Suppression of Tumorigenesis by Adaptive Response in Mice

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Adaptive response has been defined as radioresistance induced by a small priming dose given prior to a large challenge dose. In the protocol which involves the priming dose and the challenge dose, the latter is given just to demonstrate that the resistance is induced by the former. It is known that in response to low dose radiation certain biological protective functions, including antioxidative capacity, DNA repair capacity, apoptosis, and immune functions, are induced or enhanced. Therefore, the essential event in the adaptive response is the enhancement of the protective capacity by the priming dose. With this extended definition of the adaptive response in mind, we have investigated the effects of low-dose-rate irradiation on the process of tumorigenesis at a whole body level in mice.

Thymic lymphomas were induced by four weekly X-irradiations of 1.8 Gy each (total dose: 7.2 Gy) in a group of 30 female C57BL/6N mice, 10 weeks old at the beginning of the repeated irradiation. The cumulative incidence of thymic lymphoma was 90 %. When a group of 20 female mice, was exposed to gamma rays from a ^{137}Cs source at a dose rate of 1.2 mGy/hr throughout life, starting 35 days before the first 1.8-Gy X-irradiation, the incidence of thymic lymphoma was suppressed to 43 %.

A group of 5-week-old female ICR mice, 35 in each group, was irradiated at 3.5, 1.2, or 0.35 mGy/hr for 35 days. The mice were then injected in the groin with 0.5 mg of 20-methylcholanthrene (MC) dissolved in olive oil and irradiation was continued. A statistically significant suppression of cumulative tumor incidences up to 216 days after MC injection was observed in the group irradiated at 1.2 mGy/hr. The suppression of tumor incidence was also observed in C57BL/6N strain.

Ability of C57BL/6N mice to reject MC-induced tumor cells was examined using a TD_{50} technique to determine the number of cells needed for 50 % tumor take at the site of injection. In mice irradiated by the low-dose-rate irradiation more number of tumor cells was needed for tumor take, indicating the increased ability for tumor rejection in the irradiated mice.

The results presented here suggest that the adaptive response is effective for tumorigenesis by high doses of ionizing radiation and chemical carcinogens.