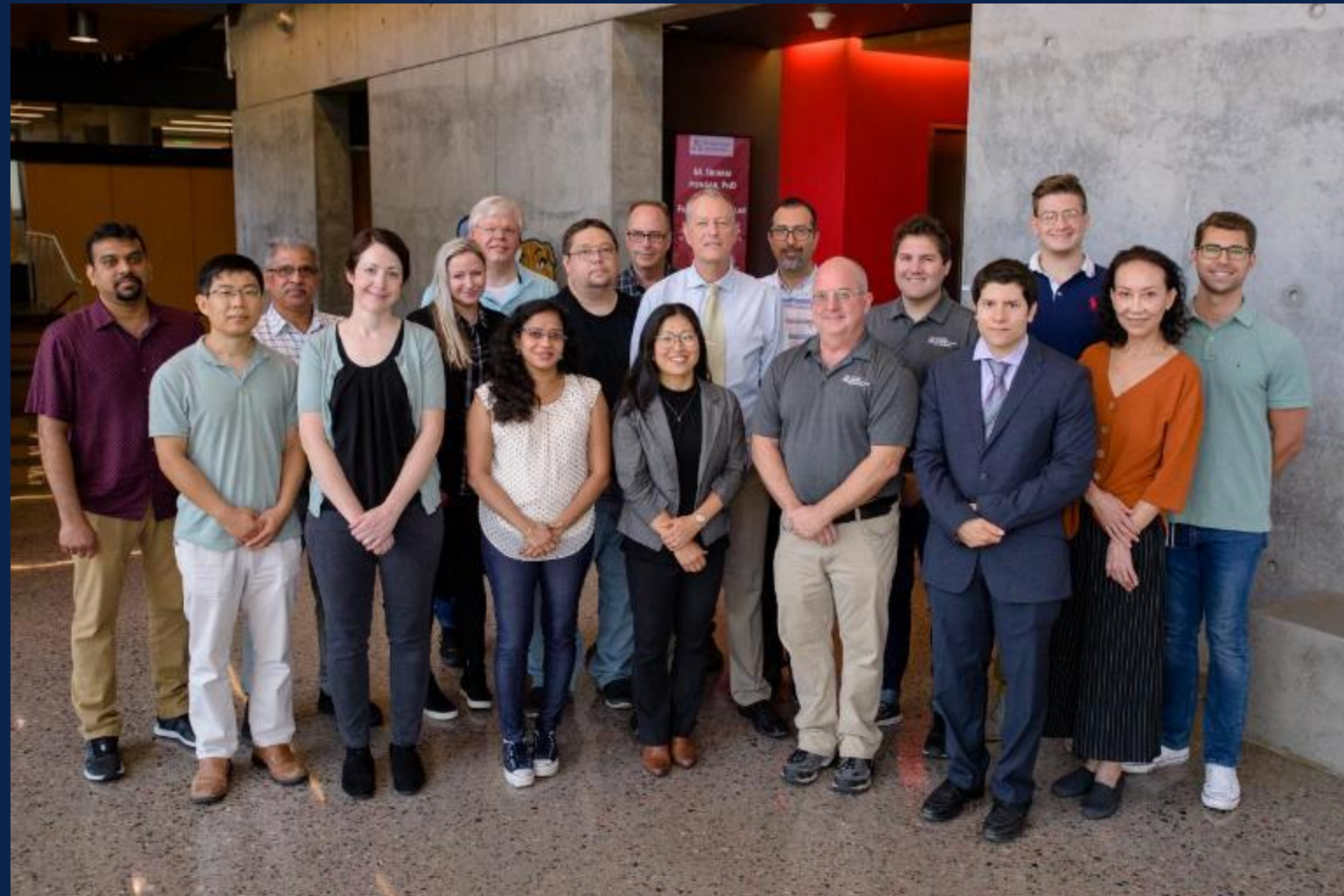
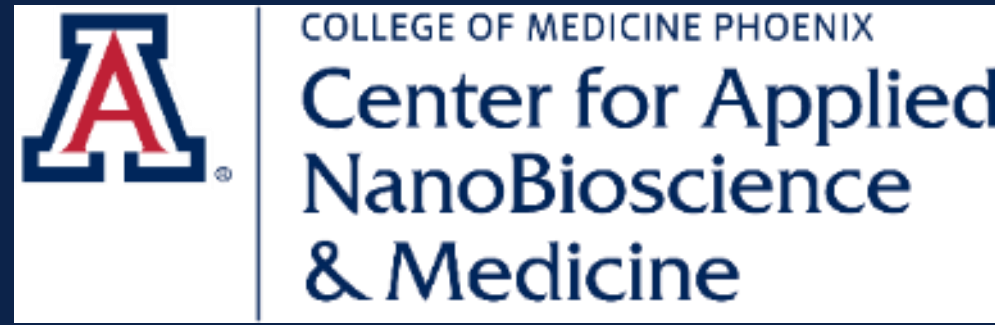
The Cellular Pump system is a microgravity-enabled modification of a microfluidics platform. The unit provides controlled and continuous media perfusion to simulate fluidic flow experienced by cells and organs within the body. Effluent is collected in sample-specific reservoirs allowing researchers to analyze tissue output, including metabolomics. The fresh media supply and effluent reservoirs are assembled in a single cassette, allowing for facile exchange, thus maintenance of long term culture and time course experiments. In addition, the fluid components and concentrations in the cassettes can be customized on a per-sample basis enabling a wide variety of experimental designs, including preservation and fixation.

Cellular Pump is designed to integrate into SABL, BioServe's next-generation incubator. SABL accommodates up to two pump units, in addition to an ACM for CO2 control. The hardware can



# ACKNOWLEDGMENTS

## TO:



### - Our collaborators



### - Our sponsors



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# QUESTIONS ?

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