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TITLE: Adaptive response against spontaneous neoplastic transformation induced by low dose ionizing radiation.

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Grant Project Officers: Arthur Katz and Justine Alchowiak
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Research Objective

This project is being conducted to ascertain the shape of the dose response curve for neoplastic transformation *in vitro* over the dose range 0.0 to 10 cGy, and to determine how this depends on radiation quality and dose fractionation. Preliminary data already have indicated that at a dose of 1 cGy the induced transformation frequency is less than the spontaneous transformation frequency. The results will be compared with animal and human epidemiological data on the induction of cancer by low doses of radiation. This will hopefully allow for a more informed estimation of the risk of cancer induction at low doses.

Research Progress and Implications

This report summarizes work after year 2 of a 3 year project. We have now completed a study of neoplastic transformation of human HeLa x skin fibroblast hybrid cells induced by doses of 0.1, 0.5, 1.0, 5.0, 10.0, 30.0, 50.0 and 100.0 cGy of Cs-137 gamma radiation. The induced frequencies have been compared to those for unirradiated cells, i.e. the spontaneous transformation frequency. The experiments also compared immediate with delayed post-irradiation plating. The results indicate that for delayed post-irradiation plating the induced frequencies at doses of 0.1, 0.5, 1.0, 5.0 and 10.0 cGy were ALL lower than that seen for unirradiated cells. In the absence of a dose effect, either positive or negative, the probability that all doses would show a reduced transformation frequency compared to unirradiated controls by chance is given by $1/2^n$ where n is the number of dose points, which in our case is 5. Thus the probability is $1/2^5 = 0.031$. It is therefore reasonable to conclude that an adaptive response against neoplastic transformation is occurring over this dose range of Cs-137 gamma radiation. Comparison of these low dose data with that seen at the higher doses of 30, 50 and 100 cGy shows that the values lie SIGNIFICANTLY below the linear extrapolation of the higher doses through zero dose. These observations clearly indicate that linear extrapolation from high doses overestimated the effect at low doses for delayed plating in this *in vitro* transformation assay using Cs-137 gamma radiation. Extrapolation of these findings to the human *in vivo* situation must be approached with caution. Nonetheless, relative risk estimates from these *in vitro* data show surprising similarity to those from human epidemiologic studies. A manuscript describing these studies has just been accepted by *Radiation Research*.

Planned Activities

In the remaining year of this project we plan to essentially repeat the Cs-137 work using 60 kVp x-rays. Because of time constraints we may not be able to complete as many as 5 low dose points but we will do at least two (e.g. 0.5 and 5.0 cGy). The rationale for these experiments is that there is reason to believe that the adaptive response may well be dependent on radiation quality