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Fabrication and Potential Use of Apical-Out Bronchial Organoids from Asthmatic Patients for Viral Infection Studies

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Introduction

With **4 millions people affected in France**, asthma is a serious public health issue. The development of new models mimicking lung tissue complexity and functionalities is essential to fight and understand this pathology.

Respiratory viruses are the first incriminated in asthma exacerbation¹ with a predominance of Respiratory syncytial viruses (RSV) and human Rhinovirus (RV) even in co-infections (30%)², but aim of viruses in asthma etiology still misunderstood

NEW MODEL : ORGANOIDS

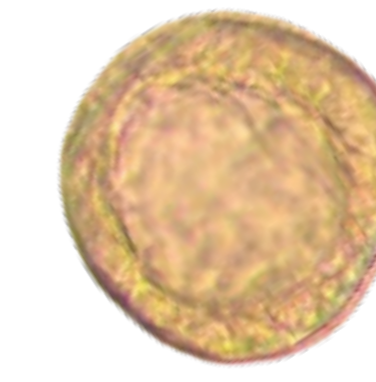
3D multicellular tissues, aim is to mimic human organs complex functionalities

2022 : development of **healthy respiratory organoids with inverted polarity** (ciliated cells on external face, allow exposure of virus target cells) and infected with RV and Influenza³.

Goals

→ Develop apical out organoids with bronchial cells of asthmatic patients

Primary bronchial epithelial cells from asthmatic donors (provided by Epithelix)



- 1) Production
- Characterize the model
 - Confirm apical out configuration
 - Define cellular composition

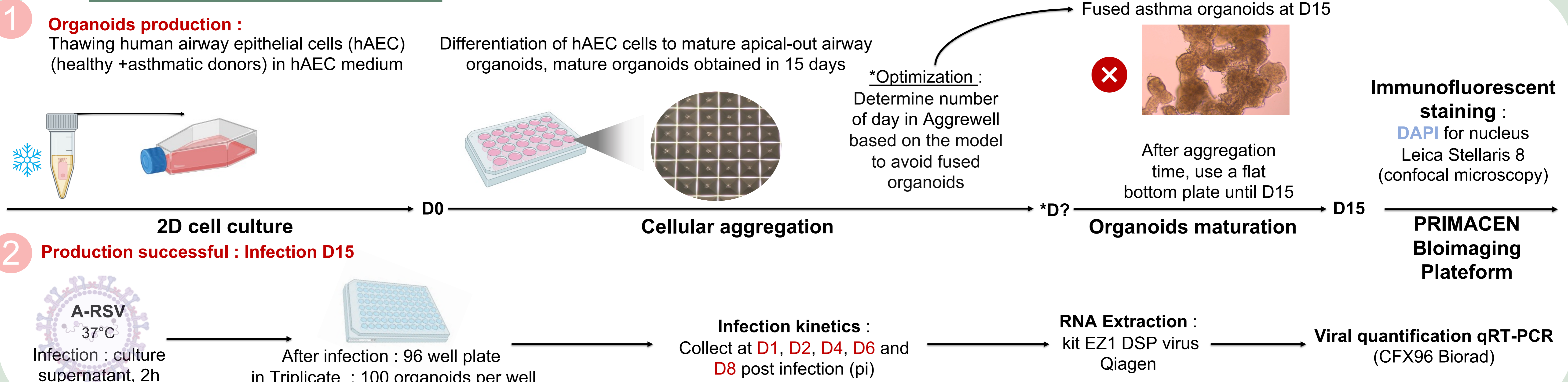
Pilot study : produce preliminary data

Characterize Improve Criticize

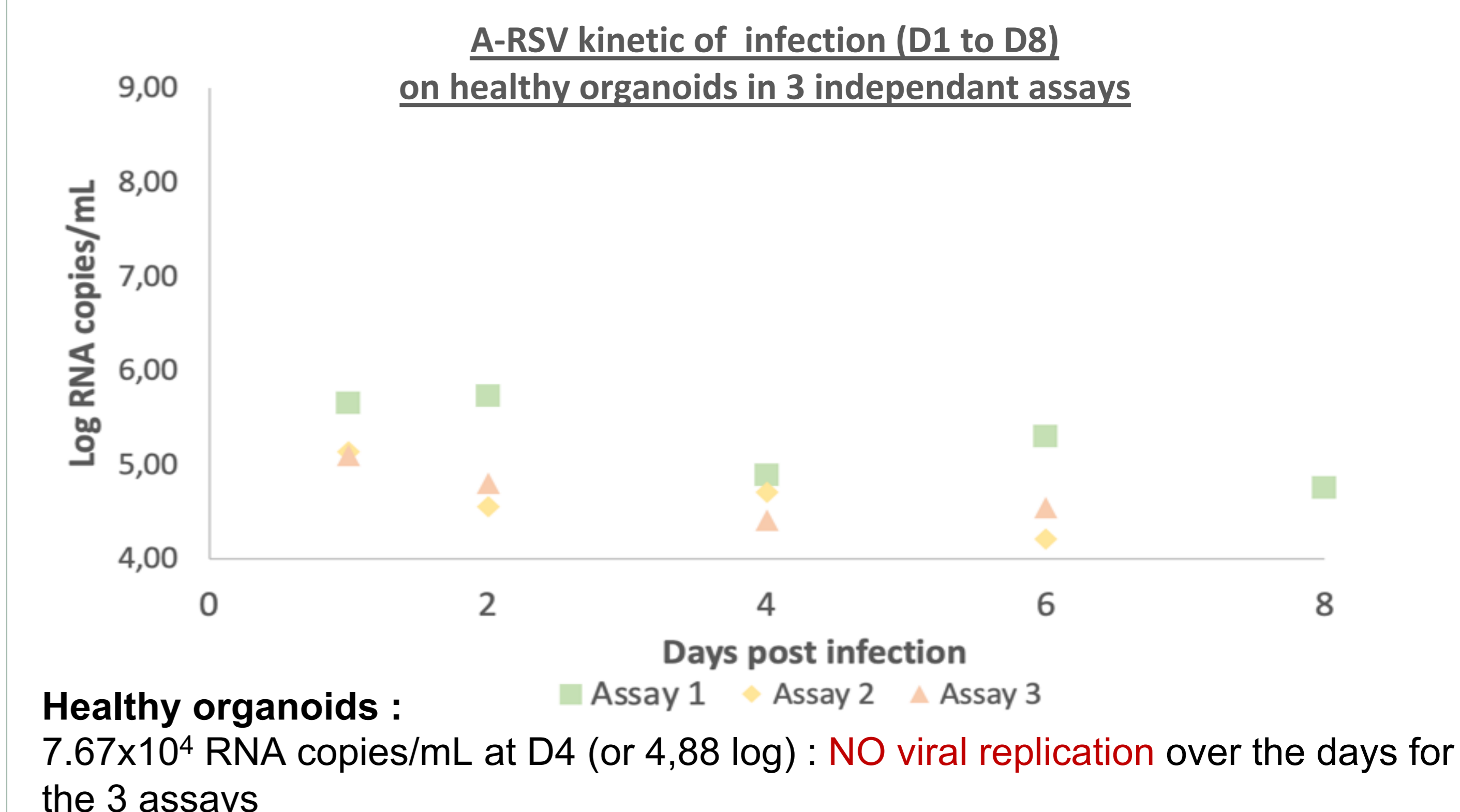
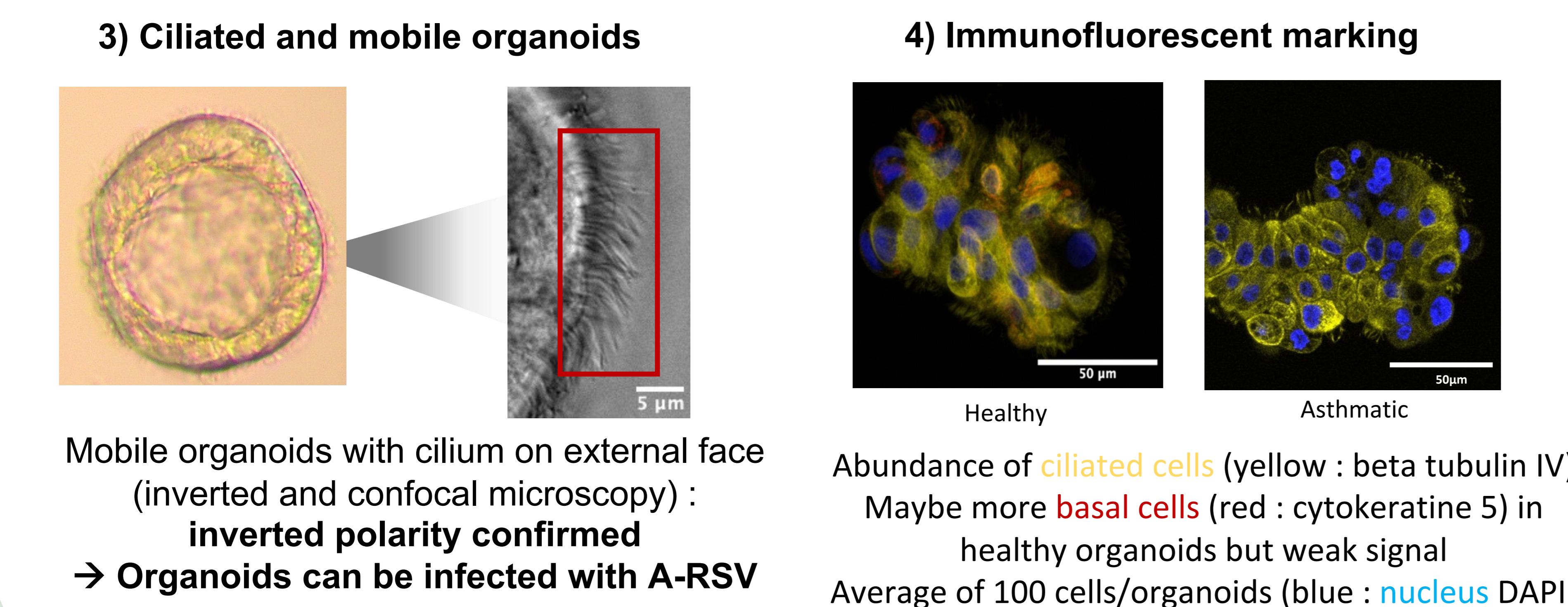
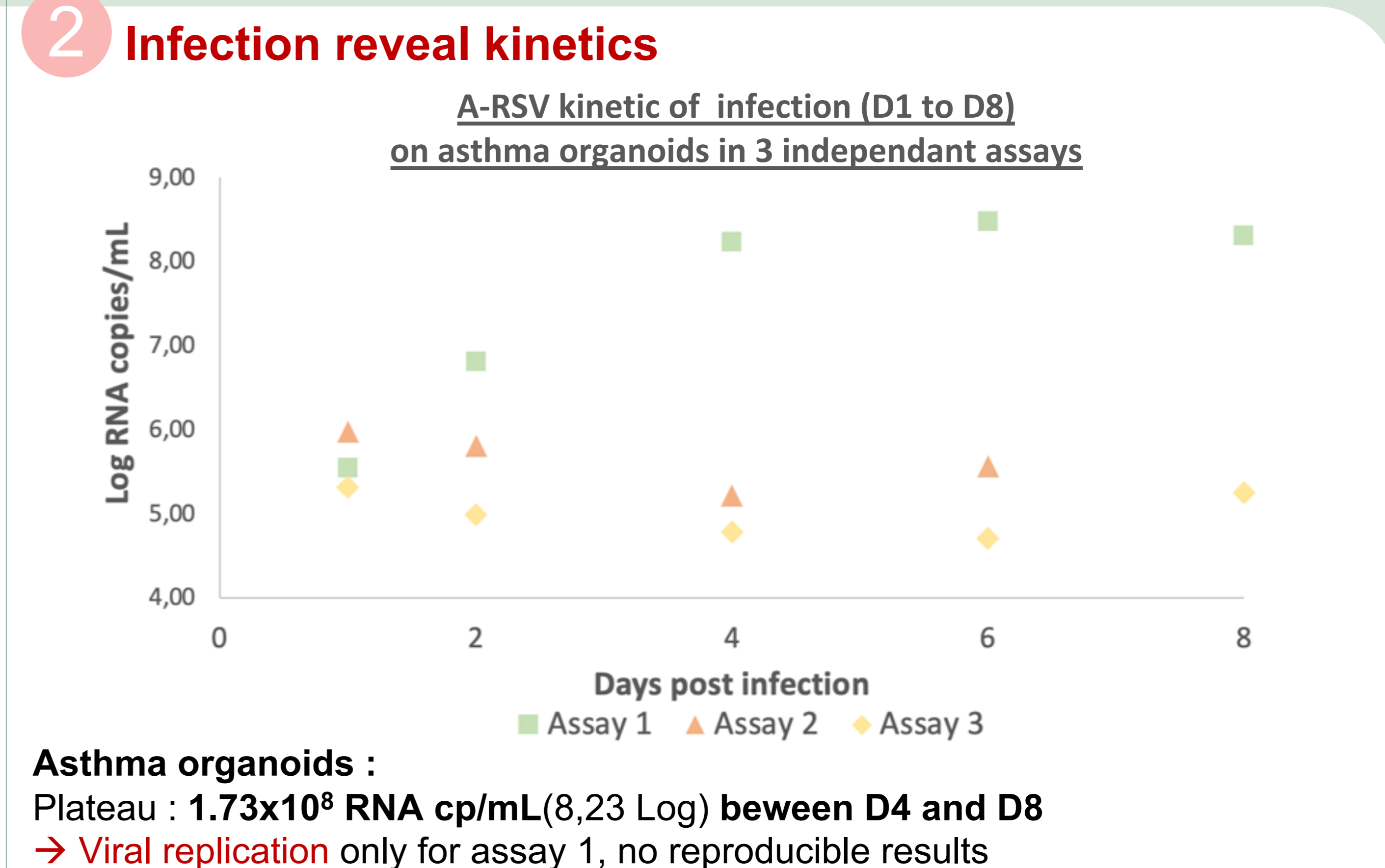
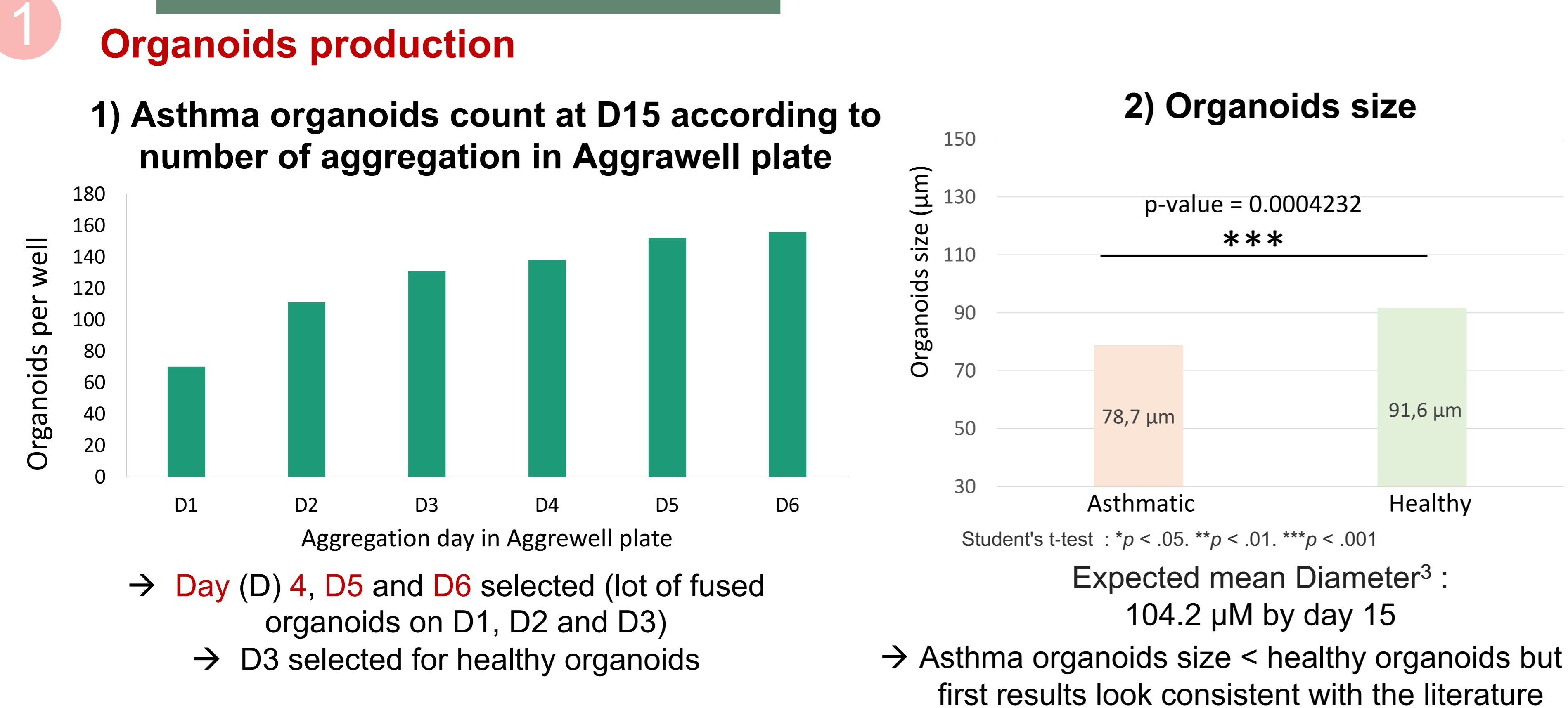
- 2) Successful production
- Analyse the impact of **A-RSV** infection on asthmatic organoids

Compare to a control (healthy cells)

Materials and methods



Results



Conclusions

The production of reversed polarity organoids from bronchial cells of asthmatic patients has been a success. The results will be used for larger projects such as the development of **personalized medicine**. Organoids will be able to play a leading role in comparison to previous models (2D culture, ALI, animal experimentation) due to the **faithful reconstitution of tissue in vivo**.

The infection with A-RSV on asthma organoids is successful but result are not reproducible → hypothesis : work on infectious dose and ratio virus/number of organoids. RV infection on organoids and **co-infection RV/RSV** are in progress on this model

→ Need to improve model robustness by **adding immune** cells and work on infection **reproducibility**

Bibliography and Acknowledgements

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³ Stroulios, G. *et al* (2022). Apical-out airway organoids as a platform for studying viral infections and screening for antiviral drugs.
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