

## 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, whereby 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