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Genetics

# Movement of yeast transposable elements by gene conversion

**(gene replacement/recombination/transposition/controlling elements/gene expression)**

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**ABSTRACT** **We have constructed yeast strains in which Ty (*t*ransposon *y*east) elements at the *HIS4* locus are genetically marked with the yeast *URA3* gene. By isolating and analyzing Ura$^-$ derivatives of these strains, we have detected a variety of Ty-mediated recombination events. In this paper, we describe events in which the DNA sequence of the Ty element at the *HIS4* locus is replaced by the DNA sequence of a different Ty element. These replacements occur without alterations in the flanking DNA sequence and without chromosomal aberrations. We believe that these events result from gene conversion between the Ty element at *HIS4* and a Ty element at a different site in the yeast genome. Gene conversion can occur between Ty elements that differ by large insertion and substitution mutations. These recombination events result not only in the movement of Ty sequences but also in alterations in expression of the adjacent *HIS4* gene. Different Ty elements at the same site in the *HIS4* regulatory region can result in His$^-$, His$^+$, and cold-sensitive His$^+$ phenotypes. Several Ty elements render expression of the *HIS4* gene subject to control by genes at the mating type locus.**

Haploid cells of *Saccharomyces cerevisiae* carry more than 30 copies of a DNA sequence known as Ty (*t*ransposon *y*east). Ty elements are approximately 6,000 base pairs long and are flanked by direct repeats of a 330-base-pair sequence called $\delta$ (1). Ty elements are capable of transposition to new sites in the yeast genome. Insertion of a Ty element into or near a functioning yeast gene can result in a mutant phenotype. We have previously described two mutations at the *HIS4* locus that result from events of this sort. These mutations, known as *his4-912* and *his4-917*, result from the insertion of Ty elements, called Ty*912* and Ty*917*, respectively, into the 5′-noncoding region of the *HIS4* gene (2–5).

Ty elements display considerable sequence heterogeneity. Ty*912* and Ty*917* differ from each other by many base-pair changes and by two large substitution mutations that cover two-thirds of the internal region of the Ty (5–7). Ty*912* and Ty*917* are representative of the two main classes of Ty elements that exist in the yeast cell. Both classes of Ty elements display restriction site polymorphisms indicating sequence heterogeneity within each group (6). There are approximately 30 Ty*912*-like elements and 6 Ty*917*-like elements per haploid genome (5–7).

To facilitate the study of Ty elements, we have constructed yeast strains in which Ty*912* and Ty*917* are genetically marked with the yeast *URA3* gene. By isolating and characterizing Ura3$^-$ derivatives of strains carrying the *URA3*-marked transposons, we have been able to demonstrate a variety of Ty-mediated recombination events. In this paper, we describe recombination events in which the DNA sequence of the Ty element at the *HIS4* locus is replaced by the DNA sequence of a different Ty element. These replacements occur without any alteration in the flanking DNA sequences and without any chromosomal aberrations. We believe that these events result from gene conversion between the Ty element at *HIS4* and one at a different site in the yeast genome. These conversion events result not only in the movement of Ty sequences but also in alterations in expression of the adjacent *HIS4* gene.

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## RESULTS

**Construction of Strains Carrying Genetically Marked Transposons.** The construction of strains carrying genetically marked Ty elements took place in three stages: (*i*) cloning of the mutant *HIS4* genes containing the transposons, (*ii*) introduction of the *URA3* gene into the cloned Ty elements, and (*iii*) replacement of the chromosomal *HIS4* gene in a yeast cell with the modified genes constructed *in vitro*.

The cloning of the *his4-912* and *his4-917* mutant genes has been described (3, 5). The plasmids obtained contain pBR322 vector sequences, the Ty element, and the flanking *HIS4* DNA. Both plasmids carry a single *Hin*dIII restriction site lying within the Ty element. A 1,200-base-pair *Hin*dIII restriction fragment containing the yeast *URA3* gene was inserted into this site in both plasmids to yield the plasmids shown in Figs. 1*a* and 2*a*.

The last step in strain construction was replacement of the chromosomal *HIS4* gene in a yeast strain with the modified genes constructed *in vitro*. When a plasmid containing yeast DNA is introduced into a yeast cell by transformation, it engages in recombination with the homologous yeast DNA in the genome. When a circular plasmid containing a Ty element is introduced into a yeast cell, it most often recombines with one of the 35 Ty elements present in the genome. To increase the frequency with which the plasmids shown in Figs. 1*a* and 2*a* recombined with *HIS4* DNA, we took advantage of the following observations made by Orr-Weaver *et al.* (8). (*i*) Restriction enzyme digestion of a plasmid within a region of yeast DNA causes the resulting linear plasmid to recombine specifically at the chromosomal location homologous to the ends of the molecule. (*ii*) Linear molecules in which both ends are homologous to yeast DNA recombine with chromosomal DNA so that the entire plasmid becomes integrated into the genome. This gives rise to a duplication of yeast DNA with plasmid vector sequences inserted between the two copies of the duplication. (*iii*) Linear molecules that have only one end homologous to yeast DNA transform by substitution. DNA on the plasmid is simply substituted for DNA in the chromosome without any integration of vector sequences.

Construction of the Ty*912* (*URA3*)-containing strain is outlined in Fig. 1. Plasmid integration was directed to the *HIS4* locus by cleaving the plasmid with *Xho* I. This enzyme cuts in the *HIS4* DNA and generates a linear molecule whose ends are homologous to the *HIS4* locus. The linear plasmid was introduced into a yeast strain carrying the wild-type *HIS4* gene and a *ura3*$^-$ mutation. Genetic analysis of the Ura$^+$ transformants

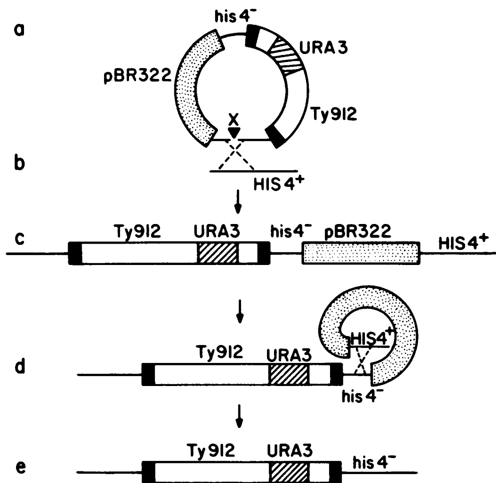


FIG. 1. Introduction of Ty*912* (*URA3*) into yeast. Diagram of procedure used to replace the chromosomal *HIS4* gene with the Ty*912* (*URA3*)-containing gene. —, *HIS4* DNA; ⊡, pBR322 vector sequences; □, Ty element; ■, δ sequences; ▨, *URA3* DNA; X, position of the *Xho* I site at which the plasmid was cleaved prior to transformation; ---, positions of reciprocal crossovers. (*a*) The Ty*912* (*URA3*)-containing plasmid represented as a circle opened at the *Xho* I site. (*b*) The wild-type *HIS4* gene on the chromosome. (*c*) The chromosomal *HIS4* region after integration of the plasmid shown in *a*. (*d*) Pairing of the homologous duplicated *HIS4* sequences. (*e*) The chromosomal *HIS4* region after excision of the vector sequences and the wild-type *HIS4* gene.

showed that the linear plasmid had integrated at the *HIS4* locus. Southern hybridization analysis showed that the transformants contain pBR322 vector sequences flanked on both sides by a copy of the *HIS4* gene (Fig. 1*c*). One copy is the wild-type *HIS4* gene and one copy carries the *URA3*-marked Ty element. These transformants are unstable since reciprocal recombination between the homologous duplicated regions (Fig. 1*d*) can result in excision of the plasmid sequences and one copy of the duplicated segment. Recombination events that excise the wild-type *HIS4* gene and the vector sequences retain the modified *his4-912* gene and result in a His⁻ phenotype. His⁻ cells were isolated by inositol starvation (9), and these were shown by Southern hybridization analysis to carry a single copy of the *HIS4* gene. This gene carried Ty*912* (*URA3*) as shown in Fig. 1*e*.

Construction of the Ty*917* (*URA3*)-containing strain is outlined in Fig. 2. The Ty*917* (*URA3*)-containing plasmid was digested with *Eco*RI, which cleaves at the junction between *HIS4*

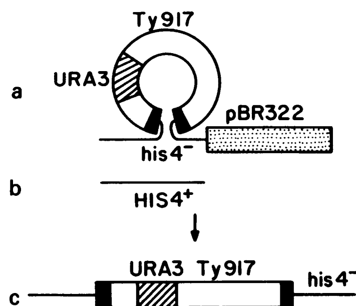


FIG. 2. Introduction of Ty*917* (*URA3*) into yeast. Diagram of procedure used to replace the chromosomal *HIS4* gene with the Ty*917* (*URA3*)-containing gene. —, *HIS4* DNA; ⊡, pBR322 vector sequences; □, Ty element; ■, δ sequences; ▨, *URA3* DNA. (*a*) The Ty*917* (*URA3*)-containing plasmid represented as the linear molecule resulting from cleavage at the *Eco*RI site. (*b*) The wild-type *HIS4* gene on the chromosome. (*c*) The chromosomal *HIS4* region after conversion of the wild-type gene to the mutant gene carried by the plasmid.

DNA and the pBR322 vector sequences. The resulting linear plasmid contains only one end that is homologous to *HIS4* DNA. Transformation of a *HIS4⁺ ura3⁻* strain by the *Eco*RI-cleaved plasmid results in *his4⁻ URA3⁺* transformants. Southern hybridization analysis of these transformants indicated that the *HIS4* gene on the chromosome was directly converted to the Ty*917* (*URA3*)-containing *HIS4* gene carried by the plasmid (Fig. 2*c*).

**Detection of Ty Replacement Events.** We have used two procedures for isolating cells in which Ty*917* (*URA3*) or Ty*912* (*URA3*) have been lost or rearranged. In the first approach, Ura⁻ derivatives of Ty*917* (*URA3*)- or Ty*912* (*URA3*)-containing strains were isolated by inositol starvation as described by Henry *et al.* (9). In the second approach, His4⁺ revertants were selected and these were analyzed for the ability to grow in the absence of uracil. Only those His4⁺ revertants that were Ura⁻ will be discussed in this paper. Both spontaneous and UV-induced mutations were isolated by using these techniques. All mutations were isolated in haploid cells growing mitotically.

Ura⁻ derivatives of Ty*917* (*URA3*) and Ty*912* (*URA3*) can result from a variety of recombination events. The events that are the subject of this paper are those in which the DNA sequence of the Ty element at *HIS4* is replaced by the DNA sequence of a different Ty element. These replacement events occur without any alterations in the flanking *HIS4* DNA and without any associated chromosomal aberrations (see Fig. 6).

Twenty-one independent Ura⁻ derivatives of Ty*917* (*URA3*) have been isolated. Thirteen of these are the result of Ty replacement events of the sort just described. Many Ura⁻ derivatives of Ty*912* (*URA3*) have been isolated, but the majority of these are the result of Ty*912* excision due to δ–δ recombination (3, 4). Only two Ty*912* (*URA3*) replacement events were detected. The properties of the cells that have undergone Ty replacement are summarized in Table 1.

**Genetic Analysis.** The strains listed in Table 1 were mated with suitably marked yeast strains of opposite mating type. Diploids were sporulated and tetrads were dissected. In every case, the tetrads showed normal spore viability, indicating that no chromosomal aberrations had occurred. The map distance between *HIS4* and *LEU2* was approximately 20 centimorgans, indicating that the *HIS4* gene was at its normal location on chromosome III (10).

**Southern Hybridization Analysis.** DNA from the strains listed in Table 1 was digested with a variety of restriction enzymes and analyzed by Southern hybridization. The probe used was a *Sal* I restriction fragment of the wild-type *HIS4* gene. This probe hybridizes to DNA sequences on both sides of Ty*912* and Ty*917*. For all of the strains listed in Table 1, at least one restriction enzyme generated a single fragment that hybridized to the *HIS4* probe. This fragment was always 6,000 base pairs larger than the fragment present in wild-type *HIS4⁺* strains. These results suggest that the *HIS4* region is still intact in these strains and that a Ty element is still present in the *HIS4* regulatory region.

**Restriction Maps.** The Ty elements present at the *HIS4* locus were analyzed by restriction mapping. In some cases, the mutant *HIS4* genes containing the new Ty elements were cloned by integration and excision as described (3, 5). The restriction maps were then determined by analysis of the cloned sequences. In other cases, the restriction maps were deduced by Southern hybridization using the flanking *HIS4* DNA as a probe.

This analysis indicates that the Ty elements derived from Ty*917* (*URA3*) fall into at least six classes. The most frequent kind of element (Fig. 3*b*) is one that differs from the parental Ty*917* (*URA3*) (Fig. 3*a*) only by the deletion of the *URA3* gene.

Table 1. Properties of yeast strains that have undergone Ty replacement

| Parent | Ura⁻ derivative | Restriction map | Origin* | Phenotype | MAT control |
|---|---|---|---|---|---|
| Ty917(*URA3*) | S456 | Fig. 3*b* | Spontaneous | His⁻ | na |
| | S467 | Fig. 3*b* | Spontaneous | cs His⁺ | + |
| | S469 | Fig. 3*b* | Spontaneous | His⁻ | na |
| | S497 | Fig. 3*b* | Spontaneous | His⁺ | + |
| | S480 | Fig. 3*b* | UV | His⁺ | + |
| | S483 | Fig. 3*b* | UV | His⁺ | + |
| | S487 | Fig. 3*b* | UV | His⁺ | + |
| | S486 | Fig. 3*c* | UV | His⁺ | − |
| | S492 | Fig. 3*d* | UV | cs His⁺ | ± |
| | S485 | Fig. 3*d* | UV | His⁺ | − |
| | S454 | Fig. 3*e* | Spontaneous | His⁺ | + |
| | S458 | Fig. 3*f* | Spontaneous | His⁺ | − |
| | S455 | Fig. 3*g* | Spontaneous | His⁺ | + |
| Ty912(*URA3*) | S260 | Fig. 4*b* | UV | His⁺ | − |
| | S577 | Fig. 4*c* | Spontaneous | His⁻ | na |

cs, Cold sensitive; na, not applicable; MAT, mating type.
* Ura⁻ derivatives arose spontaneously or after UV irradiation.

The parental Ty*917* (*URA3*) contains two *Hin*dIII sites flanking 1,200 base pairs of *URA3* DNA but the elements in Fig. 3*b* contain a single *Hin*dIII site and no *URA3* DNA. All other restriction sites are unchanged. Several derivatives of Ty*917* (*URA3*) are elements of the Ty*912* class (Fig. 3 *c–g*). They differ from the parental element by two large substitution mutations, by the deletion of *URA3* DNA, and by many restriction sites. The Ty*912*-like elements derived from Ty*917* (*URA3*) display restriction site polymorphisms characteristic of the Ty*912* class of elements.

Both of the Ura⁻ derivatives of Ty*912* (*URA3*) are similar to Ty*912* in their restriction maps (Fig. 4). The *URA3* DNA has been deleted and a few restriction sites have been changed. The restriction site polymorphisms shown among the Ty elements in Fig. 4 are a subset of those shown in Fig. 3.

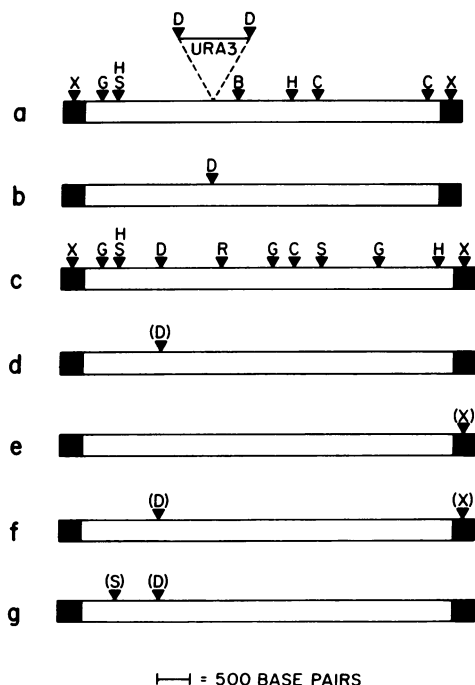


FIG. 3. Restriction maps of Ty*917* (*URA3*) and its Ura⁻ derivatives. □, Internal regions of Ty elements; ■, δ sequences; —, *URA3* DNA. Restriction sites: X, *Xho* I; G, *Bgl* II; S, *Sal* I; H, *Hpa* I; D, *Hin*dIII; B, *Bam*HI; C, *Cla* I. (*a*) Ty*917* (*URA3*). (*b–g*) Ura⁻ derivatives of Ty*917*(*URA3*). The Ty element in *b* is identical to that in *a* except where indicated. The map in *c* is the map of a Ty*912*-like element. The Ty elements in *d–g* are identical to that in *c* except where indicated. Restriction sites in parentheses are absent.

**Phenotypes.** The Ura⁻ derivatives of Ty*917* (*URA3*)- and Ty*912* (*URA3*)-containing strains display many different phenotypes with respect to *HIS4* expression. As shown in Table 1, these phenotypes range from His⁻, through weakly His⁺ and cold-sensitive His⁺, to those that are strongly His⁺. Cells with a His⁺ phenotype are found even among the survivors of an inositol starvation that demanded only that the surviving cells be Ura⁻.

**Mating Type Control.** In some of the His⁺ Ura⁻ derivatives of Ty917 (*URA3*)-containing strains, expression of the *HIS4* gene is under mating type control (Table 1). These mutants are His⁺ in haploid cells but His⁻ in diploid cells that are heterozygous, *MATa/MATα*, at the mating type locus. The His⁻ phenotype of the diploids is the result of heterozygosity at *MAT* rather than a result of diploidy since diploids that are homozygous, *MATa/MATa* or *MATα/MATα*, are His⁺.

**A Deletion Associated With Ty Replacement.** The yeast strains used in these studies carry a Ty element, known as Ty*1–17*, near the *Leu2* locus on chromosome III (7). This Ty element is approximately 20 centimorgans away from the *HIS4* gene. Ty*917* and Ty*1–17* lie in the same orientation on the chromosome and have identical restriction maps. In one of the Ura⁻ derivatives of Ty*917* (*URA3*), S484, the entire region between these two Ty elements has been deleted (Fig. 5).

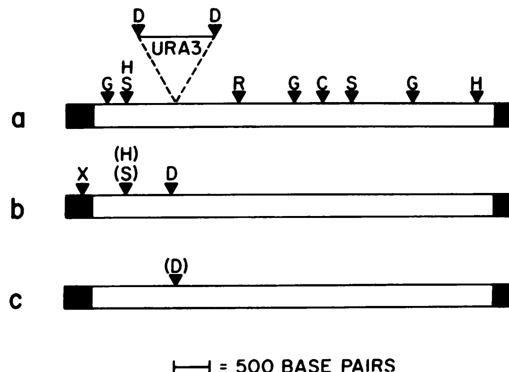


FIG. 4. Restriction maps of Ty*912* (*URA3*) and its Ura⁻ derivatives. □, Internal regions of the Ty elements; ■, δ sequences; —, *URA3* DNA. Restriction sites: X, *Xho* I; G, *Bgl* II; S, *Sal* I; H, *Hpa* I; D, *Hin*dIII; B, *Bam*HI; C, *Cla* I. (*a*) Ty*912* (*URA3*). (*b* and *c*) Ura⁻ derivatives of Ty*912* (*URA*). The Ty elements in *b* and *c* are identical to that in *a* except where indicated. Restriction sites in parentheses are absent.

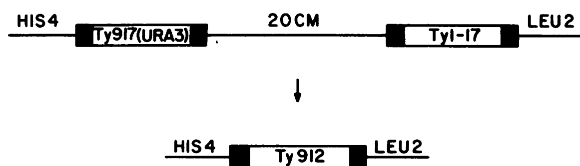


FIG. 5. A deletion associated with Ty element replacement. □, Internal regions of the Ty elements; ■, δ sequences; —, unique-sequence yeast DNA from the left arm of chromosome III. The parental Ty*917* (*URA3*)-containing strain contains two Ty elements on the left arm of chromosome III—Ty*917* near *HIS4* and Ty*1-17* near *LEU2*. There are 20 centimorgans (CM) of DNA between these two Ty elements. In strain S484, a Ura⁻ derivative of the Ty*917* (*URA3*)-containing strain, *HIS4* and *LEU2* are separated by a single Ty*912*-like element.

Southern hybridization analysis of S484 DNA using *HIS4* DNA as a probe indicates that the *HIS4* gene is now adjoined by a Ty*912*-like element. Southern hybridization using *LEU2* DNA as a probe indicates that *LEU2* also abuts a Ty*912*-like element. Southern hybridization using DNA from the region between *HIS4* and *LEU2* indicates that this region has been deleted. Genetic analysis indicates that *HIS4* and *LEU2* are less than 1 centimorgan apart in the S484 strain.

## DISCUSSION

Several Ura⁻ derivatives of Ty*917* (*URA3*)- and Ty*912* (*URA3*)-containing strains retain an intact Ty element at the *HIS4* locus. The Ty elements are in the same position and in the same orientation as the original elements; however, they differ from the parental Ty elements by the loss of *URA3* DNA and by changes in their restriction maps. The new restriction maps are characteristic of Ty elements known to exist elsewhere in the yeast genome. The simplest interpretation of these observations is that the *HIS4* Ty element engaged in recombination with a Ty element from a different site in the genome.

Ty replacement events could result from either gene conversion or double reciprocal crossing-over. Fig. 6*a* shows the pairing or alignment of homologous Ty elements from different sites in the genome. Fig. 6*b* shows the result of two reciprocal crossovers. Reciprocal crossing-over can be most easily thought of as the breakage of DNA molecules at homologous sites followed by their rejoining in a recombinant configuration. In Fig. 6*b*, two reciprocal crossovers have occurred, one near each end of the Ty element. Fig. 6*c* shows the results of a gene conversion event. In nonreciprocal recombination or conversion, the two

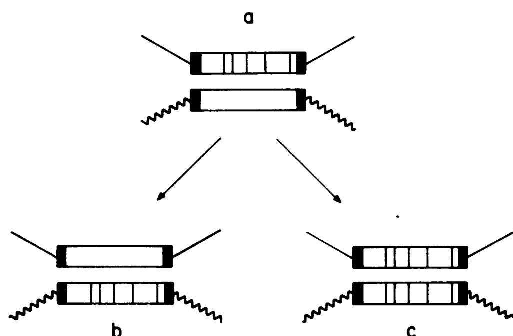


FIG. 6. Recombination between Ty elements. □, Internal regions of the Ty elements; ■, δ sequences; — and ∿, unique-sequence yeast DNA flanking the Ty elements. Vertical lines, differences between the recombining Ty elements; these could be base-pair changes or they could be insertion, deletion, or substitution mutations. (*a*) Two Ty elements from different sites in the genome pair with each other as the first step in recombination. (*b*) The products of two reciprocal crossovers between the Ty elements shown in *a*. (*c*) The products of gene conversion between the Ty elements shown in *a*.

Ty elements interact with each other in such a way that part or all of the sequence of one becomes identical to the sequence of the other. The sequence of one Ty element is lost and the sequence of the other is duplicated. Both double crossing-over and gene conversion can result in the replacement of one Ty sequence by another without any alteration in the configuration of flanking markers.

Several observations indicate that Ty replacement events result from gene conversion rather than double crossing-over. First, mitotic gene conversion of non-Ty sequences occurs more frequently than reciprocal crossing-over. If the Ty replacement results from double crossovers, the frequency of these events should be the product of the probabilities of two single crossovers. However, the frequency of chromosome aberrations ($10^{-8}$) due to single crossovers and the frequency of Ty replacement ($10^{-7}$) are very similar. Therefore, the double crossover hypothesis requires an unusual coupling between single crossover events. Furthermore, the double crossover hypothesis does not explain the loss of the *URA3* marker from cells in which the *HIS4* Ty has been replaced. The double crossover hypothesis requires that the recombination occur at the two-chromatid stage of chromosome replication and that the *URA3*-containing chromatids be lost during a subsequent segregation event.

When Ty*917* (*URA3*) or Ty*912* (*URA3*) are corrected (converted) by using another Ty element as a template, they lose the *URA3* DNA and acquire the restriction map displayed by the second Ty element. This conversion occurs between Ty elements that share extensive sequence homology and also between elements that differ by large substitution mutations. It is surprising that Ty elements that exist at dispersed sites in the genome and differ by extensive regions of nonhomology can still pair with each other and engage in recombination. However, conversion between dispersed repeated genes is not unique to Ty elements. It occurs between *HIS3* genes inserted at different sites in the genome by transformation (11), between the non-allelic *CYC1* and *CYC7* genes (12), and between dispersed tRNA genes (13). Furthermore, high-frequency gene conversion in a unique direction is responsible for mating type switching in homothallic yeast strains (14). In higher eukaryotic cells, gene conversion is thought to be involved in the correction of globin genes (15) and in the evolution of the immunoglobulin genes (16, 17).

Gene conversion is generally considered a mechanism for maintaining sequence homogeneity. Since one sequence is corrected to be identical to another, conversion will eventually force identity on any family of homologous sequences. However, gene conversion may also be an important mechanism for generating diversity. Consider a gene conversion event between two Ty elements that differ at several positions. A conversion event that covers only part of the element can generate a new Ty element that is different from both of the parental elements. It has been suggested that gene conversion may be an important mechanism in the generation of immunoglobulin diversity (18).

The sites of insertion of Ty*912* and Ty*917* are 161 and 71 base pairs, respectively, upstream of the *HIS4* coding sequence. Ty*912* and Ty*917* have inserted into the *HIS4* regulatory region in opposite orientations such that transcription of Ty*912* proceeds toward the *HIS4* gene and transcription of Ty*917* proceeds away from the *HIS4* gene. Gene conversion has generated yeast strains containing many different Ty elements at the *HIS4* locus. In every case, the derivative Ty element occurs at the same site and in the same orientation as the parental element. The yeast strains resulting from conversion of Ty*912* (*URA3*) and Ty*917* (*URA3*) display a variety of phenotypes with respect to *HIS4* expression. These results suggest that the phenotype of a Ty insertion mutation depends on the DNA sequence of the

inserted Ty and that different Ty elements can have radically different effects on the expression of adjacent genes.

There is no correlation between the restriction map of a Ty element and its effect on gene expression. Both Ty*912*- and Ty*917*-like elements can turn the *HIS4* gene on or off, render its expression cold sensitive, or subject it to control by genes at the *MAT* locus. There may be a correlation between the orientation of a Ty element and its ability to effect mating type control. There are several $His^+$ derivatives of the Ty*917* (*URA3*)-containing strain that show control by *MAT*; however, the one $His^+$ derivative of the Ty*912* (*URA3*)-containing strain does not show mating type control. Furthermore, in all the *ADR3* (19) and *CYC7* (20) insertion mutations under *MAT* control, the direction of Ty transcription is opposite to the direction of transcription of the affected gene.

Control of gene expression by mating type occurs in the ROAM (regulated overproducing alleles responding to mating type) described by Errede *et al.* (21). Ty insertion mutations at the *CYC7*, *CAR1*, *CAR2 DUR1,2* (21), and *ADR3* (19) loci result in constitutive overproduction of the products of these genes. In every case, the overproduction that occurs in haploid cells is greatly diminished in diploids that are heterozygous at *MAT*.

The mechanism by which Ty elements subject genes to mating type control remains to be elucidated. It is known that transcription of the Ty elements themselves is repressed in diploid cells heterozygous at *MAT* (22). The behavior of ROAM mutants could be explained very simply if a transcript subject to mating type control started in the Ty element and proceeded through the adjacent structural gene. However, two observations make this explanation untenable. First, in all the ROAM mutants examined, the direction of Ty transcription is opposite to that of the adjacent gene (19–21). Second, the transcript of the affected gene is known to start at the normal initiation site in several ROAM mutants (23).

Analysis of strain S484 suggests that Ty replacement may sometimes be associated with the deletion of unique sequence DNA. Fig. 7 diagrams a single recombination event that explains the simultaneous alterations of the Ty elements at *HIS4* and *LEU2* as well as the deletion of the intervening DNA. According to this model, a Ty*912*-like element pairs with the left end of Ty*917* and the right end of Ty*1-17*. This causes the formation of a loop containing Ty sequences and all the unique sequence DNA between Ty*917* and Ty*1-17*. Conversion of the chromosome III sequence to the sequence of the Ty*912* element

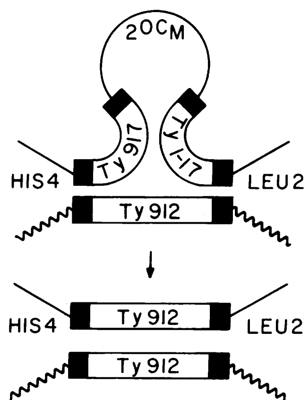


FIG. 7. Model for deletion formation by gene conversion. □, Internal regions of the Ty elements; ■, δ sequences; —, unique-sequence yeast DNA from chromosome III; ～, unique-sequence yeast DNA from another chromosome.

would delete all of the DNA in the loop and leave behind a single Ty element. The sequence of this Ty element would be identical to the sequence of the Ty*912* element used as template during conversion. Strains that have lost the DNA between *HIS4* and *LEU2* are viable as haploid cells, indicating that the DNA between *HIS4* and *LEU2* is nonessential for yeast cell viability.

The Ty replacement events described here provide the yeast cell with a means of moving Ty sequences to new sites in the genome. This movement of Ty sequences by homology-dependent recombination events occurs 10- to 100-fold more frequently than insertion into nonhomologous DNA segments by transposition. Both mechanisms provide the yeast cell with a means of altering gene expression and rapidly adapting to changes in environmental conditions. It is possible that the heterogeneity among Ty elements is of selective advantage to the yeast cell. By having different Ty elements that affect gene expression in different ways, the yeast cell can effect many different alterations in gene expression through the processes of transposition and gene conversion.

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