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TRITIATED URACIL, TRITIATED THYMIDINE, AND BROMODEOXYURIDINE-INDUCED MUTATIONS IN EUCARYOTIC CELLS

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Abstract --- The induction of gene conversion at the ARG-4 locus in strain BZ34 of *Saccharomyces cerevisiae* was examined after the cells incorporated 6-^{3}H uracil under optimum growth conditions for 16 hours, and then received damage at 4^{0} C from tritium decays at very low dose rates of 1.4-27.6 tritium decays per hour. The results were compared to the results of gene conversion induced by ^{60}Co. Each decay of tritium under these conditions was equivalent to a dose of 3.67 rads. This value is very similar to the estimated value of 2.6 rads expected when uniform distribution of dose in the cells is taken into consideration. These results are contrasted with results from acute $^{3}H_2O$ experiments that suggest a relative biological effectiveness (RBE) of 2.8. The induction of resistance to 6TG in Chinese hamster ovary (CHO) cells has been studied after incorporation of ^{3}H-methyl thymidine, 6-^{3}H-thymidine, and bromodeoxyuridine under several experimental conditions. The induction of mutations by incorporated 6-^{3}H-thymidine is about three times as effective as the induction of mutations by tritiated-methyl thymidine. Since these results are obtained for cells frozen in the G_1 stage of the cell cycle, it may be influenced by the loss of indirect effects of tritium radiation and by life cycle effects since G_1 is a sensitive time for mutations induced by ionizing radiation. The induction of mutations by BUdR depends on the portion of the DNA that is replicated during exposure to BUdR: early replicating DNA damage is associated with induction of 6TG resistance. These results suggest that the determination of the RBE for tritium decays in model eucaryotic systems like yeast and cultured Chinese hamster cells will be influenced by the precise experimental conditions employed. In particular, experiments with mammalian cells will be affected by ‘hot times’ for mutagenesis in the cell cycle and ‘hot positions’ within the DNA in the nucleus, and also by the position of tritium decay within the DNA-incorporated molecule.