Elucidation of the Mechanisms of Low Dose Radiation Effects

Background and Objective

The linear non-threshold (LNT) model, which is the basis of current system for radiological protection, uses linear extrapolation to estimate the possible risks from epidemiological data at high dose down to low dose, where there is limited data reliable enough. This model has been a foundation to assert that radiation is harmful even at a tiny dose; however, recent studies on the low-dose radiation effects have provided evidence that risks associated with exposure to low-dose and low-dose-rate radiation are lower than those estimated by the LNT model. The accurate estimation of health risks of low-dose radiation should lead to the establishment of reasonable protection criteria supported by the scientific evidence, and the relief of public anxiety for radiation exposure.

With the epidemiological study in the residents of high background radiation areas, this project has shown that the effects of long-term low-dose-rate radiation exposure would be lower than those observed in the life span study of A-bomb survivors who were exposed in a minute. To clarify the underlying mechanisms, the project obtains a series of experimental data in animals and cultured cells. Thus, the scientific basis for the optimization of radiological protection standards will be strengthened.

Main results

1. Activation of DNA repair function by low dose radiation

Somatic mutation is considered to initiate cancer development. The frequency of somatic mutations on wings of fruit flies *Drosophila melanogaster* was analyzed after 0.2 or 1 Gy X-irradiation (Fig. 1). 0.2 Gy irradiation reduced the mutation frequency in the DNA repair-proficient wild-type flies compared with non-irradiated counterparts. This result suggests that irradiation in the order of 0.2 Gy enhances the repair of background somatic mutations.

A similar reduction was observed in DNA double-strand break repair-deficient flies, but not in DNA single-strand break repair-deficient flies. This indicates that 0.2 Gy irradiation activates single-strand break repair gene that reduces background somatic mutations. Because of an orthologous gene, similar phenomenon may also occur in humans.

2. Response of non-damaged cells in the vicinity of directly irradiated cells

A radiation-induced bystander response is defined as the response of cells that have not themselves been directly irradiated, but are in the neighborhood of the irradiated cells. The bystander response may have important biological consequences under low dose irradiation conditions where irradiated and non-irradiated cells coexist in the same population. In this study, we examined the dose response for induction of bystander cell killing where only 5 cells among 7 x 10^5 cells were irradiated with microbeam X-rays. We found that the X-ray induced bystander cell killing effect was not detected at 0.12 Gy (Fig. 2). This was in contrast to the case for charged particle radiation that has been known to induce bystander cell killing even at a tiny dose.

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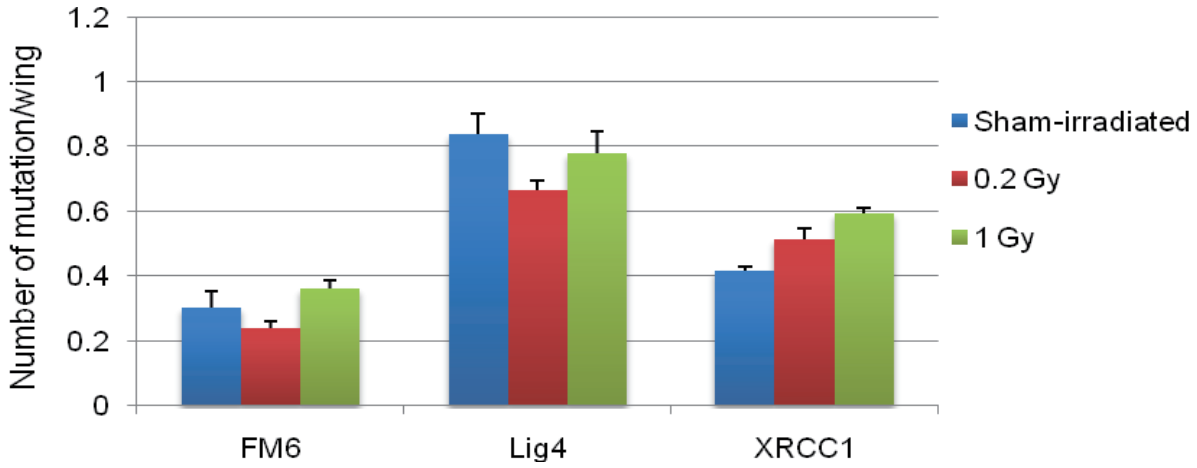

Fig. 1 Dose response for the frequency of somatic mutations in fruit flies

Irradiation with 0.2 Gy of X-rays reduced the mutation frequency in the DNA repair-proficient wild-type FM6 strain and the DNA double-strand break repair-deficient Lig4 strain. In contrast, the frequency increased with dose in the DNA single-strand break repair-deficient XRCC1 strain. These results suggest that single-strand break repair function accounts for the dose response observed in FM6 and Lig4, and that its activation by 0.2 Gy irradiation reduces background somatic mutations.

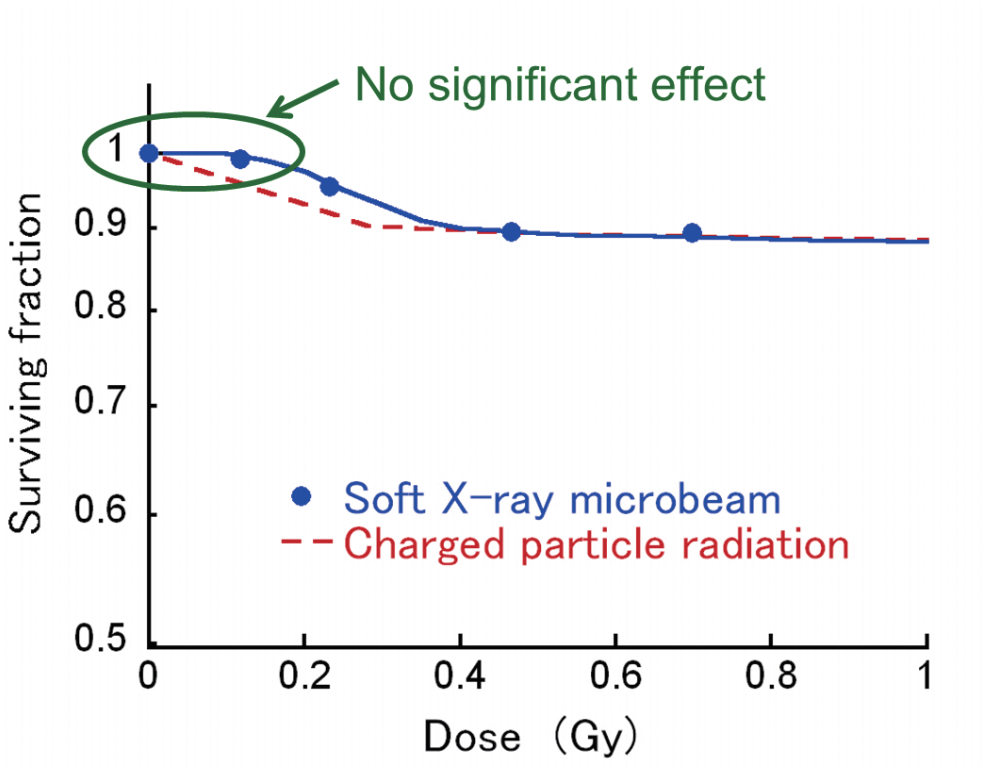

Fig. 2 Dose response for bystander cell survival as a function of the dose to targeted cells

Microbeam X-ray-induced bystander cell killing was not detected at 0.12 Gy. Even at lower doses, charged particle radiation is known to decrease the bystander cell survival (dotted line). This result suggests that X-rays and charged particle radiation have a different effect on bystander cell killing at low doses.