Carbonic anhydrase regulation and CO(2) sensing in the fungal pathogen Candida glabrata involves a novel Rca1p ortholog.

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Abstract

Carbon dioxide (CO2) is a ubiquitous gas present at 0.0391% in atmospheric air and 5.5% in human blood. It forms part of numerous carboxylation and decarboxylation reactions carried out in every cell. Carbonic anhydrases (CA) enhance the hydration of CO2 to generate bicarbonate, which is subsequently used in cellular metabolism. In microorganisms, including the yeasts Candida albicans and Saccharomyces cerevisiae, inactivation of CA leads to a growth defect in air, which is complemented in an atmosphere enriched with CO2. In this study we characterize the CA from the fungal pathogen of humans Candida glabrata, CgNce103p, and report a comparable phenotype following its inactivation. Furthermore, we show that expression of the C. glabrata CA is strongly regulated by environmental CO2 at both the protein and transcript level. Similar to what we have previously reported for C. albicans and S. cerevisiae, C. glabrata CA regulation by CO2 is independent from the cAMP-PKA pathway and requires the novel bZIP transcription factor CgRca1p. We show that CgRca1p is an ortholog of the transcription factors Rca1p from C.

albicans and Cst6p from S. cerevisiae and prove that CA induction in low CO2 involves the conserved DNA-binding motif TGACGTCA located on this C. glabrata promoter. However, in contrast to what is found in C. albicans CgRca1p expression itself is not affected by CO2. Although our results suggest a high level of similarity between the CO2 sensing pathways from C. glabrata, S. cerevisiae and C. albicans, they also point out significant intrinsic differences.

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