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SNF3 as High Affinity Glucose Sensor and Its Function in Supporting the Viability of *Candida glabrata* under Glucose-Limited Environment

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Candida glabrata is an emerging human fungal pathogen that has efficacious nutrient sensing and responsiveness ability. It can be seen through its ability to thrive in diverse range of nutrient limited-human anatomical sites. Therefore, nutrient sensing particularly glucose sensing is thought to be crucial in contributing to the development and fitness of the pathogen. This study aimed to elucidate the role of *SNF3* (Sucrose Non Fermenting 3) as a glucose sensor and its possible role in contributing to the fitness and survivability of *C. glabrata* in glucose-limited environment. The *SNF3* knockout strain was constructed and subjected to different glucose concentrations to evaluate its growth, biofilm formation, amphotericin B susceptibility, *ex vivo* survivability and effects on the transcriptional profiling of the sugar receptor repressor (SRR) pathway-related genes. The *CgSNF3*Δ strain showed a retarded growth in low glucose environments (0.01 and 0.1%) in both fermentation and respiration-preferred conditions but grew well in high glucose concentration environments (1 and 2%). It was also found to be more susceptible to amphotericin B in low glucose environment (0.1%) and macrophage engulfment but showed no difference in the biofilm formation capability. The deletion of *SNF3* also resulted in the down-regulation of about half of hexose transporters genes (four out of nine). Overall, the deletion of *SNF3* causes significant reduction in the ability of *C. glabrata* to sense limited surrounding glucose and consequently disrupts its competency to transport and perform the uptake of this critical nutrient. This study highlighted the role of *SNF3* as a high affinity glucose sensor and its role in aiding the survivability of *C. glabrata* particularly in glucose limited environment.

Keywords: ***Candida glabrata*, glucose sensor, *SNF3*, glucose-limited environment, hexose transporter**

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INTRODUCTION

Glucose is commonly known as an important carbon source and energy for many organisms. Several studies have attempted to establish the linkage between glucose availability and physiological response of *Candida* species, including the biofilm formation, oxidative stress, and antifungal resistance (Rodaki et al., 2009; Uppuluri et al., 2010; Ene et al., 2012;