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Ppz protein phosphatases in fungi: characterization of the *C. albicans* ortholog

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The Ppz phosphatases are Ser/Thr protein phosphatases that are restricted to fungi. These enzymes have been largely characterized in *S. cerevisiae*, where they are involved in cation homeostasis and cell cycle control. We became interested in the study of the functional role of this kind of proteins in pathogenic fungi and to this end we cloned the genes from *C. albicans*, *Aspergillus nidulans* and *Aspergillus fumigatus,* characterized the expression products in *S. cerevisiae* and investigated the phenotypes of the mutants. Our data indicates that the single *C. albicans* PPZ1 performs similar functions that its orthologs Ppz1 and Ppz2 in *S. cerevisiae*. Interestingly, the gene presents natural polymorphisms and their study allowed the identification of three amino acid residues that affect enzyme activity or stability. The mutant was sensitive to salts such as LiCl and KCl, to caffeine, and to agents that affect cell wall biogenesis such as Calcofluor White and Congo red, but was tolerant to spermine and hygromycin, confirming the results observed by heterologous expression. In addition, the germ tube growth rate and the virulence in the BALB/c mouse model were reduced in the null mutant, suggesting a novel function for CaPpz1 in the yeast to hypha transition that may have medical relevance.

In contrast, the characterization of the *A. nidulans ppzA* revealed that although ppzA acted as the functional equivalent of the known PPZ enzymes, its disruption in *A. nidulans* did not result in the expected phenotypes (salt tolerance, cell wall integrity effects, ..). However, the inactivation of *ppzA* resulted in increased sensitivity to oxidizing agents like tert-butylhydroperoxide, menadione, and diamide. Further work demonstrated that sensitivity to oxidizing agents is a common phenotype for other fungi, such as *S. cerevisiae* or *C. albicans,* thus revealing a novel function for the Ppz enzymes that is conserved in very distantly related fungi.

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