DOE/ER/60393-4

Mutagenic Effect of Tritium on DNA of *Drosophila melanogaster*

DOE/ER/60393--4

DE89 015925

Comprehensive Performance Report

for

June 1, 1988 - June 30, 1989

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Prepared for the U.S. Department of Energy

under contract number DE-FG05-86ER60393

Division of Biomedical and Environmental Research

Department of Energy

PUBLICATIONS:

Publications and manuscripts resulting from the period of this report:

Byrne, B.J. and W.R. Lee (1989) Relative biological effectiveness of tritiated water to gamma radiation for germ line mutations. *Radiation Research* 117: 469-479.

Lee, W.R., RBE of tritium beta radiation to gamma radiation and X-rays analyzed by both molecular and genetic methods. pp. 173-179. In: *Proceedings of the Third Japan-US Workshop on Tritium Radiobiology and Health Physics*. Edited by S. Okada. Institute of Plasma Physics, Nagoya University, Chikusa-ku, Nagoya 464-01, Japan, 1989.

(7 copies enclosed)

THE MAIN RESEARCH ACCOMPLISHMENTS WITH SPECIAL REFERENCE TO ORIGINALLY STATED OBJECTIVES:

The first objective was to induce mutations at the *Adh* locus in *Drosophila melanogaster* using the procedures and dosimetry that we have developed in our publications (Byrne and Lee, 1989, reprints attached). reprints removed, The linear dose response for the doses used in Byrne and Lee (1989), would indicate that at the high dose used in Byrne and Lee (1989) the mutations will be based predominantly on the same mechanisms of mutagenesis as that of lower exposure levels. The frequency of mutations induced at 25 G (Byrne and Lee, 1989) is 100 times the spontaneous frequency; therefore, the mutation spectrum should be that of the tritium beta radiation with a non significant contribution from spontaneous mutations. These tritium induced null mutations were then analyzed by complementation genetic tests using both deletions and specific locus mutations near the *Adh* locus. Following the genetic analysis, molecular analysis will be conducted on these mutations.

The second objective of this proposal was to develop a method of exposure and dosimetry for spermatogonia cells in *Drosophila melanogaster* with the objective of studying mutagenesis in spermatogonial cells to complement the data from spermatozoa in objective 1. The third objective based on the use of repair deficient stocks was not planned for initiation until the fourth or fifth year of the five year proposal. Since the project was funded for only three years with a 50% reduction in the level of each year's funding, there must be a substantial reduction in our objective. With the reduced level of funding and length of the project, only objective 1 can be achieved to avoid spreading our efforts too thinly over too many objectives.

An important contribution of this work will be relating classical genetic analysis, ranging from complementation tests at specific loci to chromosome aberrations, to molecular analysis which we are carrying out as described in our previous publication Batzer *et al.* (1988). A logical progression of this project is to induce and recover the mutations and then analyze them first by genetic and subsequently by molecular analysis. This logical progression is economical because several mutations can be analyzed concurrently with the same labeled probe. Therefore, our first year's work and most of the second will consist of mutation induction, recovery and genetic analysis of the mutant. Seven mutations thus far have been analyzed, and all failed to complement the three deficiencies *DfA47*, *DfA48*, and *DfA63*. The results of complementation tests of loci near the *Adh* locus are presented in Table 1. Three of these mutations (*nBR100*, *nBR105*, and *nBR106) have at least one break point within the noc* to *1(2)br3* region. For four of

these mutations with break points outside the *Adh* region, additional complementation tests are being conducted as well as the continuation of these tests on new mutations as they are recovered.

Only with considerable caution will I comment about data from incomplete experiments, but it does appear that the increased RBE of 2.7 for tritium beta radiation over that of gamma radiation is due to higher LET. If this is due to multiple breaks in DNA from the same track, considerable folding of DNA is necessary to give the results of Table 1 with all 7 deletions being multi locus deletions. We do not have enough data to justify computer modeling at this time, but by the completion of this project we expect to be able to model the degree of folding necessary to permit multiple breaks that are as far apart as observed in our combination of classical and molecular analysis of the mutants.

TABLE 1

GENETIC COMPLEMENTATION DATA FOR TRITIUM BETA RADIATION INDUCED MUTATIONS

Adh^{n} mutation	Genetic loci			
	l(2)br22	*noc*	*osp*	*l(2)br3*
nBR100	-	-	-	+
nBR101	-	-	-	-
nBR102	-	-	-	-
nBR103	-	-	-	-
nBR105	+	+	-	-
nBR106	+	+	-	-
nBR107	-	-	-	-

+, Complements mutation.
-, Does not complement mutation.