Roles of Glutathione Reductase and γ -Glutamylcysteine Synthetase in Candida albicans

Yong-Un Baek, Hyung-Soon Yim, and Sa-Ouk Kang

Laboratory of Biophysics, School of Biological Sciences, and Institute of Microbiology, Seoul National University

We have cloned the CGR1 gene encoding glutathione reductase (GR) which catalyzes the reduction of oxidized glutathione (GSSG) to reduced glutathione (GSH) from Candida albicans. The cgr1/cgr1 mutants were not viable when CaMAL2 promoter repressed the CGR1 expression. The growth of the mutants could be partially overcome by thiol compounds such as GSH, dithiothreitol, cysteine, N-acetylcysteine and GSSG. Interestingly, C. albicans with CGR1 overexpressed showed defective hyphal growth on solid medium and attenuated virulence. We have also cloned the GCS1 gene encoding γ-glutamylcysteine synthetase which catalyzes the first step of glutathione biosynthesis. The gcs1/gcs1 mutants were nonviable in minimal defined medium. The growth of the mutants could be resumed by supplementing with GSH, GSSG and γ-glutamylcysteine in the medium. The mutants had increased intracellular D-erythroascorbic acid level up to 2.25-fold when transferred to GSH-free medium. When the mutants were depleted of GSH, they showed typical markers of apoptosis. In conclusion, these results suggest that glutathione is an essential metabolite, and involved in hyphal growth, virulence and apoptosis in C. albicans.