Study on mutations associated with chromosome-structure alterations in *Saccharomyces cerevisiae*

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Mendel has shown that genes are stably transmitted from a generation to the next. However, it is later found that genes change (or mutate) though at very low frequency, and now it is widely accepted that mutations are main driving force of evolution. It is further later found that genes consist of DNA and that mutations are alterations of the structure of DNA. Studies of mutation at molecular level have focused mainly on base substitutions of DNA (and thus amino acid substitutions of protein). Consequently, mutations that associate with alterations of chromosome-structure remained obscure. The role of retrotransposons in generation of chromosome polymorphism became apparent recently. Because this notion relies mainly on experiments done under sophisticated, and thus artificial, conditions, there remaines questions whether the obtained results truly represent natural events.

In this study, I showed that *Saccharomyces cerevisiae sir4-11* strains were useful in the study of mutations in the *HMR***a** locus (especially, mutations that caused alteration of the chromosome structure). It had been previously established that an *S. cerevisiae* strain bearing a *sir4-11* mutation (*HML*α *MAT*α *HMR***a** *sir4-11*) formed diploid clones, at a very low frequency, when mated with an **a** mating strain (*HML*α *MAT***a** *HMR***a** *SIR*$^{+}$) and that the diploid clones obtained from such a cross often had altered forms of the *HMR***a**-containing restriction fragment. I extended this study and obtained evidence that the target of alteration was the **a** cassette rather than the *HMR* locus. I moreover found that the mutations in *HMR***a** locus were generated in the *sir4-11* strain before its mating with the **a** mating partner; that is, a mutation that causes loss of the function of **a** cassette in *HMR* changes the *sir4-11* strain to α-mating, and the mutated *sir4-11* strain then undertakes the normal mating reaction against an **a**-mating partner. As the result, the mutation occurred in the *sir4-11* strain is recovered in the resultant diploid clone. In this thesis, I present the results of analyses of the structure of the altered forms of restriction fragment containing *HMR.* In conclusion, I found that they were associated with "conversion of *HMR***a** (638 bp) to *HMR*α(742 bp)", "insertion of a Ty element (6 kbp) into Y**a** of *HMR*" and "more complex rearrangements of chromosome III (elongation of chromosome III by 120 kbp or more)". Based on these observations, I discuss roles of "DNA repair", "Ty insertion" and "δ mediated recombination" in dynamism of genome.