Acquisition of resistance to high-dose radiation by low-dose pre-irradiation
− Mechanism of recovery from radiation injury −

Background

Living cells exposed to low-dose radiation prior to high-dose radiation exposure show higher resistance to high-dose radiation than the cells exposed only to high-dose radiation. This effect is known as the radiation adaptive response. This response is also observed in whole-body level, i.e., low-dose pre-irradiated mice show efficient survival rate after lethal dose of radiation than the mice exposed only to lethal dose of radiation. However, the mechanism of whole-body radiation adaptive response is still unknown. Since the cause of death by lethal dose of radiation exposure is mainly due to the failure of reproduction of blood cells, improvement of survival rate of mice after lethal dose of radiation may be owing to mitigation of damage to blood cells in low-dose pre-irradiated mice. If the radiation adaptive response is induced by recovery of the number of blood cells, it would support the mechanism of whole-body radiation adaptive response, and finally, it could show that the radiation-induced damage is not simply determined by the accumulated dose of radiation.

Objectives

To identify the whole-body radiation-induced adaptive response that is supported by the recovery of the number of blood cells, mice were exposed to low-dose (0.5 Gy) radiation two weeks prior to high-dose (6 Gy) radiation exposure, and the number of blood cells and bone marrow cells were measured. Furthermore, in order to disclose the process of recovery of blood cell reproduction in low-dose pre-irradiated mice, the growth factor which contributes to such a production of blood cells was identified.

Principal Results

1. Chronological changes in the number of red blood cells

The reduction of red blood cells 21 days after high-dose radiation exposure was significantly mitigated by low-dose pre-irradiation in comparison with that in mice exposed to high-dose radiation only (Fig 1). The result shows that tissue damage caused by poverty of blood is not heavy in low-dose pre-irradiated mice.

2. Chronological changes in the number of primitive bone marrow cells

To investigate the mechanism of efficient maintenance of red blood cells in low-dose pre-irradiated mice, the number of primitive bone marrow cells, as a source of red blood cells, was measured. It was indicated that primitive bone marrow cells were extensively increased in the early stage after high-dose radiation exposure in the low-dose pre-irradiated mice (Fig 2).

3. Identification of growth factor induced in the low-dose preirradiated mice

In the low-dose pre-irradiated mice, one of the blood-producing proteins (G-CSF) was rapidly increased after high-dose radiation exposure (Fig 3). This protein is known as a growth factor which contributes to proliferation of primitive cells upstream of red blood cells.

In this study, we found a process to acquisition of whole-body radiation adaptive response; it is caused by the recovery of primitive bone marrow cells which is rapidly induced by the production of growth supporting protein (G-CSF), and finally, improvement of the number of red blood cells after high-dose radiation exposure plays an important role in avoiding lethal effect in mice.

Future Developments

To clarify the biological effect of low-dose ionizing radiation, the detailed mechanism of how G-CSF was rapidly induced in low-dose pre-irradiated mice should be investigated.

Main Researcher: Kensuke Otsuka, Ph. D.,
Research Scientist, Radiation Safety Research Center, Nuclear Technology Research Laboratory

Reference

K. Otsuka, 2006, “Whole-body radiation adaptive response in terms of the recovery of hematopoietic system”, CRIEPI Report L06 (in Japanese)

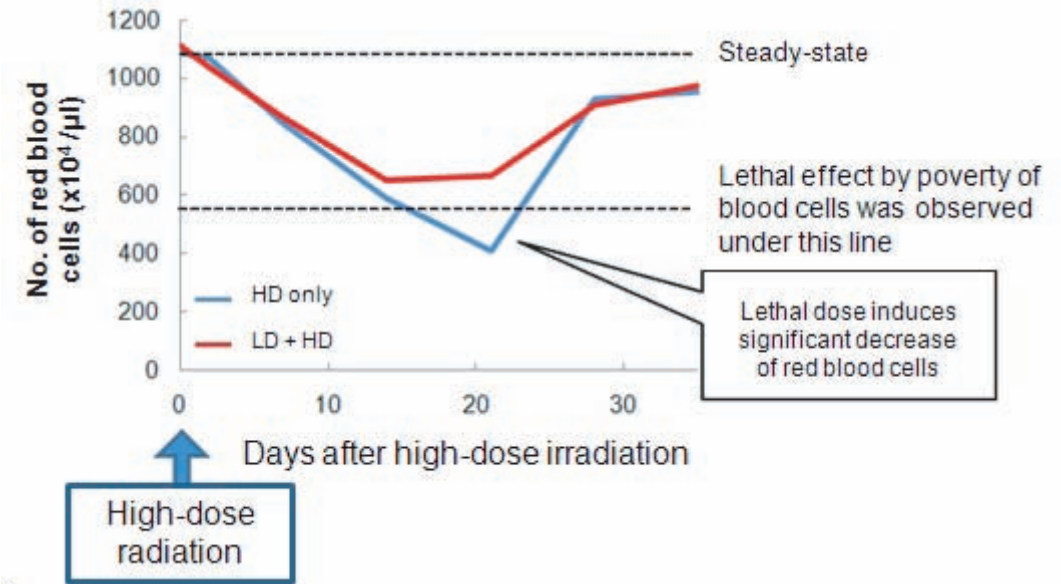

Fig.1 Low-dose pre-irradiation leads to suppression of decrease of red blood cells after high-dose radiation exposure. HD: high-dose irradiation, LD: low-dose irradiation.

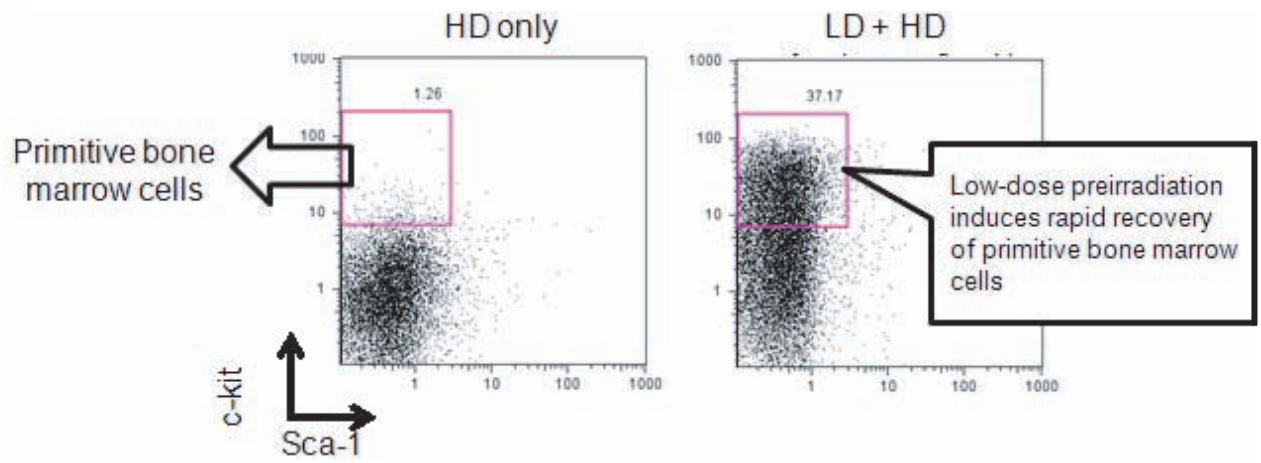

Fig.2 Low-dose pre-irradiation induces rapid recovery of primitive bone marrow cells. The figure dots denote cells which are able to discriminate each other by two primitive markers of protein (Sca-1, c-kit) and gated areas meaning primitive bone marrow cells. HD: high-dose irradiation, LD: low-dose irradiation.

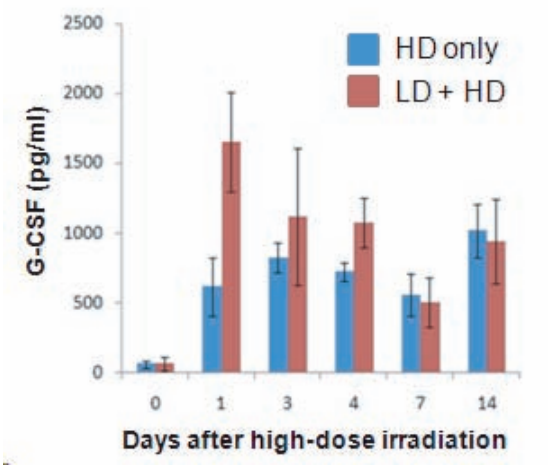

Fig.3 Growth factor G-CSF was more rapidly produced in low-dose pre-irradiated mice than in mice irradiated with high-dose radiation. HD: high-dose irradiation, LD: low-dose irradiation.