# Persistence versus escape: *Aspergillus terreus* and *Aspergillus fumigatus* employ different strategies during interactions with macrophages.

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## Abstract

Invasive bronchopulmonary aspergillosis (IBPA) is a life-threatening disease in immunocompromised patients. Although Aspergillus terreus is frequently found in the environment, A. fumigatus is by far the main cause of IBPA. However, once A. terreus establishes infection in the host, disease is as fatal as A. fumigatus infections. Thus, we hypothesized that the initial steps of disease establishment might be fundamentally different between these two species. Since alveolar macrophages represent one of the first phagocytes facing inhaled conidia, we compared the interaction of A. terreus and A. fumigatus conidia with alveolar macrophages. A. terreus conidia were phagocytosed more rapidly than A. fumigatus conidia, possibly due to higher exposure of β-1,3-glucan and galactomannan on the surface. In agreement, blocking of dectin-1 and mannose receptors significantly reduced phagocytosis of A. terreus, but had only a moderate effect on phagocytosis of A. fumigatus. Once phagocytosed, and in contrast to A. fumigatus, A. terreus did not inhibit acidification of phagolysosomes, but remained viable without signs of germination both

in vitro and in immunocompetent mice. The inability of A. terreus to germinate and pierce macrophages resulted in significantly lower cytotoxicity compared to A. fumigatus. Blocking phagolysosome acidification by the v-ATPase inhibitor bafilomycin increased A. terreus germination rates and cytotoxicity. Recombinant expression of the A. nidulans wA naphthopyrone synthase, a homologue of A. fumigatus PksP, inhibited phagolysosome acidification and resulted in increased germination, macrophage damage and virulence in corticosteroid-treated mice. In summary, we show that A. terreus and A. fumigatus have evolved significantly different strategies to survive the attack of host immune cells. While A. fumigatus prevents phagocytosis and phagolysosome acidification and escapes from macrophages by germination, A. terreus is rapidly phagocytosed, but conidia show long-term persistence in macrophages even in immunocompetent hosts.

**Beteiligte Forschungseinheiten**

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