Alteration of Mutation Frequency by Treatment with Actinomycin D

Abstract. The frequency of lethal mutations occurring in *Drosophila melanogaster* was reduced by approximately one-half when irradiated males were treated with actinomycin D, which also inhibited the appearance of melanotic atypical growths in the strain used for the study.

In the course of investigations on alteration of mutations, actinomycin D was administered to a strain of *Drosophila* developing tumors, and mutation frequency and tumor incidence were determined after irradiation. The *st sr e^s ro ca; tu 36^a* strain, which has an unusually constant but low incidence of tumors due to multiple recessive genes, was used in these studies. Preliminary tests on sex ratios in individual matings were used to reduce the likelihood of antecedent lethal mutations. One-half of the males raised on medium containing antibiotic in 1×10^{-3}-percent concentration were irradiated with 3000 r [6 ma, 100 kv (peak), 1.0 mm of Al, 15 cm] at the age of 3 days. The *sc^{81} B InS w^a sc^8* inversion and sequential matings of the Muller 5 type were utilized to detect lethal mutations on the X chromosome (Table 1). Semilethals and visibles are not included in the tabulations. Determinations of tumor incidence in P_2 and F_1 generations (*1*) were also recorded and are presented in Tables 2 and 3. Untreated cultures and cultures treated with actinomycin D alone and irradiation alone were also studied in a similar manner.

The usual frequency of mutation was found in the control cultures (two lethals among 1375 chromosomes tested), and no significant difference was encountered when actinomycin D was added to the medium. However, the frequency with irradiation, 5.73 percent, was reduced to 3.25 percent when actinomycin D was present in irradiated cultures. In the P_2 generation, any tumors formed had regressed, leaving a pigmented residue before irradiation, so that no difference was expected between irradiated and nonirradiated cultures. The presence of actinomycin D resulted in significant reduction ($p < .05$) in tumor incidence in each group, however. In the F_1 generation, the antibiotic alone and irradiation alone reduced the number of tumors as compared to the control group. Irradiation did not reduce the number of tumors by a significant additional amount when used as a supplement to treatment with actinomycin D.

The current studies show a reduction in the number of atypical growths in *Drosophila* after treatment with actinomycin D, but inhibition of tumors by both the antibiotic and irradiation suggests that in neither case is this effect mediated through the mechanism of mutation. Actinomycin D undoubtedly reduces the number of lethal mutations occurring after x-irradiation ($p < .05$). Whether a similar reduction in the frequency of natural mutations can be demonstrated by extending the scope of the tests remains to be seen. Although the mechanism (*2*) is obscure at present, the implications of the effective reduction of irradiation-induced mutation in metazoa by an agent which can be administered in therapeutic dosage would seem of some interest (*3*).

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Table 1. Effect of actinomycin D on mutation rate in *Drosophila*.

Treatment	Chromosomes tested	Lethal mutations	
	(No.)	No.	%
Control	1375	2	0.14
Actinomycin D	978	1	0.10
Irradiation (3000 r)	1168	67	5.73
Irradiation (3000 r) plus actinomycin D	952	31	3.25

Table 2. Effect of actinomycin D on incidence of tumors in *Drosophila*.

Treatment	Males			Females			Total		
	Tumors	Total	%	Tumors	Total	%	Tumors	Total	%
Control	133	1644	8.1	127	1520	8.4	260	3164	8.2
Actinomycin D	20	514	3.9	24	493	4.9	44	1007	4.4
Irradiation (3000 r)	88	971	9.1	79	1069	7.4	167	2040	8.2
Irradiation (3000 r) plus actinomycin D	22	502	4.4	11	505	2.3	33	1007	3.3

Table 3. Effect of actinomycin D and irradiation on incidence of tumors in *Drosophila*.

Treatment	Males			Females			Total		
	Tumors	Total	%	Tumors	Total	%	Tumors	Total	%
Control	387	6110	6.3	378	6217	5.38	765	12357	6.2
Actinomycin D	34	1762	1.9	34	1731	1.96	68	3593	1.9
Irradiation (3000 r)	119	4474	2.7	145	4416	3.24	264	8890	3.0
Irradiation (3000 r) plus actinomycin D	29	1113	2.6	20	1115	1.79	49	2228	2.2

References and Notes

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Modification of Cortically Induced Responses in Brain Stem by Shift of Attention in Monkeys

Abstract. The long-latency electrical response of the brain stem evoked by stimulation of the cortex of freely moving monkeys is modified by a change of attention. The modification may be either suppression or augmentation, according to the background activity prior to the shift of attention.

In conscious cats the size of sensory evoked potentials is modified as far down as second-order sensory neurons according to the state of attentiveness of the animal (*1*). This phenomenon is interpreted as due to inhibitory influences descending through the reticular core. While it is obvious that the focusing of attention requires a selective facilitation of certain sensory input above other sensory afferents, it is not clear whether a similar mechanism applies to the situation where a corticifugal impulse is interacting with sensory afferents, or vice versa.

In this study of the central biological action of urine extracts from schizophrenic subjects (*2*), a number of *Macaca* monkeys with a system of 42 to 50 permanently implanted electrodes were used (*3*). In these animals which were kept from over 6 months to 2