The human epithelial lung cell line “A549” as a suitable tool in in vitro inhalation toxicity testing

Detlef Ritter, Jan Knebel
Fraunhofer ITEM, Germany

Background
- Air-lifted interface (ALI) culture methods represent a state-of-the-art approach for investigations on biological effects of inhalable, gases, vapors or aerosols.
- Usually, such investigations aim at a high in vivo relevance by application of more complex cell models such as primary cells, 3D co-cultures or similar.
- Due to a demand for high numbers of cultures for routine testing especially in toxicity screening studies, “cheap and easy-to-use” cell culture models are urgently needed.

Objectives
- The human alveolar epithelial type-II like cell line A549 represents a comprehensively characterized culture model (> 20,000 references)
- Although lacking tight-junctions and also with a carcinogenic origin, many studies have also confirmed primary characteristics (CYP-expression, surfactant biosynthesis, etc.)
- The objective of this overview is to highlight the qualities of A549 ALI cultures in inhalation toxicity testing in vitro with respect to applicability, in vivo relevance and reproducibility
- Summary of selected inhalation in vitro data from studies of the ITEMs lab during recent years

Inhalation toxicity testing in vitro: Methods

Applicability to gases, vapors and aerosols from test items, experimental or environmental atmospheres

In vivo relevance by in vitro ↔ in vivo correlations

Reproducibility of in vitro inhalation toxicity data over years

Conclusions
- A549 human lung ALI cultures represent a relatively easy-to-use biological model that can be made available in the lab in large culture numbers (e.g. > 100/week) at moderate costs.
- Inhalation toxicity studies using A549 human lung ALI cultures have been shown to lead to a relevant prediction of in vivo toxicity.
- If applied under appropriate conditions, considerable reproducibility can be achieved, necessary for establishment of in vitro toxicity databanks and historical lab controls.
- These characteristics qualify A549 ALI cultures as biological models in first stages of tiered in vitro inhalation approaches, mechanistic studies may follow applying more complex cell models.