Phagocytosis of melanized Aspergillus conidia by macrophages exerts cytoprotective effects by sustained PI3K/Akt signalling.

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Projects

Molecular mechanisms of the interaction between *Aspergillus fumigatus* and alveolar macrophages
Details

Molecular study of apoptotic processes in *Aspergillus* ssp. and the influence of *Aspergillus fumigatus* on apoptosis in host immune effector cells
Details

Abstract

Host cell death is a critical component of innate immunity and often determines the progression and outcome of infections. The opportunistic human pathogen Aspergillus fumigatus can manipulate the immune system either by inducing or by inhibiting host cell apoptosis dependent on its distinct morphological form. Here, we show that conidia of Aspergillus ssp. inhibit apoptosis of macrophages induced via the intrinsic (staurosporine) and extrinsic (Fas ligand) pathway. Hence, mitochondrial cytochrome c release and caspase activation were prevented. We further found that the anti-apoptotic effect depends on both host cell de novo protein synthesis and phagocytosis of conidia by macrophages. Moreover, sustained PI3K/Akt signalling in infected cells is an important determinant to resist apoptosis. We demonstrate that pigmentless pksP mutant conidia of A. fumigatus failed to trigger protection against apoptosis and provide evidence that the sustained survival of infected macrophages depends on the presence of the grey-green conidial pigment consisting of dihydroxynaphthalene-melanin. In conclusion, we revealed a novel potential function of melanin in the pathogenesis of A. fumigatus. For the first time, we show that melanin itself is a crucial component to inhibit macrophage apoptosis which may contribute to dissemination of the fungus within the host.

Identifier

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