Rajaraman, R. and O.P. Kamra. Dalhousie University, Halifax, Canada. Effect of pretreatment with DNA bases and base analogs on the incidence of the sex-linked recessive lethal mutations in irradiated sperms of D. melanogaster.

It is known that the incorporation of the halogenated base analogs in the DNA increases the radiation damage to DNA (Szybalski, 1967) and that U.V. or X-irradiation stimulates the incorporation of bases or base analogs in the DNA strands even in the non-S-phase cells, a phenomenon known as "unscheduled DNA synthesis" or "repair replication" (Rasmussen and Painter, 1966; Painter and Cleaver, 1967; Evans and Norman, 1968). During our studies on the disputed question of radiosensitization by the halogenated base analogs in the premeiotic germ cells of male D. melanogaster (Rajaraman and Kamra, 1970), we also included a study of the effects of these chemicals on the radiosensitivity of the postmeiotic germ cells (mature sperms). This note reports the results obtained with the mature sperms.

The effect of the base Thymidine (Tdr) and base analogs 5-bromo deoxycytidine (BCdR) and 5-bromo deoxyuridine (BUdR) on the radiosensitivity of D. melanogaster sperms was studied by intra-abdominal injection of 0.1% base or analog solution in 0.7% NaCl followed by gamma irradiation (^{137}Cs source at the dose rate of 4.2 R/sec.) with proper controls. Treated 1-day-old $X^{c2}y$ B/sc^{8} Y males were individually mated with six 3-day-old y sc^{S1} In-49 sc^{8};bw;st p^{p} virgins for two days and the frequency of the sex-linked recessive lethal mutations was studied through F_2. The treatments and the results are shown below:

Treatments*	No. Chrom. Tested	No. Leth.	% Leth.
1. NaCl + 1.2kR gamma rays	907	28	3.1
2. BCdR + 1.2kR gamma rays	905	11	1.1
3. BUdR + 1.2kR gamma rays	385	7	1.7
4. TdR + 1.2kR gamma rays	667	9	1.3

$\chi^2 = 8.76$ d.f. = 3 $P = <0.05$

* Unirradiated control experiments in all the four treatments showed a lethal frequency well within the range of the spontaneous mutation frequency.

The results indicate that the presence of the exogenous bases or base analogs reduce the frequency of the sex-linked lethal mutation significantly at 0.05 level. Preliminary studies on the fecundity and dominant lethals did not show any appreciable difference between the different treatments. Hence, it seems unlikely that the reduction in the frequency of the sex-linked recessive lethals was due to a selective elimination of sperms with induced lethals. Subsequent studies using 7-day-old males and a higher radiation dose showed a similar reduction in the incidence of lethals (to be reported elsewhere). Hence, it is highly unlikely to be an artifact.

The mechanism of reduction (repair?) of radiation induced genetic damage is not known. Since the DNA in the sperm nucleus has been synthesized long before the injection of the base analogs, they are not likely to be incorporated in the sperm nuclear DNA at the time of irradiation and hence no radiosensitization. Nevertheless, the "fixation" of the radiation induced genetic damage has been reduced by the presence of the exogenous base or base analogs. This effect may be ascribed to radiation stimulated non-semiconservative incorporation of nucleosides in the damaged sites of the DNA strands (repair replication) in the sperm nucleus. On the other hand, any other indirect metabolic effects (Wolf, 1966; Smets, Hallman, Lause and Kuyper, 1967) may also result in the repair of the chromosomal damage. Studies are in progress to elucidate the mechanism involved in the reduction of radiation-induced sex-linked recessive lethals in the mature sperms of D. melanogaster following the injection of bases or base analogs.

References: Evans, R.G. and A. Norman, 1968 Nature 217: 455; Painter, R.B. and J.E. Cleaver, 1967 Nature 216: 369; Rajaraman, R. and O.P. Kamra, 1970 Can. J. Genet. Cytol. 12: 392; Rasmussen, R.E. and R.B. Painter, 1966 J. Cell Biol. 29: 11; Smets, L.A., P. Hallman, P. Lause and Ch.M.A. Kuyper, 1967 Int. J. Radiat. Biol. 13: 269; Wolf, S., 1966 in Genet. Aspects of Radiosensitivity: Mechanisms of Repair, I.A.E.A., Vienna, 1.

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