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Cedars-Sinai researchers explore role of fungus in digestive disorders

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Cedars-Sinai researchers say their examination of the fungi in the intestines suggests an important link between these microbes and inflammatory diseases such as ulcerative colitis.

In the new study, published in the June 8 issue of *Science*, researchers at Cedars-Sinai's Inflammatory Bowel and Immunobiology Research Institute identified and characterized the large community of fungi inhabiting the large intestine in a model of the disease.

The digestive tract is home to a large number of micro-organisms. In fact, with an estimated 100 trillion bacteria residing in the gut, microbes outnumber human cells in the body. Some are necessary to aid in digesting food, producing necessary vitamins and suppressing the growth of harmful microbes. Others are harmful to the body, contributing to illnesses such as Crohn's disease, ulcerative colitis and obesity.

Modern DNA-sequencing technology has revolutionized the study of these microbes in the last decade, allowing the role of bacteria in disease to be understood more clearly, as is shown in the Cedars-Science research published in *Science*.

"It's long been recognized that fungi must also exist in the gut, but we're among the first to investigate what types, how many, and whether they're important in disease," said David Underhill, PhD, associate professor and director of the Graduate Program in Biomedical Science and Translational Medicine, who led the study. "We were truly stunned to see

just how common fungi are, identifying more than 100 different types" and seeing linkages to digestive disorders.

An estimated 1.4 million Americans have Inflammatory Bowel Disease, or IBD, a chronic digestive disorder, and about 30,000 new cases are diagnosed annually. Ulcerative colitis, one of the most common types of IBD, causes inflammation and ulcers in the top layers of the lining of the large intestine. Common symptoms include abdominal pain, diarrhea, bleeding, fatigue, weight loss and loss of appetite. Ulcerative colitis patients can be at increased risk of developing colorectal cancer.

"This study takes us an important step closer to understanding how fungi contribute to disease, as well as significantly expanding our understanding of what types of fungi are living in our bodies," said Iliyan Iliev, PhD, a Cedars-Sinai research scientist and lead author on the study.

To determine fungi contribute to inflammatory disease, the study homed in on a protein called Dectin-1, produced by white blood cells and used by the immune system to detect and kill fungi. In an animal model of the disease, researchers found that the protein is important in protecting against inflammation caused by indigenous fungi. The finding has significant implications for human disease, as scientists at the Cedars-Sinai Medical Genetics Institute found a variant of the gene for Dectin-1 that is strongly associated with severe forms of ulcerative colitis.

Provided by Cedars-Sinai Medical Center