An interspecies regulatory network inferred from simultaneous RNA-seq of *Candida albicans* invading innate immune cells.

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Abstract

The ability to adapt to diverse micro-environmental challenges encountered within a host is of pivotal importance to the opportunistic fungal pathogen Candida albicans. We have quantified C. albicans and M. musculus gene expression dynamics during phagocytosis by dendritic cells in a genome-wide, time-resolved analysis using simultaneous RNA-seq. A robust network inference map was generated from this dataset using NetGenerator, predicting novel interactions between the host and the pathogen. We experimentally verified predicted interdependent sub-networks comprising Hap3 in C. albicans, and Ptx3 and Mta2 in M. musculus. Remarkably, binding of recombinant Ptx3 to the C. albicans cell wall was found to regulate the expression of fungal Hap3 target genes as predicted by the network inference model. Pre-incubation of C. albicans with recombinant Ptx3 significantly altered the expression of Mta2 target cytokines such as IL-2 and IL-4 in a Hap3-dependent manner, further suggesting a role for Mta2 in host-pathogen interplay as predicted in the network inference model. We propose an integrated model for the functionality of

these sub-networks during fungal invasion of immune cells, according to which binding of Ptx3 to the C. albicans cell wall induces remodeling via fungal Hap3 target genes, thereby altering the immune response to the pathogen. We show the applicability of network inference to predict interactions between host-pathogen pairs, demonstrating the usefulness of this systems biology approach to decipher mechanisms of microbial pathogenesis.

Beteiligte Forschungseinheiten

Mikrobielle Pathogenitätsmechanismen Bernhard Hube Mehr erfahren

Microbiome Dynamics Gianni Panagiotou Mehr erfahren

Leibniz-HKI-Autor*innen



Sascha Brunke

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Reinhard Guthke

Details



Bernhard Hube

Details



Jörg Linde

Details

Themenfelder

Netzwerke der Wirt-Pilz-Pathogen Interaktion

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