

## QUANTIM- Quantification of Innate Immune Function in Whole Blood Infection Assay

T. Lehnert, I. Leonhardt, D. Thomal-Rüddel, R. Martin, M.T. Figge, O. Kurzai

02/02/2017

**Center for Sepsis Control & Care**

### QUANTIM- Quantification of Innate Immune Function in Whole Blood Infection Assays

**Autoren:** Oliver Kurzai Principal Investigator, Marc Thilo Figge Principal Investigator, Daniel Thomas-Rüddel Clinician Scientist, Teresa Lehnert Scientist, Ines Leonhardt Scientist, Ronny Martin Scientist

**Problem:**

- 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:**

- Individual quantification of altered 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 for the 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 (Hünigter et al., 2014 and Lehnert et al., 2015):

Human whole-blood infection assay (WBIA)      Virtual infection models

State-based model      Agent-based model

FACS analysis      Immune reaction rates      Immune cell migration

Activation with neutrophils (PN) and monocytes (MC)      Activation patterns on immune cells

**Results obtained during the funding period:**

**WP1: Analysing pathogen association and immune activation in blood from healthy volunteers**

Activation of immune cells      Association with immune cells

**WP2: Quantification of immune effector mechanisms by biomathematical analyses**

Model simulation results      Immune reaction rates

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

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

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

**WP3: Analysing pathogen association and innate immune activation in blood from clinical samples**

White blood cell count      Activation of immune cells

Blood cell count was quantified via hematology analysis

- Increase in white blood cell count observed with a maximum after surgery
- High neutrophil numbers exceeding the reference range after surgery
- Increased monocyte numbers
- Increased lymphocyte numbers

Activation of neutrophils was markedly reduced post-operatively and one day after surgery

Monocytes showed an activated phenotype following stimulation by both pathogens at all 3 time points examined

Activation of neutrophils      Phagocytosis rates of PN and MC increase after surgery

One day after surgery, PN show lower phagocytosis rate

**Next steps...**

In ongoing experiments, we will analyze the behavior of neutrophils in more detail and visualize differences in immune effector functions using live cell imaging and advanced spatial biomathematical modeling. Once optimized, analyses of blood samples of patients from CandiSep cohort will follow in future studies.

**gefördert von:** Bundesministerium für Bildung und Forschung

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