E321 Copper- and Zinc-Containing Superoxide Dismutase Null mutant of *Candida albicans*: Oxidative Stress Sensitivity and Lysine Auxotrophy

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Recently, we reported the characterization of copper and zinc-containing superoxide dismutase and its gene (SOD1) from *Candida albicans* [*Biochim. Biophys. Acta* 1427 (1999) 245-255]. In order to investigate the role of copper- and zinc-containing superoxide dismutase in the molecular mechanism of oxygen metabolism of *C. albicans*, its gene has been deleted by the targeted gene disruption method. The *SOD1* disruption was verified by southern hybridization analysis and superoxide dismutase activity staining after native gel electrophoresis. The null mutant of *SOD1* was more sensitive to menadione which was known as a redox-cycling agent than isogenic wild-type cell, though it still showed adaptive oxidative stress response. The cell exhibited a slow growth in Salt-Dextrose minimal medium, whereas it appeared to grow slightly fast in Yeast extract-Peptone-Dextrose complex medium. The growth retardation in minimal medium was restored by the addition of lysine or flusing with nitrogen gas. These results suggest that copper- and zinc-containing superoxide dismutase in *C. albicans* not only protects the cell from oxidative stress but also is associated with lysine metabolism.

E322 A *Candida albicans* Mutant Lacking PRF1 (Pseuodhypha Regulatory Factor 1) Homologous to *Saccharomyces cerevisiae* SSN6 Showed the Promotion of Pseudohyphal Growth and Resistance to Oxidative Stress

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The most common fungal pathogen, *Candida albicans*, regulates its cellular morphology in response to environmental conditions. Hyphal development is under both positive and negative control. TUP1 forms a general transcriptional repressor complex with SSN6 in *Saccharomyces cerevisiae*. The deletion of *C. albicans* TUP1 homolog results in a constitutive filamentous phenotype under all growth condition, suggesting that TUP1 is responsible for maintenance the yeast morphology through repression of genes required for filamentous growth. By means of a sequence trace from the Stanford *C. albicans* sequencing project that resembled a portion of *S. cerevisae* SSN6, we have identified and disrupted a C. *albicans* PRF1 (pseudohypha-regulatory-factor 1) gene, which was highly homologous to *S. cerevisiae* SSN6 in the TPR (tetratricopeptide repeat) region. The deduced amino acid sequence of the PRF1 contains 9 consecutive TPR units as well as Q repeats. Homozygous *prf1* null mutant showed the promotion of phenotypic switching and pseudohyphal growth in all conditions tested. Interestingly, the mutant was more resistant to oxidants such as menadione and hydrogen peroxide, and more heat-stable than isogenic wild-type cell. Thus, It is proposed that PRF1 be an important regulator to be related morphogenesis and stress response.