Title: Investigation of Regulation of Expression of *SKS1* mRNA in *Saccharomyces cerevisiae*

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ABSTRACT:

Regulation of gene expression is the vital activity of all organisms to sustain their life processes under the changing environmental conditions and stress. Nutrient stress is one such situation, in which limiting glucose and nitrogen stimulate a transition of rounded yeast cells to elongated/filamentous pseudohyphal form in pathogenic fungi. It is believed that the filamentous pseudohyphae is the pathogenic and virulent form of these fungal pathogens. However, neither the bona fide master regulator that controls the yeast to hyphal transition nor the detailed mechanistic insight of this transition is known. The protein kinase Sks1p was implicated in the integration of signals for nitrogen and glucose limitation, resulting in pseudohyphal growth in baker's yeast *S. cerevisiae*. The *SKS1* gene being orthologous to *SHA3* gene of pathogenic *C. albicans*, is also associated with the organism's virulent form. In *Saccharomyces cerevisiae, SKS1* mRNA belongs to a special class of "Nuclear Retained mRNAs" (NR mRNAs) representing a subset of otherwise normal transcripts, which typically undergo very slow export and an unusually long intra-nuclear dwell time owing to the presence of a 202 nt "export-retarding" nuclear zip code (NZ) element. However, the regulation of the expression of the *SKS1* gene is entirely unknown. Recent findings in our laboratory indicated that the cellular repertoire of *SKS1* mRNA is regulated at the post-transcriptional level via its Nuclear Zip-code sequence, which leads to its intranuclear retention followed by its rapid degradation by the Exosome and its cofactor CTEXT. This research work focuses on the identification of any Nuclear Zip-code element associated *trans*-acting factor(s), as well as the mechanism involved in the regulation of *SKS1* gene as well as other "NR mRNAs". The final conclusion of this analysis reveals a reversible mechanism of post-transcriptional regulation of these "NR mRNAs" involving modulation of intranuclear decay and nuclear export, which plays a crucial role in the adaptability and viability of the yeast cells. This work would provide a useful knowledge base in hunting the target for therapeutic intervention in pathogenic fungi like *Candida albicans*.

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