

139 Accumulation of iNOS by Radiation and/or Hyperthermia in Human Glioblastoma Cell Lines

Hideki MATSUMOTO, Sachiko HAYASHI, Hiroki SHIOURA, Ryuhei KITAI¹, Toshio OHTSUBO², Eiichi KANO

Depts. of Expt'l. Radiol., ¹Neurosurg., ²Otorhinolaryngol., Fukui Med. Univ., Fukui 910-11

The accumulations of inducible nitric oxide synthase (iNOS) after exposure to radiation and/or hyperthermia in two human glioblastoma cell lines (A-172 and T98G) were studied by Western blot analysis. The accumulation of iNOS after exposure to radiation was only seen in T98G cells. In addition, we found that the prominent accumulation of iNOS by hyperthermia was only seen in T98G cells. We also found that after simultaneously exposure radiation and hyperthermia, the level of iNOS decreased in A-172 cells, whereas in T98G the level of iNOS increased over that after exposure to radiation or hyperthermia alone. Our observations that the responsibilities of iNOS accumulation by radiation and/or hyperthermia are different between the two cell lines suggest that iNOS accumulation may be induced indirectly through certain signal transduction pathway having different responsibilities between the two cell lines after irradiation and/or hyperthermia.

140 Function of the introduced gadd45 gene in ataxia telangiectasia cells

Seiji KODAMA*, Kentaro YAMAGUCHI*, Keiji SUZUKI*, Kanji ISHIZAKI**, and Masami WATANABE*, *Div. of Radiat. Life Science, Schl. Pharm. Sciences, Nagasaki Univ., Nagasaki 852, **Dept. Radiat., Aichi Cancer Inst., Nagoya 464.

Ataxia telangiectasia (AT) cells defect the p53 dependent pathway regulating growth arrest at G₁ checkpoint of the cell cycle. Gadd45 is one of the genes involved in the p53 pathway and its induction is suboptimal in AT cells. To study the role of the GADD45 in the p53 pathway at G₁ checkpoint, we introduced the gadd45 gene into AT5BIVA cells and isolated the AT cells showing inducible expression of the introduced gadd45 gene. The analyses of growth curve and colony formation revealed that the elevated expression of the GADD45 inhibited the cell growth of the AT cells. This suggests that the product of the introduced gadd45 gene functions as a cell growth regulatory protein in the AT cells. Radiosensitivity of the AT cells, however, was not changed by the induction of the GADD45, indicating that the suboptimal response of the gadd45 gene to radiation is not responsible for hyper-radiosensitivity of the AT cells.

141 Disappearance of Binding Activity to the Upstream Sequence of IL-1 β Gene in X-irradiated Murine Cells

Hiroshi ISHIHARA, Izumi TANAKA, Masako FURUSE, Kazuko TSUNEOKA
The First Res. Group, Natl. Inst. Radiol. Sci., Chiba 263

Interleukin (IL)-1 β gene which encodes a radioprotector is transcriptionally stimulated immediately after x-irradiation in mouse monocytic cells. To analyze the immediate-early induction, we isolated genomic DNA corresponding to the mouse IL-1 β gene with the 10 kb-upstream region. We found specific binding to the three fragments in the nuclear extract from normal monocytic cells; the fragments correspond to 1.5k-, 8.0k- and 8.5k-base upstream from the predicted transcriptional starting point. Immediately after irradiation of 20 Gy x-ray, the binding activity to the fragments disappeared in the monocytic cells. Each fragment has a unique sequence in size of approx. 50 nt respectively, which is essential to the binding. One of the fragment was present in the adjacent site of the p53-binding motif of the long terminal repeat of the retrotransposon GLN which exists in normal murine genome at 1000 copies. In contrast to the increase in binding activity to the motif as later response, disappearance of binding activity beside the motif may occur as the immediate-early response.