Persistence within dendritic cells marks an antifungal evasion and dissemination strategy of *Aspergillus terreus*.

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Details

Abstract

Aspergillus terreus is an airborne human fungal pathogen causing life-threatening invasive aspergillosis in immunocompromised patients. In contrast to Aspergillus fumigatus, A. terreus infections are associated with high dissemination rates and poor response to antifungal treatment. Here, we compared the interaction of conidia from both fungal species with MUTZ-3-derived dendritic cells (DCs). After phagocytosis, A. fumigatus conidia rapidly escaped from DCs, whereas A. terreus conidia remained persisting with long-term survival. Escape from DCs was independent from DHN-melanin, as A. terreus conidia expressing wA showed no increased intracellular germination. Within DCs A. terreus conidia were protected from antifungals, whereas A. fumigatus conidia were efficiently cleared. Furthermore, while A. fumigatus conidia triggered expression of DC activation markers such as CD80, CD83, CD54, MHCII and CCR7, persistent A. terreus conidia were significantly less immunogenic. Moreover, DCs confronted with A. terreus conidia neither produced pro-inflammatory nor T-cell stimulating cytokines. However, TNF-α addition resulted in activation of DCs and provoked the expression of migration markers without

inactivating intracellular A. terreus conidia. Therefore, persistence within DCs and possibly within other immune cells might contribute to the low response of A. terreus infections to antifungal treatment and could be responsible for its high dissemination rates.

Involved units

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