Cellular growth optimization on a Dynamic model for ALveolar Interface (DALI) and nanomaterials aerosolization optimization to compare cellular effects on a 3D static and dynamic human lung model.

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Introduction:

To improve the physiological relevance of *in vitro* lung models and to investigate the effects of aerosolized nanoparticles under mechanical strains, a sophisticated bioreactor system called DALI (Dynamic model for ALveolar Interface) was used which is capable of simulating breathing motions and cellular media flow. The DALI-bioreactor is composed of an aerosol generator in the apical part and separated by a semi-permeable membrane made of Bionate® from the basal part, where cellular media flow was integrated. The DALI system has been developed by project partners (University of Pisa) within the framework of PATROLS (H2020). It features an air-liquid interface (ALI), cellular culture media flow to mimic blood flow, lung breathing by membrane stretching made of Bionate® and an aerosol deposition system for nanoparticle exposures. The aim was to optimize the lung cell growth on this biocompatible membrane with different coatings under static and breathing conditions.

Results:

The membranes used were composed of Bionate®, which is biocompatible and stretchable. Bionate® sheets represents the extracellular matrix of the alveoli, used to reproduce the cyclic motion during breathing because it ensures membrane flexibility and enhance the cell adhesion. *In vitro* experiments were carried out using the human alveolar epithelial cell line A549 on uncoated, human umbilical artery endothelial cells (HUAEC), and rat-tail collagen (RTC) coated membranes under submerged conditions to optimize cell growth. The A549 cells reached a higher degree of confluency with the coated membranes. When cells were cultured for 1 day submerged and 2 days at ALI on RTC coated membranes in bioreactors, optimal cell growth was observed.

Conclusion:

In conclusion, A549 cells are well adapted to a culture in DALI-bioreactor and a confluent cell layer could be obtained that remained stable under stretching conditions mimicking breathing conditions. In future experiments, A549 cells will be exposed to aerosolized (nano)particles in DALI-bioreactor with and without breathing and cell effects will be compared.

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