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Vogel, E. Zentrallaboratorium für Mutagenitätsprüfung, Freiburg i. Br., Germany. Strain variations in response to certain indirect mutagens in D. melanogaster.

Strain differences in sensitivity to insecticides such as DDT, parathion and others, as well as cross-resistance are well-known in Drosophila. Among the factors considered to cause such effects is variation in enzyme activity of mixed-function oxidases localized in the microsomes (e.g. R.L. Metcalf, Ann. Rev. Entomol. 12:229, 1967). Since metabolic activation of indirect carcinogens such as aryldialkyltriazenes and azoxyalkanes is also performed by mixed-function oxidases (R. Preussmann et al., Ann. Acad. Sci. 163:697-716, 1960), the question that presented itself was whether similar effects might occur with respect to chemical mutagens.

The strains selected to study this question were our wild strain Berlin K and a resistant one, Hikone R. Dosage-mortality effects and the induction of X-chromosome recessive lethals were analyzed by treating adult males of the two strains. 1-2 day old males were exposed to test solutions of 1.0 mM/l 2,4,6-trichloro-phenyldimethyltriazene or 1.3 mM/l azoxymethane for three days and recessive lethals tested for. To recover stage-dependent sensitivity differences, three broods of three days duration each were set up (Table 1).

Table 1. Frequencies of X-chromosome recessive lethals induced by 2,4,6-trichloro-phenyldimethyltriazene (a) and azoxymethane (b).

Expt.	Strain	Brood I leth./chrom.	%	Brood II l./chr.	%	Brood III l./chr.	%	I-III (II) l./chr.	%
a	Berlin K	131/553	23.7	102/364	28.0	sterile		233/917	25.4 ± 1.4
	Hikone R	29/617	4.7	39/603	6.5	20/753	2.7	88/1973	4.5 ± 0.5
b	Berlin K	6/617	0.97	27/582	4.6	2/202	0.99	35/1401	2.5 ± 0.4
	Hikone R	5/608	0.82	49/603	8.1	sterile		54/1211	4.5 ± 0.6

The experiments revealed pronounced differences in mutation frequencies between both strains. Recessive lethals were induced to a much greater extent in Berlin K males by the triazene, while more lethals were produced by azoxymethane in Hikone R males. Analyses of the data from the different brood pattern experiments (I - III) using the χ^2 test revealed highly significant differences between the samples.

With the compounds so far tested, there was a positive correlation between toxicity and genetic activity for triazenes and azoxyalkanes. Triazenes were more toxic to Berlin K males, while Hikone R males showed higher sensitivity to azoxymethane (as well as the structural isomer of azoxyethane-diethylnitrosamine).

The data are interpreted to be due to genotype-dependent differences in activation of these indirect mutagens resulting in differing concentrations of mutagenic products in various parts of the body including the gonads. This assumption is supported by:

(1) the positive correlation between mutation frequency and the observed sterilizing effects.

(2) the inhibitory action of proper enzyme inhibitors on mutation induction by indirect mutagens (Vogel, unpublished), and

(3) our finding that the mutation frequency in Berlin K - Hikone R hybrids (Berlin K ♀♀ x Hikone R ♂♂) treated with the triazenes is almost exactly half that in the wild strain.

Whatever the correct explanation of the result is, the data show that group-specific cross-resistance to certain chemical mutagens seems to exist in Drosophila.