

217 **Recovery of heat inactivated DNA-PK activity and repair of DNA double strand break**

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DNA-PK was inactivated by heat treatment at 44°C for 15 min. Recovery of DNA-PK activity was observed during the incubation at 37 °C followed by heat treatment at 44°C. 60% of activity was recovered after 10 h of incubation. When the cells were treated at 44°C for 30 min, the recovery of activity was delayed and recovered activity was decreased compared as 15 min treatment. DNA-PK activity was not observed after 10 h of incubation when the cells were treated for 45 min. The repair activity for the DNA double strand breaks (dsb) induced by X-ray irradiation was also depressed by heat treatment. The recovery of repair activity of DNA dsb was correlated with that of DNA-PK activity.

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Heat treatment induces condensation and disintegration of nuclei but not apoptosis
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Human tumor cells are more sensitive to heat-treatment than normal human embryonic (HE) cells *in vitro*. One of the reasons may be the higher frequency of apoptosis in tumor cells. We have observed that heat treatment at 43°C for several hours induced nuclear condensation and chromosome condensation in human tumor cells. In contrast, they were less frequently detected in normal human cells. In this study, we examined whether heat treatment induce apoptosis or not. We used DNA-ladder assay and Apop Tag Direct assay (Oncor) kit. The results indicated that apoptosis was not induced by heat treatment. During the subsequent incubation for up to 4 days at 37°C, we observed that large cells with many small nuclei appeared in 5% - 10% of the tumor cells. However, Apop Tag Direct assay proved that these cells were not apoptotic. We showed that heat treatment induced the morphological alteration of nuclei but not apoptosis in all tumor cell lines, and that normal cells were less affected than tumor cells by heat treatment.

219 **p53- Dependent Hyperthermic Enhancement of Cell Killing by Radiations in Human Glioblastoma Cells (A-172/wtp53) Transfected with mp53 Gene.**

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We have previously reported that hyperthermic synergism depends on p53 gene status in C-beam-irradiated glioblastoma cells (A-172 and U87MG/wild-type p53, T98G and A7/mutant p53) having different p53 gene status. However, it remains unclear that such hyperthermic synergism may be dependent on other genetic factors. Therefore, we examined the cytotoxicities of hyperthermia and/or radiations using three kinds of human glioblastoma cells which are the parental cell line bearing wild-type p53 gene (A-172), the transformed cell line with pCMV-Neo-Bam vector (A-172/vector) and the transformed cell line with mutant p53^{Tp248} gene. The synergism of hyperthermic enhancement in cytotoxicity was observed only in wild-type p53 cells (A-172 and A-172/vector). The average of thermal enhancement ratio in them after γ -ray or C-beam irradiation was about 2.0. We have obtained confirmatory evidence that the hyperthermic enhancement of cell killing is p53-dependent. The possible mechanisms of hyperthermic enhancement to radiations were discussed.