

The fungal quorum-sensing molecule farnesol activates innate immune cells but suppresses cellular adaptive immunity.

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Abstract

Farnesol, produced by the polymorphic fungus *Candida albicans*, is the first quorum-sensing molecule discovered in eukaryotes. Its main function is control of *C. albicans* filamentation, a process closely linked to pathogenesis. In this study, we analyzed the effects of farnesol on innate immune cells known to be important for fungal clearance and protective immunity. Farnesol enhanced the expression of activation markers on monocytes (CD86 and HLA-DR) and neutrophils (CD66b and CD11b) and promoted oxidative burst and the release of proinflammatory cytokines (tumor necrosis factor alpha [TNF- α] and macrophage inflammatory protein 1 alpha [MIP-1 α]). However, this activation did not result in enhanced fungal uptake or killing. Furthermore, the differentiation of monocytes to immature dendritic cells (iDC) was significantly affected by farnesol. Several markers important for maturation and antigen presentation like CD1a, CD83, CD86, and CD80 were significantly reduced in the presence of farnesol. Furthermore, farnesol modulated migrational behavior and cytokine release and impaired the ability of DC to induce T

cell proliferation. Of major importance was the absence of interleukin 12 (IL-12) induction in iDC generated in the presence of farnesol. Transcriptome analyses revealed a farnesol-induced shift in effector molecule expression and a down-regulation of the granulocyte-macrophage colony-stimulating factor (GM-CSF) receptor during monocytes to iDC differentiation. Taken together, our data unveil the ability of farnesol to act as a virulence factor of *C. albicans* by influencing innate immune cells to promote inflammation and mitigating the Th1 response, which is essential for fungal clearance.

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