A scientific framework for epidemic and pandemic research preparedness

Developing humanized models with an eye on potential for generalizability: how to do it?

Human organ on chip (MPS) infection model development

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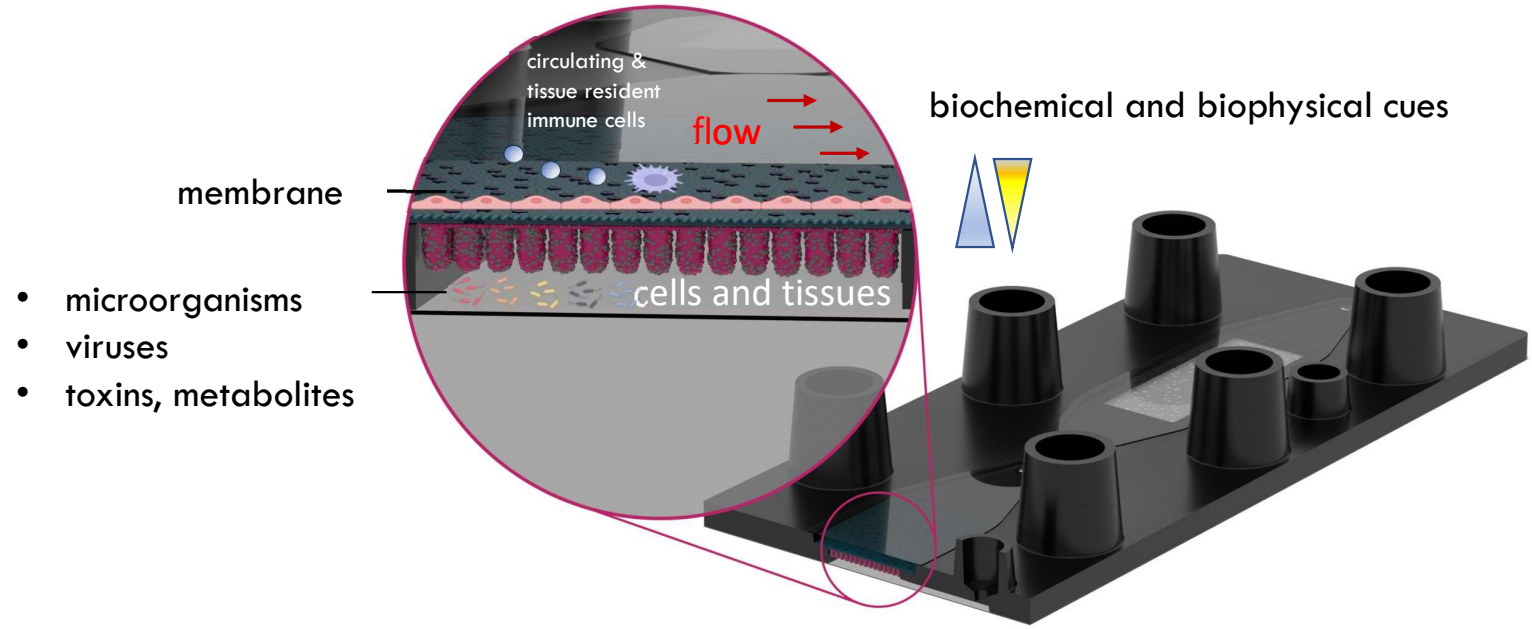
Introduction

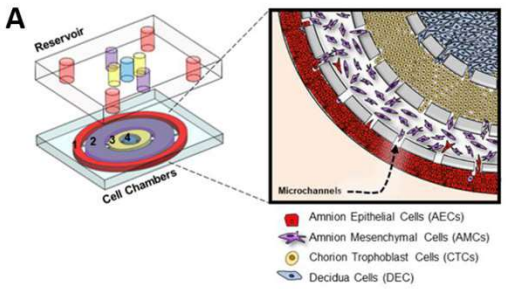
What is organ-on-chip (OoC)?

"An Organ-on-Chip (OoC) is a fit-for-purpose ***microfluidic device****, containing* ***living engineered organ substructures in a controlled microenvironment****, that recapitulates one or more aspects of the* ***organ's dynamics, functionality and (patho)physiological response*** *in vivo under real-time monitoring"* – ***ORCHID report***

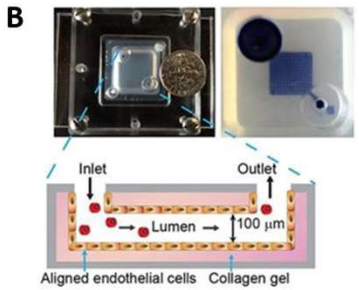


Organ-on-chip to Study Human Infections

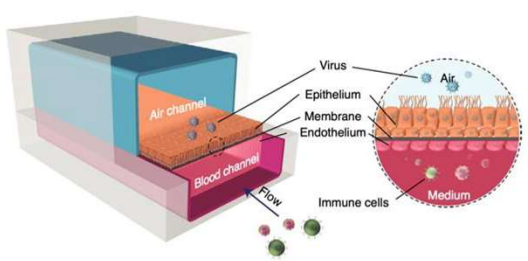
Foeto-maternal interface-on-chip



Microvessel-on-chip



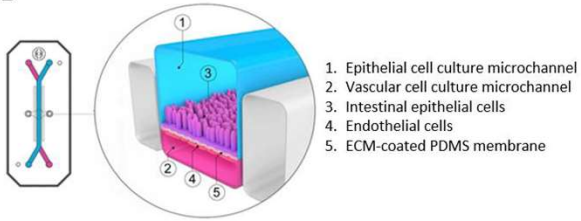
Lung-on-chip



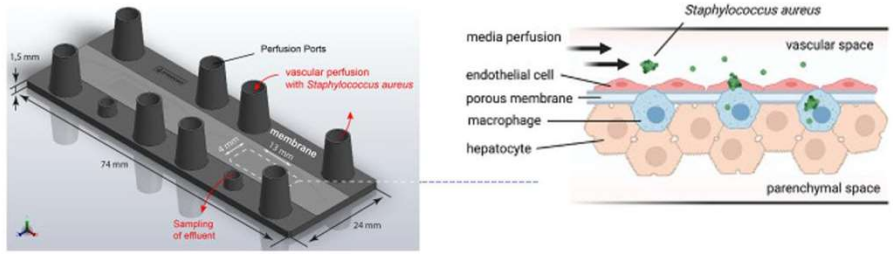
use of human cell material

- **cell lines** (affordable, characterized, fast)
- **primary cells** (patient-specific, physiologically relevant)
- **stem cells** (complex, reflects cellular diversity, personalized and autologou
- avoiding bias through interspecies differences

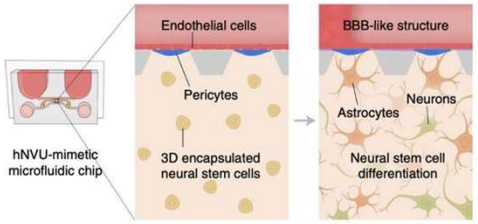
Intestine-on-chip



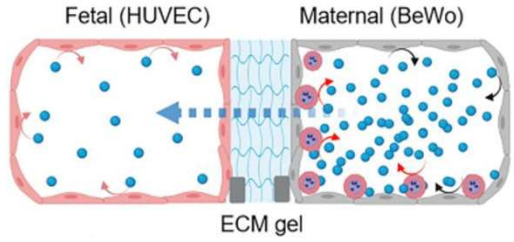
Liver-on-chip



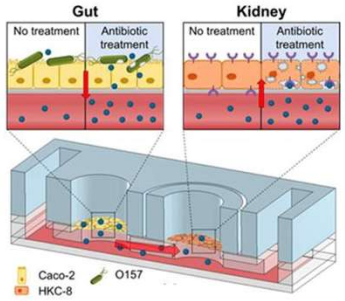
Neurovascular unit-on-chip



Placenta-on-chip



Gut & Kidney -on-chip

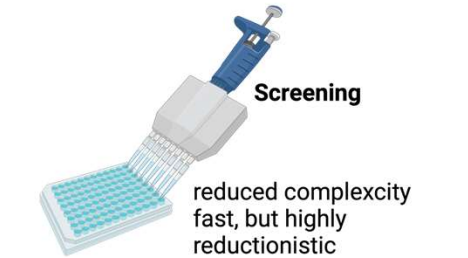


Alonso et al. 2024 (*in revision*)

Radnaa, E. et al, Lab Chip (2021); Bernabeu, M. et al. mBio (2019); Si, L. et al. Nat Biomed Eng (2021); Kasendra, M. et al. Elife (2020); Siwczak, F. et al. Biomaterials (2022); Kim, J. et al. Nat Biomed Eng (2021); Mosavati, B et al. Sci Rep (2022); Lee, Y. et al. Toxins (Basel) (2021).

Organ-on-chip to Study Human Infections

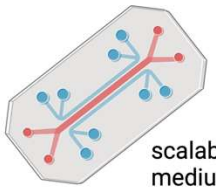
Advantages and limitations



Screening

reduced complexcity
fast, but highly
reductionistic

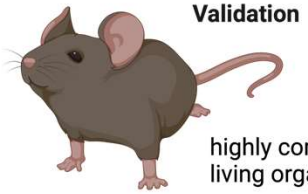
informed
studies



Building a hypothesis by dissecting critical factors of human infection

scalabale complexcity
medium troughput,
still reductionistic

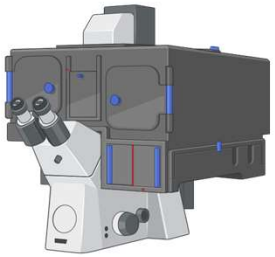
informed
studies

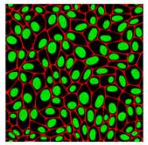


Validation

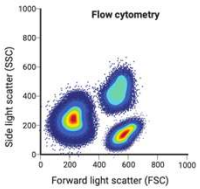
highly complex
living organism

photonics

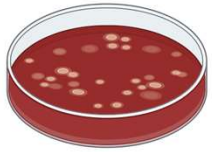


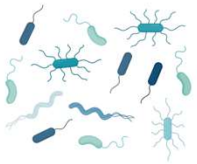


flow cytometry

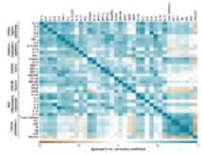


microbiology

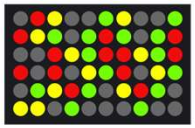




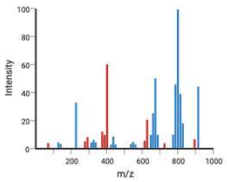
transcriptomics



proteomics



metabolomics



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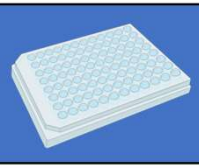
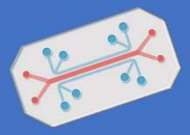
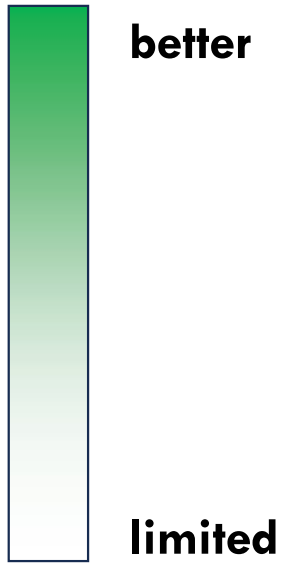
Advantages and limitations

				
precision and control	clear infection interface	variability in shape and size	clear infection interface, precise control	standardization of MOI is time-consuming
cellular diversity	limited	limited to certain cell types	scalable	full organism
Immune cells	static co-culture		tissue-resident and circulating cells	full organism, but species-specific differences
Donor diversity	can reflect individual human donors			non-human
Troughput	high	high	medium	low
Costs	low	medium	medium	high



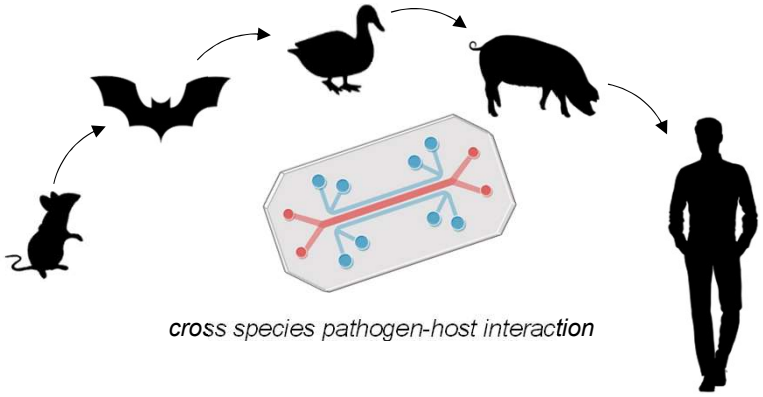
Organ-on-chip to Study Human Infections

Limitations of animal-based research is acknowledged by the Food and Drug Administration (FDA) – in OoC models are implemented in the Modernization Act 2.0 , **abolishing the requirement for all drugs to be tested in animal models**

"Nonclinical tests" for testing drug safety and efficacy that occur before or during the clinical trial phase may include: "(1) Cell-based assays, **(2) Organ chips and microphysiological systems,** (3) Computer modeling, (4) Other nonhuman or human biology-based test methods, such as bioprinting, and (5) Animal tests."

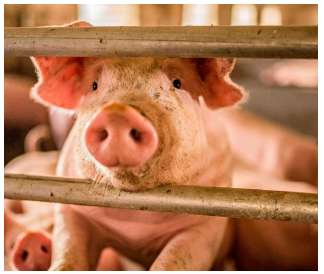
Utility in Rapid Response to Pathogen X

- can be rapidly adapted to emerging pathogens i.e., zoonotic pathogens



Modelling Human-Animal Interface

- replicating human tissue along animal tissue in standardized platforms
- understanding of interspecies transmission dynamics
- identification of therapeutic targets across species barriers



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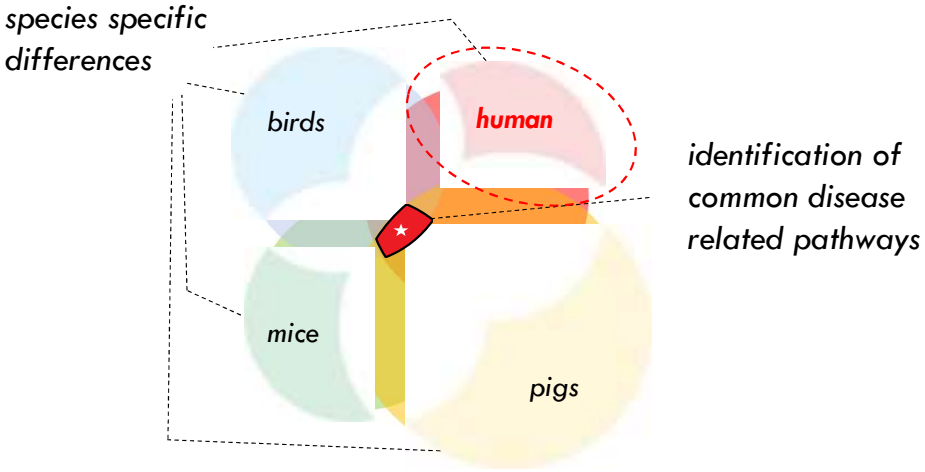

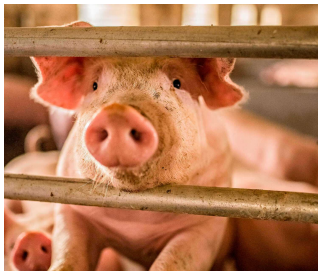

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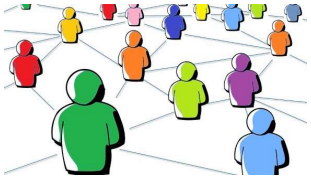
Utility in Rapid Response to Pathogen X

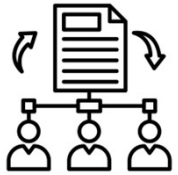
- rapid turnaround time for **studying organotropism** (single and multi-organ model systems)

- **realtime monitoring** of cellular response infection and treatment

- identification of **personalized novel biomarkers** and its **validation in parallelized clinical studies speeding up bench to bedside process**

- **cross-disciplinary collaboration** and **global data sharing**





Cross-Cutting Scientific Actions and Challenges

- advancing OoC technology in international colaborations
  - sharing research, methodologies and study findings as **open access**

OPEN ACCESS

  - development of **standardized protocols, assays and platform solutions**

INTERNATIONAL MPS SOCIETY
CONNECT, EXCHANGE, EDUCATE

EUROoCS
EUROPEAN ORGAN-ON-CHIP SOCIETY

ORCHID
organ-on-chip in development

SMART OoC

IQ MPS
IQ Microphysiological Systems Affiliate

  - implementing OoC technology in low and mid-income countries by **capacity building initiatives, technology transfers agreements** and **colaborative research grants**

Summary – A Generalizable Research Approach

- **Generalizable Research Methods for OoC**: to provide consistent and reliable results across diverse populations that can be widely applied and accepted

- **Flexibility** and **Adaptability**: to study a wide range of pathogens including viruses, bacteria, and fungi, on different human tissues in OoC

- Integration of OoC in **Global Research Frameworks**: facilitating global collaboration and multidisciplinary research (biomaterials, biophysics, cell biology, microbiology, medicine, pharmaceutics...)

- global research community, policymakers, and funding agencies to support OoC development as part of a generalized research approach – commitment towards **funding, resource allocation, broader adaption and standardization of OoC, and transfer of technologies and knowledge on a global scale**

Thank you!