



An In Vitro Model of Human Airway Epithelium (EpiAirway) for In Vitro Metabolism, Toxicity Screening and Drug Delivery Applications

Patrick Hayden, Robert Jackson, Jennifer Bolmarcich, Gina Stolper, Helena Kandarova, Mitch Klausner

[MatTek Corporation](#), Ashland, MA

ABSTRACT

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™) (Figures 2-3). The model is produced by culturing normal human tracheal/bronchial epithelial cells on microporous membrane inserts at the air-liquid interface (Figures 1, 4). The useful lifespan of the cultures is at least 1 month. Here we present physical and biochemical characterization of EpiAirway morphology barrier function and drug metabolizing capability morphology, capability. Histological cross-sections of EpiAirway cultures show an in vivo-like, pseudo-stratified structure with numerous apical cilia (Figure 2). Transmission electron microscopy reveals ultrastructural detail of cilia and tight junctions between cells (Figure 3). Dot blot analysis demonstrates apical mucin secretion (Figure 5). 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 isoforms in EpiAirway cultures derived from individual donors. (weak), CYP1B1, CYP2A6, CYP2B6 (weak), CYP2C8 (weak), CYP2C19 (weak), CYP2D6, CYP2E1 (weak) and CYP3A5 are constitutively expressed, while CYP3A4 and CYP3A7 were not detected (Figure 6). 3-Methylcholanthrene (3MC) strongly increased expression of CYP1A1 and slightly increased CYP2B6 and CYP2C8 expression (Figures 7-8). Thus, CYP expression in EpiAirway shows a high concordance with CYP expression of in vivo human bronchial epithelium. Finally total GST activity in EpiAirway was demonstrated by measuring conjugation of glutathione with 1-chloro-2,4-dinitrobenzene (Figure 9).

To be presented at EUROTOX 2007, October 7-10, 2007, in Amsterdam, The Netherlands