RADIATION DOSE-RESPONSE OF MURINE METH-A FIBROSARCOMA AS A MODEL OF RADIATION THERAPY AND ITS MODIFICATION BY HYPOXIC RADIOSENSITIZERS

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The response of murine Meth-A fibrosarcoma cells to X-irradiation was assayed by three different methods. First, to get the survivals of the tumor cells according to an *in situ* irradiation-*in vivo* assay method, the cells were transplanted into the right thigh of the BALB/c mouse and exposed to X-rays *in situ*, and then the survivals were obtained by an *in vivo* method using the growth delay phenomena of the solid tumor. Second, the estimation of the survivals according to an *in situ* irradiation *-in vitro* assay method was carried out by examining the infinite growth capacity of the cells after they were irradiated *in situ*, extracted to the single cell state and cultured *in vitro*. Third, the infinite growth capacity of the cells was also assayed after they were X-irradiated in single-cell suspension and subsequently assayed by their cloning ability in the cultured state.

These three methods gave three different X-ray dose-response curves having D_0 =1.7Gy and Dq=11.2Gy, D_0=1.3Gy and Dq=4.4Gy, and D_0=1.1Gy and Dq=2.4Gy, respectively, where D_0 and Dq represent the mean lethal dose and quasi-threshold dose, respectively. The results indicate that (1) the radiation sensitivity of the tumor cells varies depending on both the irradiation conditions and the assay method, and (2) the tumor cells irradiated *in situ* and assayed *in vivo* were most radiation-resistant bacause they had the largest D_0- and Dq-values.

The radiosensitizing abilities of two nitroimidazole compounds, misonidazole and SR–2508, as hypoxic radiosensitizers, were tested using these assay methods. These compounds were shown to sensitize the cell-killing effects of X-rays by a factor of 1.25-2.1 for D_0-values, and by a factor of 1.1–2.0 for Dq-values in all experimental methods, indicating that both should be evaluated as good radiosensitizers for clinical use.