

**Stony Brook University  
The Graduate School**

Doctoral Defense Announcement

**Abstract**

Mek1 regulates partner choice during meiotic recombination in yeast

By

**Hengyao Niu**

Meiotic recombination between homologs generates crossovers, which are critical for properly segregating homologs at Meiosis I (MI). In contrast, sister chromatids are the preferred templates for mitotic recombination. The bias in meiotic recombination for homologs is created in two ways: (1) a meiosis-specific RecA ortholog, Dmc1, actively promotes recombination between homologous chromosomes; and (2) a barrier to sister chromatid repair (BSCR) suppresses recombination between sister chromatids. Hop1, Red1 and Mek1 are meiosis-specific proteins that form a complex required for BSCR formation. Mek1 is a serine/threonine protein kinase whose activation requires both Hop1 and Red1. Studies on the BSCR can be broken down into two basic questions: (1) how is Mek1 kinase activity regulated to create a BSCR? and (2) what is the mechanism by which Mek1-phosphorylated substrates create a BSCR? My thesis involved experiments designed to address both questions.

The Hop1 protein contains two distinct functional domains: the C-domain, made up of the last 20 amino acids, and the N-domain (the remainder of the protein). My research revealed that the C-domain of Hop1 functions in BSCR formation by promoting Mek1 dimerization, which then enables activation of Mek1 through auto-phosphorylation of conserved threonines in the activation loop of the kinase. This work, in combination with other results from the Hollingsworth lab, has led to a model where DSB formation triggers Hop1 C-domain phosphorylation and Mek1 recruitment to Red1. Subsequent Mek1 auto-activation as a result of Hop1 C-domain promoted dimerization then allows creation of a BSCR in a region around where DSBs are formed.

Using a selected candidate approach to identify Mek1 targets revealed Rad54 as a good substrate for Mek1 *in vitro*. The phosphorylation sites were mapped by mass spectrometry. Overexpression of one phosphorylation site mutant, *rad54-T132A*, allows *dmc1* to sporulate. The resulting spores are viable, indicating that *rad54-T132A* promotes interhomolog recombination and that the BSCR is intact. Therefore, in addition to creating the BSCR, Mek1 regulates meiotic recombination by down-regulating the activity of Rad54.

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**Dissertation Advisor:** Dr. Nancy Hollingsworth