Validation of a simplified *in vitro* Transwell® model of the alveolar surface to assess host immunity induced by different morphotypes of *Aspergillus fumigatus*.

Morton CO, Wurster S, Fliesser M, Ebel F, Page L, Hünniger K, Kurzai O, Schmitt AL, Michel D, Springer J, Einsele H, Loeffler J (2018) Validation of a simplified *in vitro* Transwell® model of the alveolar surface to assess host immunity induced by different morphotypes of *Aspergillus fumigatus*. *Int J Med Microbiol* 308(8), 1009-1017.

Abstract

Interactions between fungal pathogens such as Aspergillus fumigatus with host alveolar epithelium and innate immune cells are crucial in the defense against opportunistic fungal infections. In this study a simplified Transwell® system with a confluent layer of A549 cells acted as a model for the alveolar surface. A. fumigatus and dendritic cells were added to simulate the spatial and cellular complexity in the alveolus. Fungal growth into the lower chamber was validated by galactomannan assays. Addition of moDCs to the upper chamber led to a reduced GM signal and fungal growth, indicating moDC antifungal activity. Minimal cell death was documented by analyses of lactate dehydrogenase concentrations and pro-apoptotic gene expression. Measurement of trans-epithelial dextran blue movement confirmed tightness of the epithelial barrier even in presence of A. fumigatus. Cytokine measurements in supernatants from both chambers of the Transwell® system documented distinct response patterns during early and late stages of epithelial invasion,

with A549 cells appearing to make a minimal contribution to cytokine release. Concentrations of cytokines in the lower chamber varied distinctly from the upper chamber, depending on the molecular weight of the cytokines. Low inter-assay variability of fungal biomarkers and cytokines was confirmed, highlighting that in vitro models closely mimicking conditions in the human lung can facilitate reproducible measurement of the dynamics of cytokine release and fungal penetration of host epithelia.

Involved units

Fungal Septomics Oliver Kurzai Read more

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