A roadmap for regulatory implementation of in vitro models for evaluation of vaccine efficacy

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Introduction

The Inno4Vac Aim: Facilitate use of in vitro models in **preclinical and clinical studies** in vaccine development**.**

Next-generation human *in vitro* 3D infection models for gastro-intestinal (GI), respiratory (RESP) and urovaginal (UV) mucosae that include relevant immune system components

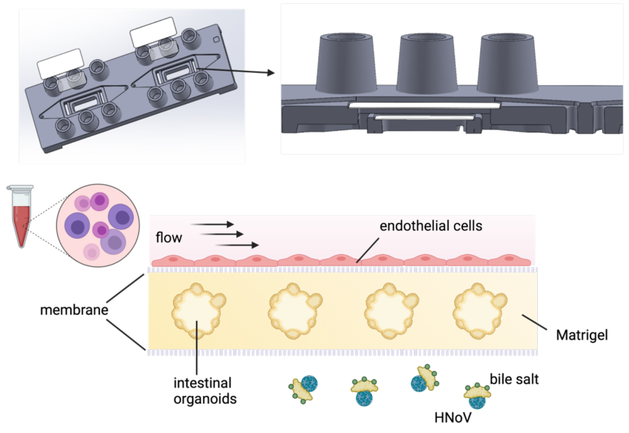
- ❖ *Clostridium difficile*, Norovirus (GI)
- ❖ Respiratory Syncytial Virus, Influenza Virus (RESP)
- ❖ *Neisseria gonorrhoeae*, Herpes Simplex Virus-2 (UV)

Methods

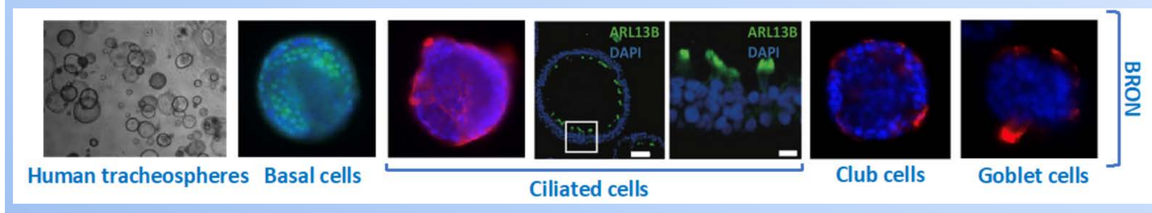
We conducted a workshop with model developers, industry and regulators in 2022 to gather regulatory feedback on:

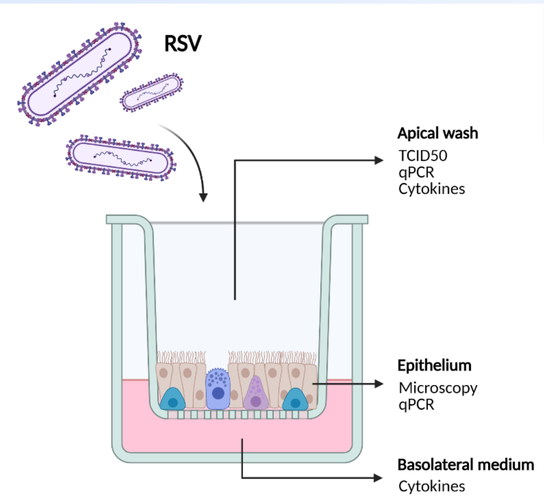
- ❖ **Choosing applications** for models
- ❖ Model **specifications and qualification**

From this feedback, a technical roadmap was created to assist models in identifying **the attributes or characteristics necessary to succeed** in their chosen applications. The roadmap also helps identify necessary standards, assays and comparators.



Left: intestinal organoid on chip
Right: primary bronchial epithelial cells at air liquid interface
Below: bronchiolar organoid





Results

Key Findings

Choose Applications Thoughtfully

How can the model determine if a vaccine candidate will succeed/fail?

Be Relevant

Accurately model the essential human response to infection

Add Value over existing assays

Increase scientific relevance, predictability and number of insights

Technical Roadmap

Define the **essential features** of the *in vivo* infection context

Use **human clinical data** as a reference

- Identify weaknesses of current assays
- Identify defined readouts of infection parameters the model captures well
- Identify assays to measure essential model features
- Identify sources of clinical data
- Identify traceable controls, standards and reference materials
- Identify established and accepted comparators for infection readouts

Further Considerations

- ❖ **Choosing an application is a prerequisite** for completing the technical roadmap successfully. A lack of or poorly defined application will not identify meaningful features or functions for the model.
- ❖ A comprehensive understanding of not only the model tissue, but also appropriate disease pathology is required for the success of the technical roadmap.
- ❖ Demonstrating improvement over traditional assays is crucial to convincing regulators to accept model data.

Conclusions

- ❖ The technical roadmap is an efficient method to identify model attributes and needs critical for success in regulatory settings
- ❖ Outputs can inform model acceptance criteria and qualification
- ❖ The technical roadmap can be used to prioritize work or make go/no go decisions

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