

Analyzing Effects of Low Dose-Rate Radiation on Endothelial Cells Regulating Hematopoietic Stem Cell Maintenance

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Abstract

Hematopoietic stem cells (HSCs) are surrounded by blood vessels in the bone marrow. Endothelial cells in arteries and sinusoids play an important role in regulating HSC behaviors. Sinusoidal endothelial cells (SECs) anchor HSCs in vascular niches, and arterial endothelial cells (AECs) secrete stem cell factors (SCFs) and Cxcl12 that promote self-renewal of HSCs. These endothelial cells were sensitive to a lethal dose of high dose-rate radiation, resulting in rupture and hemorrhage. The sensitivity of SECs and AECs to low dose-rate (LDR) radiation is unknown. Previously, we showed that ex vivo HSCs isolated from the bone marrow were highly sensitive to 20 mGy/day of LDR radiation as compared to in vivo HSCs irradiated in the bone marrow. Results suggest that the microenvironment surrounding HSCs, such as the SECs and AECs may attenuate the antiproliferative effects of LDR radiation on HSCs. Since the sensitivity of AECs and SECs and their response to LDR radiation has not been investigated, the object of this study is to clarify roles of AECs and SECs on maintenance of HSCs during and after irradiation, as well as the possible contribution of the irradiated AECs and SECs towards the transformation of HSCs into leukemic stem cells.

Table 1. List of monoclonal fluorescent antibodies used for flow cytometry

Cell surface antigen	Clone name	AEC	SEC	Endothelial vascular stem cell
Sca-1	D7	++	+	
CD45	30-F11	-	-	-
TER119	TER119	-	-	-
CD31	MEC13.3, 390	+	+	+
CD54(ICAM1)	YN1/1.7.4	-	+	
PDPN (podoplanin)	8.1.1	-	+	
CD157	BP-3			+