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SPONTANEOUS MUTATION RATE IN THE DUMPY REGION OF DROSOPHILA

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SPONTANEOUS mutational events have been examined at a number of different loci in *Drosophila* and the one consistent observation in all studies is the variability in mutation rates at the various loci. This study reports the spontaneous mutation frequency of the dumpy region (*dp*, 2, $13 \pm$) in *Drosophila* to be at least three times greater than for any other gene studied in *Drosophila*, and coupled with the data on chemical and ionizing radiation mutagenesis, makes it appear highly unlikely that dumpy is a single gene. Indeed, dumpy is probably a nest of at least 20 genes and possibly many more.

This study was carried out largely over the course of three years. Wild-type Oregon-R *Drosophila* males were mass-mated to virgin *ed dp^{ov1} cl* females (*ed*: 2, 11.0; *cl*: 2, 16.5). Half-pint milk bottles containing the standard cornmeal-agar-molasses medium housed 10 parental males and 30 parental females apiece. All flies were raised at $25 \pm 1^\circ\text{C}$. The F_1 was scored for the presence of dumpy mutants by the technique of JENKINS (1967). F_1 mutants were mated through the F_2 with *ed dp^{ov1} cl* in order to distinguish mosaic from complete mutants.

The results of the spontaneous mutation analysis are seen in Table 1. A total of 108 spontaneously arising dumpy mutants were collected from 356,400 F_1 progeny. On only 4 occasions was more than one dumpy mutant recovered per bottle, but on each such occasion the mutants differed pseudoallelically from each other, eliminating the possibility of a clone of mutant chromosomes being generated from one mutant lesion. About 90% of the mutants were mosaic, indicating an event occurred on only one strand of a post-meiotic DNA duplex or else it occurred during early embryogenesis. About 10% of the mutants were classified as complete, suggesting both strands of a post-meiotic DNA duplex were mutant. The overall spontaneous mutation rate was 108 mutants chromosomes out of 356,000, or 3×10^{-4} .

The study of other genetic loci in *Drosophila* reveals a much lower spontaneous

TABLE 1

The spontaneous mutation spectrum of the dumpy region in Drosophila
(*M* = Mosaic; *C* = Complete)

progeny scored	M	C	M	C	M	C	M	C	M	C	M	C	M	C	Σ
Number of	<i>dp^{ov1}</i>		<i>dp^{ov1}</i>		<i>dp^{ov1}</i>		Classification of dumpy		pseudoalleles		Σ		Σ		
356,400	42	5	22	1	26	4	4	0	2	1	1	0	97	11	108

mutation rate. MULLER, VALENCIA and VALENCIA (1949) analyzed 11 sex-linked loci in females—prune, white, ruby, carmine, singed, raspberry, vermilion, garnet, forked, miniature, and cut. The average mutation rate per locus was about 2×10^{-5} . GLASS and RITTERHOFF (1956) examined a total of 23 loci in both males and females, and found a twenty-fold difference in the spontaneous mutation rates in males and females: for the four loci examined in both sexes (yellow, brown, ebony and eyeless), the average mutation rate per locus, exclusive of mosaics, was 2.5×10^{-6} in females and 5.75×10^{-5} in males. Mosaics would, of course, serve to increase these rates. MUKAI (1970) in a preliminary report, analyzed the loci determining alcohol dehydrogenase (ADH), α -glycero-phosphate dehydrogenase (α -GDP), and malic dehydrogenase (MDH) and estimated the average spontaneous mutation rate in male germ cells to be 1.3×10^{-6} per locus. This is similar to the findings of TOBARI and KOJIMA (1972) who analyzed ten loci (ADH, α -GDP, MDH, isocitrate dehydrogenase, esterase-6, adult alkaline phosphatase, esterase-C, octanol dehydrogenase, xanthine dehydrogenase, and aldehyde oxidase) and found the spontaneous mutation rate to average 1.2×10^{-6} per locus, including mosaics.

The dumpy spontaneous mutation frequency of 3×10^{-4} is most closely comparable to the rate GLASS and RITTERHOFF (1956) found at the yellow locus in males: 1.1×10^{-4} . The rates for other gene loci are smaller than this, going down to essentially zero. However, using the average spontaneous mutation rates per locus as determined by TOBARI and KOJIMA (1972), MUKAI (1970), and GLASS and RITTERHOFF (1956) for males, including mosaics and completes, an evaluation of the dumpy region might be made:

It has been estimated by GRACE (1970) that dumpy is a region composed of 7 to 10 genes. This was an estimate based largely on a recombinational analysis of the region. Using spontaneous mutation rates as a means of estimating the number of genes comprising the dumpy region, the minimal number would be about 20 and a maximal could be as high as 200. These values are obtained by comparing the spontaneous dumpy mutation rate of 3×10^{-4} with a low value of about 1.2×10^{-6} per gene locus obtained by TOBARI and KOJIMA (1972) for 10 separate autosomal loci, and a high value of 14.5×10^{-6} per gene locus obtained by GLASS and RITTERHOFF (1956) for 4 separate autosomal loci. It is unlikely that the high dumpy spontaneous mutation rate is due to "hot spots" because the spectra of pseudoallelic mutants induced by various mutagenic agents are remarkably similar (JENKINS 1967). To give that similarity, the hot spots would have to be randomly distributed throughout the region. It is also unlikely that the dumpy region is equivalent to a single gene, given the high spontaneous mutation rate, and the multiple phenotypic expressions of the region.

Thus we can view the dumpy region as a nest of several functionally related genes. The specific function of these genes, however, remains obscure.

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