178 The radiation induced apoptosis in spontaneously hypertensive rats jejunum with low-dose irradiation

Mutsumi MATSUU, Kazuko SHICHIJO, Masahiro ITO, Yuji IKEDA, Shinji NAITO and Ichiro SEKINE, Dept. of Molecular Pathology, Nagasaki Univ.

The degree of radiation sickness and radiation injury which observed during and after irradiation therapy seems to have an individual variation. We use spontaneously hypertensive rats (SHR) as a genetic experimental model, which has a hyperfunction of sympathetic nervous system, to investigate the relation between acute irradiation injury and autonomic nervous system. We histologically examined the difference of radiation induced apoptosis in jejunum crypt cells between WKY and SHR treated with low-dose irradiation, and to confirm whether the high radiosensitivity of SHR is due to the sympathetic nerve system, chemical sympathectomy was done. Male 6-week-old WKY/Izm and SHR/Izm were exposed to whole body X-ray irradiation as a one shot, by dose of 0.25, 0.5 and 0.75 Gy, and observed at 2 hour after irradiation to count the number of apoptosis per crypt in jejunum (apoptosis index). WKY and SHR were treated with reserpine (Daiichi pharmaceutics co. 5 mg/kg, I.P.) and vehicle control were exposed to irradiation at dose of 0.5, 1.0 and 2.0 Gy, and counted apoptosis index at 2 hour after irradiation. Apoptosis index of jejunum crypt cells in WKY and SHR increased dose-dependently and it was significantly greater in SHR than in WKY at 0.5Gy and 0.75Gy. Apoptosis index in WKY and SHR treated with reserpine was significantly suppressed compared with in control WKY and SHR at every doses. These results revealed that the sympathetic nervous system involved in the mechanism of high susceptibility to radiation induced apoptosis in jejunum crypt cells.

179 Dose rate effects on cell killing by γ-irradiation in ataxia telangiectasia lymphoblastoid cells

Ikuko FURUNO-FUKUSHI, Kouichi TATSUMI, Natl. Inst. Radiol. Sci., Chiba 263-8555

To investigate the dependency of dose rate effect on *ATM* gene , loss of the clonogenicity of lymphoblastoid cells derived from a patient with ataxia telangiectasia(AT1-1) was studied after exposure to γ-rays at dose rates of 30 Gy/h, 0.21 Gy/h and 0.0048 Gy/h. AT1-1 cells were very sensitive to killing by high dose rate γ-rays, and showed a comparable sensitivity to those for SCID (XRCC7) and LX830 (XRCC4) cells. Survival curves showed an increase in D_0 when AT1-1 cells were irradiated at the lower dose rates compared to the high dose rate. We have determined that SCID and LX830 cells were defective in the repair of DNA double strand breaks(DSBs) and that the two cell lines failed to show the dose rate effect of γ-rays. AT cells have been believed to result from cell-cycle checkpoint defects, especially since no substantial defect in the capacity to rejoin DNA DSBs has been successfully detected for AT cells following irradiation. Hence, we suggest that the dose rate effect on cell killing by γ-rays is strongly associated with the efficient repair processes of DNA DSBs.

180 Effect of the Insulin-like growth factor I receptor (IGF-IR) on radiosensitivity of human glioblastoma cells grown in multicellular spheroids.

Hiroshi Watanabe, Masahiko Miura, Takehito Sasaki
(Department of Dental Radiology and Radiation Research, Faculty of Dentistry, Tokyo Medical and Dental University)

It is well known that IGF-IR plays a crucial role in cell proliferation, transformation, and protection from cell death. We have studied the effect of the IGF-IR on radiosensitivity of human glioblastoma GBA7 cells grown in multicellular spheroids. For this purpose, we used A7(R) and A7(puro) cells expressing the IGF-IR at high or naturally occurring densities, respectively. Spheroids were made by liquid-overlay (LOC) or spinner cultures (SPC) after 20 days of culture. Overexpressed IGF-IR did not affect radiosensitivity in monolayer growth conditions. Histological analysis revealed that a central necrosis region was observed in the spheroid of A7(puro) cells, but the corresponding region was almost completely filled with intact cells in that of A7(R) cells irrespective of how the spheroid was made. When the spheroids made by LOC were X-irradiated, clonogenic cell survival obtained from the dispersed single cells of A7(R) was same again to that of A7(puro) cells. However, in the spheroids made by SPC, unexpectedly, A7(R) cells were significantly more radiosensitive than A7(puro) cells. These results imply that overexpressed IGF-IR could act as a death factor in certain growth conditions following X-irradiation.