

Transgenerational Effects in the Progeny of Mice Exposed to Acute High
and Chronic Low Dose-rate Gamma-rays
– Germ Cell Mutation Analyses–

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Abstract

Transgenerational effects of low dose-rate (LDR) radiation have not been well studied. We have estimated the incidence of copy number variations (CNVs) in the progeny born from 65 week-old male C57BL/6J mice after continuous exposure to gamma-rays at several LDRs (0.05, 1 or 20 mGy/day for 400 days to total doses of 20, 4000 or 8000 mGy, or 20 mGy/day for 150 days to a total dose of 3000 mGy) or from 18 week-old male C57BL/6J mice after exposure to a high dose-rate (HDR) of 770 mGy/min (total dose 3 Gy). This year, using array CGH to screen for CNVs, we analyzed the progeny born from male mice after exposure to a LDR of 20 mGy/day (total dose 3000 mGy) and the progeny born from male mice after exposure to a LDR of 1 mGy/day (total dose 400 mGy). To identify “real new mutations,” we tested all candidate CNVs found using quantitative PCR and estimated that the frequencies of F1 mice containing CNVs in these groups are 30.0% and 11.0%. So far, we observed a statistically significant increase in the frequency of F1 mice with CNVs born from male mice exposed to 20 mGy/day LDR radiation for 400 days (total dose 8000 mGy).

Table 1 The numbers of the (candidate) CNVs detected by array CGH and confirmed by qPCR

Number of positive probes in 1st screening	Number of positive probes in 2nd screening	Non-irradiated		20 mGy/day (8000 mGy)		20 mGy/day (3000 mGy)		1 mGy/day (400 mGy)	
		Detected by CGH	Confirmed by qPCR	Detected by CGH	Confirmed by qPCR	Detected by CGH	Confirmed by qPCR	Detected by CGH	Confirmed by qPCR
≥ 2 (Type L)		9	9 [1]	23	23 [1]	5	5	6	6 [1]
	≥ 5	1	1 [1]	5	5	2	2	0	0
1 (Type S)	4	1	0	2	1	0	0	1	1
	3	3	1 [1]	2	1	1	1	4	2
	2	21	3	3	2	10	0	14	9 [1]
	(Total)	26	5 [2]	12	9	13	3	25	15 [1]
	(Type L + S)	35	14 [3]	35	32 [1]	18	8	6	3 [1]
	(No. of mice analyzed)	156		142		20		100	

The numbers in brackets indicate those of duplications (internal numbers).

There were 1, 3, 1 and 4 mice with two CNVs in individual groups. They are included in both Tables 1 and 2.

There were 2, 4, 1, and 0 mice with 4 or more CNVs in individual groups. They are excluded from Table 1 but included in Table 2.

Table 2 The numbers of F1 mice with CNVs

		No. of mice analyzed	No. of mice with CNV(s) (%)		
			Type L	Type S	Type L+S
Non- irradiated	Female	81	5 (6.2)	5 (6.2) [2]	10 (12.3) [2]
	Male	75	4 (5.3) [1]	2 (2.7)	6 (8.0) [1]
	Total	156	9 (5.8) [1]	7 (4.5) [2]	16 (10.3) [3]
20 mGy/day (8000 mGy)	Female	67	9 (13.4) [1]	7 (10.4)	16 (23.9)* [1]
	Male	75	13 (17.3)	5 (6.7)	16 (21.3)*
	Total	142	22 (15.5)** [1]	12 (8.5)	32 (22.5)** [1]
20 mGy/ day (3000 mGy)	Female	11	3 (27.3)	2 (18.2)	4 (36.4)
	Male	9	1 (11.1)	1 (11.1)	2 (22.2)
	Total	20	4 (20.0)	3 (15.0)	6 (30.0)
1 mGy/ day (400 mGy)	Female	43	2 (4.7)	4 (9.3) [2]	6 (14.0) [2]
	Male	57	4 (7.0) [1]	1 (1.8)	5 (8.8) [1]
	Total	100	6 (6.0) [1]	5 (5.0) [2]	11 (11.0) [3]
0.05 mGy/ day (20 mGy)	Female	21	1 (4.8)	0 (0.0)	1 (4.8)
	Male	25	0 (0.0)	1 (4.0)	1 (4.0)
	Total	46	1 (2.2)	1 (2.2)	2 (4.3)
770 mGy/min (3000 mGy)	Female	28	2 (7.1)	0 (0.0)	2 (7.1)
	Male	31	3 (9.7)	2 (6.5)	5 (16.1)
	Total	59	5 (8.5)	2 (3.4)	7 (11.9)
770 mGy/min (3000 mGy)	Female	25	1 (4.0)	1 (4.0)	2 (8.0)
	Male	19	0 (0.0)	1 (5.3) [1]	1 (5.3) [1]
	Total	44	1 (2.3)	2 (4.5) [1]	3 (6.8) [1]

The numbers in brackets indicate those of mice with duplications (internal numbers). *P<0.05, **P<0.01