

Environmental dimensionality controls the interaction of phagocytes with the pathogenic fungi *Aspergillus fumigatus* and *Candida albicans*.

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Abstract

The fungal pathogens *Aspergillus fumigatus* and *Candida albicans* are major health threats for immune-compromised patients. Normally, macrophages and neutrophil granulocytes phagocytose inhaled *Aspergillus* conidia in the two-dimensional (2-D) environment of the alveolar lumen or *Candida* growing in tissue microabscesses, which are composed of a three-dimensional (3-D) extracellular matrix. However, neither the cellular dynamics, the per-cell efficiency, the outcome of this interaction, nor the environmental impact on this process are known. Live imaging shows that the interaction of phagocytes with *Aspergillus* or *Candida* in 2-D liquid cultures or 3-D collagen environments is a dynamic process that includes phagocytosis, dragging, or the mere touching of fungal elements. Neutrophils and alveolar macrophages efficiently phagocytosed or dragged *Aspergillus* conidia in 2-D, while in 3-D their function was severely impaired. The reverse was found for phagocytosis of *Candida*. The phagocytosis rate was very low in 2-D, while in 3-D most

neutrophils internalized multiple yeasts. In competitive assays, neutrophils primarily incorporated *Aspergillus* conidia in 2-D and *Candida* yeasts in 3-D despite frequent touching of the other pathogen. Thus, phagocytes show activity best in the environment where a pathogen is naturally encountered. This could explain why

Involved units

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