

**Stony Brook University  
The Graduate School**

**Doctoral Defense Announcement**

**Abstract**

**Identification of a Novel Eukaryotic N-Acetylglucosamine Transporter**

**By**

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*Candida albicans* is an opportunistic fungal pathogen in humans. It typically lives as a harmless commensal as part of the human gut and skin flora, but under some conditions it causes mucosal infections. In immunocompromised patients it can also cause life-threatening systemic infections. *C. albicans* is a multimorphic organism, and the ability to undergo morphological transition from budding to hyphal growth is associated with its virulence. This morphological switch can also be mimicked in vitro in different ways, one of which is to grow the cells at 37°C in the presence of the amino sugar N-acetylglucosamine (GlcNAc). To learn more about differences between buds and hyphae, a proteomic comparison of plasma membrane proteins from cells grown in the presence or absence of the hyphal inducer GlcNAc was performed. 137 plasma membrane proteins, one third of which were only detected in hyphae, were identified. The characterization of one novel hyphal protein (Ngt1) became the focus of investigation. An Ngt1-GFP fusion was detected in the plasma membrane after induction with GlcNAc or upon macrophage phagocytosis. *NGT1* was needed for efficient GlcNAc uptake and for the ability to induce hyphae at low GlcNAc concentrations. High concentrations of GlcNAc could bypass the need for *NGT1* to induce hyphae, indicating that elevated intracellular levels of GlcNAc induce hyphal formation. Ngt1 acts directly as a GlcNAc transporter, since heterologous expression of *NGT1* in *S. cerevisiae* conferred ability to this yeast to take up GlcNAc. Transport mediated by Ngt1 was specific, as other sugars could not compete for the uptake of GlcNAc. Thus, Ngt1 represents the first eukaryotic GlcNAc transporter to be discovered. The presence of *NGT1* homologs in the genome sequences of a wide range of eukaryotes from yeast to mammals suggests that they may also function in the cellular processes regulated by GlcNAc, including those in important diseases such as cancer and diabetes. Altogether, this proteomic approach has successfully identified a novel GlcNAc transporter that mediates morphological switching in *C. albicans*, as well as a set of other uncharacterized plasma membrane proteins yet to be studied for a role in morphogenesis and virulence.

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**Program:** Genetics

**Dissertation Advisor:** James B. Konopka