Title:	Glutathione utilization by Candida albicans requires a functional glutathione degradation (DUG) pathway and OPT7, an unusual member of the oligopeptide transporter family
Authors:	Bachhawat, A.K. (/jspui/browse?type=author&value=Bachhawat%2C+A.K.)
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Abstract:	Candida albicans lacks the ability to survive within its mammalian host in the absence of endogenous glutathione biosynthesis. To examine the ability of this yeast to utilize exogenous glutathione, we exploited the organic sulfur auxotrophy of C. albicans met15Δ strains. We observed that glutathione is utilized efficiently by the alternative pathway of glutathione degradation (DUG pathway). The major oligopeptide transporters OPT1-OPT5 of C. albicans that were most similar to the known yeast glutathione transporters were not found to contribute to glutathione transport to any significant extent. A genomic library approach to identify the glutathione transporter of C. albicans yielded OPT7 as the primary glutathione transporter. Biochemical studies on OPT7 using radiolabeled GSH uptake revealed a Km of 205 μM, indicating that it was a high affinity glutathione transporter. OPT7 is unusual in several aspects. It is the most remote member to known yeast glutathione transporters, lacks the two highly conserved cysteines in the family that are known to be crucial in trafficking, and also has the ability to take up tripeptides. The transporter was regulated by sulfur sources in the medium. OPT7 orthologues were prevalent among many pathogenic yeasts and fungi and formed a distinct cluster quite remote from the Saccharomyces cerevisiae HGT1 glutathione transporter cluster. In vivo experiments using a systemic model of candidiasis failed to detect expression of OPT7 in vivo, and strains disrupted either in the degradation (dug3Δ) or transport (opt7Δ) of glutathione failed to show a defect in virulence.
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