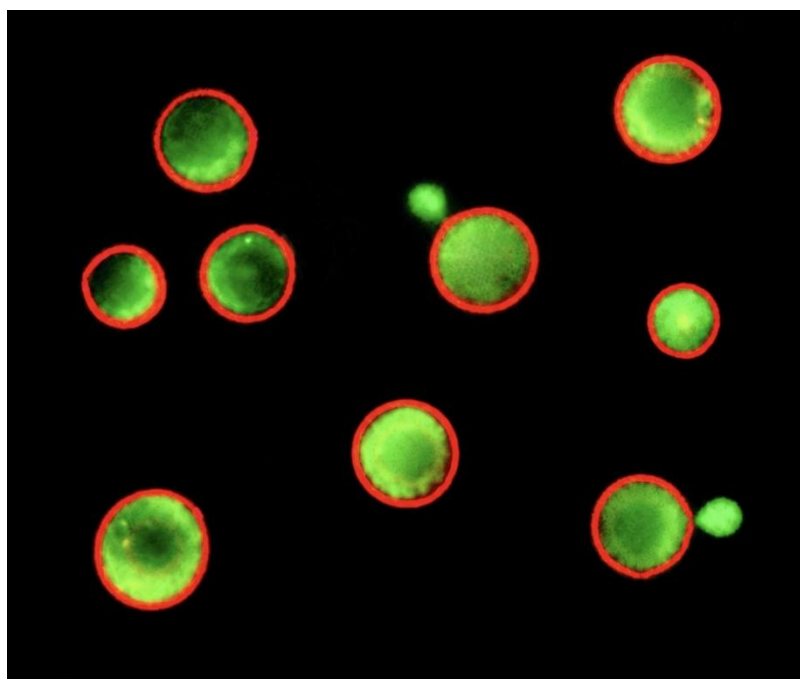




CCMB Scientists Discover the Hidden Mechanism That Helps a Deadly Fungus Infect the Brain



Cryptococcus neoformans Giant Cells

Hyderabad, 21st August, 2026: Fungal infections are increasingly emerging as one of the world's most serious yet overlooked public health threats. Invasive fungal pathogens are responsible for hundreds of thousands of deaths every year, particularly among people with weakened immune systems. Yet treatment options remain alarmingly limited. Antifungal drugs are few in number, can be toxic, and resistance against them is steadily increasing. Recognizing this growing crisis, the World Health Organization (WHO) has identified several fungal pathogens as critical priorities for research and new drug development. Among the deadliest of these is *Cryptococcus neoformans*.

Unlike many fungal infections that remain confined to the skin, *Cryptococcus neoformans* begins as a lung infection but can spread through the bloodstream to the brain, causing cryptococcal meningitis—a devastating disease responsible for nearly one in every five AIDS-related deaths worldwide. Although relatively unknown outside the medical community, cryptococcal meningitis affects more than 150,000 people annually across the globe, including thousands in India, and continues to carry an unacceptably high mortality rate.

The Bigger, the Better: A Deadly Fungal Survival Strategy:

One of the greatest "superpowers" of *Cryptococcus neoformans* is its remarkable ability to transform itself after entering the lungs. While most fungal cells are only a few micrometres in diameter, some enlarge dramatically to become enormous "**Titan cells**"—giant fungal cells several times larger than their normal counterparts. These oversized cells are far more difficult for immune cells to engulf and destroy, allowing the fungus to survive, evade immune attack, and establish persistent infections inside the body.

Scientists have known about titan cells for nearly two decades. However, despite their central role in cryptococcal infection, one fundamental question has remained unanswered:

How does the fungus decide to become a Titan cell?

Researchers led by **Dr. Sriram Varahan** at the CSIR–Centre for Cellular and Molecular Biology (CCMB), Hyderabad, have now uncovered an unexpected answer. Their [study](#) identifies a previously unknown biological circuit that enables *Cryptococcus neoformans* to form titan cells by linking the fungus's energy metabolism to one of its most important cellular signalling systems. The discovery reveals an entirely new layer of regulation governing fungal virulence and opens promising possibilities for developing future antifungal therapies.



Dr Sriram Varahan's team; Dr Varahan is third from left.

A Hidden Circuit Inside the Giant Cells

Scientists have long regarded metabolism as the process that simply provides cells with energy. But the new study reveals that metabolism also acts as a powerful

decision-making system that determines whether the fungus can become more dangerous.

"We uncovered an unexpected biological connection between the fungus's energy hub and one of its most important survival pathways," said Dr. Sriram Varahan. "Our findings show that metabolism is not merely supplying fuel—it is actively controlling the cellular signals that allow the fungus to transform into titan cells."

The researchers discovered that efficient glucose metabolism helps the fungal cell maintain a proper balance of intracellular calcium. While calcium is best known for building strong bones, inside living cells it functions differently. It acts as a tiny molecular messenger that carries information from one part of the cell to another. When calcium levels are maintained, they activate "**Calcineurin**", a master signalling pathway that enables the fungus to survive stressful conditions inside the human body and ultimately grow into giant titan cells.

Disarming One of the Fungus's Deadliest Weapons

The discovery establishes, for the first time, a direct connection between the fungus's energy metabolism, calcium signalling, and calcineurin activation in controlling Titan cell formation. Rather than acting as independent processes, these systems work together as a coordinated biological network that allows the pathogen to adapt and survive within its host.

By identifying this hidden vulnerability, the study suggests an entirely new strategy for combating cryptococcal disease. Instead of simply trying to kill the fungus, future therapies may be designed to prevent it from ever producing titan cells—effectively disarming one of its most powerful disease-causing weapons before severe infection can become established.

A New Direction for Antifungal Therapy

At a time when invasive fungal infections are rising worldwide and new antifungal drugs are desperately needed, these findings reveal a previously unrecognized weakness in one of the world's deadliest fungal pathogens. By targeting the metabolic circuitry that drives titan cell formation, scientists may be able to develop therapies that weaken the fungus, improve immune clearance, and ultimately reduce the burden of cryptococcal meningitis.

Rather than attacking fungal growth alone, the next generation of antifungal drugs may instead prevent the pathogen from activating the very survival strategy that makes it so dangerous.