

**Stony Brook University
The Graduate School**

Doctoral Defense Announcement

Abstract

Role of Sir3 N-terminus in Yeast Transcriptional Silencing

By

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This study focuses on the function of the Sir3 (Silencing information regulator) BAH (Bromo adjacent homology) domain which is located at the N-terminus of *Saccharomyces cerevisiae* Sir3 protein. Previous work has shown that the N-terminus of Sir3 is crucial for the function of Sir3 in transcriptional silencing. However, the precise biological role of the BAH domain is not fully understood.

My data show that the BAH domain, amino acids 1-214 of Sir3, can partially silence the *HM* loci in a *sir3* Δ strain as long as Sir1 is overexpressed. This BAH silencing requires the other silencing proteins, Sir1, Sir2 and Sir4. Chromatin-IP reveals that Sir3 N-terminal fragments spread from the silencers to the silenced loci, suggesting that the Sir3 BAH domain is sufficient to establish and maintain a heterochromatin state. The Sir3 BAH domain was found to bind to DNA and nucleosomes *in vitro*. This DNA and nucleosome binding capability probably contributes to silencing.

In an attempt to understand the role of the Sir3 BAH domain, I used mutagenesis to determine the specific residues within this domain that are required for the function of full-length Sir3 in silencing. A mutant library was constructed and screened for BAH mutations that affect silencing at telomeres. Ten mutants were obtained. All of them caused a telomeric silencing defect but *HMR* silencing was normal. All of them are *eso* (Enhancers of the *sir1* mutant) mutants in that their phenotypes are greatly exacerbated by a *sir1* Δ mutation. A136T, C177R and S204P are the three most drastic *sir3* BAH mutations; they lead to a lack of *HML* silencing. According to the crystal structure of Sir3 BAH, these three residues are located around the same region of Sir3, implying this region is important for the function of the Sir3 BAH domain.

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