Aspergillus cell wall melanin blocks LC3-associated phagocytosis to promote pathogenicity.

Akoumianaki T, Kyrmizi I, Valsecchi I, Gresnigt MS, Samonis G, Drakos E, Boumpas D, Muszkieta L, Prevost MC, Kontoyiannis DP, Chavakis T, Netea MG, van de Veerdonk FL, Brakhage AA, El-Benna J, Beauvais A, Latge JP, Chamilos G (2016) *Aspergillus* cell wall melanin blocks LC3-associated phagocytosis to promote pathogenicity. *Cell Host Microbe* 19(1), 79-90.

Abstract

Concealing pathogen-associated molecular patterns (PAMPs) is a principal strategy used by fungi to avoid immune recognition. Surface exposure of PAMPs during germination can leave the pathogen vulnerable. Accordingly, β-glucan surface exposure during *Aspergillus fumigatus* germination activates an Atg5-dependent autophagy pathway termed LC3-associated phagocytosis (LAP), which promotes fungal killing. We found that LAP activation also requires the genetic, biochemical or biological (germination) removal of *A. fumigatus* cell wall melanin. The attenuated virulence of melanin-deficient *A. fumigatus* is restored in Atg5-deficient macrophages and in mice upon conditional inactivation of Atg5 in hematopoietic cells. Mechanistically, Aspergillus melanin inhibits NADPH oxidase-dependent activation of LAP by excluding the p22phox subunit from the phagosome. Thus, two events that occur concomitantly during germination of airborne fungi, surface exposure of PAMPs and melanin removal, are necessary for LAP activation and fungal killing. LAP blockade is a general property of melanin pigments, a

finding with broad physiological implications.

Beteiligte Forschungseinheiten

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