Study suggests when dealing with fungi, it's best to attack from both sides

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(PhysOrg.com) -- Each year, 83,000 life-threatening fungal infections cost us $2.6 billion. And this number will only go up as HIV infection, cancer chemotherapy, and organ transplants bump up the immune-compromised population where these fungi thrive.

Or maybe not.

Dr. David E. Levin, Professor of Molecular and Cell Biology at Boston University Henry M. Goldman School of Dental Medicine, and his team suggest in a new study that combining a therapy that increases pressure from within the fungal cell with existing antifungal drugs that weaken the cell wall, is the right mix to kill the infection.

After less than eight years on the market, clinical use of the new front line drugs for treating systemic fungal infections, known as echinocandins, is already being threatened by the appearance of clinical isolates with increased resistance to their antifungal activity. Echinocandin drugs, like caspofungin, attack the cell surface by interfering with cell wall biosynthesis. To enhance the sensitivity of fungal pathogens to these drugs, Dr. Levin looked to increase the internal force against the cell wall by exploiting a new target in fungi that is absent from human cells.

That target is what Dr. Levin calls the Rgc (abbreviation for Regulators of the glycerol channel) proteins. The paper is the first to describe the function of these proteins, which is to open a molecular “pressure valve”

at the fungal cell surface. Inhibiting the Rgc proteins alone does not kill the fungal cells but makes them more sensitive to the effect of echinocandins.

“We envision a form of combination therapy for systemic fungal infections based on adding Rgc protein inhibitors to existing antifungal drugs,” Dr. Levin says.

The study, Identification of positive regulators of the yeast Fps1 glycerol channel, is available online in *PLoS Genetics*.

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