

Effect of Continuous Exposure to Gamma-Rays at Low Dose Rate on Murine Hematopoietic Stem Cell Lineage

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Abstract

The origin of radiation-induced leukemic stem cells (LSC) is still unknown and is often a source of controversy in many studies. Our previous report showed that LSCs in acute myeloid leukemia (AML), induced in mice exposed to low-dose-rate (LDR) γ -ray exposure for 400 days at a rate of 20 mGy/22h/day, are similar to common lymphoid progenitors, whereas, AMLs induced by acute radiation exposure at 1.0 Gy/min resemble common myeloid progenitors. To determine whether the radiation dose rate (i.e. high-dose-rate versus low-dose-rate) effect on the origins of radiation-induced leukemias is quantitative or qualitative, 8 week-old male B6C3F1 mice were exposed to a total accumulated dose of 8 Gy at LDRs. The components of the bone marrow from the humerus and femur of both irradiated and non-irradiated mice were analyzed at pre-determined intervals within the irradiation period (400 days). The population of hematopoietic stem cells in the bone marrow of irradiated mice showed no increase in number after 200 days of irradiation and was significantly decreased compared to non-irradiated mice after 400 days of irradiation. Both multi-potent and common lymphoid progenitors did not show any increase in number after 200 days of irradiation. An increase in the number of common myeloid progenitors was observed in both age-matched non-irradiated control mice and irradiated mice after 200 days of irradiation. Although a sharp decline in the number of common myeloid progenitors was seen after 300 days of irradiation, the numbers gradually returned to original levels 100 days after the radiation exposure was completed. These results indicate that continuous LDR γ -ray exposure affects the population of the lymphoid progenitors and stem cells, but not myeloid progenitors.

Table 1. Experiment schedule showing the number of male B6C3F1 mice examined at each time.

IR-day ^a (age)	non-IR	IR
Day 0 (8 weeks)	10	-
Day 100 (22 weeks)	9	10
Day 150 (29 weeks)	14	10
Day 200 (36 weeks)	4	10
Day 300 (50 weeks)	8	10
Day 400 (65 weeks)	5	11
^b Day 500 (79 weeks)	0	13
^c Day 600 (93 weeks)	0	3

^aDays from the start of exposure to γ -ray at dose rate of 20 mGy/day.

^b100 days after 400 days exposure.

^c200 days after 400 days exposure.

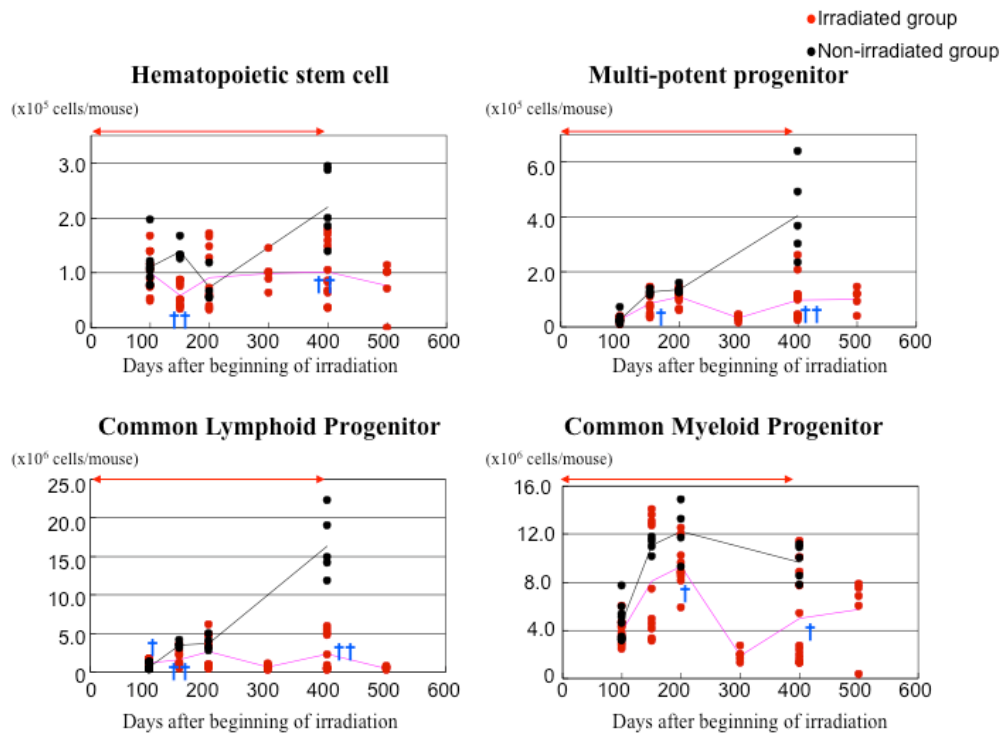


Fig. 1 Population of bone marrow cells, classified into four differentiation stages, collected from male B6C3F1 mice exposed to 20 mGy/22h/day γ -rays as compared to the non-irradiated controls.