Quantitative Simulations Predict Treatment Strategies Against Fungal Infections in Virtual Neutropenic Patients.

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Abstract

The condition of neutropenia, i.e., a reduced absolute neutrophil count in blood, constitutes a major risk factor for severe infections in the affected patients. Candida albicans and Candida glabrata are opportunistic pathogens and the most prevalent fungal species in the human microbiota. In immunocompromised patients, they can become pathogenic and cause infections with high mortality rates. In this study, we use a previously established approach that combines experiments and computational models to investigate the innate immune response during blood stream infections with the two fungal pathogens C. albicans and C. glabrata. First, we determine immune-reaction rates and migration parameters under healthy conditions. Based on these findings, we simulate virtual patients and investigate the impact of neutropenic conditions on the infection outcome with the respective pathogen. Furthermore, we perform in silico treatments of these virtual patients by simulating a medical treatment that enhances neutrophil activity in terms of phagocytosis and migration. We quantify the infection outcome by comparing the response to the two fungal pathogens relative to non-neutropenic individuals. The analysis reveals that these fungal infections in neutropenic patients can be successfully cleared by cytokine treatment of the remaining neutrophils; and that this treatment is more effective for C. glabrata than for C. albicans.

Identifier

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