

## Effects of *In Utero* Low Dose-rate Gamma-ray Exposure in B6C3F1 Mice

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### Abstract

For the second year of study, pregnant mice were irradiated with gamma-rays at medium dose-rates (MDRs) of 200 or 400 mGy/day for the entire gestation period (18 days, total doses: 3600 or 7200 mGy, respectively), or at a high dose-rate of 770 mGy/min at 11 days post-coitus (period of organogenesis, total dose: 2000 mGy). All fetuses from the irradiated groups had significantly smaller body sizes, and the extent of reduction in body size increased as the dose rate increased. Ossification was significantly retarded in the 400 mGy/day and 770 mGy/min irradiation groups (Table 1). Embryonic gonadal cells in gestation day (GD) 15 fetuses exposed to 200 and 400 mGy/day from GD 6 to 15 were stained with DDX4/MVH (protein expressed in germ cells) and counted. Results show a significant decrease in the number of DDX4/MVH positive cells in both males and females (Table 2). These results suggest that radiation exposure at MDRs from GD 6 to 15 strongly inhibits either one or all of the processes (differentiation of primordial germ cells, migration to the reproductive tract or proliferation in the gonads) in the developing fetuses. Previous work also found similar findings in the gonads of irradiated fetuses at 10 weeks of age. To investigate the long-term effects, mice born after in utero exposure are currently being studied with corresponding non-irradiated control mice.

Table 1 Ossification in B6C3F1 fetuses on gestation day 18.

	Non-irradiated (0 mGy) <sup>a</sup> n = 47 n (%)	20 mGy/day (360 mGy) <sup>a</sup> n = 37 n (%)	200 mGy/day (3600 mGy) <sup>a</sup> n = 46 n (%)	400 mGy/day (7200 mGy) <sup>a</sup> n = 31 n (%)	770 mGy/min (2000 mGy) <sup>a</sup> n = 36 n (%)		
Metacarpal							
8	47 (100)	37 (100)	46 (100)	19 (61)	**	19 (52)	**
<8	0	0	0	11 (36)	**	17 (47)	**
Absent	0	0	0	1 (3.2)		0	
Metatarsal							
10	46 (98)	35 (95)	42 (91)	12 (39)	**	19 (53)	**
<10	1 (2)	2 (5)	4 (9)	15 (48)		12 (33)	
Absent	0	0	0	4 (13)	*	2 (6)	
Tarsal							
10	7 (15)	1 (3)	1 (2)	0	*	2 (6)	
8	37 (79)	35 (95)	38 (83)	3 (10)	**	2 (6)	**
<8	2 (4)	1 (3)	1 (2)	2 (7)		16 (44)	**
Absent	1 (2)	0	6 (13)	26 (84)	**	16 (44)	**
Calcaneus							
2	30 (64)	29 (78)	18 (39)	0	*	3 (8)	**
1	3 (6)	0	0	0		0	
Absent	14 (30)	8 (22)	28 (61)	31 (100)	**	33 (92)	**
Sternebrae							
6	47 (100)	36 (97)	46 (100)	23 (74)	**	33 (92)	**
<6	0	1 (3)	0	5 (16)	**	2 (6)	
Absent	0	0	0	3 (10)		1 (3)	
Coccygeal Vertebrae							
13	0	1 (3)	0	0		0	
11	1 (2)	1 (3)	1 (2)	0		0	
10	2 (4)	0	0	0		1 (3)	
9	6 (13)	4 (11)	3 (7)	0		2 (6)	
8	18 (39)	18 (49)	10 (22)	0	**	0	**
<8	20 (43)	13 (35)	32 (70)	31 (100)	**	33 (92)	**
Absent	0	0	0	0		0	

<sup>a</sup> Total dose

\*, P<0.05, \*\*: P<0.01 vs. Non-irradiated

Table 2 No. of DDX4/MVH positive cells per 0.004 mm<sup>2</sup> in B6C3F1 fetal gonads on gestation day 15.

	Non-irradiated (0 mGy) <sup>a</sup>	200 mGy/day (3600 mGy) <sup>a</sup>	400 mGy/day (7200 mGy) <sup>a</sup>		
Male	8.8±2.9 (n=20)	0.3±0.2 (n=8)	**	0.003±0.009 (n=13)	**‡
Female	14.4±3.4 (n=12)	1.2±1.0 (n=10)	**	0.02±0.04 (n=12)	**‡

<sup>a</sup> Total dose

\*\*‡; P<0.01 vs. Non-irradiated, ‡; P<0.01 vs. 200mGy/day