Biologists prove ZOLOFT packs potential to fight fungal meningitis

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New research conducted by biologists at Texas A&M University suggests that ZOLOFT, one of the most widely prescribed antidepressants in the world, also packs a potential preventative bonus — potent mechanisms capable of inhibiting deadly fungal infections.

The findings are the result of a two-year investigation by Xiaorong Lin, assistant professor of biology, and Matthew S. Sachs, professor of biology, involving sertraline hydrocholoride (ZOLOFT) and its effects on Cryptococcus neoformans, the major causative agent of fungal meningitis — specifically, cryptococcal meningitis, which claims more than half a million lives worldwide each year, according to a 2009 Center for Disease Control (CDC) report.

Their research, funded with grants from the American Heart Association (AHA), the Norman Hackerman Advanced Research Program, and the National Institutes of Health (NIH), is published in the June issue of the American Society of Microbiology journal *Antimicrobial Agents and Chemotherapy*. Their research team includes Ph.D. candidate Bing Zhai and postdoctoral fellows Cheng Wu and Linqi Wang.

"The point here is that if there is a drug that already exists, is known to be well-tolerated, and has alternative uses, that's a good thing," Sachs says. "The billion dollars it would take to bring a drug to the market — that's already done."

C. neoformans is a potentially dangerous fungal pathogen found in many

soils throughout the world that may cause systemic infections, particularly involving the central nervous system. In most cases, the microscopic, airborne fungal cells of *C. neoformans* cause asymptomatic colonization in the lungs. However, Lin says the fungus is particularly aggressive in people with weakened immune systems and can spread to other parts of the body, such as the brain and spinal cord, resulting in cryptococcal meningitis — a condition that, in absence of treatment, is fatal.

Lin participated in a previous study to screen a collection of FDA-approved drugs in a John Hopkins Clinical Compound Library to determine if any contained fungicidal agents. Although sertraline was shown to only moderately inhibit the effects of common fungal strains like Aspergillus nidulans, a genus of common mold often found on spoiled food, and Candida, a genus of yeast often associated with mammals, sertraline was found to be particularly effective against *C. neoformans*.

A follow-up investigation of sertraline in a mouse model of systemic cryptococcosis revealed that it combats infection similar to fluconazole, an antifungal drug used commonly since the early 1990s. Moreover, a drug combination of sertraline and fluconazole was found to work more efficiently than either drug alone.

Lin says that even though the infection ultimately proved fatal in the mice study, sertraline as a cryptoccol treatment still holds promise. Because sertraline reduced the overall fungal burden within the mice and also possesses the desirable ability to cross the blood-brain barrier as an antidepressant, there is still hope it can be altered to serve as a viable treatment option.

"The problem for many current antifungal drugs is that many cannot go to the brain, and it's very difficult for a lot of compounds to reach the

brain in the first place," Lin says. "So, you run into the problem of not killing all the fungus or having a very low level of fungus still exist. The fact is, this antidepressant can cross the blood-brain barrier and can get into the tissue at high concentrations."

It remains unclear exactly what dosage and concentration of sertraline is necessary to completely eliminate cryptococcosis, especially cryptococcal meningitis, but Lin and Sachs hope those answers will come to light with further testing.

"If this becomes useful, it could represent a truly significant increase in our ability to help people with brain cryptococcal infections," Sachs adds.

More information: aac.asm.org/content/56/7/3758.abstract?etoc

Provided by Texas A&M University