COLLEGE STATION, Texas, March. 21, 2011 – Employing a novel method to observe the evolution of microorganisms, researchers at the Artie McFerrin Department of Chemical Engineering at Texas A&M University have found an evolved fungus with an uncommon and unsettling survival advantage – an ability to thrive in the presence of the drugs meant to kill it as well in environments where such drugs are not present.

The findings by Assistant Professor Katy Kao and graduate student Mian Huang appear in the journal "Eukaryotic Cell" and detail the team's work with the fungus *Candida albicans*, a common culprit in hospital-acquired infections and a fungus that historically has shown increased resistance to several antifungal treatments.

While *Candida albicans'* increased drug resistance is well known, its concurrent ability to live – and live well – in the absence of drug therapies is highly uncommon and flies in the face of common knowledge about the way organisms evolve, Kao says. In short, the fungus shouldn't be able to thrive in both environments, she explains.

When it comes to adaptability, Kao says, there are usually trade-offs for these tiny organisms. Those trade-offs, she adds, result in a fungal pathogen evolving to be more suited for one type of environment while becoming less fit in another.

"Usually a drug-resistant microbe pays some kind of a cost for its acquired ability to survive in the presence of a drug; this cost usually results in the organism not being able to survive as well in an environment where the drug is not present," Kao says. "This can have important effects on the therapy regimen," she explains. "For example, if a microbe develops resistance to a particular drug, the doctors can stop the therapy. By then, the microbe has 'liked' the drug so much that it dies in the absence of the drug."

That was not the case in Kao's research.

Not only did *Candida albicans* show increased resistance to drug treatments, it also appeared to maintain its survival advantages when the drug was removed from its environment. In other words, there were no "trade offs." That's a finding that concerns Kao because of its potentially serious implications for treating patients with compromised immune systems who take antifungal drugs as a preventative for the damage *Candida albicans* can cause.

Although *Candida albicans* is naturally present in the human body, it is an opportunistic pathogen that can cause diseases when the immune system does not keep the microbial population in check, Kao explains. In healthy people, the fungus is regulated by the body's normal biological processes, but for people with compromised immune systems, such as those suffering from AIDS or cancer, *Candida albicans* can grow at faster rates and cause serious health issues.

To combat this, patients with natural or artificially suppressed immune systems are frequently prescribed antifungal drugs as a preventative despite not having fungal infections, Kao says. While it has been recognized that such a course of treatment can sometimes inadvertently strengthen the fungus by bolstering its drug resistance, Kao's research reveals another disturbing aspect of the treatment. Stopping the treatment may, in effect, leave the patient with a fungus that's even harder to treat.

It's a potential no-win situation, she says.

"Based on our findings, stopping the drug treatment after exposure is not going to help," she said. "In fact, it can potentially evolve drug resistant mutants within the body that are more fit even after the drug therapy is stopped. That may be one of the reasons physicians are seeing more drug-resistant cases in clinical settings," Kao says.

Key to Kao's research was the use of a technique she developed for studying how generations of microbes evolve throughout time. The technique, known as "Visualizing Evolution in Real-Time" (VERT) enables Kao to view "live" how generations of particular microbes respond to environmental pressures and subsequently evolve the adaptations that allow them to flourish. This is achieved, she explains, by genetically engineering these populations to appear a certain color. In the case of *Candida albicans,* a colored florescent protein was added to these populations that made them appear red, green or yellow.

As some of these populations evolved to develop advantageous survival mechanisms, they, in turn, grew at faster rates than other less-fit populations. When this occurred, Kao was able to observe an expansion and contraction of colors that signaled that certain populations were outpacing other populations because of their adaptations, she says.

The VERT system, Kao adds, is the rough lab equivalent of the microbial environment within a human being because microbes in the human body exist as a similar genetically diverse population in which drug resistance evolves randomly. Kao believes the system could be an invaluable tool in helping her shed light on how *Candida albicans* is able to maintain its survival advantage in or out of the presence of drug therapies.

"Going in and identifying the exact mutations that cause these resistant mechanisms would be the next step," Kao says. "Knowing this mechanism would help us design a therapy regimen which would be helpful in more personalized treatments."

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