

Analysis of Gene Expression Profiles of Hematopoietic Stem Cell of Mice 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, and that hematopoietic stem cells (HSCs) in mice irradiated with LDR γ -rays (20mGy/day) were significantly decreased at day 400 of irradiation when compared with age-matched non-irradiated mice. In this study, we investigated the changes in gene expressions that may be related to the observed decrease in HSCs of mice exposed to LDR radiation. RNA extracted from HSCs of irradiated and non-irradiated mice was subjected to gene expression microarray, and the gene expression profiles were analyzed by bioinformatic methods with the Ingenuity Pathway Analysis software. We observed that less than 1% of the total analyzed genes were differently expressed in HSCs in LDR-irradiated versus non-irradiated mice. The pathway analysis suggested a possibility that bio-functions of “cell viability”, “cell survival”, and “maturation of cells” were promoted in irradiated HSCs. Surprisingly, contrary to high-dose-rate-irradiated HSCs, no bio-function associated with cell death, such as apoptosis, was altered in LDR-irradiated HSCs. These findings suggest that the decreases in HSCs observed in LDR-irradiated mice might be a result of cell differentiation.

Table 1 Bio-functions predicted to be altered in irradiated hematopoietic stem cells

Irradiation period (days)	Category	Diseases/Functions	Predictions of activation state
200	Cell Death and Survival	cell viability	activated (significant)
		cell viability of tumor cell lines	activated (significant)
		cell survival	activated (significant)
		cell viability of cervical cancer cell lines	activated (significant)
		cell death of connective tissue cells	inactivated
		apoptosis of bone cancer cell lines	inactivated
		cell death of fibroblast cell lines	inactivated
		cell death of kidney cell lines	inactivated
		cell death of bone cancer cell lines	inactivated
		apoptosis	inactivated
	cell death	inactivated (significant)	
	necrosis	inactivated (significant)	
	cell death of tumor cell lines	inactivated (significant)	
	apoptosis of tumor cell lines	inactivated (significant)	
	Cellular Growth and Proliferation	proliferation of tumor cell lines	activated (significant)
		proliferation of cells	activated (significant)
	Cellular Development	proliferation of endothelial cell lines	activated (significant)
		proliferation of tumor cell lines	activated (significant)
	Cellular Function and Maintenance	proliferation of endothelial cell lines	activated (significant)
		endocytosis	activated (significant)
Hematological System Development and Function	Clathrin mediated endocytosis	activated (significant)	
	quantity of blood platelets	inactivated	
Tissue Morphology	quantity of blood platelets	inactivated	
Hematopoiesis	differentiation of bone marrow cells	inactivated	
	cell movement of antigen presenting cells	inactivated	
Hematological System Development and Function	quantity of blood cells	inactivated	
	quantity of leukocytes	inactivated	
Cellular Development	proliferation of melanoma cell lines	activated	
	proliferation of tumor cell lines	inactivated	
	proliferation of breast cancer cell lines	inactivated	
Cellular Growth and Proliferation	proliferation of melanoma cell lines	activated	
	proliferation of tumor cell lines	inactivated	
	proliferation of breast cancer cell lines	inactivated	
Tissue Morphology	quantity of blood cells	inactivated	
	quantity of leukocytes	inactivated	
Cell Death and Survival	necrosis	activated	
	cell viability of breast cancer cell lines	inactivated	
Organismal Injury and Abnormalities	bleeding of tissue	activated	
Metabolic Disease	glucose metabolism disorder	activated	
400	Hematological System Development and Function	aggregation of blood cells	activated
		quantity of red blood cells	activated
		hematocrit	activated
		bleeding time	inactivated (significant)
	Cancer	quantity of tumor	activated (significant)
		metastasis of lung	activated
	Cell Death and Survival	apoptosis of breast cancer cell lines	activated (significant)
		apoptosis of tumor cell lines	activated
	Tissue Morphology	permeability of blood vessel	activated
	Tissue Morphology	quantity of red blood cells	activated
	Cellular Development	differentiation of tumor cell lines	inactivated (significant)
	Cardiovascular System Development and Function	permeability of blood vessel	activated
Tissue Development	aggregation of blood cells	activated	
Hematopoiesis	quantity of red blood cells	activated	
500	Cellular Growth and Proliferation	proliferation of connective tissue cells	activated (significant)
		proliferation of fibroblasts	activated (significant)
		proliferation of cancer cells	activated
	Cellular Development	proliferation of tumor cells	activated
		proliferation of fibroblasts	activated (significant)
		proliferation of cancer cells	activated
Tissue Morphology	proliferation of tumor cells	activated	
	quantity of cells	activated	
Cell Cycle	senescence of tumor cell lines	inactivated	
	G1 phase	inactivated	
Cancer	cell transformation	activated	
	morphology of leukocytes	inactivated	
Cell Morphology	morphology of blood cells	inactivated	
	morphology of cells	inactivated	
Cell-mediated Immune Response	differentiation of thymocytes	activated	