Agent-based model of human alveoli predicts chemotactic signaling by epithelial cells during early *Aspergillus fumigatus* infection.

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Details

Abstract

Aspergillus fumigatus is one of the most important human fungal pathogens, causing life-threatening diseases. Since humans inhale hundreds to thousands of fungal conidia every day, the lower respiratory tract is the primary site of infection. Current interaction networks of the innate immune response attribute fungal recognition and detection to alveolar macrophages, which are thought to be the first cells to get in contact with the fungus. At present, these networks are derived from in vitro or in situ assays, as the peculiar physiology of the human lung makes in vivo experiments, including imaging on the cell-level, hard to realize. We implemented a spatio-temporal agent-based model of a human alveolus in order to perform in silico experiments of a virtual infection scenario, for an alveolus infected with *A. fumigatus* under physiological conditions. The virtual analog captures the three-dimensional alveolar morphology consisting of the two major

alveolar epithelial cell types and the pores of Kohn as well as the dynamic process of respiration. To the best of our knowledge this is the first agent-based model of a dynamic human alveolus in the presence of respiration. A key readout of our simulations is the first-passage-time of alveolar macrophages, which is the period of time that elapses until the first physical macrophage-conidium contact is established. We tested for random and chemotactic migration modes of alveolar macrophages and varied their corresponding parameter sets. The resulting first-passage-time distributions imply that randomly migrating macrophages fail to find the conidium before the start of germination, whereas guidance by chemotactic signals derived from the alveolar epithelial cell associated with the fungus enables a secure and successful discovery of the pathogen in time.

Involved units

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Topics

Agent-based model of Aspergillus fumigatus infection in human alveoli

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