143 Acute Irradiation Injury and Autonomic Nervous System

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We have reported that spontaneously hypertensive rats (SHRs) is a genetic experimental model which has a hyperfunction of sympathetic nervous system. We have already demonstrated that the decreases of food intake and body weight after whole body X-ray irradiation were larger in SHRs than in WKYs(Wistar-Kyoto rats) and LD50 of SHR was lower than that of WKY. The decrease of bood pressure and the increase of noradrenaline contents in small and large intestine of SHRs were observed much and earlier than those of WKYs . To investigate the mechanism of hyper radiosensitivity in SHRs, we histologically examined the difference of radiation injury between SHRs and WKYs treated with low-dose x-ray. 6-week-old male SHR/Izm and WKY/Izm were exposed to whole body X-ray irradiation at dose of 2Gy. The high-sensitivity organs were observed histologically and the expression of p53 was detected by western blotting. At the time of 1, 2, 4, 8, 12, 24 hours after irradiation, the number of apoptosis in small intestine, large intestine, thymus and spleen were larger in SHRs than in WKYs. The degree of radiation damages observed histologically were severer in SHR. These results suggest that the increase in induction of radiation-induced apoptosis in SHR with a genetic hyperfunction of sympathetic nervous system might result in severer radiation injury.

144 Flow cytometric analysis of thymocyte subpopulations in the thymus of mice early after irradiation

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The purpose of this study was to analyze phenotypic characteristics of thymocyte subpopulations undergoing apoptosis induced by radiation. Female 6-wk-old DBA1 mice were exposed to 6.8 Gy whole-body X-irradiation. Thymocyte suspensions were prepared at various time (3~168 hr) after irradiation, stained with fluorescent dye-conjugated monoclonal antibodies of different lymphocyte cell marker, and analyzed by a Cyto ACE-150. Forward scattering (FSC) was used to discriminate apoptotic cells from viable cells. DNA content of thymocytes was measured by propidium-iodide staining on the flow cytometer. The percentage of low FSC cells (FSC^{low}), indicating decreased cell size, increased until 12 hr after irradiation. This increase of FSC^{low} cells was coincident with an increase in the percentage of hypodiploid cells, indicating apoptosis. These results demonstrated that a substantial number of thymocytes undergoing radiation-induced apoptosis expressed B220, although only a small portion of thymocytes from unirradiated mice expressed B220.

145 **Mechanisms for Radiation-induced Apoptosis in a Radiosensitive Murine Thymoma Cell Line 3SB**

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Extremely radiosensitive murine thymic lymphoma cell line, 3SB undergoes apoptosis shortly after X-irradiation. Namely, more than 50% cells showed apoptosis 4 hr after 0.5 Gy irradiation. We established several radioresistant cell lines from a subclone of 3SB, 3SBH5.

Western blotting analysis revealed that p53 was not detectable in non-irradiated control, but increased gradually with time after 5 Gy irradiation before appearance of apoptotic cells, in both 3SB and resistant cell lines. However, p53 remained at low level following 0.5 Gy irradiation. A proteasome inhibitor, Z-leucyl-leucyl-leucinal, which was reported to inhibit radiation-induced apoptosis in thymocytes also inhibited the apoptosis in 3SB. Phorbol myristate inhibited apoptosis induced by 0.5 Gy irradiation appreciably. However, it was less effective at inhibiting apoptosis after 5 Gy irradiation. These results suggest that different mechanisms underlie for the induction of apoptosis by 0.5 Gy and 5 Gy irradiation.