How a common fungus knows when to attack

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The opportunistic fungal pathogen *Candida albicans* inconspicuously lives in our bodies until it senses that we are weak, when it quickly adapts to go on the offensive. The fungus, known for causing yeast and other minor infections, also causes a sometimes-fatal infection known as candidemia in immunocompromised patients. An in vivo study, published in *mBio*, demonstrates how *C. albicans* can distinguish between a healthy and an unhealthy host and alter its physiology to attack.

"The ability of the fungus to sense the immune status of its host may be key to its ability to colonize harmlessly in some people but become a deadly pathogen in others," said Jessica V. Pierce, BA, PhD student in the molecular microbiology program at the Sackler School of Graduate Biomedical Sciences at Tufts.

"Effective detection and treatment of disease in immunocompromised patients could potentially work by targeting the levels of a protein, Efg1p, that we found influenced the growth of Candida albicans inside the host," she continued.

The researchers knew from previous research that Efg1p influences the expression of genes that regulate how harmful a fungal cell can become. Surprisingly, the investigators found that lower Efg1p levels allow the fungal cells to grow to high levels inside a host. Higher levels of the protein result in less growth.

To examine how the immune status could affect the growth of *C.*

albicans within a host, the researchers fed both healthy and immunocompromised mice equal amounts of two fungal strains containing two different levels of the Efg1p protein.

Fecal pellets from the mice were tested to determine which strain of fungi thrived. In a healthy host, the fungal cells with higher levels of the protein predominated.

In immunocompromised mice, the fungal cells with lower levels of the protein flourished. The researchers noted that lack of interactions with immune cells in the intestinal tract most likely caused the necessary environmental conditions favoring fungal cells that express lower levels of the protein, resulting in fungal overgrowth and setting the stage for systemic infection.

"By having a mixed population with some high Efg1p cells and some low Efg1p cells, the fungus can adjust its physiology to remain benign or become harmful when it colonizes hosts with varying immune statuses. These findings are important because they provide the first steps toward developing more effective methods for detecting and treating serious and stubborn infections caused by Candida albicans, such as candidemia," said Carol A. Kumamoto, PhD, professor of molecular biology and microbiology at Tufts University School of Medicine and member of the molecular microbiology and genetics program faculties at the Sackler School of Graduate Biomedical Sciences.

The immune system and "good bacteria" within the body act to regulate the size of *C. albicans* fungal populations in healthy individuals. When the immune system is compromised, the fungus can spread throughout the body. Candidemia, i.e. blood-borne *Candida*, is the fourth most common blood infection among hospitalized patients in the United States and is found in immunocompromised patients such as babies, those with catheters, and the critically ill.

More information: Pierce JV, Kumamoto CA. *mBio*. "Variation in Candida albicans EFG1 Expression Enables Host-Dependent Changes in Colonizing Fungal Populations." July 24, 2012. DOI:10.1128/mBio.00117-12

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