

## Characterization of fecal mycobiota reveals yeast-host coevolution in pediatric Crohn's disease

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At variance with the well-recognized role of intestinal bacterial communities, the fungal contribution on the balance between health and disease is still debated. Here we report that gut mycobiota of 93 healthy and Inflammatory Bowel Disease (IBD) affected children is enriched in non-pathogenic species, including *Ascomycetes*. Notably, phylogenetic analysis of *Saccharomyces cerevisiae* fecal isolates provided evidence for co-evolution of strains gut-specific with the host, clustering separately with respect to *S. cerevisiae* isolated worldwide from different sources. Through cytokine production, *S. cerevisiae* isolates differently contribute to local immune homeostasis. Whole genome sequencing of 21 fecal strains discovered wild-domestic mosaic populations evolved in the human gut, unveiling selection in specific loci regulating sporulation and pseudohyphal formation as responsible for the strains' immunomodulatory properties. Also we show that the definition of pathogenic species should be reassessed investigating the variability of the pathogenic profiles of specific strains, corroborating the idea that depending on the genetic makeup of the host and of the yeast, even *S. cerevisiae* could be seen as an opportunistic pathogen.



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