YEAST GLUTATHIONE TRANSFERASES, OXIDATIVE STRESS AND VIRULENCE IN *Candida albicans*

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Glutathione transferases (GSTs) conjugate glutathione to xenobiotics, followed by elimination of the conjugates from the cell. GSTs are divided into classes based on sequence, substrate specificity or immunological properties. GSTs of omega class diverge from other GST classes because they have lower activity against standard GST substrates, whereas they are active as glutaredoxins. Thus, omega GSTs act as thiol redox regulators and, in this way, they may participate in the defence against oxidative stress. Only a few fungal GSTs have been studied in some detail, especially in *S. cerevisiae*. This yeast has two proteins with standard GST activity (Gtt1 and Gtt2), Gtt1 being associated to the endoplasmic reticulum. In addition, *S. cerevisiae* has a peroxisomal omega GST involved in sulphur amino acid metabolism (Gto1) and two cytosolic omega GSTs (Gto2 and Gto3).

In silico analysis of the *Candida albicans* genome revealed the existence of two ORFs coding for Gtt homologues (orf 19.698 for CaGtt1 and orf 19.6947 for CaGtt2) and one ORF coding for a putative omega GST (orf 19.2613 for CaGto1). CaGtt2 and CaGto1 have been purified by us from recombinant *E. coli* cells and they display enzyme activity patterns typical of standard and omega GSTs respectively. Expression of the three genes has been studied in cell cultures under environmental stresses. While *CaGTT1* is not expressed at detectable levels in any of the conditions tested, basal expression is detected for *CaGTT2* and *CaGTO1* in exponential cells, and upregulated expression for both of them is observed upon oxidative, osmotic and alkaline pH stresses, and in stationary phase cells. Induction patterns show a complex dependence on CaHog1 and CaSko1 regulators, while they are independent of CaCap1. GFP-tagged versions of CaGtt2 and CaGto1 have been constructed and their cellular localisation has been studied *in vivo*. CaGto1 diaplays a homogeneous cytosolic location, while CaGtt2 appears as forming aggregates at specific locations. Flourescence levels parallel mRNA levels in the tested conditions. Phenotypic analyses of homozygous mutants in *CaGTO1* in laboratory cultures have only revealed some resistance to cadmium stress.

We have also done *ex vivo* experiments to analyse expression of the three *C. albicans* GSTs upon phagocytosis. CaGtt1 and CaGtt2 as well as CaGto1 are modestly induced inside cultured macrophages, while a significant temporary upregulation of CaGto1 is observed after phagocytosis by human neutrophils. These results suggest some role of Gto1 during infection, which should be corroborated by *in vivo* virulence analyses.