SIP27, CCNG1/cyclin G1, EI24/PIG8, POLK, and BAX, at 1 to 10 cGy/h exposure: CDKN1A/p21 and CCNG1/cyclin G1, were significantly increased at more than 1 cGy/h, whereas MDM2 and BAX showed increase at more than 10 cGy/h exposure. Taken together, the data suggested that cells show differential response to the different doses of radiation and involve more than one pathway. (This work was supported by Aomori Prefecture, Japan.)

9 Modulation of nitric oxide-mediated bystander effects by chronic irradiation with gamma-rays

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There has been a recent upsurge of interest in radiation-induced bystander effects. Previously we reported that the accumulation inducible nitric oxide synthase (iNOS) was induced only in human glioblastoma mutant (m) *p53* cells by acute irradiation with X-rays. In the present study, we found that the accumulation of iNOS in wt*p53* cells was induced by chronic irradiation with gamma-rays followed by acute irradiation with X-rays, but not by each one. It is suggested that the accumulation of iNOS may be due to the depression of acute irradiation-induced p53 functions by pre-chronic irradiation. We found that chronic irradiation with gamma-rays did not inhibit the accumulation of p53 after exposure to the conditioned medium from the irradiated m*p53* cells. However, the decay of accumulated p53 was stimulated by chronic irradiation with gamma-rays. At the same time, the accumulation of Hdm2 was observed, suggesting that chronic irradiation with gamma-rays may stimulate the degradation of p53 accumulated by NO-mediated bystander effects.

10 Lifespan of C57BL/6 mice after radio-adaptive survival response

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We have reported that pre-irradiation with a small dose (0.3–0.5 Gy) induces radio-resistance observed as an increased survival rate from bone marrow death in ICR and C57BL/6 mice. This was also observed in splenectomized C57BL/6 mice, and the lifespan of pre-irradiated group after observation of bone-marrow death rate was significantly longer than that of non-pre-irradiated control group. In this study, lifespan of intact (without splenectomy) mice was examined. The 30-day survival rates of pre-irradiated and non-preirradiated control animals were 96% (48/50) and 58% (29/50), respectively. Increment of the survival rate was significant (Fisher's exact probability=0.0000035). Lifespan of the survived 48 (pre-irradiated) and 29 (control) animals were observed. The average survival time (and its standard error) was 347.3 (29.8) days for pre-irradiated group and 378.9 (40.9) days for control group. The difference of the lifespan was not significant both in generalized Wilcoxon's rank sum test (p=0.55) and log rank test (p=0.32).

11 Identification of transcription factor binds to upstream region of the GADD45 gene after ionizing irradiation

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It is considered that induction of the GADD45 gene after X-ray irradiation is p53-dependent, requiring binding of p53 to the p53-recognition element in the third intron. However, it is not understood whether additional transcription factors (TFs) other than p53 are required for transcriptional regulation of the GADD45 gene after X-ray irradiation. We have previously revealed X-ray-inducible binding of factors at several loci in the regulatory region of the GADD45 gene in ML-1 cells. Among them, we focused on the locus, spanning –793/–759 bp in the upstream region of the GADD45 gene, where binding of factors is induced after 0.5 Gy of X-rays irradiation. Although this locus is homologous to the consensus recognition sequences for TFs, GATA, Ikaros, and IRF, EMSA using competitor oligonucleotides revealed an association of none of these TFs. By introduction of point mutations into the probe, we revealed that this X-ray-inducible factor binds to the –775 bp/–759 bp region.

12 Spectrum of mutations at the mouse Hprt locus induced by ionizing radiation in cells of radioadaptive response

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Radioadaptive response is a biological defense mechanism that is induced by low-dose ionizing irradiation for cellular resistance to the genotoxic effects of subsequent irradiation. The response is the acquisition of resistance to the induction of mutation, chromosome aberraion, and cell killing by ionizing radiation. We have shown that the radioadaptive response is mediated through the pathways involving protein kinase C and p38 mitogen-activated protein kinase. However, its molecular mechanism is still largely elusive. We examined mutations induced by ionizing radiation with or without radioadaptive response at the Hprt locus in mouse m5S cells. We analyzed the Hprt gene in 6-thioguanine-resistant mutants by amplification of all the nine exons of the mouse Hprt