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## Unveiling Pathological Insights and Accelerating Antiviral Drug Discovery in Respiratory Viral Infections with Polarized Organoids

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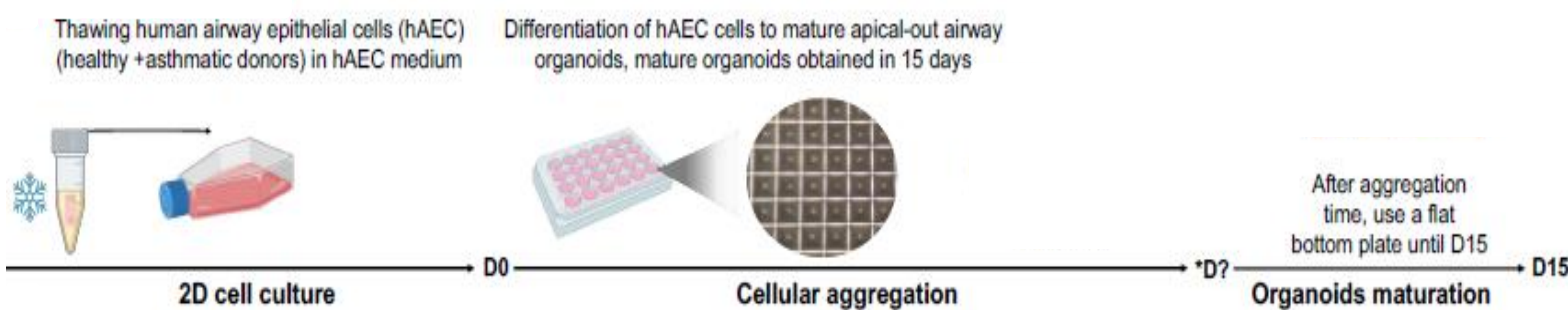
Respiratory organoids derived from human cells offer insights into diseases like asthma, COPD, and cystic fibrosis. **Polarized apical-out organoids** provide a more accurate replication of lung tissue, mimicking airway epithelial organization and barrier properties, making them ideal for studying pathogen interactions.

However, their full potential in disease research, drug testing, and personalized therapies is yet to be realized, requiring further characterization and validation

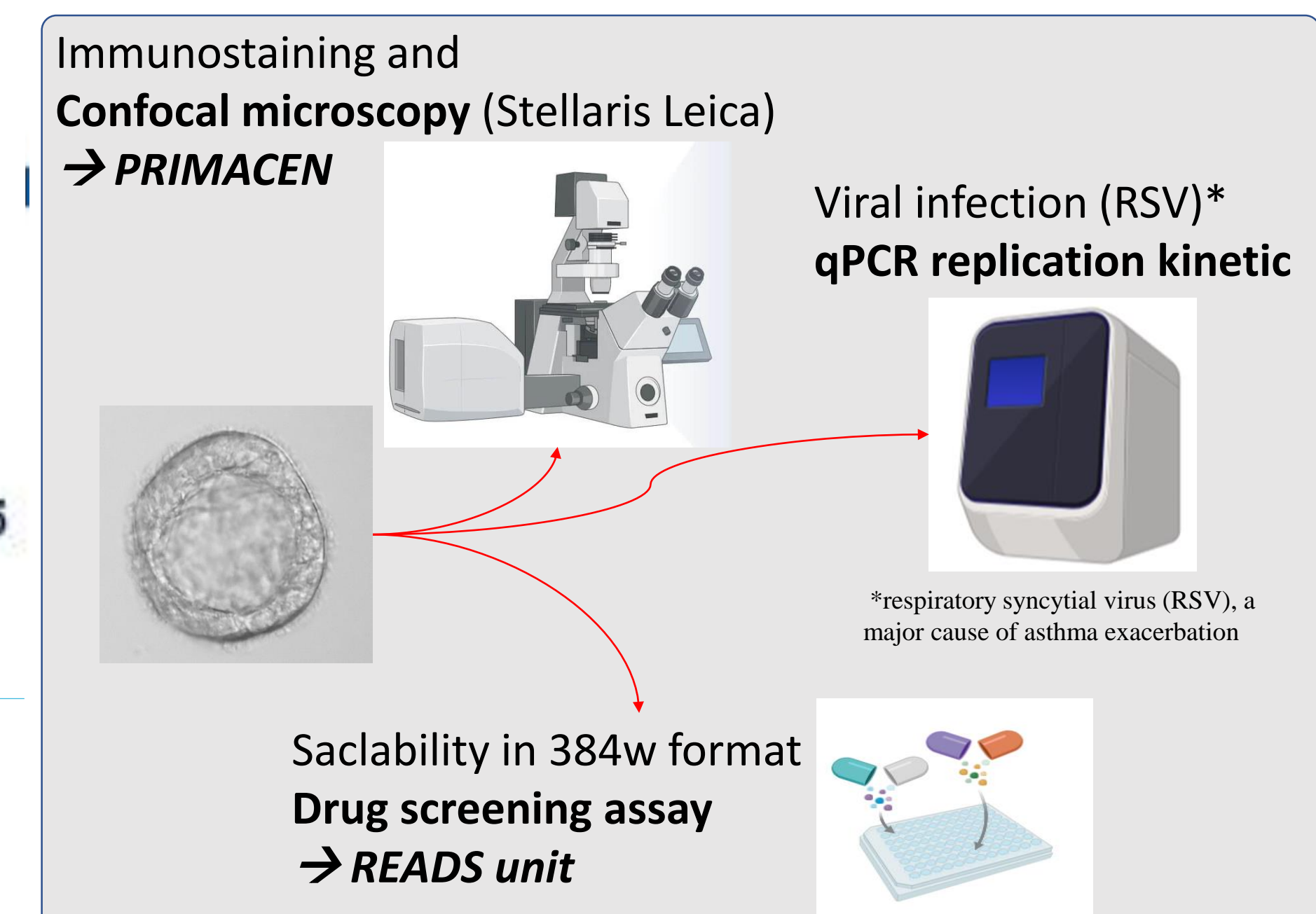
### AIMS

- Explore the potentiality of respiratory organoids in precision medicine
- Show applications in asthma/COPD
  - viral infection studies
  - personalized therapeutic approaches

### Organoids Production

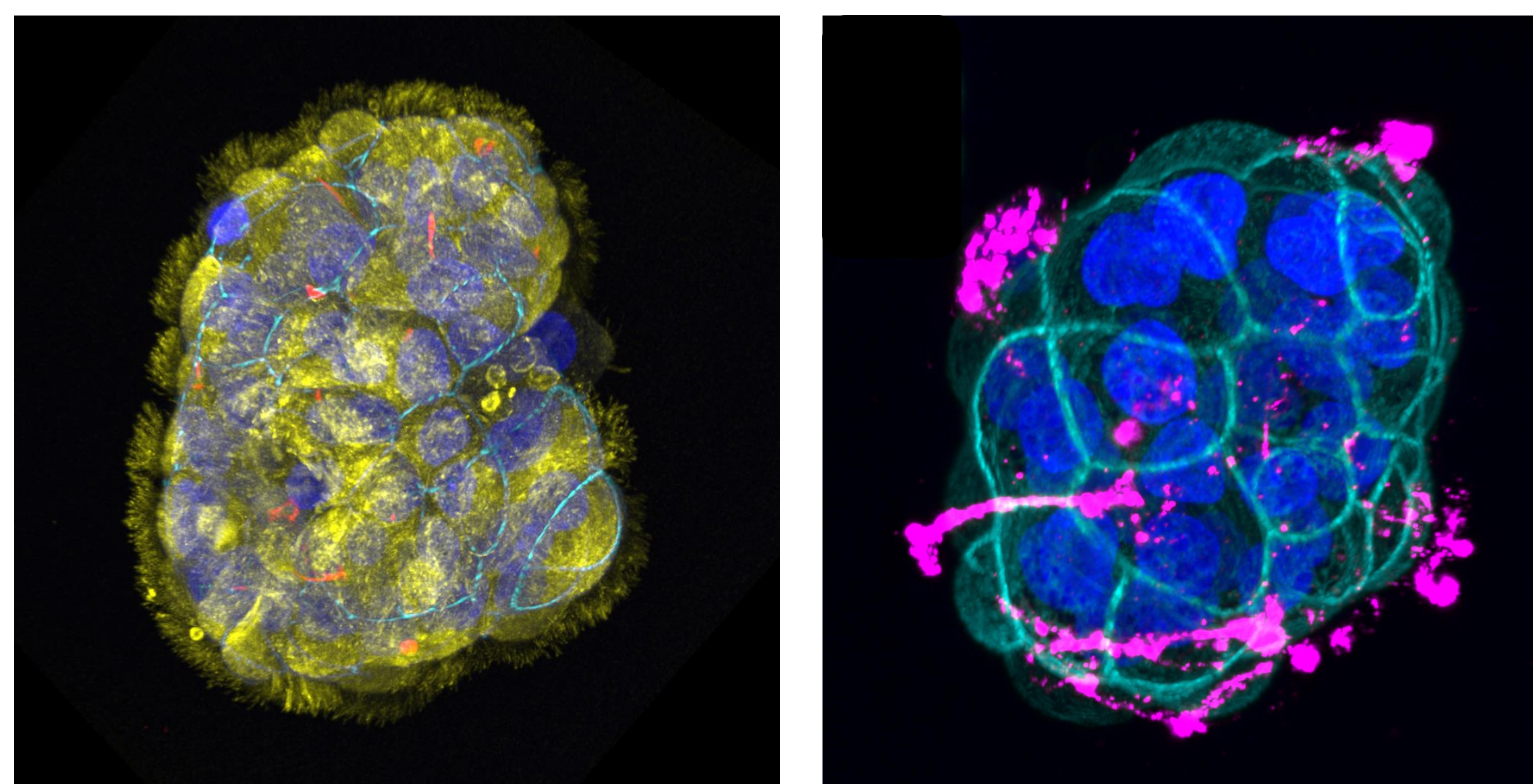


### Applications



### Tissue 3D organisation

- Rounded self-organisation of 30-60 cells (DAPI, Phalloidine), 50 to 150 µm diameter, with inconstant central lumen
  - Main epithelial bronchial cell types observed: abundant ciliated cells (BETA-TUB), weak basal cells (CY5), a few goblet cells (MUC5A)
- = 3/orga in average ( ) in healthy) organoids potentially more in asthma organoids



Healthy organoids in 3D vue (Image!)

Asthma organoids in 3D vue (Image!)

→ Need deeper characterisation (proportion cell type, motility functionality to compare healthy and asthma phenotypes in apical out polarized bronchial organoids

= Arguments for good fidelity of bronchial tissue in apical out organoids

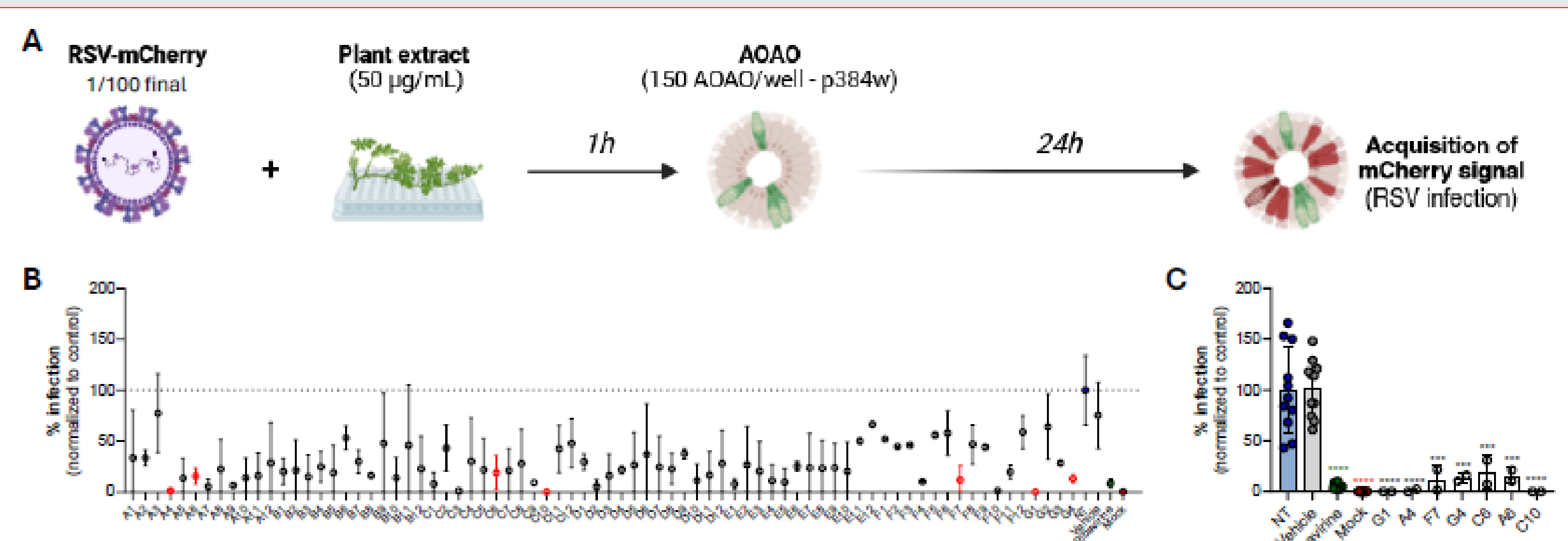
### Permissivity to viral infection

RSV infection (0.03 MOI for 2h at 37°C with 5% CO<sub>2</sub>) led to increased viral replication, reaching a plateau at 1.73E8 RNA cp/ml (8.23 Log) between day 4 and day 8 in asthma organoids

→ Encouraging preliminary results, need reproducibility and transposition to other agents = Apical out disposition facilitate the steps of viral entry during infection and open multiple perspectives in the exploration of viral interference in tissue remodeling during diseases

### Drug screening scalability

Optimal screening conditions were found to be at approx. 150 organoids per well in a 384-well plate format. Organoids were infected with RSV-mCherry (estimated MOI of 0.1) and the mCherry area is monitored 24h later (Cytation, Agilent\*).



→ Variability in the infection rate needs to be optimized. but physiologically relevant organoids remain technically suitable for performing screening assays