Fungal spores could 'hijack' human immune cells to spread infection

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Scientists have announced a major breakthrough in their understanding of how the fungus *Aspergillus terreus* - the cause of serious illness in humans - can move around the body, rather than remaining in the lungs as with similar fungal infections.

The study, led by researchers at The University of Nottingham and published in the academic journal *Cell Chemical Biology*, has discovered that infections from A.terreus could hitch a ride on immune cells in order to transport themselves and cause systemic infection.

The research, a collaboration with experts at Friedrich-Schiller University Jena and the Hans-Knoell Institute in Jena, Germany, centred on the investigation of the formation of a new type of the pigment melanin, which appears to have evolved in *A. terreus* but not other similar fungi.

Lead investigator Dr Matthias Brock, of The University of Nottingham's School of Life Sciences, said: "We now have an idea about how ecological adaptation shapes fungal components that may cause detrimental effects in human infections.

"The ongoing sequencing of fungal genomes will show whether this new type of melanin specifically evolved in *A. terreus* or also in other fungal species. The identification of a new pigment among closely-related species exemplifies how the pathogenic potential among species changes by variation of structural components."

Moulds growing on food, damp walls or compost piles produce millions of spores that are frequently inhaled by humans and can cause diseases ranging from simple asthma to life-threatening illnesses such as invasive bronchopulmonary aspergillosis.

The spores are protected from environmental stress by the coloured pigment melanin - the same pigment that gives human skin, hair and eyes their colour and offers a natural screen against damaging UV light. Scientists had long believed that fungi shared a common type of melanin but the latest research disproves this dogma.

Mould spores are frequently attacked in the environment by soil predators such as amoeba that use other microorganisms as a source of food. The melanin pigment of fungal spores generally slows down the digestion process and enables the spores to germinate and kill the predator.

However, *A. terreus* spores are different as they fight off digestion and are able to survive in the longer term. This 'sit and wait' strategy has been credited by the scientists to a different type of melanin pigment that is vital for the process.

Some fungi use pre-existing compounds in the human body during infection to build up a layer of melanin that protects it from its host's immune system. This type of melanin is similar to that found in the human body.

In contrast, spores of moulds possess a cluster of genes that have survived the evolutionary process and produce a melanin pigment without using anything from the host. This pigment protects spores from damage caused by free radicals and UV light and inhibits the acidic digestion by amoeba or immune cells.

However, the researchers found that *A. terreus* uses neither of these processes to produce melanin, although its spores are highly pigmented. They found that two genes contributed to pigment formation and were able to reconstruct in vitro the synthesis of the melanin.

Further study showed that the pigment partially protects spores from predators but does not allow them to escape once 'eaten' by amoeba. In contrast to other pH neutral-loving spores, *A. terreus* prefers an acidic environment. Since macrophages - white blood cells that eat cellular debris, foreign substances, microbes and pathogenic cells to prevent infection - behave and act in a similar way to soil amoeba, the fungal spore's ability to survive in an acidic environment could enable it to use immune cells as a transport vehicle around the body.

More information: A Non-Canonical Melanin Biosynthesis Pathway Protects Aspergillus terreus Conidia from Environmental Stress, *Cell Chemical Biology* - May 19, 2016 issue. DOI: 10.1016/j.chembiol.2016.03.014

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