Comparative assessment of aspergillosis by virtual infection modeling in murine and human lung.

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Abstract

Aspergillus fumigatus is a ubiquitous opportunistic fungal pathogen that can cause severe infections in immunocompromised patients. Conidia that reach the lower respiratory tract are confronted with alveolar macrophages, which are the resident phagocytic cells, constituting the first line of defense. If not efficiently removed in time, *A. fumigatus* conidia can germinate causing severe infections associated with high mortality rates. Mice are the most extensively used model organism in research on *A. fumigatus* infections. However, in addition to structural differences in the lung physiology of mice and the human host, applied infection doses in animal experiments are typically orders of magnitude larger compared to the daily inhalation doses of humans. The influence of these factors, which must be taken into account in a quantitative comparison and knowledge transfer from mice to humans, is difficult to measure since in vivo live cell imaging of

the infection dynamics under physiological conditions is currently not possible. In the present study, we compare *A. fumigatus* infection in mice and humans by virtual infection modeling using a hybrid agent-based model that accounts for the respective lung physiology and the impact of a wide range of infection doses on the spatial infection dynamics. Our computer simulations enable comparative quantification of *A. fumigatus* infection clearance in the two hosts to elucidate (i) the complex interplay between alveolar morphometry and the fungal burden and (ii) the dynamics of infection clearance, which for realistic fungal burdens is found to be more efficiently realized in mice compared to humans.

Involved units

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