Modified yeast used to treat common bacterial intestinal infection

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A medical illustration of Clostridioides difficile bacteria, formerly known as Clostridium difficile, presented in the Centers for Disease Control and Prevention (CDC) publication entitled, Antibiotic Resistance Threats in the United States, 2019. Credit: CDC

A team of researchers from the University of Maryland School of Dentistry and FZata Inc. has found that modifying a common type of yeast in a certain way made it an effective treatment for Clostridioides difficile infections in mice. In their paper published in the journal *Science Translational Medicine*, the group describes how they modified Saccharomyces boulardii to produce antibodies that neutralize the toxins generated by C. difficile infections and how well it worked when tested.

C. difficile infections typically involve people (usually older people) who have been prescribed antibiotics to treat a bacterial infection —when the antibiotics kill off good bacteria in the gut, the gut is vulnerable to C. difficile infections. Such infections are very common in nursing homes and some hospitals—they account for approximately 30,000 deaths in the U.S. annually. Treatment generally involves more antibiotics. And while antibiotics are effective against C. difficile, medical scientists are concerned that using them in such cases is leading to resistance. In this new effort, the researchers have found a way to combat the bacteria without using antibiotics.

The new approach involved designing antibodies for two toxins produced by C. difficile and then engineering Saccharomyces boulardii (a common yeast found in many probiotic supplements) to produce them. The team then fed the resulting product to mice after killing their gut biomes using antibiotics; the mice were then infected with C. difficile. The researchers found that this resulted in reduced inflammation in the intestines, which in turn kept the mice from dying from the infection. The researchers also gave the treatment to test mice first and then infected them with C. difficile. They found that doing so reduced symptoms and once again prevented the mice from dying. Testing of colon tissue in both cases showed not only reduced inflammation, but an absence of the tissue damage generally associated with C. difficile infections.

The researchers suggest more testing is required before clinical trials can start and note also that they need funding to continue their research. They predict that their efforts will lead to therapies for treatment and prevention of C. difficile infections in just a few years.

More information: Kevin Chen et al. A probiotic yeast-based immunotherapy against Clostridioides difficile infection, *Science Translational Medicine* (2020). DOI: 10.1126/scitranslmed.aax4905

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