

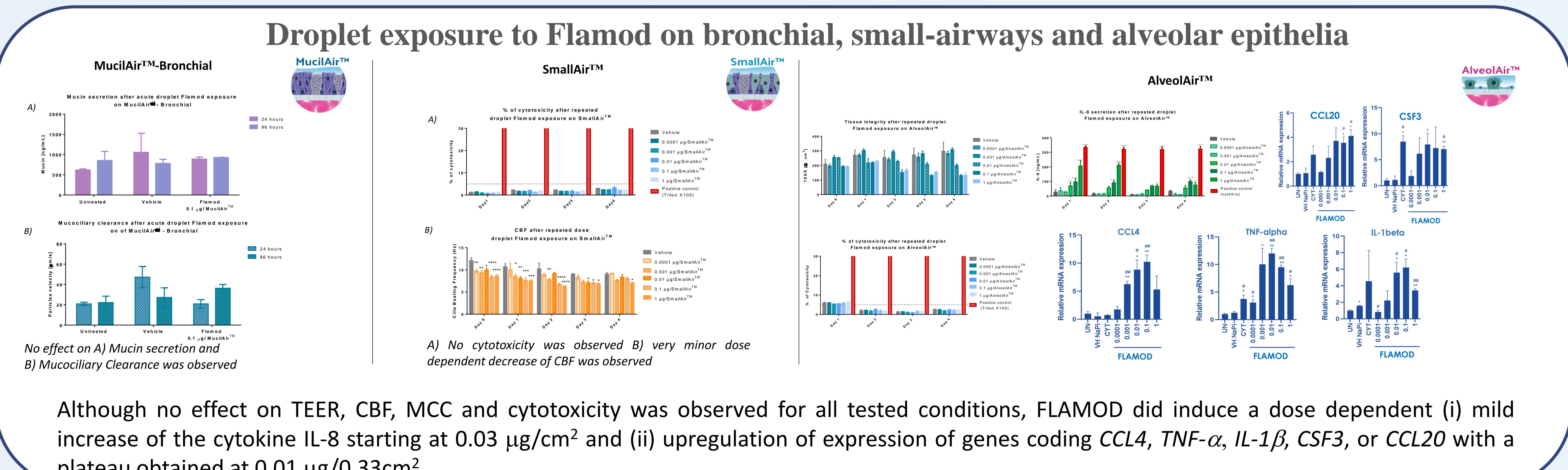
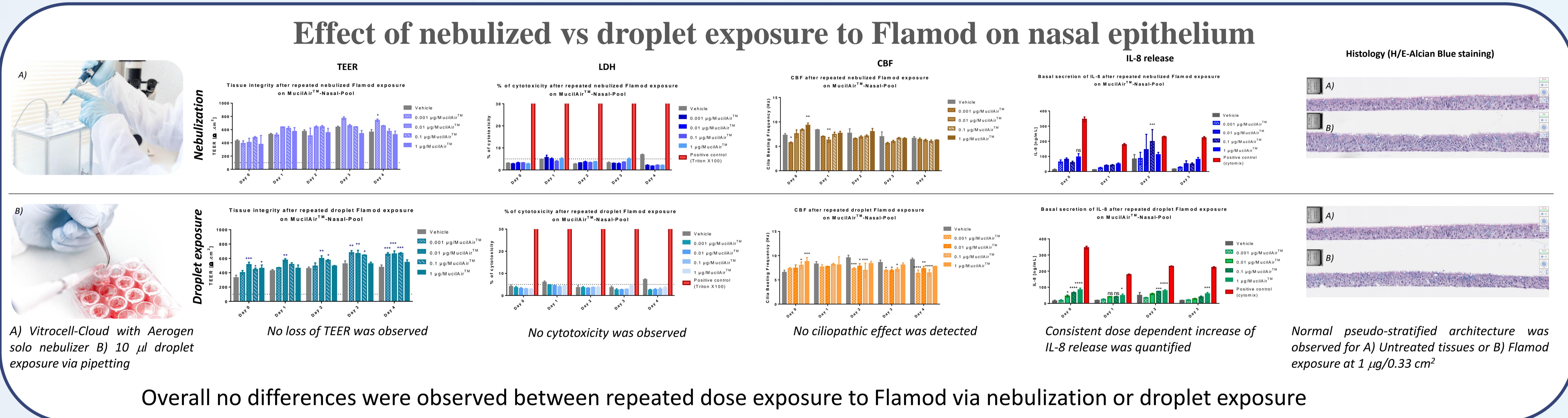
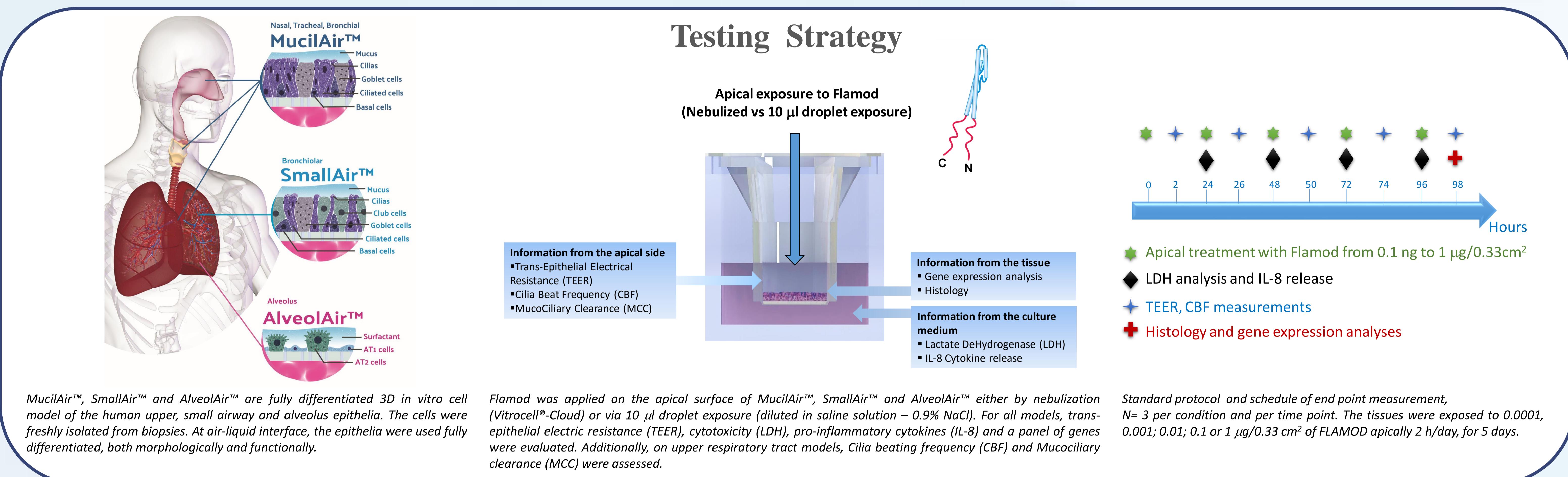
Evaluation of the local tolerance of flagellin aerosol therapy (FLAMOD) on primary human cell-based 3D *in vitro* nasal, bronchial, small-airway and alveolar models

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Bacterial pneumonia is a major cause of morbidity and mortality in humans. To counter this, the European consortium FAIR aims to develop more efficient therapies, based on recombinant flagellin FliCΔ174-400, to treat pneumonia with or without a concomitant uptake of antibiotics. Recombinant flagellin works as an immune-modulator which boosts the innate immunity of airway epithelia via the activation of TLR-5. Delivery of recombinant flagellin to the lung via nebulization has the advantage of directly targeting the airway epithelial cells while conferring minimal systemic immune activation.

We herein describe the local tolerance evaluation of a flagellin-based formulation (FLAMOD) for mesh-nebulization on primary human airway and lung epithelial models. Regional effects on fully differentiated nasal, bronchial (MucilAir™), small airways (SmallAir™) and alveolar (AlveolAir™) epithelial function were evaluated using a multi-parametric approach and a dynamic analysis.



Conclusion

Altogether, FLAMOD was well tolerated by nasal, bronchial, small airway and alveolar epithelia. Apical exposure induced biomarkers upregulation, thus highlighting FLAMOD's immunomodulation potential all along the respiratory and lung mucosa.