Radiation Effects on Regulation of Gene Expression

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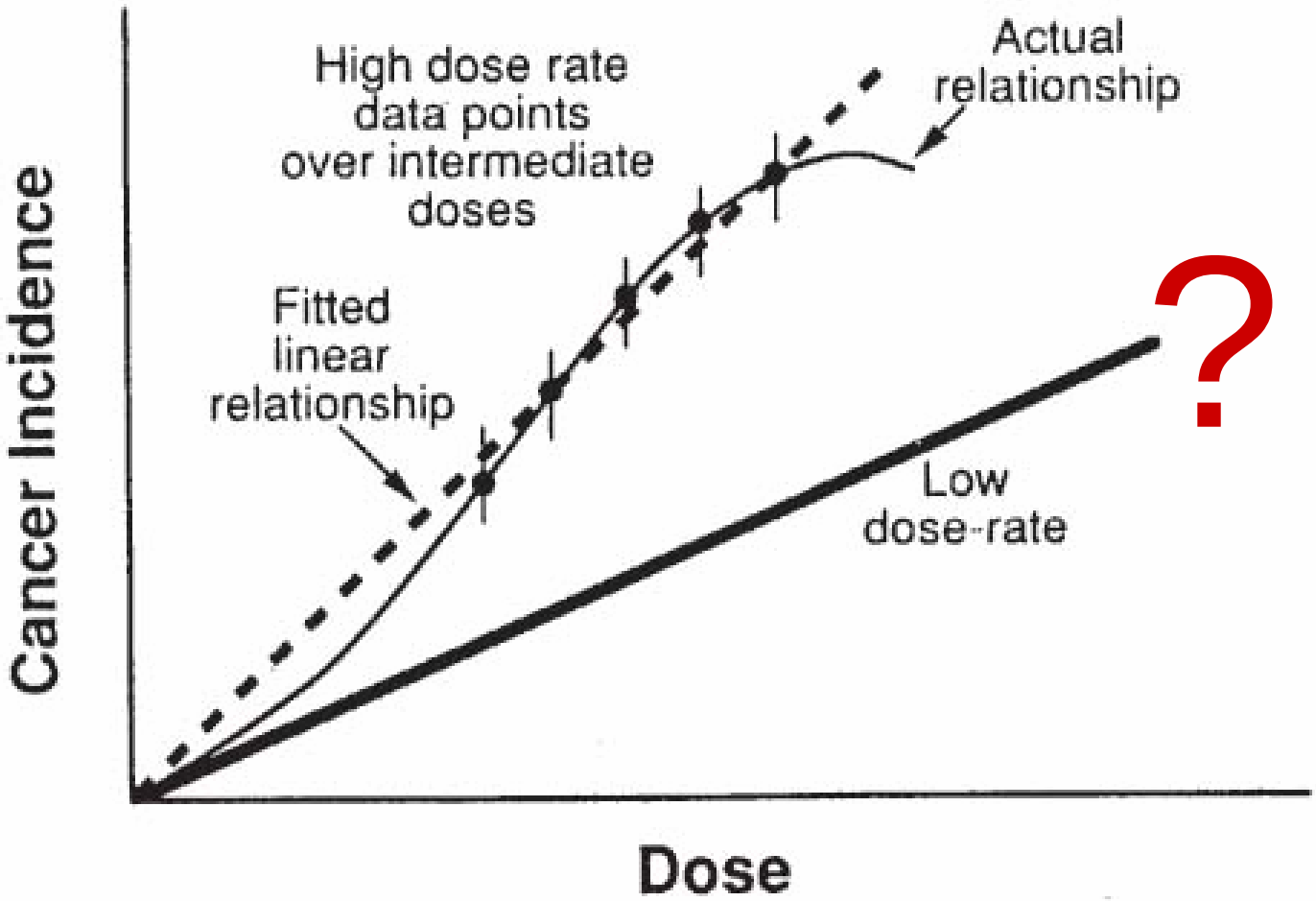
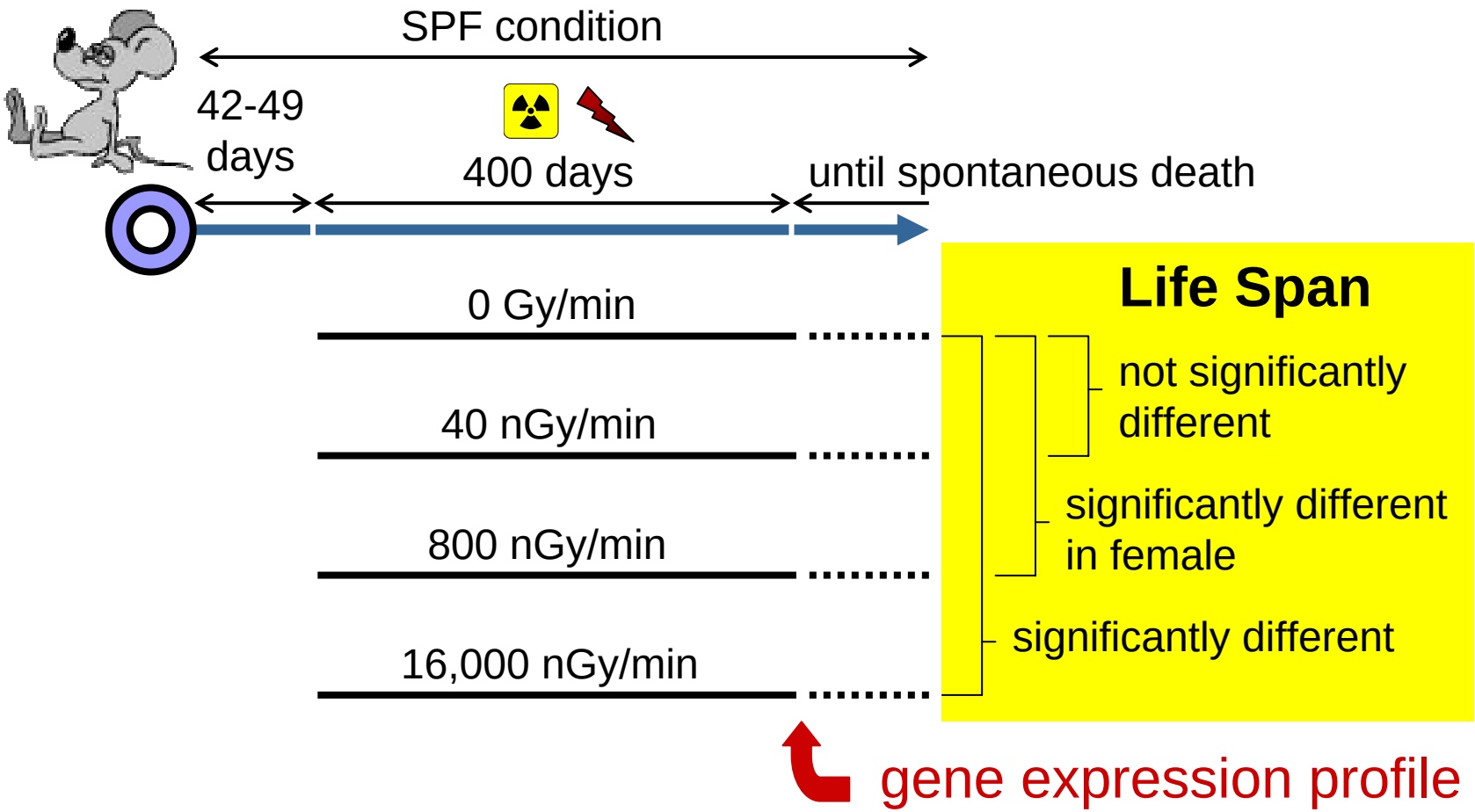
Risk of Radiation-Induced Cancers

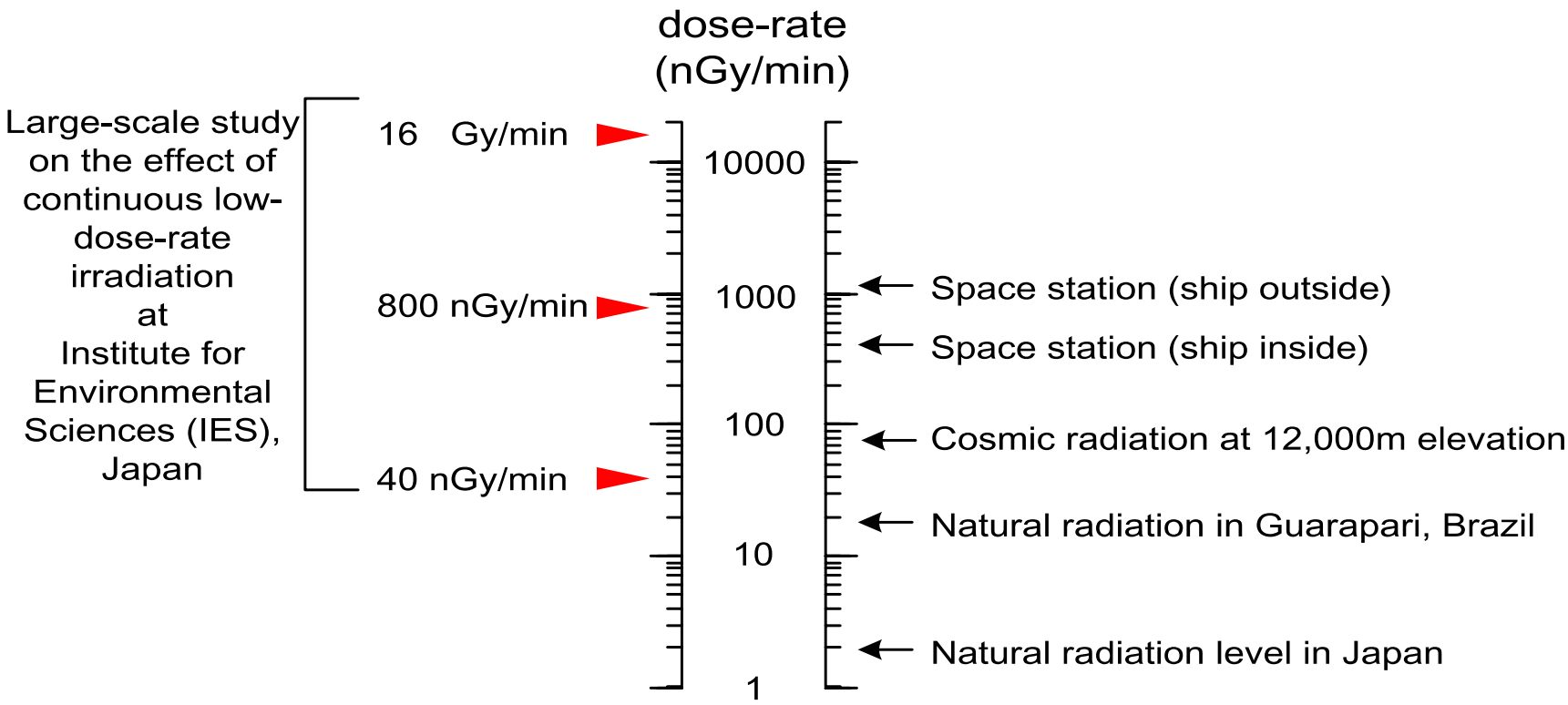


From Hall,E.J., Radiobiology for the Radiologist. J.B. Lippincott Company

Experiment of continuous low-dose-rate irradiation at IES



Dose-rate range used in the study at IES

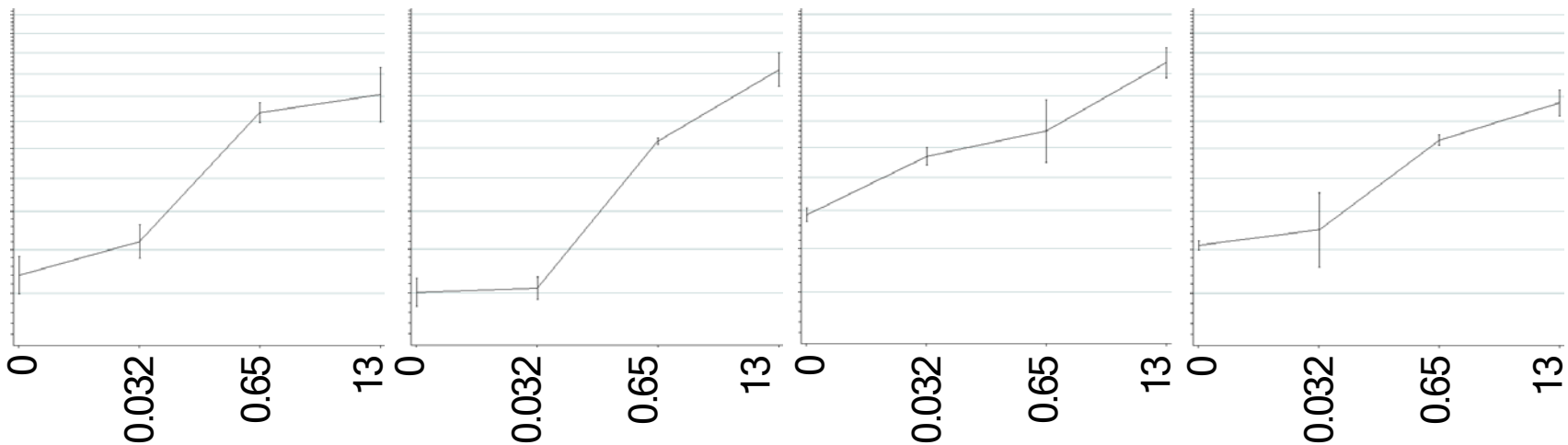


Number of genes whose expression levels were changed more than 1.6-fold by irradiation

dose-rate (nGy/min)	up-regulated	down-regulated	total
32	1	5	6
650	18	3	21
13,000	16	11	27
32 & 650	1	0	1
650 & 13,000	3	1	4
13,000 & 32	0	0	0

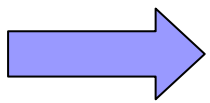
Functional analysis of deregulated genes

- Four genes whose expression was enhanced after irradiation at 650 nGy/min and 13,000 nGy/min were involved in mitochondrial oxidative phosphorylation pathway.



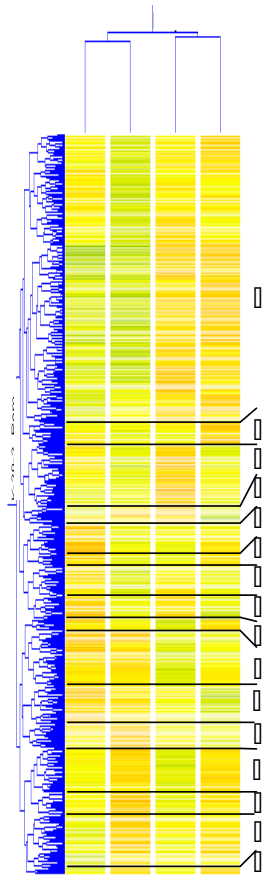
Genes whose expression levels were significantly varied by irradiation

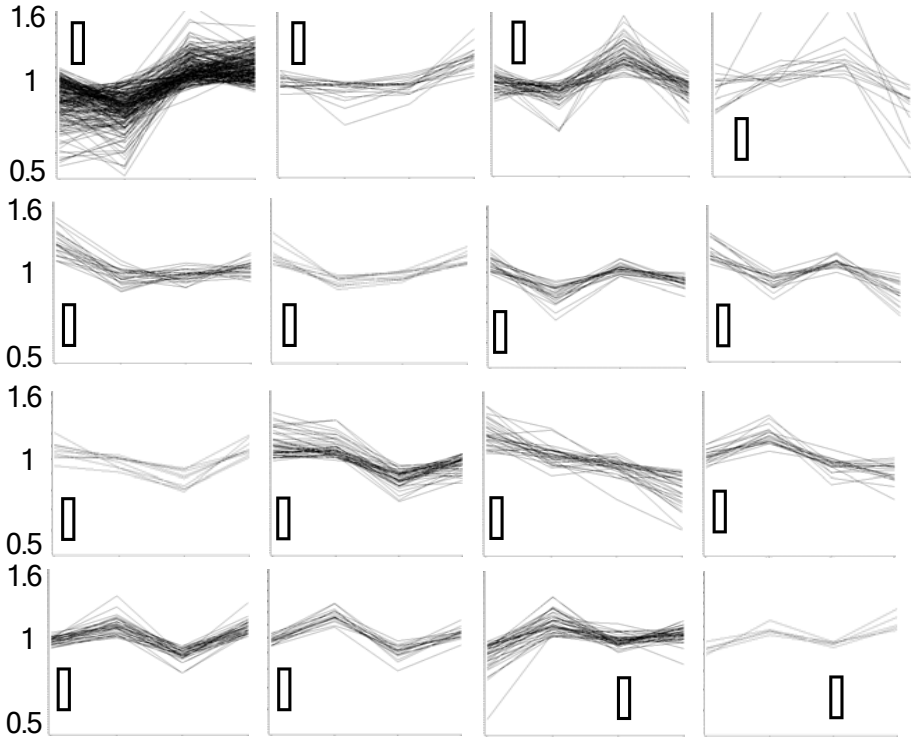
- Welch's ANOVA
  - $p<0.05$
  - MTC: None



621 genes

Clustering analysis of selected genes





GO category containing similar gene list to the clusters

	GO category	Overlapped gene number	p value
□	cytoplasm	78	2.8E-07
	mitochondrion	22	5.7E-04
	mitochondrion organization and biogenesis	24	0.0013
	energy pathways	24	0.0055
	organelle organization and biogenesis	37	0.0071
	cell organization and biogenesis	37	0.0071
	cytoplasm organization and biogenesis	37	0.0071
	transferase	48	0.031
□	cell organization and biogenesis	17	1.4E-05
	cytoplasm organization and biogenesis	17	1.4E-05
	organelle organization and biogenesis	17	1.4E-05
	cytoplasm	22	0.0016
	mitochondrion	9	0.0061
	nucleosome	4	0.012
	mitochondrion organization and biogenesis	9	0.032
	GO SLIMS Cellular Component	39	0.040

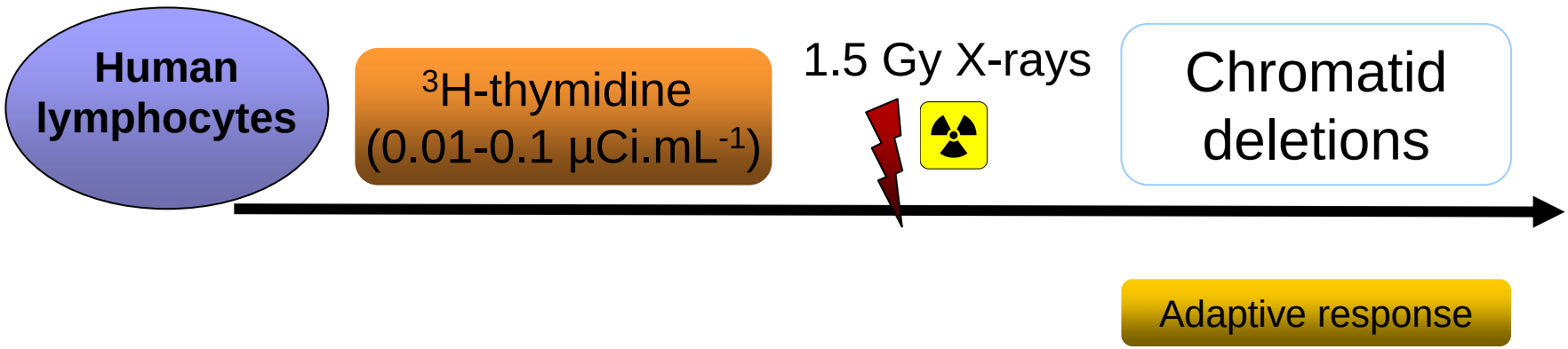
Conclusion1

- Mitochondrial oxidative phosphorylation was suggested to be elevated after irradiation at 650 nGy/min and 13,000 nGy/min.
- Mice irradiated with low dose-rate radiation in this range may suffer oxidative stresses caused by elevated mitochondrial respiratory activity. This oxidative stress may be one of the factors that cause life spans-shortening of irradiated mice.
- Multiple genes were found whose expression was changed more than 1.6-fold after 32 nGy/min, but their biological significances are unclear.

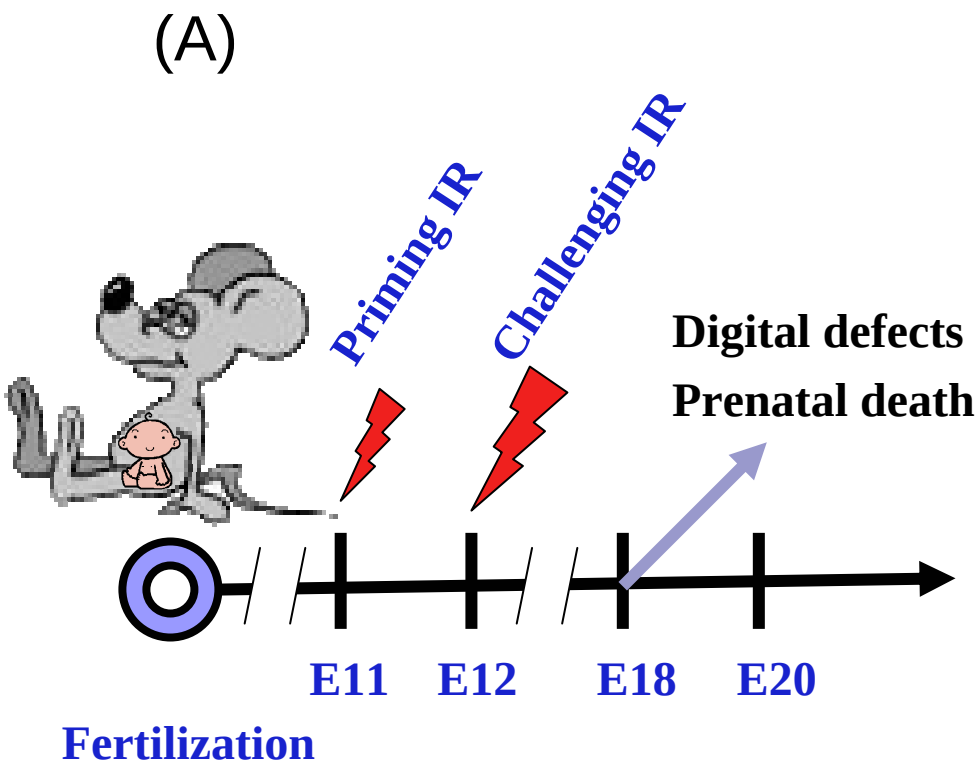
Radioadaptive response

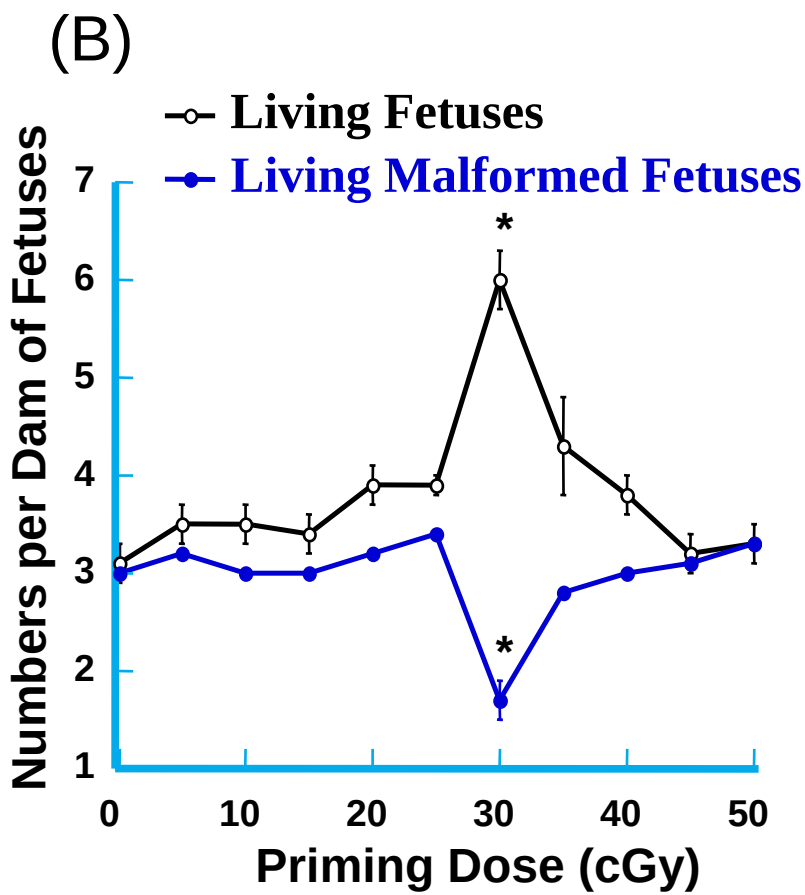
When cells are exposed to a priming low-dose or low dose-rate of radiation, they show a reduced biological response to a challenging high dose of radiation.

Olivieri *et al.*, 1984

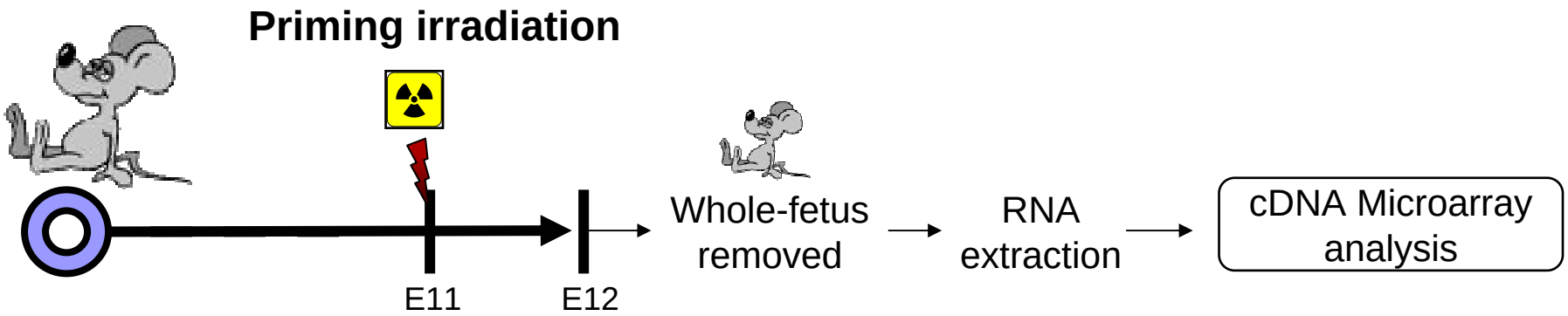


Radioadaptive response in mice during late embryogenesis





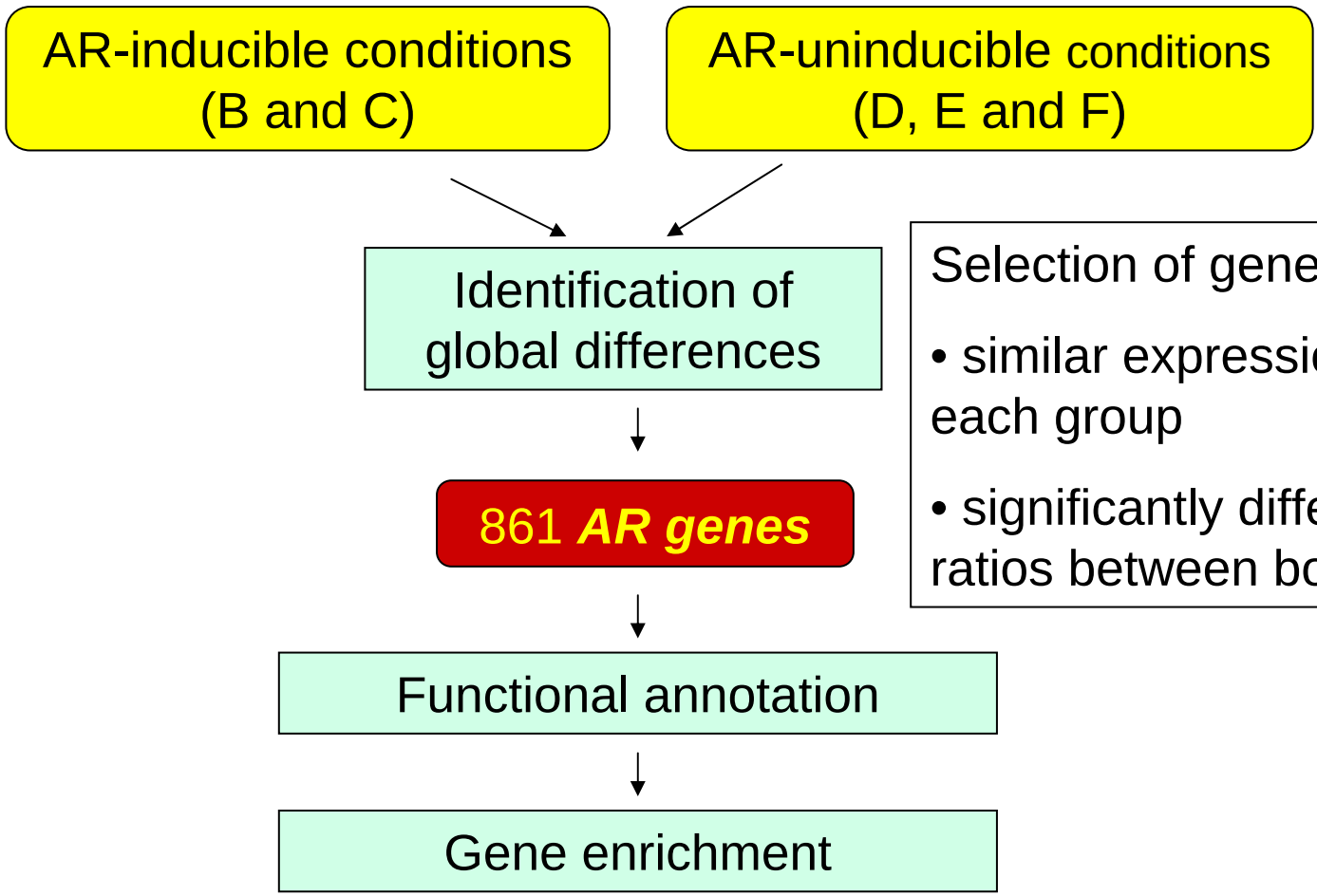
Experimental model



Priming irradiation parameters:

	Dose Rate (Gy/min)	DOSE (Gy)	Description
A	0	0	Control
B	0.34	0.3	Effective dose-rate (DR)
C	4.2	0.3	
D	2.5	0.3	Non-effective DR
E	0.34	0.5	Non-effective dose
F	0.34	1	

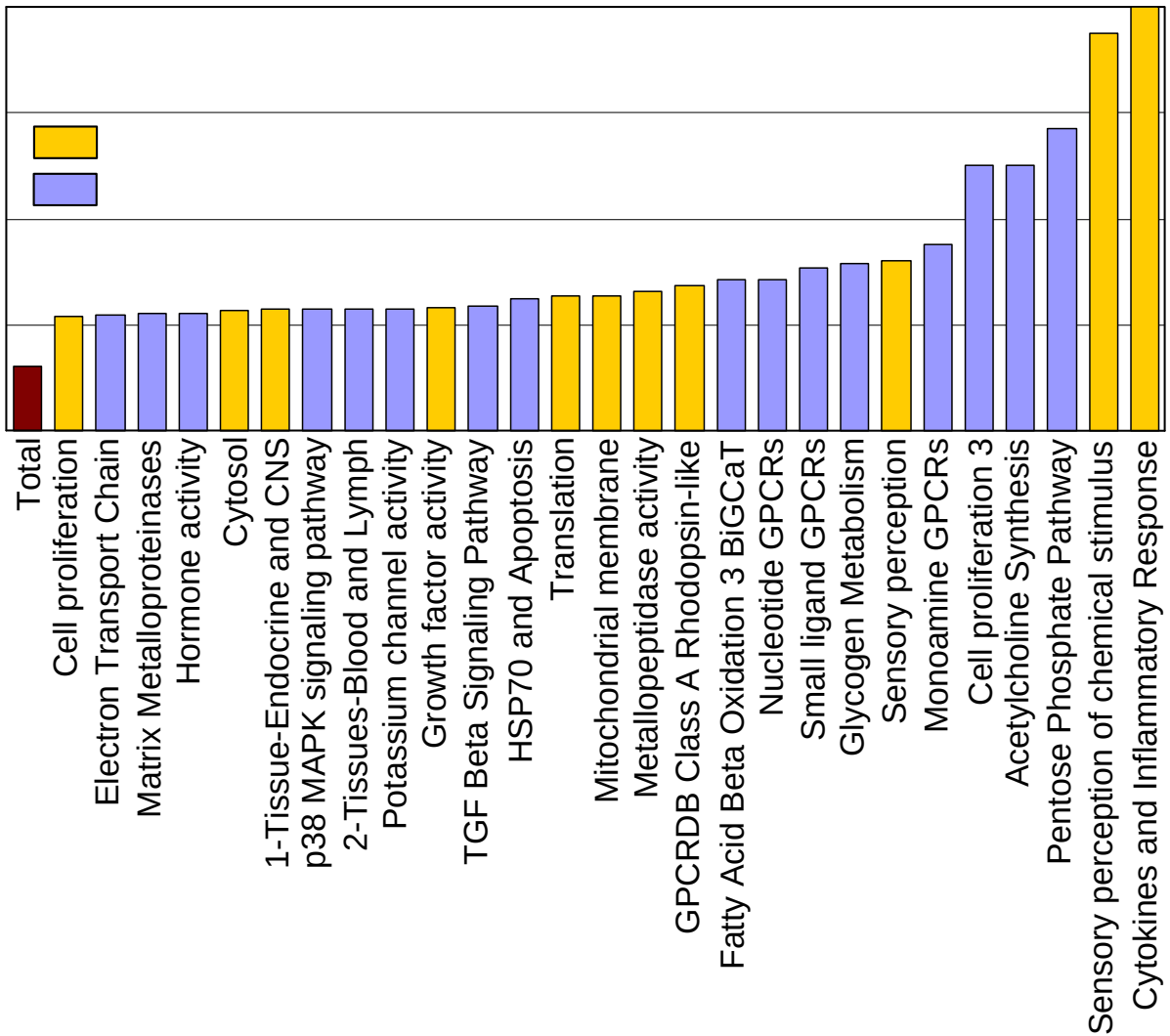
AR genes



Selection of genes with:

- similar expression ratios inside each group
- significantly different modulation ratios between both groups

Functional annotation and gene enrichment analysis



Conclusion2

- Intracellular and intercellular signaling activities are suggested to be important bases for radioadaptive response in mouse fetuses during late organogenesis.

- The present cDNA microarray analysis failed to show evidences for involvement of DNA damage repair genes in the radioadaptive response.

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