Deciphering chemokine properties by a hybrid agent-based model of *Aspergillus fumigatus* infection in human alveoli.

Pollmächer J, Figge MT (2015) Deciphering chemokine properties by a hybrid agent-based model of *Aspergillus fumigatus* infection in human alveoli. *Frontiers in Microbiology* 6(503),

Abstract

The ubiquitous airborne fungal pathogen *Aspergillus fumigatus* is inhaled by humans every day. In the lung, it is able to quickly adapt to the humid environment and, if not removed within a time frame of 4-8 hours, the pathogen may cause damage by germination and invasive growth. Applying a to-scale agent-based model of human alveoli to simulate early *A. fumigatus* infection under physiological conditions, we recently demonstrated that alveolar macrophages require chemotactic cues to accomplish the task of pathogen detection within the aforementioned time frame. The objective of this study is to specify our general prediction on the as yet unidentified chemokine by a quantitative analysis of its expected properties, such as the diffusion coefficient and the rates of secretion and degradation. To this end, the rule-based implementation of chemokine diffusion in the initial agent-based model is revised by numerically solving the spatio-temporal reaction-diffusion equation in the complex structure of the alveolus. In this hybrid agent-

based model, alveolar macrophages are represented as migrating agents that are coupled to the interactive layer of diffusing molecule concentrations by the kinetics of chemokine receptor binding, internalization and re-expression. Performing simulations for more than a million virtual infection scenarios, we find that the ratio of secretion rate to the diffusion coefficient is the main indicator for the success of pathogen detection. Moreover, a subdivision of the parameter space into regimes of successful and unsuccessful parameter combination by this ratio is specific for values of the migration speed and the directional persistence time of alveolar macrophages, but depends only weakly on chemokine degradation rates.

Beteiligte Forschungseinheiten

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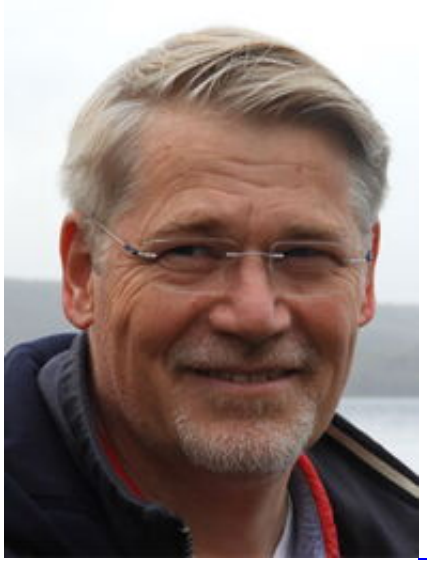

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Details

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Themenfelder

Agenten-basiertes Model der *Aspergillus fumigatus* Infektion in menschlichen Alveolen

Identifier

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