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Title: A human airway mucosa tissue model to investigate whooping cough

Dr. Maria 5566 Steinke maria.steinke@uni-wuerzburg.de [1], Prof. Dr Roy 5567 Gross roy@biozentrum.uni-wuerzburg.de [2], Susanne 5568 Bauer s.bauer@biozentrum.uni-wuerzburg.de [2], Prof. Dr Thorsten 5569 Walles Walles_T.htc@klinik.uni-wuerzburg.de MD [3] and Prof. Dr Heike 5570 Walles heike.walles@uni-wuerzburg.de [1]. [1] Department of Tissue Engineering and Regenerative Medicine, University Hospital Wuerzburg, Wuerzburg, Germany ; [2] Department of Microbiology, University of Wuerzburg, Wuerzburg, Germany and [3] Department of Cardiothoracic and Thoracic Vascular Surgery, University Hospital Wuerzburg, Wuerzburg, Germany .

Body: The pathomechanism of human obligate Bordetella pertussis eliciting whooping cough is not completely elucidated, yet. Tissue-engineered human airway models (TAM) are promising tools to investigate interrelations between B. pertussis and the airway mucosa. Our aim was to generate a TAM that closely resembles natural airway mucosa and to establish optimal conditions for infections studies with B. pertussis. Human bronchial epithelial cells (hBEC) and fibroblasts (Fb) obtained from surgical specimen were grown on a collagen scaffold derived from a porcine jejunum segment and cultivated in an airlift environment for two weeks. To establish optimal conditions for infection studies pieces of human bronchus biopsies were incubated with B. pertussis with varying incubation time, whereas untreated biopsy pieces served as controls. All samples were prepared for light and transmission electron microscopic analyses. Histologic evaluation of TAM sections revealed a pseudostratified respiratory epithelium consisting of ciliated, mucus-producing and basal cells. Kinocilia, cell-cell contacts and a continuous basement membrane were verified by ultrastructural analyses. Whereas hBEC remained at the apical side of the collagen scaffold, Fb migrated into the scaffold. Infection of bronchus pieces with B. pertussis led to cytoplasmatic vacuoles, damaged mitochondria, cell extrusions and completely destroyed epithelial cells, which were not detected in controls. With respect to morphology and barrier characteristics, TAM highly represents natural human airway mucosa. Infection studies with B. pertussis on natural human bronchus tissue reproduced morphologic changes as observed elsewhere (Wilson, R. et al. Infect Immun 1991; 337-345).