

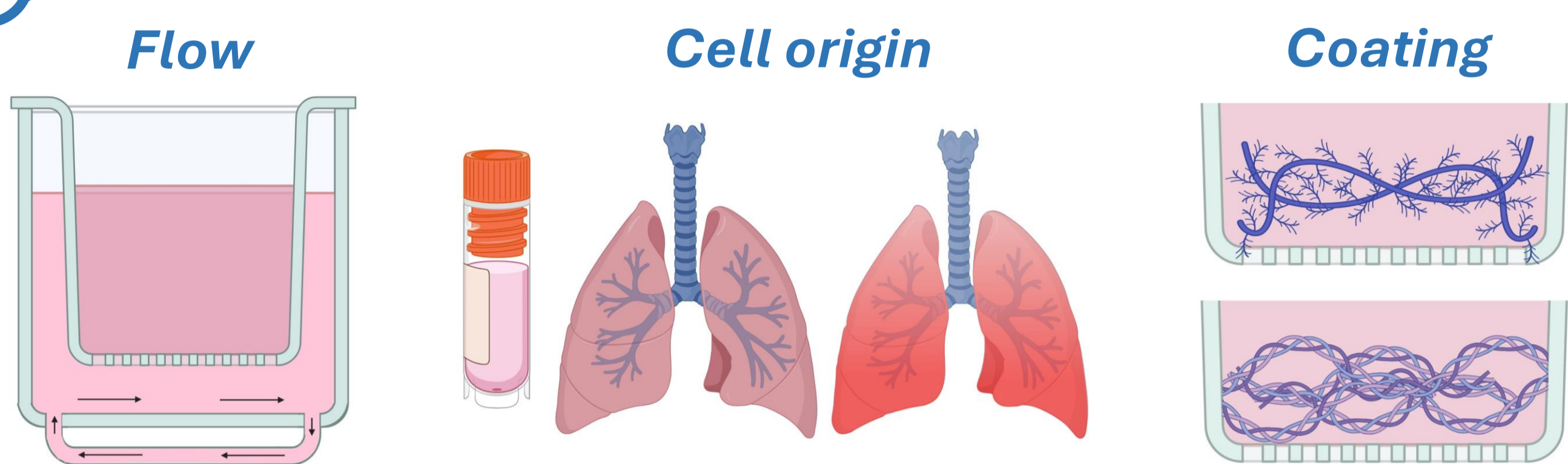
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## 1 Introduction

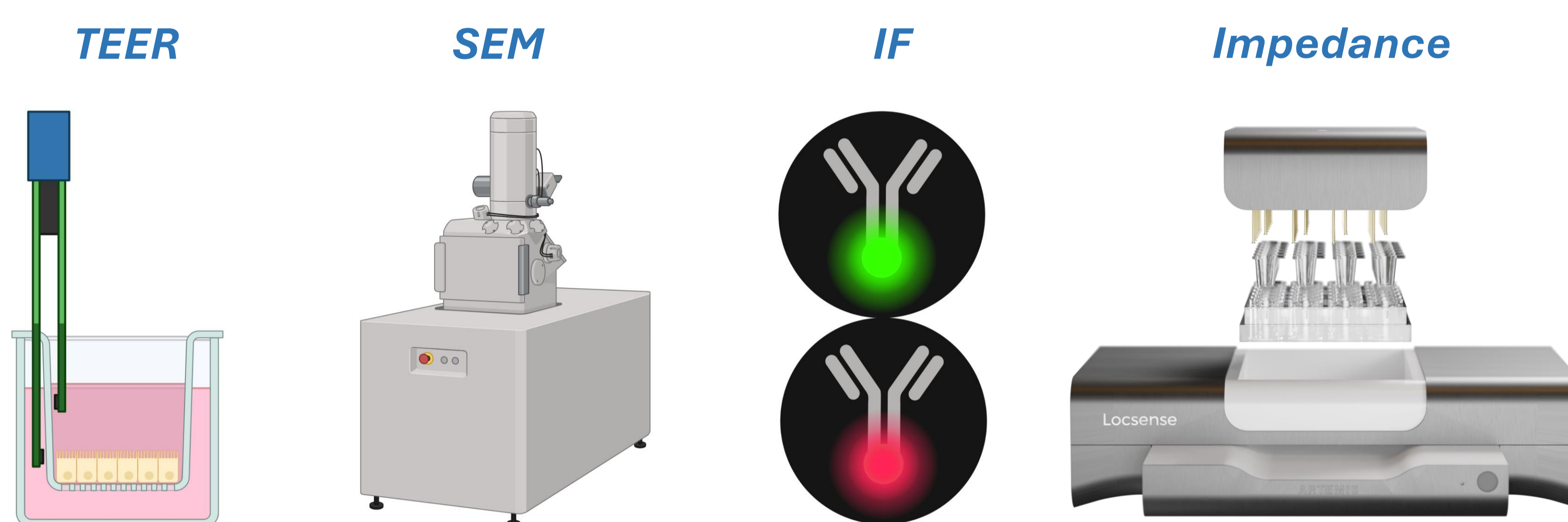
- COPD is a major global cause of mortality, but current treatments only provide symptomatic relief.
- Limited progress in developing new therapies is attributed to the absence of reliable lung models for testing.

**We formulated a healthy and COPD *in vitro* lung mimic that incorporates (1) microcirculation (2) extracellular matrix (ECM) and, (3) a diseased COPD primary cell line. To assess our model, we created an extensive quality control (QC) for barrier integrity and physical characteristics.**

## 3 Methods

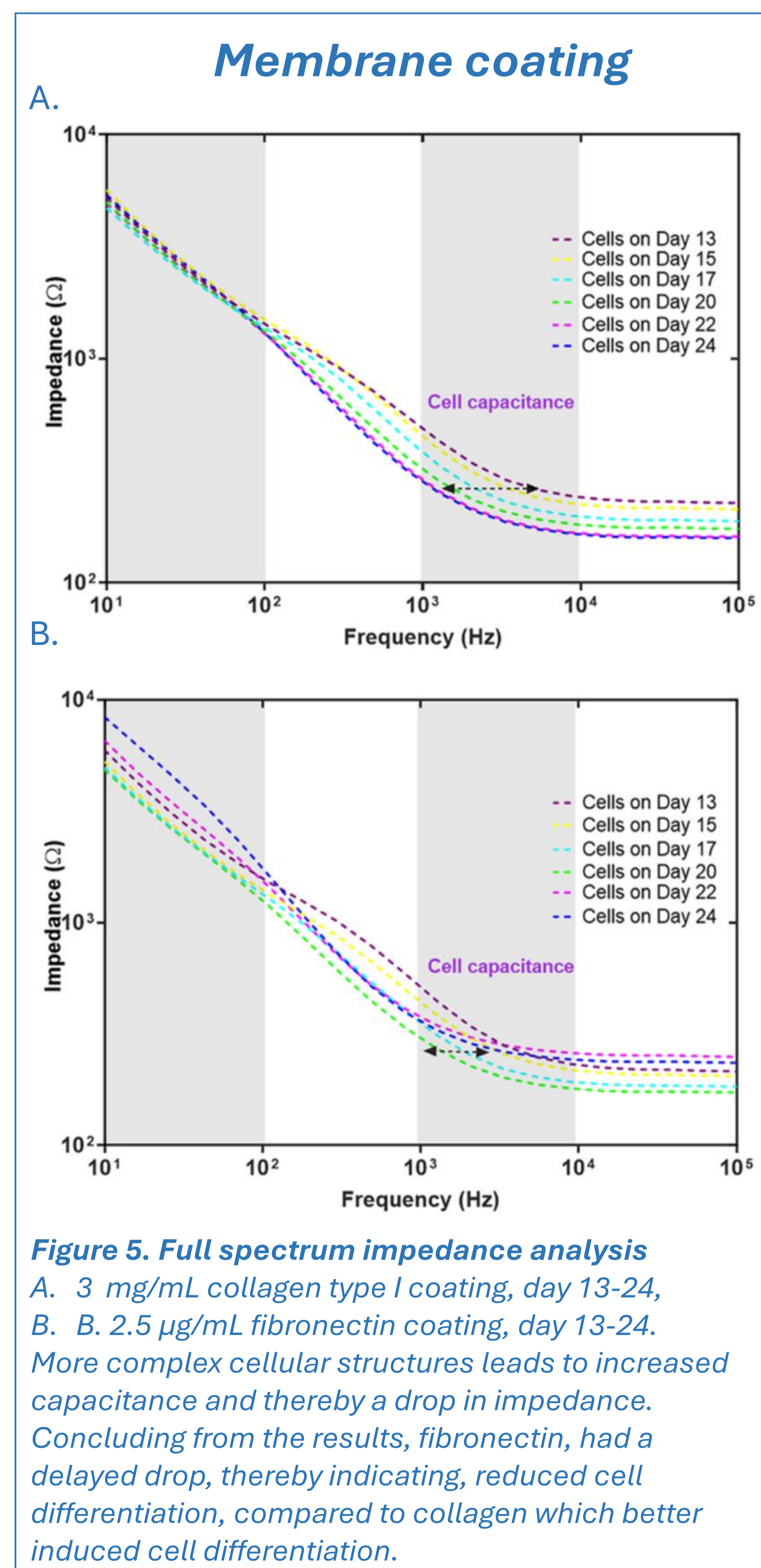
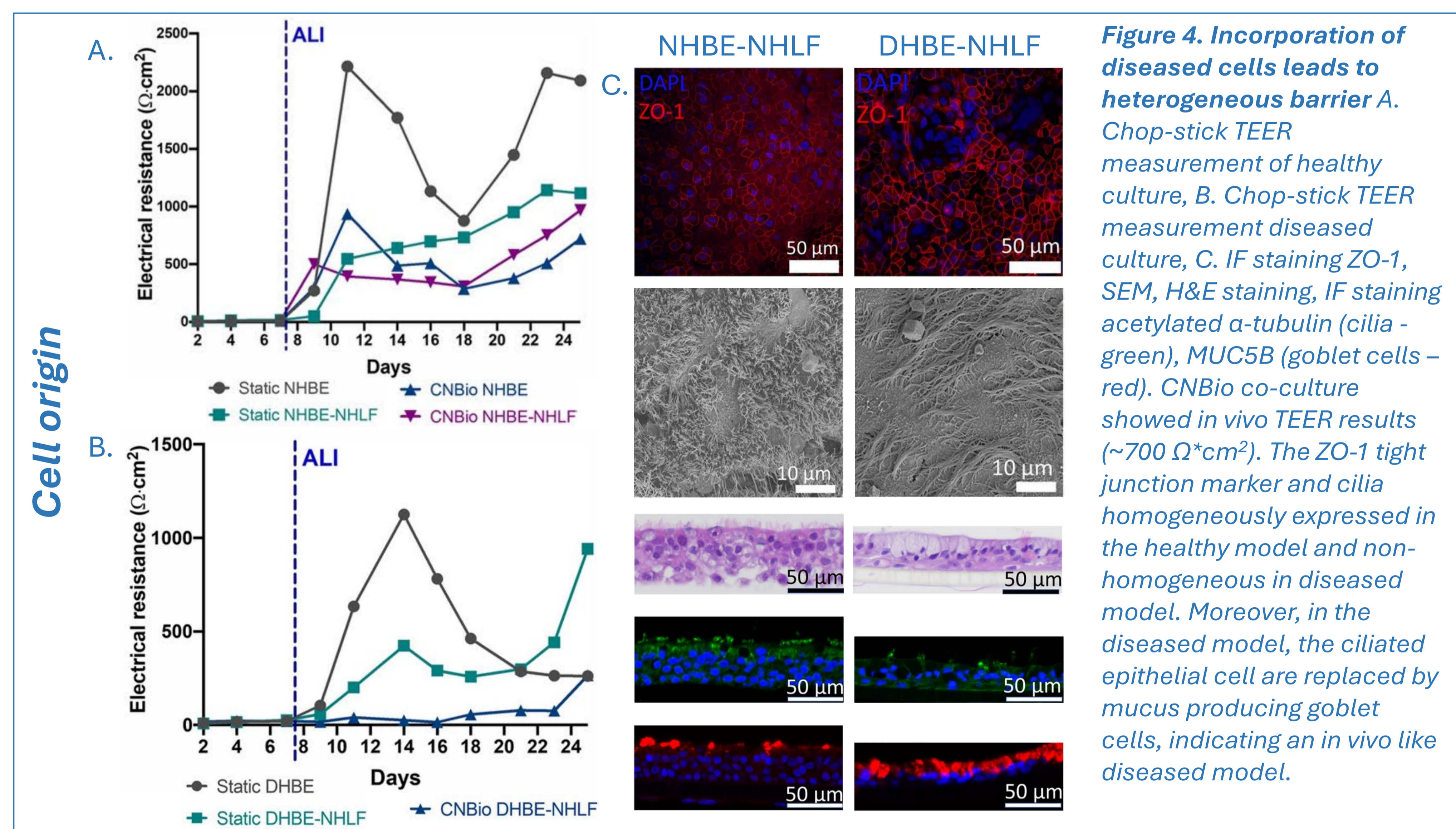
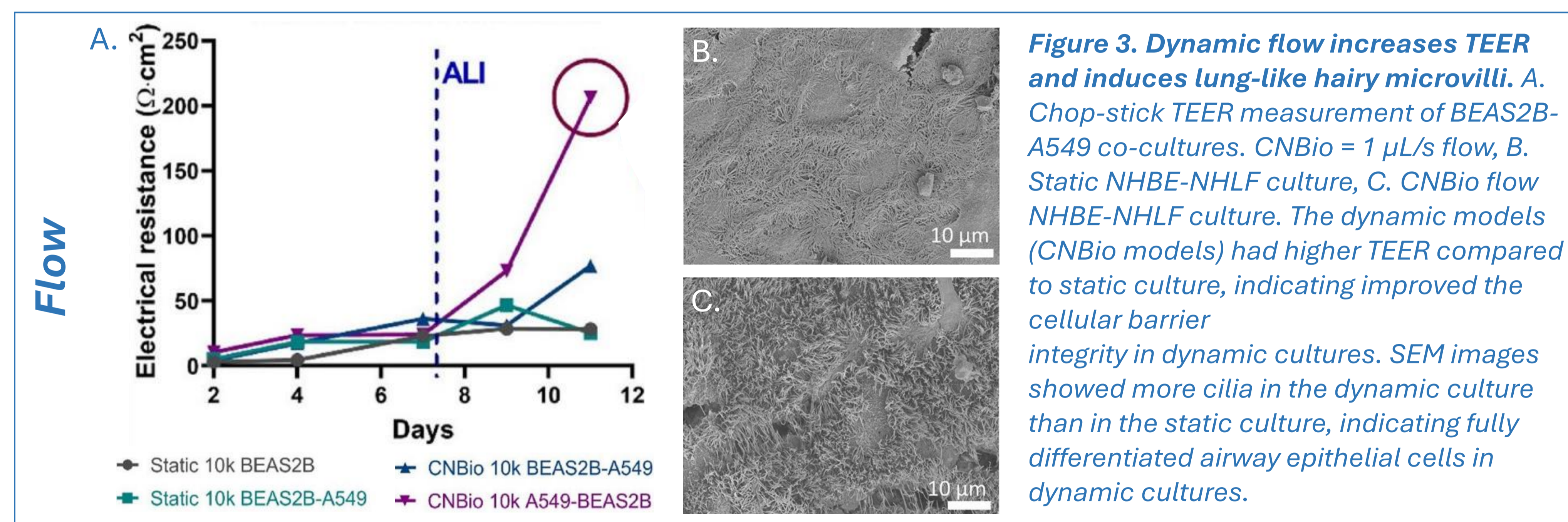


**Figure 1. Model improvement parameters.** (1) Flow: CNBio's PhysioMimix<sup>®</sup> microfluidic system was used to emulate physiologically relevant conditions, (2) Cell origin: immortalized cell line (bronchial epithelial cell line (BEAS2B), lung cancer cell line (A549)), were compared to healthy primary cells (normal human bronchial epithelial cells (NHBEs) normal human lung fibroblasts (NHLFs)), and diseased primary cells (diseased human bronchial epithelial cells (DHBEs)), and (3) Membrane coating: fibronectin and collagen-I were compared to replicate biochemical aspects



**Figure 2. Quality control.** (1) Transepithelial electrical resistance (TEER) to assess barrier function, (2) scanning electron microscopy (SEM) to analyze the cilia of the cells, (3) Immunofluorescence (IF) to analyze ZO-1 tight junction expression, and (4) full spectrum impedance spectroscopy to analyze cellular development.

## 4 Results



## 5 Conclusions

- Dynamic flow improved the barrier function and cell differentiation
- Collagen-I coated Transwells improved cell differentiation
- Replacing immortalized cell lines with primary cell improved the barrier and differentiation
- Using diseased human bronchial/tracheal epithelial cells COPD was effective in recapitulating the features observed in COPD patients

## 6 Personalia

