Metabolic adaptation via regulated enzyme degradation in the pathogenic yeast Candida albicans

ABSTRACT

The virulence of Candida albicans is dependent upon fitness attributes as well as virulence factors. These attributes include robust stress responses and metabolic flexibility. The assimilation of carbon sources is important for growth and essential for the establishment of infections by C. albicans. Previous studies showed that the C. albicans ICL1 genes, which encode the glyoxylate cycle enzymes isocitratelyase are required for growth on non-fermentable carbon sources such as lactate and oleic acid and were repressed by 2% glucose. In contrast to S. cerevsiae, the enzyme CaIcl1 was not destabilised by glucose, resulting with its metabolite remaining at high levels. Further glucose addition has caused CaIcl1 to lose its signal and mechanisms that trigger destabilization in response to glucose. Another purpose of this study was to test the stability of the Icl1 enzyme in response to the dietary sugars, fructose, and galactose. In the present study, the ICL1 mRNAs expression was quantified using Quantitative Real Time PCR, whereby the stability of protein was measured and quantified using Western blot and phosphoimager, and the replacing and cloning of ICL1 ORF by gene recombination and ubiquitin binding was conducted via co-immuno-precipitation. Following an analogous experimental approach, the analysis was repeated using S. cerevisiaeas a control. Both galactose and fructose were found to trigger the degradation of the ICL1 transcript in C. albicans. The Icl1 enzyme was stable following galactose addition but was degraded in response to fructose. C. albicans Icl1 (CaIcl1) was also subjected to fructose-accelerated degradation when expressed in S. cerevisiae, indicating that, although it lacks a ubiquitination site, CaIcl1 is sensitive to fructose-accelerated protein degradation. The addition of an ubiquitination site to CaIcl1 resulted in this enzyme becoming sensitive to galactose-accelerated degradation and increases its rate of degradation in the presence of fructose. It can be concluded that ubiquitin-independent pathways of fructose-accelerated enzyme degradation exist in C. albicans.

Keyword: Candida albicans; Glyoxylate cycle; Isocitratelyase; Adaptation; Virulence; Pathogenicity