Aspergillus fumigatus melanins: interference with the host endocytosis pathway and impact on virulence.

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Abstract

The opportunistic human pathogenic fungus Aspergillus fumigatus produces at least two types of melanin, namely pyomelanin and dihydroxynaphthalene (DHN) melanin. Pyomelanin is produced during tyrosine catabolism via accumulation of homogentisic acid. Although pyomelanin protects the fungus against reactive oxygen species (ROS) and acts as a defense compound in response to cell wall stress, mutants deficient for pyomelanin biosynthesis do not differ in virulence when tested in a murine infection model for invasive pulmonary aspergillosis. DHN melanin is responsible for the characteristic gray-greenish color of A. fumigatus conidia. Mutants lacking a functional polyketide synthase PksP, the enzyme responsible for the initial step in DHN-melanin formation, i.e., the synthesis of naphthopyrone, produce white spores and are attenuated in virulence. The activity of PksP was found to be essential not only for inhibition of apoptosis of phagocytes by interfering with the host PI3K/Akt signaling cascade but also for effective inhibition of acidification of conidia-containing phagolysosomes. These features allow A. fumigatus to survive in phagocytes and thereby to escape from human immune effector cells and to become a

successful pathogen.

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