**Effects of low-dose and low-dose-rate irradiation in mouse model system**

1. Effects of split priming doses on the adaptive response in ICR mice

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The importance of low-dose and low-dose-rate radiation induced has been well recognized. Different systems have been used to study this phenomenon induced by low doses and low dose rates of radiation using various biological endpoints such as chromosomal aberration and micronuclei. However, the data from epidemiological studies are still insufficient to define its implications for human health and especially for risk assessment for radiation workers in the fields of medicine and nuclear power. Therefore, the results of the animal model system, particularly cytogenetical effects, are considered to be extremely important. We previously found that single gamma-irradiation to define the adaptive response decreased the level of micronuclei frequency in priming low-dose irradiated mice. In these studies, we have analyzed adaptive response in terms of the frequency of micronuclei in polychromatic erythrocytes of mice to evaluate the modulation by split conditioning low-dose to challenging high-dose irradiated mice. Six-week-old ICR mice (Female, 24-28g) were given whole-body irradiation via a gamma-ray machine (IBL-147). The dose rate of the priming (0, 0.01, 0.1) and challenge dose (2Gy) irradiations was 0.8Gy/min. The mice were pre-irradiated with priming doses for 10 days with the same doses. The animals assigned for adaptive response were again irradiated with a challenging dose at 11 days (Fig. 1). For all experiments, no irradiated controls were run concurrently with the pre-treated groups. The frequency of micronucleated polychromatic erythrocytes (MN-PCE) in mice was evaluated using the Acridine orange staining method (Hayashi et al, 1990). Irradiating mice with conditioning doses of 0 and 0.01Gy (cumulative dose of 0.1Gy) caused no significant increase in MN-PCE compared to 0.1Gy (cumulative dose of 1Gy) irradiated groups. The split conditioning doses of 0 and 0.1Gy did not influence induction of an adaptive response. However, when a conditioning dose was given, then split with 0.01Gy, the subjects were able to modulate the response of the challenging dose of 2Gy. These results clearly showed the occurrence of adaptive response in terms of hematopoietic microenvironment the conditioning given in small fractions continuously seemed to be more effective.

| Groups | Split conditioning dose/days on | | | | | | | | | | CD | MN-PCE |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | | |
| 1 | | | | | 0Gy | | | | | | X | O |
| 2 | | | | | 0Gy | | | | | | O | O |
| 3 | | | | | 0.01Gy | | | | | | O | O |
| 4 | | | | | 0.01Gy | | | | | | X | O |
| 5 | | | | | 0.1Gy | | | | | | O | O |
| 6 | | | | | 0.1Gy | | | | | | X | O |

CD: challenge dose (2Gy) on day11th. O: irradiated, X: non-irradiated. MN-PCE: micronucleated polychromatic erythrocytes.

Fig. 1. Experimental designs.

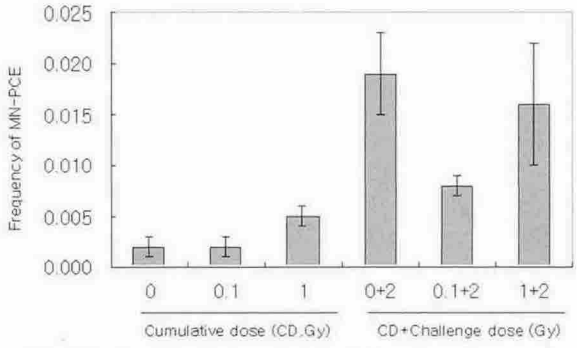


Fig. 2.The frequency of micronucleated polychromatic erythrocytes after pretreatment with split conditioning dose of 0, 0.01 and 0.1Gy for 10 days, followed by challenge dose of 2Gy ($P<0.001$, 0.1+2 vs 0+2 and 1+2).