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Virtual infection model for *Aspergillus fumigatus* in human alveoli

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Aspergillus fumigatus is one of the most dangerous human fungal pathogens that can cause life-threatening diseases. Since humans inhale hundreds to thousands of fungal conidia every day, the lower respiratory tract is the primary site of infection. In a previous doctoral study, we implemented a spatio-temporal agent-based model of a human alveolus and performed *in silico* experiments of a virtual infection scenario under physiological conditions. However, our investigations were so far limited to study the detection of pathogens by alveolar macrophages (AM) in a single alveolus. We compared the time duration of first pathogen-encounter for different migration modes of the phagocytic cells and deciphered properties of a chemokine that directs AM to the invaded pathogen. The objective of this project is to exploit the flexibility and extensibility of the agent-based modeling framework by including more complex aspects of host-pathogen interactions to enable simulations of the immune response at a substantially higher level of realism. In particular, it will be investigated how the concurrent buildup in the dynamic interplay between infection and inflammation might be regulated and affected, for example, by the dose of infection. In order to achieve this challenging goal within a spatio-temporal modeling approach, the whole time course of the innate immune network will be simulated on the computer, including the impact of the complement system, phagocytosis by resident AM as well as by recruited neutrophils (PMN) and dendritic cells (DC). This will be realized within a multi-scale approach comprising cytokine dynamics at the molecular level up to inter-alveolar communication within alveolar sacs. Since the peculiar physiology of the lung generally

complicates *in vivo* imaging of cell dynamics, predictive computer simulations are a convenient and adequate option to decipher the dynamics of the immune network and to direct future experimental investigations.

Publications

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