

# Hypoxia-inducible factor 1 $\alpha$ modulates metabolic activity and cytokine release in anti-*Aspergillus fumigatus* immune responses initiated by human dendritic cells.

Fliesser M, Morton CO, Bonin M, Ebel F, Hünninger K, Kurzai O, Einsele H, Löffler J (2015) Hypoxia-inducible factor 1 $\alpha$  modulates metabolic activity and cytokine release in anti-*Aspergillus fumigatus* immune responses initiated by human dendritic cells. *Int J Med Microbiol* ,

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## Abstract

The mold *Aspergillus fumigatus* causes life-threatening infections in immunocompromised patients. Over the past decade, new findings in research have improved our understanding of *A. fumigatus*-host interactions, including the recent identification of myeloid-expressed hypoxia-inducible factor 1 $\alpha$  (HIF-1 $\alpha$ ) as a relevant immune-modulating transcription factor and potential therapeutic target in anti-fungal defense. However, the function of HIF-1 $\alpha$  signaling for human anti-*A. fumigatus* immunity is still poorly understood, including its role in dendritic cells (DCs), which are important regulators of anti-fungal immunity. This study investigated the functional relevance of HIF-1 $\alpha$  in the anti-*A. fumigatus* immune response initiated by human DCs. Hypoxic cell culture conditions were included because hypoxic microenvironments occur during *A. fumigatus* infections and may influence the host immune response. HIF-1 $\alpha$  was stabilized in DCs following stimulation with *A. fumigatus* under normoxic and hypoxic conditions. This stabilization was partially dependent on dectin-1, the major receptor for *A. fumigatus* on human DCs. Using siRNA-based

HIF-1 $\alpha$  silencing combined with genome-wide transcriptional analysis, a modulatory effect of HIF-1 $\alpha$  on the anti-fungal immune response of human DCs was identified. Specifically, the difference in the transcriptomes of HIF-1 $\alpha$  silenced and non-silenced DCs indicated that HIF-1 $\alpha$  contributes to DC metabolism and cytokine release in response to *A. fumigatus* under normoxic as well as hypoxic conditions. This was confirmed by further down-stream analyses that included metabolite analysis and cytokine profiling of a time-course infection experiment. Thereby, this study revealed a so far undescribed functional relevance of HIF-1 $\alpha$  in human DC responses against *A. fumigatus*.

## Involved units

[Fungal Septomics](#) [Oliver Kurzai](#) [Read more](#)

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**Identifier**

**doi:** S1438-4221(15)30005-9

**PMID:** 26387061