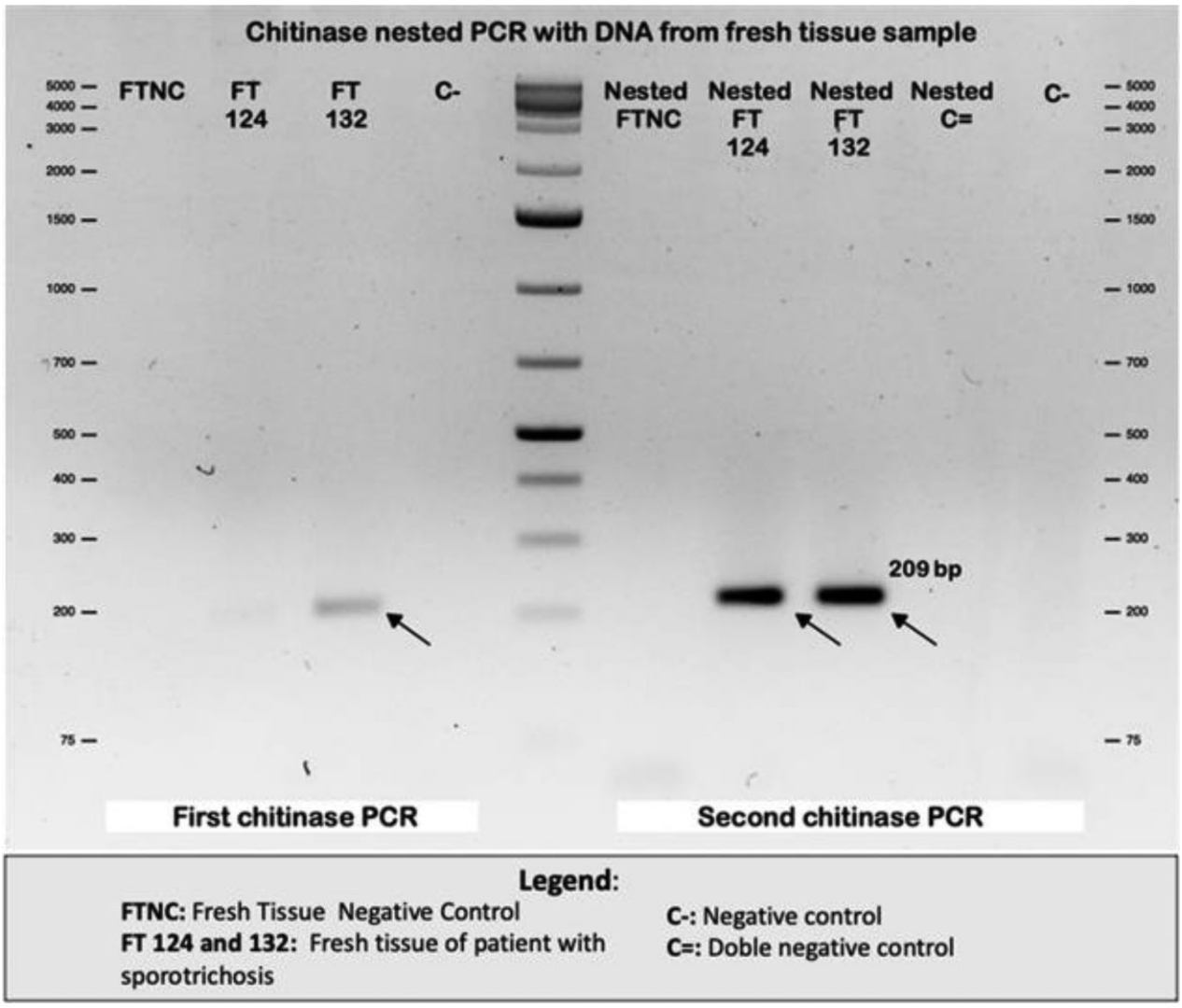

is necessary to improve this test, which we believe is affected by the type of sample used for DNA extraction, so further studies are required.

S10.2d

Fungal beta-glucans and mannan performances in HIV-associated histoplasmosis

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S10.2 Fungal Infections in Transplant Patients, September 24, 2022, 10:30 AM - 12:00 PM

Objectives: Diagnosis of histoplasmosis in people living with HIV (PLWHIV) remains challenging despite developments in Histoplasma antigen and molecular detection tools. Fungal markers such as Beta-(1,3)-D-glucan (BDG) and galactomannan *Aspergillus* antigen (GM) are widely available, but the experience is limited during PLWHIV workup for suspicion of histoplasmosis. Our objective was to evaluate and compare BDG and GM performances for the diagnosis of HIV-associated histoplasmosis.

Methods: We performed a diagnostic accuracy study using primary serum samples stored frozen in a certified biorepository (CRB Amazonie-DC-2021-4649). Samples consisted of consecutive hospitalized PLWHIV unexposed to oral antifungals during the previous month (EDIRAPHIS study-NCT01884779). All patients gave consent for biobanking and ancillary studies on fungal markers.

Histoplasmosis cases, proven (EORTC/MSG criteria) and probable (polyclonal or monoclonal Histoplasma antigen detections in urines or serum), as well as negative controls, were randomly selected. Patients with a proven or suspected *Pneumocystis jirovecii* infection were excluded. Following manufacturers' instructions, samples were blindly tested for BDG and GM using Fungitell® and PlateliaTM *Aspergillus* Ag assays, respectively.

Gold standard definition used three scenarios: EORTC scenario (cases and controls defined according to the EORTC/MSG 2020 criteria for endemic mycoses); strict scenario with proven cases restricted to those positives to all three previous Histoplasma antigen detections, and controls conversely negatives for all methods; and a large scenario with proven or probable cases and controls negatives for all methods.

Results: We included 121 samples, 92 HIV-associated histoplasmosis cases (34 proven and 58 probable), and 29 negative controls. Compared with controls, histoplasmosis cases were significantly younger and advanced in the course of HIV disease [median CD4 count level 33/mm3 (15-87) vs 116 (62-245)].

BDG and GM median detection levels were significantly higher among histoplasmosis cases compared with controls across all scenarios [368 (176-441) pg/ml vs 142 (89-211) for BDG and 2.5 (1.3-4.8) vs 0.19 (0.14-0.36) for GM, in cases vs controls of the strict scenario, respectively].

In the strict scenario, at 150 pg/ml and 0.5 for BDG and GM respectively, sensitivity, specificity, positive and negative likelihood ratios were respectively: 95% [95%confidence interval (CI), 85-100] vs 90% [77-100], 52% [34-70] vs 83% [69-97], 2 [1.4-3.0] vs 5.3 [2.4-12.0], and 0.1 [0.01-0.7] vs 0.12 [0.03-0.45]. ROC curves found AUCs of 0.82 [0.68-0.91] vs 0.92 [0.80-0.98], and optimal thresholds at 288 pg/ml and 1.29, for BDG and GM, respectively (Fig. 1). Post-test probabilities showed best performances at the lowest thresholds for negative testing of both BDG and GM, and at the 0.7 thresholds for a positive GM test (Fig. 2).

Conclusion: BDG and GM may not be used for the same objective when searching for HIV-associated histoplasmosis. Although a negative BDG test at the lowest thresholds should rule out histoplasmosis in a screening context, limitations of a positive BDG test, even at the highest thresholds, call for a consecutive positive GM test before starting patients on antifungal therapy targeting histoplasmosis. Still, when considering the highest costs of BDG testing, higher balanced diagnostic performances, and lower costs of GM testing alone, one may favor the use of GM, notably in resources-limited settings.

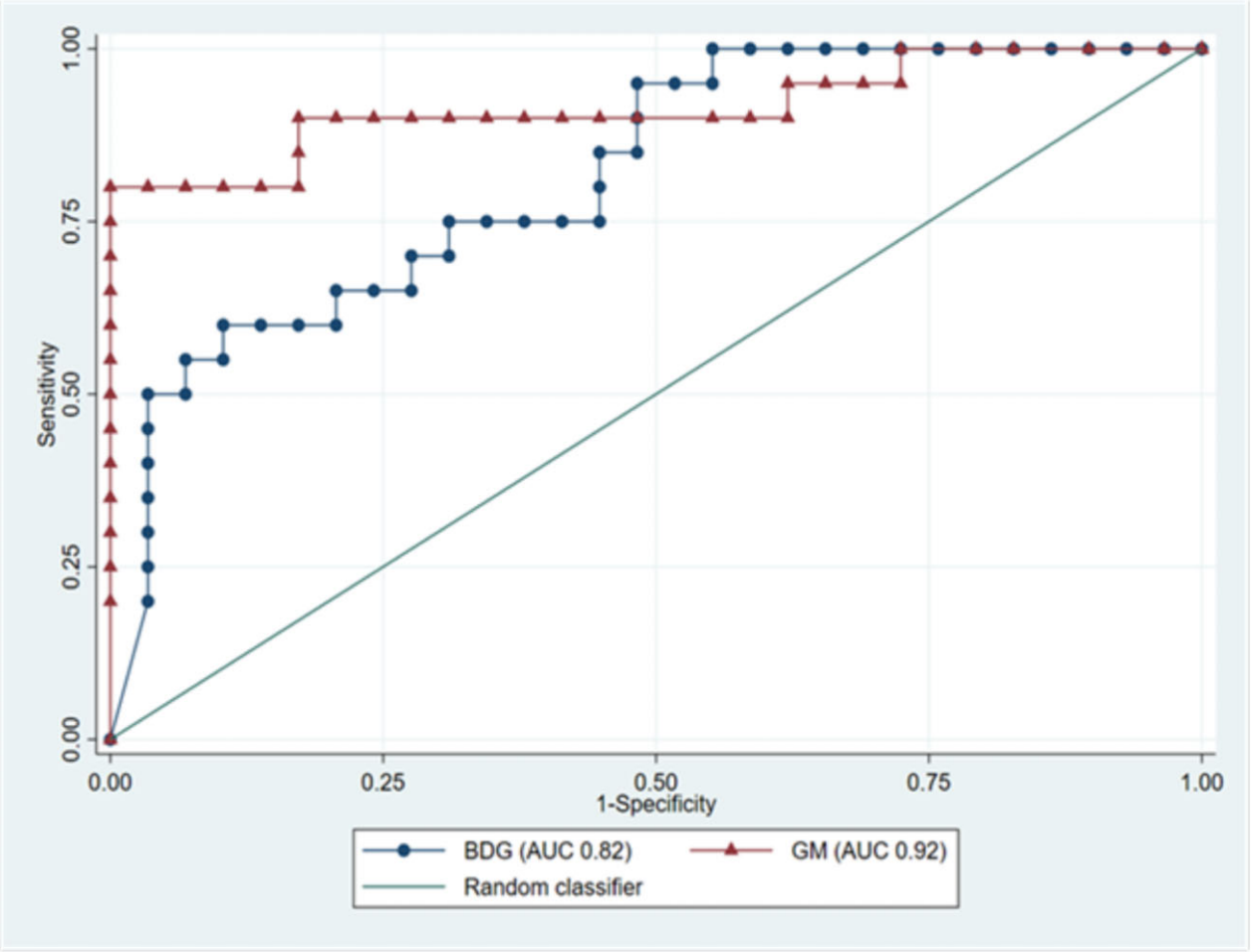

Figure 1. ROC curves and Areas Under Curves (AUC) of β-(1,3)-D-glucan (BDG) and galactomannan *Aspergillus* antigen (GM) detection levels for the diagnosis of HIV-associated histoplasmosis in serum samples according to a strict gold standard definition

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.