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Fraunhofer-Institut für Zelltherapie und Immunologie IZI

Organ-on-Chip Platforms for One Health Applications and beyond

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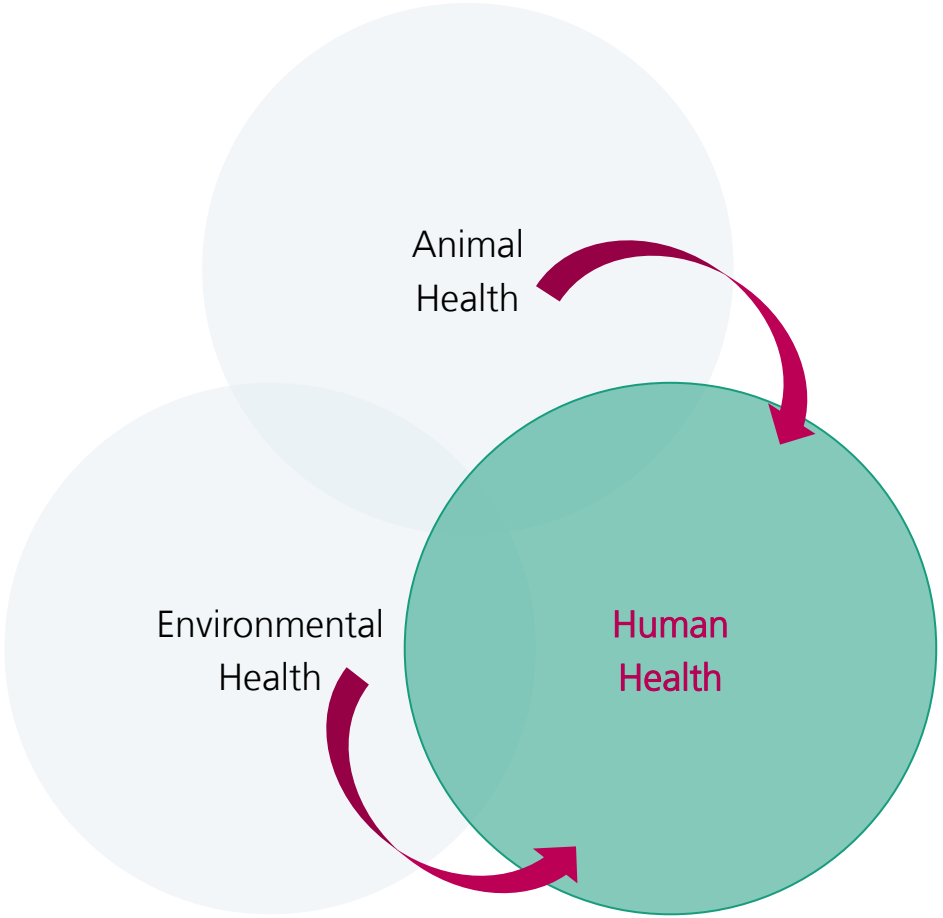
One Health and Global Medical Challenges

Human, animal, and environmental health are interconnected

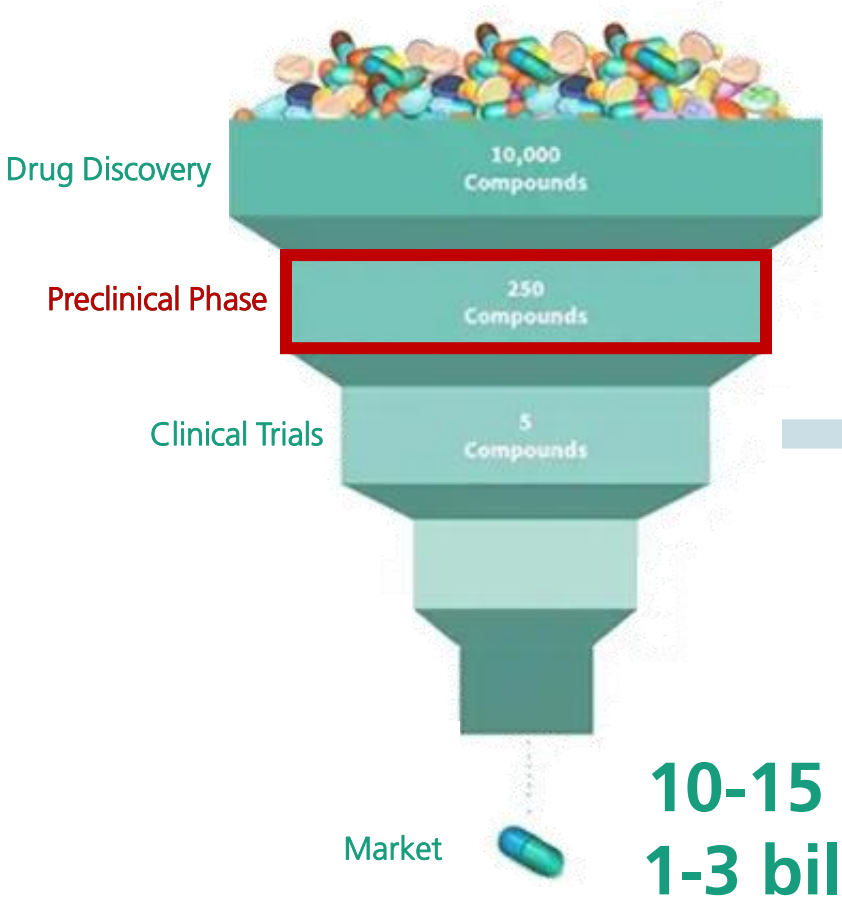


Global Health challenges:
Zoonotic infections
Antimicrobial resistance
Cancer & chronic diseases

Urgent need to develop new and effective therapies to protect human health!

The challenge: Inefficiency of drug development pipeline

Traditional preclinical model systems fail to model human diseases



90% Failure rate

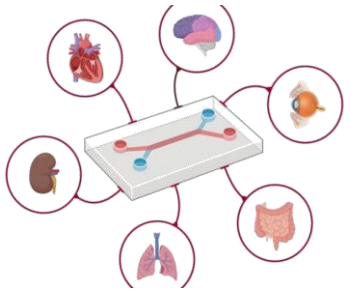
10-15 years
1-3 billion €

Traditional preclinical model systems

✗ Human
√ Complex

√ Human
✗ Complex

Advanced in vitro systems



√ Human
√ Complex

Organ-on-Chip: Potential vs. Acceptance

Advantages over animal models are clear — the challenge is industry integration

Advantages of OoC technologies over traditional preclinical model systems

- Higher predictive power
- Faster and more cost-effective
- Personalized disease-modelling
- Reduction of animal testing

Lacking acceptance of pharma to include OoCs in DD pipeline:

- Accuracy
- Scalability
- Biological Validation
- Standardization
- Regulatory approval

Motivation: Bridging the Gap Between Potential and Implementation

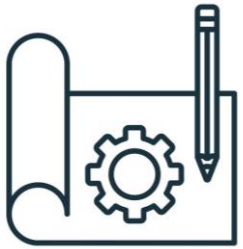
Developing advanced preclinical model systems that match industrial standards

Standardized and Modular Model Development

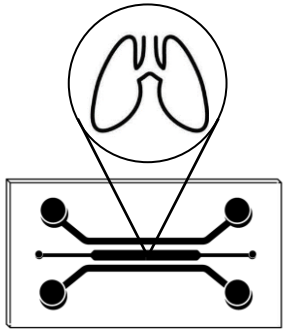
Non-Standardized OoC model systems

- Non standardized:
  - Design variety
- PDMS-based:
  - Molecule adsorption
  - Not scalable
- End-point based assays (qPCR, flow cytometry)

Microfabrication: rapid prototyping



Organ model generation: Long-term cell culture



Biological validation: In-line microscopy and sensor-based assays

Standardized, modular preclinical model systems

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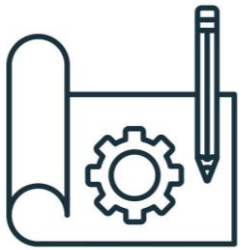

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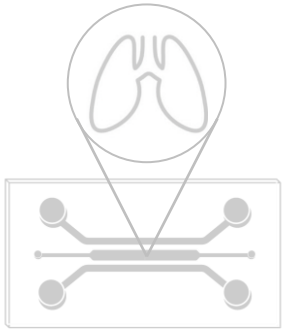
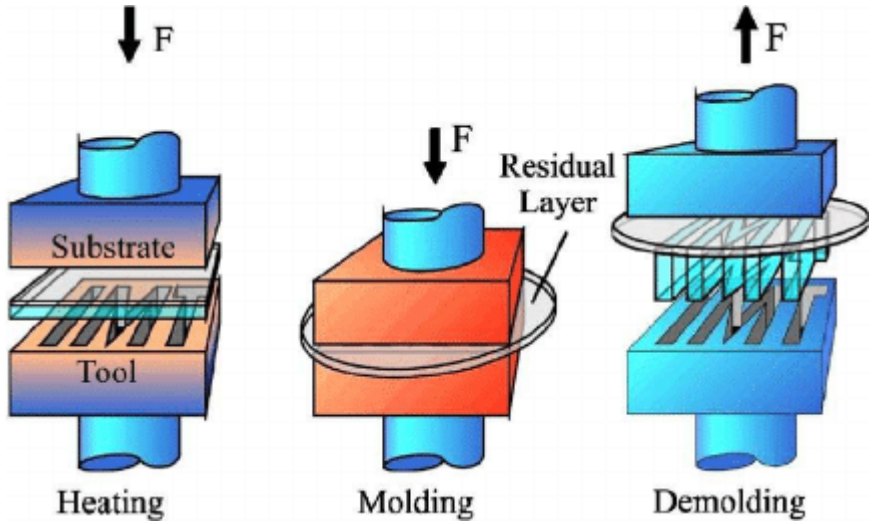


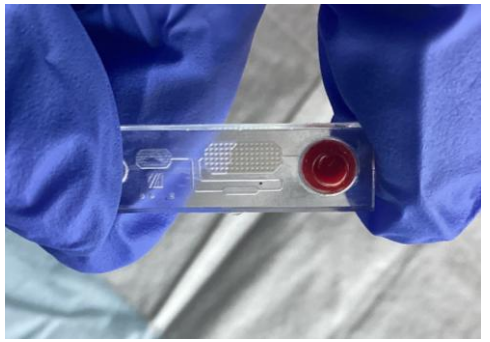
Biological validation: In-line microscopy and sensor-based assays

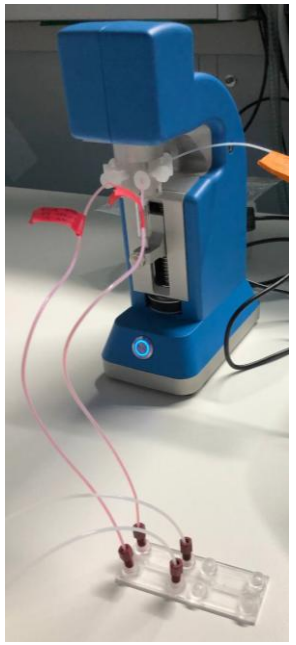
Rapid Prototyping of Microfluidic Devices via Hot Embossing

Flexible, scalable, and compatible with Organ-on-Chip applications

Hot embossing process using thermoplasts



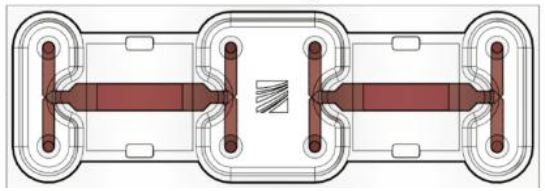




Hot embossing enables rapid, versatile, and scalable fabrication of microfluidic devices for diagnostics and Organ-on-Chip

Quality assessment of our in-house chip fabrication

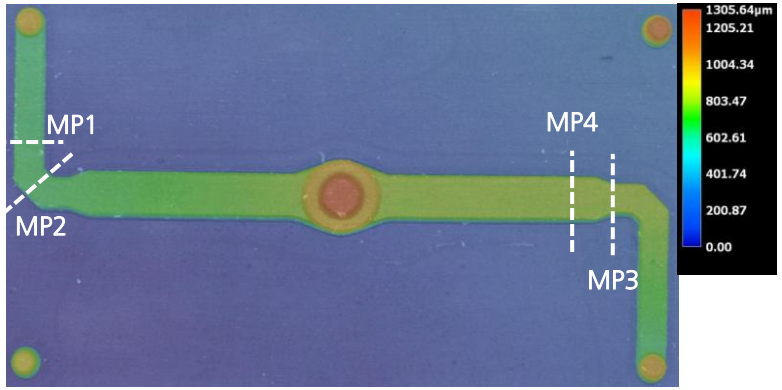
Checking channel Geometries at different measurement points

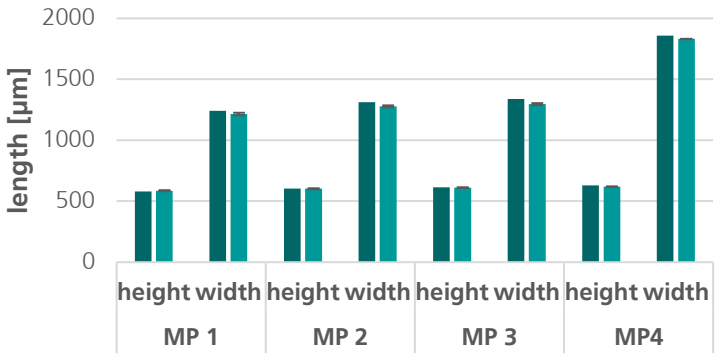


Fabricated Membrane-Chip

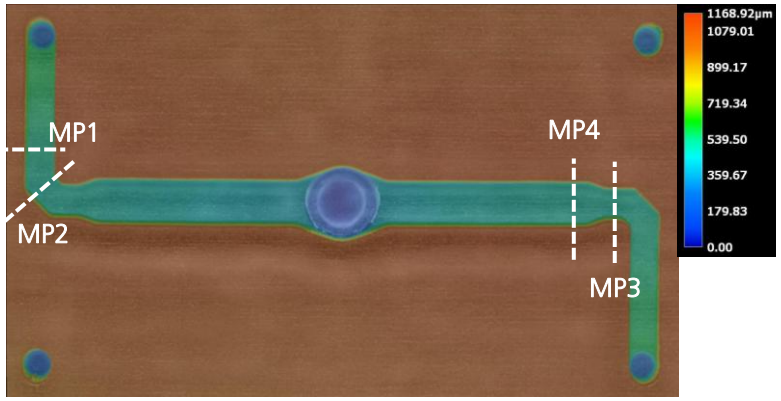
Two-channel chip with integrated membrane for barrier models

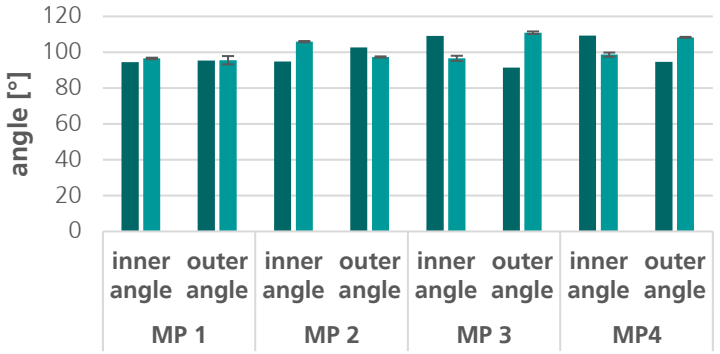
3D printed mold





Fabricated chip, after hot embossing

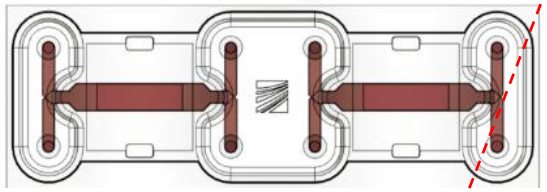




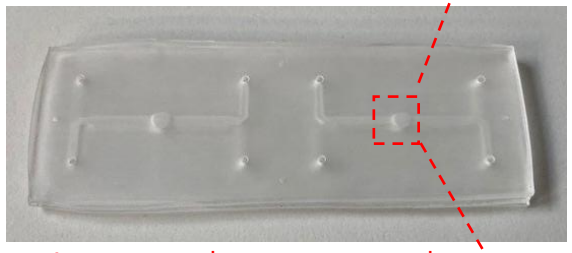
Fabricated chips closely match the designed geometry, confirming precision of the embossing process.

Quality assessment of our in-house chip fabrication

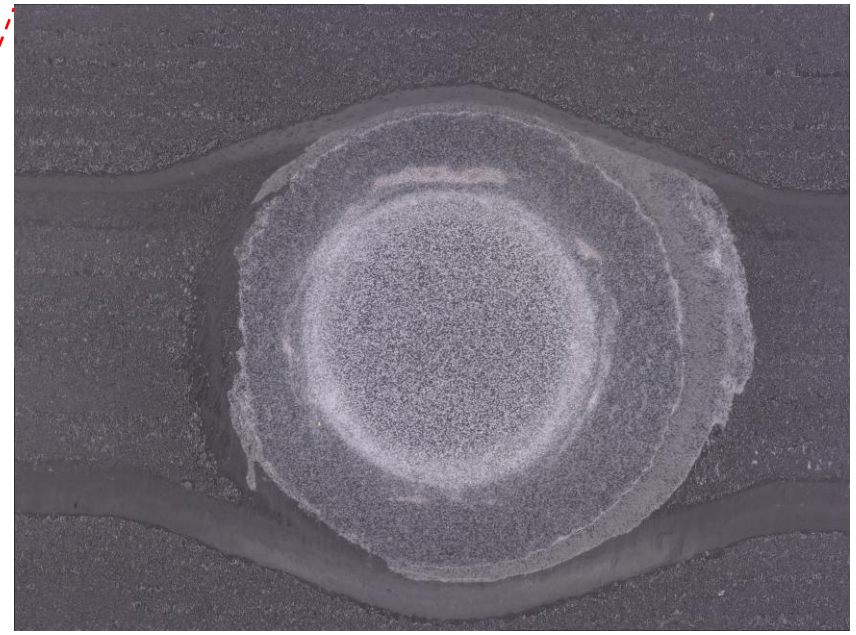
Membrane Integrity: Testing stability of membranes under heat and pressure



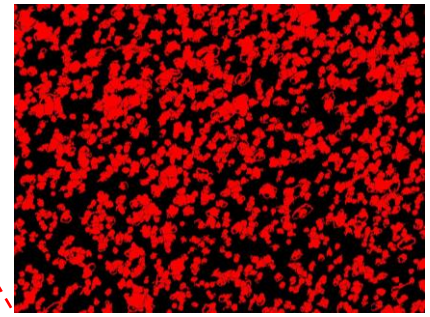
Fabricated Membrane-Chip



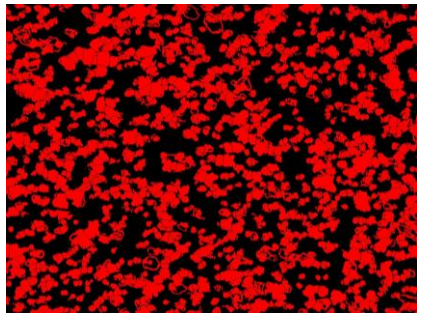
Integrated porous membrane



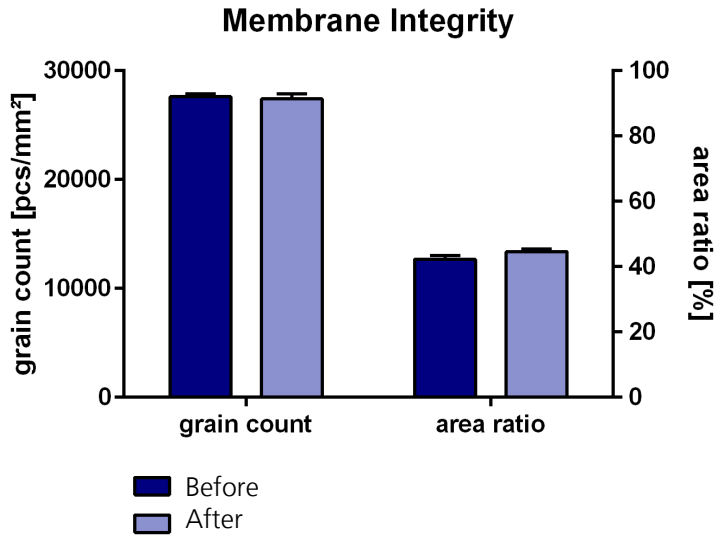
Before



After



Pores in membrane

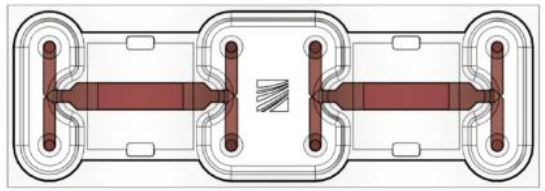


Both channel geometry and membrane integrity remain unchanged after hot embossing, confirming the robustness and reproducibility of our fabrication process.

Our Organ-on-Chip Systems

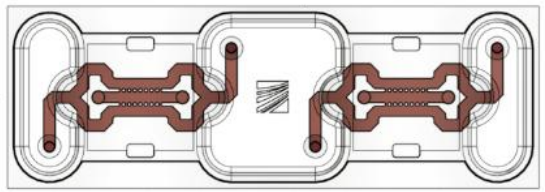
Standardized, versatile, and microscopy-compatible

- Standardization: size matches conventional glass slide
- Compatibility with standard lab equipment e.g. microscopy, pumps
- Design: 2 chips per system for parallel testing of conditions



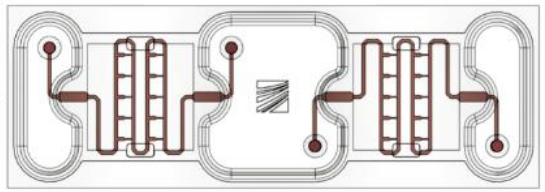
Membrane-Chip

- Barrier tissues (e.g. lung, gut, skin, liver)



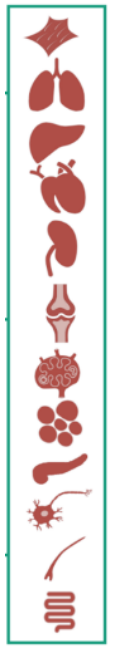
Matrix-Chip

- Complex cellular 3D microenvironments



Spheroid-Chip

- 3D cell models (e.g. Spheroids, tumoroids, organoids)



Versatility: compatible with various cell types – generation of various organ/tissue models

Three standardized microfluidic devices each designed for different biological application and to generate diverse tissue models.

Summary: Robust and Standardized Chip Fabrication

Hot embossing enables precise, reproducible, and integration-ready OoC devices

Standardized and versatile microfluidic devices for generation of various OoC models

Robust and reproducibile fabrication

Cost and time efficient
design of microfluidic devices

Scalable fabrication
compatible with industrial production techniques (e.g. injection molding)

High experimental accuracy
through minimal molecule absorption

Hot embossing delivers precise, cost-efficient, and scalable OoC devices — a strong foundation for industrial adoption

Motivation: Bridging the Gap Between Potential and Implementation

Developing advanced preclinical model systems that match industrial standards

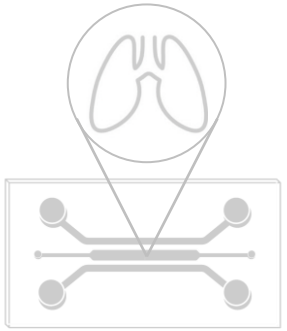
Non-Standardized OoC model systems

Standardized and Modular Model Development

Standardized, modular preclinical model systems

Microfabrication: rapid prototyping

Organ model generation: Long-term cell culture



Biological validation: In-line microscopy. and sensor-based assays

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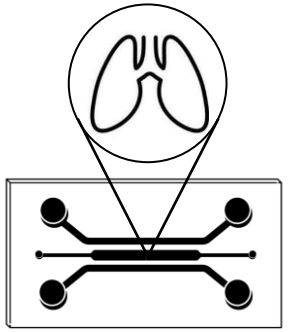
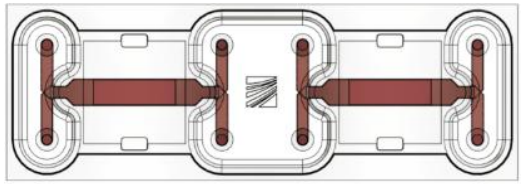


Biological validation: In-line microscopy. and sensor-based assays

Three Organ-on-Chip Systems for One Health Application

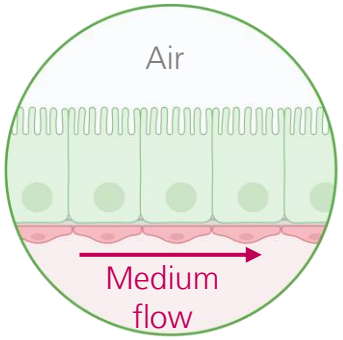
Distinct microfluidic devices – versatile models for infection, cancer, and immune diseases

Membrane-Chip: Lung on Chip



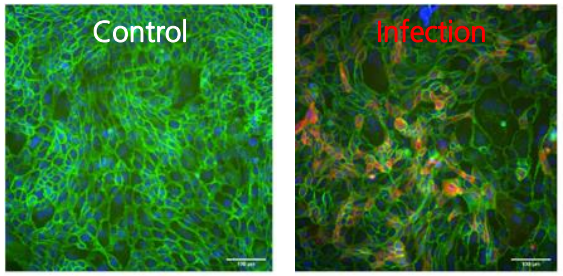
Generate Barrier-models

Culture of lung epithelial and endothelial cells on an air-liquid interface.

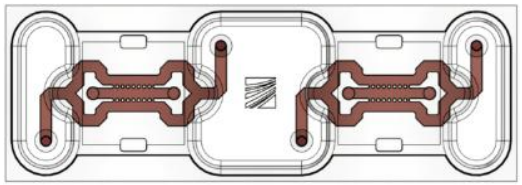


Model for zoonotic virus infections

Infection of lung epithelial cells with a virus.

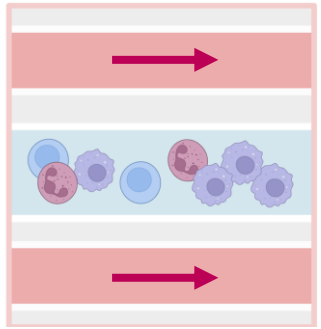


Matrix-Chip: AML Chip



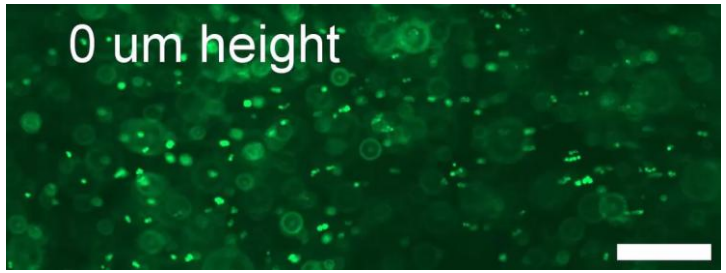
Mimic 3D microenvironment

Medium flow in outer channels

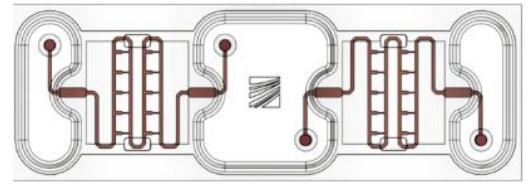


Immune cells in hydrogel channel

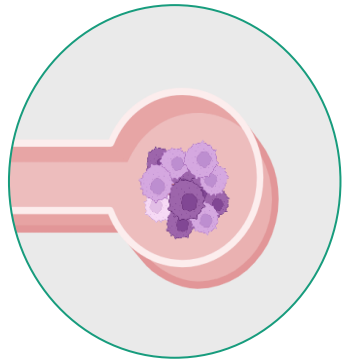
Mimic the bone marrow microenvironment and evaluate the efficiency of cell therapies



Spheroid-Chip: Breast Cancer Chip

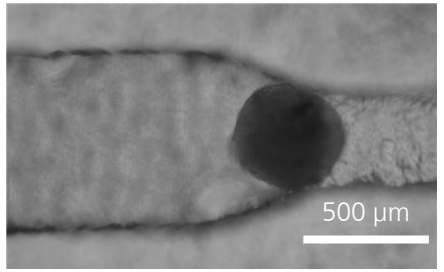


Culture individual 3D cell models.



Pockets to culture individual spheroids.

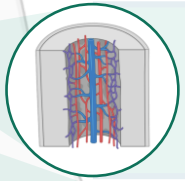
Personalized breast cancer model for drug screening.



Establishing Organ Models on Our Chips

Versatile platforms for infection, cancer, and immune diseases

- **Membrane-Chip:** Lung tissue models for infection and cancer immunotherapy



- **Matrix-Chip:** 3D hydrogel cultures to study leukemia

- **Spheroid-Chip:** Patient-derived tumoroids for translational cancer therapy testing

Potential to test new therapies and compounds in a personalized, patient-relevant way

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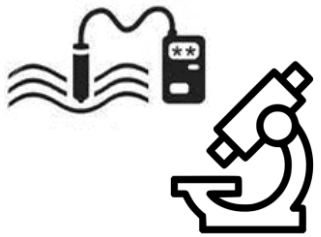
Microfabrication: rapid prototyping

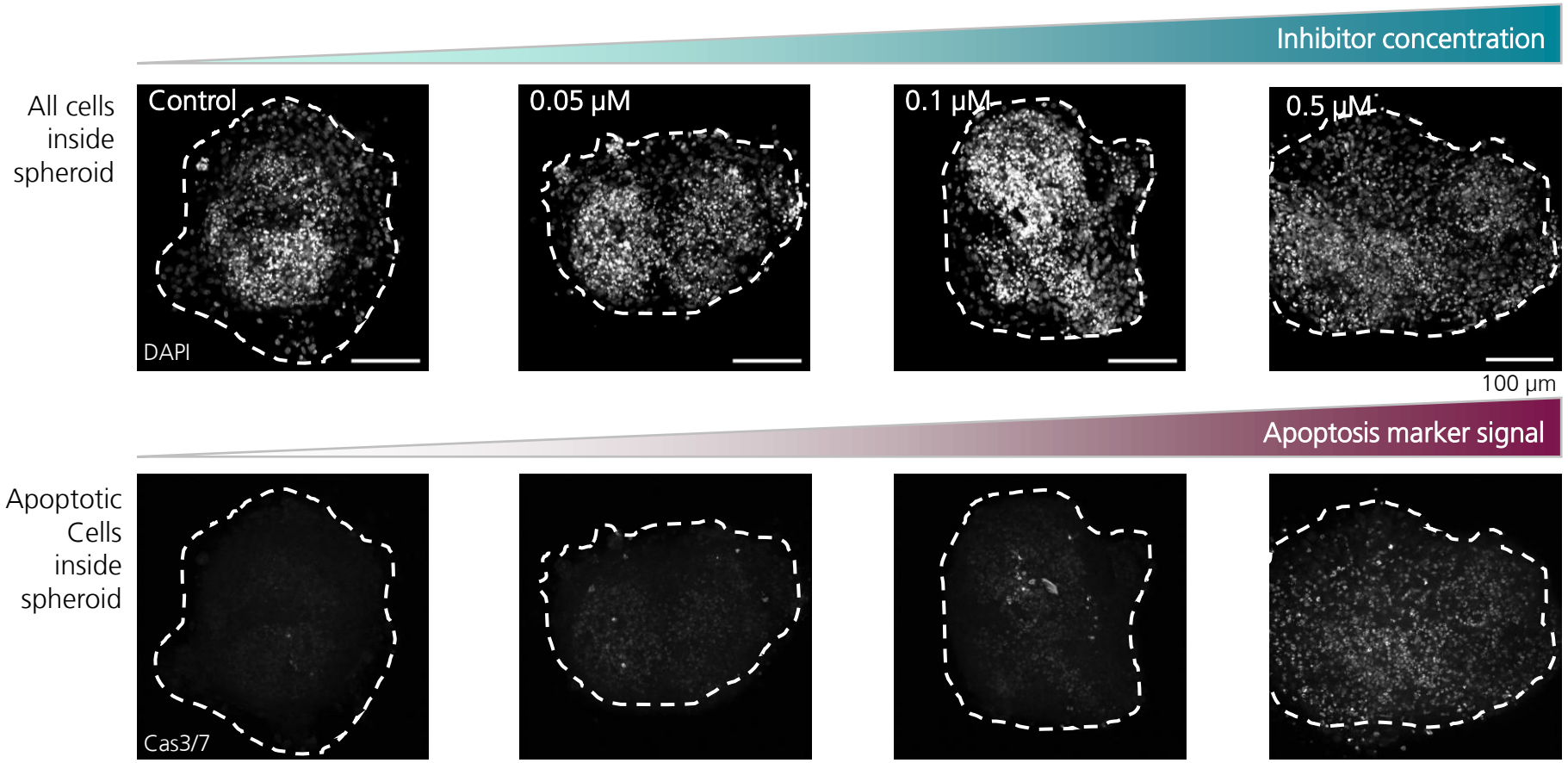
Organ model generation: Long-term cell culture

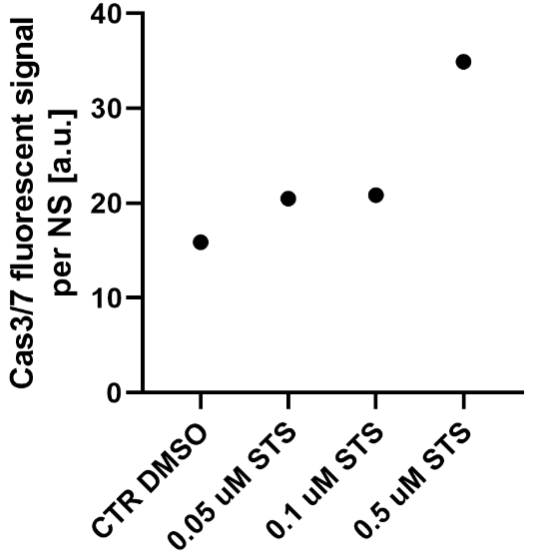
Biological validation: In-line microscopy and sensor-based assays



Generating biological endpoint assays

Microscopy-based measurement of cell death/apoptosis





Microscopy-based assays allow to assess the efficacy of drugs and therapies in our Organ-on-Chip systems

Towards automatization and high-throughput analysis

A modular approach of sensor integration in OoCs

Microscope-based assays:

- Time and labour extensive
- Generate a big set of data
- Intensive Image analysis

Lack scalability, hindering adoption in industry workflows

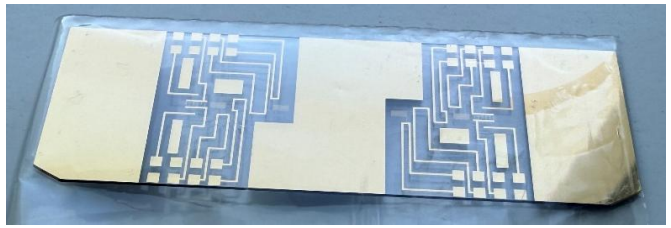
Sensor-based real-time analysis:

- Observe cell status in chip in real time
- See drug effect
- Non-destructive measurement

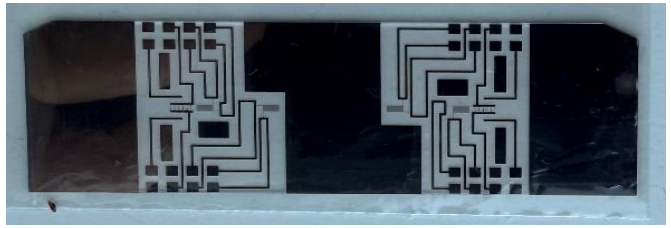
Scalable, high-throughput assays aligned with industrial drug pipelines

Sensor slide fabrication: gold electrodes on glass

Front side



Back side



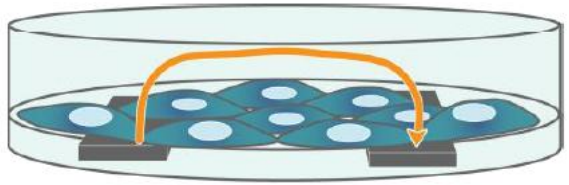
Integrated sensors turn our chip systems into real-time drug testing platforms — with modularity and standardization ensuring seamless integration across all devices.

High-throughput measurement of Barrier Function using TEER

Example: Axion biosystems – TEER measurements using the Maestro Z platform

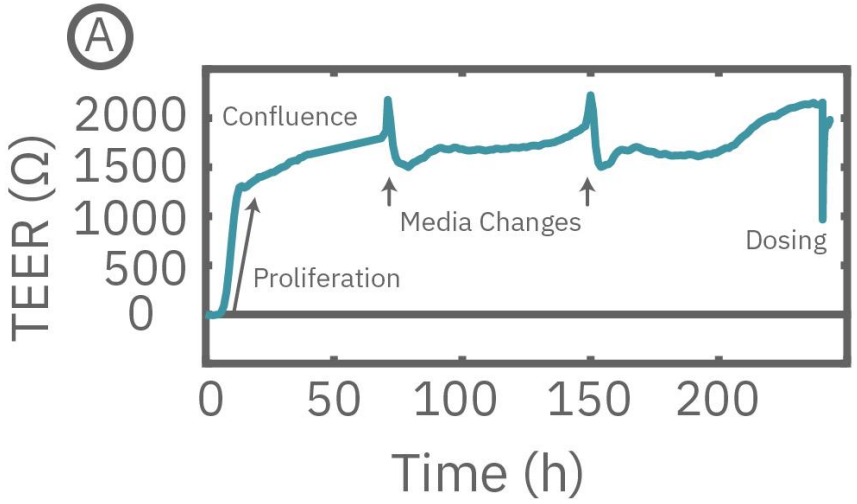
Monitoring of cell behaviour and environment :

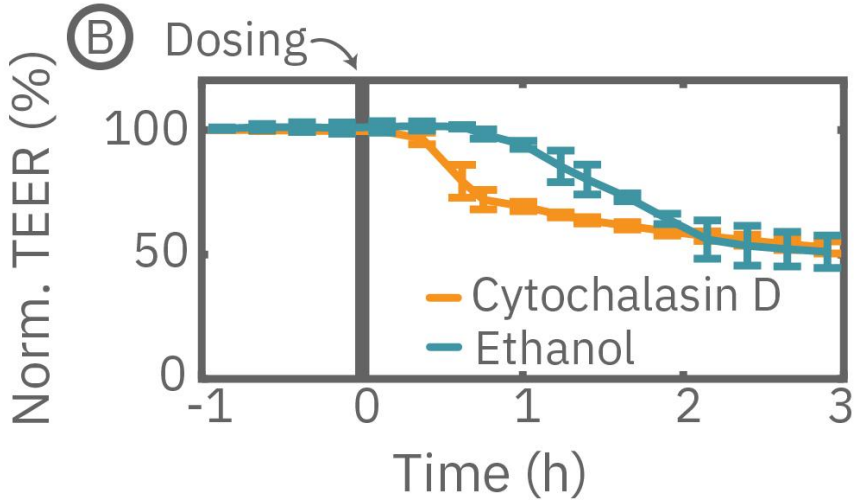
- Cell proliferation
- Barrier function formation
- Media changes



Monitoring of drug effect

- Decrease in barrier integrity
- Cell death





In-line sensor assays provide continuous, non-destructive, and highly sensitive monitoring — bringing Organ-on-Chip systems closer to the scalability and standardization required for industry adoption.

Example curves: Flyer for Maestro Z from Axion Biosystems

Motivation: Bridging the Gap Between Potential and Implementation

Developing advanced preclinical model systems that match industrial standards

Standardized and Modular Model Development

Non-Standardized OoC model systems

Standardized, modular preclinical model systems

Microfabrication: rapid prototyping

for robust, scalable device fabrication

Organ model generation: Long-term cell culture

to establish Infection & cancer models

Biological validation: In-line microscopy and sensor-based assays

for quantitative tissue and drug analysis

Ultimate goal: increase industry relevance for OoC systems by closer alignment with pharma workflows → scalability, reproducibility, and automatization

Fraunhofer ENAS

Interested in our technologies? Let´s collaborate !

Fraunhofer IZI

- Mario Baum
- Andreas Morschhauser
- Mohammed Salah Mohammed Rajeh

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