PRODUCTION OF INTERLEUKINS BY WHOLE-BLOOD CELL CULTURE FROM INFLAMMATORY BOWEL DISEASE PATIENTS IN THE PRESENCE OF SEVERAL YEASTS

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Introduction:
Inflammatory bowel diseases are characterized by both a dysbiosis and a disturbance of the mucosal inflammatory homeostasis. Probiotics may favorably influence these two aspects. Beside bacteria, some yeast strains may also be considered as probiotics. However, apart from Saccharomyces boulardii no other yeast has been tested clinically for the treatment of IBD or IBS. Furthermore, their ability to modulate the immune response has been little studied. Our aim was to test several yeast strains for their ability to modulate the production of interleukin-1β, interleukin-10, interleukin-12+p40 and interleukin-17 by whole blood cell cultures.

Methods:
Patients affected with inflammatory bowel disease were recruited and their blood was put in whole blood cells culture with lipopolysaccharide, Saccharomyces boulardii ATY-SB-101, Saccharomyces cerevisiae Σ 1278b, Yarrowia lipolytica ATY-YL-103, Brettanomyces bruxellensis Van der Walt MUCL 27700, Debaryomyces hansenii ATY-DH-110 or Candida albicans ATCC 14053. A negative control was also performed without any stimulus. Interleukin-1β, interleukin-10, interleukin-12+p40 and interleukin-17 were measured in the supernatants. Results were compared using Mann-Whitney U test. Differences were considered to be significant when p < 0.05.

Results:
Eleven patients with Crohn’s disease and six patients with ulcerative colitis were recruited. As compared to negative controls, all yeast strains were able to stimulate production of significantly higher amount of interleukin-1β, interleukin-10, interleukin-12+p40 and interleukin-17 with the exception of Brettanomyces bruxellensis Van der Walt MUCL 27700 regarding the levels of IL-12+p40 and IL-17. IL-10 concentrations varied between 10.43 (± 15.88) pg/ml and 131.94 (± 113.27) pg/ml depending on the yeast. The highest production of interleukin-10 was obtained with Yarrowia lipolytica ATY-YL-103 and Debaryomyces hansenii ATY-DH-110. These strains were also among those that stimulate the highest production of interleukin-1β, while the lowest concentrations of this pro-inflammatory cytokine were obtained with Saccharomyces boulardii ATY-SB-101 and cerevisiae Σ 1278b (respectively p<0.001 and p<0.01 compared to LPS). Saccharomyces cerevisiae Σ 1278b was also among the strongest inducers of interleukin-10 and was the strongest inducer of interleukin-17. The production of interleukin-17 was also highly stimulated with Yarrowia lipolytica ATY-YL-103 and Saccharomyces boulardii ATY-SB-101. About interleukin-12+p40, the strongest inducers were Yarrowia lipolytica ATY-YL-103 and Saccharomyces cerevisiae Σ 1278b, however the observed values were much lower than those obtained with LPS. The lowest interleukin-12+p40 concentrations were obtained with Brettanomyces bruxellensis Van der Walt MUCL 27700 and Saccharomyces boulardii ATY-SB-101.

Discussion:
Different yeast strains show highly significant differences in their ability to stimulate interleukins by whole blood cell cultures in patients with inflammatory bowel disease. This suggests very different probiotic properties which have to be taken into account when contemplating probiotic treatment for inflammatory bowel disease. According to these results, Saccharomyces cerevisiae Σ 1278b and Saccharomyces boulardii ATY-SB-101 may be considered as having a favorable profile to be tested in a disease like IBD or IBS, while the profile of Yarrowia lipolytica ATY-YL-103 may be interesting in infectious diseases.
**Keywords:** Yeast, Probiotics, Crohn’s disease, Ulcerative colitis, Cytokine

**Citation:**