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CENTER FOR HUMAN RADIOBIOLOGY

Fact Sheet on

Transformation of Cells in Culture Irradiated by Alpha Particles

The study of the mechanisms of action of different carcinogens, using cells in culture, without the complexity of the in vivo system, has had a revolutionary effect on our ability to obtain basic information about many of the important steps in carcinogenesis.

Our experiments were designed specifically to simulate the effect of alpha emitters, such as plutonium and radium on cells at bone surfaces. A parallel beam of alpha particles from a Tandem Van de Graaff with an energy of 5.6 MeV was used to irradiate cells from a well characterized cell line of normal mouse embryo fibroblasts (C3H 10T1/2).

At the outset of the experiment, it was far from clear that cells could be malignantly transformed in culture because many previous workers had concluded that a single alpha particle hitting the cell nucleus anywhere had a high probability of killing the cell, thereby preventing it from becoming malignant. In contrast with this hypothesis, our early experiments showed that using flattened cells, the mean lethal dose corresponded not to one, but to ten or more alpha particles passing through each nucleus.

In eight separate experiments carried out in the last year where cultures were irradiated as described, cells were shown to be transformed by producing malignant tumors when injected back into C3H mice. Unirradiated control cells injected at the same concentration have, so far, failed to produce tumors.

Dose responses for the transformation frequencies obtained by counting the number of transformed foci in the culture dishes have been shown to vary with the number of cells irradiated but all show a very steep increase (approximately cubic) with dose up to a maximum of $1.5-2.5 \times 10^7$ alphas per cm^2 (205-342 rads). The maximum transformation frequency observed was 4% of the surviving cells, which is an order of magnitude higher than has been observed by others for x-rays using the same cell system.

The present results permit us, for the first time, to conclude that alpha irradiation may, indeed, be able to exert a direct effect on the genome of the cell to produce malignancy without any external immunological or hormonal influences.

Prepared by E. L. Lloyd

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