

Analysis of Gene Expression Profiles of Hematopoietic Stem and Progenitor Cells Exposed to Continuous Low dose-rate Gamma-rays

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Abstract

We have previously shown that continuous exposure to low dose-rate (LDR) radiation is leukemogenic in mice. In this study, we investigated how LDR radiation changes cell numbers and gene expressions of immature hematopoietic cells, involving stem cells (HSCs) and three kinds of progenitor cells (HPCs). Mice irradiated with LDR (20mGy/day) γ -rays for 400 days were subjected to FACS and gene expression analysis, and the analysis results were compared with those of age-matched non-irradiated control mice. HSCs and HPCs in irradiated mice were decreased during and after the irradiation, but manners of the cell decreases showed different patterns. Although HSC decreases were the most prominent and prolonged, annotations of gene expression profiles of HSCs during and after the irradiation suggested that bio-functions associated with “cell survival” and “cell viability” were frequently promoted, and that “cell death”- and “apoptosis”-related bio-functions were suppressed. Annotation analyses of gene expression profiles of HPCs resulted similar trends. The similarities among HSCs and HPCs were more clearly found after 300-day irradiation, such that many transcription factors and biological networks predicted to be important for responding LDR radiation were identical among HSCs and HPCs at days 300 and 400. These results suggest unique LDR radiation-induced responses in immature hematopoietic cells.

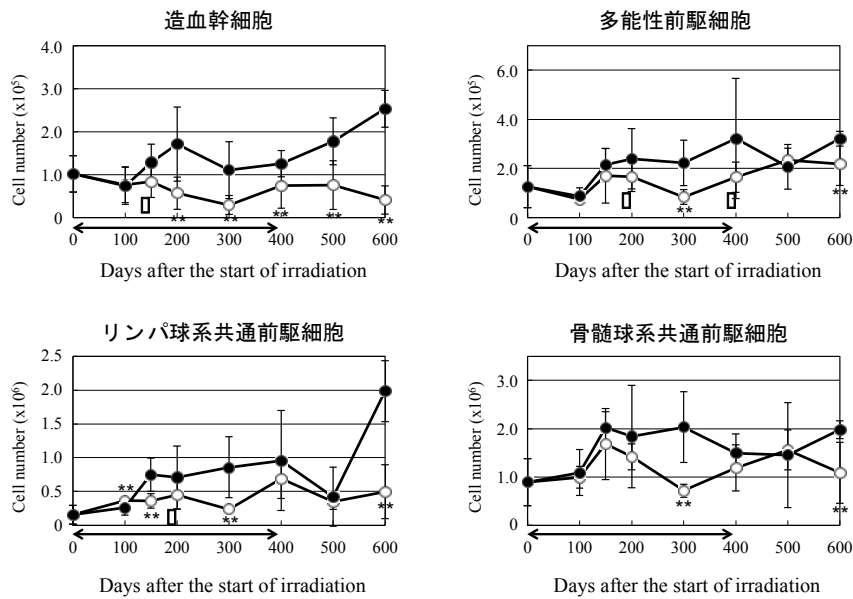


Fig. 1 Alterations in number of hematopoietic stem cells (HSCs) and three kinds of hematopoietic progenitor cells (HPCs) during and after irradiation of B6C3F1 male mice with γ -rays at a dose rate of 20 mGy/day for 400 days from 8 weeks of age. Bone marrow cells were obtained at a 100-day interval, and hematopoietic stem cells (A), multi-potent progenitor cells (B), common lymphoid progenitor cells (C) and common myeloid progenitor cells (D) were counted. Closed and open circles indicate values of non-irradiated mice and irradiated mice, respectively. Bars represent standard deviation. (*:p<0.05, **:p<0.01, *t* test)

Table 1 A part of the analysis of the gene expression profiles of hematopoietic stem cells (HSCs) in B6C3F1 male mice exposed to γ -rays at a dose rate of 20 mGy /day for 200 days from 8 weeks of age. Only cell death- or survival-related bio-functions are listed here. The activation z-scores of the bio-functions were calculated from expression profiles of top 1%, 2%, 4%, 8% or 10% of the total analyzed genes; positive z-scores predict promotion; negative z-scores predict suppression.

Diseases and Bio Functions	1%	2%	4%	8%	10%
cell survival	3.4	4.3	5.4	6.4	6.4
cell viability	3.2	4.3	5.5	6.2	6.3
organismal death			-9.7	-11.4	-1.6
apoptosis	-2.4	-1.8	-4.6	-4.0	-3.8
cell death	-2.4	-2.2	-3.7	-3.1	-3.1
necrosis	-2.8	-2.3	-3.2	-1.7	-1.4
apoptosis of leukemia cell lines	-2.9	-2.4	-0.3	-0.9	
cell death of leukemia cell lines		-2.6	-2.7	-0.5	-0.3
apoptosis of lymphoid organ				1.9	2.2
cell death of T lymphocytes				1.7	2.3
cell death of granule cells			2.6		
activation-induced cell death of T lymphocytes					2.4