

# CARD9+ microglia promote antifungal immunity via IL-1 $\beta$ - and CXCL1-mediated neutrophil recruitment.

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## Abstract

The C-type lectin receptor-Syk (spleen tyrosine kinase) adaptor CARD9 facilitates protective antifungal immunity within the central nervous system (CNS), as human deficiency in CARD9 causes susceptibility to fungus-specific, CNS-targeted infection. CARD9 promotes the recruitment of neutrophils to the fungus-infected CNS, which mediates fungal clearance. In the present study we investigated host and pathogen factors that promote protective neutrophil recruitment during invasion of the CNS by *Candida albicans*. The cytokine IL-1 $\beta$  served an essential function in CNS antifungal immunity by driving production of the chemokine CXCL1, which recruited neutrophils expressing the chemokine receptor CXCR2. Neutrophil-recruiting production of IL-1 $\beta$  and CXCL1 was induced in microglia by the fungus-secreted toxin Candidalysin, in a manner dependent on the

kinase p38 and the transcription factor c-Fos. Notably, microglia relied on CARD9 for production of IL-1 $\beta$ , via both transcriptional regulation of Il1b and inflammasome activation, and of CXCL1 in the fungus-infected CNS. Microglia-specific Card9 deletion impaired the production of IL-1 $\beta$  and CXCL1 and neutrophil recruitment, and increased fungal proliferation in the CNS. Thus, an intricate network of host-pathogen interactions promotes antifungal immunity in the CNS; this is impaired in human deficiency in CARD9, which leads to fungal disease of the CNS.

## Beteiligte Forschungseinheiten

[Mikrobielle Pathogenitätsmechanismen Bernhard Hube](#) [Mehr erfahren](#)

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## Themenfelder

[Interaktion mit Immunzellen \(MPM\)](#)

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## Identifizier

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