

Team identifies fungus in humans for first time as key factor in Crohn's disease

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A Case Western Reserve University School of Medicine-led team of international researchers has for the first time identified a fungus as a key factor in the development of Crohn's disease. The researchers also linked a new bacterium to the previous bacteria associated with Crohn's. The groundbreaking findings, published on September 20th in *mBio*, could lead to potential new treatments and ultimately, cures for the debilitating inflammatory bowel disease, which causes severe abdominal pain, diarrhea, weight loss, and fatigue.

"We already know that bacteria, in addition to genetic and dietary factors, play a major role in causing Crohn's disease," said the study's senior and corresponding author, Mahmoud A Ghannoum, PhD, professor and director of the Center for Medical Mycology at Case Western Reserve and University Hospitals Cleveland Medical Center "Essentially, patients with Crohn's have abnormal immune responses to these bacteria, which inhabit the intestines of all people. While most researchers focus their investigations on these bacteria, few have examined the role of fungi, which are also present in everyone's intestines. Our study adds significant new information to understanding why some people develop Crohn's disease. Equally important, it can result in a new generation of treatments, including medications and probiotics, which hold the potential for making qualitative and quantitative differences in the lives of people suffering from Crohn's."

Both bacteria and fungi are microorganisms – infinitesimal forms of life that can only be seen with a microscope. Fungi are eukaryotes: organism whose cells contain a nucleus; they are closer to humans than bacteria, which are prokaryotes: single-celled forms of life with no nucleus. Collectively, the fungal community that inhabits the human body is known as the mycobiome, while the bacteria are called the bacteriome. (Fungi and bacteria are present throughout the body;

previously Ghannoum had found that people harbor between nine and 23 [fungal species](#) in their mouths.)

The researchers assessed the mycobiome and bacteriome of patients with Crohn's disease and their Crohn's-free first degree relatives in nine families in northern France and Belgium, and in Crohn's-free individuals from four families living in the same geographic area. Specifically, they analyzed fecal samples of 20 Crohn's and 28 Crohn's-free patients from nine families and of 21 Crohn's-free patients of four families. The researchers found strong fungal-bacterial interactions in those with Crohn's disease: two bacteria (*Escherichia coli* and *Serratia marcescens*) and one fungus (*Candida tropicalis*) moved in lock step. The presence of all three in the sick [family members](#) was significantly higher compared to their healthy relatives, suggesting that the bacteria and fungus interact in the intestines. Additionally, test-tube research by the Ghannoum-led team found that the three work together (with the *E. coli* cells fusing to the fungal cells and *S. marcescens* forming a bridge connecting the microbes) to produce a biofilm – a thin, slimy layer of microorganisms found in the body that adheres to, among other sites, a portion of the intestines – which can prompt inflammation that results in the symptoms of Crohn's disease.

This is first time any fungus has been linked to Crohn's in humans; previously it was only found in mice with the disease. The study is also the first to include *S. marcescens* in the Crohn's-linked bacteriome. Additionally, the researchers found that the presence of beneficial [bacteria](#) was significantly lower in the Crohn's patients, corroborating previous research findings.

"Among hundreds of bacterial and fungal species inhabiting the intestines, it is telling that the three we identified were so highly correlated in Crohn's patients," said Ghannoum. "Furthermore, we found

strong similarities in what may be called the 'gut profiles' of the Crohn's-affected families, which were strikingly different from the Crohn's-free families. We have to be careful, though, and not solely attribute Crohn's disease to the bacterial and fungal makeups of our intestines. For example, we know that family members also share diet and environment to significant degrees. Further research is needed to be even more specific in identifying precipitators and contributors of Crohn's."

In addition to Ghannoum, other Case Western Reserve University investigators equally contributing to the study are Pranab Mukherjee, Chris Hager, Jyotsna Chandra, Mauricio Retuerto, and Hisashi Fujioka. Other members of the study team are from France and Belgium, as well as the Icahn School of Medicine at Mt. Sinai in New York City.

More information: G. Hoarau et al. Bacteriome and Mycobiome Interactions Underscore Microbial Dysbiosis in Familial Crohn's Disease, *mBio* (2016). DOI: 10.1128/mBio.01250-16 , [dx.doi.org/10.1128/mBio.01250-16](https://doi.org/10.1128/mBio.01250-16)

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