INHIBITION OF DNA REPAIR IN X-IRRADIATED CHINESE HAMSTER V79' CELLS BY NUCLEOSIDE ANALOGUES

Wakako HIRAOKA

Department of Radiation Biology,
Faculty of Veterinary Medicine,
Hokkaido University, Sapporo 060, Japan

The effects of DNA purine nucleoside analogues such as cordycepin and its 2-chloro, 2-bromo and 2-iodo derivatives on the recovery of X-irradiated Chinese hamster V79 cells from potentially lethal damage were investigated with reference to their metabolism within a cell. The recovery from potentially lethal damage was suppressed when the cells were exposed to cordycepin during post-irradiation incubation. The other nucleosides had no ability to inhibit the recovery of the cells. Analysis of the metabolic products of each nucleoside, using high pressure liquid chromatography, showed that cordycepin was phosphorylated to the triphosphate form in the cell, whereas the other halogenated analogues were not. Thus, a clear relationship between the inhibiting ability of the drugs and the degree of the phosphorylation of the drugs was obtained.

The effect of cordycepin on enzymatic repair of X-ray-induced DNA strand breaks was also investigated. An examination by the filter elution method proved that this drug prevented the rejoining of DNA double strand breaks but did not prevent rejoining of DNA single strand breaks.

This finding indicates that the recovery of the cells from potentially lethal damage reflects the rejoining of the double strand breaks. From these results, it was inferred that cordycepin incorporated into the cell was first phosphorylated and thereby interfered with the enzymatic processes of the rejoining of DNA double breaks, resulting in the inhibition of cell recovery.