New drugs hope for 'superbug' yeast and thrush

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(Medical Xpress) -- Researchers are a step closer towards creating a new class of medicines and vaccines to combat drug-resistant and deadly strains of fungal infections, following a new study published today in *Proceedings of the National Academy of Sciences.*

Yeast infections are the fourth most common cause of infection acquired by people in hospitals, although in healthy people they are most usually associated with vaginal or oral yeast infections known as thrush. In extreme cases in vulnerable patients, such yeasts can circulate in the bloodstream and spread throughout the body, causing systemic candidiasis. This is life-threatening in around half of patients when the infection spreads in this way.

Researchers from Imperial College London have now found out how yeast cells identify and attach to human tissue in order to colonise it and cause an infection. They have identified the key features in this process and now plan to create and test prototype drug-like molecules that interfere with the yeast and prevent the infection from taking hold.

There are already treatments that are effective at suppressing yeast infections and eliminating them from medical equipment, but microorganisms are constantly evolving to outsmart existing drugs and many strains of yeast have already become completely resistant to antifungal treatments. Scientists are seeking new ways to effectively kill them or prevent infection.

"Most healthy women will have thrush or other mild yeast infection at some point in their lives, but what is less well known is that yeasts can be lethal, and a major health concern for vulnerable hospital patients," said Dr Paula Salgado from the Department of Life Sciences at Imperial College London, one of the main investigators who carried out the research. "What I find most concerning is the fact that we don't seem to have an effective way to control the most severe cases of these infections. Our work allows us to understand the details involved and provide vital clues to develop new drugs and clinical applications."

Lead author of the research, Dr Ernesto Cota, and his colleagues from the Department of Life Sciences and the Centre for Structural Biology used data from high field magnets in Imperial's state-of-the-art Nuclear Magnetic Resonance (NMR) Centre as well as large x-ray research facilities across Europe to study a protein called Als adhesin on the surface of the yeast Candida albicans, in order to explore the role it plays in helping the yeast recognise human tissues.

To help visualise the fine details of the recognition mechanism, they probed the structure of this fungal protein attached to a complementary human cell molecule using powerful x-rays at the UK's national synchrotron facility, Diamond Light Source, in Oxfordshire. This allowed the researchers to fully identify which tiny part of Als adhesin attaches the yeast cell to human tissues and the exact features of that interaction.

"We have shown the unique way that Candida albicans has evolved to recognise and latch on to a wide variety of human cells. Als adhesin proteins give the yeast an ability to thrive throughout the human body, which is what makes it such a dangerous infection," said Dr Cota. "We hope this new knowledge will allow us to create drug-like molecules that prevent the yeast cells from taking hold, by blocking this specific molecular mechanism."

The researchers say their findings pave the way for commercial vaccines and anti-fungal compounds that are effective against a wide range of infection-causing fungi. The next step is to test small, drug-like compounds in the laboratory to analyse whether they behave as expected. These could then be developed into the first stages of new treatments.

"This work is exciting because it shows the great amount of insight that can be gained through interdisciplinary collaborations", said another author, molecular microbiologist Dr Lois Hoyer from the University of Illinois at Urbana-Champaign, who first discovered and characterized the Als adhesins. "The new data transform this field of study and highlight the next set of questions that can be answered by combining the structural biology in Dr Cota's group with the cellular biological expertise in my laboratory."

More information: www.pnas.org/content/early/201 … /1103496108.abstract

Provided by Imperial College London