Melanin targets LC3-associated phagocytosis (LAP): A novel pathogenetic mechanism in fungal disease.

Chamilos G, Akoumianaki T, Kyrmizi I, Brakhage A, Beauvais A, Latge JP (2016) Melanin targets LC3-associated phagocytosis (LAP): A novel pathogenetic mechanism in fungal disease. *Autophagy* 12(5), 888-889. (Review)

Abstract

Intracellular swelling of conidia of the major human airborne fungal pathogen *Aspergillus fumigatus* results in surface exposure of immunostimulatory pathogen-associated molecular patterns (PAMPs) and triggers activation of a specialized autophagy pathway called LC3-associated phagocytosis (LAP) to promote fungal killing. We have recently discovered that, apart from PAMPs exposure, cell wall melanin removal during germination of *A. fumigatus* is a prerequisite for activation of LAP. Importantly, melanin promotes fungal pathogenicity via targeting LAP, as a melanin-deficient *A. fumigatus* mutant restores its virulence upon conditional inactivation of Atg5 in hematopoietic cells of mice. Mechanistically, fungal cell wall melanin selectively excludes the CYBA/p22phox subunit of NADPH oxidase from the phagosome to inhibit LAP, without interfering with signaling regulating cytokine responses. Notably, inhibition of LAP is a general property of melanin pigments, a finding with broad physiological implications.

Involved units

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