Problems of Extrapolation from High Dose to Low Dose in *Tradescantia* Mutation Studies

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Inflorescences of several clones of *Tradescantia* heterozygous for flower color have been treated with ionizing radiation and with the gaseous form of several known or suspected chemical mutagens. Pink somatic mutations were subsequently scored in the stamen hair cells of mature flowers and exposure/dose response curves were constructed. Results indicate clearly that there is no threshold for mutation response following x or neutron irradiation. Results so far obtained for gaseous chemicals are less clear, but also suggest that there is no threshold for mutation response.

Following exposure to 0.43-MeV neutrons, the mutation response is directly proportional to dose, forming a +1 slope on a log-log plot, from 10 mrads to the area of mutation saturation beginning at ca 10 rads. The x-ray mutation response curve (determined at a dose rate of 30 rads/min) is more complex, forming a +1 slope between doses of 0.25 and 5 rads; a slope of +1.4 may be fitted to the data for doses from 5 to 100 rads. Clearly, an extrapolation from the high-dose portion of the curve to lower doses would have increasingly underestimated the mutagenic potential of doses lower than 5 rads. In addition, a threshold effect would have been predicted.

Since neutron and x-ray curves are converging above 5 rads, RBE decreases as dose increases. However, since the curves are parallel below 5 rads, RBE is constant and maximum in that region. Extrapolation of high-dose x-ray data to lower doses would have predicted an ever increasing RBE.

Departure of the x-ray dose-response curve

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above 5 rads to a slope steeper than +1 on a log-log plot indicated a quadratic component to the curve, due to a dose-rate effect. This prediction proved true when it was demonstrated that mutation frequency decreased over 5-fold when dose rate required to deliver 80 rad was decreased over five orders of magnitude, from 105 rad/min to 3.6 Mrad/min. The dose-rate effect indicates that there is a rapid component to the repair process, i.e., repair of premutational lesions during irradiation. Thus, the dose rate at which a radiation dose-response curve is determined can have a significant influence on any downward extrapolation: the lower the dose rate the closer the curve will approach a +1 slope and the more accurately would an extrapolation to lower doses predict the mutagenicity in that low-dose region.

The x-ray dose fractionation also demonstrated a sparing effect for pink mutation induction in clone 02. Compared to an unfractionated dose of 60 rad, fractionation intervals (between two 30 rad doses) up to ca. 12 min did not reduce the mutation frequency. Progressively longer intervals resulted in a reduction in mutation frequency, but only by about 20% for an interval of 24 hr. This slow and limited decline in mutation rate indicates a slow component to the repair process.

Following exposure to gaseous 1,2-dibromo-ethane (DBE) and ethyl methanesulfonate (EMS) for 6 hr, exposure-response curves have been determined for three clones. Slopes of the curves vary from +0.6 to +2.4 for these two chemicals. Comparison of these curves to those for x-rays shows that exposure to 250 ppm of EMS is four times as mutagenic as 160 rad of acute x-rays in one clone.

Separate exposure-response curves have been constructed for DBE when duration of exposure to

0.5-100 ppm was varied between 2 hr and 6 days. In general, slopes increase from +1 to +1.5 as exposure time is increased. Data from all of these individual curves can be plotted to construct a single curve when the product of concentration and duration of exposure is expressed as total exposure on the abscissa. The overall slope of this curve on a log-log plot is +1.23. Mutation response to chemicals is always more variable than to ionizing radiation and the data which make up this curve at low total exposure are somewhat scattered. However, there is some indication, especially in the 6-hr data, that the slope may be decreasing at low exposures. If this preliminary indication is correct, extrapolation of high exposure to low exposure would give an underestimated prediction of the danger of a low exposure to DBE. Further investigation of the shape of the curve in the low-exposure region is planned.