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EDITORS' CHOICE | FOCIS HIGHLIGHTS

Barrier busting yeast brew trouble in the gut

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Article

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A healthy microbiota, composed of bacteria, archaea, fungi, and viruses, is important for effective immune responses. Many disease states are associated with alterations in these microbial communities. Most prior studies have focused on commensal bacteria, but a recent study by Chiaro *et al.* calls attention to the fungus among us.

Patients with Crohn's disease often have antibodies against the yeast *Saccharomyces cerevisiae*, and an overgrowth of yeast compared to bacteria is often observed in patients with inflammatory bowel disease (IBD). Mice colonized with *S. cerevisiae* had more severe intestinal disease when treated with two different chemicals that induce colitis. The increased disease severity in *S. cerevisiae*-colonized mice was caused by a loss of barrier function in the gut, not by changes in immune responses. Metabolomic profiling demonstrated that in the presence of *S. cerevisiae*, intestinal epithelial cells produced increased levels of purine breakdown products, including uric acid. Administration of uric acid to mice worsened intestinal damage, and the blockade of uric acid production by allopurinol prevented worsening of colitis in *S. cerevisiae*-colonized mice. These results suggest that *S. cerevisiae* signals the gut epithelium to produce levels of uric acid that are toxic to the intestinal barrier.

In addition, the authors linked *S. cerevisiae* colonization to uric acid production by demonstrating that increased levels of circulating antibodies to *S. cerevisiae* significantly correlated with increases in uric acid in blood of healthy humans.

These studies suggest that *S. cerevisiae* may signal the intestinal epithelium to overproduce uric acid at levels that can inhibit barrier function in the gut. Patients with IBD who have circulating anti-*S. cerevisiae* antibodies and increased uric acid may benefit from allopurinol therapy. Future studies are needed to identify the signals produced by *S. cerevisiae* that induce uric acid production by intestinal epithelia and to more definitively establish the role of *S. cerevisiae* in human gut flora with excessive uric acid production and decreased barrier function.

Highlighted Article

T. R. Chiaro, R. Soto, W. Zac Stephens, J. L. Kubinak, C. Petersen, L. Gogokhia, R. Bell, J. C. Delgado, J. Cox, W. Voth, J. Brown, D. J. Stillman, R. M. O'Connell, A. E. Tebo, J. L. Round, A member of the gut mycobiota modulates host

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Ray Soto et al., Sci Transl Med, 2017

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Elizabeth M. Adler, Sci Signal, 2008

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American Association for the Advancement of Science, Sci Transl Med, 2019

Butyrate benefits the intestinal barrier
Annalisa M. VanHook, Sci Signal, 2015

Calming the Gut
John F. Foley, Sci Signal, 2011

Baker's yeast linked to worsening of symptoms in Crohn's disease
Healio

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Healio, 2020

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Srikanth KatlaSrikanth KatlaBioPAT Laboratory et. al., Next Generation Biomanufacturing Technologies, 2019

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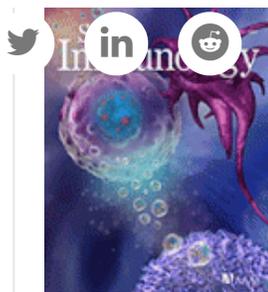
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