



The Use of a Human In Vitro Airway Epithelium Tissue Model (EpiAirway) for Metabolism, Toxicity Screening and Drug Delivery Applications

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In vitro airway models are urgently needed as alternatives to animal testing for compliance with REACH legislation. The current poster describes a highly differentiated in vitro model of human tracheal/bronchial epithelium (EpiAirway). The model is produced by culturing normal human tracheal/bronchial epithelial cells on microporous membrane inserts at the air-liquid interface. Here we present physical and biochemical characterization of EpiAirway morphology, barrier function and drug metabolizing capability. Histological cross-sections of EpiAirway cultures show an in vivo-like, pseudo-stratified structure with numerous apical cilia. The useful lifespan of the cultures is at least 1 month. Dot blot analysis demonstrates apical mucin secretion. Transmission electron microscopy reveals ultrastructural detail of cilia and tight junctions between cells. Transepithelial electrical resistance (TEER) of 300-500 ohms x cm² demonstrates functionality of tight junctions. RT-PCR gene expression experiments were conducted to evaluate baseline and inducible expression of CYP isoforms in EpiAirway cultures derived from 4 individual donors. CYP1A1 (weak), CYP1B1, CYP2A6, CYP2B6 (weak), CYP2C8 (weak), CYP2C19, CYP2D6, CYP2E1 and CYP3A5 are constitutively expressed, while CYP3A4 and CYP3A7 were not detected. 3-Methylcholanthrene (3MC) strongly increased expression of CYP1A1 and slightly increased CYP2B6 and CYP2C8 expression. Thus, CYP expression in EpiAirway shows a high concordance with CYP expression of in vivo human bronchial epithelium. Total GST activity in EpiAirway was demonstrated by measuring conjugation of glutathione with 1-chloro-2,4-dinitrobenzene. The results demonstrate that the EpiAirway model possesses in vivo-like physical and biochemical attributes for evaluating airway irritation, toxicity potential, metabolism and delivery of drugs and environmental/occupational chemicals.

Keywords: EpiAirway, REACH, CYP expression, TEER, metabolism, delivery of drugs

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