

DBT/ National Centre for Cell Science (NCCS), Pune

NCCS scientists pave the way to fight a fungal pathogen

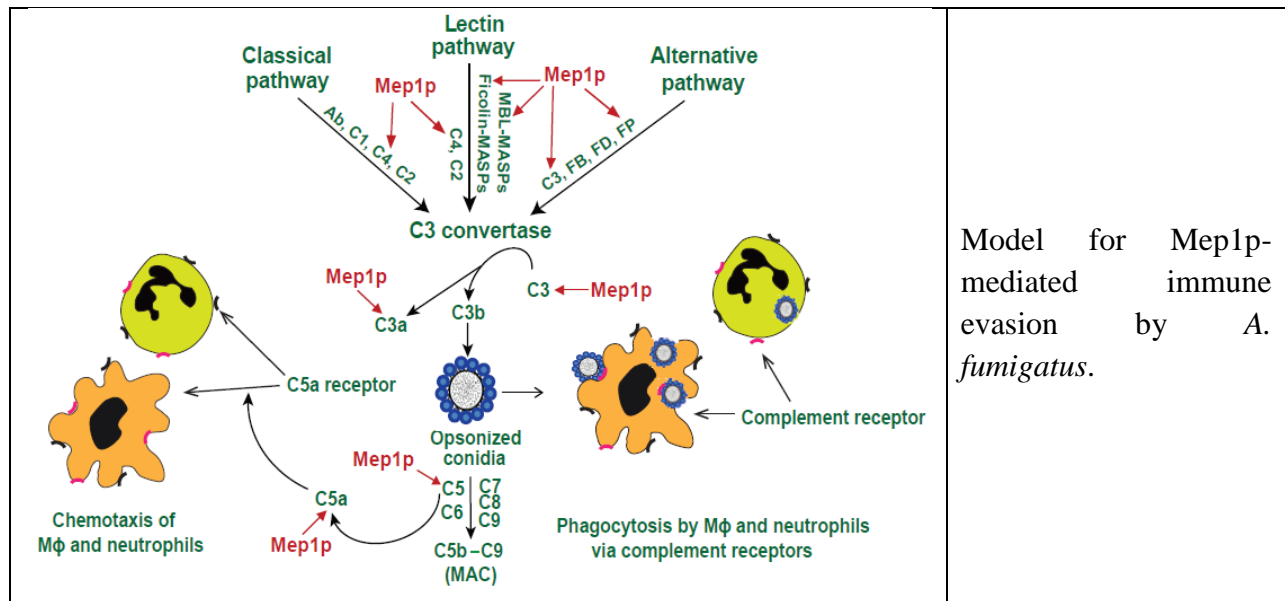
By Sunderarajan Padmanabhan

New Delhi, February 19: Innate immunity refers to the nonspecific defense mechanisms that protect us from infections immediately upon exposure to pathogens. These mechanisms include physical barriers like the skin, specific chemicals in the blood, and cells of the immune system that attack foreign entities like pathogens, including fungi.

Aspergillus fumigatus (*A. fumigatus*) is a species of fungus that is commonly found in our environment, including in soil and dust. Consequently, it is not uncommon for spores of this fungus, called conidia, to be inhaled. Usually, resident immune cells in our lungs engulf and destroy these conidia, and prevent them from causing an infection. However, when the immune system becomes impaired, the body becomes susceptible to infection by the fungus. Conidia can then germinate and invade the host systemically by crossing the lung barrier and target the vital tissues.

The innate immune system has an important component called 'complement system'. It is involved in immune surveillance. It comprises a series of inactive protein components that become sequentially activated in a cascade of enzymatic events. The activated parts of the complement system, in particular, two proteins called C3b and C5a, aid in clearing the conidia from the lung by augmenting engulfment of the conidia by cells of the immune system called phagocytes, which ingest the conidia and destroy them by a process called phagocytosis. Foreign particles like fungal conidia are marked by a process called opsonisation, to be ingested and destroyed by the phagocytes.

A team of scientists at the National Centre for Cell Science (NCCS) in Pune led by Dr. Arvind Sahu has shown that the fungal conidia have evolved a mechanism to avoid the detrimental effects of activation of the host's complement system. They secrete a specific type of protein molecule, called metalloprotease Mep1p, which degrades the C3, C4 and C5 components of the complement system and their activation products. This group has further demonstrated that Mep1p also inhibits the opsonization of conidia by C3b and their recognition by phagocytic cells. Their findings thus provide evidence to support the hypothesis that early secretion of Mep1p by conidia is imperative for inhibiting complement-mediated phagocytosis, and could help the fungus to colonize and invade the host. Therefore, identification of Mep1p as one of the key players in infection, and the insights gained into the mechanisms through which it operates, have paved the way to explore strategies to use Mep1p as a potential target to manage infections by *A. fumigatus*.



Model for Mep1p-mediated immune evasion by *A. fumigatus*.

Links related to this story -

Research article: <https://www.jbc.org/content/293/40/15538.long>

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