Center for Sepsis Control & Care

Quantification of Innate Immune Function in Whole-blood Infection Assays

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Introduction

- Marked heterogeneity of sepsis as a clinical syndrome
- Caused by highly diverse pathological conditions and shows variable kinetics in individual patients

➡ Classification of sepsis patients by their immune status is necessary for immunomodulatory therapy approaches

Objectives

- Individualised quantification of altering immune effector functions of septic patients

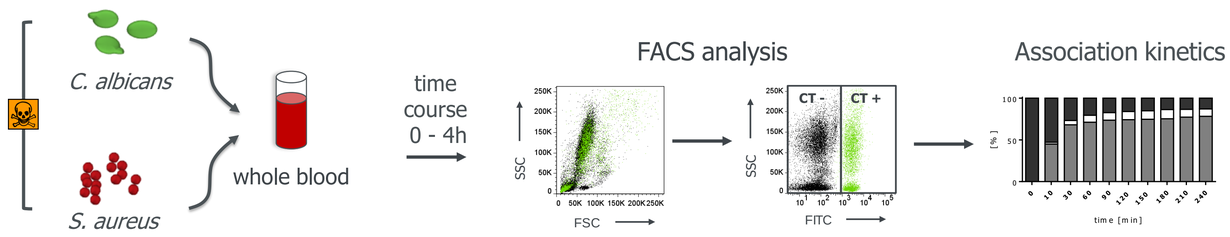
Are there pathogen-specific patterns of immune activation during whole blood infection?

Are there immune effector functions that allow stratification of sepsis patients?

Approach

Within this project, we will use data from a human whole blood model of infection combined with advanced mathematical modeling.

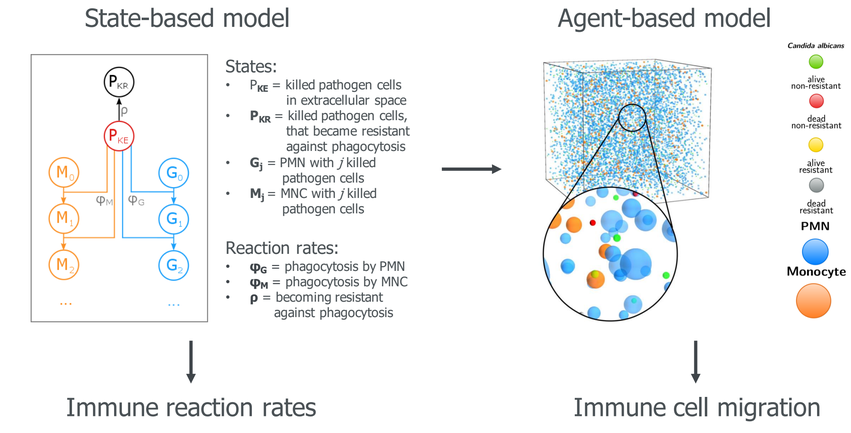
Human whole-blood infection assay (WBIA)



- Association with neutrophils (PMN) and monocytes (MoC)
- Activation patterns on immune cells

(Hünniger *et al.* 2014, Lehnert *et al.* 2015)

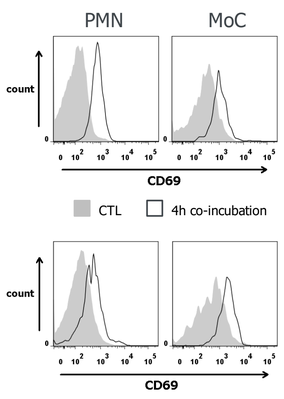
Virtual infection models



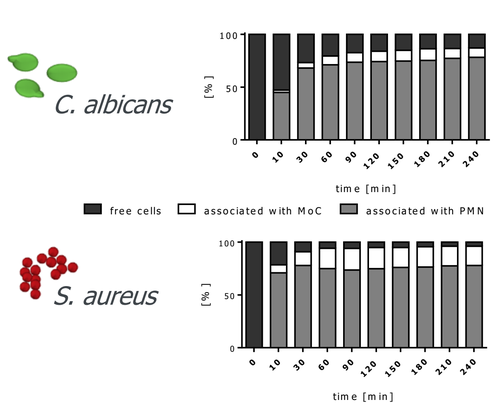
Results

Analysing pathogen association and immune activation in blood from healthy volunteers

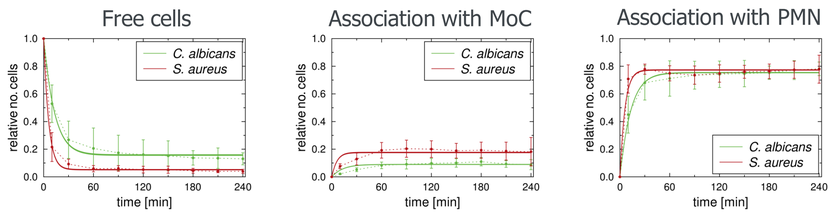
Activation of immune cells



Association with immune cells



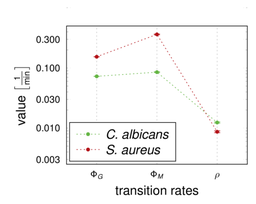
Model simulation results



Comparison of infection with *C. albicans* and *S. aureus*

- Greater association of *S. aureus* cells with MoC
- Larger number of free *C. albicans* cells
- *S. aureus* infection causes steeper slope of immune cell association kinetics

Immune reaction rates

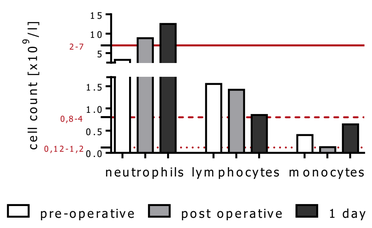


- Larger phagocytosis rates for whole-blood infection with *S. aureus*

Analysing pathogen association and innate immune activation in blood from HLM patients

- Within a pilot study, blood samples of 3 patients that underwent cardiac surgery with extracorporeal circulation (heart-lung machine, HLM) were analysed
- Blood samples were obtained before cardiac surgery (pre-operative), immediately after surgery (post-operative), and 1 day after admission to ICU

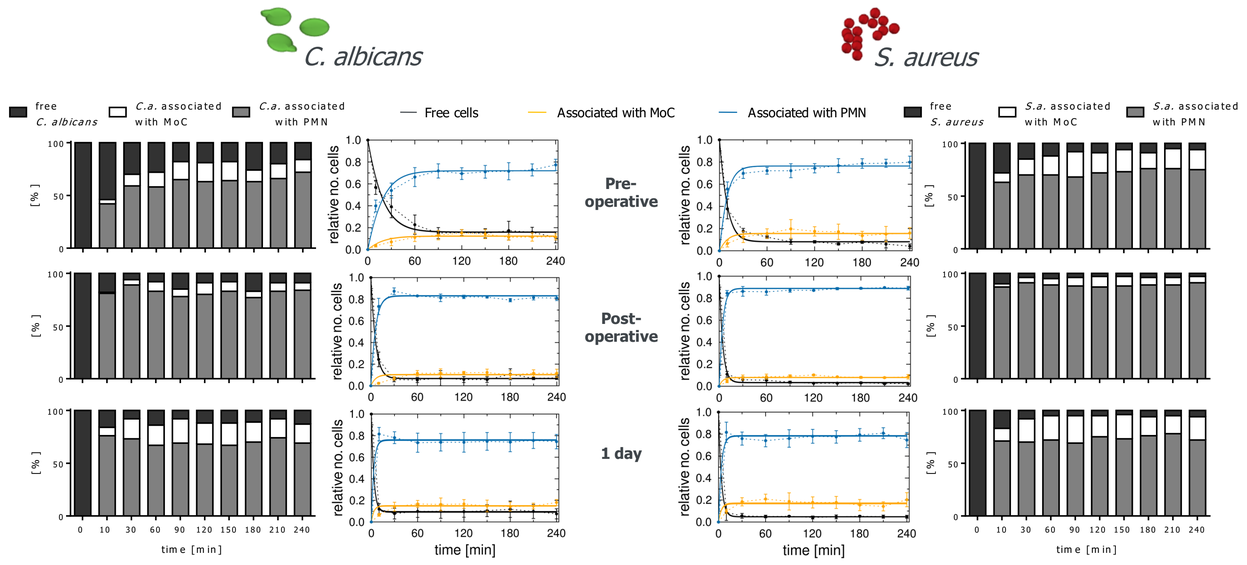
White blood cell count



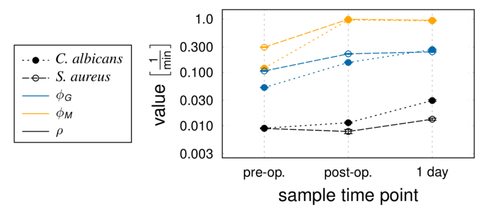
Blood cell count was quantified via hematological analyzer.

- Increase in white blood cell count after surgery with a maximum at one day
- High neutrophil numbers exceeding the reference range after surgery
- Monocyte number increases
- Lymphocyte number decreases

Association with immune cells



Immune reaction rates



C. albicans

- Phagocytosis rates of PMN and MoC as well as immune evasion rate increases

S. aureus

- Phagocytosis rates of PMN and MoC increase after surgery, but decrease one day later
- Immune evasion rate increases

Conclusions

Once optimized, analyses of blood samples from sepsis patients and patients who have survived severe sepsis will follow. This will allow identifying patterns of the dysregulated immune homeostasis providing functional classifiers for the differentiation of sepsis patients, thereby forming a basis for future patient stratification.

GEFÖRDERT VOM

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