Low–LET, large–mutation spectra at hemizygous loci: evidence for intrachromosomal proximity effects

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ABSTRACT

A mathematical model is used to analyze mutant spectra for large mutations induced by low–LET radiation. The model equations are based mainly on two–break misrejoining leading to deletions or translocations. It is assumed, as a working hypothesis, that initial low–LET radiation damage is located randomly in the genome. Specifically, we analyzed data for two hemizygous loci: *CD59*$^-$ mutants, mainly very large–scale deletions (> 3 Mbp), in human–hamster hybrid cells; and data from the literature on those *HPRT*$^-$ mutants which involve at least deletion of the whole gene, and often of additional flanking markers (~50 kbp to ~4.4 Mbp deletions). For five data sets we estimated *f*, the probability that two given breaks on the same chromosome will misrejoin to make a deletion, as a function of the separation between the breaks. We found that *f* is larger for nearby breaks than for breaks that are more widely separated, i.e. there is a "proximity effect". For acute irradiation, the values of *f* determined by the data are consistent with corresponding break misrejoining parameters previously found in quantitative modeling of chromosome aberrations. Somewhat surprisingly, *f* was comparable for acute and prolonged irradiation at a given total dose, i.e. the mutation data do not show a pronounced dose–rate effect.