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Researchers hone in on new strategy to treat common infection

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Researchers at Georgetown University Medical Center (GUMC) have successfully tested a genetic strategy designed to improve treatment of human infections caused by the yeast *Candida albicans*, ranging from diaper rash, vaginitis, oral infections (or thrush which is common in HIV/AIDS patients), as well as invasive, blood-borne and life-threatening diseases.

Their findings confirm that inhibiting a key protein could provide a new drug target against the yeast, which inhabits the mucous membranes of most humans. The research was presented today at the 48th Annual Interscience Conference on Antimicrobial Agents and Chemotherapy/46th Annual Meeting of the Infectious Diseases Society of America (ICAAC/IDSA) in Washington, DC.

"This is a genetically intelligent approach to target identification and drug design," says the study's lead author, Richard Calderone, PhD, professor and chair of the department of microbiology and immunology and co-director of the PhD program in the global infectious disease program at GUMC.

"*Candida* infections are often treatable, however, in patients that are immunocompromised following cancer chemotherapy, bone marrow transplantation, or surgery, diagnosis is often delayed, postponing therapy," he says. "Also when drug-resistant yeast pathogens cause the infection, clinical management of the patient becomes a problem."

Candida invasive, blood-borne infections are the fourth most common hospital-acquired infection in the United States, costing the healthcare system about $1.8 billion each year, Calderone says.

"More drug resistance is being seen clinically, so there is significant room for improvement in the therapies used today," he says

This study continues research in which Calderone and his colleagues identified a protein, the product of the Ssk1 gene that *Candida* needs to infect its host. To date, this protein has not been found in humans or in animals, which means it could be "targeted" with a novel drug without producing toxicity because such an agent should only attack the fungus.

The researchers found that if the Ssk1 gene is deleted from *Candida albicans*, the "triazole" drugs that are now used to treat these diseases are much more effective in the laboratory. "This allows the triazole drugs to do their job," Calderone says. "We propose that this finding might lead to other, possibly more effective, treatment options."

In this study, the researchers used a gene microarray analysis to further understand what knocking out the Ssk1 gene does to the organism, and they discovered that the gene is critical to the pathogenic nature of the fungi.

What this means is that an Ssk1 inhibitor might work in synergy with a triazole or perhaps as an effective stand-alone drug to treat *Candida* infections, the researchers say. If it works in *Candida*, it may have broader activity in other pathogens because Ssk1p is found in other fungi.

"Using the genome of the organism to find genes to target is a logical approach to drug design," he says. The researchers are now working with other groups to find the right agent to target the Ssk1protein.

Source: Georgetown University Medical Center