X-RAY-INDUCED KILLING OF CHINESE HAMSTER V79 CELLS IN THE PRESENCE OF SEVERAL ENZYME INHIBITORS AND ACTIVATORS

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It has been reported that killing efficiency of X-rays to mammalian cells is altered by post-irradiation treatment with some enzyme inhibitors and activators. This is termed "fixation of repair of potentially lethal damage (PLD)". In order to elucidate the mechanisms of enzymatic repair of PLD, many studies have been focused on the effects of enzyme inhibitors on the repair. In the present study, the effects of several enzyme inhibitors and activators on Chinese hamster V79 cells, which were exposed to X-rays when growing exponentially in the log-phase or resting stationally in the plateau-phase, were investigated. The drugs tested for this study were DNA synthesis inhibitors (2–C1-deoxyadenosine, 2-Br-deoxyadenosine, 2'-deoxyadenosine, cordycepin and hydroxyurea) and histone-structure modifiers (sodium butyrate, which inhibits histone deacetylase, and 12–O–tetradecanoylphorbor-13-acetate and polymyxin B, which activates and inhibits protein kinase C, respectively). In the case of the log-phase, the cells were incubated for 2 hours with medium containing these drugs after X-irradiation. In the case of the plateau-phase, the cells were incubated for 4 hours with medium containing these drugs after X-irradiation. The medium was then exchanged with fresh normal medium and the cells were incubated for 7–8 days for colony formation. Among the drugs tested, 2–C1-deoxyadenosine and sodium butyrate could enhance the killing efficiency of X-rays in the log-phase cells. In the plateau-phase cells, only 2–C1–deoxyadenosine significantly enhanced the efficiency of X-rays. From these results, one possible conclusion is that histone-acetylation correlates the fixation of PLD, and another is that the inhibition of DNA synthesis is responsible for the fixation of PLD, since 2–C1–deoxyadenosine is known to change the ballance of the cellular deoxyribonucleotide pools by inhibiting ribonucleotide reductase. The drugs which activate the repair ability of the cells were not found in the present study.