

Direct Binding of the pH-Regulated Protein 1 (Pra1) from *Candida albicans* Inhibits Cytokine Secretion by Mouse CD4(+) T Cells.

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Abstract

Opportunistic infections with the saprophytic yeast *Candida albicans* are a major cause of morbidity in immunocompromised patients. While the interaction of cells and molecules of innate immunity with *C. albicans* has been studied to great depth, comparatively little is known about the modulation of adaptive immunity by *C. albicans*. In particular, direct interaction of proteins secreted by *C. albicans* with CD4(+) T cells has not been studied in detail. In a first screening approach, we identified the pH-regulated antigen 1 (Pra1) as a molecule capable of directly binding to mouse CD4(+) T cells in vitro. Binding of Pra1 to the T cell surface was enhanced by extracellular Zn(2+) ions which Pra1 is known to scavenge from the host in order to supply the fungus with Zn(2+). In vitro stimulation assays using highly purified mouse CD4(+) T cells showed that Pra1 increased proliferation of CD4(+) T cells in the presence of plate-bound anti-CD3 monoclonal antibody. In contrast, secretion of effector cytokines such as IFN γ and TNF by CD4(+) T cells upon anti-CD3/ anti-CD28 mAb as well as cognate antigen stimulation was reduced in the

presence of Pra1. By secreting Pra1 *C. albicans*, thus, directly modulates and partially controls CD4(+) T cell responses as shown in our in vitro assays.

Beteiligte Forschungseinheiten

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