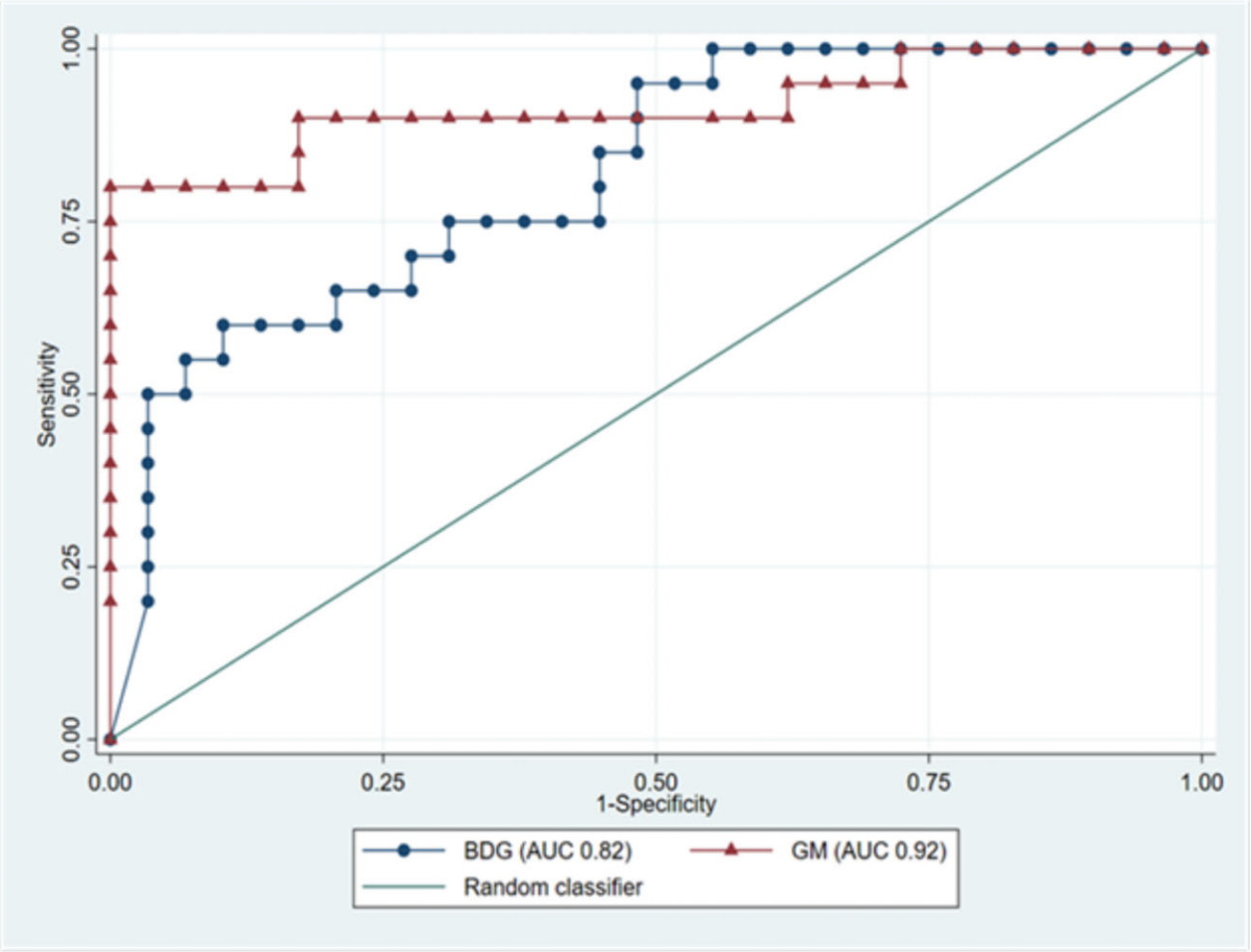

Figure 1. ROC curves and Areas Under Curves (AUC) of β-(1,3)-D-glucan (BDG) and galactomannan *Aspergillus* antigen (GM) detection levels for the diagnosis of HIV-associated histoplasmosis in serum samples according to a strict gold standard definition

S10.3c

Clinical studies provide new insights on the association between the microbiota and host resistance to *Candida albicans* intestinal colonization

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S10.3 The mycobiome characterization: future perspectives or just a trend?, September 24, 2022, 10:30 AM - 12:00 PM

Objectives: *Candida albicans* is both a harmless commensal intestinal yeast in healthy individuals and a harmful opportunistic pathogen in immunocompromised patients, causing life-threatening invasive candidiasis. *C. albicans* intestinal overgrowth is a prerequisite for intestinal translocation, which is at the root of invasive candidiasis. Therefore, to prevent invasive candidiasis in immunocompromised patients, it is necessary to curb intestinal *C. albicans* overgrowth. However, little is known of the role of bacterial species of the microbiota in dampening *C. albicans* intestinal colonization.

We aimed to decipher the influence of the bacterial and fungal intestinal microbiota on *C. albicans* gut colonization in healthy individuals in whom their microbiota was modified or not by antibiotic treatment.

Methods: We studied two cohorts of healthy individuals: the first cohort included 22 volunteers for which fecal samples were collected before, during and after a 3-day regimen of third-generation cephalosporin antibiotics. The second cohort gathered 1000 healthy individuals for which a single fecal sample was collected. We quantified *C. albicans* carriage using a specific quantitative PCR approach. We monitored the antibiotic effect on the composition of the fungal microbiota—the so called mycobiota—in the gut of the individuals up to 180 days post-antibiotic exposure, using both the qPCR data and ITS1 targeted metagenomic. We also monitored the level of fecal β-lactamase activity, which is known to modulate the intensity of post-cephalosporin intestinal dysbiosis. Finally, to identify potential *C. albicans* inhibiting bacteria, we used MaAsLin2 to search for associations between *C. albicans* levels and bacterial species abundance, deduced from shotgun metagenomics data obtained from all individuals and annotated at the species level.

Results: A very high level of *C. albicans* carriage was observed in both cohorts, with a prevalence of 95.2% and 83.1% in the first and second cohort, respectively. Yet, the quantity of *C. albicans* DNA detected varied greatly between subjects. The mycobiota composition was significantly altered by antibiotics and the fungal load was increased both at short and long term. Particularly, *C. albicans* abundance was increased but with wide inter-subject variations. A part of these variations was explained by changes in the levels of endogenous fecal β-lactamase activity, with subjects characterized by a low increase of β-lactamase activity displaying a higher increase of *C. albicans* levels. Finally, using shotgun metagenomics data, we identified a first set of 50 bacterial and archaeal species whose abundance inversely correlated with *C. albicans* abundance.

Conclusion: These results (1) bring a new understanding of *C. albicans* overgrowth in healthy individuals, (2) lead to the identification of microbial signatures with a potential key role in controlling *C. albicans* gut colonization, and finally (3) show for the first time that changes in endogenous fecal β-lactamase activity is a key factor for *C. albicans* overgrowth in the gut after antibiotic exposure. Taken together, these results open the way for new intervention strategies to curb *C. albicans* intestinal overgrowth.

S10.3d

Yeast Microbiome in patients with inflammatory bowel disease (IBD)

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S10.3 The mycobiome characterization: future perspectives or just a trend?, September 24, 2022, 10:30 AM - 12:00 PM

Objective: The intestinal microbiota plays major roles in host-protective functions and inflammatory bowel diseases (IBDs). Although some data suggest a role of the yeast microbiota in IBD pathogenesis, the available data are rare. The aim of this study was to evaluate the fecal yeast microbiota in patients with IBD.

Methods: Fungal isolates of the fecal microbiota of 120 patients with IBD and 30 healthy control individuals were determined using conventional and molecular (ITS sequencing and RFLP) methods.

Results: The mean age of the patients was 37.4 ± 12.2 years (range 15-72 years). Of 120 patients included, 67 had ulcerative colitis (55.8%) and 53 had Crohn's disease (44.2%). Ulcerative colitis was more prevalent in women than Crohn's disease (61.7% vs 50.2%, P <.005). The median time between the onset of symptoms and diagnosis was 9.58 ± 8.56 years. In total, 73 colonies of *Candida* spp. were isolated from 60 patients with IBD. The most common identified species of *Candida* were *C. albicans* (42.4%), *C. glabrata* (20.5%), and *C. krusei* (6.8%). The incidence of non-*albicans Candida* species (57.6%) was higher than *C. albicans* (42.4%). We observed an increased proportion of *C. albicans* compared with healthy individuals (28.5% vs 21.6%). The frequencies of *C. glabrata* were significantly higher among IBD patients rather than the control group (20.5% vs 9.8%).

Conclusion: *Candida albicans* were found to be increased in abundance in the IBD samples. These data emphasize the potential importance of yeast microbiota signatures as biomarkers. Moreover, we unravel here disease-specific-*Candida* species network alterations in IBD, suggesting that, *Candida* species might play a role in IBD pathogenesis.