240 Modification of Hyperthermia-Induced Apoptosis by a Spin Trapping Agent, α-Phenyl-N-Tert-Butyl Nitrone

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α-phenyl-N-tert-butyl nitrone (PBN) has been widely used as a spin trapping agent. We investigated the effects of PBN and its derivatives on hyperthermia-induced apoptosis in U937 cells in order to examine the role of active oxygen in the apoptosis. PBN dose-dependently inhibited DNA fragmentation induced by heat-treatment (44℃, 30min). PBN also prevented the expression of phosphatidylserine on the cell surface, which was a index of early apoptosis. The ability of PBN and its derivatives to inhibit DNA fragmentation was in the order of PBN>POBN>SPBN and this order coincided with that of hydrphobicity of the compounds. In heat-treated cells, PBN enhanced the expression of HSP70. These results suggest that active oxygen is a cause of heat-induced apoptosis and the protective effect of PBN against the apoptosis might be due to the increase of HSP70 expression.

241 Restoration of Mutant P53 to Normal P53 Function by Hsp in Human Tumor Cells.

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We examined whether Hsp induced by hyperthermic treatment can act as a molecular chaperon to correct the mutant p53 conformation. No WAF1 expression was induced after X-rays of 6 Gy in A-172/248 cells carrying mutant p53. In contrast, A-172/248 showed WAF1 expression when they were irradiated with X-rays 16 h after heating at 44°C for 15 min, which was similar to the response of A-172/neo cells carrying normal p53. These results suggests that Hsp induced by heating in tumor cells with mutant p53 is effective in restoring mutant p53 to normal p53 function.

242 Induction of HSP 70 in Some Organs of the Adrenalectomy Mice under Heat Stress or Non-Stress.

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It is known well that an adrenal gland is in the center of the stress response. Already, we had reported that a large quantity of heat shock protein ( HSP 70 ) was expressed in the adrenal glands by heat stress. In order to study the relation ship between the adrenal glands and HSP 70, we used the adrenalectomy mouse which was extirpated both adrenal glands. Adrenalectomy mice were sacrificed on 1, 3, 7, 14 and 28 days after the extirpation of adrenal glands. Also, they were heated with whole-body heating at 37℃ for 30 min on 28 days. Induction of HSP 70 in some organs of adrenalectomy mice and normal mice were measured by ELISA method. The level of HSP 70 in some organs of adrenalectomy mice was lower than that of normal mice. Induction of HSP 70 in some organs of normal mice by heat stress was significantly increased, but that of the adrenalectomy mice was not increased. From these results it was suggested that the adrenal gland was the contact point of the stress response and the induction of HSP 70.