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RADIATION SENSITIVITY DEPENDS ON OGG1 ACTIVITY STATUS IN HUMAN LEUKEMIA CELL LINES

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To assess the role of 8-oxoguanine glycosylase (OGG1) in the cell defense against radiation injury, the radiation-induced cytotoxicities were compared between the mutant type KG-1 featuring a loss of OGG1 activity due to a homozygous mutation of Arg 229 Gln, and the wild type U937. While the following three obvious toxicities were displayed in KG-1, they were observed only minimally in U937. These were: a dramatic arrest at the G2/M phase indicated by a marked increase in both the number of G2/M cells and the expression of cyclin B1, cdc2, and mitotic phosphoprotein monoclonal-2 (MPM-2)-reactive proteins; a severe apoptosis shown by a marked increase in the number of cells with hypo-diploid DNA and DNA fragmentation; and as a result, a severe inhibition of cell growth and proliferation measured by the MTT test and [3H]-thymidine uptake assay. As expected, KG-1 exhibited a significant increase in the 8-hydroxyguanine level in DNA whereas U937 did not. However, the level of irradiation induced lipid peroxidation was almost the same in both cell lines. All of these symptoms evidenced by KG-1 were observed in Molt-4 and CEM-CM3, which were also found to feature low OGG1 activity. These findings suggest that OGG1 plays an important role in cell survival from radiation-induced damage and are also indicative of the capability of 8-hydroxyguanine in DNA to induce cellular toxicities.

keyword : 8-Hydroxyguanine, OGG1, Apoptosis, Cyclin B1, Cdc2, Radiation