

Establishing immunocompetent respiratory infection models to study nasal mucosal immunity

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FACTS & FIGURES

Inno4Vac:

Innovations to accelerate
vaccine development and manufacture



Start

01-09-2021

End

28-02-2028



EU Contribution

€18,600,000

EFPIA Contribution

€20,742,552

Total

€39,342,522



Website



CHALLENGE

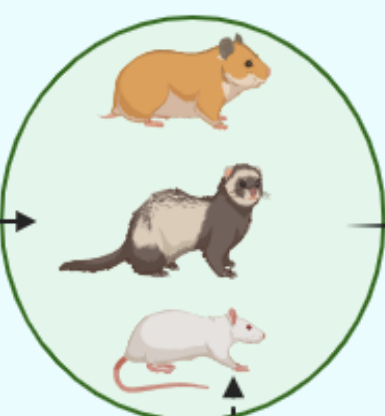
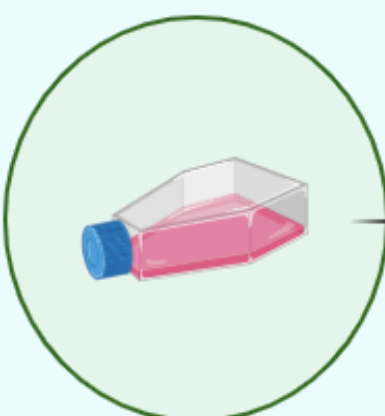
Current status:

Cell lines

Animal models

Clinical trials

Only 10% of
drugs succeed



Accelerating and de-risking the development of vaccines:

Human 3D
in vitro models



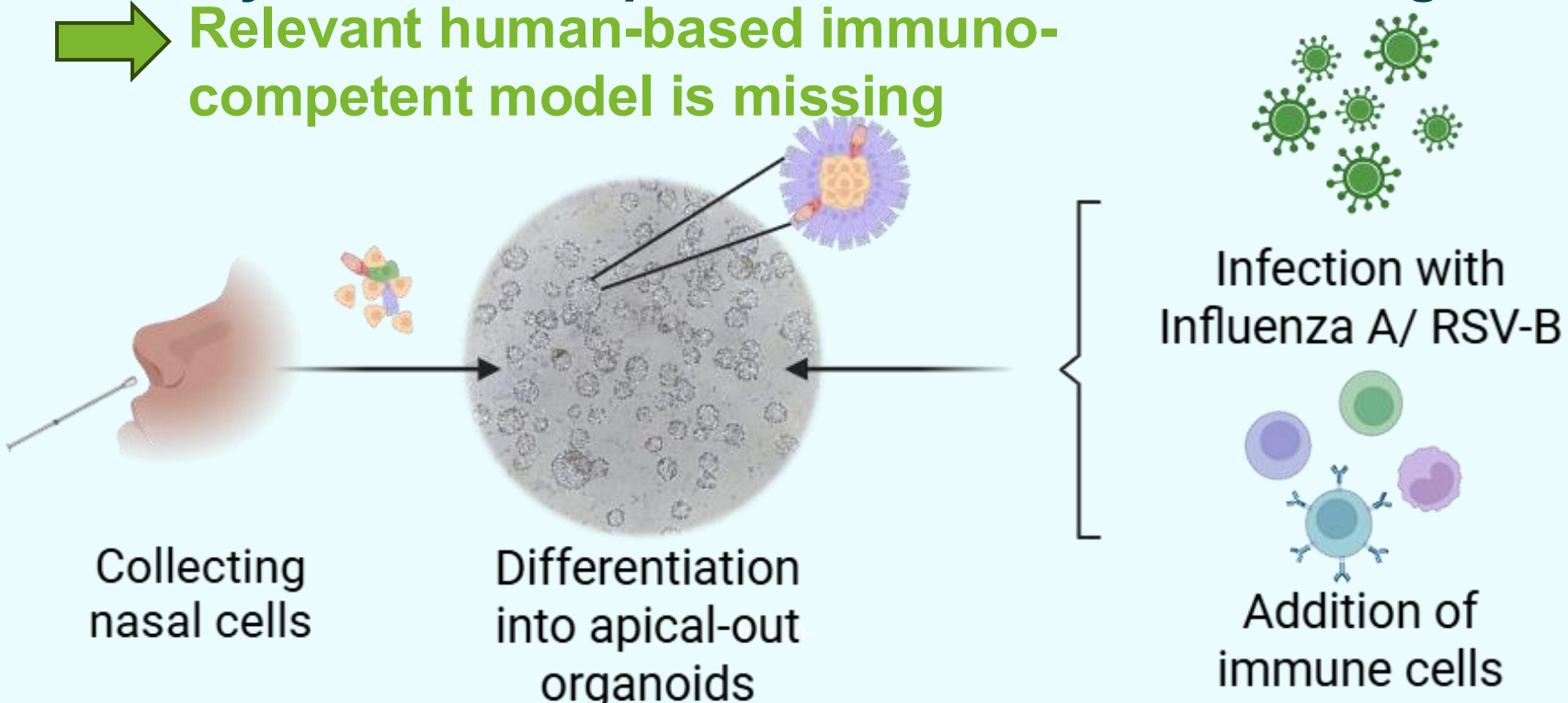
Pre-screen with human
cell-based models:

resources/money/
time/animals

APPROACH & METHODOLOGY

1. Developing organoid-based respiratory infection models to study anti-viral responses and test anti-viral drugs

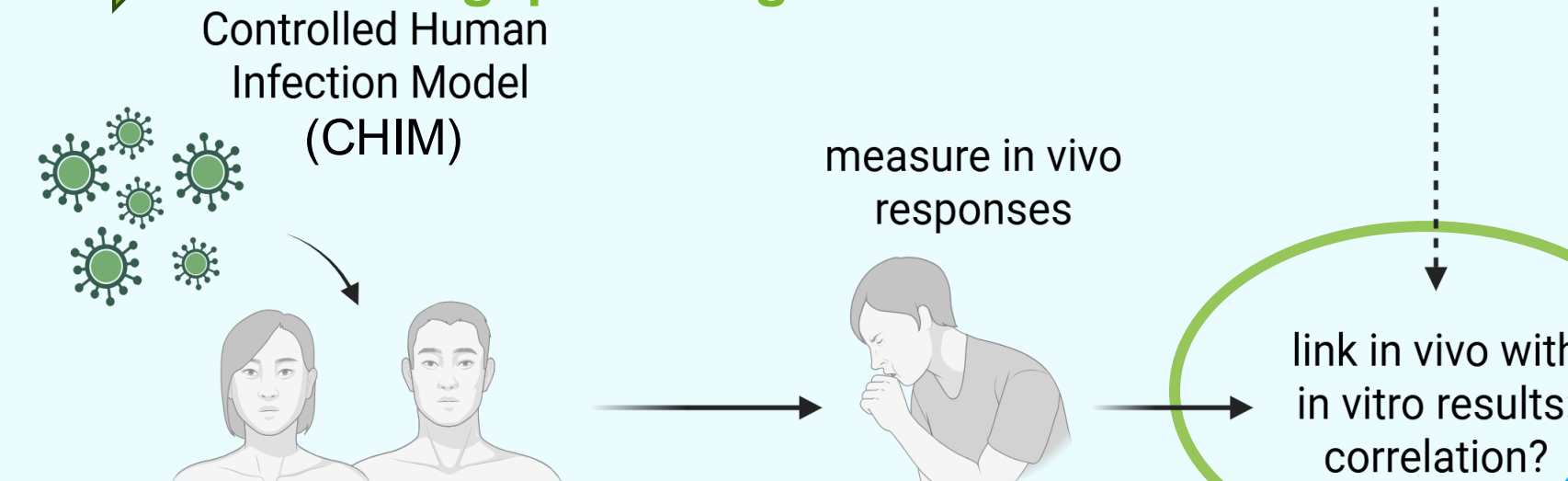
➔ Relevant human-based immuno-competent model is missing



2. Comparing in vitro and in vivo anti-viral responses:

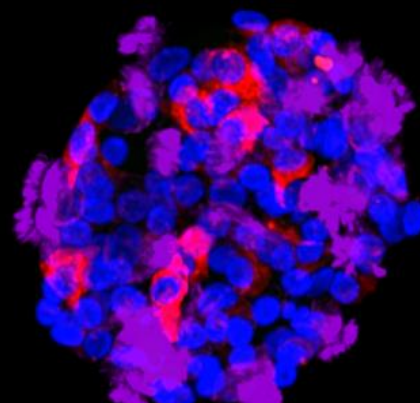
Is this model system clinically relevant? (planned)

➔ Validation gap missing in the field

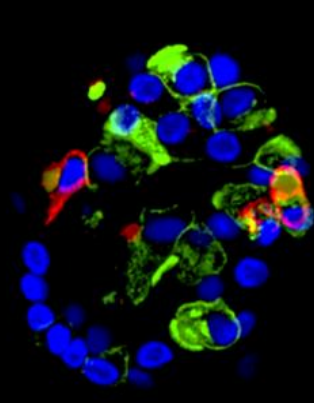


RESULTS

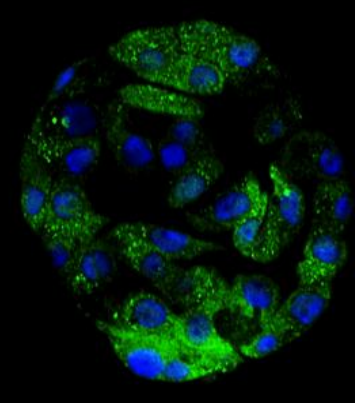
1. Organoids consist of differentiated cell types and express viral entry receptors:



Cell nuclei
Goblet cells
Ciliated cells



Cell nuclei
 α -2,3 sialic acid
 α -2,6 sialic acid



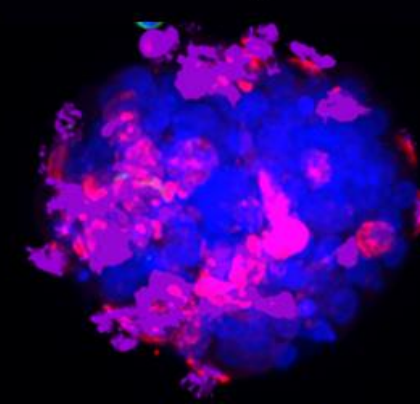
Cell nuclei
CX3CR1

2. Organoids can be infected by different respiratory viruses:

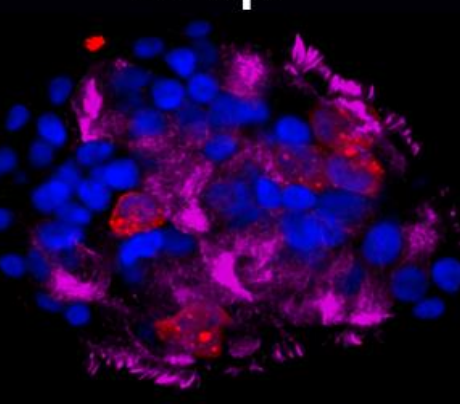
48 hpi

24 hpi

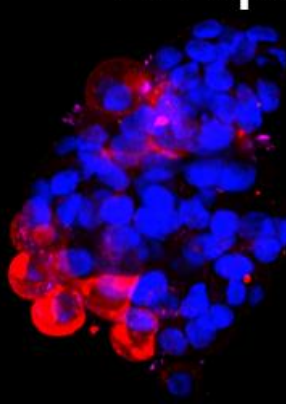
144 hpi



Cell nuclei
Influenza A H1N1
Ciliated cells



Cell nuclei
RSV-B
Ciliated cells



3. Influenza-specific T cells inhibit viral replication:

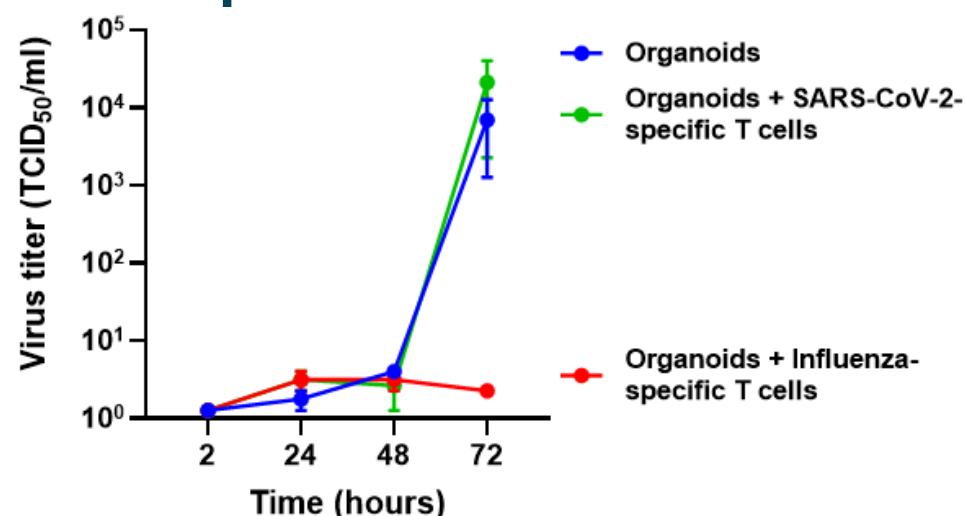


Figure legends
1. & 2. Organoids were fixed, permeabilized and stained. Z stacks were made using a confocal microscope.

3. Organoids (n=2 donors) were incubated for 2, 24, 48 and 72 hours with or without autologous virus-specific T cells (5:1 T cell:organoid cell ratio) in the presence of Influenza A H1N1 (0.01 MOI). TCID₅₀ assays with MDCK cells were used to quantify viral titers in supernatant

We have developed an immunocompetent organoid model that will be validated within Inno4Vac using in vivo CHIM samples, thereby strengthening the translational relevance

VALUE OF IMI COLLABORATION

1. Effective collaborations with academic researchers and industry partners (i.e. GSK & Sanofi)
2. Aligning research questions with real-world clinical and industry needs
3. Developing consensus-based methodologies and standardized procedures across institutions

CAREER IMPACT

1. Gained experience in working in a large, international, multidisciplinary consortium
2. Expanded professional network across Europe and sectors
3. Worked at the academia-industry interface

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