Jena School for Microbial Communication
Graduate School of Excellence

PhD project title

Unravelling the impact of interferon-immunotherapy on epithelial resistance to *Candida albicans* translocation and dissemination

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Abstract:

Invasive candidiasis is one of the most common opportunistic fungal infections threatening immunocompromised patients. Candidiasis is caused by *Candida* species, with *Candida albicans* being the most common pathogen isolated. Under normal conditions, this yeast is a commensal that resides in the gastrointestinal tract of most individuals. However, use of broad-spectrum antibiotics fosters *C. albicans* overgrowth, and a dysfunctional intestinal epithelial barrier allows translocation from the gut into the bloodstream. When the innate immune defenses are compromised the fungi can reach the bloodstream and cause disseminated infection. Immunotherapy has already been posited as an approach to augment host defense of immunocompromised patients. Despite the immunological interferon gamma (IFN-γ), type II IFNs, communication that augments antifungal effects of myeloid cells, it remains largely unclear how an acute increase in IFN-γ levels influence infection at epithelial barriers. Particularly, since chronic IFN-γ release has been associated with interferonopathy and compromised epithelial barrier function. Conversely, type I IFNs (IFN-I) have been associated with increased epithelial resistance to *C. albicans* infection. Using an *in vitro* intestinal epithelial model to study *C. albicans* translocation, we will evaluate the association between fungal translocation and breakdown of epithelial barrier integrity, upon treatment with IFN-I/II. This will be specifically investigated using microbiological translocation assays, monitoring of tissue damage, confocal microscopy of tight junctions and biophysical assays for assessment of epithelial integrity. Collectively, the project will shed light on the potential detrimental or beneficial effects of interferons on *C. albicans* colonization, infection, and translocation.