COPD-on-Chip: Validation and Technical Development of a Continuous Flow Inhalation Chamber

Aurélien Dorn

Supervisors: Prof. Dr. Olivier Guenat, Dr. Arunima Sengupta
Institution: University of Bern, ARTORG Center for Biomedical Engineering Research
Examiners: Prof. Dr. Olivier Guenat, Dr. Arunima Sengupta

Introduction

Airborne nanoparticles (NPs) and cigarette smoke (CS) are major concerns for pulmonary health globally as they represent major risks factors for chronic lung diseases. Organs on chip technologies present promising platforms to study the effects of these air pollutants in vitro. Hence advanced lung-on-chip models along with exposure systems to mimic inhalation are needed to develop a valuable physiological model for COPD.

The aim of this study is the validation and the technical development of two inhalation systems: the aerosol nebulizer (Cloud AX12) for nanoparticles exposure and the continuous flow exposure system (CF-AX12) for cigarette smoke exposure.

Materials and Methods

Different suspensions of NPs were nebulized with the Cloud AX12 System (Vitrocell systems GmbH, Waldkirch, Germany) to asses the effects of various parameters on the dose deposition inside the chamber. A suspension of SiO2 NPs was nebulized on human alveolar cells to assess the biological validation of the system.

The CF-AX12 exposure system (Vitrocell systems GmbH, Waldkirch, Germany) was used to conduct cigarette smoke exposures experiments following the Health Canada Intense (HCI) standard smoking regime. The smoke distribution in the cell wells was tested using the native autofluorescence signal from tobacco. Cells cultured in the advanced lung-on-chip model AX12 were exposed to the cigarette smoke to further validate the system.

Results

The Cloud AX12 demonstrated homogenous dose deposition in the wells within the exposure chamber. Nebulization of SiO2 NPs induced significant variation in transbarrier electrical resistance (TER) [Fig.1] and viability of the cells, confirming alveolar barrier disruption due to the toxic dose of these NPs.

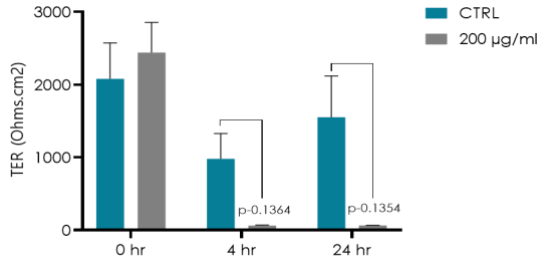

Fig. 1 TER evolution on the AX12 after the SiO2 NPs exposure. (n=3)

The CF-AX12 showed equal distribution of smoke in the cell wells (±15%) [Fig.2]. Furthermore, CS exposure on human alveolar cells cultured in the AX12 was found to demonstrate significant barrier disruption measured by TER decrease.

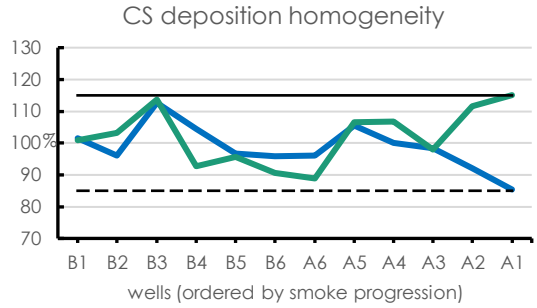

Fig. 2 Relative cigarette smoke deposition between wells (n=2). Acceptance range (±15%) indicated by the CF-AX12 manufacturer.

Discussion

The preliminary results confirm the relevance of such in vitro inhalation systems. However, additional exposure data are needed to thouroghly validate both systems.

In combination with the AX12, the Cloud AX12 and the CF-AX12 systems present great potential to model in vitro inhalation of toxic compounds, nanoparticles and cigarette smoke exposure.

References

[1] Ding et al., Quartz crystal microbalances (QCM) are
suitable for real-time dosimetry in nanotoxicological studies using VITROCELL®Cloud cell exposure systems, 2020.

[2] Thorne D. and Adamson J., A review of in vitro cigarette smoke exposure systems, 2013.

[3] Benam et al., Biomimetic smoking robot for in vitro inhalation exposure compatible with microfluidic organ chips, 15: 183-206, 2020.

Acknowledgements

The OOC group members at ARTORG center were a great support during my thesis and I am very thankfull for their help. The important contribution of AlveoliX AG and Vitrocell systems GmbH is gratefully acknowledged.