FungiNet

CRC/Transregio 124 Pathogenic fungi and their human host: Networks of interaction

B4 // Image data analysis and agent-based modelling of the spatio-temporal interaction between immune cells and human-pathogenic fungi

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Summary

- Analysis, interpretation and modelling of microscopic image data
- Investigation of morphological, functional and dynamical aspects of host-pathogen interactions
- Generation of hypothesis to be tested in experiment

Image-based systems biology approach:
1. Automated image processing
2. Derivation of quantitative measures
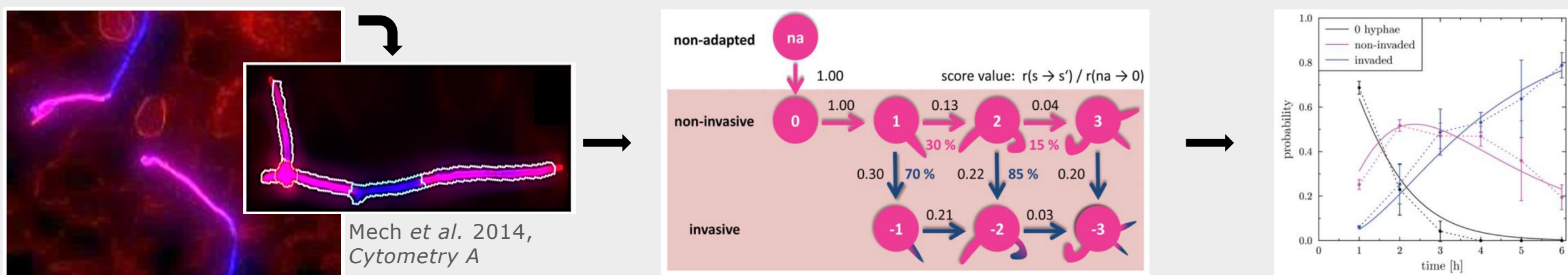3. Virtual infection modelling and computer simulation

Project progress to date

Image-based systems biology of infection involves the development of strategies and methods for the quantitative analysis and modelling of information contained in microscopic images.
Project B4 focuses on all three aspects of image-based systems biology and applies this approach to the image data on infection processes acquired by our CRC/TR partners.
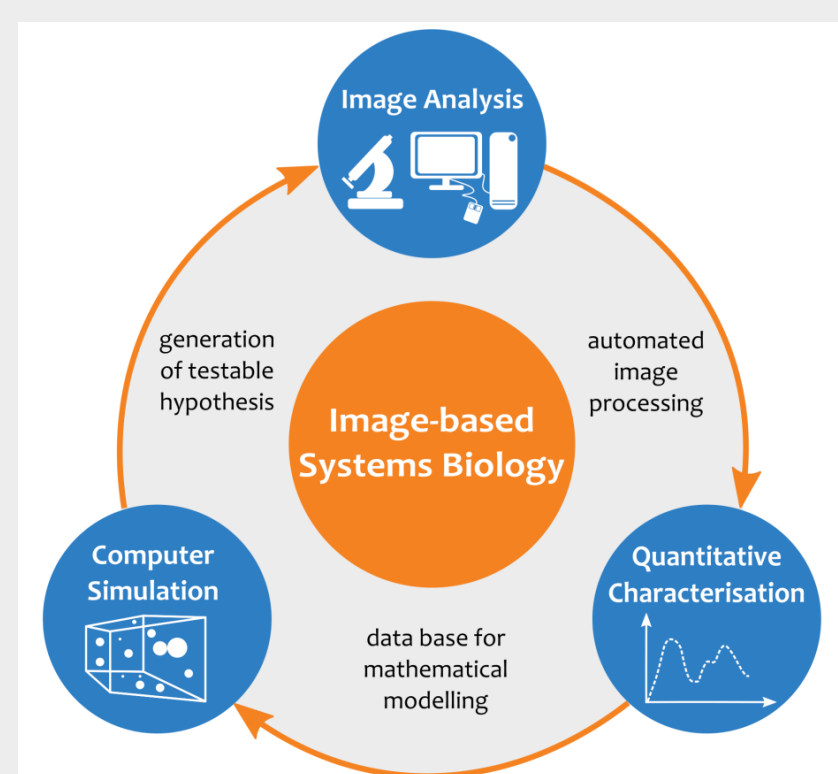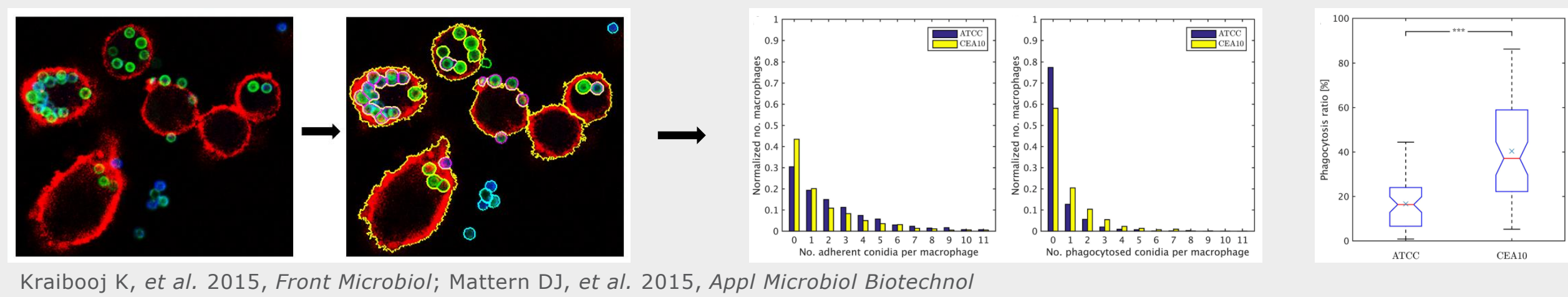
Automated pipeline for analysis of microscopic images:

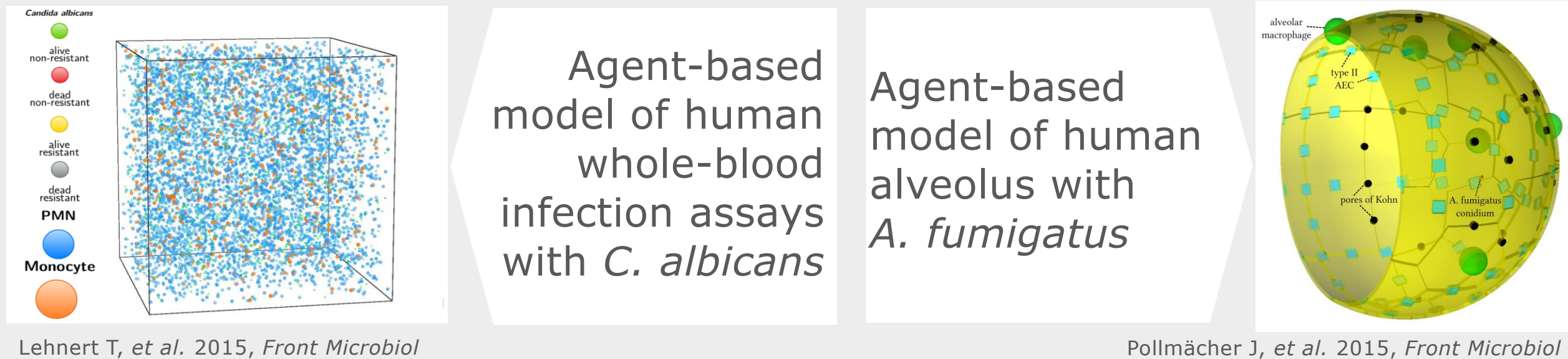- Segmentation and modelling of hyphal growth (B4 + C1):

Mech *et al.* 2014, *Cytometry A*

- Quantification of phagocytosis assays (B4 + A1):

Kraibooj K, *et al.* 2015, *Front Microbiol*; Mattern DJ, *et al.* 2015, *Appl Microbiol Biotechnol*

Virtual infection models in whole blood and in lung alveoli:

- Agent-based computer simulations (B4 + C3):

Agent-based model of human whole-blood infection assays with *C. albicans*

Agent-based model of human alveolus with *A. fumigatus*

Lehnert T, *et al.* 2015, *Front Microbiol*

Pollmächer J, *et al.* 2015, *Front Microbiol*

- Evolutionary game theory on graphs (B4 + A1 + B1 + C5):

Counterplay of pathogen-driven infection and host-induced inflammation across various time scales in alveolar sacs

Role of alveolar macrophages depends on infection-dose

Pollmächer J, *et al.* 2016, *Sci Rep*
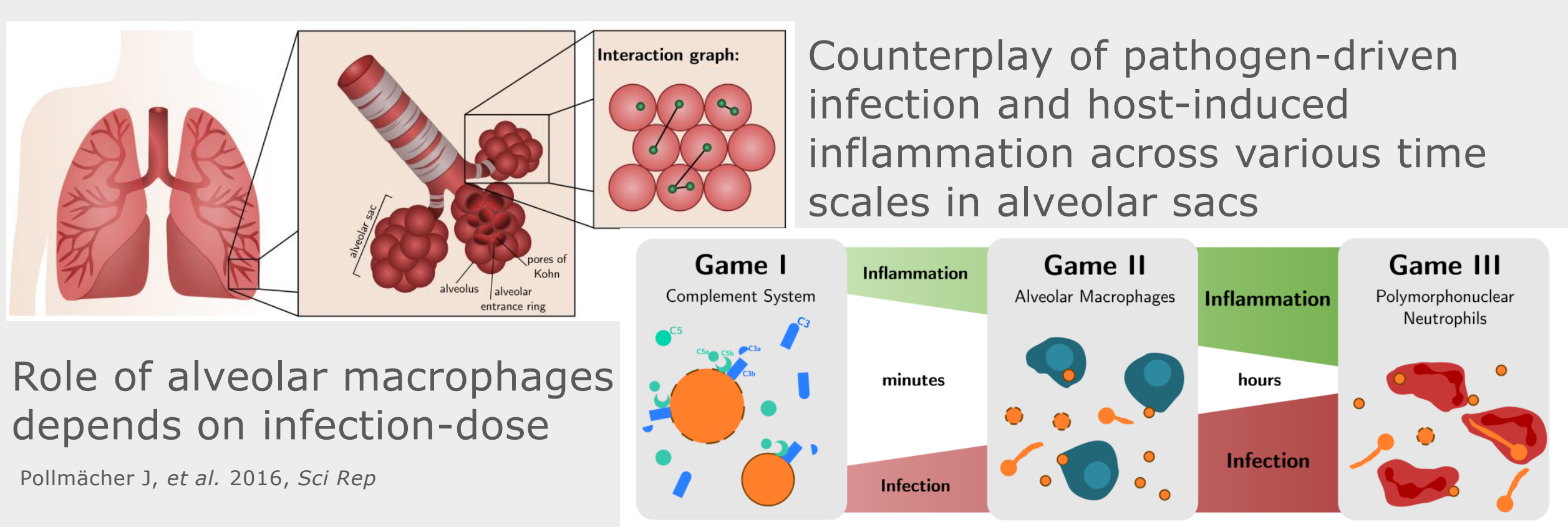
Publications

1. Pollmächer J, Timme S, Schuster S, Brakhage AA, Zipfel PF, **Figge MT** (2016) Deciphering the counterplay of *Aspergillus fumigatus* and host inflammation by evolutionary games on graphs. *Sci Rep* **6**: 27807.
2. Brandes S, Dietrich S, Hünniger K, Kurzai O, **Figge MT** (2016) Migration and Interaction Tracking for Quantitative Analysis of Phagocyte-Pathogen Confrontation Assays. Medical Image Analysis 36, 172-183.
3. Kraibooj K*, Schoeler H*, Svensson CM, Brakhage AA, **Figge MT** (2015) Automated quantification of the phagocytosis of Aspergillus fumigatus conidia by a novel image analysis algorithm. Front Microbiol 6: 549. (*equal contribution)
4. Lehnert T*, Timme S*, Pollmächer J, Hünniger K, Kurzai O, **Figge MT** (2015) Bottom-up modeling approach for the quantitative estimation of parameters in pathogen-host interactions. Front Microbiol 6: 608. (*equal contribution)
5. Mattern DJ, Schoeler H, Weber J, Novohradská S, Kraibooj K, Dahse HM, Hillmann F, Valiante V, **Figge MT**, Brakhage AA (2015) Identification of the antiphagocytic trypacidin gene cluster in the human-pathogenic fungus Aspergillus fumigatus. Appl Microbiol Biotechnol 99: 10151-61.
6. Medyukhina A, Timme S, Mokhtari Z, **Figge MT** (2015) Image-based systems biology of infection. Cytometry A 87: 462-70. (review)
7. Buhlmann D*, Eberhardt HU*, Medyukhina A, Prodinger WM, **Figge MT**, Zipfel PF, Skerka C (2016) Complement factor H related protein 3 (FHR3) blocks C3d-mediated co-activation of human B cells. J Immunol, 197: 620-9. (*equal contribution)
8. Brandes S, Mokhtari Z, Essig F, Hünniger K, Kurzai O, **Figge MT** (2015) Automated segmentation and tracking of non-rigid objects in time-lapse microscopy videos of polymorphonuclear neutrophils. Med Image Anal 20: 34-51.
9. Pollmächer J, **Figge MT** (2015) Deciphering chemokine properties by a hybrid agent-based model of Aspergillus fumigatus infection in human alveoli. Front Microbiol 6: 503.
10. Hünniger K*, Lehnert T*, Bieber K, Martin R, **Figge MT**+, Kurzai O+ (2014) A virtual infection model quantifies innate effector mechanisms and Candida albicans immune escape in human blood. PLoS Comput Biol 10: e1003479. (*equal contribution, +corresponding authors)
11. Mech F, Wilson D, Lehnert T, Hube B, **Figge MT** (2014) Epithelial invasion outcompetes hypha development during Candida albicans infection as revealed by an image-based systems biology approach. Cytometry A 85: 126-39.

Project aims of the second funding period

Design of new tools and workflows to investigate morphological, functional and dynamical aspects of host-pathogen interactions by the *image-based systems biology* approach:

- Processing of live cell microscopy data on confrontation assays
- Automated recognition and statistics of time-ordered event patterns
- Advancement of virtual infection models for a higher level of detail
- Improvement of model parameter estimation algorithms
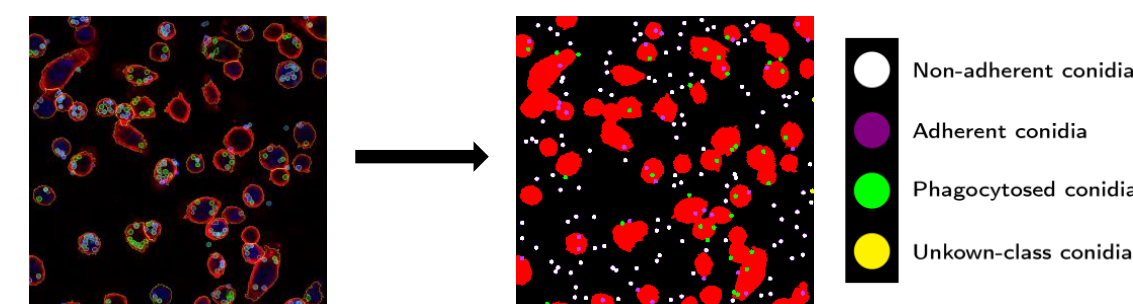- Experimental design of confrontation assays by computer simulations

Project plan

WP1: Development of algorithms for the automated analysis of time-resolved image data
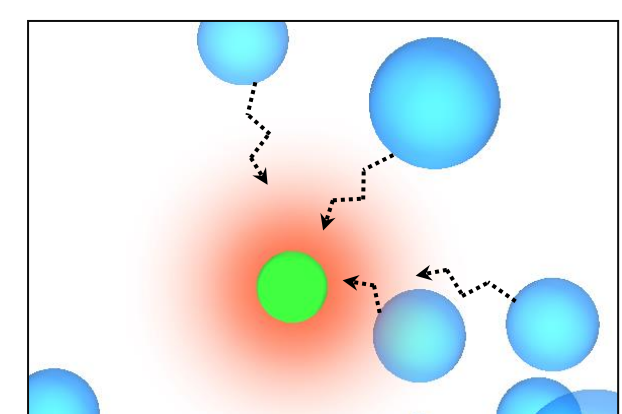
WP2: Automated high-throughput and high-content screening of time-resolved image data
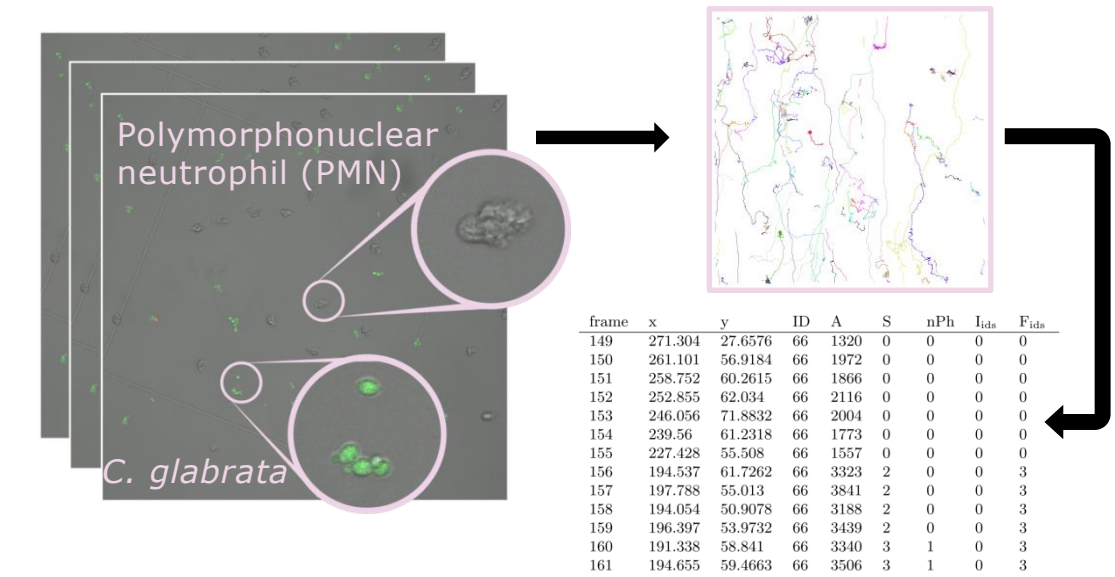
WP3: Experimental design of phagocytosis assays via computer simulations

WP4: Advancement of virtual infection modelling and of estimation of model parameters

WP5: Quantitative predictions of sensitive parameters in infection scenarios

WP6: Support of CRC/TR partners based on methods developed in the first funding period

Role within CRC/Transregio 124

A1 (Brakhage)
Live cell imaging of confrontation assays

A5 (Slevogt)
CEACAM receptor properties from confrontation assays

A6 (Voigt)
Comparison of confrontation assays for *A.fumigatus* and *Lichthemia spp.*

A3 (Beilhack, Heinze, Terpitz)
LSFM and MPM on infection scenarios

B4 (Figge)
Image data analysis and agent-based modelling

B1 (Dandekar, Schuster)
Game-theoretical modelling

INF (Linde)
FungiNet-SEEK
Standadised description of image data acquisition

C1 (Hube, Pérez)
Correlated assays on adhesion, invasion and damage

C3 (Kurzai)
Live cell imaging of confrontation assays; Pathogen resistance in whole blood infection assays

C5 (Bauer, Jacobsen)
C. albicans colonisation and translocation in gut mucosa by FISH

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