

# Lec 8. Organ on chips

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# Overview

- Significance of organ chip
- Organ chip

# Drug Development Cycle

1. Discovery and Development
2. Preclinical Research
3. Clinical Research
4. FDA Review
5. FDA Post-Market Safety Monitoring



# Discovery and Development

- Cellular targets include cell receptors, enzymes, membranes, genes, etc.
- Mechanism of action
- Potential benefits
- Effectiveness
- Pharmacodynamics (how the drug affects the body)
  - Including how it affects different populations
- Pharmacokinetics
  - How it is absorbed, distributed, metabolized, and excreted
- Best dose and route of administration
- Adverse effects
- Interaction with other treatments

# Drug development

## Summary of clinical research phase studies.

<i>Phase</i>	<b>Phase I</b>	<b>Phase II</b>	<b>Phase III</b>	<b>Phase IV</b>
<i>Purpose</i>	Safety and dosage	Efficacy and side effects	Efficacy and monitoring of adverse reactions	Safety and efficacy
<i>Participants</i>	20 to 100 healthy volunteers or people with the disease/condition	Up to several hundred people with the disease/condition	300 to 3,000 volunteers who have the disease or condition	Several thousand volunteers who have the disease/condition
<i>Length of Study</i>	Several months	Several months to 2 years	1 to 4 years	Months-Years

# Preclinical Research

- The two types of pre-clinical research
  - *in vitro*, or outside a living organism such as in a test tube,
  - *in vivo* studies which involve studies done in living organisms.

FDA NEWS RELEASE

# FDA Announces Plan to Phase Out Animal Testing Requirement for Monoclonal Antibodies and Other Drugs

For Immediate Release: April 10, 2025

<https://www.fda.gov/news-events/press-announcements/fda-announces-plan-phase-out-animal-testing-requirement-monoclonal-antibodies-and-other-drugs>



# Roadmap to Reducing Animal Testing in Preclinical Safety Studies

## Executive Summary

This roadmap outlines a strategic, stepwise approach for FDA to reduce animal testing in preclinical safety studies with scientifically validated new approach methodologies (NAMs), such as organ-on-a-chip systems, computational modeling, and advanced *in vitro* assays. By partnering with federal agencies like NIH and VA through ICCVAM, FDA can accelerate the validation and adoption of these human-relevant methods, improving predictive accuracy while reducing animal use. This transition will enhance public health by streamlining drug development and ensuring safer therapies reach patients faster, while positioning FDA as a global leader in modern regulatory science and innovation.

# Overview — Failures of Animal Testing in Preclinical Research

- Over **90% of drugs** that are safe/effective in animals **fail in human trials**
- Major reason: **biological and immune system differences** between species
- Leads to **unreliable predictions** for human safety and efficacy

# Disease-Specific Failures

- **Cancer**
  - Many cancer drugs effective in mice **fail in human trials**
  - Tumor microenvironment and immune responses **differ between species**
- **Alzheimer's Disease**
  - Animal models **do not replicate human disease mechanisms**
  - Contributed to repeated **failures of Alzheimer's drug candidates**
- **Inflammatory Diseases**
  - Mouse immune responses **poorly mimic human inflammation**
  - Studies show **genomic responses diverge greatly** between mice and humans

# Safe in Animals, Harmful in Humans

- Example: **TGN1412 Monoclonal Antibody**
- Appeared **safe in monkey studies**
- Caused **life-threatening cytokine storm** in human volunteers
- Exposed **critical flaw** in predicting immune reactions across species
- Led to development of **human-based cytokine release assays**

# Harmful in Animals, Safe in Humans

- **Example: Aspirin**
- **Toxic in several animal species**, would not pass modern safety tests
- Yet **safe and widely used** in humans
- Demonstrates how animal tests can **block beneficial drugs**

# Immunogenicity Mismatch

- Animals often **produce immune responses** to human monoclonal antibodies
- Alters exposure and **confounds toxicity results**
- **Animal immune reactions ≠ human immunogenicity**
- Makes animal data **unreliable for predicting human safety**

# Ethical and Welfare Concerns

- Millions of animals are used annually in research, often experiencing pain, confinement, or euthanasia.
- Growing public opposition and ethical concerns are driving calls for more humane, **non-animal alternatives** that do not compromise scientific progress.

# High Costs and Time Consumption

- Animal studies require **specialized facilities, long study periods**, and regulatory oversight.
- They are **expensive** to conduct and often add months or years to the preclinical process.
- In contrast, **AI-based modeling and human cell systems** can generate results faster and at a fraction of the cost.

# NAMs (New Approach Methodologies)

- **NAMs** = Human-relevant, non-animal testing methods
- Aim to **predict human safety and efficacy** more accurately
- Include **in vitro, in silico, and other innovative platforms**
- Designed to **reduce or replace animal testing** while improving reliability

# In Vitro Human-Based Systems

- **Organoids**
  - 3D miniature human tissues grown from stem cells
  - Replicate key organ structures (e.g., liver, gut, brain)
  - Used to study toxicity, metabolism, and immune effects
- **Microphysiological Systems (Organ-on-a-Chip)**
  - Chips recreate human organ functions using living human cells
  - Can simulate blood flow, immune activity, and mechanical forces
  - Examples:
    - **Human Liver-Chip** → predicted 87% of drugs causing human liver injury
    - **Cardiac tissue chips** → detect heart toxicity or arrhythmia risk
    - **Immune organoids / blood-on-a-chip** → detect cytokine release and immune toxicity

- **In Silico & Computational Modeling**
  - **1. Physiologically-Based Pharmacokinetic (PBPK) Models**
    - Simulate drug absorption, distribution, metabolism, and excretion (ADME) in humans
    - Help set **first-in-human dosing** and replace animal PK studies
  - **2. Machine Learning (ML) & Artificial Intelligence (AI) Models**
    - Analyze molecular features to **predict toxicity or immunogenicity**
    - Example: **AbImmPred** model predicts antibody immune reactions before trials
  - **3. Quantitative Systems Pharmacology (QSP)**
    - Simulates **drug interactions with human biological networks**
    - Predicts therapeutic and toxic outcomes in virtual “human” systems
  - **4. Bioinformatics / In Silico Off-Target Screening**
    - Uses protein databases and AI to find **unintended human binding targets**
    - Replaces broad receptor binding or animal tissue cross-reactivity studies

# What is an Organ-on-a-Chip?



## Definition

A small bioengineered device that mimics the structure and function of a human organ using living cells and microfluidic technology.

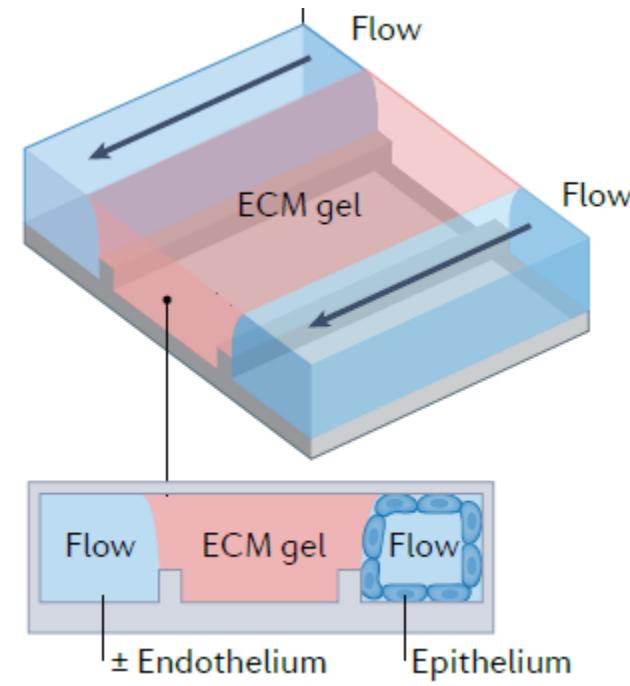
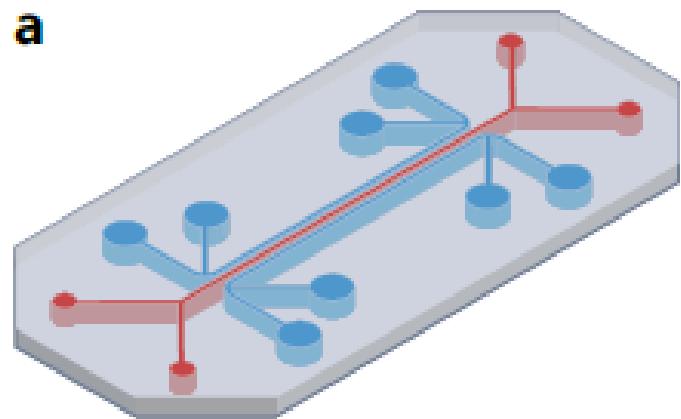


## Key Features

- Microchannels simulate **blood flow and nutrient exchange**
- **Human cells** arranged to replicate organ-level structure and function
- Applies **mechanical forces** (e.g., breathing, heartbeat) for realism

# Reported Organ-on-Chip Systems

- **Central Nervous System:** Brain, spinal cord, blood-brain barrier (BBB)
- **Cardiovascular System:** Heart, blood vessels, microvasculature, aortic valve
- **Respiratory System:** Lung (alveolus & airway)
- **Digestive System:** Liver, intestine, colon, stomach
- **Renal System:** Kidney (proximal tubule, glomerulus)
- **Immune System:** Lymph node, spleen, immune-cell circulation models
- **Endocrine & Metabolic:** Pancreas (islet chips), adipose tissue
- **Sensory Organs:** Eye (retina, choroid), inner ear
- **Reproductive System:** Placenta, uterus, testis, ovary
- **Musculoskeletal:** Bone, cartilage, skeletal muscle
- **Multi-Organ “Body-on-a-Chip”:** Linked liver-kidney-intestine-heart systems for drug metabolism and toxicity

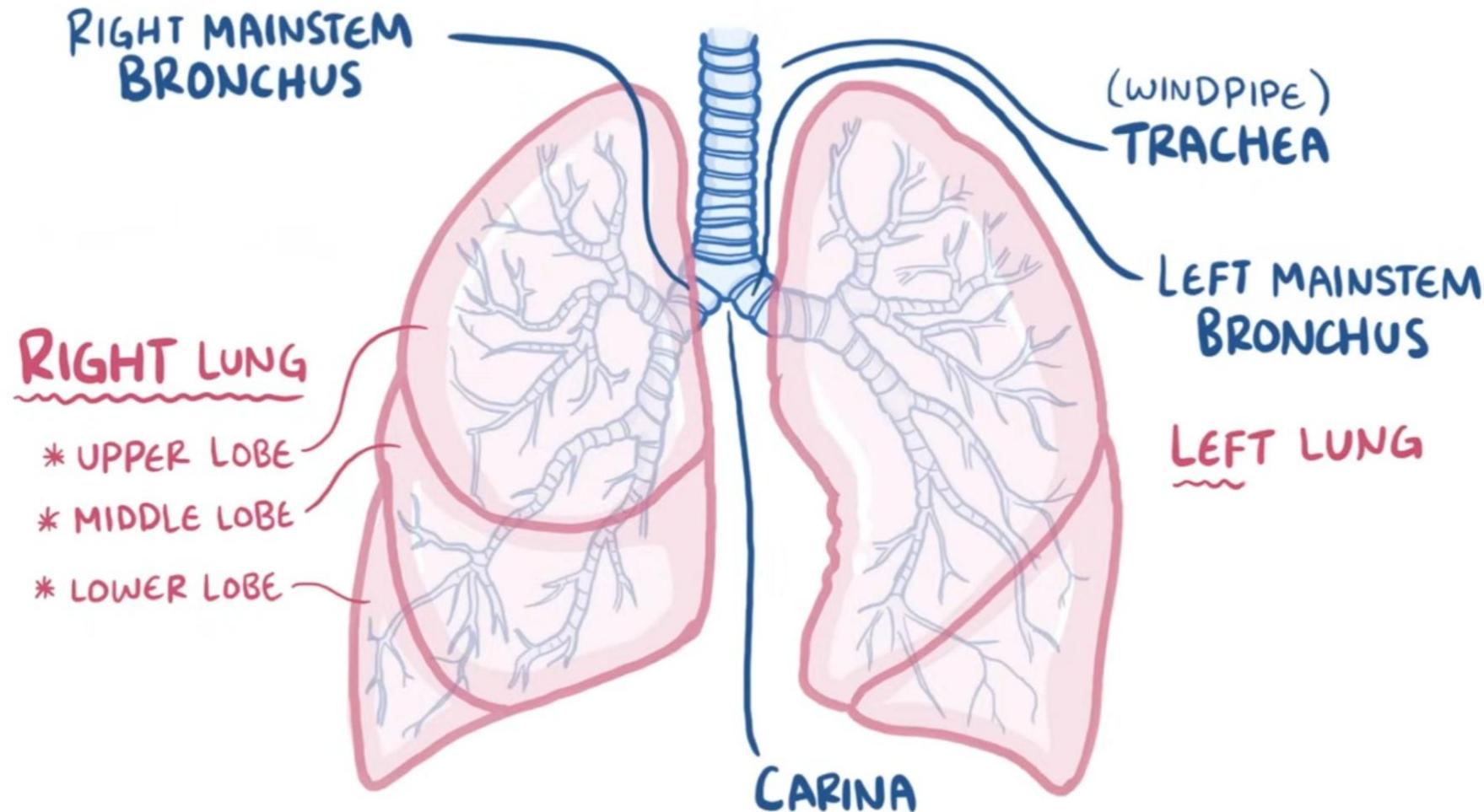


# Different types of organ chips

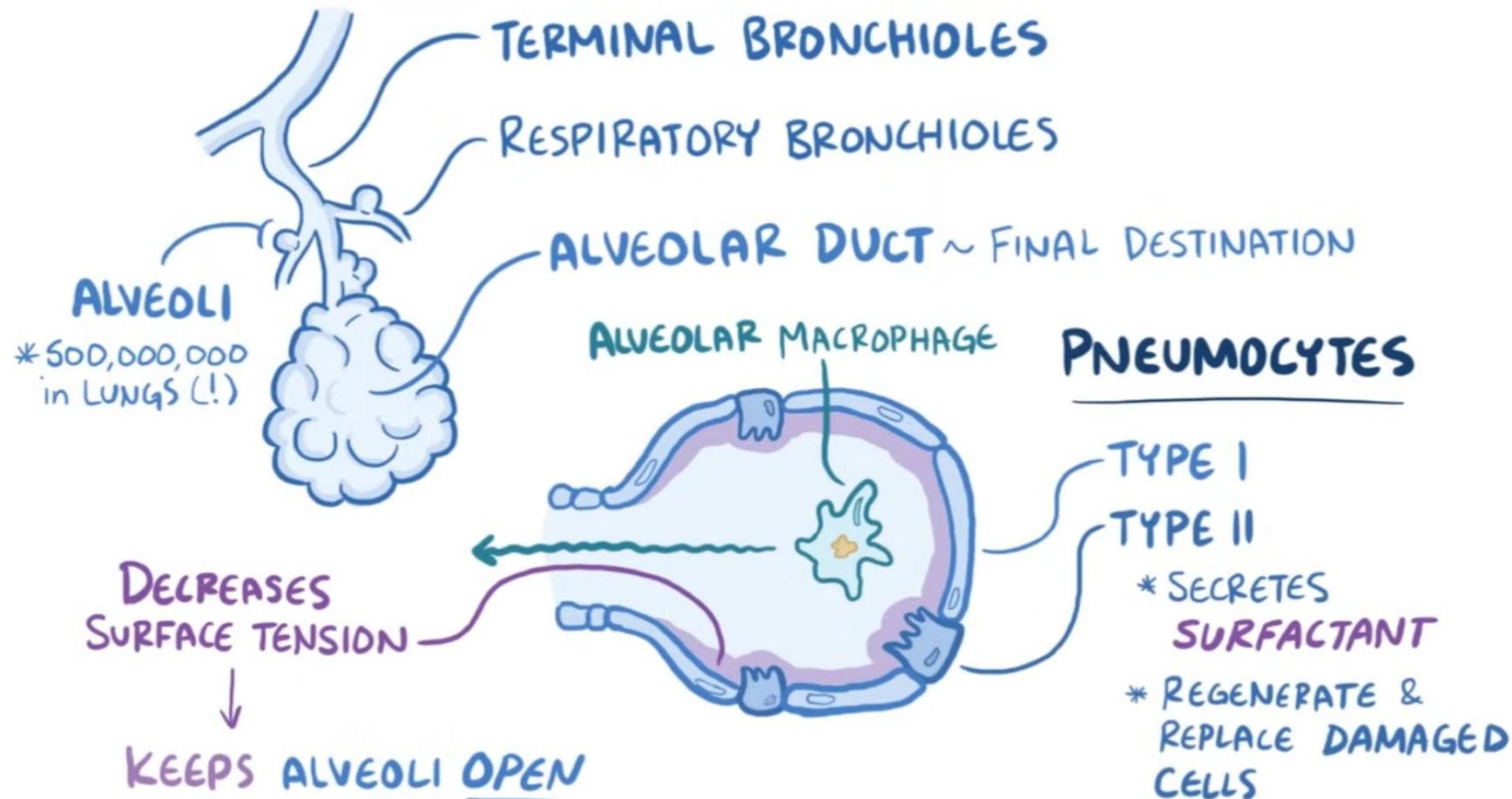
- Lung
- Bone marrow
- Blood-brain barrier
- Liver

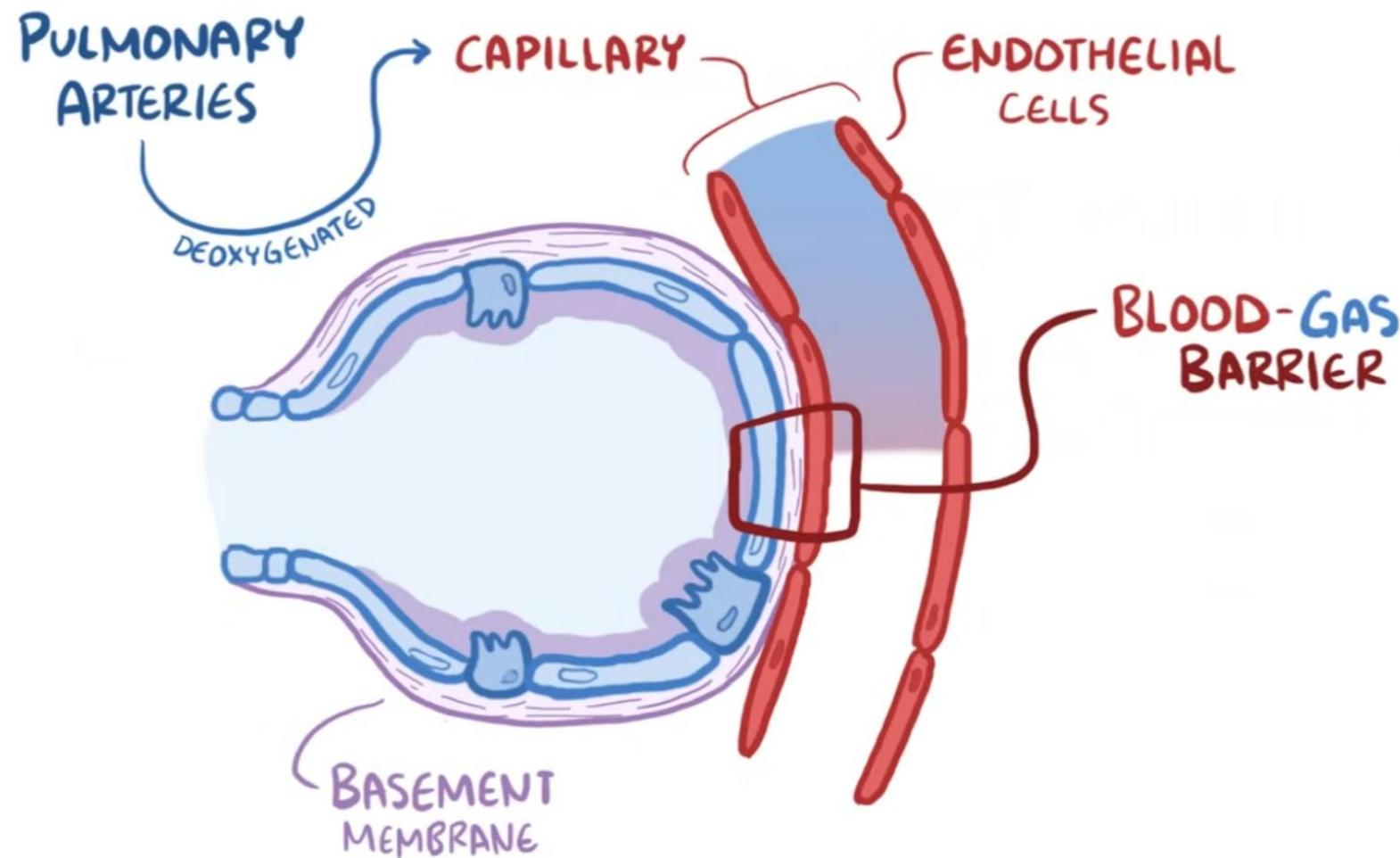
# Lung chip

# Lung



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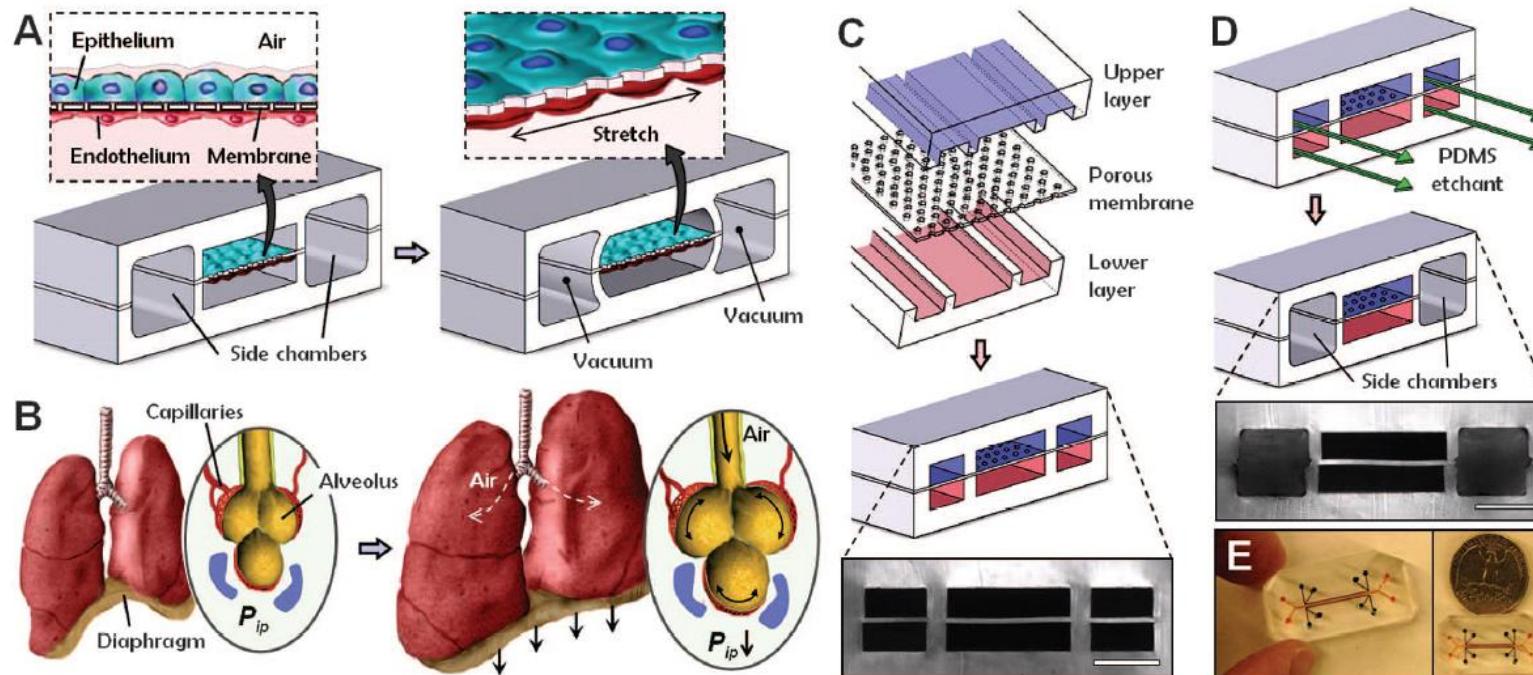




# Reconstituting Organ-Level Lung Functions on a Chip

Dongeun Huh,<sup>1,2</sup> Benjamin D. Matthews,<sup>2,3</sup> Akiko Mammoto,<sup>2</sup> Martín Montoya-Zavala,<sup>1,2</sup> Hong Yuan Hsin,<sup>2</sup> Donald E. Ingber<sup>1,2,4\*</sup>

Here, we describe a biomimetic microsystem that reconstitutes the critical functional alveolar-capillary interface of the human lung. This bioinspired microdevice reproduces complex integrated organ-level responses to bacteria and inflammatory cytokines introduced into the alveolar space. In nanotoxicology studies, this lung mimic revealed that cyclic mechanical strain accentuates toxic and inflammatory responses of the lung to silica nanoparticles. Mechanical strain also enhances epithelial and endothelial uptake of nanoparticulates and stimulates their transport into the underlying microvascular channel. Similar effects of physiological breathing on nanoparticle absorption are observed in whole mouse lung. Mechanically active “organ-on-a-chip” microdevices that reconstitute tissue-tissue interfaces critical to organ function may therefore expand the capabilities of cell culture models and provide low-cost alternatives to animal and clinical studies for drug screening and toxicology applications.



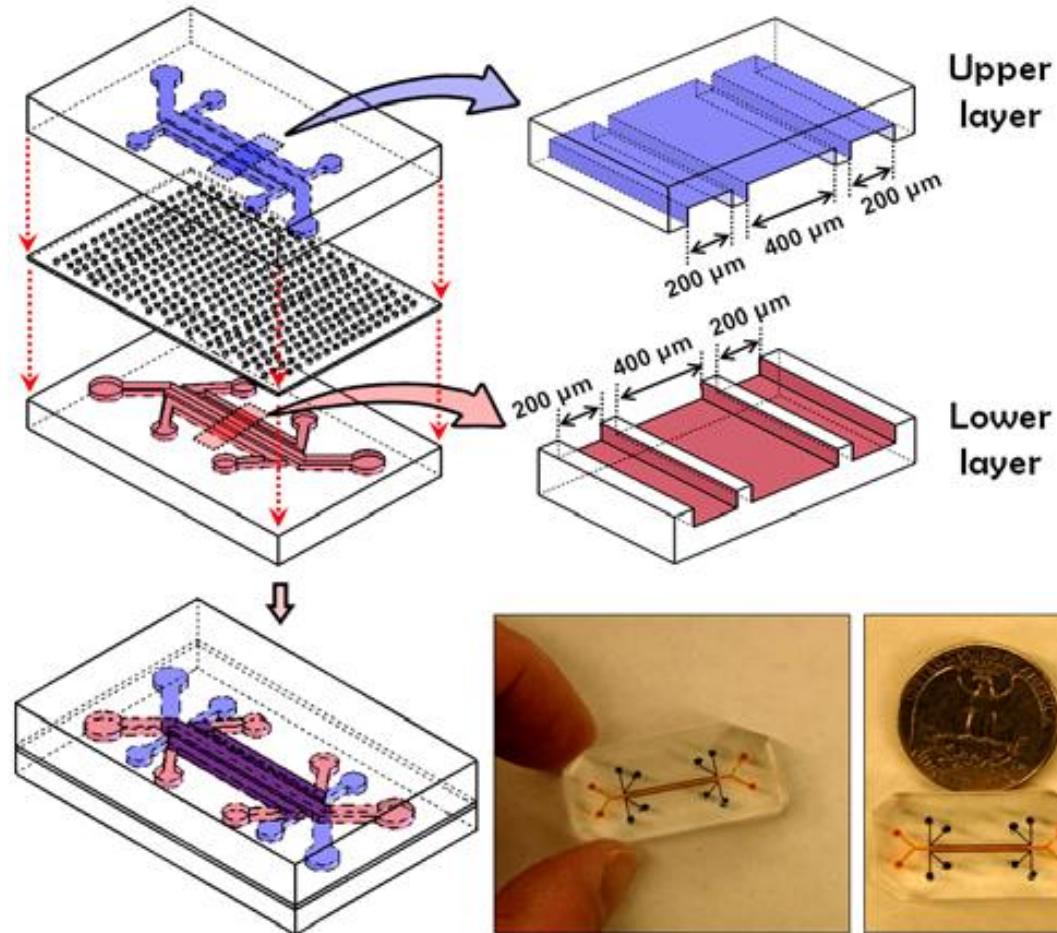
- **Key Idea:** The device mimics the alveolar–capillary interface.

- **Design Features:**

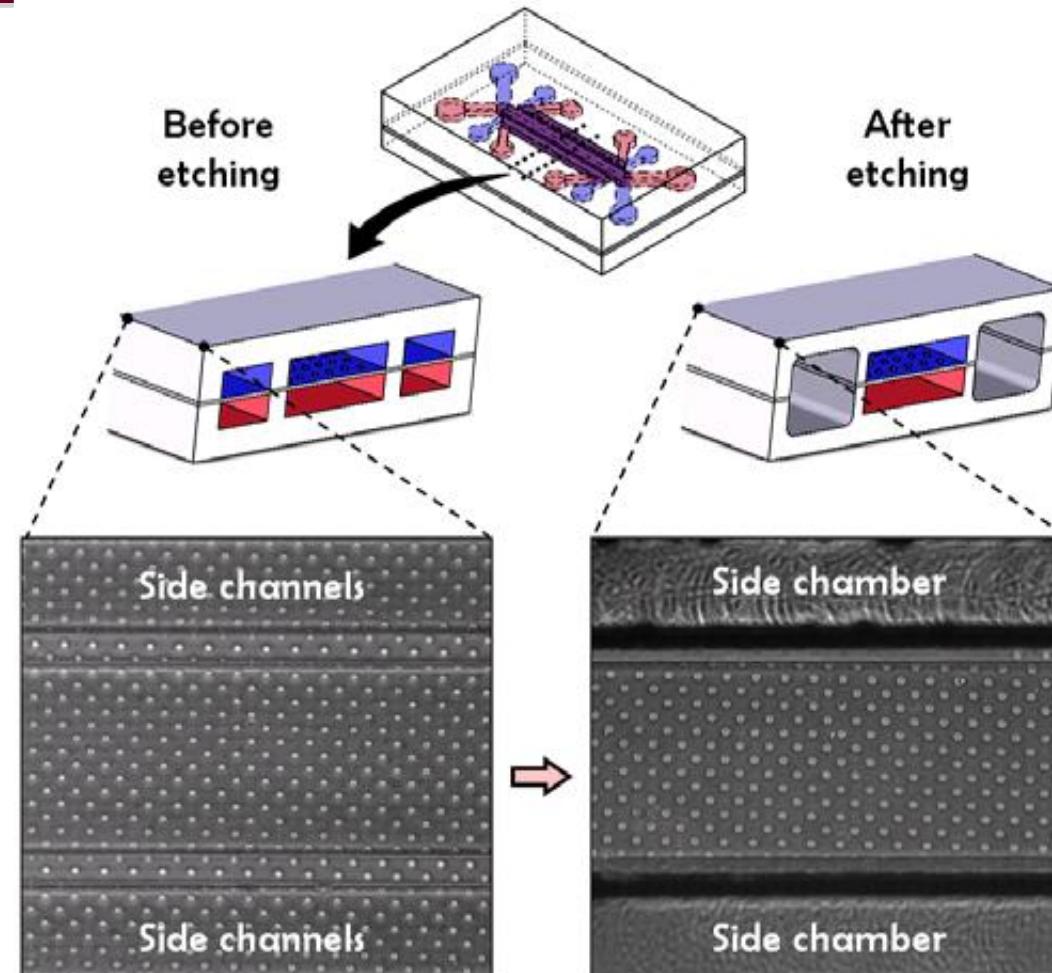
- Two microchannels (air & blood) separated by a **porous, flexible PDMS membrane** coated with ECM.
- **Vacuum side chambers** stretch the membrane to simulate breathing motions.
- Enables independent control of **air flow, fluid flow, and mechanical strain**.
- **Takeaway:** Recreates lung architecture and mechanics on a microscale platform.

# Question:

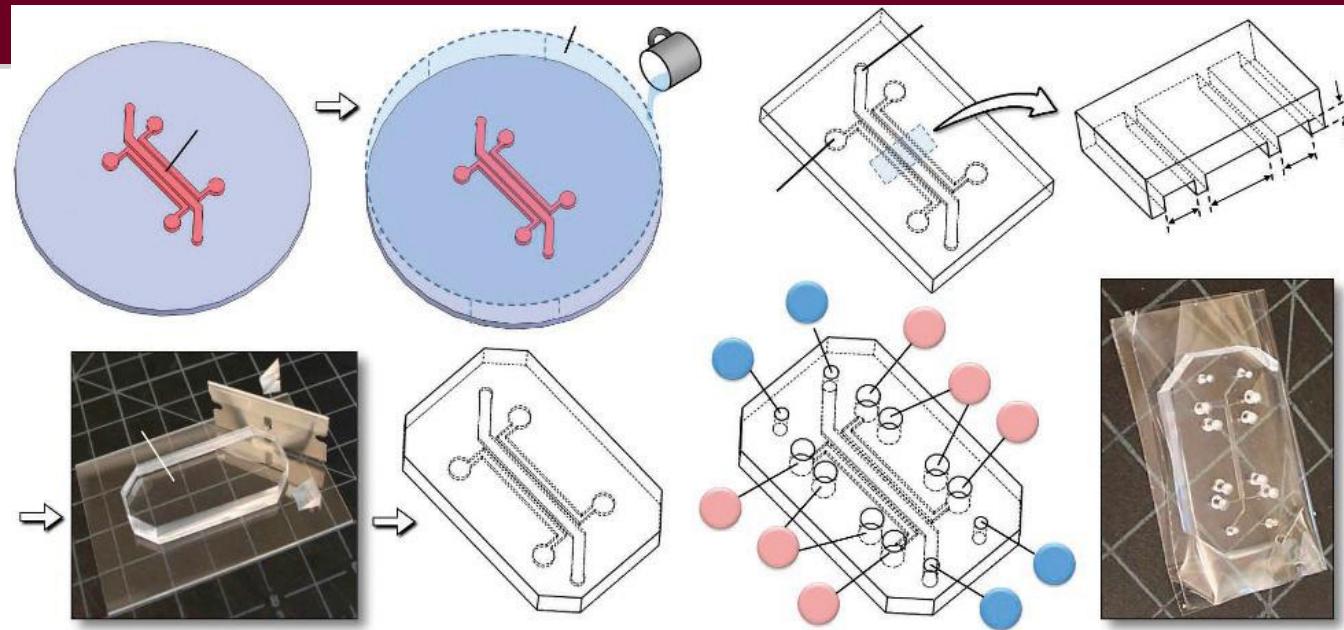
- How to fabricate such microfluidic devices?



Layer-by-layer bonding

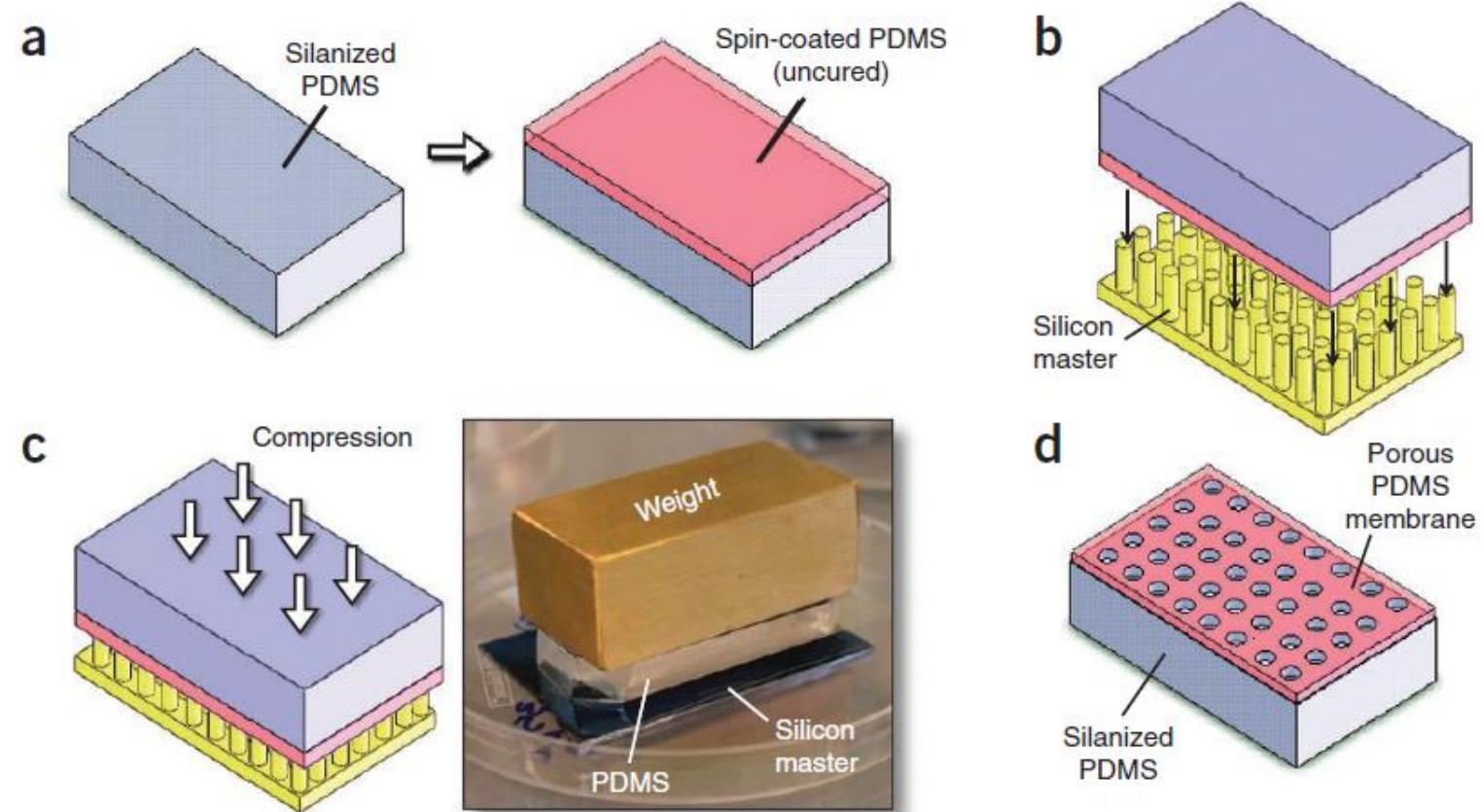


**Membrane etching**

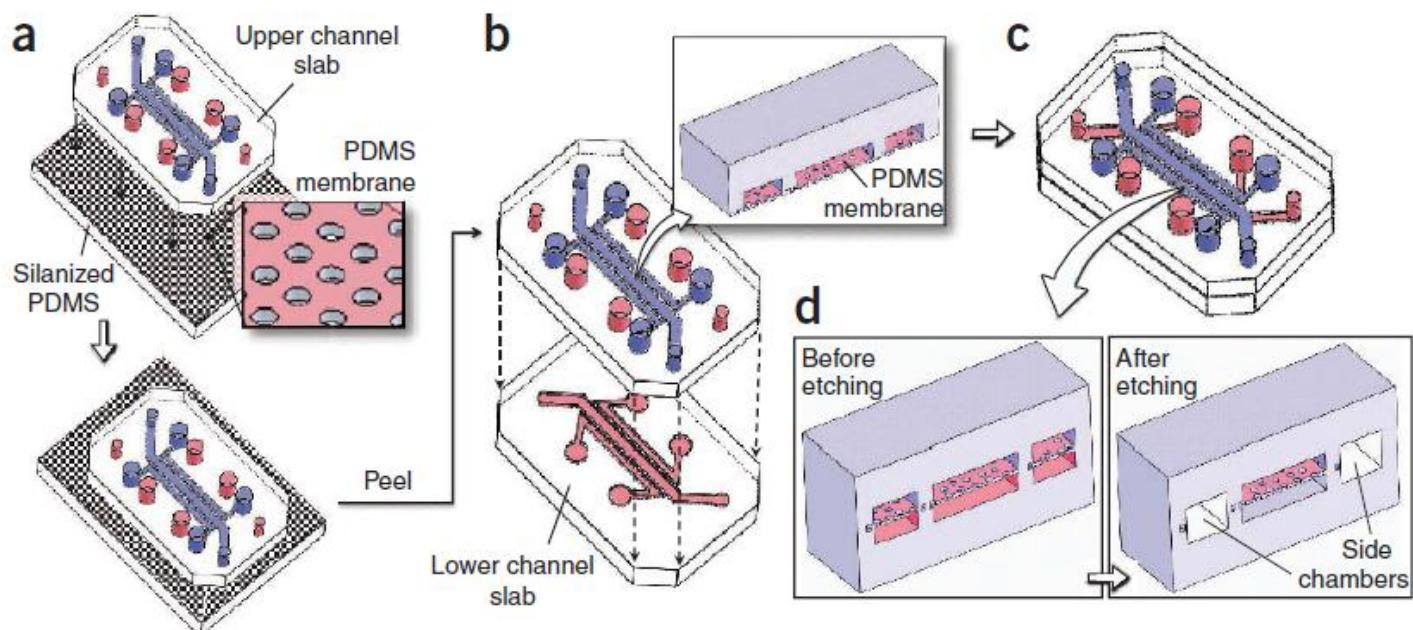


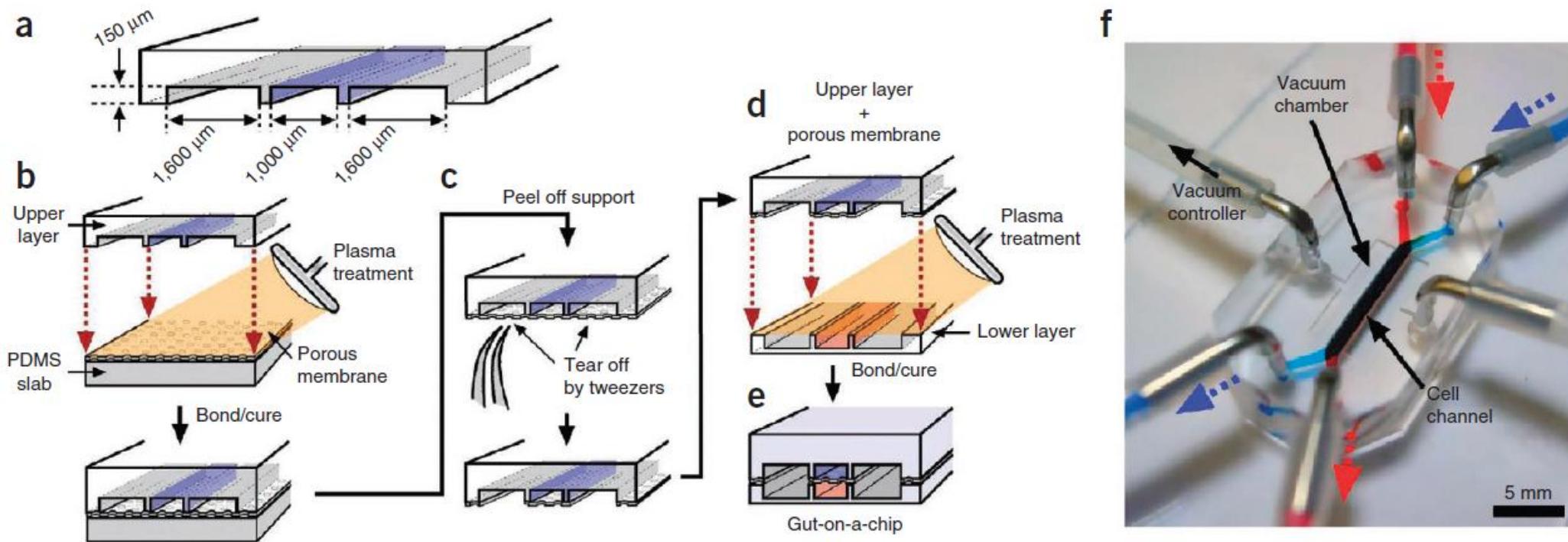
Fabrication of the upper microchannels of the lung-on-a-chip. **(a)** Prepolymer of PDMS mixed with curing agent is poured onto the photolithographically prepared SU-8 microchannel features and subsequently cured at an elevated temperature. **(b)** The fully cured PDMS is peeled off of the master and cut into a rectangular block embossed with three parallel upper microchannels that are 100  $\mu\text{m}$  in thickness. The widths of the central cell culture channel and two side vacuum channels are 400  $\mu\text{m}$  and 200  $\mu\text{m}$ , respectively. **(c,d)** The corners of the PDMS slab are removed **(c)**, and access ports are made to the microchannels using hole punches **(d)**. Cell culture and vacuum channels are denoted by C and V, respectively, and asterisks mark access holes for the lower microchannels. **(e)** The upper PDMS slab is cleaned and wrapped in packaging tape for later use.

**Figure 3 |** Fabrication of porous PDMS membranes. (a) PDMS is spin-coated on a silanized PDMS slab to form a 10- $\mu\text{m}$ -thick film of uncured PDMS. (b,c) Subsequently, the PDMS slab is placed on a silicon wafer patterned with an array of microfabricated pillars (b) and compressed uniformly against the master using weight during PDMS curing (c). The diameter and height of the pillars are 10  $\mu\text{m}$  and 50  $\mu\text{m}$ , respectively. (d) After complete curing of PDMS, the weight and silicon master are removed to produce a 10- $\mu\text{m}$ -thick PDMS membrane with microfabricated through-holes that is reversibly attached to a silanized PDMS surface.



**Figure 4 |** Alignment, bonding and chemical etching of the lung-on-a-chip microdevice. (a) After brief surface treatment with corona, the upper PDMS slab is irreversibly bonded to the membrane. (b) Once bonding is accomplished, the upper microchannel slab is carefully separated from the silanized PDMS block, primed with corona and aligned/bonded to the lower microchannels. (c,d) This results in the production of a fully assembled microfluidic device (c) in which the membrane layers in the vacuum microchannels are etched away to form two hollow side chambers (d).

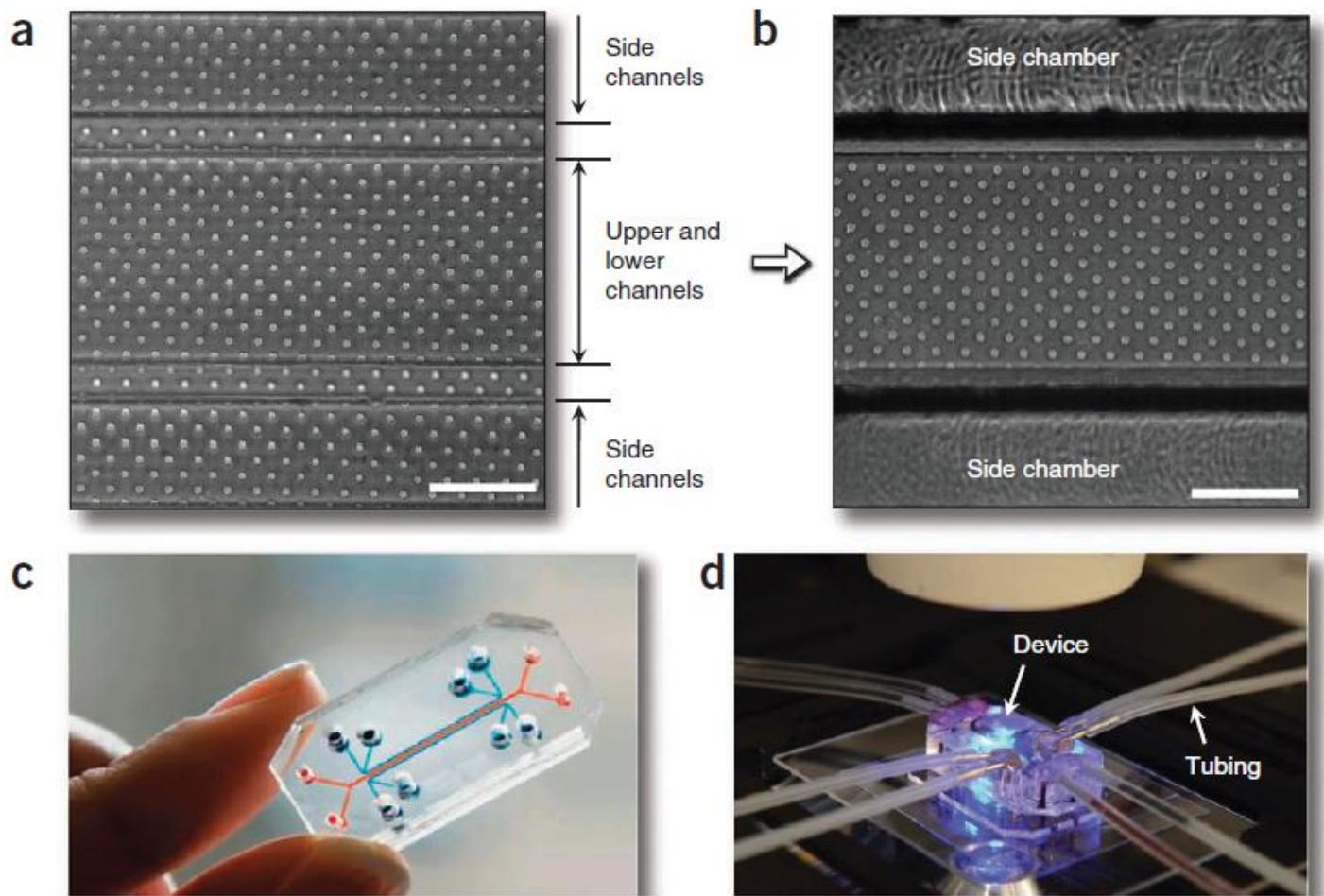




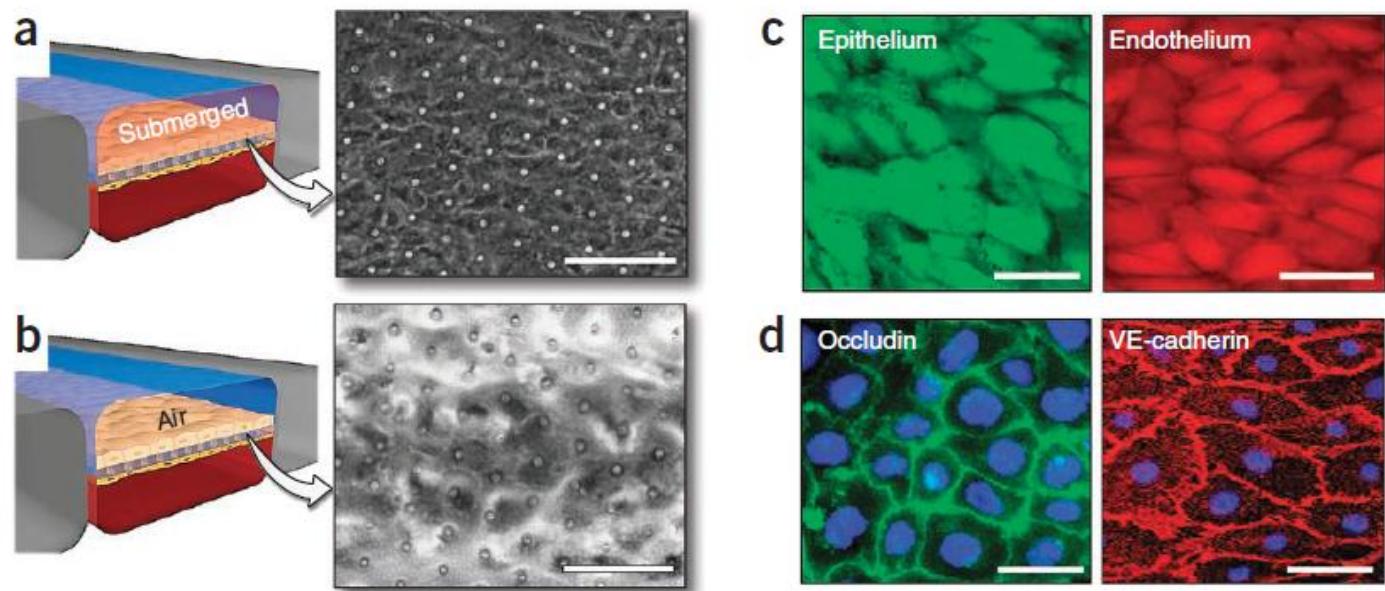
**Figure 5 |** Microfabrication of gut-on-a-chip. (a) Dimensions of the central cell culture microchannel and side vacuum chambers in the upper layer of the gut-on-a-chip device. The size of microchannels in the lower layer is the same as that in the upper layer. (b–e) Layer-by-layer microfabrication process. The gut-on-a-chip microdevice is composed of the upper layer, a porous membrane and the lower layer. Each layer is sequentially bonded and cured to fabricate the upper (blue) and lower (orange) cell culture microchannels and two lateral vacuum chambers (gray). The porous PDMS membrane in the vacuum chambers is manually torn off by using tweezers to create full-height vacuum chambers. (f) A photograph of the fully assembled gut-on-a-chip microdevice with the upper and lower microchannels filled with blue and red dyes, respectively.

alveolar channel can become flooded

**Figure 6 |** A multilayered 3D microfluidic device for the production of the human breathing lung-on-a-chip. **(a)** A micrograph of well-aligned upper and lower microchannels separated by a thin porous PDMS membrane in an assembled microdevice. Scale bar, 200  $\mu$ m. **(b)** Chemical etching of PDMS successfully removes the porous membrane in the side channels and causes the thinning of the PDMS walls between the central microchannels and the side chambers. Scale bar, 200  $\mu$ m. **(c)** Optical transparency of PDMS permits direct visualization of individual microchannels embedded in the device. In this image, the cell culture microchannels and vacuum chambers are shown in orange and blue, respectively. **(d)** Tubing is attached to the assembled device by using bent needles inserted into the access ports. The final PDMS microdevice can be placed on a regular microscope stage for imaging.

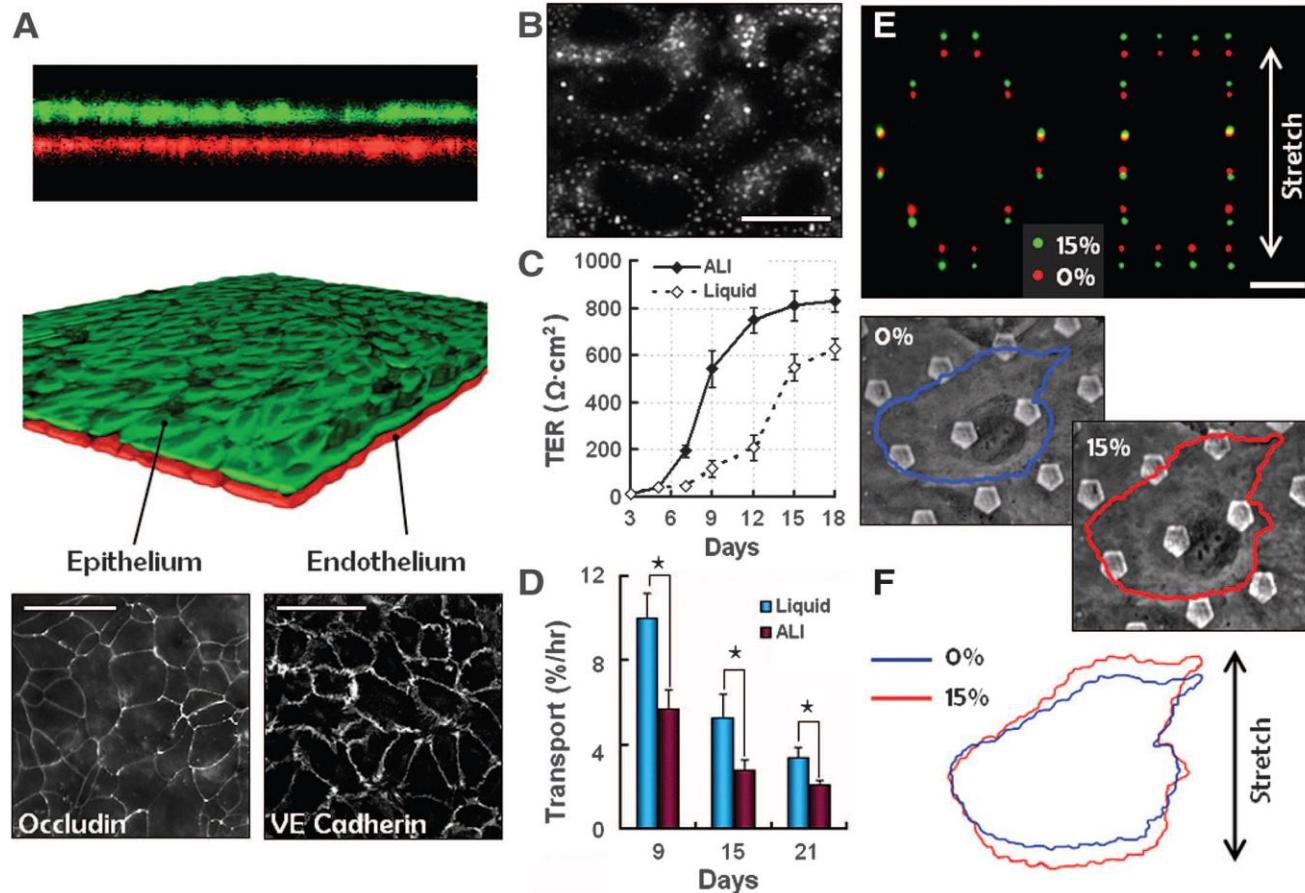


**Figure 7 |** Production and microfluidic engineering of the alveolar epithelium and microvascular endothelium in the lung-on-a-chip microdevice. (a) Confluent monolayers of human lung epithelial cells and microvascular endothelial cells are formed on the opposite sides of the membrane within 5 d of cell seeding. During this period, both the upper and lower microchannels are continuously perfused with appropriate culture media. This phase-contrast image (right) was taken on day 5. Scale bar, 75  $\mu$ m. (b) A micrograph of the human alveolar epithelial tissue (right) in the air-filled alveolar microchannel on day 10 in air-liquid interface (ALI) culture. When exposed to air, the confluent monolayer of the alveolar epithelial cells serves as a barrier to fluid leakage from the lower vascular microchannel, facilitating the maintenance of ALI culture conditions for extended periods. Scale bar, 75  $\mu$ m. (c) The majority of the epithelial and endothelial cells in the microdevice are maintained highly viable at the completion of ALI culture (day 20), as evidenced by their staining with CellTracker Green CMFDA (epithelial) and CellTracker Red CMTPX (endothelial) live cell-specific dyes. Scale bar, 25  $\mu$ m. (d) ALI culture in our system also leads to the formation of tight (green; anti-occludin antibody conjugated with Alexa Fluor 488) and adherens (red; anti-VE-cadherin antibody conjugated with Alexa Fluor 594) junctions in the epithelial and endothelial cells, respectively. Blue shows nuclear staining. Scale bars, 25  $\mu$ m.



# Downstream analysis

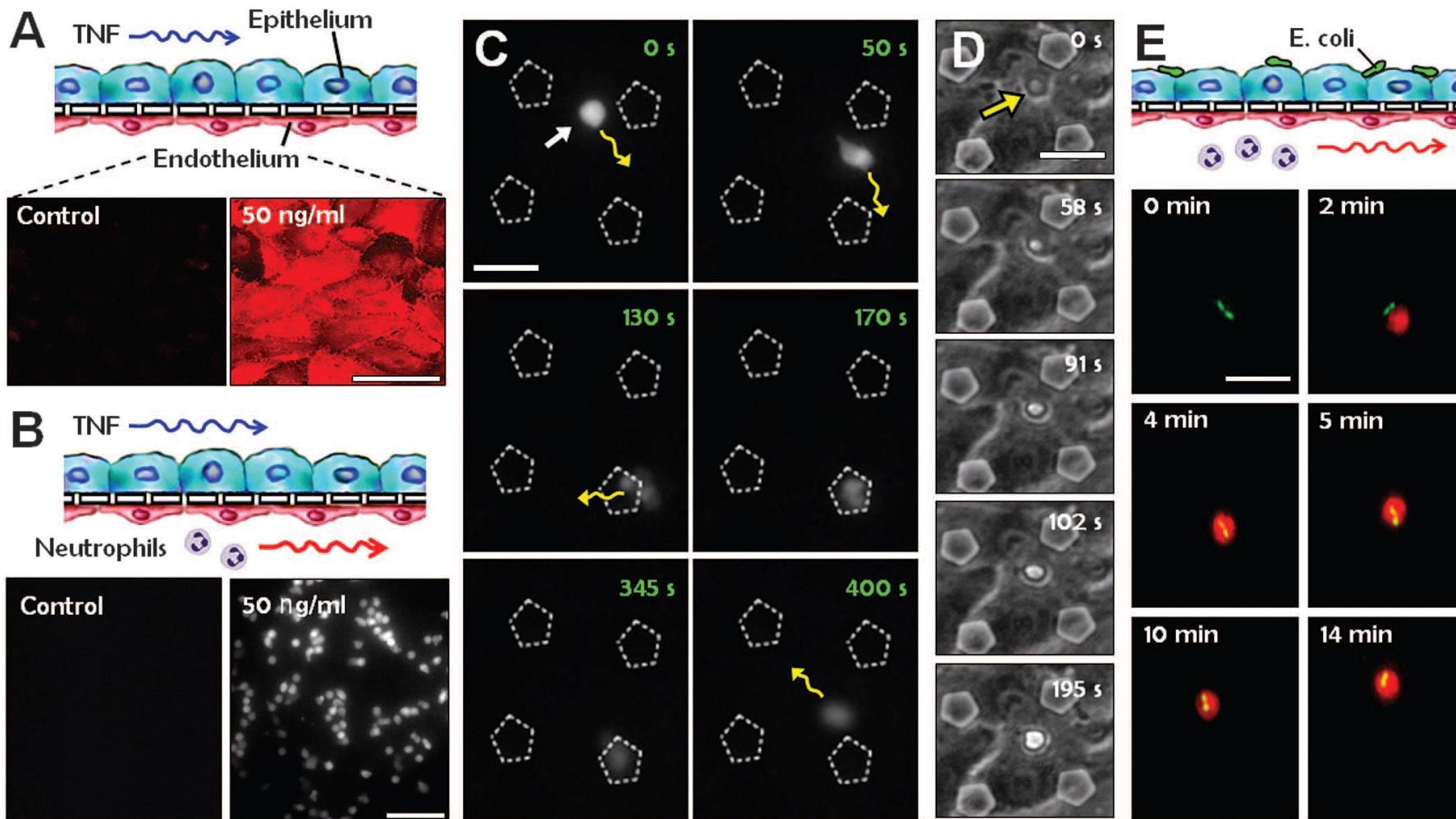
# Formation and Stretching of Alveolar-Capillary Interface

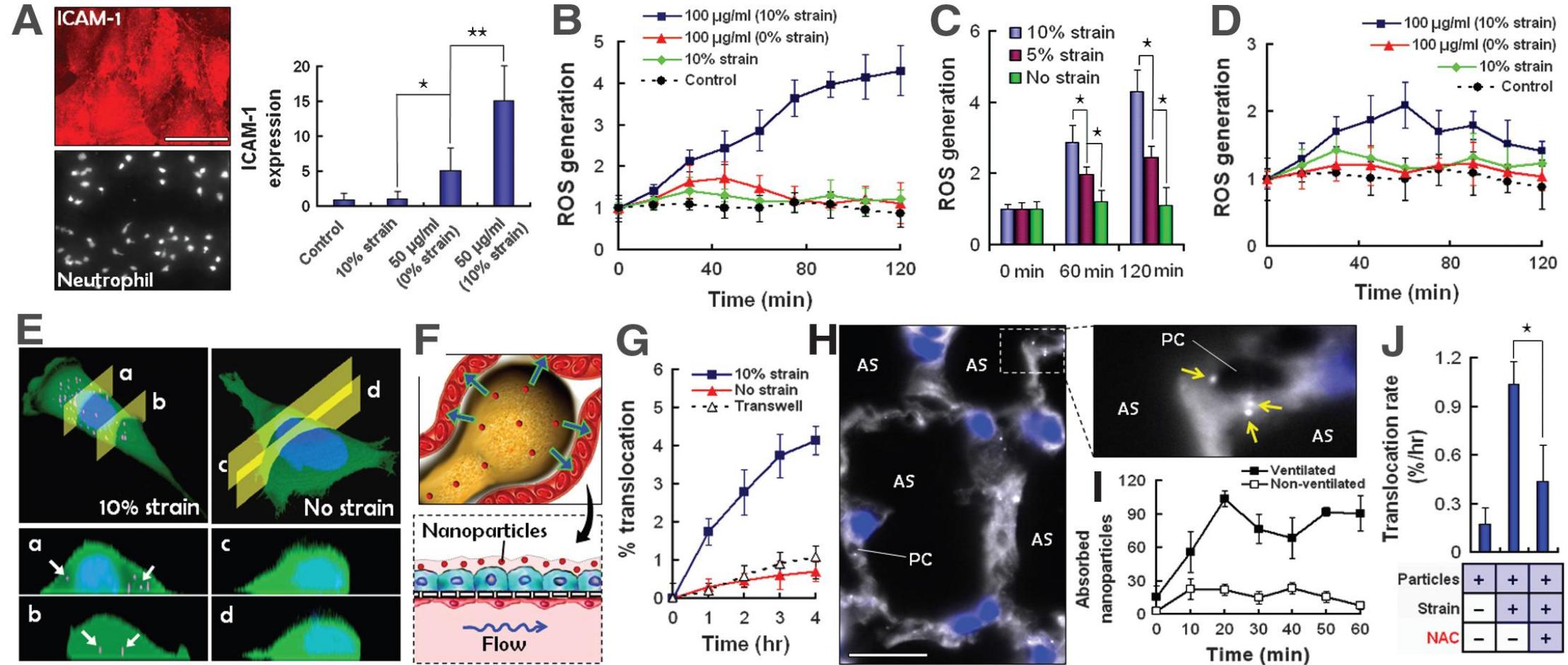


## •Features:

- Co-culture of **human alveolar epithelial cells** and **microvascular endothelial cells** on opposite sides of the membrane.
- Cells form **tight junctions** and exhibit **surfactant production** under air–liquid interface conditions.
- Applied cyclic strain (5–15%) mimics physiological breathing.
- Outcome:** The chip reproduces realistic **barrier function**, **electrical resistance**, and **mechanical cell responses**.

# Simulating Pulmonary Inflammation and Infection





# Design Principles of Organ-on-a-Chip

- **Goal:** Recreate human organ-level structure and function in vitro.
- **Key Design Principles:**
  - **Structural Biomimicry:** Reproduce tissue architecture (e.g., vessel lumen, alveolar interface).
  - **Mechanical Cues:** Integrate breathing, stretching, or fluid shear forces.
  - **Chemical Gradients:** Maintain nutrient, oxygen, and signaling gradients.
  - **Cellular Microenvironment:** Include multiple human cell types arranged in 3D.
  - **Dynamic Flow Control:** Simulate blood or air movement through microchannels.
  - **Integration with Sensors:** Enable real-time monitoring of physiological responses.

# Role of Microfluidics in Organ Chips

- **Microfluidics = Engineering cells with controlled microscale fluid environments.**
- **Key Advantages:**
  - Precise control of **flow rate, shear stress, and gradient formation.**
  - Enables **continuous nutrient exchange** like capillary blood flow.
  - Supports **miniaturization and parallel testing** for drug screening.
  - Allows **co-culture of multiple tissue types** under physiological flow conditions.

# Mimicking Vessels and Lumens

Example: Lung Alveolus-on-a-Chip, Gut-on-a-Chip, Blood Vessel-on-a-Chip

## Microfluidic Design Elements:

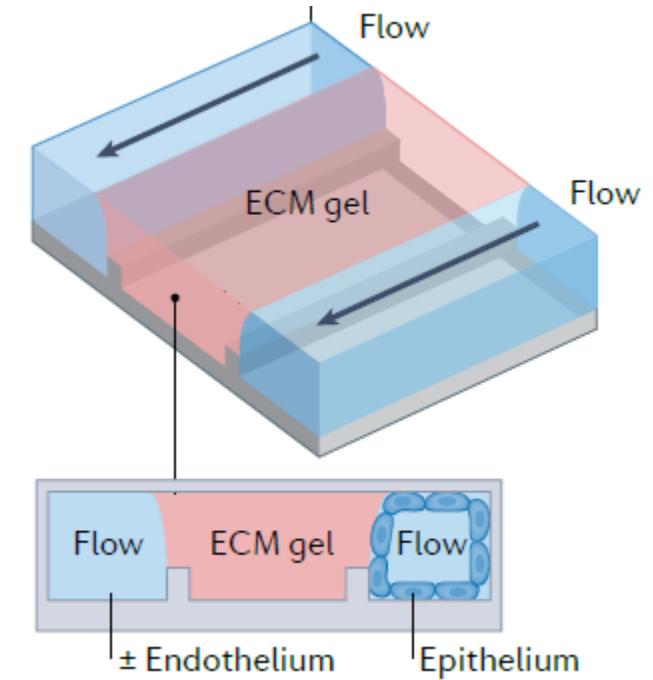
- Two parallel microchannels separated by a **porous flexible membrane**.
  - **Air channel** (epithelial side) and **liquid channel** (endothelial side).
  - **Vacuum chambers** alongside channels apply **cyclic mechanical strain** to mimic breathing or peristalsis.
  - Recreates a **vascularized tissue barrier** where gas or solute exchange occurs.
- 肺 *Used to study pulmonary infection, immune response, and nanoparticle toxicity.*

# Mimicking the Extracellular Matrix (ECM)

**Design Concept:** Integrate gel regions to simulate 3D tissue scaffolds.

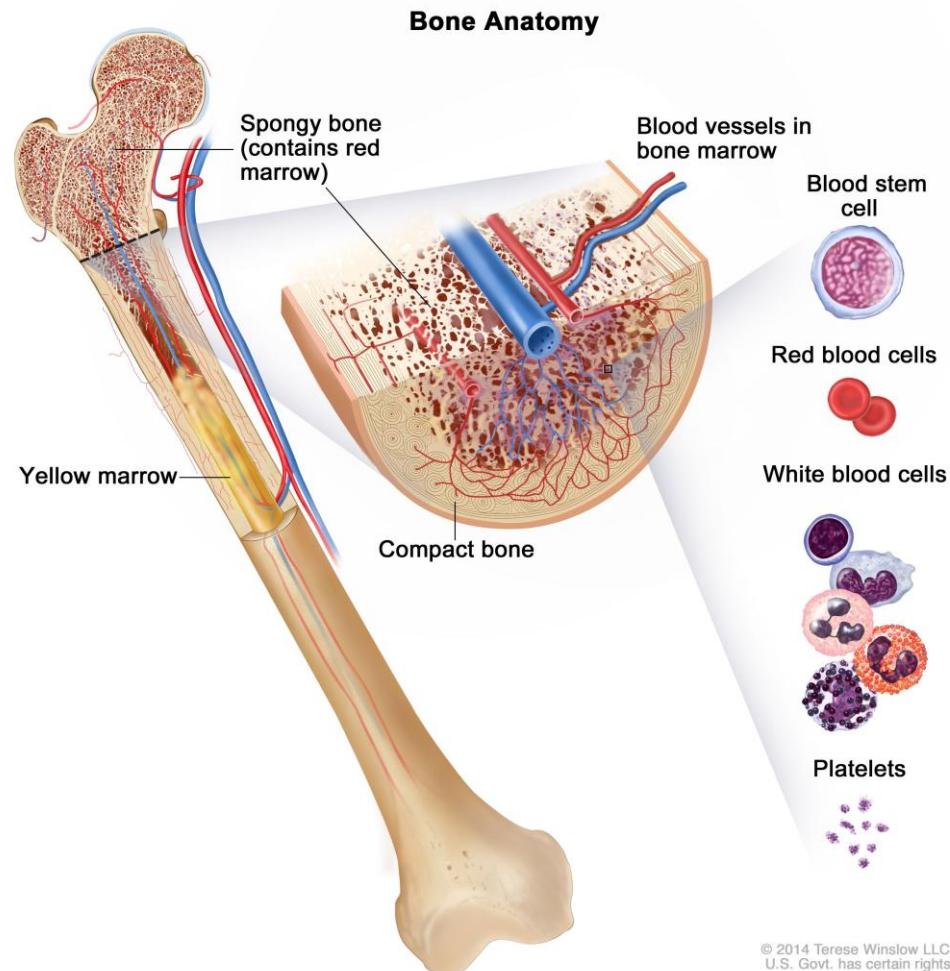
## Microfluidic Implementation:

- Central **gel channel** filled with ECM materials (e.g., collagen, Matrigel).
- Adjacent **flow channels** lined with endothelial or parenchymal cells.
- Diffusion across the gel mimics **nutrient, cytokine, and oxygen gradients**.
- Supports **cell migration, angiogenesis, and cancer invasion** studies.



# Leukemia chip (bone marrow chip)

# Anatomy of the bone



# Bone marrow

## Structure

- Located within the **medullary cavities** of bones.
- Composed of a **network of blood vessels, stromal (support) cells**, and developing blood cells.
- Two main types:
  - **Red bone marrow:** Active in blood cell production (hematopoiesis).
  - **Yellow bone marrow:** Primarily fat storage; can convert to red marrow if needed (e.g., after blood loss).



## Function

### 1. Hematopoiesis (Blood Cell Production)

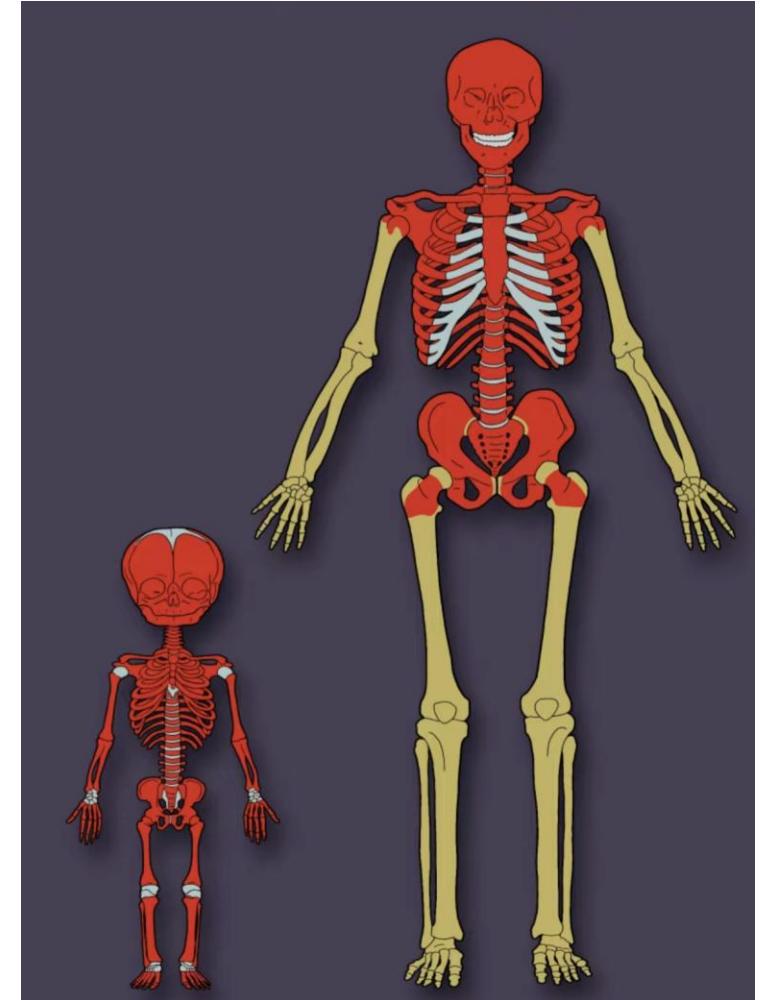
1. Produces all major blood cell types:
  1. **Red blood cells (RBCs)** – carry oxygen.
  2. **White blood cells (WBCs)** – fight infection.
  3. **Platelets** – help blood clot.
2. This occurs in red bone marrow through differentiation of **hematopoietic stem cells (HSCs)**.

### 2. Immune System Support

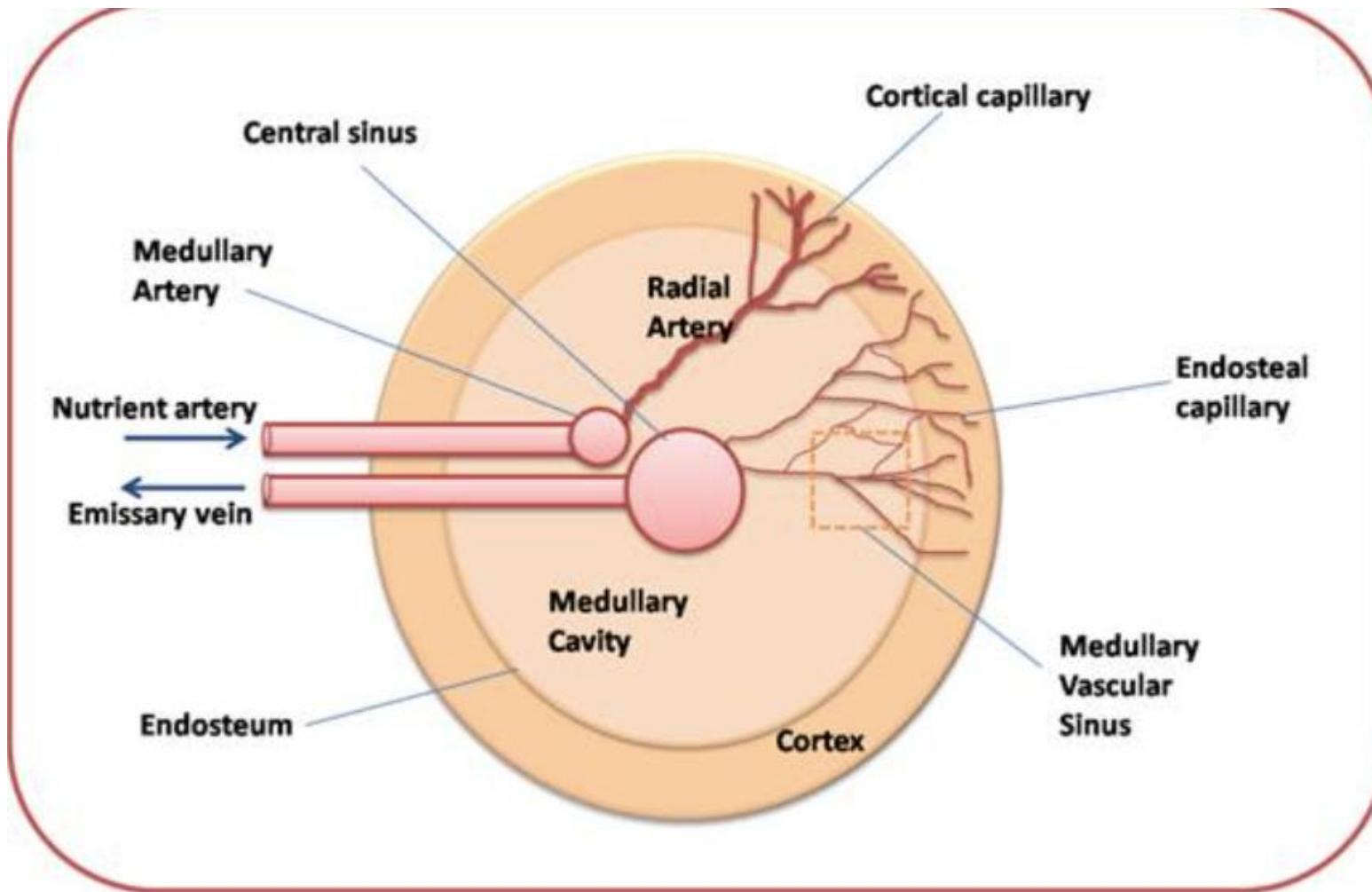
1. Source of **lymphoid progenitors** that give rise to B cells (which mature in the marrow) and T-cell precursors (which migrate to the thymus).
2. Produces immune cells critical for defense and inflammation regulation.

### 3. Storage & Regeneration

1. Stores **fat, iron, and immune cells**.
2. Can regenerate after injury or transplantation due to its **stem cell population**.



# Bone marrow



## Leukemia-on-a-chip: Dissecting the chemoresistance mechanisms in B cell acute lymphoblastic leukemia bone marrow niche

Chao Ma<sup>1,2</sup>, Matthew T. Witkowski<sup>3,4</sup>, Jacob Harris<sup>2</sup>, Igor Dolgalev<sup>3,4</sup>, Sheetal Sreeram<sup>3</sup>, Weiyi Qian<sup>1</sup>, Jie Tong<sup>1</sup>, Xin Chen<sup>1</sup>, Iannis Aifantis<sup>3,4</sup>, Weiqiang Chen<sup>1,2,4,\*</sup>

B cell acute lymphoblastic leukemia (B-ALL) blasts hijack the bone marrow (BM) microenvironment to form chemoprotective leukemic BM “niches,” facilitating chemoresistance and, ultimately, disease relapse. However, the ability to dissect these evolving, heterogeneous interactions among distinct B-ALL subtypes and their varying BM niches is limited with current *in vivo* methods. Here, we demonstrated an *in vitro* organotypic “leukemia-on-a-chip” model to emulate the *in vivo* B-ALL BM pathology and comparatively studied the spatial and genetic heterogeneity of the BM niche in regulating B-ALL chemotherapy resistance. We revealed the heterogeneous chemoresistance mechanisms across various B-ALL cell lines and patient-derived samples. We showed that the leukemic perivascular, endosteal, and hematopoietic niche-derived factors maintain B-ALL survival and quiescence (e.g., CXCL12 cytokine signal, VCAM-1/OPN adhesive signals, and enhanced downstream leukemia-intrinsic NF-κB pathway). Furthermore, we demonstrated the preclinical use of our model to test niche-cotargeting regimens, which may translate to patient-specific therapy screening and response prediction.



## Bioengineered immunocompetent preclinical trial-on-chip tool enables screening of CAR T cell therapy for leukaemia

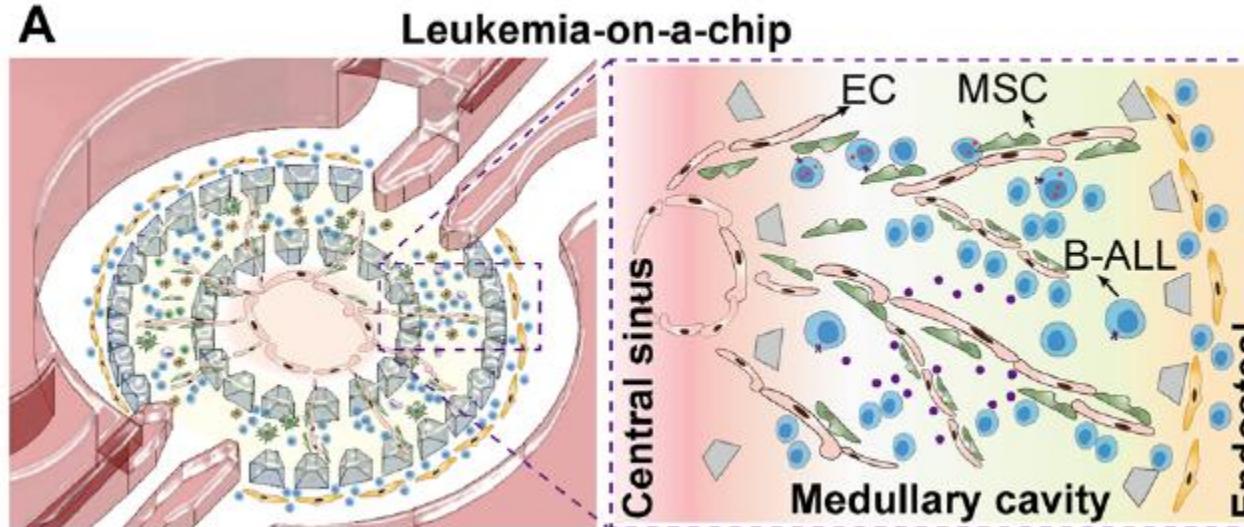
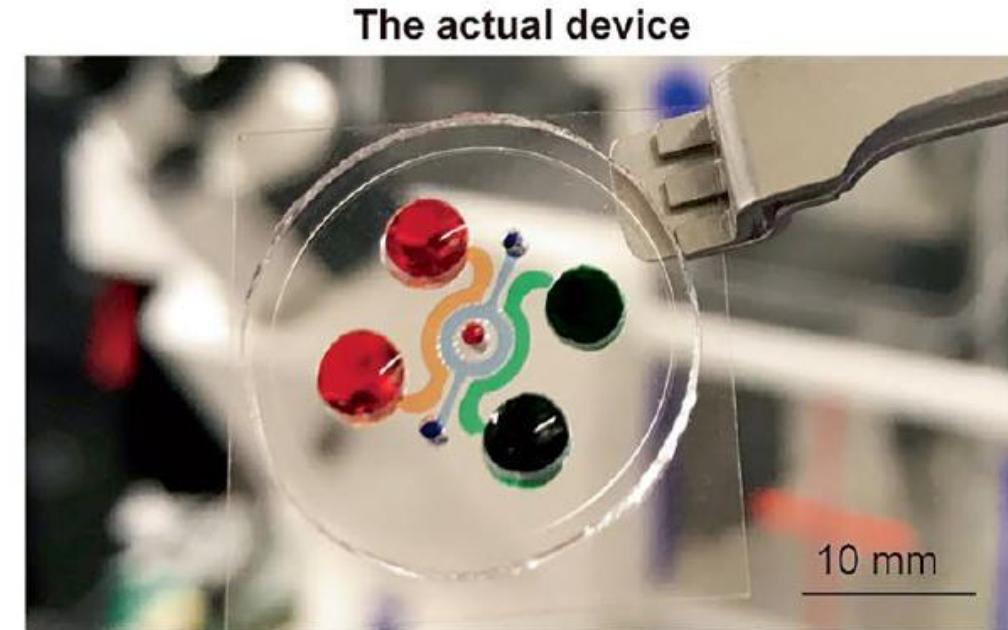
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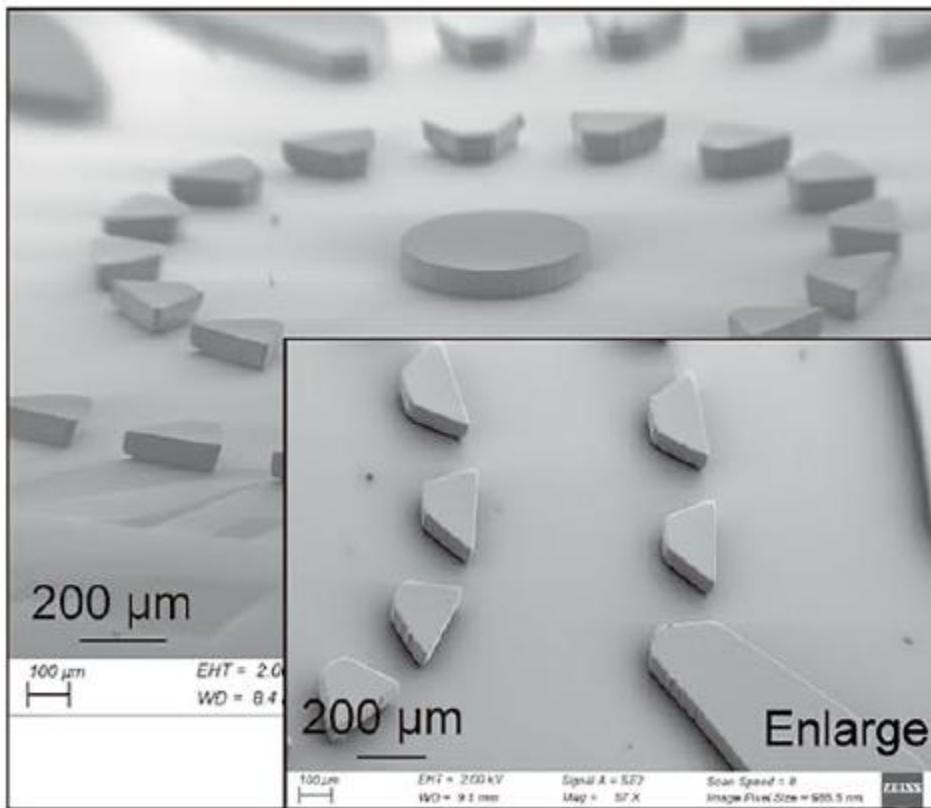
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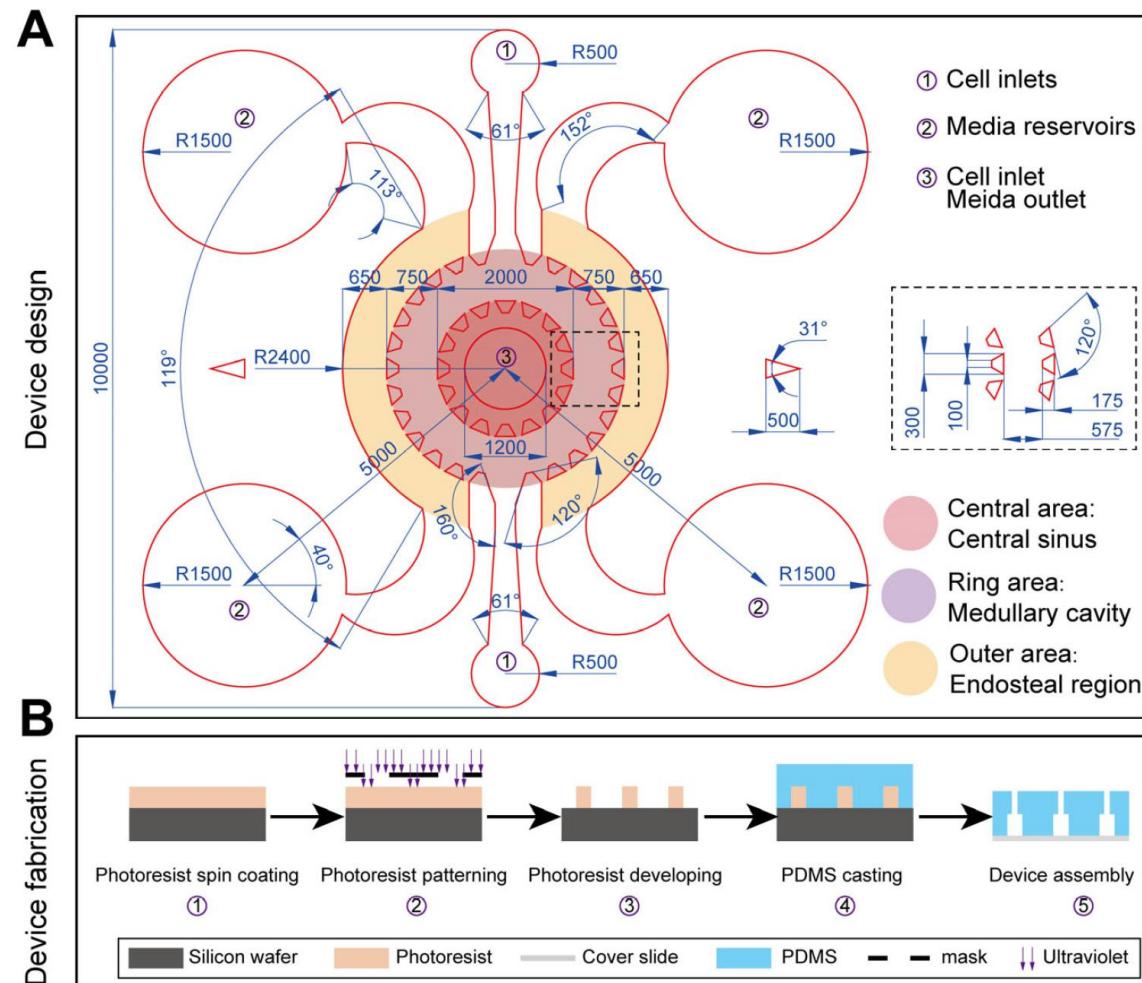
Chao Ma<sup>1,2,9,10</sup>, Huishu Wang<sup>1,10</sup>, Lunan Liu<sup>1</sup>, Ruiqi Chen<sup>2</sup>, Nandana Mukherjee<sup>3,4</sup>, Jie Tong<sup>1</sup>, Shadab Kazmi<sup>3,4</sup>, Xiangyi Fang<sup>3,5</sup>, Matthew T. Witkowski<sup>6,7,8</sup>, Iannis Aifantis<sup>6,7</sup>, Saba Ghassemi<sup>10,3,4,11</sup>✉ & Weiqiang Chen<sup>1,2,7,11</sup>✉

**A****a**

**b**

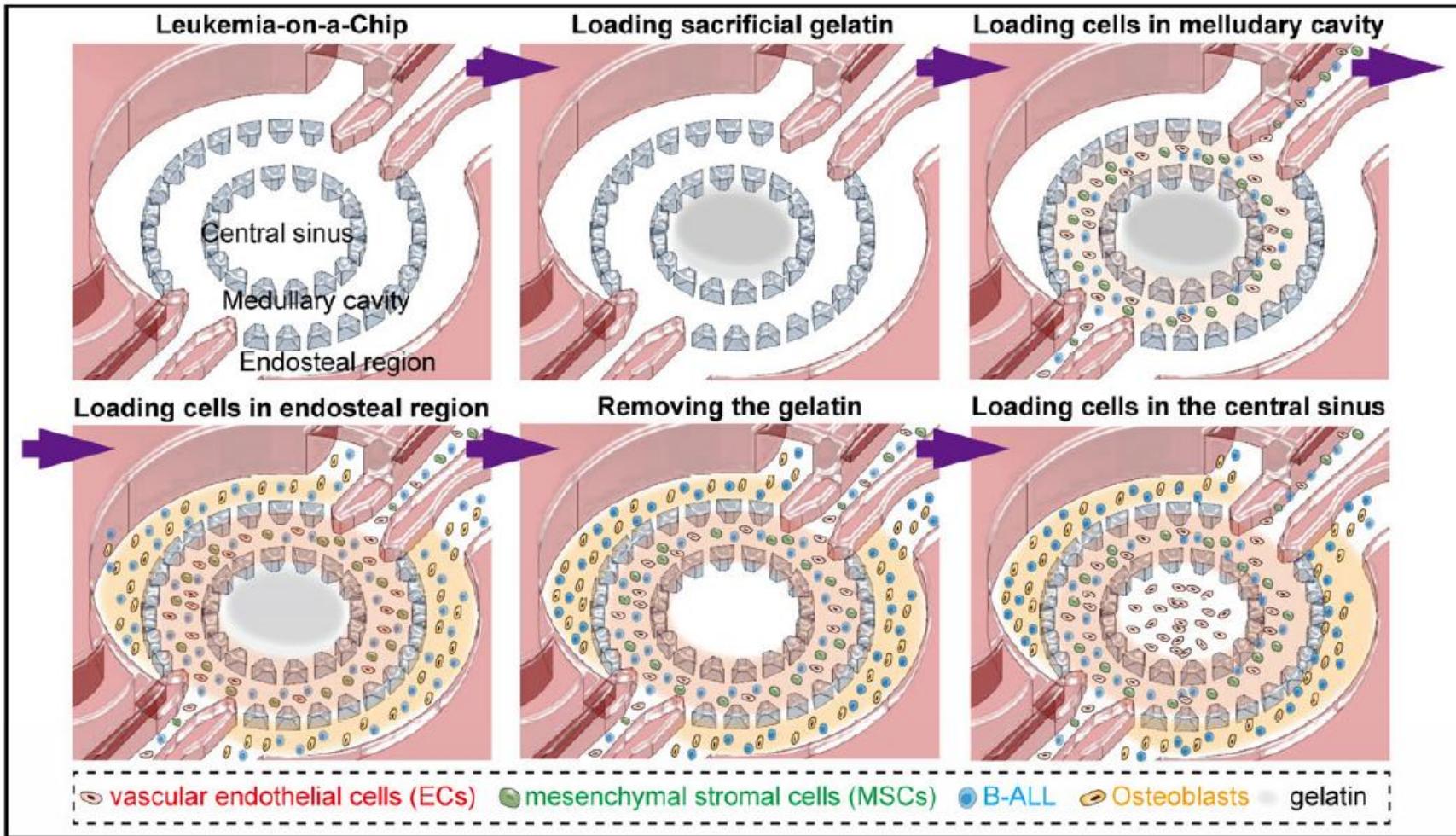
The SEM image of whole device



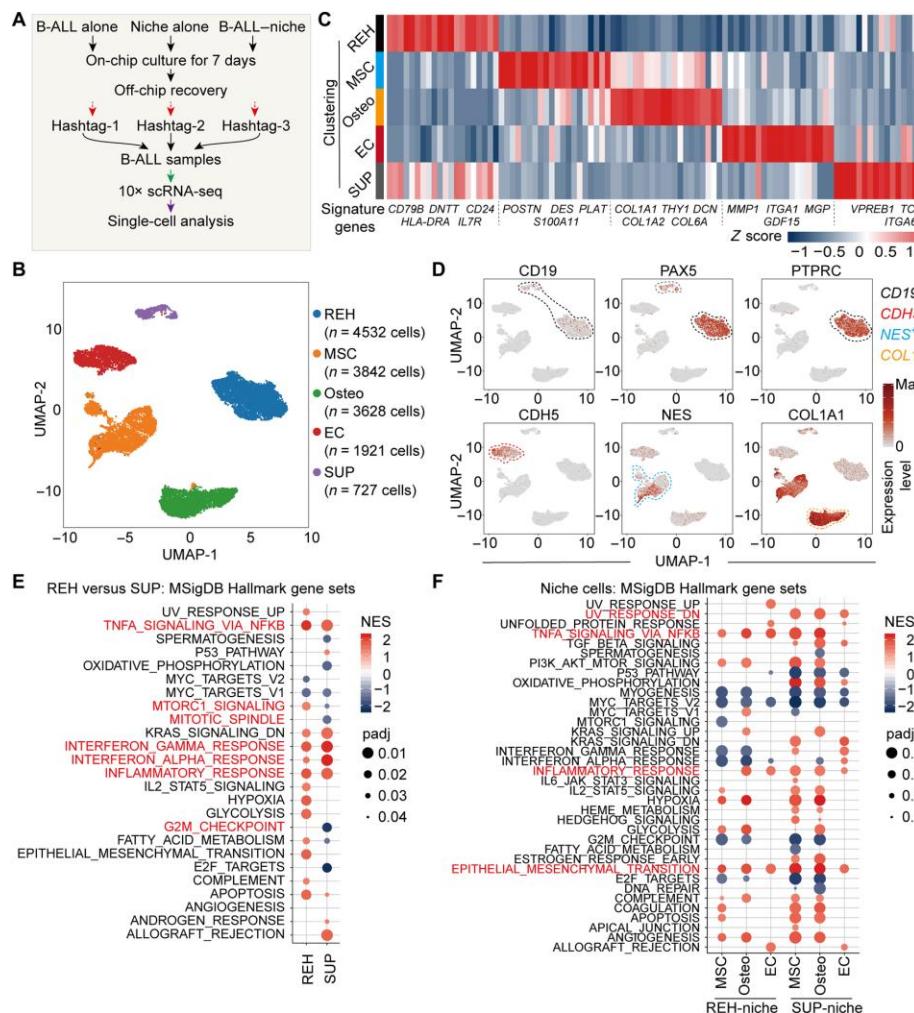


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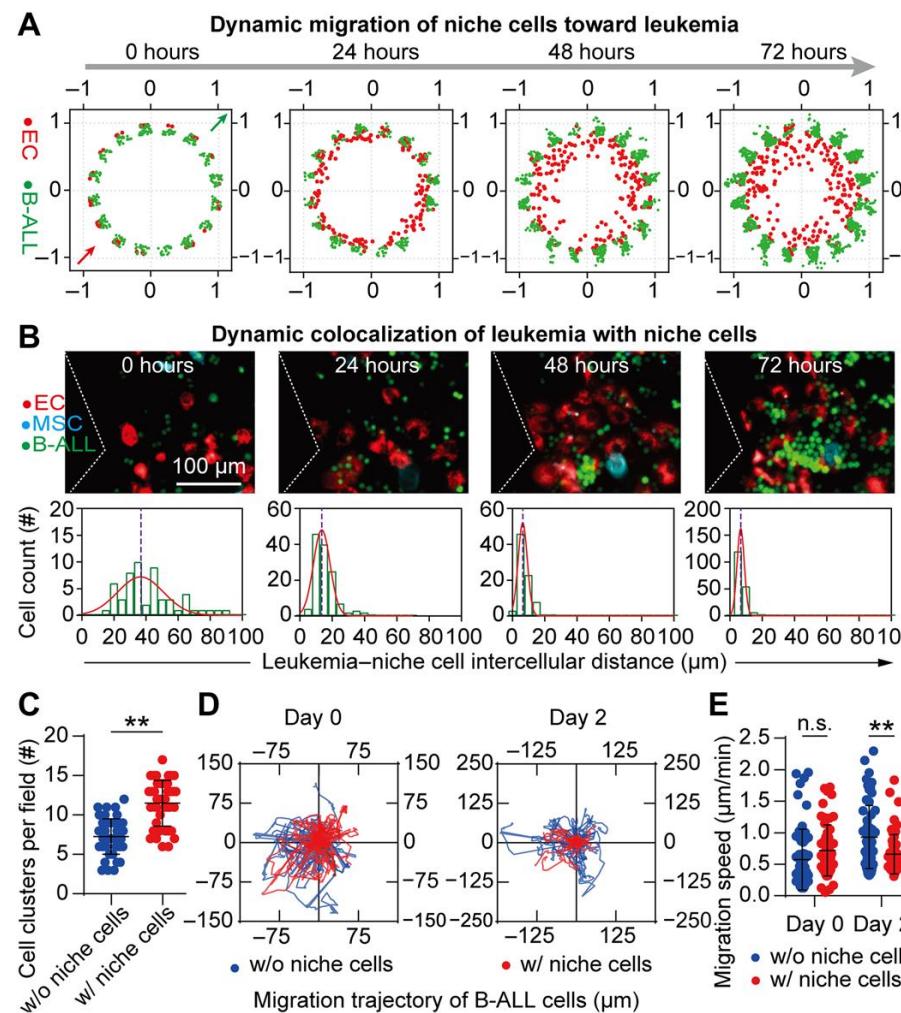
Cell loading



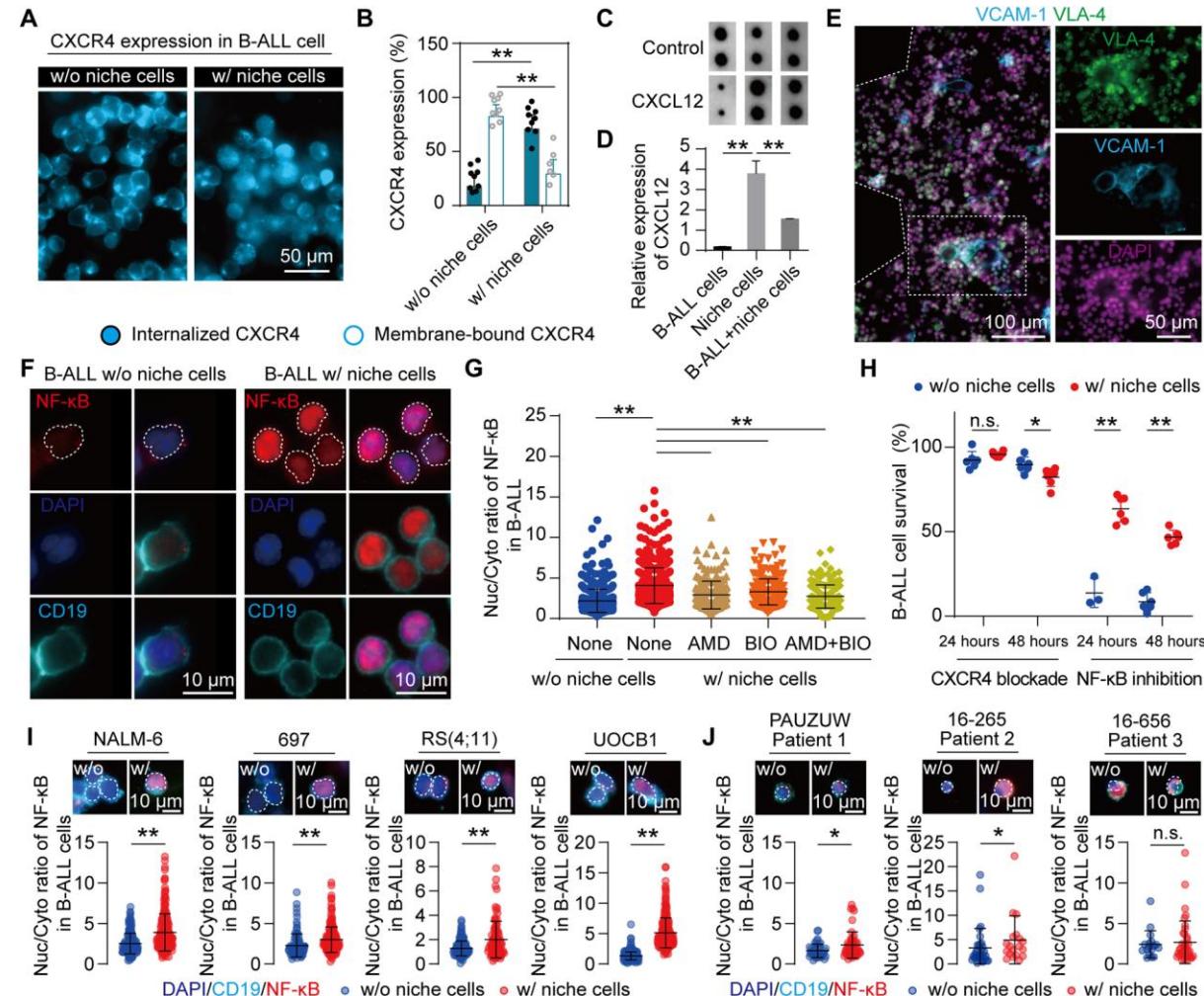
# scRNA-seq mapping of engineered human leukemic BM niches



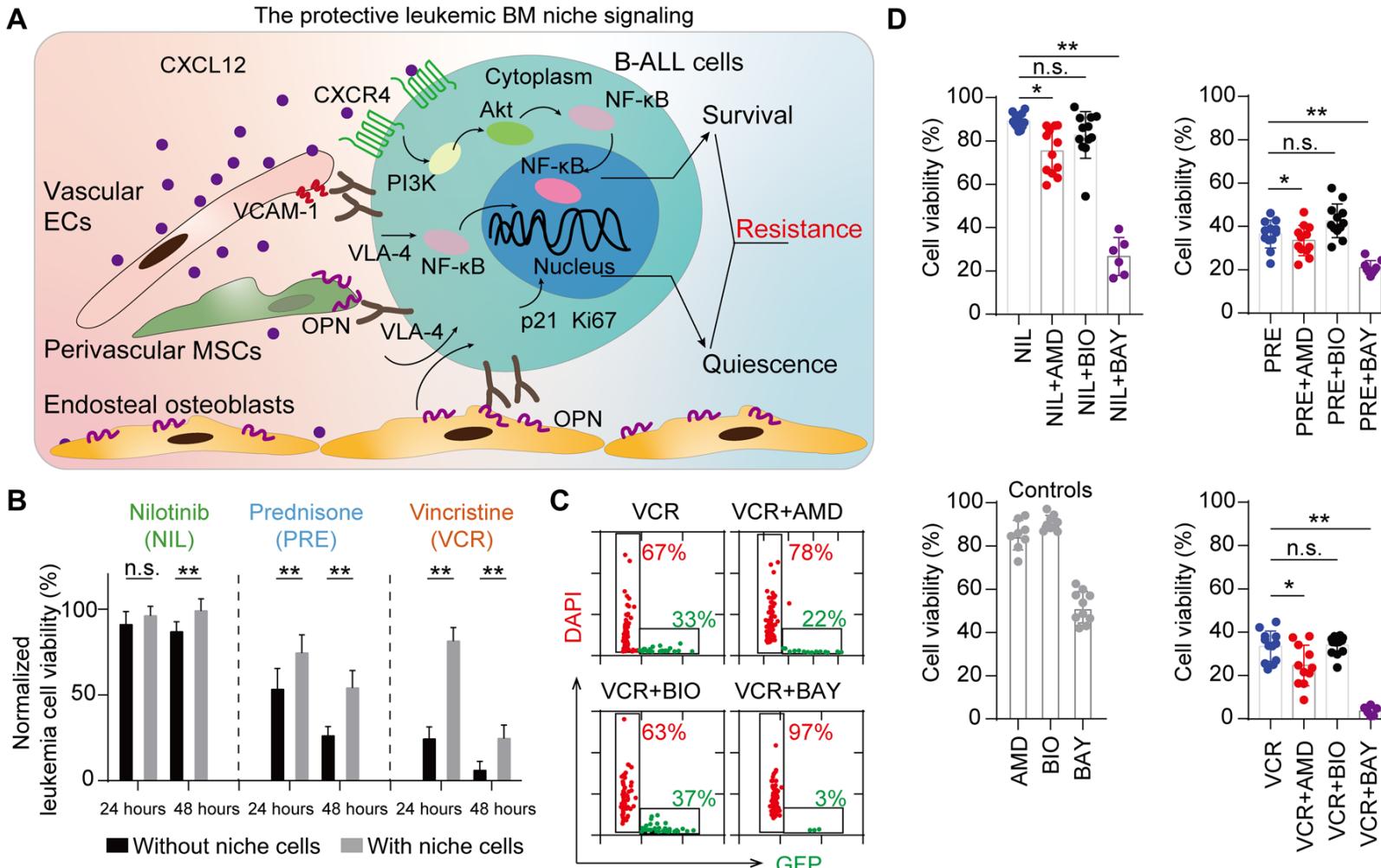
# Real-time monitoring of the leukemia-niche cell interaction dynamics



# Niche cells promoting leukemia progression via cytokine and adhesive signaling



# On-chip testing of cotargeting niche signaling to eradicate leukemic burden



ARTICLES

<https://doi.org/10.1038/s41551-021-00743-8>

nature  
biomedical engineering

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# Fungal brain infection modelled in a human-neurovascular-unit-on-a-chip with a functional blood-brain barrier

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## Significance

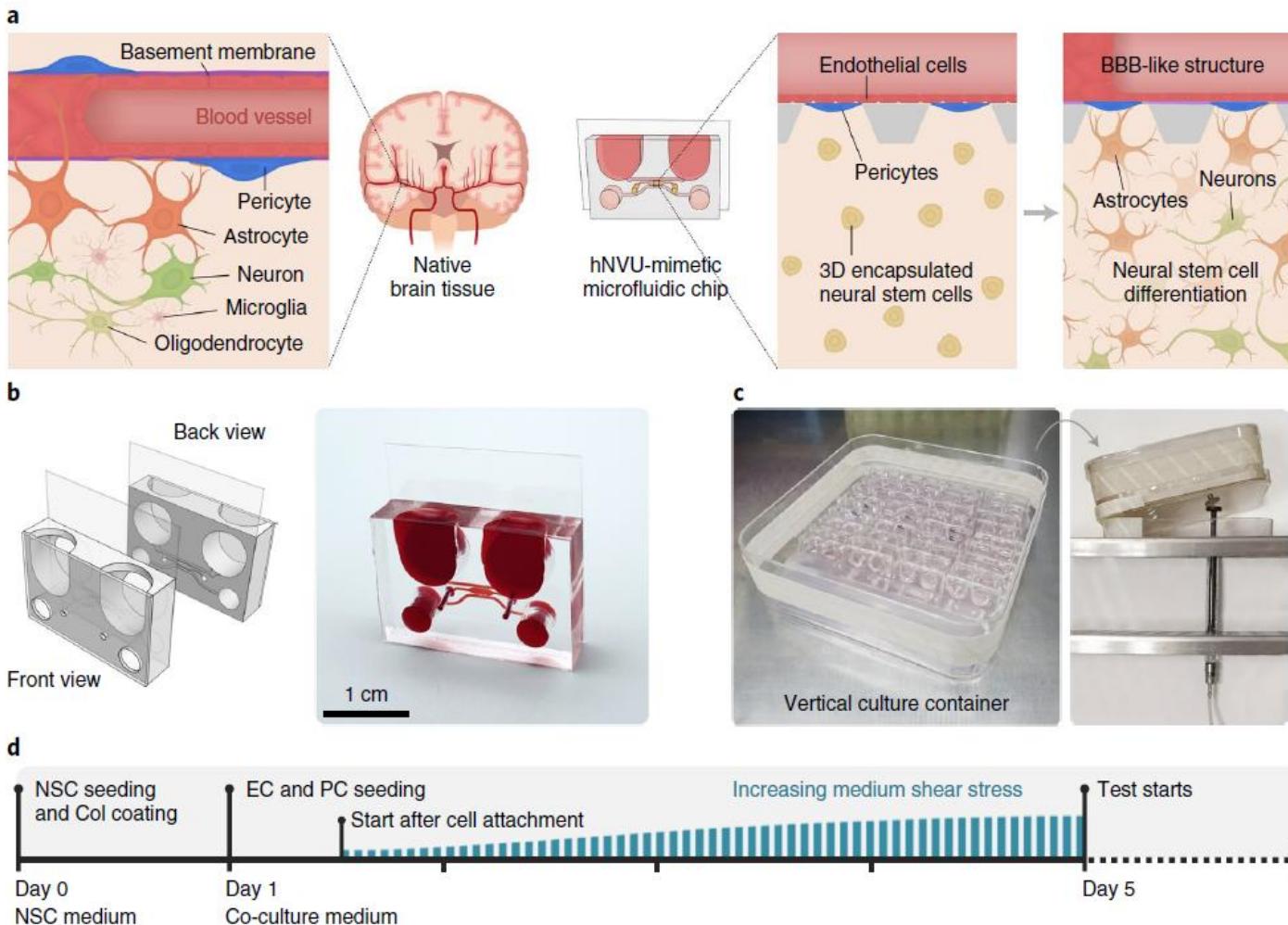
- First **human-relevant 3D BBB infection model** enabling real-time visualization of pathogen–brain interactions.
- Provides a **powerful platform** for studying **pathogen neuroinvasion** and testing **BBB-targeted drugs**.

## Overview

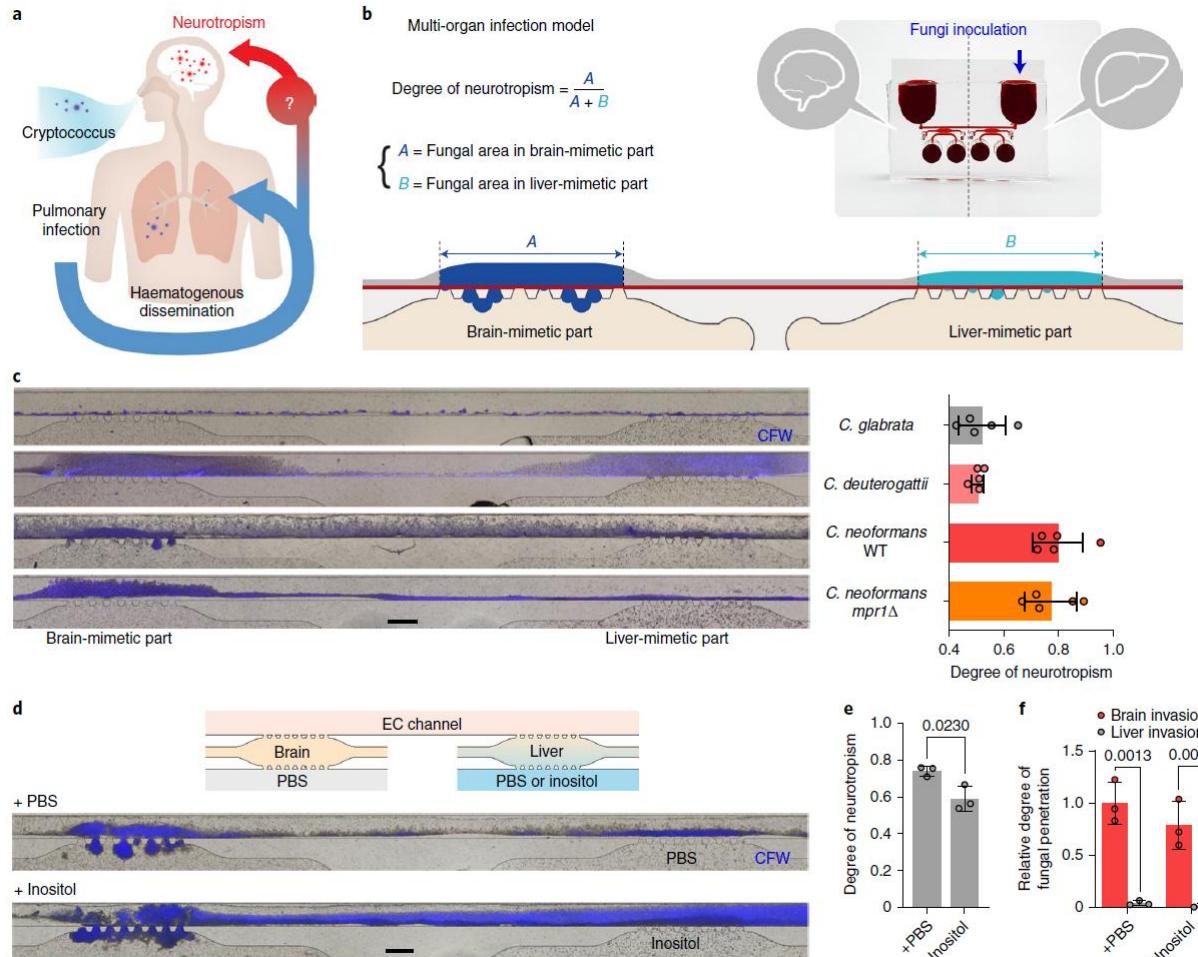
- Developed a **microfluidic human neurovascular unit (hNVU) chip** simulating the **blood-brain barrier (BBB)**.
- Co-cultures **human neural stem cells (NSCs)**, **brain endothelial cells (ECs)**, and **pericytes (PCs)** in a **3D brain-like hydrogel**.
- Maintained under **gravity-driven unidirectional flow**, recapitulating physiological BBB function.

## Key Findings

- **Functional BBB Formation:**
  - Tight junctions (ZO-1), P-glycoprotein efflux, and selective permeability similar to native BBB.
  - Dynamic flow and EC-PC-NSC interactions essential for barrier integrity.
- **Infection Modeling:**
  - Successfully mimicked ***Cryptococcus neoformans*** infection, showing:
    - **Transcytosis-mediated BBB penetration** without tight-junction disruption.
    - **Cluster formation beneath endothelial layer** mirroring *in vivo* infection.
    - Induction of host responses ( $\uparrow$ PTX3,  $\uparrow$ TSP-1,  $\uparrow$ IL-8).
- **Mechanistic Insight:**
  - Neurotropism of *C. neoformans* replicated and quantified.
  - Mutant (*mp1 $\Delta$* ) strain defective in BBB penetration but retained neurotropic preference.
  - Multi-organ chip (brain-liver) confirmed *C. neoformans*' **selective brain tropism**.



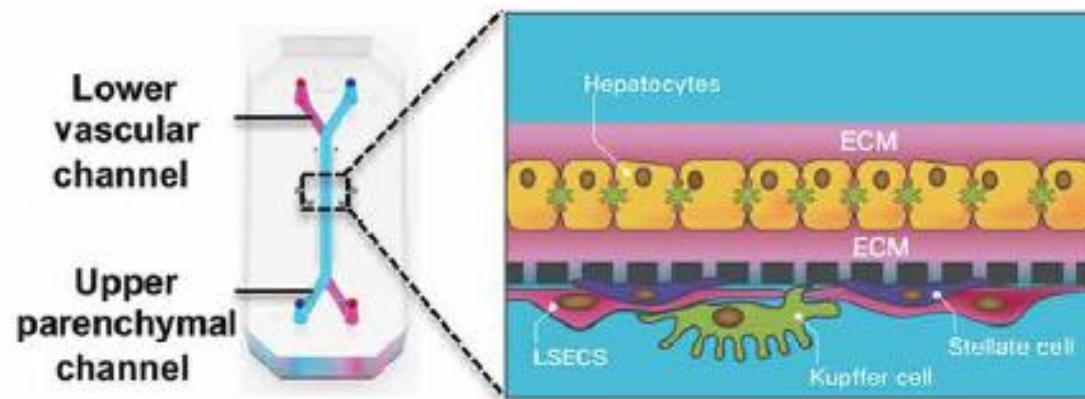
# A multi-organ hNVU chip model for fungal neurotropism study



DRUG TESTING

# Reproducing human and cross-species drug toxicities using a Liver-Chip

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## Overview

- Developed a **3D human brain-on-a-chip platform** to simulate **traumatic brain injury (TBI)** at microscale resolution.
- Integrated **neurons, astrocytes, and microglia** in a **gel-based microfluidic system** that recreates brain cytoarchitecture and neurovascular responses.

## Key Findings

### • Mechanical Injury Simulation

- Induced **neuronal damage, axonal injury, and astrocytic reactivity**.

### • Inflammatory Cascade Activation

- Demonstrated **neuroinflammatory cross-talk** between glia and neurons post-injury.

### • BBB and Neurovascular Interaction

- When coupled with endothelial layers, reproduced **BBB dysfunction** after injury.
- Observed increased permeability and reactive oxygen species production.

### • Drug Screening Potential

- Tested **anti-inflammatory and neuroprotective compounds** that reduced neuronal loss and cytokine release.
- Demonstrated the chip's use as a **preclinical screening tool** for TBI therapeutics.

# Final paper

- Due on Nov 15.
- See website announcement.

# Suggested Topics

## Fundamentals and Fabrication

- Paper-based microfluidics for low-cost diagnostics
- 3D printing of microfluidic devices
- Integration of sensors into microfluidic chips

## Fluid Control and Droplet Systems

- Digital microfluidics using electrowetting
- Droplet-based PCR and digital PCR
- Controlled coalescence and splitting of droplets

## Biomedical Applications

- Microfluidic devices for rapid infectious disease testing

## • Organs-on-chips

- Point-of-care immunoassays
- Liquid biopsy using microfluidics

## Single-Cell and Molecular Tools

- Single-cell RNA sequencing on chips
- Microfluidic sorting of cells by mechanical or optical properties
- CRISPR-based diagnostics integrated with microfluidics

## Challenges and Outlook

- Scaling up microfluidic manufacturing
- Standardization in microfluidics
- Sustainability and green fabrication