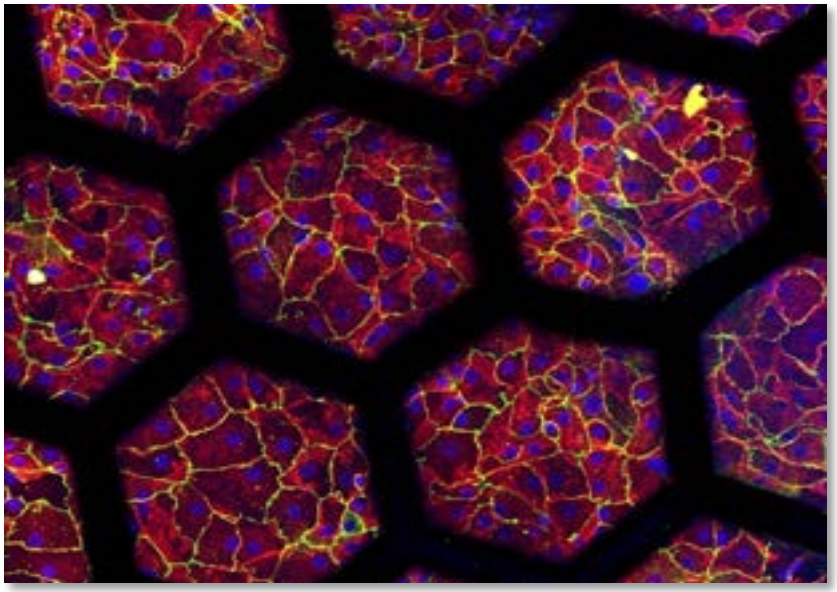
From Research to Application: Lung-on-Chip Models



Zamprogno et al., Nat. Com. Biol. 2021

Prof. Dr. Olivier T. Guenat

- University of Bern, ARTORG Center
- Bern University Hospital, Pneumology Clinic & Thoracic Surgery Clinic

NRP79 Symposium, Transition in Practice, Bern, November 27th, 2025

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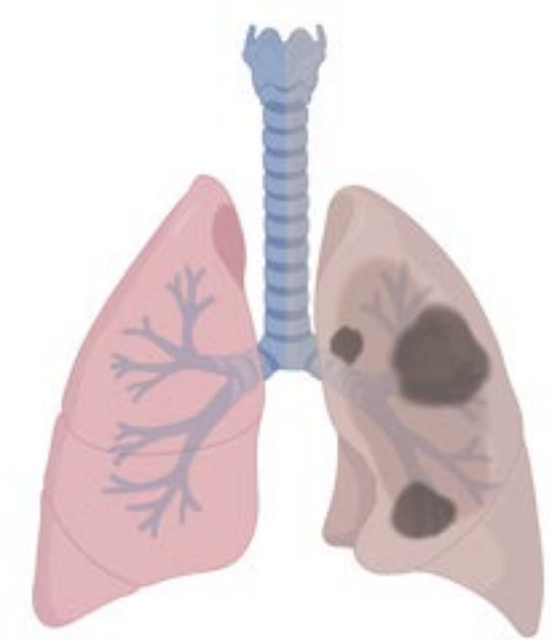
Why Lung Disease Research Needs New Models

Clinical Need: Respiratory diseases (0.5bn patients worldwide)



Lung cancer, COPD, IPF, COVID-19,…

- **Animal models**: different biology

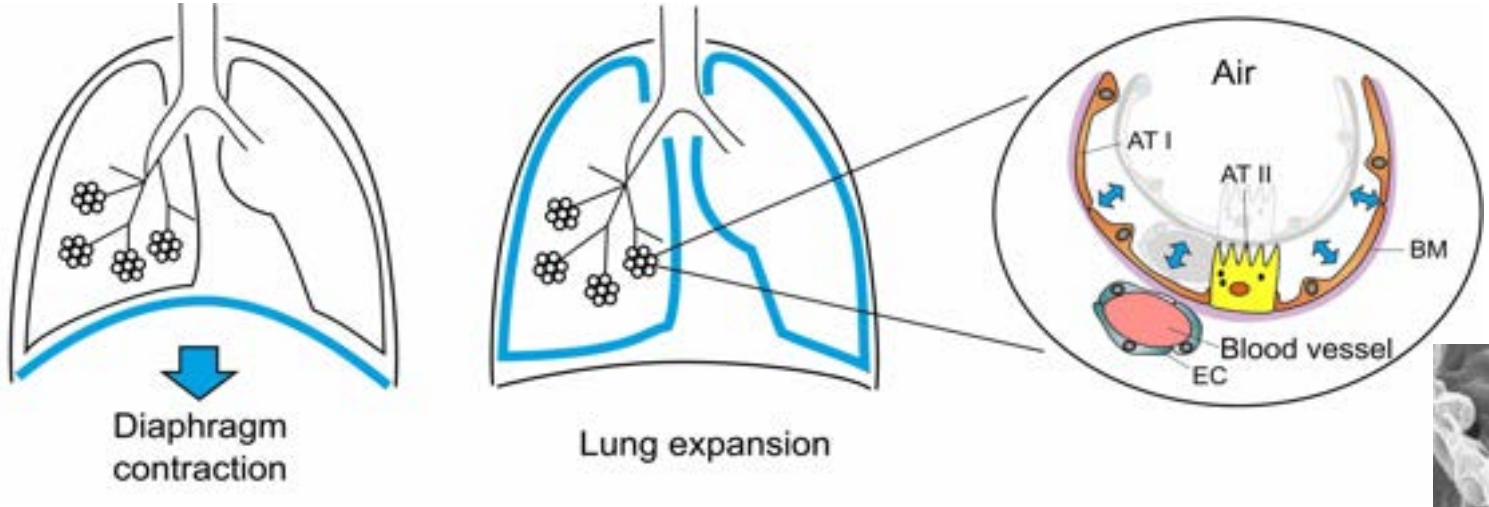
- **In-vitro models**: often over-simplified

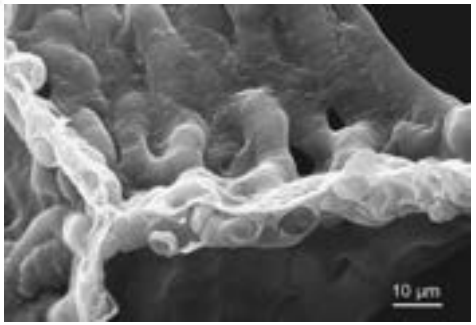
- **Lung-on-chip models**: physiologically relevant

Illustrations: Biorender

Beitler et al. Lancet 2022; Eur. Respir. J. 2015

Requirements for Transitioning to Practice





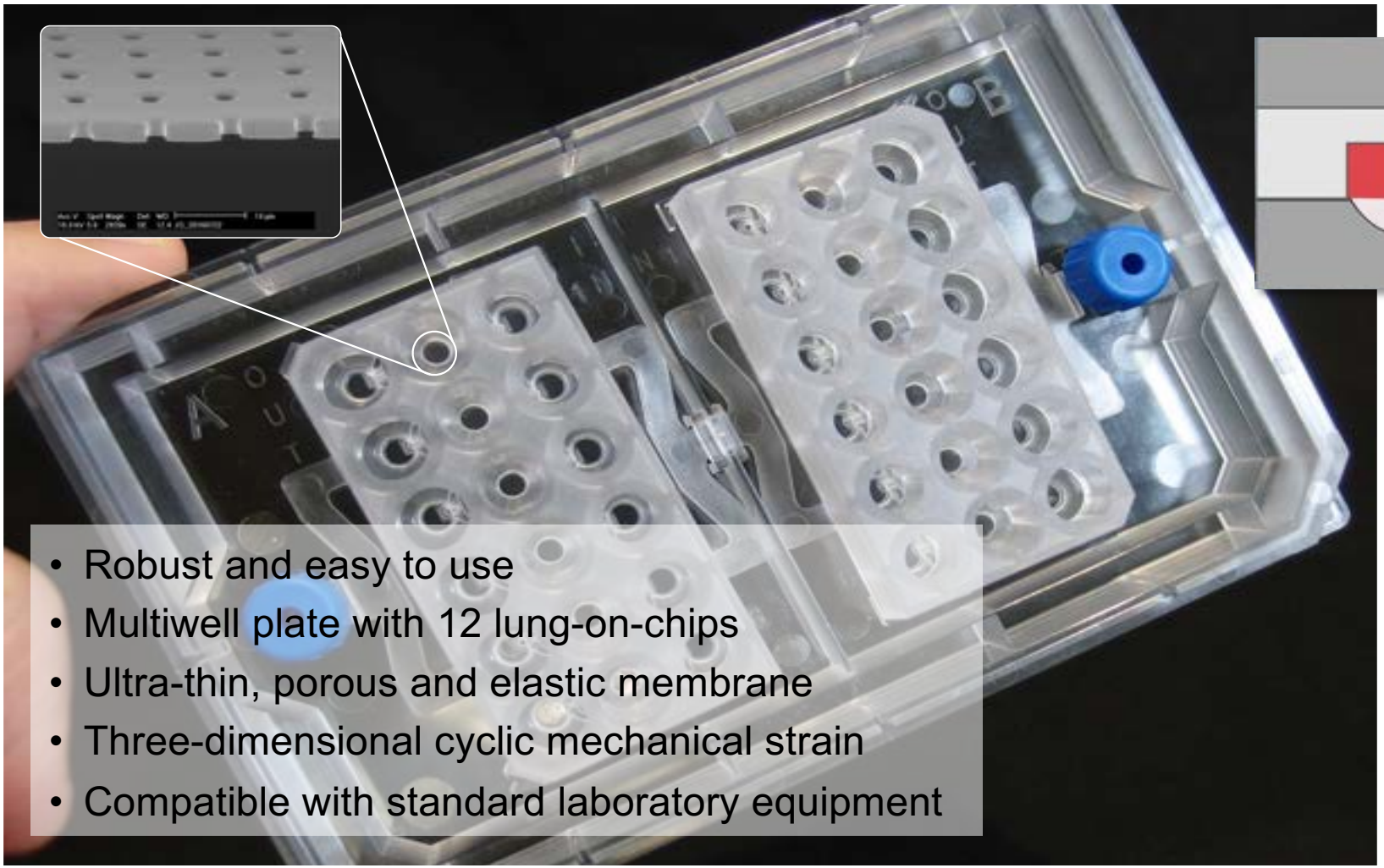
Weibel, Swiss Med Wkly. 2009

Key requirements:

- Reproducible system, robust architecture
- Mimic the air-blood barrier (thin membrane, breathing motions)
- Enable relevant cells to maintain their phenotype
- Provide required information
- Mimic specific disease

Stucki A. et al., Lab Chip 2015
Stucki J. et al, Nat. Scientific Reports, 2018

AlveoliX Lung-on-Chip Specifications



- Robust and easy to use
- Multiwell plate with 12 lung-on-chips
- Ultra-thin, porous and elastic membrane
- Three-dimensional cyclic mechanical strain
- Compatible with standard laboratory equipment

SWISS MEDTECH AWARD 2022

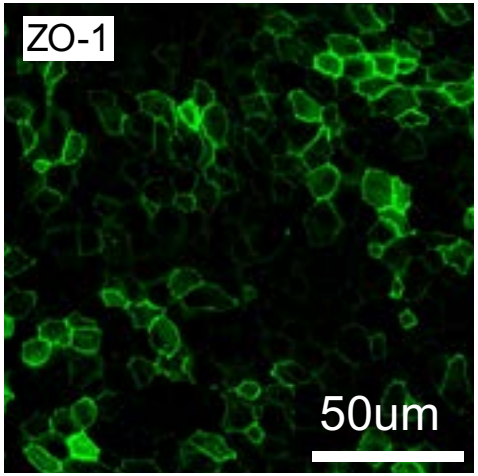
Stucki A. et al., Lab Chip 2015; Stucki J. et al, Nat. Scientific Reports, 2018; Sengupta et al., Front. Toxicol. 2022


AlveoliX Lung-on-Chip System
AlveoliX
In-vitro models inspired by nature
Adopted by Roche & other pharmaceutical companies

Modeling Idiopathic Pulmonary Fibrosis

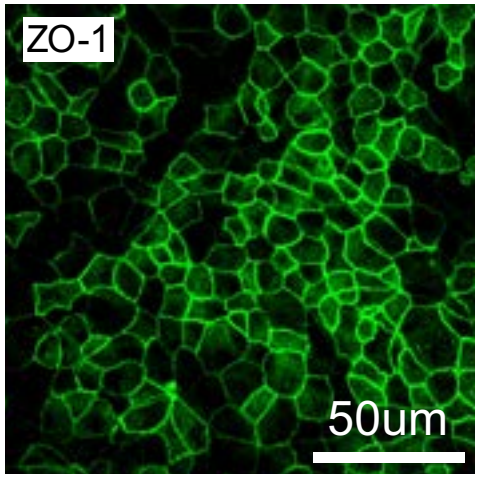
- **IPF pathology**: Alveolar epithelial injury → impaired wound healing → fibrosis
- **Model**: TGFβ-induced barrier disruption (ZO-1 loss)
- **Drug testing**: Nintedanib restores barrier integrity

Diseased

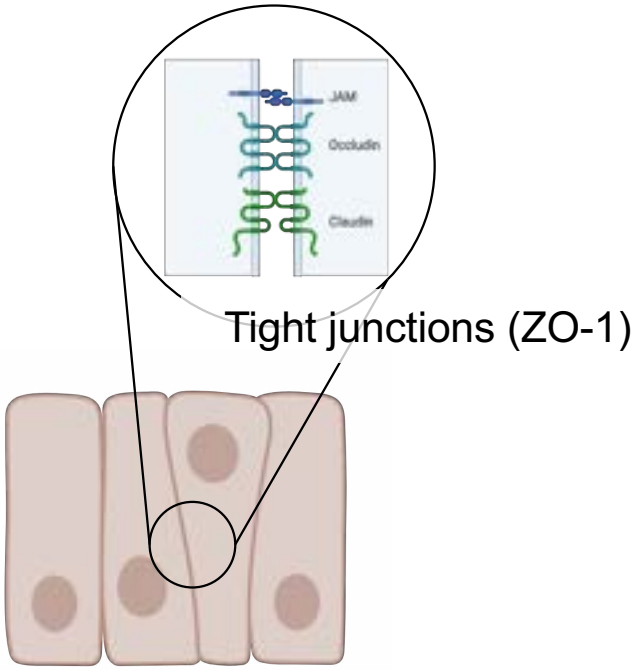


TGFb injury

After treatment



TGFb injury + Nintedanib



Healthy epithelium

Alveolar epithelial cells: human derived immortalized alveolar epithelial cell line (AXiAEC) from AlveoliX

Weber et al., Biofabrication (ahead of print)

Illustrations: Biorender

Next Candidate for Translation: Vascularised Tumor-on-Chip

- **Clinical context:** Metastasis causes 90% of cancer deaths - understanding CTC extravasation is critical

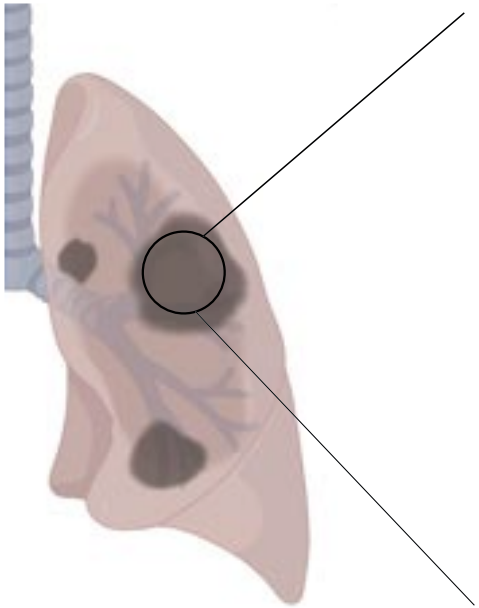
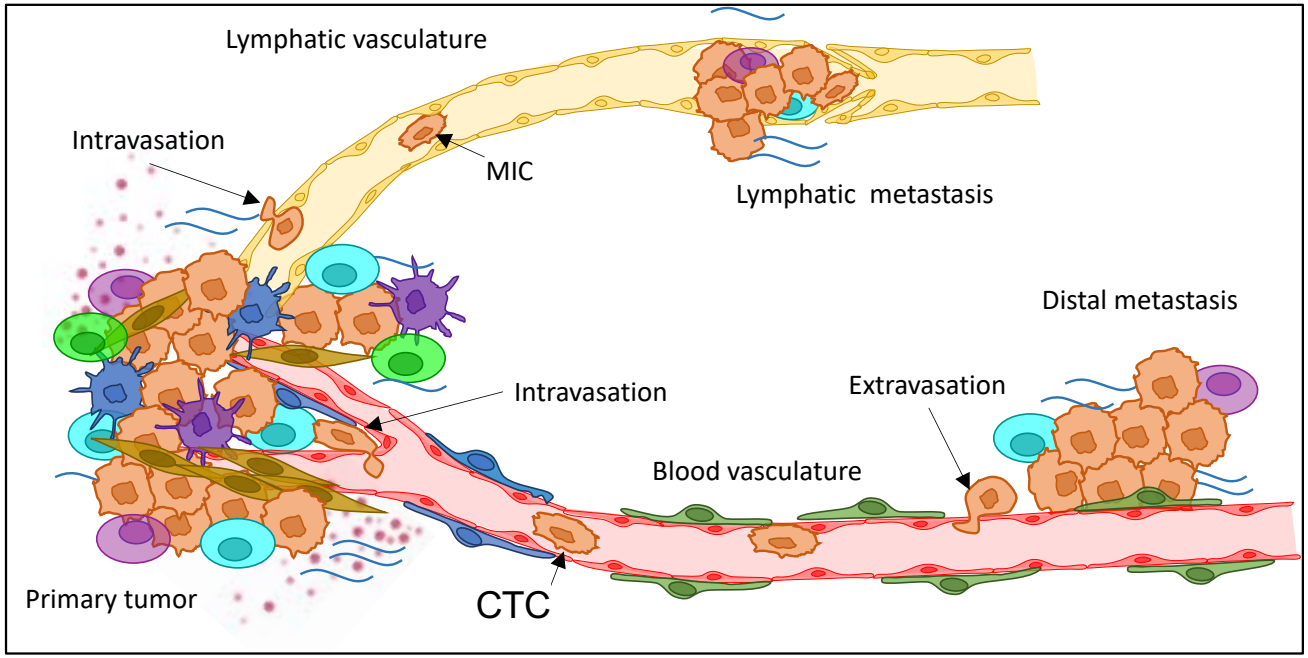


Illustration: Biorender



Circulating Tumor Cells: CTC

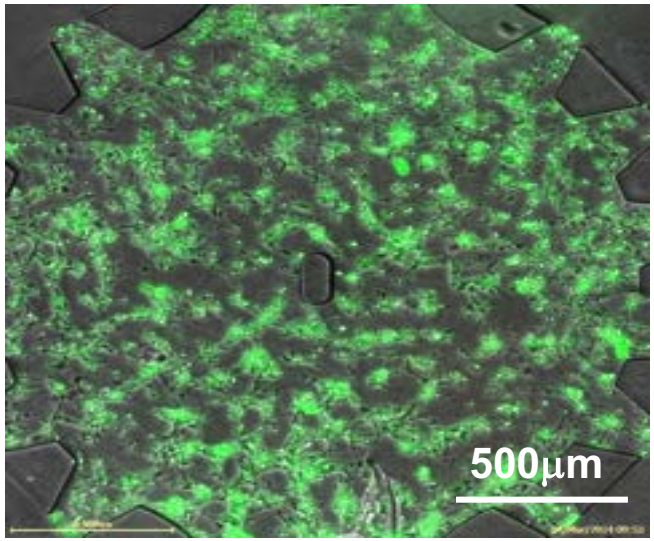
Vascularised tumor-on-chip:

- Enables study of tumor-vessel interactions and metastasis
- Enables drug efficacy and toxicity assessments

Microvasculature Formation

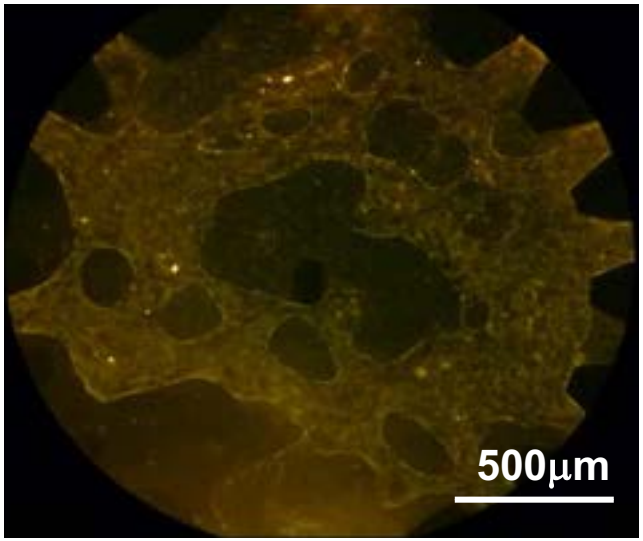
Co-culture with primary endothelial cells and primary lung pericytes (from patients)

Vasculogenesis

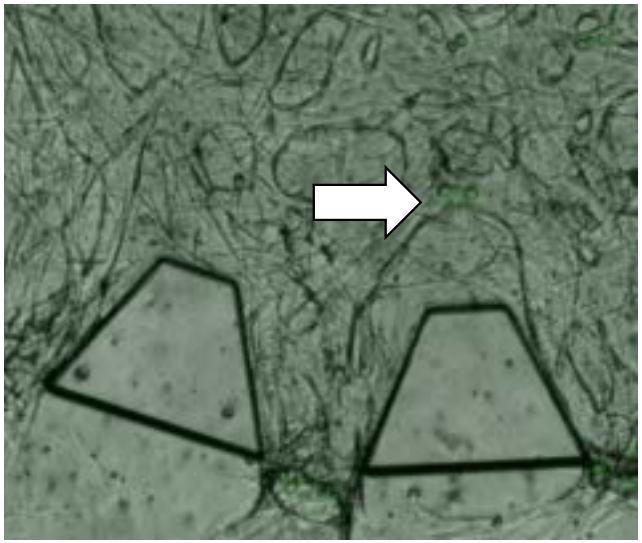


Mature networks in 3-5 days

Perfusable microvessels



Perfusion with rhodamine dyed solution



Perfusion of immune cells (PBMC) (white arrow)

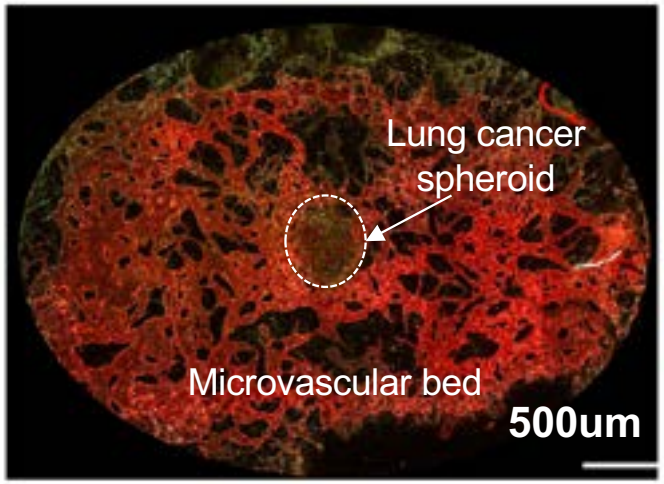
Key requirements:

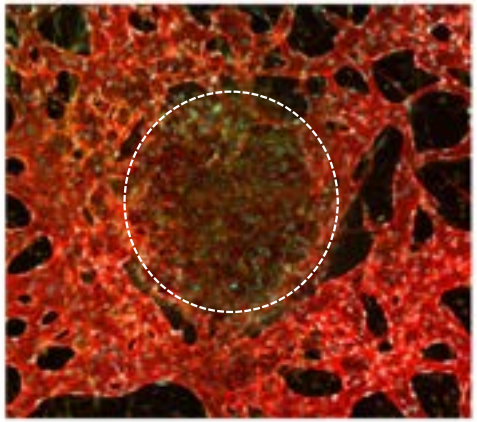
- Reproducible system
- Functional microvasculature (self-assembled vascular network, perfusable, vasoactive, ..)
- Enables circulation of immune cells
- Provide required information for oncology models

Bichsel et al., Tissue Eng. A, 2015
Zeinali et al. unpublished

Vascularised tumor-on-chip

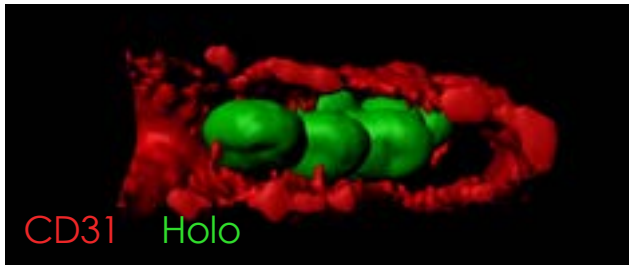
- Combination of spheroids and organs-on-chip technology
- Integration of lung cancer spheroid in a perfusable microvasculature

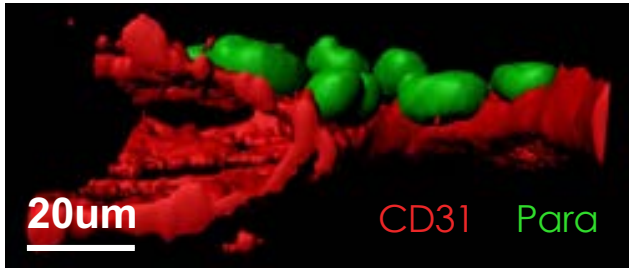




Zeinali et al., World MPS conference, 2025

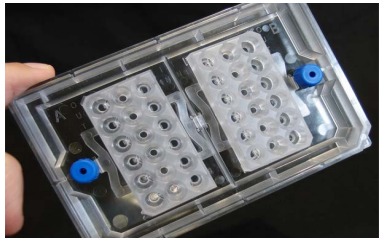
Metastatic cascade: extravasation of CTC



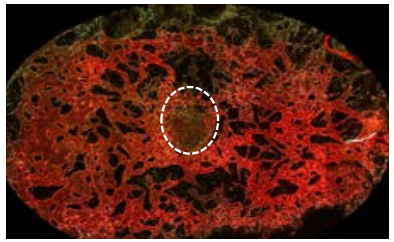


Schmid, Zeinali, et al., Frontiers Biotech. Bioeng. 2024

Transitioning Organs-on-Chip to Practice



- **Lung-on-Chip**: commercialized (AlveoliX), disease modeling, drug testing



- **Vascularised tumor-on-chip**: development stage, metastasis modeling, drug testing

- **Key requirements**: Reproducibility, biological relevance, practical utility

Pictures: Top: AlveoliX; Bottom: Zeinali et al., World MPS conference, 2025

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