

Multiple signaling pathways involved in human dendritic cell maturation are affected by the fungal quorum-sensing molecule farnesol.

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Details



Abstract

The quorum-sensing molecule farnesol is produced by the opportunistic human fungal pathogen *Candida albicans*. Aside from its primary function of blocking the transition from yeast to hyphal morphotype, it has an immunomodulatory role on human dendritic cells (DC) through the alteration of surface markers, cytokine secretion, and their ability to activate T cells. Nonetheless, the molecular mechanisms by which farnesol modulates DC differentiation and maturation remained unknown. In this study, we demonstrate through transcriptional and functional assays that farnesol influences several signaling pathways during DC differentiation and in response to TLR agonists. In particular, farnesol increases the expression of the Ag-presenting glycoprotein CD1d through the nuclear receptors PPAR γ and RAR α , as well as p38 MAPK. However, the higher expression of CD1d did not confer these DC with an enhanced capacity to activate CD1d-restricted invariant NKT cells. In the presence of farnesol, there is reduced secretion of the Th1-inducing cytokine, IL-12, and increased release of proinflammatory cytokines, as well as the anti-inflammatory

cytokine IL-10. These changes are partially independent of nuclear receptor activity but, in the case of TNF- α and IL-10, dependent on NF- κ B and MAPK pathways. Interestingly, renewal of the IL-12/IL-10 milieu restores the ability of farnesol-differentiated DC to activate invariant NKT, Th1, and FOXP3+ regulatory T cells. Our results show that farnesol modulates nuclear receptors, NF- κ B, and MAPK-signaling pathways, thereby impairing the capacity of DC to activate several T cells subsets and potentially conferring C. albicans, an advantage in overcoming DC-mediated immunity.

Beteiligte Forschungseinheiten

[Fungal Septomics](#) [Oliver Kurzai](#) [Mehr erfahren](#)

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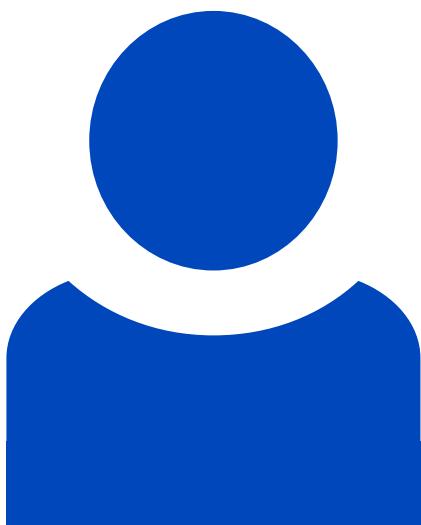
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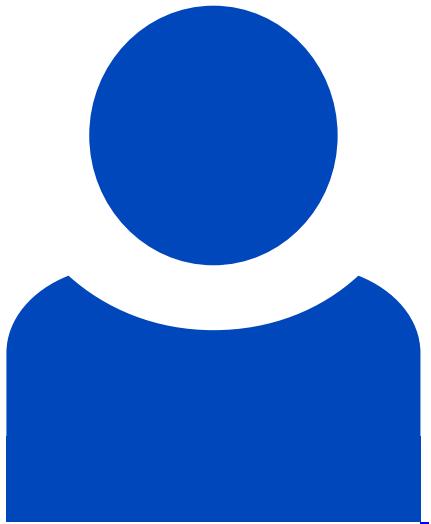
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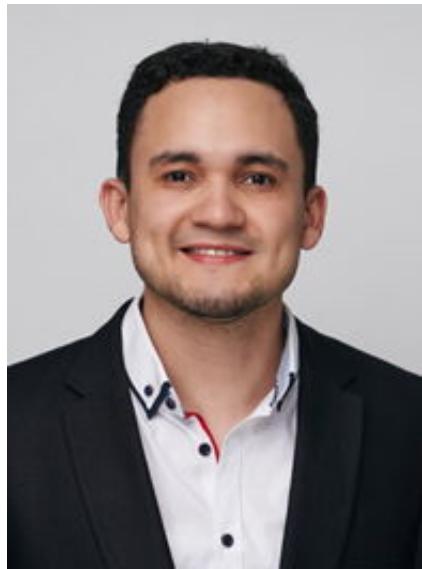
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