

- 132 Expression of p53 and p21 proteins after ionizing irradiation in tumor cells express wild-type p53

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DNA damage caused by ionizing radiation leads normal cells to accumulate p53 and increase p21, which result in G1 arrest. It is predicted that tumor cells even if they express wild-type p53 arrest in G1 phase following exposure to ionizing radiation. However, previous studies have suggested that G1 arrest is abnormal in tumor cells even if they express wild-type p53. Here, we examined the levels of p53 and p21 proteins with Western blotting analysis after exposure to 6Gy of X-rays in HT1080, RKO and MCF-7, all of which have wild-type p53. In HT1080 and RKO, p53 and p21 proteins kept increased level for 4 hours. Whereas p53 protein level, in MCF-7 cells, peaked at 2 hours after irradiation, then decreased to control level after 4 hours. p21 level reached maximum 2~4 hours after irradiation, and it didn't decreased to control level until 12 hours after irradiation. Because the kinetics is similar to those of normal human cells, it is suggested that down stream to p53/p21 pathways are abnormal in tumor cells even if they express wild-type p53.

- 133 Radio-adaptive Response in Mice - Suppression of p53 and Bax Accumulation in the Spleen after 3 Gy by Pre-irradiation with 0.45 Gy

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Pre-irradiation with 0.3-0.5 Gy of X-rays results in acquired radio-resistance (decreased bone-marrow death) 2 weeks later in ICR and C57BL strains of mice. Molecular mechanism was studied by measuring p53 and Bax accumulation in tissues of irradiated C57BL/6 mice. The pre-irradiation significantly suppressed p53 accumulation 5 hr after exposure to 3 Gy in the spleen measured by Western blotting method, even to the lower level than that in intact animal. A similar result was obtained in tissue histology of the spleen, stained with anti-p53 or anti-Bax antigen, of mice 7 days after 3 Gy. These results suggest that the radio-adaptive response might be induced as follows; (i) apoptosis of highly radio-sensitive cells in the spleen after 0.45 Gy, (ii) replacement by neighbouring healthy (radio-resistant) cell proliferation during the interval time of 2 weeks, (iii) less apoptosis, good recovery of hematopoietic function of the spleen after 3 Gy.

- 134 Regulatory mechanisms of MAP kinase activation in response to UVC irradiation.

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UVC irradiation activates MAP kinases (MAPK) in various cells, however, the regulatory mechanisms of this activation are not understood. We investigated the role of receptor tyrosine kinases (RTK) and intracellular redox level in UVC-irradiated normal human embryonic (HE) cells. Among MAPK, ERK and JNK were markedly and immediately activated by UVC irradiation. When cells were cultured in hypoxic condition (5% O₂) or in the presence of an antioxidant, N-acetyl-cysteine (NAC), UVC-induced JNK activation and DNA fragmentation was selectively inhibited. In contrast, ERK activation by UVC was inhibited by suramine, an RTK inhibitor. These results suggested that responses of MAPK to UVC irradiation are regulated in part by intracellular redox level and by RTK.