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Fungal chitin treatment reestablishes the anaerobic bacteria and decreases the intestinal inflammation in mice

The gastrointestinal (GI) microbiota acts a natural barrier to colonization and proliferation of opportunistic pathogens, thereby decreasing the risk of intestinal infection and disease. Deregulation of the dynamic crosstalk between the microbiota, intestinal epithelial cells and immune cells is critically involved in the development of inflammatory bowel disease. Clinical and experimental studies have shown that either *Candida albicans* or *Candida glabrata* aggravates the intestinal inflammation-induced by dextran sulfate sodium (DSS) in mice, and, conversely, that DSS induced-colitis promotes the fungal colonization. *C. glabrata* is an opportunistic yeast pathogen that has adapted to colonize all segments of the human GI tract. The fungal cell wall is the predominant site of interaction between the fungus and its host. *C. glabrata* cell wall consists of a complex structure of polysaccharides, proteins, and lipids, but its composition is dynamic, responding to changes in the local environment. Expansion of the fungal wall during growth involves permanent remodeling of the cell wall polysaccharide network, which is comprised of three major types of polysaccharide: mannans, β-glucans, and chitin. Chitin is a homopolymer of β1,4-N-acetylglucosamine (GlcNAc) and is essential for biological functions in fungi, including cell division, forming the primary septum of all septa, hyphal growth, and virulence. Deregulation of chitin biosynthesis is a potential mechanism of virulence and resistance to antifungal treatments.

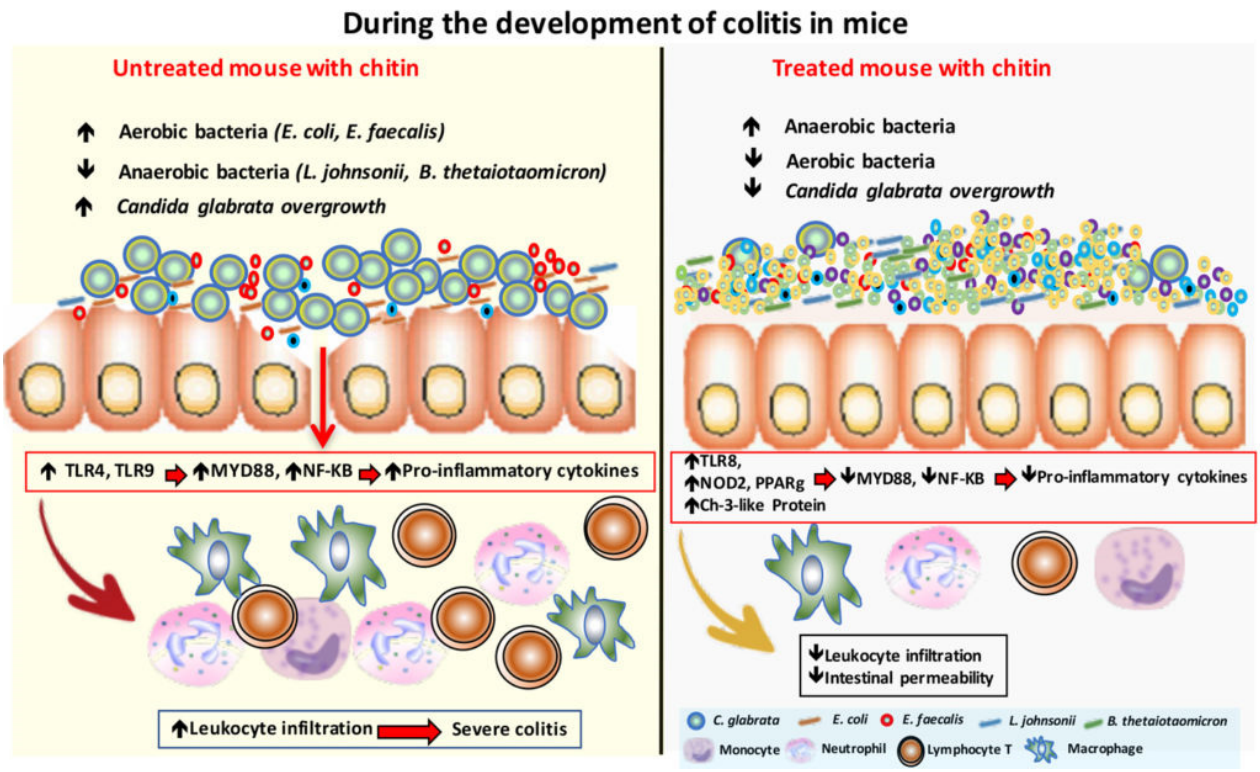

Fig. 1. Effect of oral administration of fungal chitin on intestinal inflammation, *C. glabrata* overgrowth and the gut microbiota.

In the present study, we investigated the impact of *C. glabrata* colonization on the diversity of the gut microbiota in a DSS-induced colitis model, and assessed how the *C. glabrata* cell wall is remodeled in order to persist in the gut environment. We also analyzed the effect of fungal chitin treatment on *C. glabrata*-host interactions in the DSS mouse model.

We observed an increase in *Escherichia coli*, *Enterococcus faecalis*, and *Bacteroides vulgatis* populations and a decrease in *Lactobacillus johnsonii*, *Bacteroides thetaiotaomicron*, and *Bifidobacterium animalis* in mice with DSS-induced colitis. This reduction was more pronounced for *L. johnsonii* during *C. glabrata* overgrowth. In addition, *C. glabrata* overgrowth increased mouse mortality and inflammatory parameters, and modulated the expression of intestinal receptors and signaling pathways. The *C. glabrata* cell wall underwent various changes during the course of *C. glabrata* colonization, and showed a significant increase in chitin. *C. glabrata* deficient in chitin synthase-1, which has a high level of b-mans, expressed in the outer fungal cell wall layer, induced more inflammatory parameters than the parental strain during intestinal inflammation. Oral administration of chitin decreased the inflammatory parameters, and reduced the number of aerobic bacteria and *C. glabrata* overgrowth. Additionally, chitin treatment increased chitinase-3-like protein-1, enabling chitin digestion and the generation of small sized chitin particles that induced IL-10 production via PPARg, NOD-2, and TLR-8 sensing, promoting the attenuation of colitis and *C. glabrata* elimination.

This study provides evidence that inflammation of the gut alters the microbial balance and leads to *C. glabrata* cell wall remodeling through an increase in chitin, which is involved in promoting persistence of *C. glabrata* in the gut while the oral administration of chitin to mice reduced the overgrowth of aerobic bacteria and *C. glabrata* as well the production of inflammatory parameters through stimulation of intestinal receptors.

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Publication

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