Effects of Medium and High Dose-rate Irradiation Exposure on Hematopoietic Stem Cells in Ex Vivo Culture

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Abstract

The hematopoietic stem cell (HSC) niche microenvironment is essential for hematopoiesis. While it is known that irradiation causes hematopoietic damages, there are few reports on effects of irradiation on the HSC niches, particularly the effects of radiation at lower dose-rates. Chronic whole body radiation exposure at a low dose-rate (LDR) of 20 mGy/day in mice has been shown to increase the incidence of leukemia. Gene expression analyses of the irradiated HSCs demonstrated that apoptosis and DNA damage responses were rarely induced at LDR unlike that of high dose-rate exposure. Although the microenvironment in HSC niches are also exposed to radiation, very little is known about the changes induced in these niches. Since the microenvironment of HSC niches play an important roles in maintaining of HSCs, we studied the effects of LDR irradiation on HSC niches by comparing it with the effects found in those exposed middle dose-rate (MDR) and high dose-rate (HDR) irradiations, using an *ex vivo* experimental approaches. *Ex vivo* cultures of HSCs were isolated from C3H males aged 100 to 200 days, exposed to 359 mGy/22hours/day (chronic MDR) or 870 mGy/min (acute HDR) of gamma rays. Total doses of both chronic MDR and acute HDR irradiations were 1100, 2200, or 4600 mGy, and total culture periods of all experiments were 21 days. The solo HSC cultures without HSC niche-constructing cells showed higher radio-sensitivity both to chronic MDR and acute HDR exposures. The cell counts in acute MDR experiments were decreased at total doses of 2200 and 4600 mGy, and were equivalent to only 23% and 0.1% of those in non-irradiated control cells at day 21 respectively. On day 21 at acute HDR exposure, the cell counts at the total dose of 2.2 Gy were equivalent to 16% of the non-irradiated control cell counts, and at the total dose of 4600 mGy, cells were rarely found. These results suggest that HSCs isolated from HSC niches become more radiosensitive than those in HSC niches.

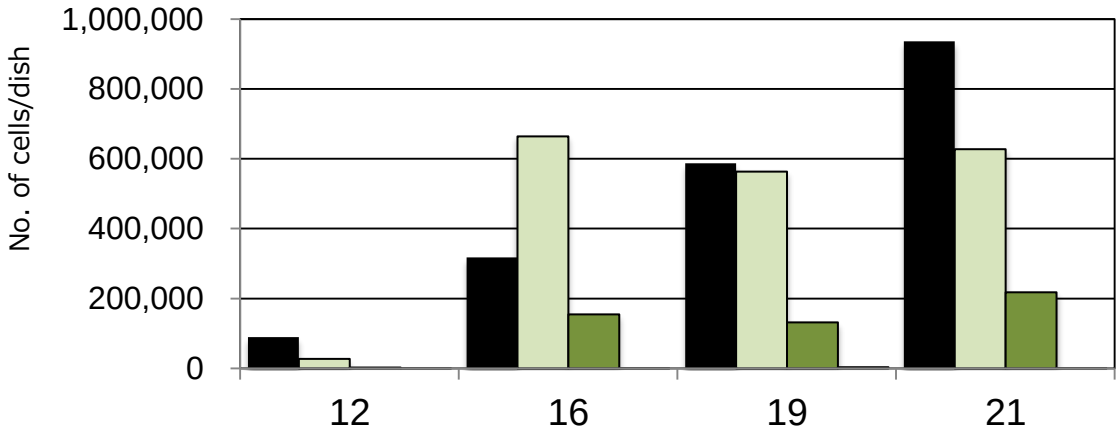

Fig. 1 Time-dependent changes in cell counts of *ex vivo*-cultured hematopoietic stem cells exposed to medium dose-rate gamma rays. Hematopoietic stem cells were irradiated to total doses of 1100 (■), 2200 (■) and 4600 mGy (■) (■) at a dose-rate of 359 mGy/22 hours/day, and then cultured for a total of 21 days after radiation exposure with corresponding non-irradiated control cells (■).

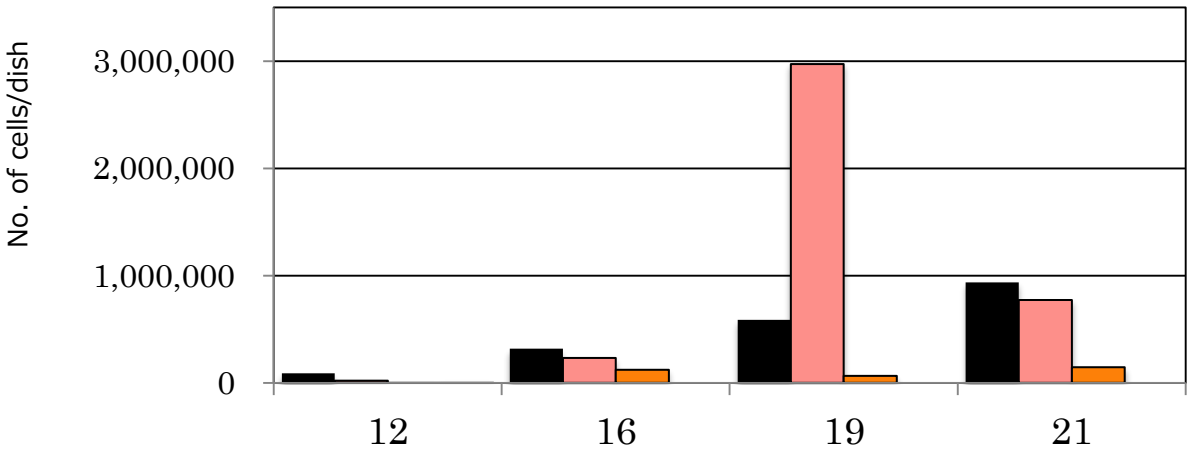

Fig. 2 Time-dependent changes in cell counts of ex vivo-cultured hematopoietic stem cells exposed to high-dose rate gamma rays. Hematopoietic stem cells were irradiated to total doses of 1100 (■), 2200 (■) and 4600 mGy (■) at a dose rate of 870 mGy/minute, and then cultured for a total of 21 days after radiation exposure with corresponding non-irradiated control cells (■).