Leibniz Institute for Natural Product Research and Infection Biology - Hans Knöll Institute

Virtual infection model of the







Teresa Lehnert^{1,2}, Kerstin Hünniger^{2,3}, Oliver Kurzai^{2,3}, Marc Thilo Figge^{1,2} ¹ Applied Systems Biology² Friedrich Schiller University Jena³ Fungal Septomics, Septomics Research Center

Motivation

The opportunistic human fungal pathogen *Candida albicans* causes severe sys-temic infections such as bloodstream infections and is becoming an increasing clinical problem associated with a high mortality rate. We quantified the different routes of immune response to *C. albicans* in human blood by developing a virtual infection model that simulates the host-pathogen interaction using time resolved data of whole-blood infection assays.



Virtual Infection Model



States and transitions:

Transition rates:



State types:



Extracellular killing

Estimation of transition rate values

Simulated annealing based on Metropolis Monte-Carlo:

Predictions on Dynamics of Host-pathogen Interaction

Identifying the main route of immune response







 \rightarrow phagocytosis by PMN more probable than by monocytes



Simulation algorithm



- explore parameter space
- compare simulated and experimental data
- always accept parameter values that improve fitting
- accept parameter values that impair fitting based on Boltzmann distribution

Resulting transition rates:

	rate	standard deviation [%]
ϕ_G	2.69 $\cdot 10^{-2}$ min ⁻¹	1.24
$\phi_{G^{\star}}$	3.58 $\cdot 10^{-2}$ min ⁻¹	5.24
ϕ_M	$0.63 \cdot 10^{-2} \min^{-1}$	5.25
κ_M	6.08 $\cdot 10^{-2}$ min ⁻¹	6.64
κ_G	4.26 $\cdot 10^{-2}$ min ⁻¹	4.76
ρ	0.41 $\cdot 10^{-2}$ min ⁻¹	3.25
γ	3.16 $\cdot 10^{-2}$ min ⁻¹	6.8
κ_{EK}	29.13 $\cdot 10^{-2}$ min ⁻¹	4.93



killing of *C. albicans:* • 67.3% in PMN • 30.0% in extracellular space • 2.7% in monocytes

\rightarrow killing of *C. albicans* in human blood mainly mediated by PMN

Determining the distribution of *C. albicans* in PMN

Manual evaluation of microscopy images





C. albicans in PMN

 \rightarrow majority of PMN bear one fungus during infection time

Quantifying the immune escape of *C. albicans*



 \rightarrow mechanism of *C. albicans* escape still under investigation

Outlook

In the future, we will simulate neutropenia for comparison to experiments with blood of neutropenia patients. Furthermore, we are very interested in the identification of the escape mechanism of *C. albicans* in human blood.

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Contact: teresa.lehnert@hki-jena.de