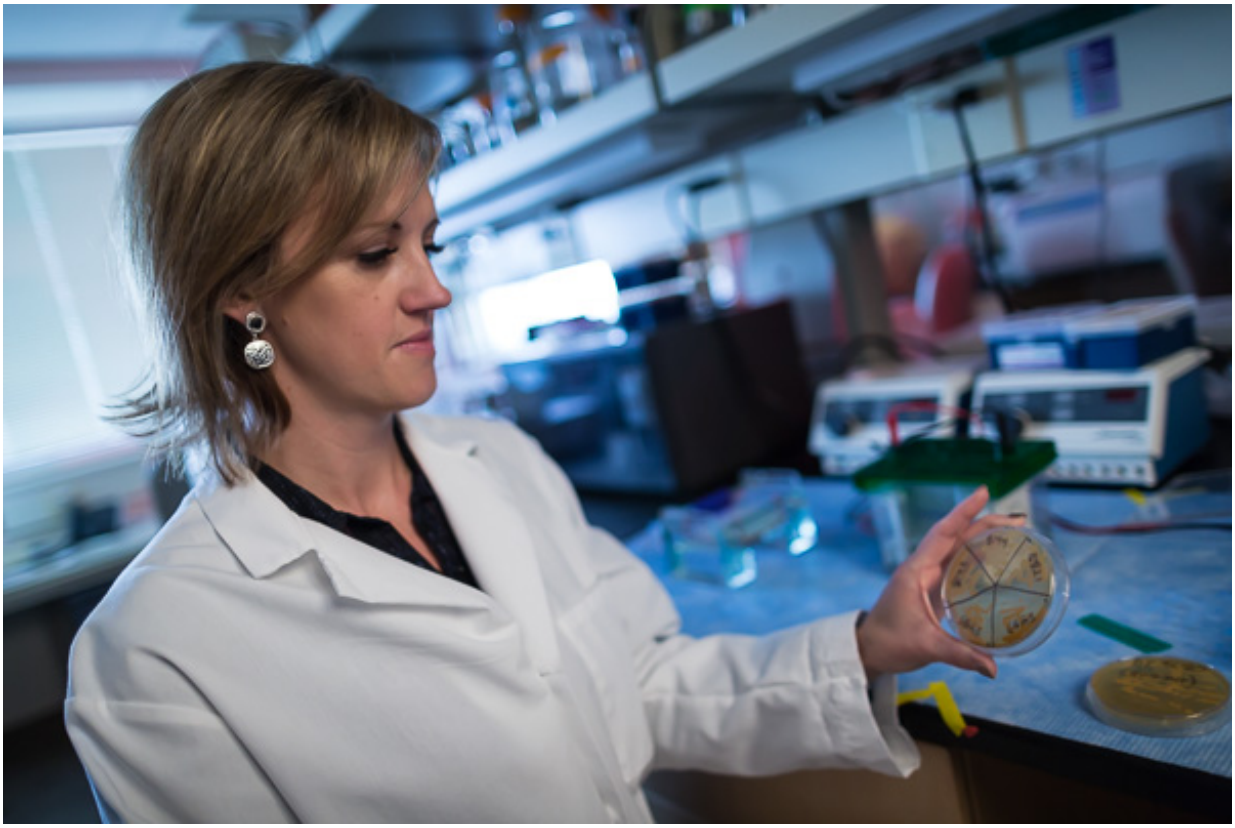
Common yeast may worsen IBD symptoms in Crohn's disease

March 8 2017



June Round, Ph.D. associate professor in pathology at the University of Utah School of Medicine. Credit: University of Utah Health Science

During the past decade, the gut has experienced a renaissance as investigations focus on the role of the microbiome on human health.

While most studies have focused on bacteria, the dominant microbial inhabitants in the gut, scientists at University of Utah Health Sciences used mouse studies to show the role of yeast in aggravating the symptoms of Inflammatory Bowel Disease (IBD). Their work suggests that allopurinol, a generic drug already on the market, could offer some relief. The results of the study will be published online in March 8 issue of *Science Translational Medicine*.

IBD is an autoimmune disease characterized by chronic inflammation of the gastrointestinal tract that produces severe diarrhea, pain, fatigue and weight loss. For several decades, doctors have used the presence of yeast antibodies, specifically antibodies to the cell wall of the yeast *Saccharomyces cerevisiae*, to differentiate between Crohn's disease and ulcerative colitis, two variations of IBD. But it was unclear the role that yeast played in relation to IBD.

"To me this was a huge hole in our understanding of the role of yeast in IBD and our health," begins June Round, Ph.D. associate professor in pathology at the University of Utah School of Medicine.

Broad surveys of yeast in the human gastrointestinal system are just now being published, but the research team chose two types of yeast that are common in the gut microbiota of healthy and IBD patients.

Saccharomyces cerevisiae, also called Baker's yeast, is a prominent organism in our environment and our food. *Rhodotorula aurantiaca* is commonly found in our environment, as well as milk and fruit juice.

In this study, the scientists gave each type of yeast to mice that had been treated with chemicals to induce IBD-like symptoms. The symptoms increased in mice fed *S. cerevisiae*, but not in those fed R aurantiaca. "The mice fed *S. cerevisiae* experienced significant weight loss, diarrhea, bloody stool, just like a person with IBD," said Tyson Chiaro, graduate

student in Round's lab.

The researchers were curious as to why.

They looked at mouse intestinal compounds to decipher this mystery. Mice fed *S. cerevisiae* had a higher concentration of nitrogen-rich compounds, called purines, than mice fed *R. aurantiaca*.

Unlike other yeast varieties, *S. cerevisiae* cannot break down purines that accumulate in the intestinal tract and transition to another compound called uric acid. Uric acid exacerbates inflammation, which may worsen IBD symptoms.

In addition to the mouse study, the scientists examined serum samples from normal adults. "We found that every human serum sample with high *S. cerevisiae* antibodies also had high uric acid levels," she said. While only a subset of patients with IBD are colonized by *S. cerevisiae*, the findings of this study support the idea that yeast exacerbates the illness in those individuals, and that relief may be within reach.

To test the idea, the scientists treated mice with a generic drug, allopurinol, used to prevent production of uric acid in patients with gout. The drug significantly reduced intestinal inflammation in these mice.

"Our work suggests that if we can block the mechanism leading to the production of uric acid, perhaps with allopurinol, IBD patients with a high concentration of *S. cerevisiae* antibodies may have a new treatment option to reduce inflammation, which could allow the intestine time to heal," said Round.

Clinical trials will need to be done determine whether yeast exacerbates IBD in people as it does in mice.

Round wants to expand this work by investigating how bacteria and yeast interact with one another in the gut. "Yeast and bacteria might influence the biology of one another within our gut. Yet, we have no idea how that interaction effects human disease." said Round. "Our research will continue to explore the role intestinal micro-organisms play in our health with the hopes of identifying microbiota-based therapies to treat different diseases."

More information: *Science Translational Medicine*. DOI: 10.1126/scitranslmed.aaf9044

Provided by University of Utah