GENERATING COMPLEX PHYSIOLOGICAL LUNG TISSUE USING 3D BIOPRINTING TO STUDY RESPIRATORY PATHOLOGIES

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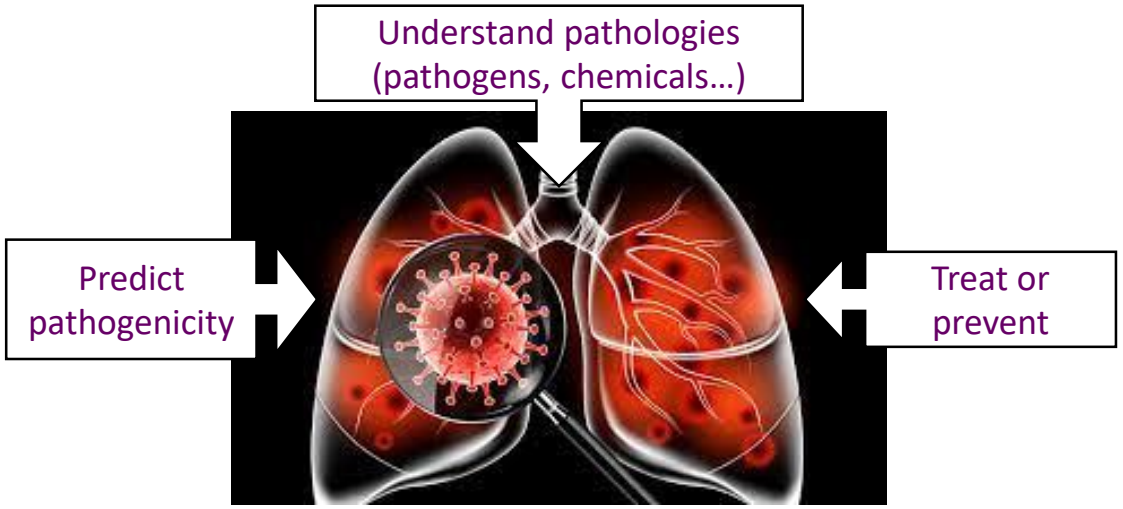
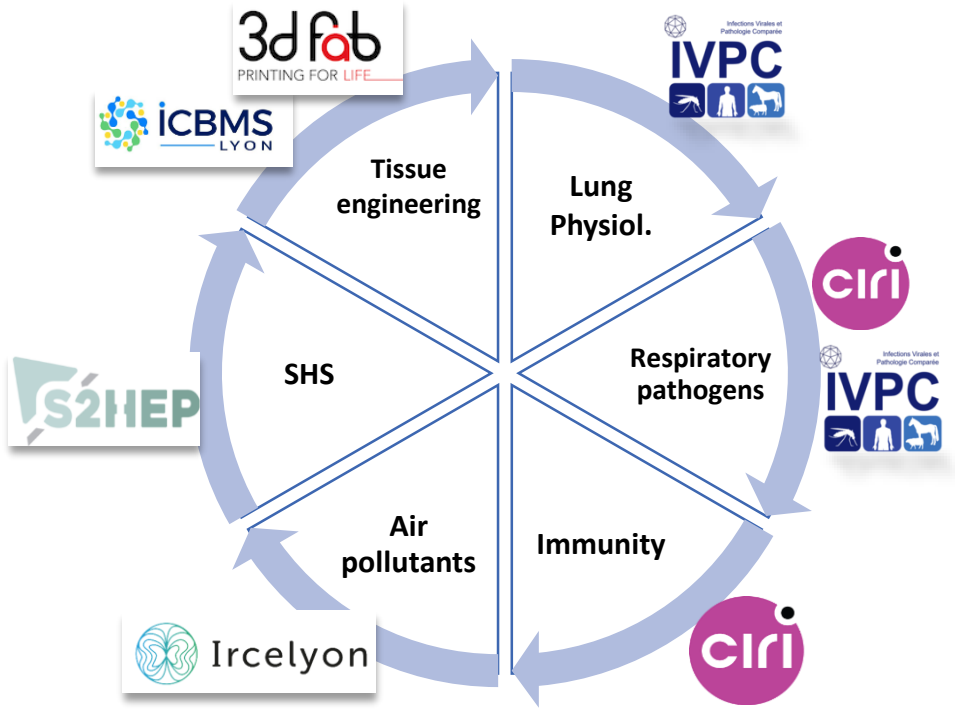


Objectives :

- *To get more physiological, and more predictive models*
- *To propose alternative to animal testing (3R rules)*



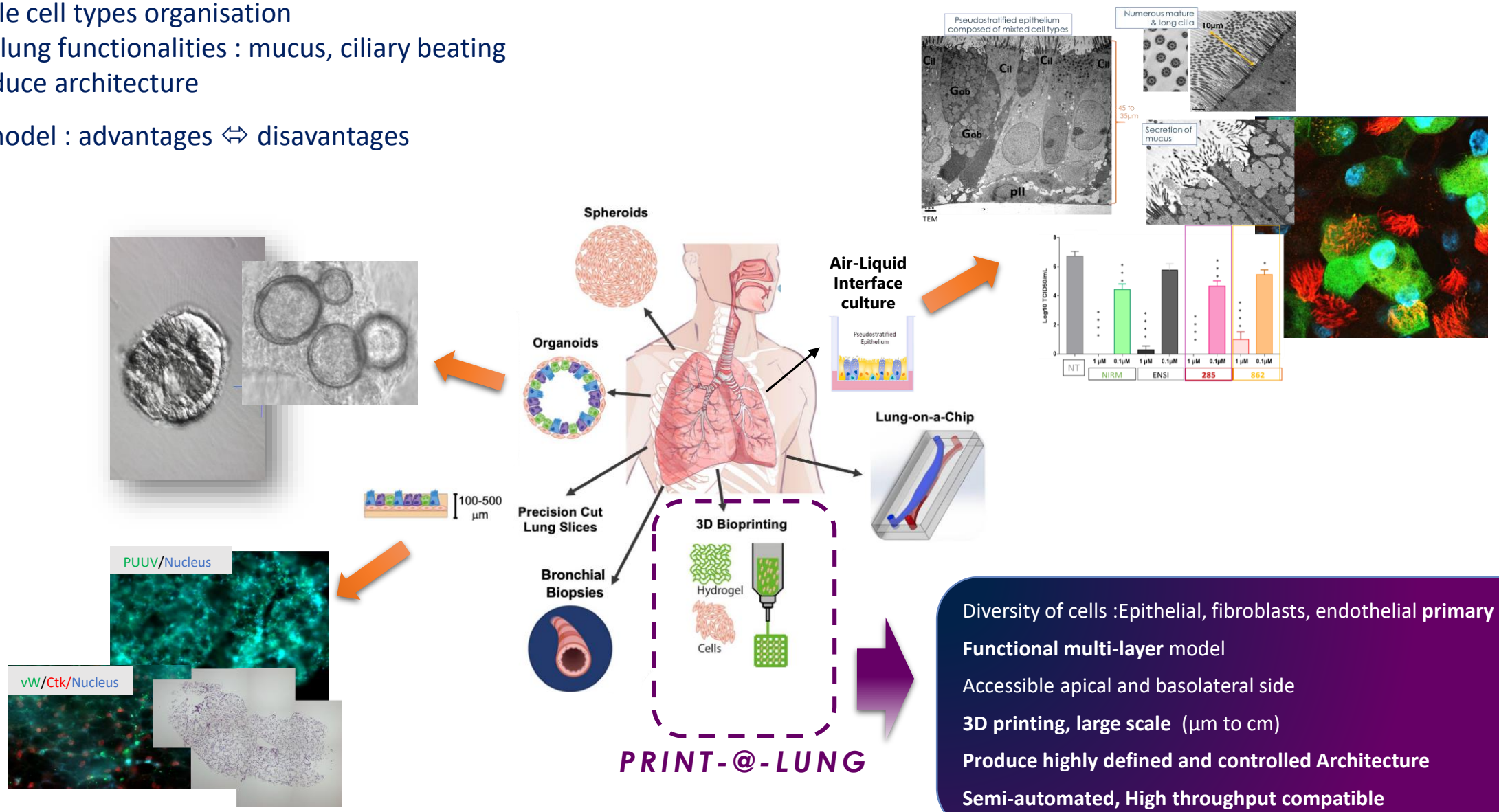
➔ ***PRINT-@-LUNG***
an interdisciplinary project

Need for more relevance

➔ Expectations :

- Multiple cell types organisation
- Mimic lung functionalities : mucus, ciliary beating
- Reproduce architecture

➔ Each model : advantages ⇔ disavantages



Diversity of cells :Epithelial, fibroblasts, endothelial **primary** cells…

Functional multi-layer model

Accessible apical and basolateral side

3D printing, large scale (µm to cm)

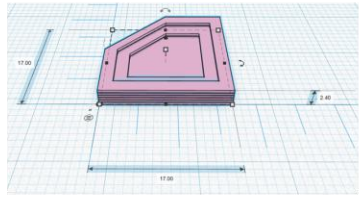
Produce highly defined and controlled Architecture

Semi-automated, High throughput compatible

Adapted from Rocio J. Jimenez-Valdes et al. 2020

Biofabrication combining two method of bio-impression 3D

1 - Computer Assisted Designing



NHLF

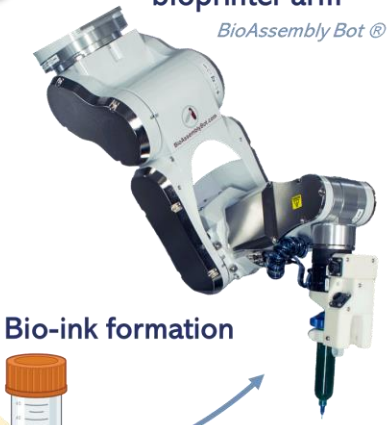
HUVEC

Gelatin
Fibrinogen
Alginate

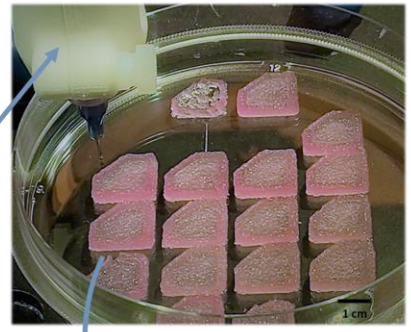
2 - Bio-ink formation

3 - Loading in the 6-axis bioprinter arm

BioAssembly Bot ®



4 - Micro-extrusion of the basal compartments



6 – Loading of the epithelial cells in the capillary

hAEC

OR

Calu-3

SciFlexArray S3 ®

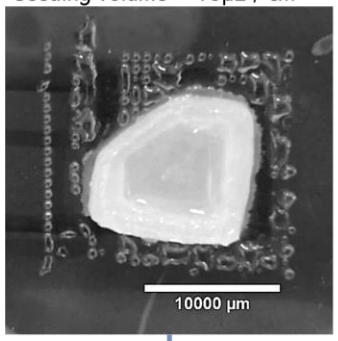
Fluid fitting tube

Piezo electric element

Dispensing capillary
Ø 80 – 100 µm

7 – Inkjet printing of the epithelial cells

Seeding volume ~ 10µL / cm²



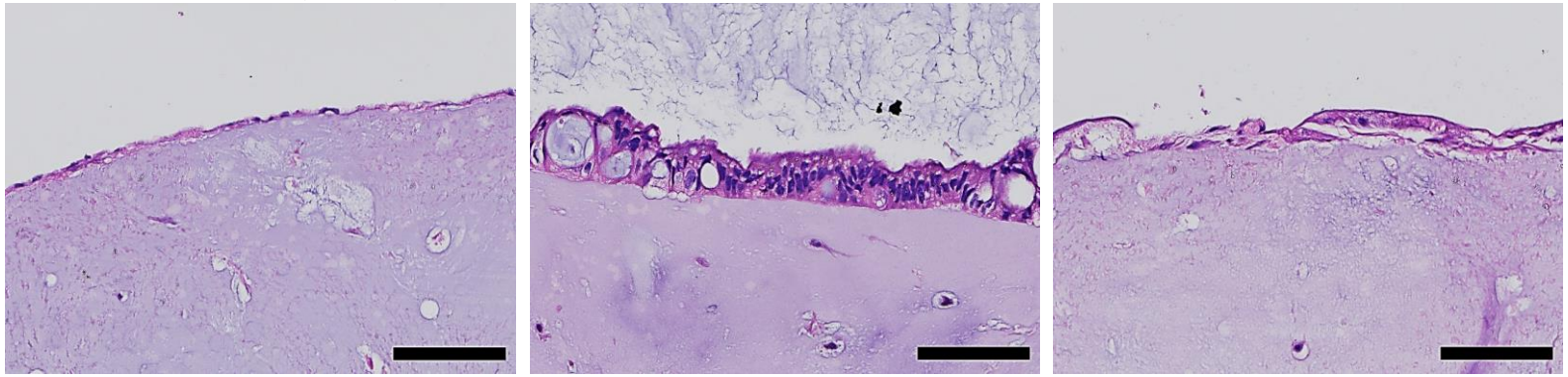
LLI : Liquid-Liquid Interface ; ALI : Air-Liquid Interface

NHLF + HUVEC (control)

NHLF + HUVEC + Calu-3

NHLF + HUVEC + hAEC

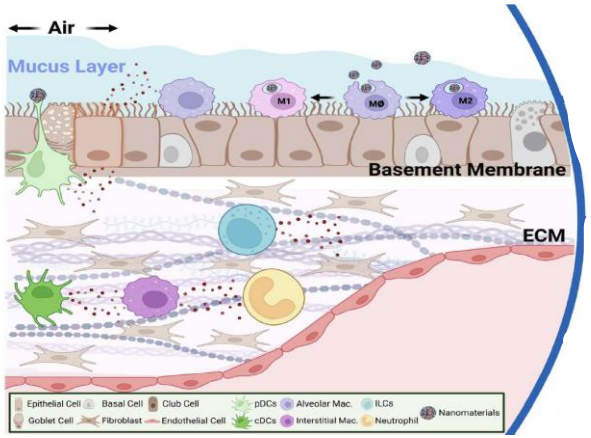
J48 Epi J34 ALI J20



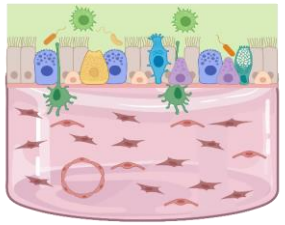
Echelle 100µm

Next step

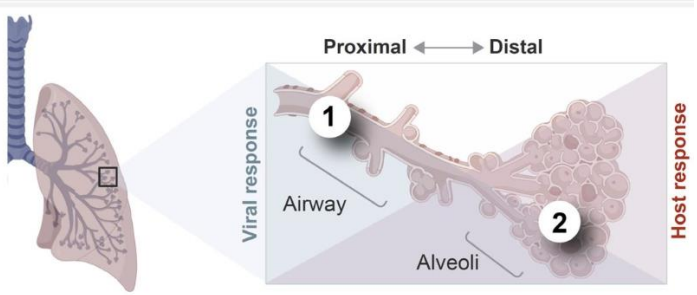
➢ **Integrate Immune cells : macrophages, monocytes, dendritic cells**



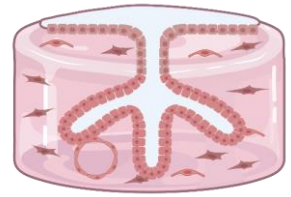
Adapted from Graf et al. EurJ Pharma.Sc 2023



➢ **Differentiate specific regions & Improve 3D architecture**



Tubule shape **VS** alveolar bag



➢ **Impact of pathogens (*S.aureus, Ps aeruginosa, Legionella*, Sars-Cov2 virus, …)**
➢ **Evaluate curative approaches (phages, antiviral drugs)**
➢ **Impact of fine particles in air pollution**