Study unravels how our immune system deals with fungal and viral infections

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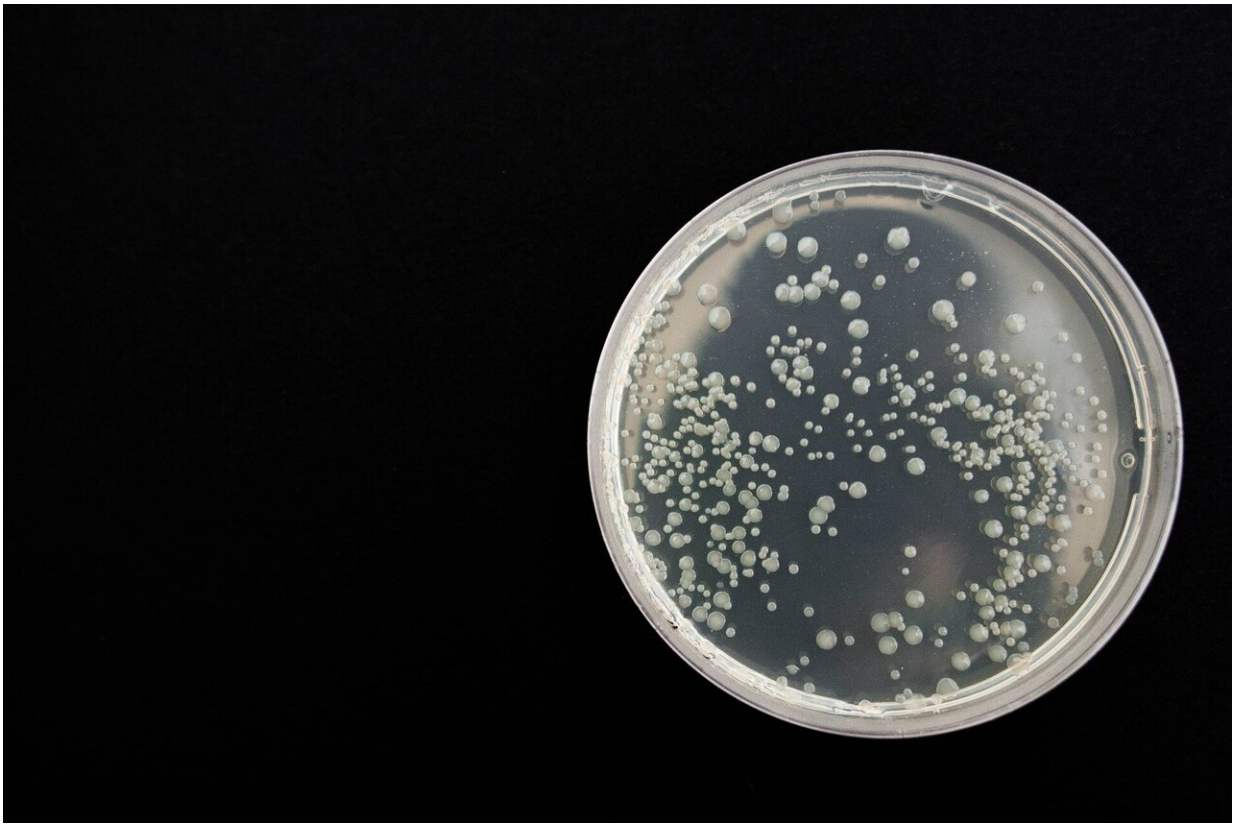

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The body's immune response to fungal infections changes when a patient is also infected by a virus, according to new research which investigated the two types of infection together for the first time.

The study, carried out by researchers at the University of Birmingham, The Pirbright Institute and University College London, sheds fresh light on the immune system's ability to deal with co-infection.

Fungal infections are major killers of patients with impaired immunity, such as AIDS patients or transplant recipients, but they usually occur alongside a secondary, viral infection. Although clinicians understand how the immune system responds to each of these types of pathogen, much less is known about what happens when both occur together.

Typically, white blood cells will attack pathogens through a process called phagocytosis—where a pathogen is engulfed by the white blood cell. In fungal infections, however, this process sometimes 'reverses' - ejecting the fungus back out of the white blood cell via a process called vomocytosis.

In a new study, published in *PLOS Pathogens*, the researchers were able to show that this process of expulsion is rapidly accelerated when the white blood cell detects a virus.

The team used advanced microscopy techniques to study live white blood cells exposed to two different types of virus, HIV, and measles, alongside the fungal pathogen, *Cryptococcus neoformans*. This opportunistic pathogen is particularly deadly among HIV+ patients, where it causes around 200,000 deaths per year worldwide.

The researchers found that, instead of becoming simply less able to deal with the fungus, the white blood cells began expelling the fungal cells much more rapidly.

Lead author, Professor Robin May, Director of the Institute of Microbiology and Infection at the University of Birmingham, explains: "We found the macrophages ejected their prey—the fungal cells—much

more quickly when the virus was present. This was very unexpected, but could be an attempt to 'free up' those white blood cells to deal with the new viral invaders."

Because the vomocytosis occurred with both viruses, the researchers concluded that the effect was likely to be a general response to viral co-infection.

Professor Robin May adds: "This is the first time that scientists have studied our immune system's response to fungal infection in the much more realistic setting of a secondary (viral) infection. We don't yet know whether this mechanism makes the white blood cells more or less effective in fighting off either infection. Although expelling the fungal cell will free up the macrophage to attack the virus, it also sets free the fungal cell to continue its spread through the body."

Dr. Dalan Bailey, head of the Viral Glycoproteins group at Pirbright, comments: "This is another interesting example of transkingdom interactions between microbes, this time fungi and viruses. We are only beginning to understand the complexity of microbe interactions within the host, and this collaboration sheds new light on this exciting new area of research"

Investigating these processes in animal models will be the next step for the team, with a longer term goal of harnessing the mechanisms used to trigger the expulsion of fungi and use them to help clear these pathogens from the body.

More information: May et al (2019). 'Viral infection triggers interferon-induced expulsion of live Cryptococcus neoformans by macrophages'. *PLOS Pathogens*.

Provided by University of Birmingham