Predictive virtual infection modeling of fungal immune evasion in human whole blood.

Prauße MTE, Lehnert T, Timme S, Hünniger K, Leonhardt I, Kurzai O, Figge MT (2018) Predictive virtual infection modeling of fungal immune evasion in human whole blood. *Front Immunol* 9, 560.

Details

Abstract

Bloodstream infections by the human-pathogenic fungi *Candida albicans* and *Candida glabrata* increasingly occur in hospitalized patients and are associated with high mortality rates. The early immune response against these fungi in human blood comprises a concerted action of humoral and cellular components of the innate immune system. Upon entering the blood, the majority of fungal cells will be eliminated by innate immune cells, i.e. neutrophils and monocytes. However, recent studies identified a population of fungal cells that can evade the immune response and thereby may disseminate and cause organ dissemination, which is frequently observed during candidemia. In this study, we investigate the so far unresolved mechanism of fungal immune evasion in human whole blood by testing hypotheses with the help of mathematical modeling. We

use a previously established state-based virtual infection model for whole-blood infection with *C. albicans* to quantify the immune response and identified the fungal immuneevasion mechanism. While this process was assumed to be spontaneous in the previous model, we now hypothesize that the immune-evasion process is mediated by host factors and incorporate such a mechanism in the model. In particular, we propose, based on previous studies, that the fungal immune-evasion mechanism could possibly arise through modification of the fungal surface by as of yet unknown proteins that are assumed to be secreted by activated neutrophils. To validate or reject any of the immune-evasion mechanisms, we compared the simulation of both immune-evasion models for different infection scenarios, i.e. infection of whole blood with either *C. albicans* or *C. glabrata* under non-neutropenic and neutropenic conditions. We found that under non-neutropenic conditions both immune-evasion models fit the experimental data from whole-blood infection with *C. albicans* and *C. glabrata*. However, differences between the immune-evasion models could be observed for the infection outcome under neutropenic conditions with respect to the distribution of fungal cells across the immune cells. Based on these predictions, we suggested specific experimental studies that might allow for the validation or rejection of the proposed immune-evasion mechanism.

Involved units

Applied Systems Biology Marc Thilo Figge Read more

Fungal Septomics Oliver Kurzai Read more

Leibniz-HKI-Authors

Marc Thilo Figge

Details

Kerstin Hünniger

Details

Oliver Kurzai

Details

Teresa Lehnert

Details

Ines Leonhardt

Details

Maria Praußе

Details

Sandra Timme

Details

Identifier

doi: 10.3389/fimmu.2018.00560

PMID: 29619027