

## **Poster 32** Development of advanced in-vitro human bronchial epithelial models in COPD enabled by thoracic surgery translational research

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### **Background**

Careful analysis of cellular differentiation in the human bronchial epithelium is important to understand patterns that characterize chronic lung diseases/CLD. A highly standardized organoid-like long-term culture based on primary human bronchial epithelial cells/pHBECs from non-CLD and end-stage COPD patients was recently developed and optimized in our laboratory (Stoleriu et al., Thorax 2024).

### **Methods**

Over 200 human bronchial tissue samples from CLD patients undergoing lung transplantation at the Thoracic Surgery Division (LMU) between 01.2018-01.2025 were processed at the CPC-M bioArchive (Institute for Lung Health and Immunity), the LMU Hospital, and the Asklepios Clinic Gauting. Long-term pHBECs cultures isolated from non-CLD and COPD patients at air-liquid-interface were used for comprehensive cell characterization after nanoparticle exposure via ALICE CLOUD system, a bioreactor mimicking environmental nanoparticle exposure.

### **Results**

COPD-IV cultures were characterized by a prosecretory phenotype at the expense of the multiciliated epithelium, resulting in an increased resilience towards particle-induced cell damage. Single cell RNA-seq analysis of pHBECs revealed a novel basal cell population, driving the hypersecretory phenotype in end-stage COPD cultures. The basal cell state was characterized by overrepresentation of Wnt and Notch canonical airway pathways involved in secretory and multi-ciliated cell differentiation.

### **Conclusion**

Thoracic surgery translational research is able to update knowledge on cellular landscape of the human bronchial epithelium and lung cell atlas, thus contributing to a better understanding of COPD pathogenesis driving therapeutic ideas.