92 Involvement of Protein Kinase C in Radiation-induced Apoptosis Regulation in 3SBH5 Cells
Tetsuo NAKAJIMA1, Osami YUKAWA1, Harumi OHYAMA1, Bing WANG1, Isamu HAYATA1, Hiroko INABA1, 1Research Center for Radiation Safety, Natl. Inst. Radiol. Sci.

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 PKCβ1 in the cytosol of 3SBH5 cells decreased outstandingly after irradiation in the cells pretreated with PMA. It was also demonstrated that immunoprecipitates by anti-PKCα 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
Masaaki TATSUKA1, Shiho SUTO1, Minori Yamada1, Zhen-Bo HAN1, Fumio SUZUKI1, 1Res. Inst. Radiat. Biol. Med. Hiroshima Univ.

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

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.