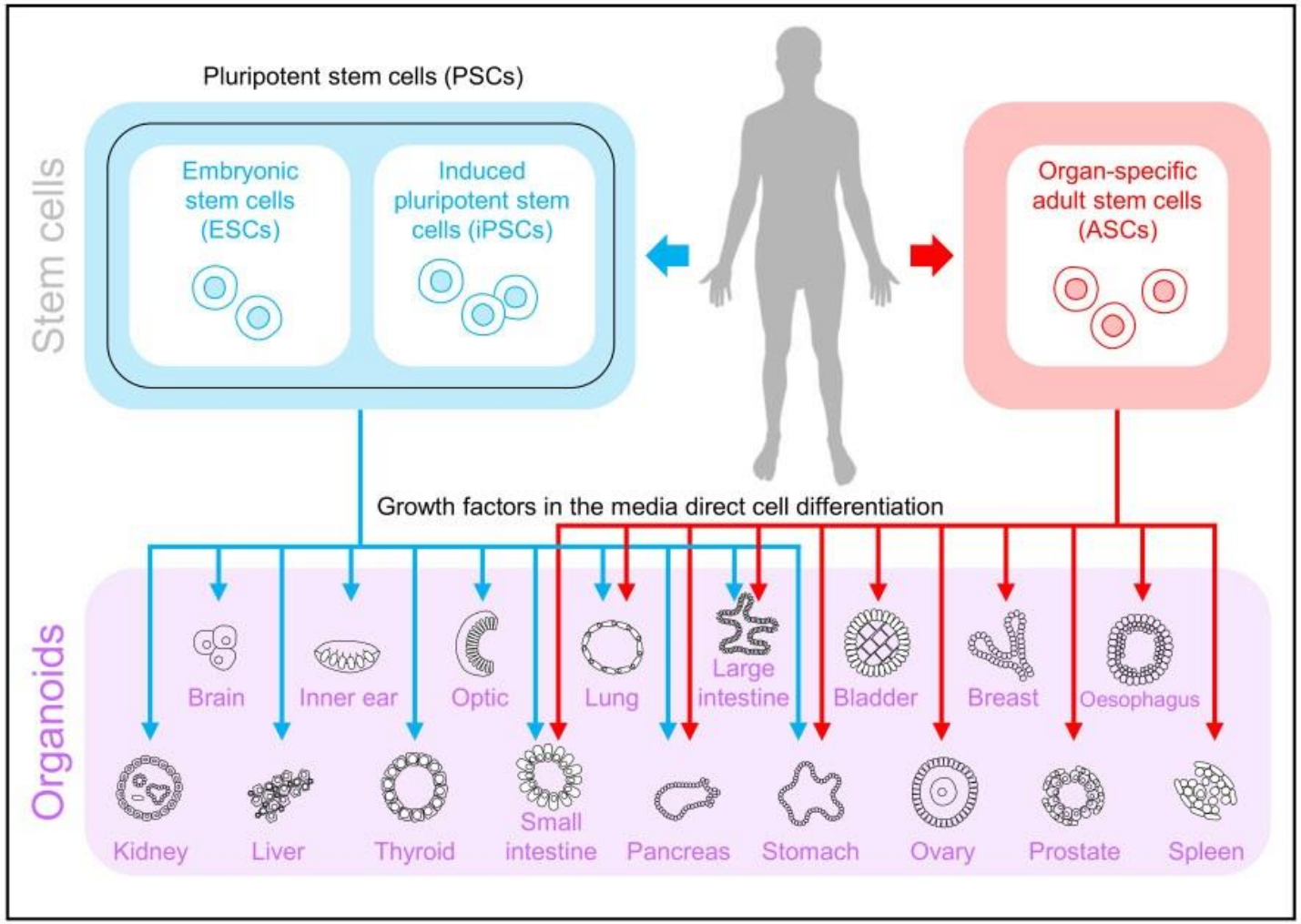
VIBIOSPHEN

From microbes to One Health

Apical out lung organoids as a relevant tool to study respiratory diseases

Patricia Martin

Organoids



https://cytosmart.com/resources/resources/organoids-definition-culturing-methods-and-clinical-applications

“**New medicines need not be tested in animals to receive U.S. Food and Drug Administration (FDA) approval,** according to legislation signed by President Joe Biden in late December 2022.

the law allows FDA to promote a drug or biologic—a larger molecule such as an antibody—to **human trials after either animal or nonanimal tests.**

[…] in clearing drugs for human trials the agency should rely more heavily on **computer modeling, “organ chips,” and other nonanimal methods** that have been developed over the past 10 to 15 years”

Vibiosphen's offer-Preclinical studies

Anti-infective drug development

R&D

***In vitro* testing**

Organoids

3D tissues

MTD – PK/PD

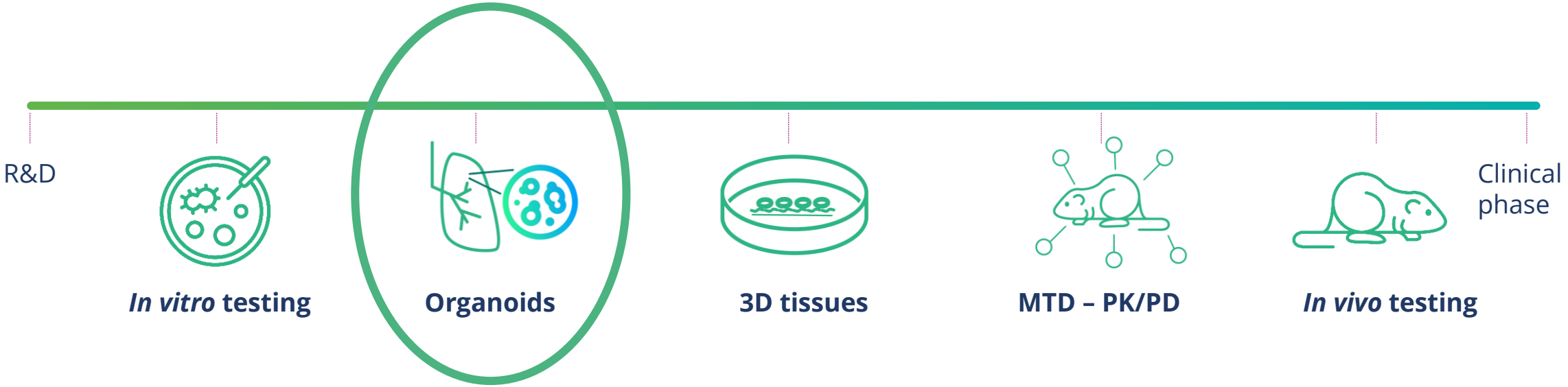
***In vivo* testing**

Clinical phase

- Safety
- Efficacy

Vibiosphen's offer-Preclinical studies

Anti-infective drug development



- To reduce the number of animals used
- To provide more relevant data (human-derived organoids)

Design better ***in vivo studies for better outcome***

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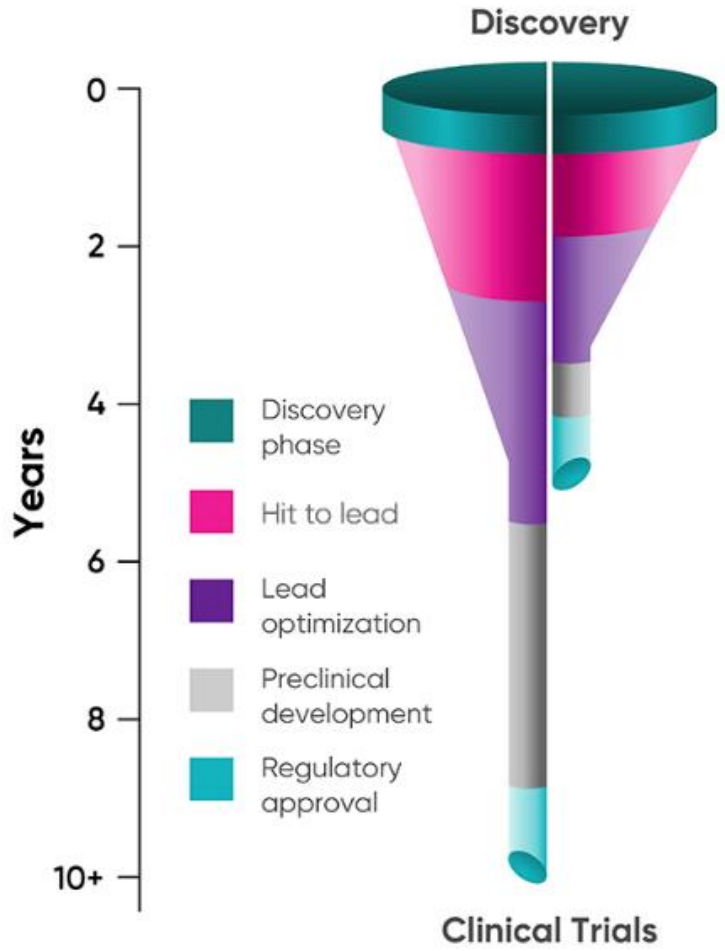
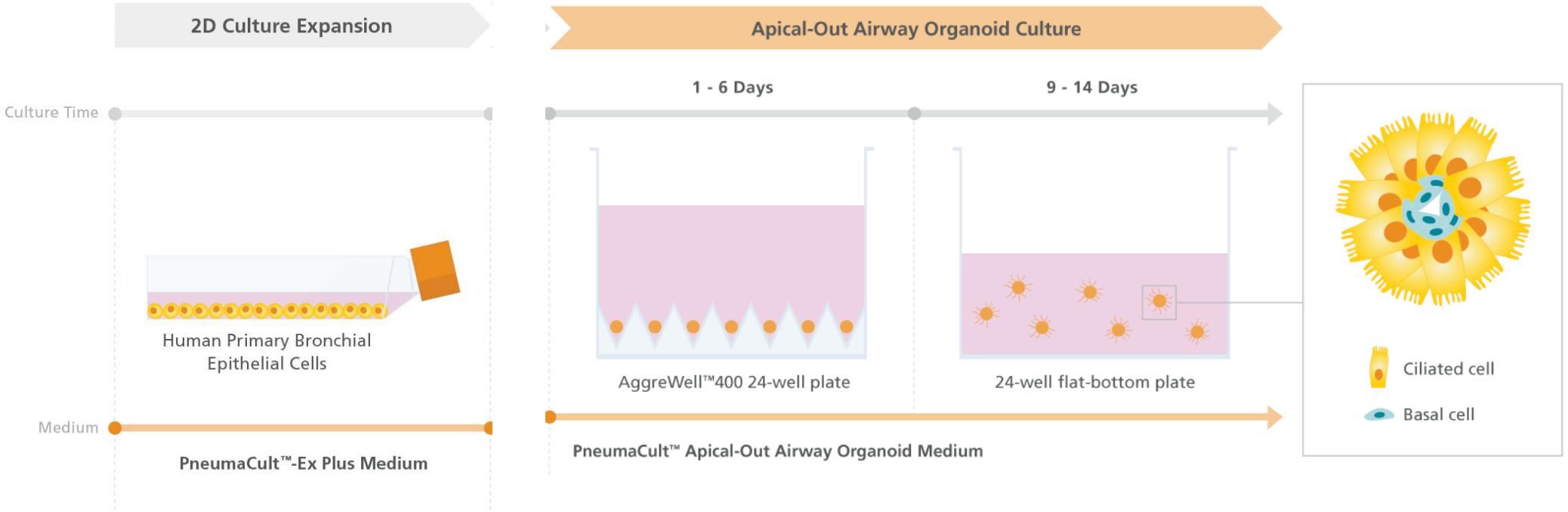
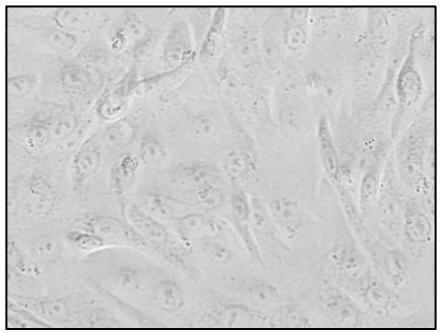
Lung organoids

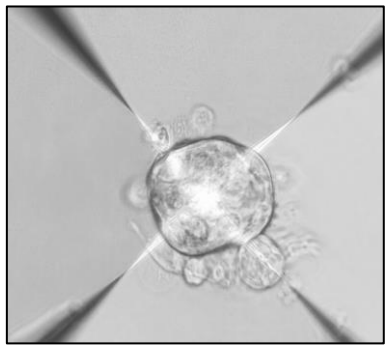


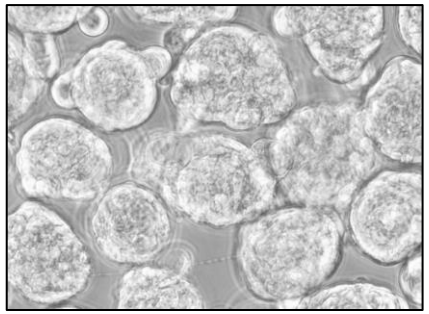
- To save time and money thanks to accuracy

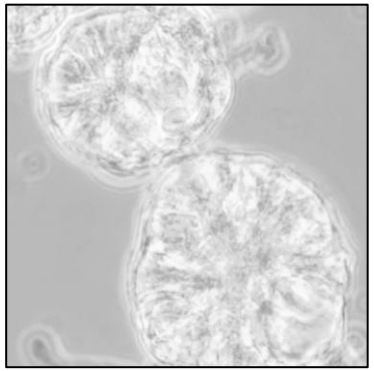
Apical out lung organoids (Epithelix, StemCell)



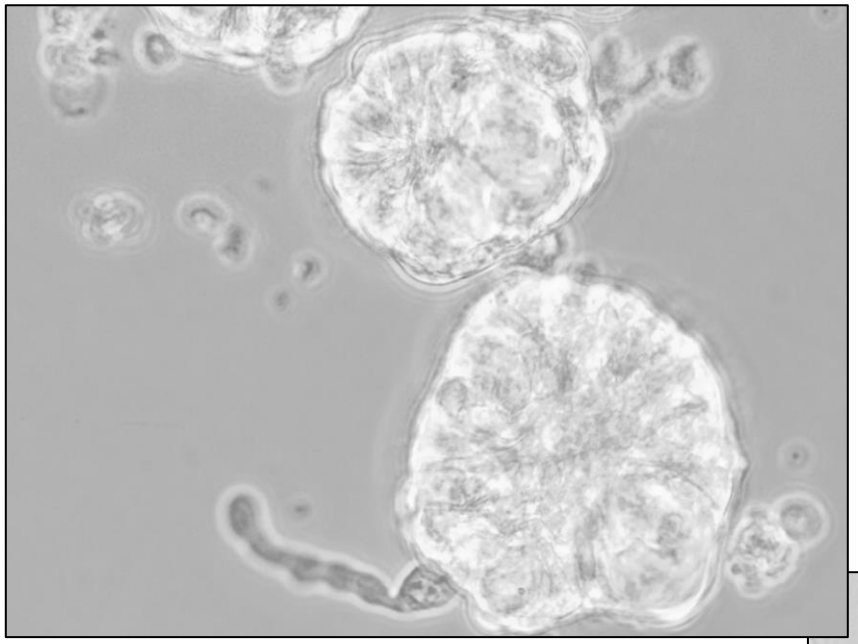


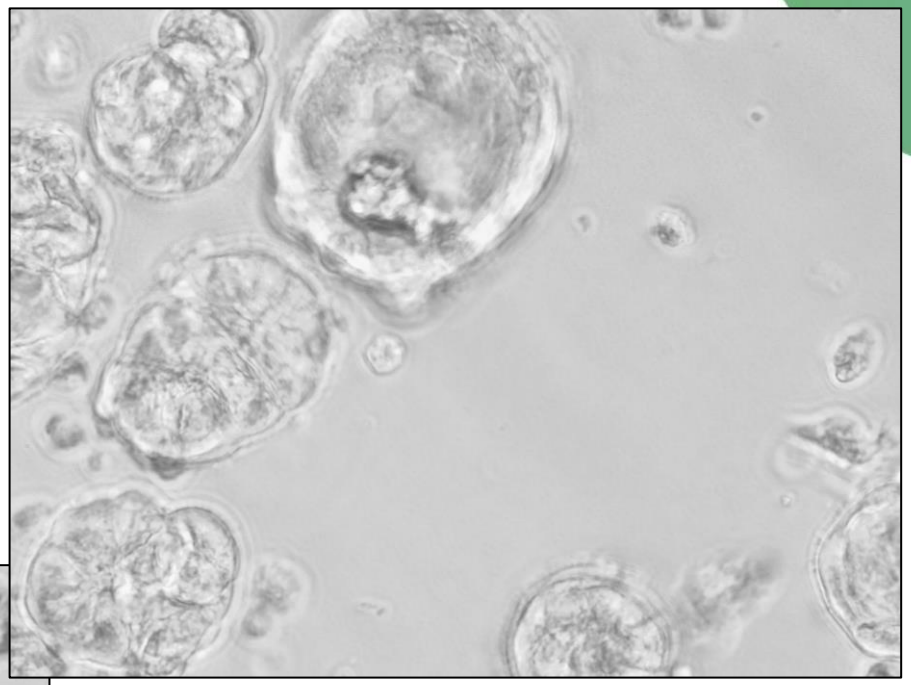


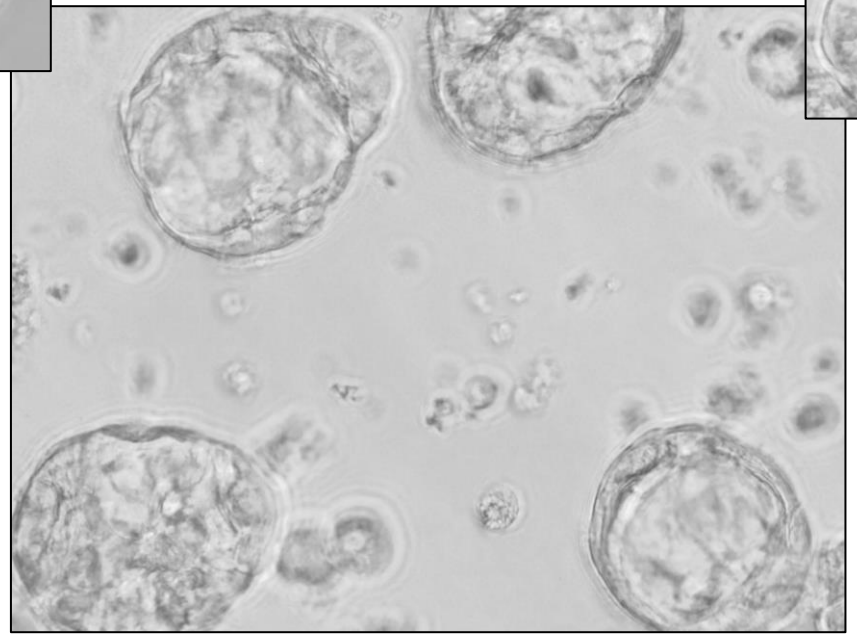




Apical out lung organoids (Epithelix, StemCell)







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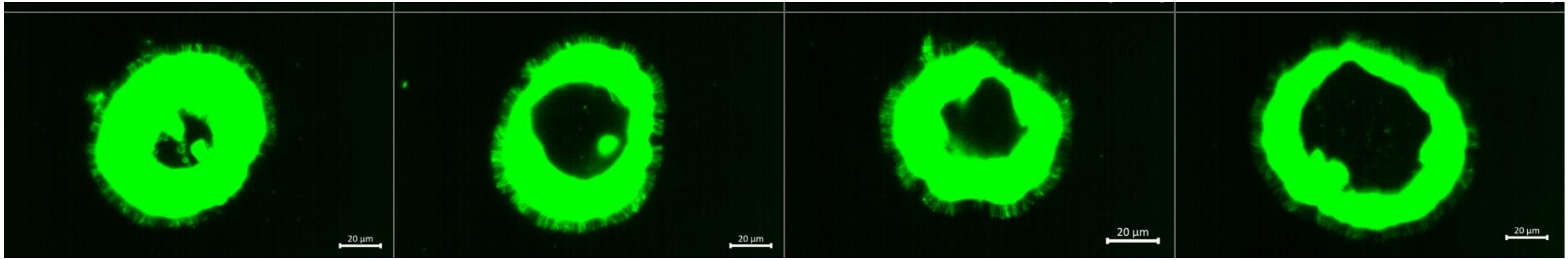
Apical out lung organoids–(Imactiv3D)
Beta-Tubulin, microtubule, cytoskeleton



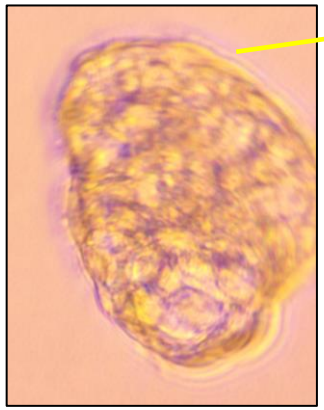
plan en z. acquisition en z-stack, 40X

- Ciliated cells are detected at the surface of the organoid
- A lumen was formed

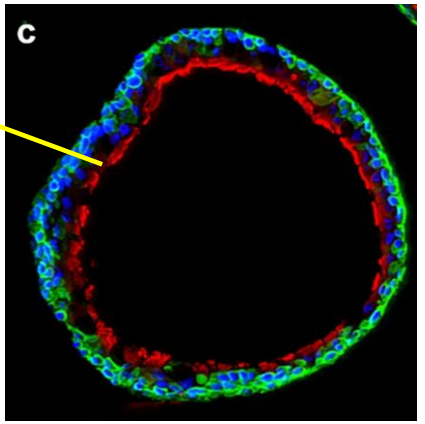
Apical out vs Apical in

Ciliated cells

Real life orientation of ciliated cells



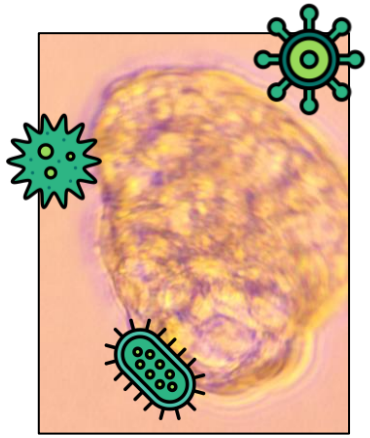
Outside-in orientation of the ciliated cells



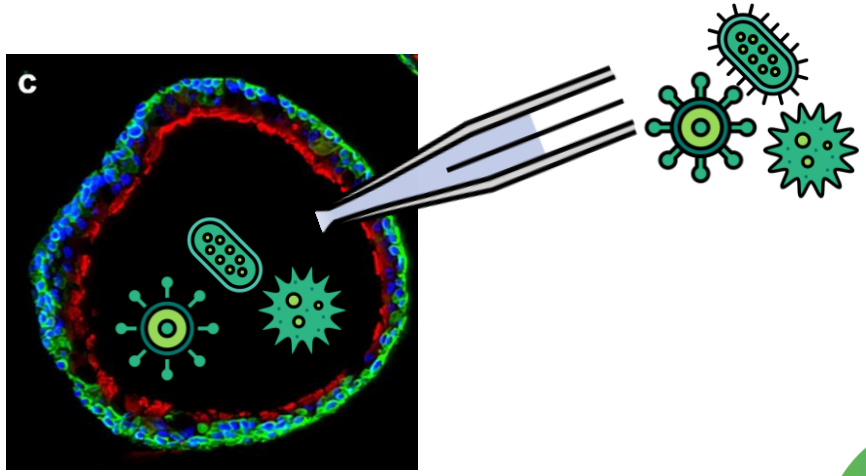
basal marker cytokeratin 5 (green)
ciliated cell marker acetylated tubulin (red)
nuclei (blue)

Cunniff et al., 2021

Real life exposition to microorganisms



Microinjection of microorganisms required



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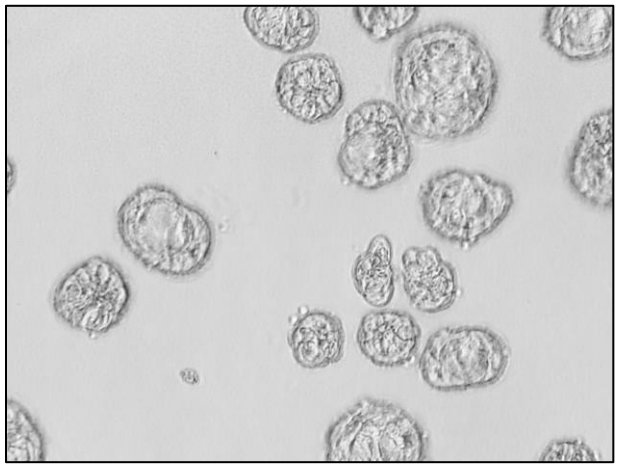
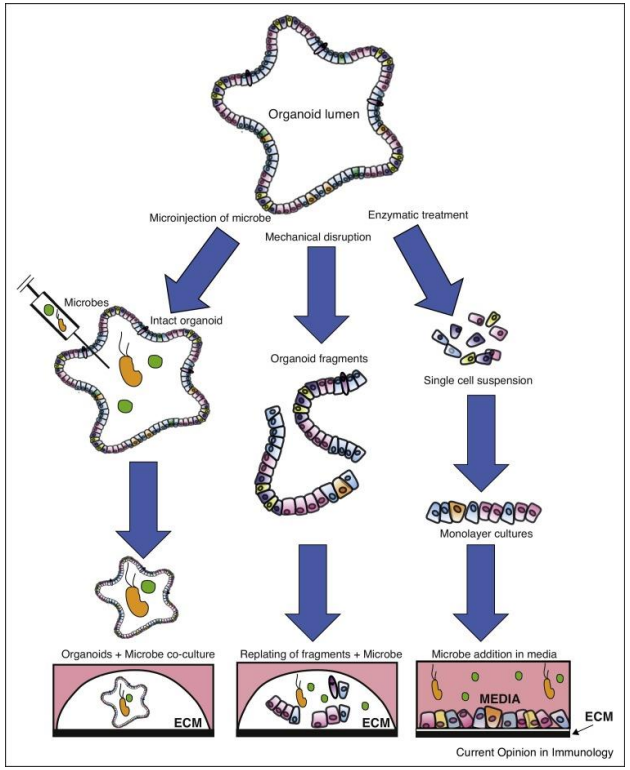
Apical out vs Apical in

Hundreds of organoids can be used for a given condition

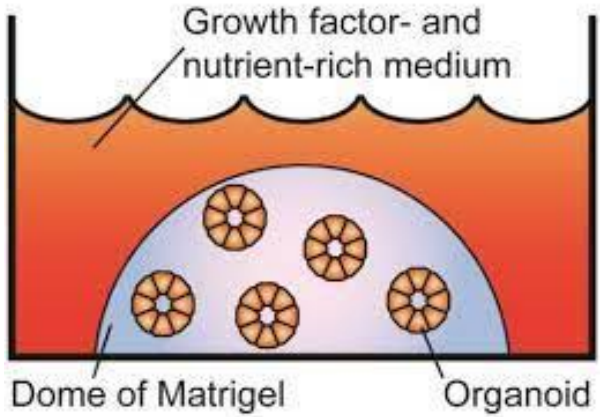


Tens of organoids can be used for a given condition



Apical out vs Apical in

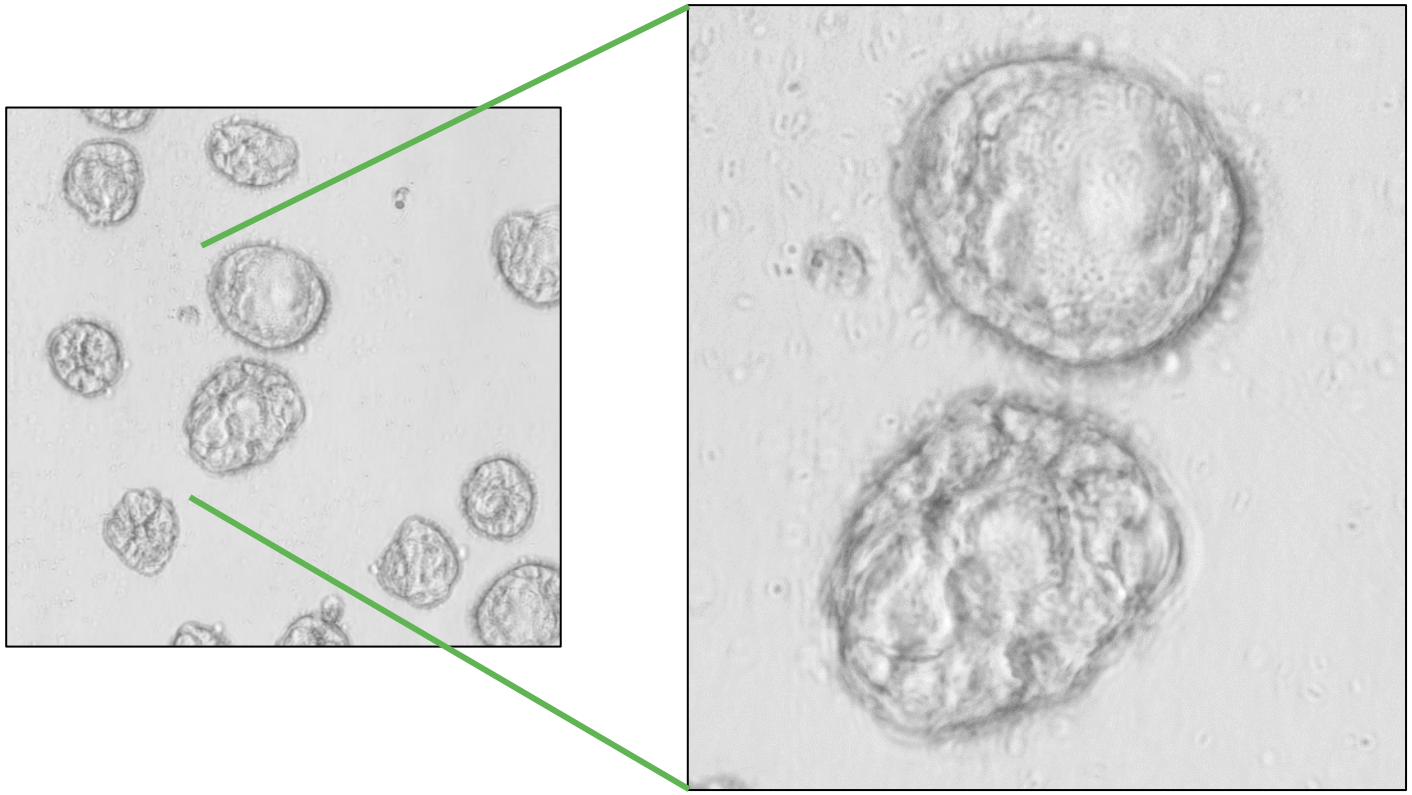
Matrigel, a basement-membrane matrix extracted from Engelbreth–Holm–Swarm **mouse sarcomas**

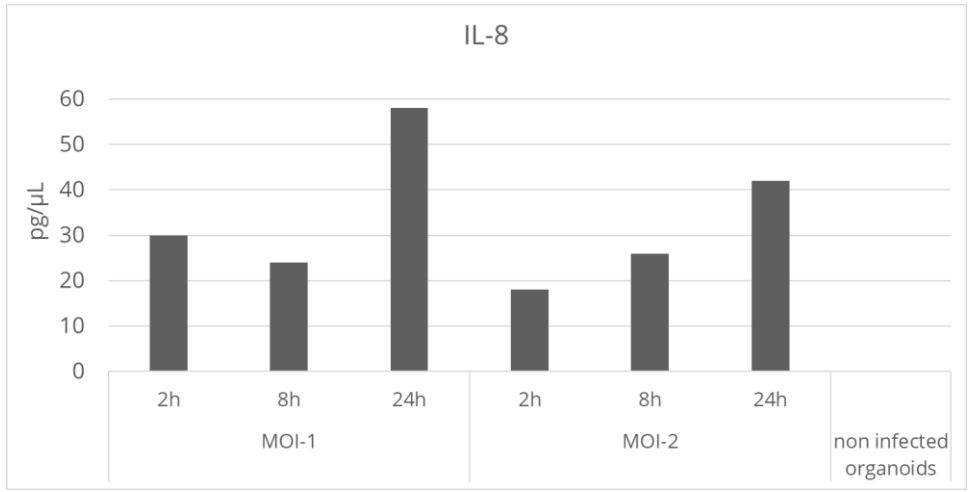


Does not fit with reduction of mouse utilisation

Lung organoids-bacterial infection

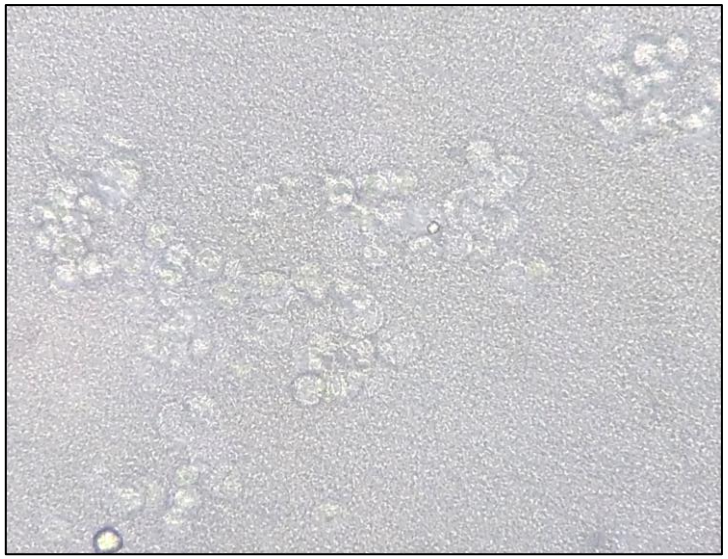
Acinetobacter baumannii



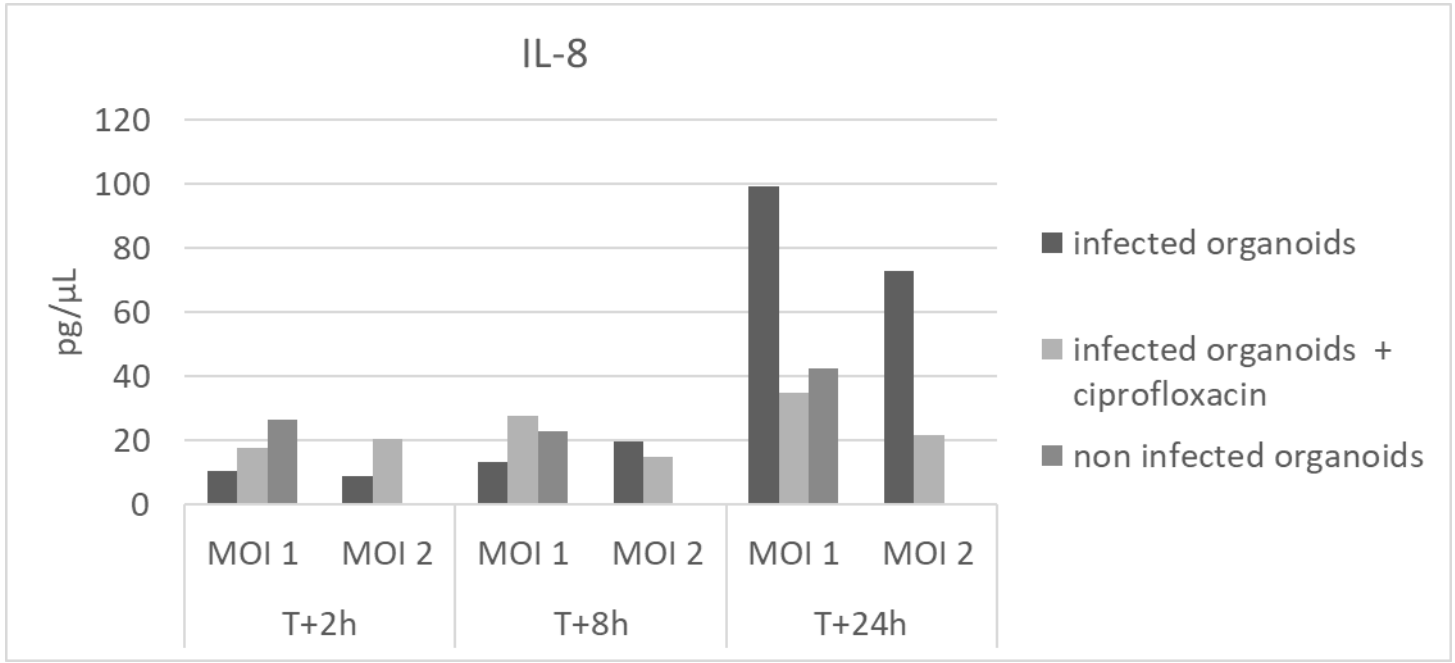


Lung organoids-bacterial infection

Pseudomonas aeruginosa

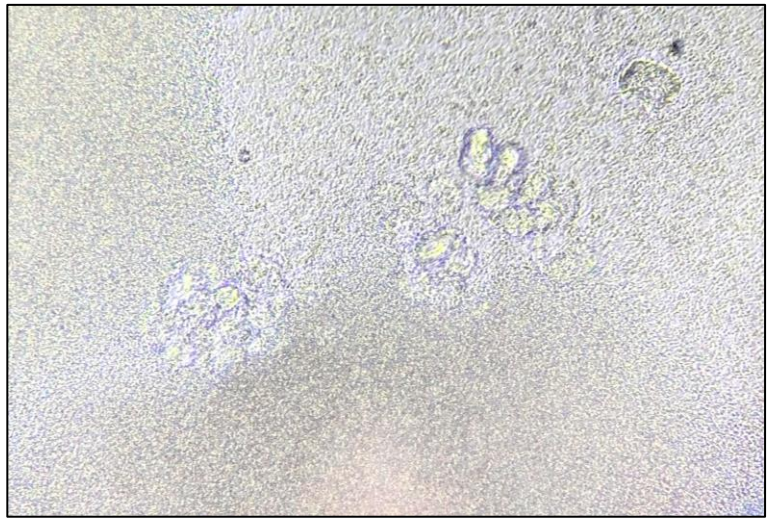


T+24h

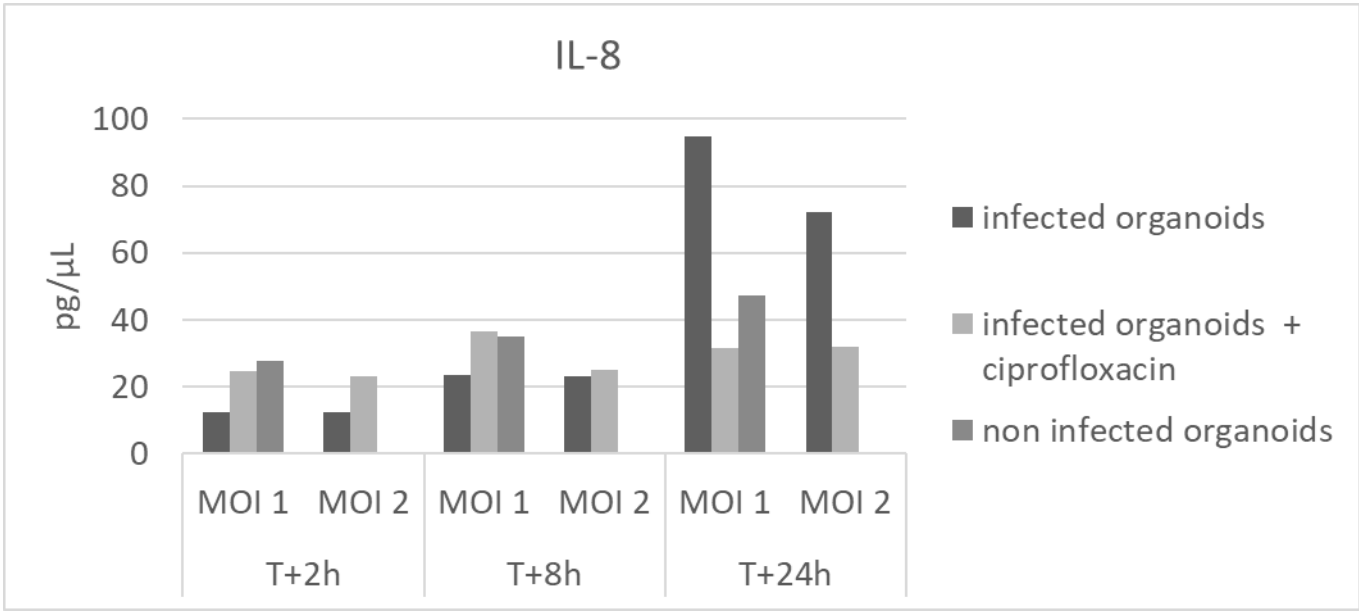


Lung organoids-bacterial infection

Staphylococcus aureus



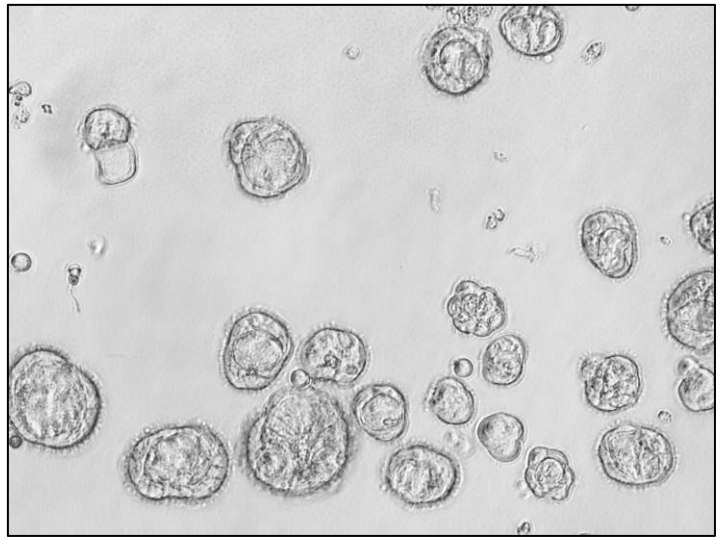
T+24h



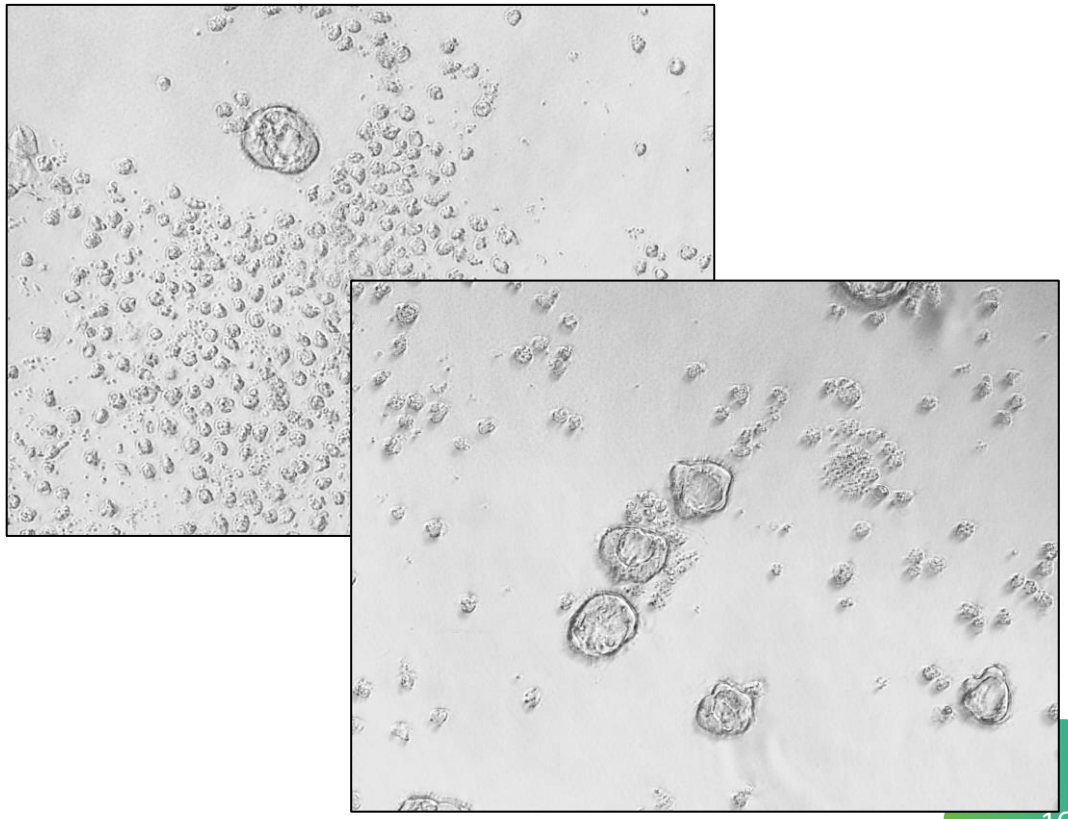
Lung organoids-viral infection

Influenza virus H1N1

Non infected organoids



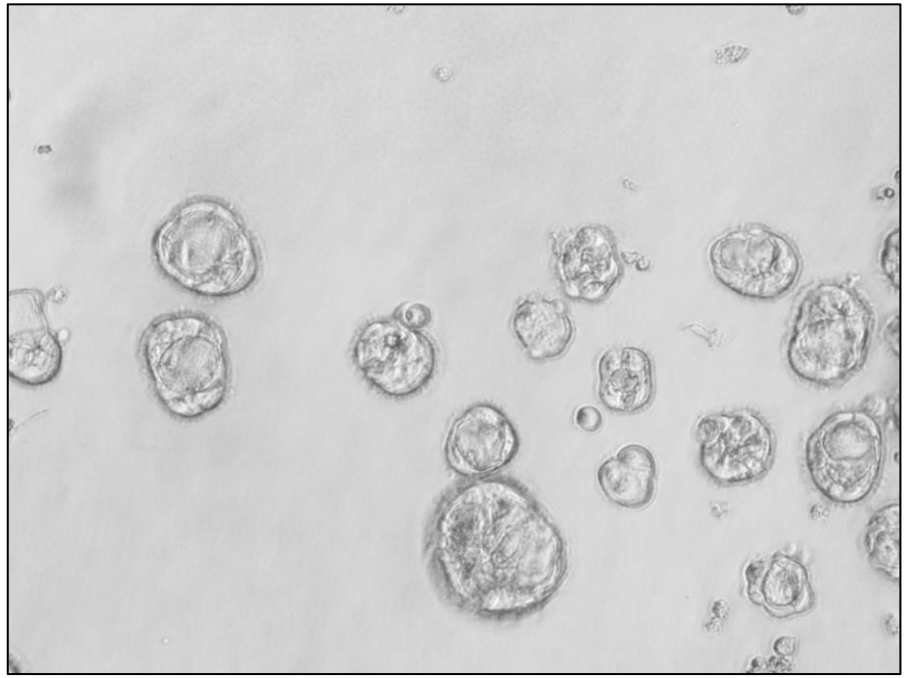
Infected organoids



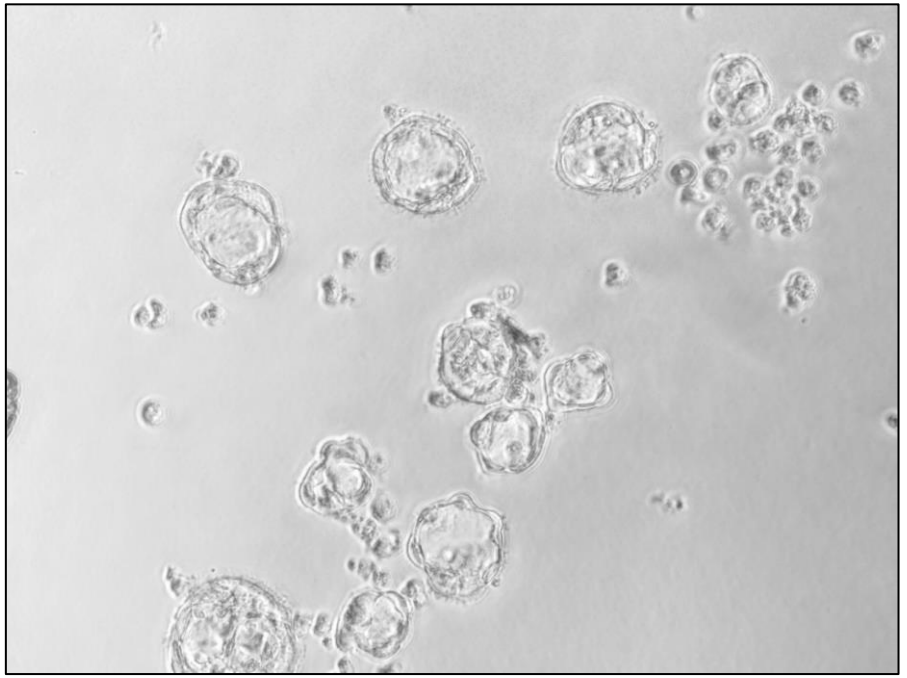
Lung organoids-viral infection

Influenza virus H1N1

Non infected organoids

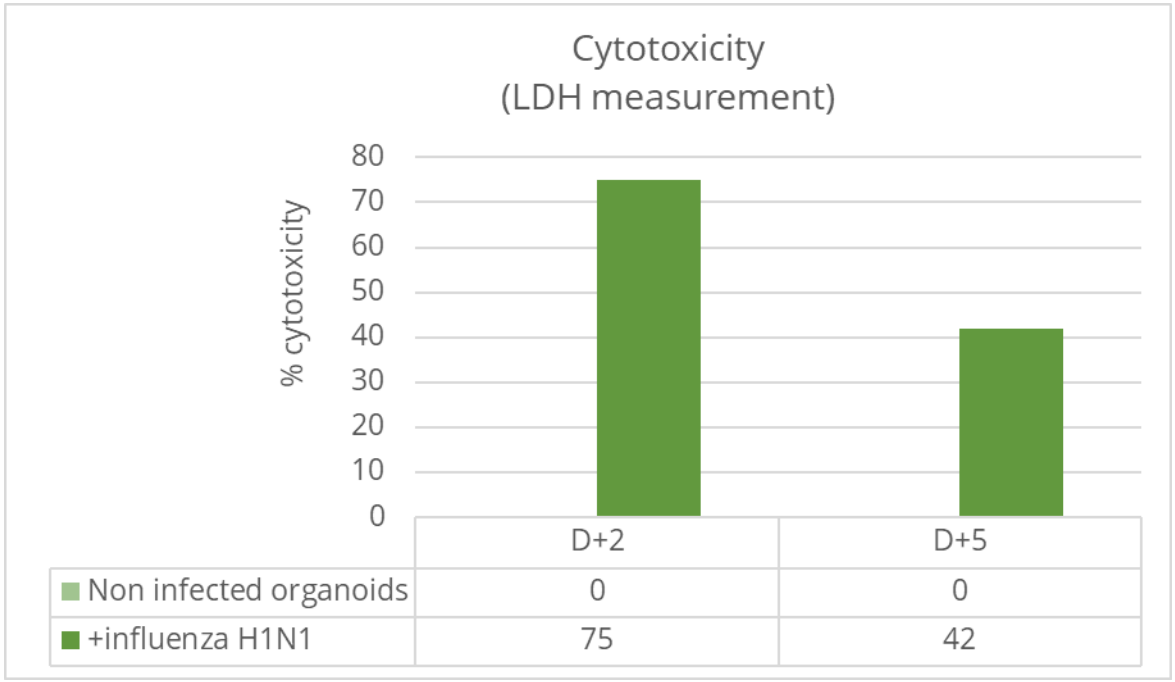


Infected organoids



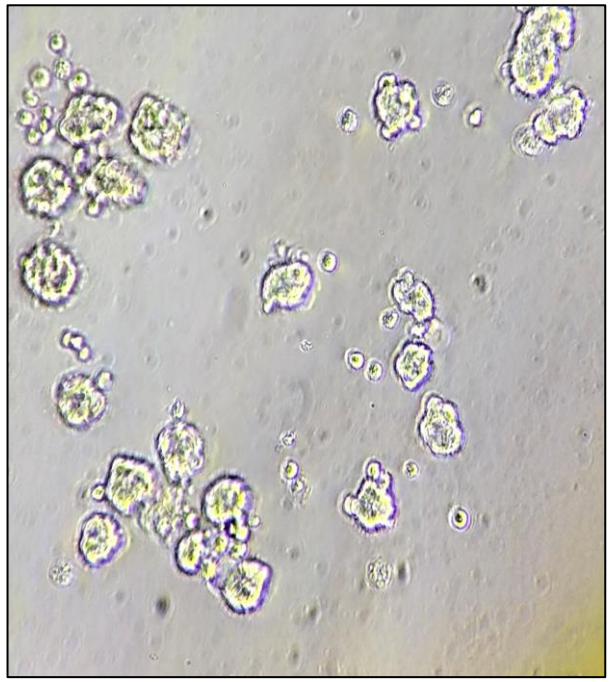
Lung organoids-viral infection

Influenza virus H1N1

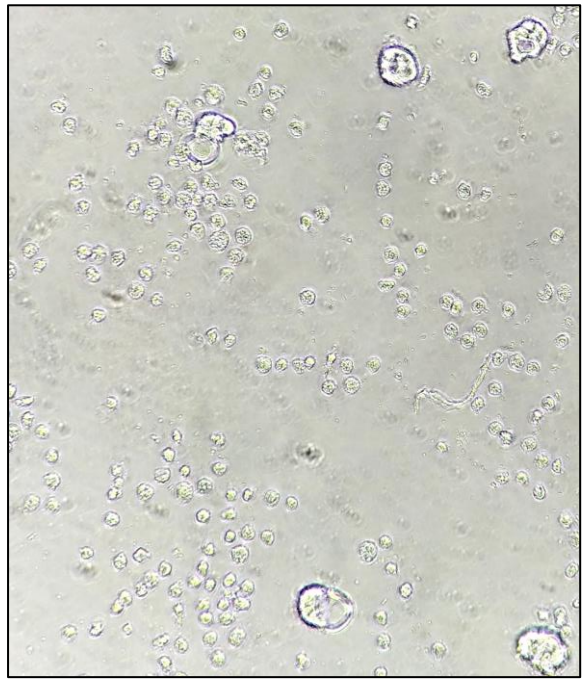


Lung organoids-viral infection

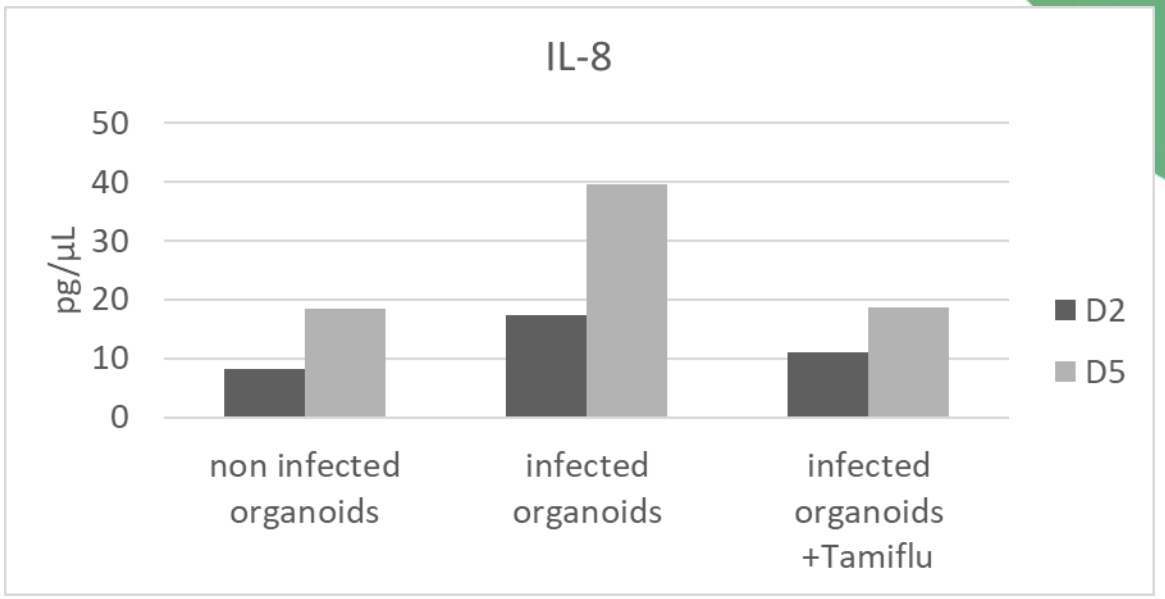
Rhinovirus

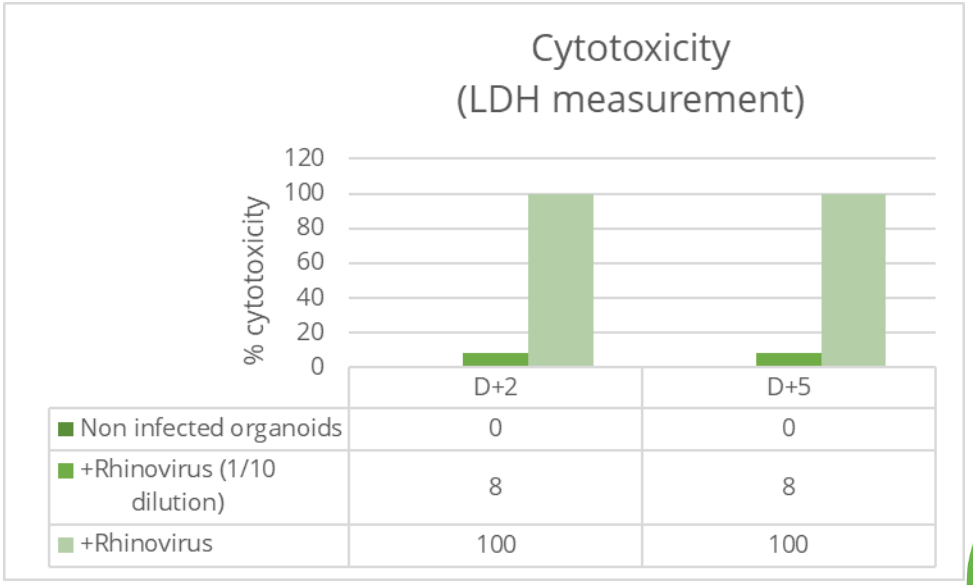


D+2



D+5

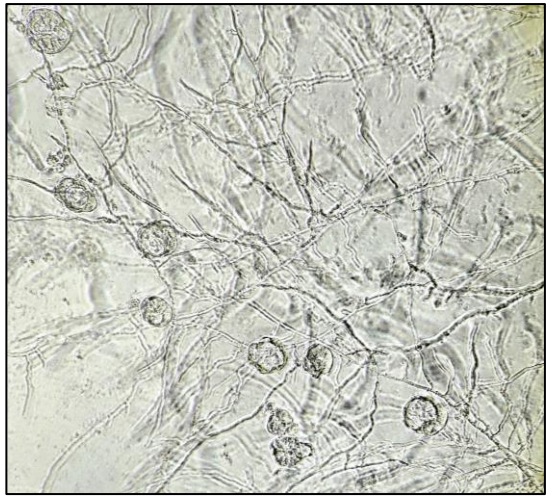




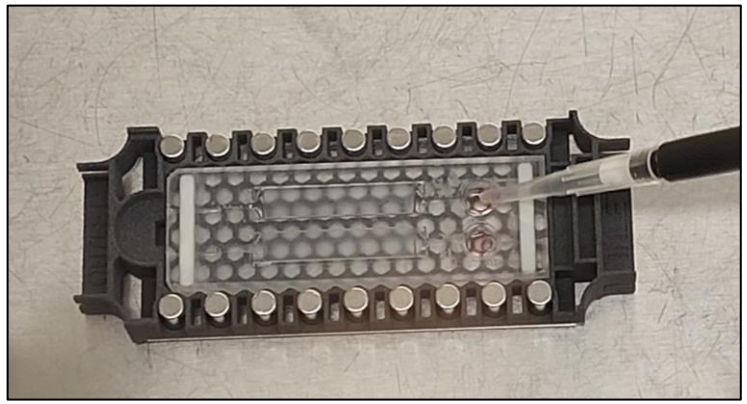
VIBIOSPHEN

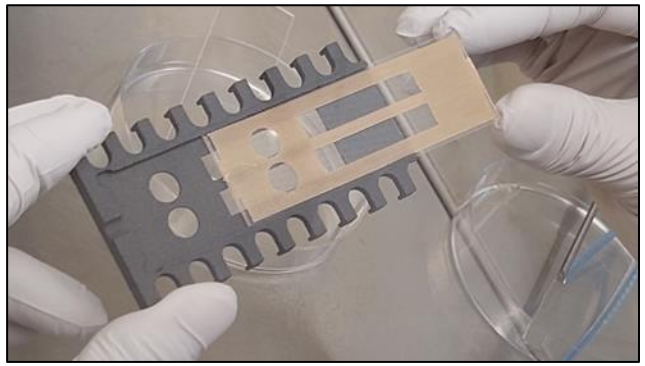
Lung organoids-fungal infection

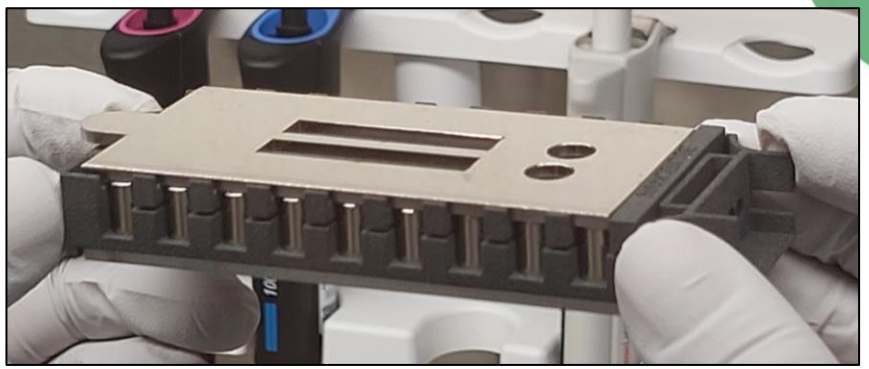
Aspergillus brasiliensis

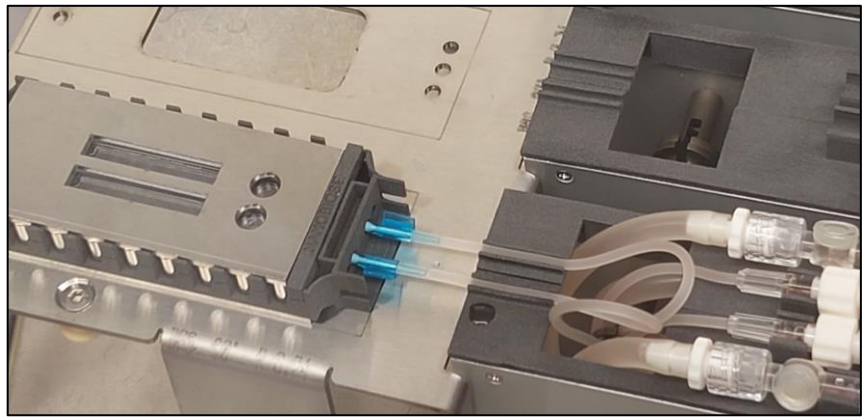


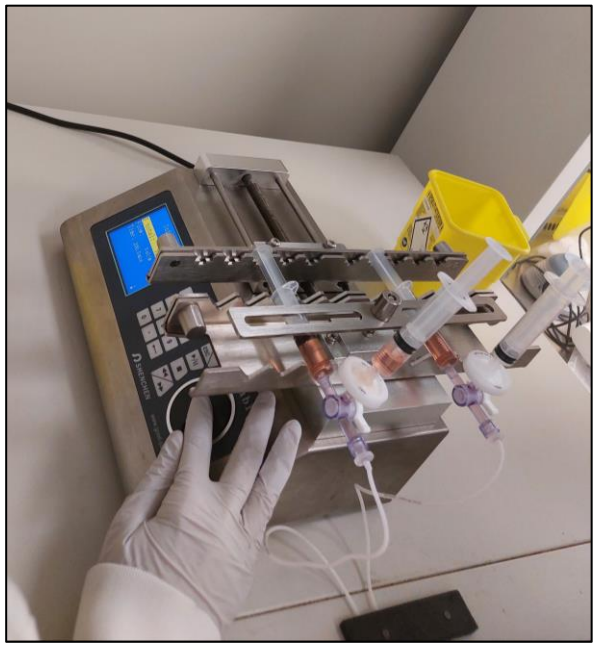
Lung organoids-microfluidic system (Nanobiose)

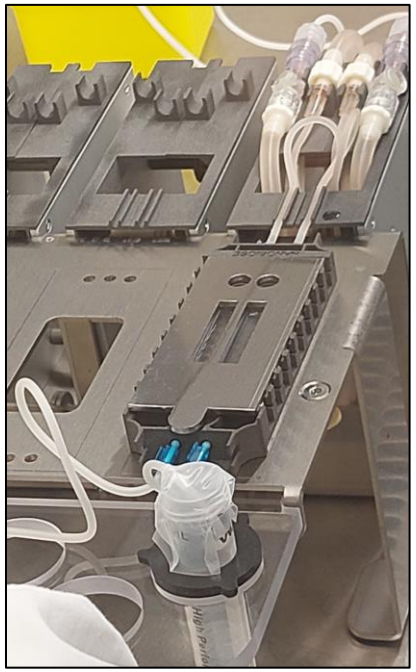












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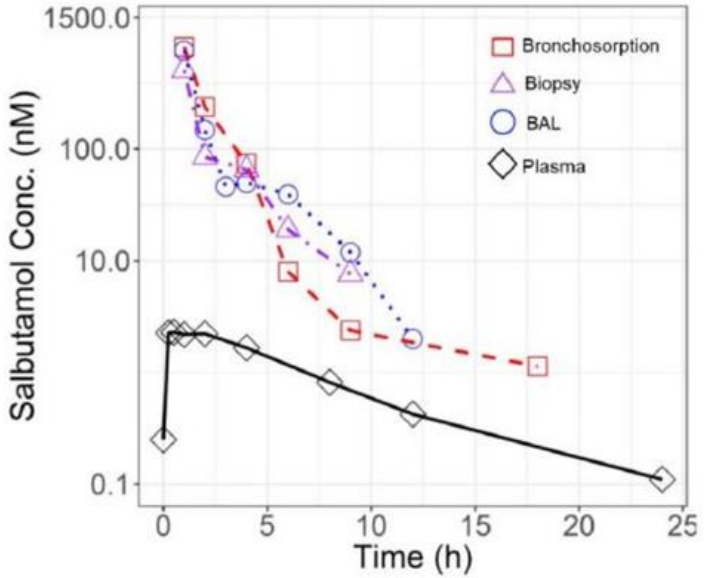
Lung organoids-microfluidic system

Modelling methods for treatment delivery

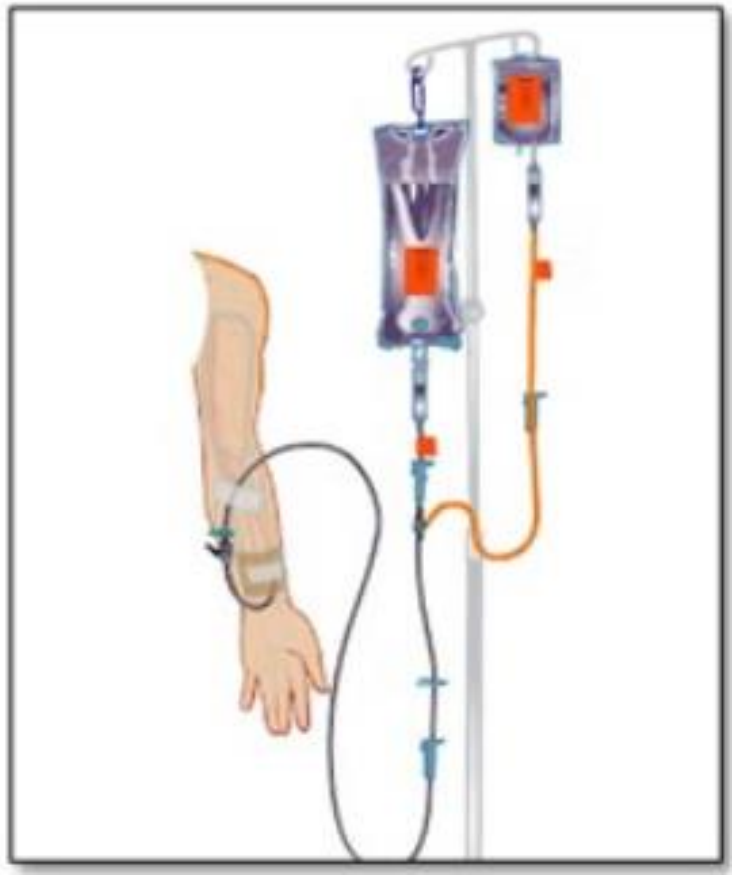
Inhalation



Distribution of drugs after inhaled administration

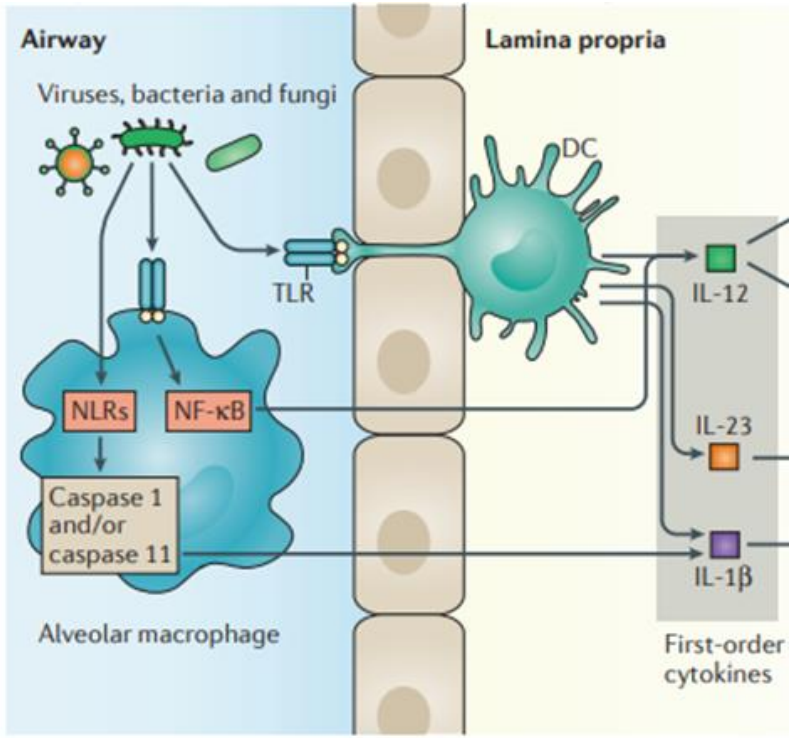
Muhammad Waqas Sadiq et al. Eur Respir J 2019;54:OA2103

Perfusion



Lung organoids + immune cells

Modelling pulmonary environment



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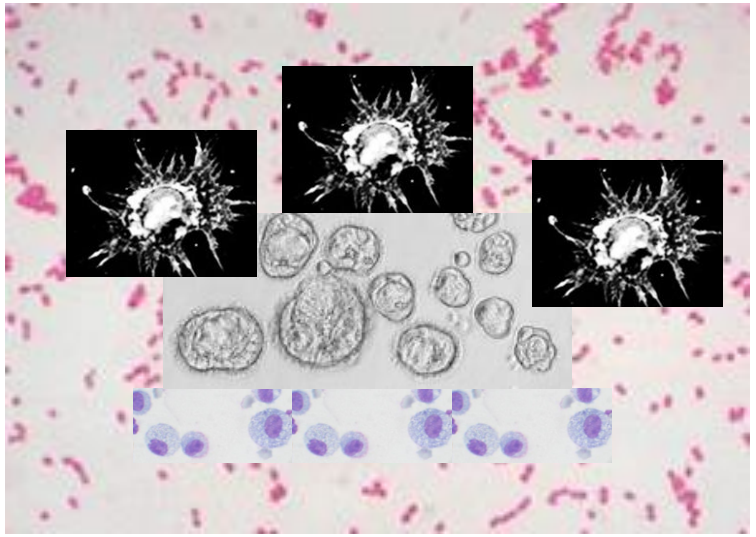
Iwasaki et al., 2016



Acinetobacter baumannii

dendritic cells

organoids

macrophages

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VIBIOSPHEN

From microbes to One Health

Maxime FONTANIE

Célia LECACHEUX
Alexandre LAURENT
Christophe FREMEZ

Robin DUMAS

Thank you for your attention