Formal Relations Between Om Mutants and Their Suppressors in Drosophila ananassae

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ABSTRACT

Optic morphology (Om) mutants associated with insertions of the tom transposable element at each of three tested loci are neomorphs as defined by the phenotypic equivalence of +/+Om with +/Om and of +/Om/Om with Om/Om. Mutants behaving as suppressors of Om mutants and mapping to at least six loci are recovered from the same source and in similar frequency as Om mutants. The semidominant and nonpleiotropic suppressors at four of the six loci display defective eye phenotypes themselves, and the phenotypically normal mutants at a fifth locus are suspected alleles of a gene represented by recessive furrowed eye mutants. These and other properties imply that the suppressors, like suppressible Om mutants, are neomorphic due to insertion of the tom element into a hypothetical sequence they share with other members of a set of genes involved in development of the eye. Concurrently premature expression of both the suppressor and suppressed mutants would allow interaction of their products just as in normal development.

IN the Om hypermutability system of Drosophila ananassae, almost all recovered mutants display defective optic morphology. Each of these semidominant Om mutants is expressed quite uniformly and they are viable and fertile as homozygotes with few, if any, other pleiotropic effects. Om mutants are distributed throughout the genome among at least 25 loci some of which are represented by two or more alleles which share a locus specific phenotype. Om mutants are recovered as independent events with an overall frequency of two per ten thousand among the progeny of females derived from a particular laboratory stock.

The genetic properties of the Om hypermutability system were attributed (HINTON 1984) to a transposable element called tom that specifically inserts into a sequence shared by a set of coordinately expressed genes involved in eye development. The existence of the postulated tom element was demonstrated by SHRIMPTON, MONTGOMERY and LANGLEY (1986) as an insert into the DNA of an exceptional singed (sn乞) bristle mutant derived from the Om system; cytogenetic analyses showed that sequences homologous to the cloned insert segregated with Om mutants at each of four X-linked loci. Similar in situ hybridization of the cloned tom element was demonstrated (MATSUHAYASHI, MATSUDA and TOBARI 1986) for Om mutants at 15 additional loci. Subsequent molecular analyses (TANDA et al. 1988) identified the tom element as a retroviral-like element with high homology to the sequenced 297 and 17.6 transposable elements of Drosophila melanogaster. Examination of host sequences flanking inserted tom elements has so far failed to provide a molecular explanation for the effect of tom insertion on gene function. One purpose of this report is to describe genetic observations that suggest a formal model of Om mutant function.

Although Om mutants are routinely transmitted with high fidelity, flies with exceptional phenotypes were encountered in stocks or outcross progeny of Om mutants (HINTON 1984). Sometimes the exceptional phenotype was more extreme than the original and attributable either to the additive effect of a second site Om mutant or to an apparent isocentric change. In other cases, the exceptional phenotype approached wild type and genetic analyses exposed either a revertant or a dominant suppressor of the Om mutant. Formal characterization of such suppressors is the major topic addressed in this paper.

MATERIALS AND METHODS

Om hypermutability originated and persists in a doubly marked stock prepared from the F2 of a cross between the ca (clare, 2-linked eye color) and px (plexus, 3-linked wing venation) mutant stocks. Optic morphology mutants are designated by the symbol Om with the chromosome number and locus letter following in parentheses which, in turn, are followed by a number indicating a specific allele. The derivation of a mutant from a preexisting one is specified in the symbol; for example, Om(1D)9 gave rise to the phenotypically more extreme isocentric mutant Om(1D)9g and to the revertant Om(1D)9r25. The suppressor (Su) mutants in this system are symbolized, for example, as Om(1K)Su86 in which (1K) gives the X-linked Om locus of the mutant and 86 refers to a particular Su allele at that locus. Most stocks of Om and Su mutants and their derivatives retain much of the ca;px antecedent stock's genotype.

Some of the observations relied on X-linked markers...
including sn (singed bristles), Iz (lozenge eye structure), cop (copper eye pigmentation), m (miniature wings), v (vermilion eye color), fu (furrowed eye structure), f6 (forked bristles), g (garnet eye color), Bz (Beadex wing margins) and w (white eyes); most of these mutants are indicated on the abbreviated genetic map of the X chromosome (Figure 1).

A similarly truncated map of chromosome 2 markers (Figure 2A) includes the loci of ca, Sb (Stubble bristles) and e3 (ebony body color) in addition to various Om mutants. Whereas the foregoing mutants are found in standard chromosome sequences, Th (Thorny bristles) is associated with a reciprocal (XR;2L) translocation. Lp (Lobed eye) and UbX (Ultrastrabismus) are coupled with pericentric inversions of the second chromosome, and both Pn (Puffed eye) and M(2)91 (Minute bristles) are linked with the pericentric In(2L).A. More detailed descriptions of the markers and rearrangements can be found in HINTON and DOWNS (1975) or HINTON (1980).

Typical experimental matings were conducted at room temperature and combined two or three, 3–5 days old, parents of each sex in a 25 × 95 mm shell vial; two one week progeny broods were obtained from most matings. The culture medium containing corn meal, brewer’s yeast, agar and molasses was fortified with propionic acid and Tegosept and seeded with live baker’s yeast. To induce revertants of sn females, four day old males were fed 5 mm diepoxybutane (DEB, Aldrich) in a one percent sucrose solution for 24 hr prior to mating (OLSEN and GREEN 1982).

RESULTS

Om mutant function: Definition of the function of Om mutants may provide a useful guide to their analysis in molecular terms. To that end, the phenotypic effects of varying Om dosage were studied using Tp(2L;2R)Sb, a rearrangement in which a proximal segment of 2L was transposed to distal 2R (Figure 2A; HINTON 1980). The 34C breakpoint of the transposed segment is marked by the Stubble phenotype which is allelic (noncomplementing recessive lethality) to Sb, an independent mutant mapping 4.4 units to the right of ca. In situ hybridization of a probe containing the tom element to polytene chromosomes with Om mutants at the 2A or 2C loci revealed their sites outside the transposed segment whereas the Om(2G), Om(2H) and, by inference, the Om(2B) loci are included in the transposed segment (MATSUBAYASHI, MATSUDA and TOBARI 1986; M. MATSUDA, personal communication). The Om(2G) and Om(2H) loci were identified by supplementary mapping which showed that Om18 and Om33, both previously assigned to the 2A locus (HINTON 1984), actually reside at the nearby loci 2C along with the previously unmapped mutants Om77 and Om78. Similarly, Om14 was erroneously included with mutants at 2B but it has been reassigned to 2H which is also occupied by the previously unmapped Om59 and Om80 mutants.

Crosses between Tp(2L;2R)Sb/In(2L)A, M(2)91 males and females from either the ca Om(2G)18, ca Om(2B)22 or ca Om(2H)80 stocks produced Tp/+ females which were then mated to In(2L)A, + males. Among the progeny of these Tp/+ females, about 1.1% were Om Sb recombinants expected from single crossovers (Figure 2B) that generate a chromosome duplicated for the transposed segment, but the complementary deficiency chromosome was not recoverable. Comparisons of the eye phenes expressed by Om/+ + recombinants with those of their Om/+ noncrossover counterparts revealed no difference; from 17 to 20 recombinants were observed for each of the three Om mutants examined.

The female Dp/In recombinant progeny from the foregoing crosses were backcrossed to males from their respective parental Om stocks; in these females, recombination in the ca-Om interval was eliminated by heterozygosity for In(2L)A and this enabled the use of the ca and Sb markers to identify recombinants (Figure 2B) which amounted to about 5% of the progeny. As in the previous generation, it was not possible to distinguish the eye phenes of +/Om and +/+ + Om; here, it was also evident that the phenotypes of noncrossover Om/Om/+ flies are equivalent to those of Om/Om crossovers. These observations show that the mutant phenotype is proportional to the number of Om alleles and independent of the dosage of the +

FIGURE 1.—An abbreviated map of the X chromosome of D. ananassae. Location of the centromere (C) is based on in situ hybridization of vermilion and forked probes to polytene bands in XL and XR, respectively (Y. N. TOBARI and M. MATSUDA, personal communication). See text for descriptions of loci indicated by mutant symbols.

FIGURE 2.—Markers and matings used to generate duplications for Om loci. A, Relations between genetic map (upper) of markers and corresponding polytene chromosome (lower) loci in proximal 2L; see text for descriptions of loci indicated by mutant symbols. B, Noncrossover (NCO) and single crossover (SCO) products recovered as duplicated (Dp) or standard (+) chromosomes; parentheses in lower left indicate presence of an inverted (In) sequence.
exceptions and their analyses identified one suppressor among the reciprocal outcrosses revealed only two atypically normal progeny of reciprocal crosses between the ca; px and f°° Om(1D)9 Bx w°° stocks

<table>
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<th>Parents</th>
<th>Females</th>
<th>Males</th>
<th>ca; px</th>
<th>f°° Om(1D)9 Bx w°°</th>
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allele; by definition (Muller 1932), the functions of Om mutants at all three tested loci are neomorphic.

Incidentally, the equivalence of bristle phenotypes among the Sb/+ and Sb/+/+ flies indicates this mutant to be neomorphic also. Parallel observations on e°° showed that this mutant, like its homolog in D. melanogaster (Muller 1932), is antimorphic, that is, the body pigmentation increased in order of the genotypic sequence +/+ , +/+ e , +/e , +e/e , and e/e.

Screen for revertants and suppressors of Om(1D)9: To establish the genetic conditions under which revertant and suppressor mutants occur, as well as their quantitative relations, reciprocal outcrosses were made between the ca; px and f°° Om(1D)9 Bx w°° stocks. Expression of the Om(1D)9 marker was monitored for its reversion or suppression, and the flanking X-linked markers served to distinguish between these two kinds of exceptions in subsequent diagnostic tests as well as to identify and exclude from further consideration exceptions due to maternal X chromosome nondisjunction (Table 1). The regularly wild-type sons of outcrossed ca; px females provided an assay for the expected recurrent Om mutants; among 45,992 sons, eight (or 2/10°) exceptions transmitted new Om mutants. No attempt was made to score more extreme Om phenotypes among the regularly mutant daughters of this cross nor among the offspring of either sex from the reciprocal cross. Of 15 atypically normal-eyed daughters among a total of 49,395 daughters from ca; px mothers, three (or 6/10°) were found to carry revertants of the paternally derived Om(1D)9 allele, whereas 12 (2/10°) carried a dominant suppressor of the Om mutant. The suppressor mutant proved to be autosomal in two cases but it was located in the maternally derived X chromosome in at least eight others. Scoring the 26,335 progeny of the reciprocal outcrosses revealed only two atypically normal exceptions and their analyses identified one suppressor and one revertant, both in the maternal X chromosome. Together, the results of the reciprocal screens suggest that suppressor mutants may be produced exclusively by females and, in the case of ca; px females, in a frequency equivalent to that of Om mutants. On the other hand, the low frequencies of Om(1D)9 revertants show no difference with respect to parental origin.

Whereas the exceptions enumerated in Table 1 all occurred as one specimen per culture, six clusters of 30 or more exceptions were detected among the progeny of the outcrossed ca; px males. Four of these clusters were shown to carry suppressors in the paternal X chromosome, one carried an autosomal suppressor and one was attributed to a revertant in the maternal X chromosome. These clusters were excluded from the foregoing tabulation and frequency calculations on the assumption that the mutations existed in the parental stocks prior to the assay. A typical suppressor mutant segregating in the ca; px stock would not be phenotypically detectable, and a heterozygous revertant or suppressor mutant segregating in an otherwise homozygous Om stock might have such a small phenotypic effect as to be overlooked when casually collecting parents for outcrosses but be readily detectable as a cluster among their progeny. This explanation, rather than premeiotic mutation in males as well as females, would readily account for the clustered exceptions reported (Table 5 in Hinton 1984) for outcrossed parents from the Om(1D)9 stock. Reexamination of the apparently extraordinary instability of the Om(1D)9 stock, using parents carefully selected for phenotypic conformity, failed to reveal any exceptions among 8608 total progeny of females or 8528 daughters of males in outcrosses to the f°° Bx w°° stock. Thus unusual instability of the Om(1D)9 mutant, if it ever existed, is no longer manifested. It is true that more derivatives of this Om mutant exist than for any other, but this may only reflect the greater attention given this mutant.

Further analysis of the Om(1D)9 revertants as well as more extreme derivatives will be reported separately (S. Tanda and C. W. Hinton, unpublished data). The remainder of this report will focus on various properties of the suppressor mutants.

Suppressor mutant phenotypes: After excluding two putative suppressors because their effects were too weak to permit reliable scoring, the remaining 10 entered in Table 1 were combined with 16 suppressors independently discovered during routine examination of Om mutant stocks or of progeny from miscellaneous outcrosses. Twenty-two of this sample of 26 suppressors proved to be X-linked and one of these, Om(1J)Su34, was mapped near X in the middle of Xl. All the other 21 X-linked suppressors were assigned to the single locus designated Om(1K)Su and located
about 1.6 map units to the left of f (Figure 1) as determined from their collective recombination frequencies in Su/f49 Om(1D)9 Bx2 w65 females (N = 12,064; values for individual Su alleles varied between 0.7 and 3.1 map units). Mapping the four autosomal suppressors established Om(2)fSu84 at 1.5 map units to the left of e (Figure 2A) and Om(2E)Su69 which was previously reported (HINTON 1984) as Om(2E)9h in 2R. On the third chromosome, the Om(3G) locus, mapping midway within the 4.2 map units separating Om(3F) and S, is represented by Su22, and Su12 was assigned to Om(3H) about 1 map unit distal to ru in 3R (HINTON 1984). None of the X-linked suppressors displays phenotypes other than the effects on Om expression, but all four autosomal suppressors have irregular ommatidial arrangements which are moderately severe in the case of Om(2E)Su69 (HINTON 1984) but rather mild in the Su84, Su22 and Su12 mutants. The eye phene of Su22 is visible only in homozygotes and the semidominant phene of Su84 is most easily scored as a recessive; for all four autosomal suppressors, the roughened eye phenotypes allowed them to be mapped independently of their suppressor effects.

Comparisons of the eyes of genotypic combinations of Om(1)fSu34 with Om(1D)9 showed that either Om9/+ or Om9/Om9 is more effectively suppressed by Su34/Su34 than by Su34/+; that is to say, Su34 is a semidominant allele. On the other hand, dominance varies between Om(1K) alleles: for example, Su63 is semidominant as in the preceding case of Su34, whereas all genotypic combinations of Su61 with Om9 are wild type. Suppressivity varies, not only from one Su allele to another, but with the particular Om mutant suppressed as shown by the progeny of matings between males from variousOm stocks and either Om(1K)Su/T(X:2)B, Th or Om(2E)Su69/Ubx, In(2LR)B females. The balancer chromosomes marked with Th or Ubx provided control + +/Om + siblings for comparison with + Su/Om + daughters, and the results (Table 2) are summarized in roughly quantitative scores ranging from complete suppression (score 3) to no suppression (score 0) based on observation of some 20 flies of each genotype. Among the (1K) alleles, Su18 is the strongest suppressor, with Su61 only slightly less effective, while Su26 and Su63 are distinctly weaker. Suppressibility of alleles at the Om(2C) locus varies approximately inversely with the severity of their Om phenotypes. The lack of locus specificity is emphasized by suppression of the Om(1E)53 mutant which, unlike all the others tested, exhibits an increase in amount of eye tissue (HINTON 1984). On the other hand, neither of the four (1K) suppressors has any effect on expression of the mutants Puffed or Lobe; these dominant eye structure, recessive lethal mutants originated in stocks unrelated to the ca;px progenitor of Om mutants. Nevertheless, the mere association of a tom element with a mutant is not a sufficient condition for suppressibility as shown by the failure of either Su61 or Su69 to modify expression of the bristle phenotype of sn% from which the tom element was cloned.

The entries for Om(2E)Su69 along the lower margin of Table 2 are of particular interest in that the semidominant Om phenotype of this suppressor is itself eliminated completely by Su18 and Su61 and partially by Su26. In combination with any of the several tested Om mutants (right hand column of Table 2), the eye phene of Su69 is expressed while that of the Om mutant is usually completely suppressed (that is, the phenotypes of Om +/+ Su69 approximate those of +/+ Su69; ordinarily, the combination of nonallelic Om mutants in a double heterozygote exhibits additivity). In contrast to Su69, combination of the weak suppressor and weak eye phenes of Su84 and Su12 confounds interpretation of the residual phenotypes exhibited by compounds of these suppressors with various Om mutants. Incidental observations show that Om(1K)Su86 reduces expression of the semidominant eye phenes of Om(2)fSu84 and Om(3G)Su12 as well as that of Om(2E)Su69. Among these three autosomal mutants, Su69 and Su12 interact additively in double heterozygotes but the weaker Su84 is apparently silent in combination with either Su69 or Su12.

Because the eye defect of Om(3G)Su22 is recessive, the possibility that other autosomal recessive mutants with optic morphology phenes might also function as dominant suppressors of Om mutants was examined. All the tested mutants arose prior to the Om hypermutability system, and they included gl, eyg, ro, gv, mot, rh and ru. Tests of each mutant in trans-heterozygotes with linked Om mutants failed to expose any influence of the recessive on Om expression.

The ca;px stock exhibiting Om hypermutability does not carry the extrachromosomally transmitted clastogenic mutator of its ca antecedent (HINTON 1984), but the possibility that the two systems are related is difficult to ignore. Thus it is of interest that neither the Th, Sh, Ubx nor Cy phenes associated with rearrangements induced by the ca stock mutator is influenced by any of several Om(1K)Su alleles or by Om(2E)Su69. Incidentally, the slight enlargement of Om eyes seen in most flies also carrying Minute mutants is not likely a matter of suppression but rather an additive effect of the larger eyes often exhibited by Minutes.

Reversion of suppressor mutants: Routine inspections of several stocks in which Su and Om mutants are combined did not yield the exceptions expected to result from reversion of the Su component. Specific assays for Su revertants were provided by reciprocal crosses between Om(1K)Su61 Om(1D)9, Om(1K)Su86;
Om(2B)86 or Om(1K)Su91; Om(3A)91 and the m² v² g³ stocks. Among 27,634 progeny of Su mothers, only two possible revertants were found, both of them females with one Om and one Om⁺ eye; neither mosaic transmitted a revertant Su allele in matings to m² v² Om(1D)9 g³ males. From the reciprocal outcrosses of Su males, two exceptional daughters among 24,916 scored were proven to carry revertants associated with recessive lethality, but only one of these, Om(1K)Su86, was established in stock. While the numbers are small, they are consistent with spontaneous reversion of Om mutants; in either case, reversion is as likely to occur in males as in females and it occurs with an overall frequency of about 4–6/10⁵.

Revertants, especially deficiencies, can be useful tools in the analysis of forward mutants. To enlarge the sample of Su revertants, Om(1K)Su86 males were fed DEB for 24 hours before mating to m² v² Om(1D)9 g³ females and 17,903 of their daughters were scored for exceptions exhibiting an Om phenotype. Of nine such exceptions recovered, one was attributable to the additive effect of second site Om mutant in the untreated maternal X chromosome, four were viable, partial or complete revertants of Su86 and four others were complete revertants associated with recessive lethals. Among the latter four revertants, Om(1K)Su86 was probably associated with a gross rearrangement because females heterozygous for it and the m² v² Om(1D)9 g³ marker chromosome produced among their progeny a high proportion of non-disjunctional exceptions but no recombinants. Mapping the recessive lethals of Su86, Su86 and Su86 as well as that of the spontaneous Su61 revertant, exposed no suppression of recombination between m and g and, in all cases, the lethal segregated from the v marker indicating less than 0.1 map unit between them (collectively, N = 1,307). Given the probability that reversion and lethality are concomitants of a DEB-induced small deficiency close to, but not including, the locus of v, a pseudodominance test was made with fu, the only other mutants available in the v-f interval (Figure 1). The furrowed mutants, not of Om mutability provenance, are very similar to those described under the same name in D. melanogaster (Lindsley and Grell 1968). Females heterozygous for fu or fu² and either Su86, Su86 or Su86 displayed a strong furrowed phenotype but those carrying either Su86 or Su61 were wild type. The suggestion that Om(1K)Su mutants are alleles of fu was examined by mapping Su8, Su12, Su53 and Su86 with respect to the m² v² Om(1D)9 g³ marker chromosome. Together, the four testcrosses produced 6,999 progeny of which just one was an Om(1D)9 g³ recombinant in the v-fu interval; the calculated map distance of 0.03 unit hardly differs from that of 0.04 map unit for the v-fu interval measured in fu/m² v² g³ females (N = 5,045; the nominal value of 0.5 map unit shown in Figure 1 is based on this direct determination averaged with several independent and indirect estimates). Tests of the fu mutants as possible suppressors ofOm(1D)9, Om(1E)53, Om(2A)28, Om(2C)1 or Om(3C)87 were negative and showed, instead, additivity of the fu and Om phenes.

**Suppressors and transposition:** The Om mutant phenotype evoked by insertion of the tom element could be attributed to abnormal expression of the flanking host sequences or to de novo expression of sequences within the tom element. In the latter case, a suppressor of the Om mutant phenotype might also suppress transposition given that this maneuver is.
encoded within the *tom* element (TANDA et al. 1988). This possibility was explored experimentally through reciprocal crosses between either *Om(1K)Su12* or *Om(1K)Su73* and the *ca;px* progenitor stock. F1 males from the reciprocal crosses, genetically equivalent except for their sex chromosomes, were backcrossed to *ca;px* stock females to generate *X1, +/+* or +/+*Su* daughters. These *X1* females, in matings to *m2v2g2* males, produced regularly wild-type offspring which were assayed for new *Om* mutants (Table 3). There were no significant differences between the *Su12* and *Su73* subsets, and reference to their sums shows the yield of *Om* mutants (2.4/10⁴) by *+/*X1 females to be equivalent to that customarily observed for *ca;px* females. Because half of the progeny of *X1 Su/+* females carried the *Su* allele and could not have exhibited an *Om* phenotype if they did carry a new *Om* mutant, the observed frequency of 1.6/10⁴ *Om* mutants reflects, if anything, a higher rate of transposition in *+/*Su females than in their *+/*+ controls. The four clusters of *Om* mutants detected in progenies of *Su/+* females were excluded from estimates of *Om* mutability on the assumption that they originated in a previous generation but could not be detected until the *Su* segregated in the progeny of the *X1* females.

**DISCUSSION**

Suppressor mutants appear to be as characteristic of the *Om* hypermutability system as the *Om* mutants themselves. Both types of mutants originate with a frequency of about 2/10⁴ as independent events among the progeny of females from the *ca;px* stock or its derivatives. The semidominant mutants of either class exhibit little visible pleiotropy, sterility or lethality; they revert only rarely, but as often in males as females. Just as *Om* mutants are found at many loci, some of them hotspots, *Su* mutants map to at least six loci of which one is roughly 20 times more mutable than the others. A shared functional relationship of *Su* to *Om* mutants is emphasized by the optic morphology phenes exhibited by *Su* alleles at four loci and a fifth locus may be concerned with eye development if the *Om(1K)* suppressors are actually furrowed alleles rather than being fortuitously nearby.

The implication that *Su* mutants should harbor a *tom* element has been examined for only two of the six suppressor loci (H. MATSUBAYASHI, personal communication). Whereas *Om(2E)Su69* was associated with hybridization of the *tom* probe by an appropriately situated polytene band in 2R, 13 tested *Om(1K)Su* alleles failed to hybridize the *tom* probe at a position consistent with their genetic map locus. That this locus is situated adjacent to, or within, underreplicated chromocentral heterochromatin provides a ready rationalization for its failure to bind the *tom* probe sufficiently for visualization. In view of the facts that all the other 19 in *situ* hybridization tests have exposed euchromatic loci and that no *Om* mutants among more than 100 analyzed have been traced to the large heterochromatic chromosome 4, it appears likely that *Om(1K)Su* also lies in euchromatin, but near its boundary with heterochromatin.

Neither the singed bristle phenotype associated with the *tom* element inserted in *m2v2* nor the eye malformations of mutants (*Pu* and *Lo*) from other sources are influenced by *Su* mutants, whereas eye deformities elicited by *tom* insertion, even those of suppressors themselves, are subject to suppression. The observation that the frequency of *Om* mutants is not reduced in the presence of *Su* mutants was interpreted to mean that intrinsic functions required for transposition of the *tom* element are not subject to suppression, at least not in the primary oocytes in which *Om* mutants apparently arise. In any case, the functions probably encoded in the genome of the *tom* element (TANDA et al. 1988) seem unlikely participants in eye development. Given their phenotypic restriction to eye tissue as well as the unique eye phenes shared by alleles at some loci, it is reasonable to expect that an explanation for *Om* mutants, and their suppressors, lies in the functions of the genes into which the *tom* element is inserted.

In view of the observed homogeneity between *Om* mutants with respect to other formal properties, it is legitimate to generalize from tests of alleles at three loci that all *Om* mutants are neomorphic. Thus every *Om* mutant expresses the normal product of its locus but this occurs at the wrong time or in the wrong
place. As for place, the simplest possibility is that both wild type and Om mutant alleles are expressed in prospective eye tissue or it would be necessary to explain why all Om mutants, regardless of what the normal tissue of expression might have been, come to be expressed almost exclusively as defects in eye structure. If, on the other hand, the tom element transposes preferentially into a nucleotide sequence that is shared by a set of genes and is responsible for their coordinate expression during normal eye development (Hinton 1984), then premature expression of one of these genes could lead to morphogenetic failure. Elaboration of this speculation in molecular detail is hardly required by any presently available information about Om mutants, but simple extension of the model to Su mutants is demanded by their parallelism with Om mutants.

The participation of numerous genes in a complex developmental program implies interactions between their products. The minimal requirement for normal development, the interaction of A with B, might be perturbed if, due to a neomorphic mutation, product A were precociously produced and accumulated as may be the case for any typical Om mutant. In contrast, the premature production of B need not necessarily alter development corresponding to the case of Om(JK) suppressor alleles. Now if both A and B are prematurely present, they could interact in their usual way so as to prevent accumulation of A and permit normal development to proceed via the interaction product. "Ad hoc" modifications of this basic notion might easily accommodate the inferences that the normal product of a suppressor locus interacts with those of all the suppressible Om loci and that nonallelic suppressor loci might function in either complementary or supplementary modes. Rather than informing us about specific molecular mechanisms in optic morphogenesis, the immediate significance of the Om hypermutability system is ostensibly its identification, through tractable mutants sharing a common cause, of a large set of genes each of which is primarily and concurrently involved in this particular developmental program.

Suppressibility of D. melanogaster mutants is highly correlated with the insertion of a retroviral-like transposable element that usually results in hypomorphic function (e.g., Rutledge et al. 1988). Perhaps the closest analogs of Om mutants in D. melanogaster are the suppressible, semidominant and neomorphic Hairy-wing alleles; their transcripts are truncated, but hyperabundant and functional (Campuzano et al. 1986) as proposed for Om mutants. Suppressor mutants in D. melanogaster are typically recessive and they carry an inserted transposable element only incidentally, if at all (Chang et al. 1986), in contrast to the inference that suppressors of Om mutants exist because of the inserted tom element. Moreover, evidence is accumulating that D. melanogaster suppressors control, in one or another of diverse ways (Parkhurst and Corces 1986a, 1986b; Chang et al. 1986; Mount, Green and Rubin 1988), the expression of the inserted sequences themselves rather than operating on the host gene product as surmised for Om suppressors. Recognition of the bias introduced by selective mutagenicity of the tom element supports the expectation that a search in either species for the kinds of suppressor systems known in the other should be fruitful.

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