

Microsatellite Instability in Malignant Lymphomas Developed from Mice Continuously Exposed to Low-Dose-Rate Gamma-Rays

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Abstract

We previously found that the life-shortening in B6C3F1 mice continuously irradiated at a low-dose-rate (LDR: 20 mGy/22h/day) accumulating to a high dose of 8000 mGy for about 400 days was due to earlier death from a variety of neoplasms including malignant lymphomas (MLs). Clustering analysis of gene expression data was performed using the 44k format of whole mouse genome array (Agilent), which suggested that MLs from irradiated and non-irradiated mice could be classified into two types (named A MLs and non-A MLs). In the present study, we investigated microsatellite instability (MSI) of 35 MLs from 19 irradiated and 16 non-irradiated mice. MSI was assessed using five selected suitable markers (D7Mit123, mBat-37, A27, Cyp1a2, and D7Mit17), and classified into three statuses as MSS (microsatellites stable, 0 markers unstable; n=7), MSI-L (microsatellites instable-low, 1 or 2 markers unstable; n=19), and MSI-H (microsatellites instable-high, 3 or more markers unstable; n=9). As a result, MSI-H MLs were found in 31.6% of the irradiated group and 18.8% of the non-irradiated group (p=0.62). In contrast, MSI-H MLs were found in 40.0% of A MLs and in 20.0% of non-A MLs (P=0.052). No MSS MLs were found in A MLs. These results suggest that DNA repair activities such as DNA mismatch repair might be reduced more in A MLs.

Table 1 Microsatellite instability (MSI) status in mice malignant lymphomas (MLs). A) Low-dose-rate (LDR) γ -ray irradiated group and non-irradiated group. B) A MLs and non-A MLs.

A) MLs from LDR γ -ray irradiated group and non-irradiated group

	Total	Number of MLs(%)		
		MSI-H	MSI-L	MSS
irradiated	19	6(31.6)	9(47.4)	4(21.1)
non-irradiated	16	3(18.8)	10(62.5)	3(18.8)

B) A MLs and non-A MLs

	Total	cases(%)		
		MSI-H	MSI-L	MSS
group A	10	4(40.0)	6(60.0)	0(0.0)
non group A	25	5(20.0)	13(52.0)	7(28.0)

MSI-H: microsatellite instable-high, ≥ 3 markers unstable; MSI-L: microsatellite instable-low, 1 or 2 markers unstable; MSS: microsatellite stable, 0 markers unstable. Numbers in parentheses show percentage in each MSI status.