

- 92 Involvement of Protein Kinase C in Radiation-induced Apoptosis Regulation in 3SBH5 Cells
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We have demonstrated that radiation induces protein kinase C (PKC) activation and diacylglycerol production. Although many studies on radiation-induced PKC signaling pathways have been performed involving radiation-induced apoptosis, roles of the PKC signaling pathways remain unknown. Here, PKC function in radiation-induced apoptosis was investigated using murine thymic lymphoma cells, 3SBH5 cells. PMA (phorbol 12-myristate 13-acetate), an activator of PKC, blocked the radiation-induced apoptosis in 3SBH5 cells. In contrast, chelerythrine, a PKC inhibitor, enhanced the radiation-induced apoptosis. These results suggest that PKC plays a key role in the regulation of radiation-induced apoptosis in 3SBH5 cells. Irradiation alone had no effect on the distribution of PKC in 3SBH5 cells. However, the amounts of PKC β I in the cytosol of 3SBH5 cells decreased outstandingly after irradiation in the cells pretreated with PMA. It was also demonstrated that immunoprecipitates by anti-PKC α antibody include Raf-1, one of stress response proteins, in 3SBH5 cells after irradiation. The relationship between PKC functions and the mechanism of radiation-induced apoptosis is discussed with reference to Raf-1 function.

- 93 Involvement of AIM-1 in ionizing radiation-induced G2 checkpoint
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AIM-1 and its related kinases, aurora family kinases, had been found in mammals by us. In our further analyses, AIM-1 was demonstrated to be a major regulator for mammalian mitotic processes including chromosomal condensation, chromosomal segregation, gene silencing, and cytokinesis. Additionally, we showed that AIM-1 is a responsible kinase for the phosphorylation of H3 histone at Ser 10 during mitosis. Here we reports that AIM-1 is involved in the ionizing radiation (IR)-induced G2 checkpoint pathway. AIM-1 kinase activity and the H3 histone phosphorylation was suppressed by irradiation. Phosphorylation status of AIM-1 at Thr 256 was also repressed. The effect was transient and corresponded with radiation-induced G2 arrest. Thus, AIM-1 is considered to involve in G2 checkpoint regulation induced by IR.

- 94 Decreased expression of c-Myc in X-ray-induced apoptotic cell death of human T-cell leukemia cell line MOLT-4
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MOLT-4 is one of the most radiosensitive cell lines and undergoes apoptotic cell death after X-irradiation. We found that the expression levels of c-Myc protein and c-myc mRNA decreased after X-irradiation or treatment with C2-ceramide, preceding apoptotic response. On the other hand, in an X-ray- or C2-ceramide-resistant MOLT-4 variant, the expression levels of c-Myc protein and c-myc mRNA were not changed. Exposure of MOLT-4 cells to c-Myc peptide inhibitor or transfection of c-myc antisense oligonucleotides significantly induced cell death. These results suggest that decreased expression of c-myc might be one of the triggers of apoptotic cell death.