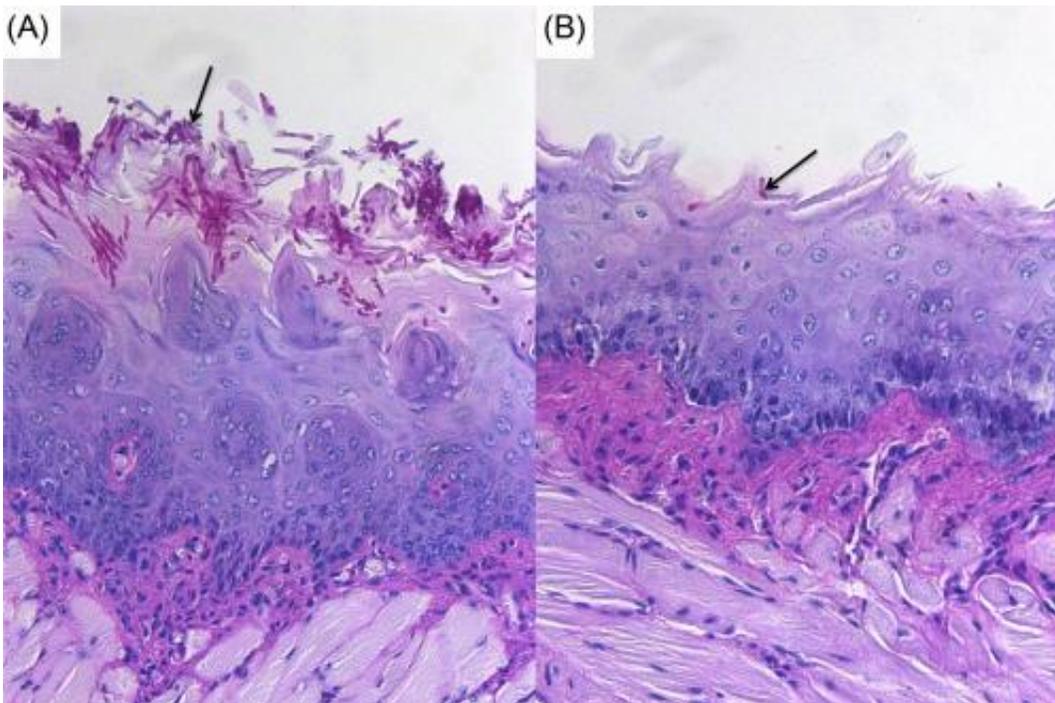


Microorganism shows promise in inhibiting thrush

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Treatment of mice with *Pichia* spent medium reduces the extent of tissue invasion by *Candida* (see arrows) in the tongue. This image shows (A) untreated and (B) *Pichia* spent medium treated mice tissue. Credit: Mahmoud Ghannoum

Scientists at Case Western Reserve School of Medicine and University Hospitals (UH) Case Medical Center have discovered how the beneficial fungal yeast, *Pichia*, holds at bay a harmful fungal yeast, *Candida*. The hope for this finding is that components in *Pichia* could one day become therapeutic agents to stave off not only thrush, but also other life-

threatening systemic fungal infections. Research findings about the effect of oral *Pichia* on *Candida* appear in the March 13 edition of *PLOS Pathogens*.

"Our aim was to try to understand what microorganisms live in our mouths. A disturbed equilibrium of these microorganisms can lead to disease," said the study's senior author Mahmoud A. Ghannoum, PhD, EMBA, professor of dermatology and pathology at the School of Medicine and director of the Center for Medical Mycology at UH Case Medical Center.

The study involved testing the mouths of 24 [patients](#) from UH Case Medical Center—12 HIV infected and 12 not infected with HIV. HIV-infected patients were selected for comparison in the study because thrush is a common occurrence for them. The oral cavity was tested for fungi and bacteria using pyrosequencing, a method that uses DNA analysis, which is more powerful with greater specificity than conventional, culture-based approaches.

"When we looked at the data, we found to our surprise that bacteria did not change much between HIV-infected patients and those who were not," Ghannoum said. "However, what changed significantly between the two groups was the composition of the fungal community. We found that when *Candida* is present, *Pichia* is not, and when *Pichia* is present, *Candida* is not—indicating *Pichia* plays an important role in treating thrush."

From these observations, investigators conducted in vitro (test tube) experiments on *Candida* and *Pichia*. When they grew *Candida* in the test tube in the presence of *Pichia*, there was a striking reduction in *Candida* growth. They also discovered that *Pichia* secretes material, or a protein, that controls *Candida*. This *Pichia*-secreted material, referred to as supernatant, inhibits biofilm formation, germination and adherence in

Candida, factors that mark a microbe's level of harmfulness.

Investigators then took their findings to the next level with experiments on three groups of *Candida*-infected mice. One group of mice was treated with *Pichia* supernatant. The next group was treated with nystatin, a topical treatment for thrush. Still another group received no treatment. The outcome? In the mouths of the *Pichia*-treated mice, the level of *Candida* was nearly eradicated, though traces remained. Even the nystatin-treated mice had far more *Candida* present than the *Pichia*-treated mice. Additionally, the physical symptoms, such as tongue appearance, improved in the *Pichia*-treated group.

"One day, not only could this lead to topical treatment for thrush, but it could also lead to a formulation of therapeutics for systemic fungal infections in all immunocompromised patients," he said. "In addition to patients with HIV, this would also include very young patients and patients with cancer or diabetes."

As a next step this year, investigators will study *Pichia* supernatant to identify its components that inhibit *Candida* and other fungi.

More information: Mukherjee PK, Chandra J, Retuerto M, Sikaroodi M, Brown RE, et al. (2014) Oral Mycobiome Analysis of HIV-Infected Patients: Identification of *Pichia* as an Antagonist of Opportunistic Fungi. *PLoS Pathog* 10(3): e1003996. doi:10.1371/journal.ppat.1003996

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