Development of a new 3D-Human Airway Epithelium/ Whole-blood Co-culture Model Combined with Multi-Analyte Profile (MAP) Analyses for Assessing Drug Effects

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Background

The dialogue between cells of the immune system and various tissues controls immune reactions and is in part mediated by a variety of cytokines, chemokines etc. This network may be strongly influenced by the application of drugs.

Aim of our investigations was to develop an innovative organo-typical human airway epithelial co-culture model for the analysis of immunopharmacological activities of drugs. A differentiated airway epithelium, MucilAir, was combined with whole-blood cultures in a two-chamber system to study the effects of betamethasone applied onto the epithelium sitting on activated immune cells from a healthy donor mimicking an inflamed tissue environment.

92 mediators and other parameters were tested in the supernatants of the cell cultures by multiplexed bead assays (RBM MAP analysis).

Results and Conclusions

In this newly developed co-culture model of human airway epithelial cells in combination with whole blood cells, Betamethasone exhibited its typical, strong pharmacological effect profile on both, the immune and the epithelial cells: It dose-dependently inhibited a variety of pro-inflammatory mediators, being either T helper cell type 1- (Th1), Th2-, or macrophage-associated, such as interferon (IFN)-gamma, interleukin (IL)-12p70, IL-4, -5, -13 and tumor necrosis factor (TNF)-alpha, respectively. In contrast, IL-10 as anti-inflammatory mediator was upregulated after 24h of co-culture. Furthermore, epithelial cells were cultured for another 6 days showing a dose-dependent effect on e.g. the monocyte chemotactic protein-1 (MCP-1) and IL-8.

From the data presented here, it is evident that the highly complex, organo-typical co-culture model provides an excellent tool to study in vitro, under in vivo-like conditions not only the pharmacokinetics and pharmacodynamics of inhaled drugs, but also the harmful effects of toxicants that get access to the human lung.

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