out as continue and several intervals treatment. Anti-tumor effects were observed in the continuous treatment than the intervals treatment group. NK cells activity were increase in the continuous treatment than the interval treatment, and also enhance the apoptosis generation. Increased the number of lymphocytes and white blood cells after continuous treatment. These results suggest that mild hyperthermia has effects the patients QOL and control the metastasis for patients after cancer treatment in clinically.

168  Mechanism of cell cycle-dependent cell death by heat shock

It has been shown that heat treatment has lethal effects on mammalian cells. Generally, cells in S phase are resistant to X-rays, whereas they are the most sensitive to heat shock. We have previously reported that heat shock induces centrosome dysfunction. Because centrosome duplication occurs during S phase, we examined the effect of heat shock on centrosome in normal human diploid (HE49) cells during S phase. HE49 cells were synchronized in G0, then 16 hr after release we labeled early S phase cells with BrdU. The frequency of cells with abnormal centrosomes was examined 72 hr after heat shock, and 86% of BrdU-positive cells showed the abnormality of the centrosome (multiple, minute and no), whereas those cells were 66% of BrdU-negative cells. Especially, cells with no centrosome were frequently detected in BrdU-positive cell. These results indicate that heat shock causes more detrimental effects on centrosomes in early S phase, the resultant failure in cell division, could result in cell death.

169  Effects of hyperthermia on DNA-PK activity and radiosensitivity
Yoshihisa MATSUMOTO1, Noriko UMEDA2, Hong-Lan YIN1, Masanori TOMITA1,2, Atsushi ENOMOTO1, Akinori MORITA1, Terumi MIZUKOSHI1, Kazuo SAKAI1, Yoshio HOSOI1, Kuni OHTOMO2, Norio SUZUKI1
DNA-PK is considered one of critical enzymes in the repair and/or signal transduction of DNA double-strand breaks. We and others have demonstrated hyperthermic lability of Ku subunits in DNA-PK as a possible mechanism for hyperthermic radioresistance. We have examined in detail the effects of hyperthermia on DNA-PK in situ, i.e., in various cultured cell lines from mouse, hamster, human and chicken. We found that DNA-PK activity in human cells was more heat resistant than that in rodent cells. In conjunction with this, human cells exhibited smaller hyperthermic radiosensitization than rodent cells. Additionally, the activity could be restored when cells were returned to normal temperature and DNA-PK became less heat-sensitive in thermotolerant cells. The elucidation of the mechanisms protecting and recovering DNA-PK from heat damage may possibly provide a new approach to improve cancer therapy through hyperthermia, either by itself or in combination with radiation.

170  Hyperthermic radiosensitization of chicken B lymphocyte DT40 and Its derivatives lacking NHEJ and/or HR pathways of DNA DSBreakpair
To explore the roles of two major pathways of DNA double-strand break repair, i.e., NHEJ and HR, in hyperthermic radiosensitization, we examined chicken B lymphocyte DT40 cells and its derivatives lacking Ku70, DNA-PKcs or Rad54. When these cells were irradiated with X-ray after 20 or 40 min-treatment at 46°C, the radiosensitivity was enhanced in any of mutants as well as wild-type cells. Notably, however, in Ku70--/-- and DNA-PKcs--/--/-, which are consisted of two subpopulations with greatly different radiosensitivity, the radioreistant fraction, rather than the radiosensitive fraction, was sensitized. It has been considered that the radioreistant fraction of these cell lines might represent cells in late S- and G2-phases, with efficient repair through HR. In conjunction with this, the present observation suggested that hyperthermia might have inhibited homologous recombinational repair of DNA double-strand breaks.