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Prediction of infection outcome by computational modeling of Yersinia enterocolitica infection

The complex interplay of a given pathogen, its virulence and fitness factors, the host immune response and the presence and composition of the endogenous microbiome determine the course and outcome of gastrointestinal infection. An expansion of pathogens within the gastrointestinal tract implies an increased risk for the development of severe systemic infections, especially in patients receiving antibiotic treatment or in the immune-compromised state.
To predict pathogen expansion, gut colonization and infection outcome we employed a powerful measure of systems biology, i.e., the development of a computational model. For implementation and challenge of the model, oral mouse infection experiments with the enteropathogen Yersinia enterocolitica (Ye) were used. Our model is able to calculate the bacterial population dynamics during gastrointestinal infection and accounts for specific pathogen characteristics, the host immune capacity and colonization resistance mediated by the endogenous microbiome. First, we performed model parameter optimization based on the experimental data we obtained by the infection of a healthy host. Afterward, we challenged our model by adopting scenarios where either a microbiome was lacking (mimicking antibiotic treatment of patients), or where the immune response was partially impaired. The predicted Ye population dynamics based on these scenarios could be approved in experimental mouse infections.
Our model is able to provide new hypotheses about the roles of host- and pathogen-derived factors within this complex interplay and might be useful for future development of personalized infection prevention and treatment strategies.

Summary

Primary author(s) : Ms GEIßERT, Janina; Prof. EICHNER, Martin; Dr BOHN, Erwin; Dr MOSTOLIZADEH, Reihaneh; Dr DRÄGER, Andreas; Prof. AUTENRIETH, Ingo B.; Ms BEIER, Sina; Dr MONIKA SCHÜTZ, Monika

Presenter(s) : Dr MOSTOLIZADEH, Reihaneh

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