



PhD project title: *Experimental dissection of the interaction of Candida albicans with antagonistic bacteria in a Gut-on-Chip model*

PhD Student: Raquel Alonso-Román

Supervisors: Bernhard Hube, Alexander Mosig

Abstract:

Microbial consortia of the human gut are extremely diverse, individualized and essential for host health and fitness. However, gut microbiomes also contain opportunistic pathogens, such as the fungus *Candida albicans*, which can cause disease when the microbiome is disturbed. Choice of diet and antibiotic use, removing the protective microbiome, can enrich *C. albicans* and cause overgrowth, predisposing individuals for systemic infections. In fact, the gut is the main source of life-threatening *C. albicans* infections.

In this project, a Gut-on-Chip model will be established to investigate the processes and dynamics of interactions of *C. albicans* with antagonistic bacteria and human intestinal epithelial cells thereby providing the basis to elucidate the principles of balances and dysbalances of the gut microbial communities containing opportunistic pathogenic fungi.

In preliminary experiments, we established a static commensal model based on human intestinal cells, lactobacilli and *C. albicans*, and identified mechanisms by which lactobacilli keep the fungus under control and prevent epithelial damage. This system will be transferred to the dynamic Gut-on-chip model to mimic the process of colonization and the shift to pathogenicity (e.g triggered by the use of antibiotics) as a proof of principle. Then, we will establish technologies and protocols for monitoring an imaging the stable colonization (commensal) phase and the processes involved in the commensal-to-pathogenic shift, ideally in situ without disturbing the system. Next, we will modify distinct parameters, in particular the absence or presence of distinct metabolites or antibiotic treatment, thereby mimicking clinical settings. Finally we will use a diverse, but defined, *C. albicans* strains and single or groups of bacterial members of the microbiome predicted to be protective to systematically investigate the commensal and/or pathogenic relationship between *C. albicans* and defined microbial consortia.