Phylogenetic and Transcripts Profiling of Glucose Sensing Related Genes in Candida glabrata

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Abstract

Background: The sensing mechanism of glucose in Saccharomyces cerevisiae is well studied. However, such information is scarcely found in other yeast species such as Candida glabrata.

Objectives: This study aimed to identify the glucose sensing pathway related genes of C. glabrata and to analyze the regulation pattern of these genes in response to different surrounding glucose concentrations through the quantitative real time polymerase chain reaction (qRT-PCR).

Materials and Methods: Phylogenetic analysis was carried out on predicted amino acid sequences of C. glabrata and S. cerevisiae to compare their degree of similarity. In addition, the growth of C. glabrata in response to different amounts of glucose (0%, 0.01%, 0.1%, 1% and 2%) was evaluated via the spot dilution assay on prepared agar medium. Besides, the SNF3 and RGT2, which act as putative glucose sensors, and the RGT1 and MIG1, which act as putative transcriptional regulators and selected downstream hexose transporters (HXTs), were analysed through qRT-PCR analysis for the gene expression level under different glucose concentrations.

Results: Comparative analysis of predicted amino acids in the phylogenetic tree showed high similarity between C. glabrata and S. cerevisiae. Besides, C. glabrata demonstrated the capability to grow in glucose levels as low as 0.01% in the spot dilution assay. In qRT-PCR analysis, differential expressions were observed in selected genes when C. glabrata was subjected to different glucose concentrations.

Conclusions: The constructed phylogenetic tree suggests the close evolutionary relationship between C. glabrata and S. cerevisiae. The capability of C. glabrata to grow in extremely low glucose environments and the differential expression of selected glucose-sensing related genes suggested the possible role of these genes in modulating the growth of C. glabrata in response to different glucose concentrations. This study helps deepen our understanding of the glucose sensing mechanism in C. glabrata and serves to provide fundamental data that may assist in unveiling this mechanism as a potential drug target.

Keywords: Glucose Transport Proteins, Facilitative, Phylogeny, Candida glabrata

1. Background

The incidence of invasive yeast infection caused by non-Candida albicans Candida (NCAC) species including Candida glabrata has increased considerably (1) in the past two decades. The emergence of C. glabrata as an important threat has been reported in an epidemiological study conducted at a tertiary care hospital, where the prevalence of C. glabrata as a causative agent for healthcare-associated candidemia has increased drastically from 0% to 16% from 1983 to 2007 (2). The candidiasis disease ranges from superficial to life-threatening disseminated types such as deep-seated candidiasis (3, 4). The wide spectrum of disease found in various anatomical regions of the human body suggests that C. glabrata has flexibility in sensing nutrients such as glucose and thus can adapt to unique environmental niches of the host.

Glucose sensing and transportation are highly regulated processes in most organisms, as glucose is an important source of carbon and energy. Previous studies have shown that Saccharomyces cerevisiae, a model organism of eukaryotes, senses the uptake of glucose through the Sugar Receptor-Repressor pathway (SRR). Basically, SRR pathway uses two glucose sensors in the cell membrane, namely Snf3 and Rgt2 that govern and regulate the expression of genes encoding for hexose transporter (HXT) with the aids of transcription regulators: RGT1 and MIG1 (5-7). In a similar fashion, another important human pathogen, C. albicans, also employs the same glucose sensing pathways, yet instead of two glucose sensors in the SRR pathway, only one has been shown to be present in this species, namely the Hgt4 (8, 9). However, little is known about the function...