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The DNA transposition system of hybrid dysgenesis in *Drosophila melanogaster* can function despite defects in host DNA repair

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SUMMARY

Genetic traits associated with the hybrid dysgenesis syndrome were quantified in strains deficient in two major host-coded DNA repair pathways, post-replication and excision repair. A defect in either (or both) pathway(s) fails to influence the frequency of male recombination or sex-linked recessive lethal mutations associated with hybrid dysgenesis, suggesting that the DNA transposable elements associated with this syndrome act independently of these cellular functions. However, when the post-replication repair pathway is blocked, the recovery of second chromosomes containing factors associated with hybrid dysgenesis activity is reduced. The decrease in recovery is associated with zygotic lethality.

1. INTRODUCTION

A correlated syndrome of related genetic abnormalities, termed hybrid dysgenesis, occurs among the progeny of certain interstrain crosses of *Drosophila melanogaster* (reviewed by Bregliano & Kidwell, 1983; Kidwell, 1983*b*; Woodruff *et al.* 1983). The hybrid dysgenesis syndrome encompasses: (1) illegitimate recombination in males (meiotic recombination does not normally occur in males of this species), (2) temperature-sensitive male and female sterility, (3) distorted Mendelian transmission ratios from heterozygous males, (4) increased frequencies of mutation induction (including lethal and visible mutations and chromosome aberrations) and (5) altered parameters of meiosis in males and females. In the *P–M* system of hybrid dysgenesis, these abnormalities are most common among the progeny of crosses between males from strains recently isolated from cosmopolitan natural populations (*P* strains) and females from strains maintained in the laboratory for many years (*M* strains). Any particular isolated chromosome from an *MR* or *P* strain may show any subset of these abnormalities, yet all appear to be characterized by increased mutation induction and male recombination. The genetic factors

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carried by these chromosomes are under the control of chromosomal and cytoplasmic factors, a condition termed cytotype (Engels, 1979*b*).

Recent molecular evidence indicates that in many strains members of a specific family of nomadic DNA sequences (*P* elements) are inserted into the sites of mutations induced by hybrid dysgenesis (Bingham *et al.* 1982; Rubin *et al.* 1982). It is not known whether all *P* strains contain the specific *P* element family, but most if not all *P* strains do contain transposable elements which can induce genetic changes. Of interest is the genetic control of such 'jumping gene' systems in eukaryotes. Do these systems require cellular functions for their activity? One approach which can be utilized to answer this question is to monitor the effects of *P–M* hybrid dysgenesis in genetic backgrounds deficient in one of the major pathways of DNA repair.

Such repair-deficient mutants have been identified by screening for hypersensitivity to killing by physical or chemical mutagens (Boyd *et al.* 1976*a*; Baker *et al.* 1976). In Drosophila, at least 20 loci controlling sensitivity to one or more mutagens have been identified (Boyd *et al.* 1980). Although some of these loci have been shown to control steps in excision repair (Boyd *et al.* 1980) or post-replication repair (Brown & Boyd, 1981), the biochemical functions of many of these loci are not understood. It is also known that many of these loci control mitotic chromosome stability (Baker *et al.* 1980), meiotic recombination (Baker & Carpenter, 1972), and female fertility (Smith, 1976), as well as chemically and radiation-induced mutation frequencies (Graf *et al.* 1979). Since hybrid dysgenesis contributes to these endpoints, it is of interest to ask whether mutants defective in DNA repair influence the behaviour of this transposable element system. In this report we examine the effects of blocks in the excision and post-replication pathways of DNA repair on the activity of a transposable element system in Drosophila, using the genetic endpoints of mutation induction, male recombination induction and transmission distortion.

2. MATERIALS AND METHODS

All experiments were carried out using standard cornmeal, agar, dextrose media, supplemented with propionic acid as a mould inhibitor. All strains and crosses of *Drosophila melanogaster* were maintained at 24 ± 1 °C. Males and females were less than 3 days old when used to begin crosses. Unless otherwise noted, parents were discarded after 7 days from the inception of the cross and progeny were scored until the 19th day.

(i) *Terminology and stocks*

Following the description of Kidwell *et al.* (1977) and Engels (1979*b*), paternal strains which contribute to the hybrid dysgenesis syndrome are known as *P* strains, while maternally contributing strains are termed *M* strains. Dysgenic progeny arise from crosses of *M* females by *P* males (cross A), whereas non-dysgenic progeny arise from the reciprocal cross, *P* females by *M* males (cross B). Thus, criteria for classifying strains as *P* rested on the observation of the production of dysgenic progeny from crosses of presumptive *P* strain males to standard *M* strain females

and the production of non-dysgenic progeny from the reciprocal cross. Strains utilized in this study were tested in this manner for *M* or *P* type.

Six independently isolated *P* strains from diverse geographic locations were assayed: *T-007* (Texas) (Hiraizumi, 1971), *N-1* (California) (Green, 1978), *Haifa-12* (Israel) (Green, 1977), *W8D* (Georgia) (Woodruff & Thompson, 1980), *OK1* (Oklahoma) (Woodruff & Thompson, 1977) and π_2 (Wisconsin) (Engels, 1978*a*, *b*). An additional *P* strain, *C(1)DX*; π_2, was also used in certain experiments. In this strain, females contain two *X* chromosomes attached to each other and a *Y* chromosome ($\widehat{XX}/Y$). Such females produce sons whose *X* chromosome is of patroclinous origin and whose *Y* chromosome is of matroclinous origin. The attached-*X* chromosome is marked with the two recessive mutants, *y* (yellow body colour, 1-0·0) and *f* (forked bristles, 1-56·7). The remainder of the chromosomes in this strain (including the *Y* chromosome) are from the π_2 strain.

These *P* strains were all tested by the procedures outlined below. However, in order to save space, only the data for *T-007*, *Haifa-12* and π_2 will be presented. The other three *P* strains showed similar results. The complete set of data, including all six *P* strains, is available upon request from the authors.

The following laboratory *M* strains of *D. melanogaster* were used in these experiments.

cn bw. An isogenic second chromosome strain containing the two recessive eye colour mutations *cn* (cinnabar eye colour, 2L-54·5) and *bw* (brown eye colour, 2R-104·5). Homozygous *cn bw* flies show white eye colour.

Canton-S. A standard wild-type strain. This strain will be abbreviated as $+^C$ in this report.

Basc. A balancer strain whose *X* chromosomes contain multiple, overlapping inversions, the dominant mutation *B* (Bar eye shape) and the recessive mutations w^a (white–apricot eye colour) and *sc* (scute bristle).

mus or mei strains. In Drosophila, as has been observed in other organisms where such parameters have been assayed, the repair of genetic damage, general recombination and fertility are controlled by overlapping genetic functions (Baker *et al.* 1976; Boyd *et al.* 1980; Smith *et al.* 1980). Mutations at two loci controlling mutagen sensitivity (symbol: *mus*) were originally isolated based upon their phenotype of increased meiotic nondisjunction and have been termed meiotic mutants (symbol: *mei*). For the purposes of this discussion, however, the general symbol *mus* will be used to designate all loci controlling mutagen sensitivity, unless reference is made to a specific locus. Specific *mus* strains utilized in this report include the following.

mei-9^a/Basc; cn bw and *mei-9^{D1}/Basc; cn bw*. Two strains containing mutations at the *X* chromosome locus *mei-9* (1–5·0), which controls excision repair (Boyd *et al.* 1976*b*). These strains are also homozygous for the second chromosome mutations *cn* and *bw*. Because homozygous *mei-9* females have reduced fertility, *X* chromosomes in these strains were kept in a balanced condition with the *Basc X* chromosome.

mei-41^{D1}/Basc; cn bw and *mei-41^{D5}/Basc; cn bw*. Two strains containing mutant alleles of the *X* chromosome locus *mei-41* (1–54·0), which controls post-replication repair (Boyd & Setlow, 1976). These strains are also homozygous for the second

chromosome mutations *cn* and *bw*. Because homozygous *mei-41* females have reduced fertility, *X* chromosomes in these strains were kept in a balanced condition with the *Basc X* chromosome.

mus-101^{D1}/Basc; cn bw. A strain containing a mutant allele of the *X* chromosome locus *mus-101* (1–44·0), which controls post-replication repair (Boyd & Setlow, 1976). This strain is also homozygous for the second chromosome mutations *cn* and *bw*. Because homozygous *mus-101* females have reduced fertility, *X* chromosomes were kept in a balanced condition with the *Basc X* chromosome.

Mus-102^{D1}/Basc; cn bw. A strain containing a mutant allele of the *X* chromosome locus *mus-102* (1–0·05) (Boyd *et al.* 1976*a*). This strain also is homozygous for the second chromosome mutations *cn* and *bw*. The biochemical nature of the repair deficiency is unknown.

mei-9^{a} mei-41^{A3}/Basc; cn bw and *mei-9^{a} mei-41^{D5}/Basc; cn bw*. Two strains containing combinations of mutant alleles at the *mei-9* and *mei-41* loci. These strains are also homozygous for the second chromosome mutations *cn* and *bw*. Because homozygous *mei-9 mei-41* females are virtually sterile, the *X* chromosomes in each strain were kept in a balanced condition.

(ii) *Sex-linked recessive lethal mutation tests*

P strain males were crossed to *mus; cn bw* (or *mus^{+}; cn bw*) females to produce F_1 sons which were then mated individually to *Basc* females. Individual F_2 *Basc/X** females from these crosses were backcrossed to *Basc* males, where *X** represents the *X* chromosome being tested for the presence of a newly induced sex-linked recessive lethal mutation. The absence of F_3 non-*Basc* males indicated the induction of a sex-linked recessive lethal mutation. Retests were performed from vials where less than 20 male progeny were present.

(iii) *Male recombination and transmission frequency tests*

Crosses of *mus; cn bw* (or *mus^{+}; cn bw*) females by *P* (or *M*) males were performed to produce F_1 sons which were heterozygous for *cn bw*. These F_1 males were then individually testcrossed to homozygous *cn bw* females and the progeny were scored for the presence of recombinants (as indicated by the presence of non-parental phenotypes, i.e. *bw* or *cn* eye colour), as well as the frequency of the non-*cn bw* homologue. This measure, termed *k*, was computed as the number of wild-type progeny divided by the total non-recombinant progeny. The *k* values thus measure the frequency of viable progeny receiving a wild chromosome from the F_1 heterozygous males. The expected Mendelian transmission frequency is 0·50, since one-half of the progeny should receive a wild-type second chromosome and one-half should receive a *cn bw* second chromosome (excluding recombinant progeny). The *k* values presented in this report have been corrected for viability, because it has been shown that the viability of *cn bw* individuals is very close to that of wild-type (Hiraizumi, 1977).

(iv) *Egg hatchability and adult eclosion tests*

As before, matings of *mus; cn bw* (or *mus*$^+$*; cn bw*) females by *P* (or *M*) males were made to produce F_1 sons. These males were crossed to three *cn bw* females for 48 h, after which they were individually mated to additional harems of three *cn bw* females for seven 24 h broods. Parental females from each brood were individually placed in fresh food vials for an additional 24 h and were transferred to fresh food vials every 24 h for a total of seven days. To better visualize oviposited eggs in these experiments, media were prepared with the addition of powdered activated charcoal. In the adult eclosion tests, flies were scored up to the eighteenth day from egg deposition. In the egg hatchability tests, eggs were scored within 36 h for the presence of hatching. All vials were double-blind coded and, as an internal check, vials in which there were a large number of eggs were scored by more than one investigator. Sets were uncoded after final adult counts were completed. Females not producing any first-instar larvae by the time of final adult counts were considered not to have been fertilized, and those egg counts were removed from the data. Hatchability was computed as the number of first-instar larvae out of the total number of eggs. Adult eclosion was computed as the number of adults out of the total number of eggs. A series of four independent experiments was performed; within each set results were homogeneous.

3. RESULTS

(i) *Sex-linked recessive lethal mutation induction*

Sex-linked recessive lethal mutation frequencies for the *mus* strains in the absence of *P* strain chromosomes have been shown previously not to differ significantly from those of the $+^C$ genotype (Mason, 1980). The results of assays for sex-linked recessive lethal mutations, in the presence of *P* strain chromosomes, are presented in Table 1. Clusters of lethals (representing pre-meiotic events) were identified by a cumulative Poisson distribution test (Owen, 1962) and were counted as individual lethals. The Kastenbaum–Bowman statistical tables were used to judge significance (Kastenbaum & Bowman, 1970). From Table 1, it can be observed that, in combination with *P–M* dysgenesis, repair-deficient mutants fail to increase sex-linked recessive lethal mutation frequencies significantly from the *Canton-S* control values.

(ii) *Male recombination induction and transmission frequencies*

Results obtained from assays of male recombination induction and of transmission frequencies are presented in Table 2. Adjustments for clusters of recombinants were made as described above (Owen, 1962), as were significance determinations (Kastenbaum & Bowman, 1970). Standard *F* tests (Snedecor & Cochran, 1980) were used to determine significance of transmission frequencies.

In the absence of *P*-bearing chromosomes, none of the *mus* mutants caused a significant increase in male recombination over that observed for the $+^C$ control. A similar result was obtained by Lutken & Baker (1979). In addition, none of the

tested combinations showed a significant change in frequency compared with the corresponding *P* chromosome control. There was also no evidence of increased clustering in any particular genotype. It appears from these results that these repair-deficient mutants fail to influence *P–M* dysgenesis-induced recombination in males.

Table 1. *Percentage of sex-linked recessive lethal mutations observed in various indicated genotypes*

	Second chromosome genotype	
X chromosome genotype	*T-007/cn bw*	*Haifa-12/cn bw*
$+^{C}$	1·21 (4471)*	0·93 (4507)
mei-9^{D1}	0·93 (857)	1·29 (1396)
mei-9^{a}	0·84 (1071)	1·03 (2324)
mei-41^{D1}	1·17 (1883)	0·72 (2075)
mei-41^{D5}	1·70 (1820)	1·03 (2129)
mus-101^{D1}	1·22 (2129)	1·05 (2198)
mus-101^{D2}	1·54 (1842)	1·15 (2426)
mus-102^{D1}	0·55 (1086)	1·23 (1547)
mei-9^{a} *mei-41*^{D5}	1·44 (823)	0·45 (1117)
mei-9^{a} *mei-41*^{A3}	1·22 (1149)	1·25 (1357)

* Values in parentheses represent the numbers of sex-linked recessive lethal mutation tests scored.

The transmission of all *P*-bearing second chromosomes, however, was significantly reduced in the presence of mutant alleles at the *mei-41* and *mus-101* loci (Table 2). These loci control post-replication repair. Two mutants of the *mei-9* locus, however, show no ability to alter this phenotype.

Of further interest are two additional observations. First, in the *mus*$^{+}$ control some *P*-bearing chromosomes (e.g. *T-007*) have a reduced *k* value compared to the *Canton S*, whereas others do not (e.g. *Haifa-12*). Post-replication repair-defective mutants which reduce this value do so to approximately the same degree for all *P*-bearing chromosomes. That is, the two types of reduction in *k* value appear to be additive. *mei-41* alleles have stronger effects than *mus-101* alleles and *mus-102* alleles. In the case of *mei-41; T-007/cn bw* males, only 2–8 % of the recovered non-recombinant chromosomes are of the *T-007* genotype, as opposed to almost 40 % in the presence of *mei-41*$^{+}$.

Secondly, males of the genotype *mei-9 mei-41; P/cn bw* are largely sterile. Fewer than 10 % of these males are fertile, and among the fertile males fecundity is very low. It is unclear why this combination leads to male sterility, especially since *mei-9* appears to have no effect upon transmission distortion.

To verify that these results follow the pattern of inheritance observed for other phenotypes associated with hybrid dysgenesis, two sets of additional crosses were performed using the *P* chromosome stock π_2 (Engels, 1979*b*), where hybrid $\pi_2/+$ F_1 males do not exhibit distorted transmission ratios. In the set A crosses, designed to produce dysgenic progeny, π_2 males were crossed to *cn bw* females (A-1), *mei-41*^{D2}*; cn bw* females (A-2) or *mei-41*^{D5}*; cn bw* females (A-3). In the set B crosses, designed to produce non-dysgenic progeny, *C(1)DX*; π_2 females were crossed to *cn bw* males

Table 2. *Transmission ratios (k) and percentage male recombination observed in various indicated genotypes*

X chromosome genotype	Second chromosome genotype: *Canton-S/cn bw*		*T-007/cn bw*		*Haifa-12/cn bw*	
	k	Recombination (%)	*k*	Recombination (%)	*K*	Recombination (%)
$+^{C}$	0·539	0·02 (13305)*	0·385	0·66 (5157)	0·529	0·41 (4124)
mei-9^{a}	0·546	0 (3437)	0·353	0·31 (1272)	0·523	0·39 (1289)
mei-9^{D1}	0·522	0 (1212)	—	— (—)	0·555	0·26 (1150)
mei-41^{D1}	0·581	0 (2778)	0·026†	0·20 (3145)	0·374†	0·29 (3147)
mei-41^{D5}	0·513	0·12 (1602)	0·083†	0·28 (1060)	0·228†	0·43 (1402)
mus-101^{D1}	0·590	0 (1687)	0·197†	0·66 (1677)	0·465†	0·15 (2009)
mus-101^{D2}	0·599	0 (2256)	0·288†	0·23 (2149)	0·463†	0·20 (2202)
mus-102^{D1}	0·549	0 (2767)	0·304†	0·55 (1447)	0·459†	0·43 (1880)
mus-9^{a} *mei-41*^{A3}	0·429	0 (1909)	0·153†	0·89 (1676)	0·299†	0·31 (1711)
mei-9^{a} *mei-41*^{D5}	0·413	0 (1219)	0·072†	0·18 (558)	0·266†	0·44 (1818)

* Values in parenthesis indicate the number of progeny scored. † $P < 0·01$.

(B-1), *mei-41*^{D1} males (B-2) or *mei-41*^{D5} males (B-3). From the six crosses in these two sets, F1 males were collected, backcrossed to *cn bw* females and transmission frequencies measured. The results from these crosses are presented in Table 3. The two *mei-41* alleles significantly decrease the transmission frequency in the dysgenic (set A) males, but not in the control (set B) males. Thus the effect of *mei-41* on transmission frequencies appears to correlate with hybrid dysgenesis.

Table 3. *Transmission frequencies (k values) among the progeny of* π_2*/cn bw males containing various indicated X chromosome genotypes*

X chromosome genotype	Set A	Set B
(1) *cn bw*	0·467 (1719)*	0·471 (1228)
(2) *mei-41*^{D1}	0·165† (168)	0·473 (349)
(3) *mei-41*^{D5}	0·207† (136)	0·462 (573)

* The value in parentheses indicates the number of progeny scored. † $P < 0{\cdot}01$.

(iii) *The mechanism of transmission distortion in P strain post-replication repair-deficient males*

Light microscopy reveals no obvious structural defect in the testis of *P*-bearing males with a post-replication repair-deficiency; there appear to be as many motile sperm as in *P*-bearing males without such a deficiency (S. Haas, unpublished). The following series of egg hatchability and adult eclosion experiments also suggest that the cause of the reduction of the transmission frequency is zygote mortality, rather than a defect in spermiogenesis.

As before, F_1 males were generated by crossing (*mus*)*; cn bw* females to *P*-strain or *Canton-S* males. These F_1 males were crossed to *cn bw* females, and the resulting eggs were scored for hatchability and eventual adult production. No significant reduction in egg hatchability occurs among the progeny of the F_1 *mus;* $+^C$*/cn bw* males (Table 4). Similar egg hatchabilities are also seen among the progeny of *mei-9* and *mus-101* males when they carry either the *T-007* or the *Haifa-12* chromosome. In contrast, there are large decreases in egg hatchability and adult eclosion among the progeny of *mei-41* males containing *P*-bearing chromosomes. The progeny of *mus-101; P*-bearing males show intermediate levels of hatchability. The reductions in adult eclosion appear to be similar in magnitude to the values obtained for the egg hatchability experiments, suggesting that most lethality in these progeny occurs in the embryo.

Because males ejaculate more sperm than can be utilized by a female, the observed reductions in egg hatchability and adult eclosion appear to be due to fertilized, but inviable, eggs. These results suggest that, in the presence of a defect in post-replication repair, breakage in *P*-bearing chromosomes cannot be repaired properly. When sperm bearing these damaged chromosomes fertilize eggs from wild-type females dominant lethality results. Matthews (1981) has shown that some 70% of the reduction in *k* values among the progeny of *T-007/cn bw* males is due to spermiogenic defects, while the remainder is due to zygotic lethality. The reduction in egg hatchability, even among the progeny of *P*-bearing males that normally show no distortion, may define a novel hybrid dysgenesis phenotype.

It should be noted that adult eclosion values for three of the *mei-41* non *P*-bearing controls were significantly lower than expected (Table 4). These results suggest that an additional lethal component exists in these genotypes at some developmental stage between egg hatch and adult eclosion.

Table 4. *Percentage of egg hatchability (top panel) and adult eclosion (bottom panel) for various male genotypes*

X chromosome genotype	Second chromosome genotype		
	Canton-S/cn bw	*T-007/cn bw*	*Haifa-12/cn bw*
*mus**	83 (462)†	75 (398)	78 (349)
mei-9^{a}	84 (243)	84 (279)	81 (491)
mei-41^{D1}	79 (378)	53 (342)*	53 (502)*
mei-41^{D5}	78 (209)	55 (403)*	55 (382)*
mus-101^{D1}	85 (418)	63 (361)*	72 (512)
mus-102^{D1}	87 (520)	83 (419)	84 (486)
mei-9^{a} *mei-41*^{A3}	79 (198)	54 (216)*	52 (231)*
mei-9^{a} *mei-41*^{D5}	77 (213)	52 (187)*	54 (224)*
*mus**	77 (4671)†	65 (467)	73 (1888)
mei-9^{a}	82 (173)	84 (623)	69 (616)
mei-41^{D1}	75 (493)	47 (188)*	48 (3642)*
mei-41^{D5}	72 (1105)*	52 (223)*	49 (3422)*
mus-101^{D1}	81 (323)	59 (217)	68 (315)
mus-102^{D1}	83 (368)	87 (536)	74 (652)
mei-9^{a} *mei-41*^{A3}	69 (459)*	49 (122)*	49 (705)*
mei-9^{a} *mei-41*^{D5}	63 (220)*	47 (108)*	51 (81)*

* $P < 0{\cdot}01$. † Numbers in parentheses indicate the number of eggs scored.

4. DISCUSSION

In this report we have examined the effects of blocks in the excision (using *mei-9* mutants) and post-replication (using *mei-41* and *mus-101* mutants) pathways of DNA repair on the activity of a transposable element system in Drosophila. Two of the endpoints which were monitored, mutation and male recombination, may be the direct result of insertion or excision of a transposable element (Bingham *et al.* 1982; Rubin *et al.* 1982; Rubin & Spradling, 1982; Spradling & Rubin, 1982). The relationship between transposition and the third endpoint, transmission distortion, however, is not clear. If transposition were blocked by a defect in DNA repair, one might expect that the frequencies of mutation and male recombination would be reduced. This result, however, is not observed, suggesting that transposition is not blocked in the presence of these mutants. Instead, in the presence of a defect in post-replication repair there is a decrease in the recovery of *P*-bearing second chromosomes.

The observations that (1) mutations in four loci controlling mutagen sensitivity have no effect on either mutation frequency or male recombination frequency and (2) mutations that block post-replication repair drastically decrease the recovery of *P*-bearing chromosomes, suggest that post-replication repair is needed for the transmission of existing copies of the transposable element, but not for its transposition. Further, the observation that much of the distortion is caused by

the inability of *P*-bearing progeny to complete development suggests that the lesions occurring in *P*-bearing chromosomes require a functional post-replication repair pathway to be corrected. Absence of proper repair is lethal.

An analogous situation was reported by Graf *et al.* (1979), who found that *mus-101*^{D1} eliminated nitrogen-mustard-induced mutation. They suggested that the pre-mutational lesion induced by nitrogen mustard is a DNA crosslink and that this lesion in the presence of *mus-101*^{D1} becomes a dominant lethal (Wurgler & Graf, 1980). Mutations at another locus controlling post-replication repair (*mei-41*) did not have a significant effect on nitrogen mustard-induced mutagenesis. It is possible that there are some steps common in the repair of DNA crosslinks and repair of lesions induced in *P*-factor-bearing chromosomes because both require a functional *mus-101* locus. However, the overlap cannot be complete because *mei-41* is required for repair of lesions in *P*-bearing chromosomes, but not nitrogen mustard-induced pre-mutagenic lesions.

Our results show that *mei-9*^{a}, a mutation in a locus controlling excision repair, has no effect on transmission distortion or the frequencies of *P*-factor-induced sex-linked recessive lethal mutations or male recombination. This is also true when *mei-9* is in a *mei-41* background. These results are at odds with the observations of Eeken & Sobels (1981), who reported that *mei-9*^{a} and *mei-41*^{D5} both increased the frequency of *Haifa-12*-induced visible mutations at the *sn* and *ras* loci, and that there was a synergistic effect when these two mutants are together. While it may be suggested that visible and lethal mutations result from slightly different processes, it has been generally assumed that they both result from similar events. The reasons for this apparent discrepancy are not known.

Based upon our results, we conclude that this transposable element family functions largely independently of host-provided DNA repair mechanisms, suggesting that these elements likely code for the products necessary for their movement. In this respect they are similar to most transposable-element families in lower eukaryotic and prokaryotic systems, supporting suggestions concerning their evolutionary relatedness.

Based upon genetic and molecular evidence, parallels exist among *IS* (insertion elements) and *Tn* (transposons) in prokaryotic systems and those of yeast, higher plants and Drosophila (reviewed by Calos & Miller, 1980; Fincham & Sastry, 1974; Green, 1980; Kleckner, 1981; *Cold Spring Harbor Symposium on Quantitative Biology* **45**, parts I and II, 1980). It has been shown that *IS* and *Tn* activities are largely independent of the host general recombination systems (*rec* genes). In one yeast transposable-element system, *Del1*, transposition and deletion formation occur in the absence of the *RAD 52* gene product (Liebman & Downs, 1980), suggesting that this transposable system also operates independently of the host-generalized recombination system. Yet mutations have been uncovered which affect the functions of the transposable elements. For example, in *E. coli*, *del* mutations reduce the frequency of transpositions and precise excision events of *IS* elements, and other *E. coli* mutations have also been found which similarly affect the transposition process (Il'ina *et al.* 1980, 1981; Nevers & Saedler, 1977, 1978).

In prokaryotic systems, transposons appear to code for products necessary for their own transposition. For example, *Tn3*, *Tn5*, *Tn9*, *Tn10* and *IS5* code for both

transposase enzymes, as well as for regulatory proteins, similar to the situation observed for the transposable mutagenic phages *P1* and *Mu*. Comparable data are not yet available from eukaryotic systems, although Rubin & Spradling (1982) and Spradling & Rubin (1982) have suggested that active *P* elements are important for transformation events in Drosophila embryos, perhaps by supplying transposase functions.

It is clear that transposable elements are widespread in prokaryotes and eukaryotes. However, the control and structure of these diverse systems are only begining to be understood. The determination of host genetic control of transposable element functions will shed further light upon evolution of these ubiquitous elements and will provide further information concerning the process of mutation in eukaryotic systems.

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