The role of innate immune receptors in *Candida albicans* skin infections

Artuso I.[1*], Borriello F.[2], Orlandi I.[1], Stamerra G.[1], Vai M.[1], Zanoni I.[1, 2], Granucci F[1].

*i.artuso@campus.unimib.it
[1]Department of Biotechnology and Biosciences, University of Milano-Bicocca, Piazza della Scienza 2, 20126 Milan, Italy.

[2]Harvard Medical School, Division of Gastroenterology, Boston Children's Hospital, 300 Longwood Ave, Enders 675, Boston, MA 02115.

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Intradermal infections with *C. albicans* are eliminated by neutrophils recruited at the site of infection with an unknown mechanism.

To dissect how neutrophils are recruited at the site of infection, we analyzed the involvement of PRR that recognize *C. albicans* (TLR4, TLR2, Dectin1 and Dectin2) as well as CARD9, activated downstream Dectins, and MyD88 that transduces the signal derived from TLRs.

WT, PRR-deficient and CARD9-deficient mice did not show any defect in neutrophil recruitment after *C. albicans* intradermal injection. Diversely, MyD88-deficient mice do not recruit neutrophils after *C. albicans* skin infection.

Since MyD88 is involved in IL-1 signaling, we tested the role of IL-1β and IL-1α in the initiation of inflammation and neutrophil recruitment. In vitro and in vivo studies revealed that both IL-1β and IL-1α were involved in this process. IL-1α is constitutively expressed in epithelial, endothelial and stromal cells and can be released through proteolytic cleavage or cell death, enhancing the production of CXCL1, a chemokine with neutrophil chemoattractant activity. We confirmed that CXCL1 production in vivo depends on IL-1α release.

We concluded that PRRs were not involved in the initiation of the inflammatory process during primary *Candida* skin exposure. Diversely, the initiation of the inflammatory process during primary infections can be due to the unspecific release of alarmins (like IL-1α) by distressed cells stimulating neutrophils recruitment at the site of infection.