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（要　旨）
(Summary)

Introduction

The fission yeast *Schizosaccharomyces pombe* has two mating types (MTs), called *P* (*plus*) and *M* (*minus*). From a single *P* or *M* cell, *S. pombe* can produce a population of haploids containing both MTs in nearly equal proportions by switching MT after cell division. Single-cell lineage analysis has revealed the asymmetrical rules of MT switching (Miyata's rules). MT is determined by genetic information present at the *mat1* locus: *mat1-P* in P cells, and *mat1-M* in M cells. The *mat1-P/M* gene can be replaced efficiently by one of the two silent donor cassettes *mat2-P* and *mat3-M* according to Miyata's rule. This process is called mating-type switching (MTS)

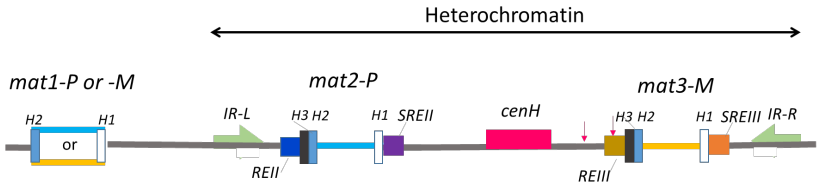

Figure 1. The *mat* region in *S. pombe*. Representation of the expressed *mat1* and the silent donor *mat2-P* and *mat3-M* localized in chromosome 2.

The correct donor choice requires two competing small recombination enhancers, *SRE2* and *SRE3*, that function in the context of heterochromatin (Figure 1 and ref [1] for a review).

Several genetic screenings have been performed to generate *S. pombe* mutants that have helped to elucidate how the MTS process works [2]–[4]. More importantly, three main models have been proposed for the Regulation of Donor selection in the MTS [4]–[6]. However, the MTS process is not completely elucidated yet. So, it is important to identify novel regulators of the MTS process.

Results

I used a semi-quantitative PCR method to perform genetic screening for Mating-Type deficient mutants in a Bioneer v.2 gene deletion library. The identification of the *shf1* gene in this screening and the *brl2* gene, as well as the six genes encoding for the Set1/COMPASS in another screening [4], suggest that HULC and Set1C are involved in MTS. Taking together the results of the systematic analysis of the subunits of HULC by Multiplex PCR and iodine staining, and analysis of the *rad18Δ* deletion mutant allows me to conclude that HULC is involved in MTS.

Southern blot analysis of *HindIII*-digested genomic DNA of the shf1 deletion mutant determines that HULC is involved in the donor selection step of the MTS process. Analysis of the *SRE* deletion mutants allowed me to pinpoint that the effect of HULC in MTS is possibly through decreased use of *SRE3* in M cells.

The phenotypes observed by the HULC subunits were similar to phenotypes of the *set1Δ* deletion mutants from an independent genetic screening[4]. The epistasis analysis that I performed indicates that HULC and Set1C are epistatic in their involvement in the MTS process. The effects of the histone residues mutants are similar to the deletion of the subunits of HULC, indicating that H2Bub and Set1C are important for the Donor Selection of MTS.

The different effects in gene silencing observed in the Shf1 and Set1 mutants show divergent effects in heterochromatin formation. I was able to compare different complexes that are involved in histone modifications, related to either Euchromatin or Heterochromatin. It was important to evaluate the effect of Chromatin-related factors and how different they behave in comparison with the HULC and Set1C in the MTS process. For instance, Paf1C is required for proper H2Bub, moreover, it is also involved in the RNA pol II transcription elongation, and interacts with Set1C. It was important to evaluate if it was required also for the MTS process. However, HULC and Set1C effects in MTS happen independently of Paf1C.

Evaluating the effects of Heterochromatin-related factors Clr4 and Clr3 was important to analyze the similarities in their biases in the Cell-type ratios with the HULC and Set1C. Although considered to promote different chromatin structures, they showed similar trends in the cell-type biases. These experiments show that HULC and Set1C might be able to fine-tune the chromatin structure to decrease the use of the *SRE3* element in M cells.

Discussion and Conclusion.

I propose a model for Regulation of MTS involving HULC and Set1C wherein M cells, HULC and Set1C inhibit the *mat3-M* donor choice at *SRE3*. Swi6 enrichments are also regulated by HULC and Set1C at *SRE2* and *SRE3*. The Swi2-Swi5 complex is associated with *SRE2* and *SRE3* in a Swi6-dependent or Swi6-independent manner and promotes *mat2-P* donor choice at *SRE2* by an unknown mechanism. In P cells, the Swi2-Swi5 complex localizes at *SRE3* specifically and promotes *mat3-M* donor choice.

Taken altogether, HULC and Set1C might be recruited in several ways to the *mat* locus where they would cooperate with Clr3 to regulate aspects of heterochromatin formation and nucleosome occupancy important for donor selection.

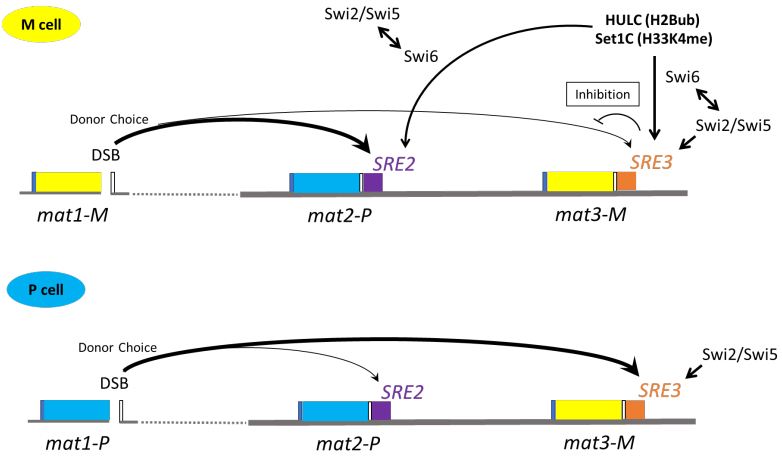

Figure 2. Proposed Model for Regulation of MTS involving HULC and Set1C.

It will be important in the future to understand how remodeling complexes might contribute to MTS, as well as how the regulation would be executed specifically to each cell-type as well as if it is executed locally, at the enhancers, or if global effects on nucleosome mobility would differ between P and M cells that might lead to the observed biases in enhancer use.

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