

G304 Platelet-Activating Factor-Induced Early Activation of NF- κ B Plays a Crucial Role for Organ Clearance of *Candida albicans*

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The yeast *Candida albicans* is a common commensal organism in humans and animals, and it is a major opportunistic fungal pathogen which can cause life-threatening infections of the internal organs in patients with impaired host defense mechanism. The kidneys and brain appear to be particularly susceptible to *C. albicans*. However, the mechanism underlying the organ susceptibility is unknown. Here we show that efficient clearance of *C. albicans* in an organ was exclusively dependent upon the early activation of NF- κ B in the organ, which was mediated by platelet-activating factor (PAF). Thus, the organ susceptibility to *C. albicans* seen in the kidneys and brain appears to be attributed to the failure of the PAF-induced early activation of NF- κ B in the organs. This may be a general protective mechanism for infections in which cellular immunity plays a major role.

G305 Selective Involvement of Reactive Oxygen Intermediates in Platelet-Activating Factor-Mediated Activation of NF- κ B

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Although it has been suggested that some biological activities of platelet-activating factor (PAF) are mediated by, at least in part, reactive oxygen intermediates (ROI), the precise mechanisms underlying the interaction between the two remains to be elucidated. Antioxidants, such as α -tocopherol acid succinate, N-acetyl-c-Cystein, pyrrolidinedithiocarbamate failed to inhibit PAF-induced immediate systemic reactions such as lethality, symptoms of disseminated intravascular coagulation 10 min following PAF injection. In contrast, antioxidants significantly inhibited both the *in vivo* and *in vitro* PAF-induced NF- κ B activation and NF- κ B-dependent TNF- α expression. The effects of the antioxidants were due to their inhibition of PAF-induced degradation of I κ B α a protein responsible for keeping NF- κ B in an inactive form. A protein tyrosine kinase and N-tosyl-L-phenylalanine chloromethyl ketone sensitive serine protease were involved in both PAF- and H₂O₂-induced NF- κ B activation. Collectively, these data indicate that the PAF-induced NF- κ B activation is selectively mediated through the generation of ROI.