nificantly smaller than that in the aerobic condition, and treatments of cells with etanidazole enhanced the radiation-induced dsb under the hypoxic condition. Moreover, in 5-bromo-2'deoxyuridine-incorporated cells, the remarkable sensitization of radiation-induced apoptosis was observed in HL 60 and not in MOLT-4 cells.

These results indicated that the radiation-induced apoptosis of HL 60 cells was initiated by DNA dsb and treatment with etanidazole sensitized apoptosis through the enhancement of dsb induction in the hypoxic condition, but the radiation-induced apoptosis of MOLT-4 cells occurred through damage other than DNA, i. e., lipid and/or protein oxidations. It seems that the incidence of oxygen effects and sensitizing effects of etanidazole on radiation-induced apoptosis are dependent on the difference of radiation targets.

The effect of estrogen receptor on the induction of cytochrome P 450 mRNA via aryl hydrocarbon receptor

Yuko Suzuki

Laboratory of Toxicology
Department of Environmental Veterinary Sciences
School of Veterinary Medicine
Hokkaido University, Sapporo 060-0818 Japan

Aryl hydrocarbon (Ah) receptor agonists, such as benzo(a)pyrene (BP) and 2,3,7,8-tetrachrolodibenzo-p-dioxin (TCDD) are known to exert the effects of endocrine disruption, and to induce certain kinds of cytochrome P 450 (CYP) as well as phase II enzymes. BP induced CYP 1 A 1 and CYP 1 B 1 mRNA in human breast cancer MCF-7 cells in dose dependent manner, but co-application of estradiol 17β (E 2) reduced CYP 1 A 1 induction with no effect on CYP 1 B 1 induction. In human hepatocyte HepG 2 cells containing no functional estrogen receptor, this reduction was not detected. These results suggested a possibility that the reduction was due to estrogen receptor activation. To elucidate the interaction between Ah receptor and estrogen receptor, I examined the effect of growth factors whose expression or sensitivity depended on estrogen receptor activation on CYP 1 A 1 induction in MCF-7 cells. Epidermal growth factor and insulin like growth factor-I did not alter CYP 1 A 1 mRNA induction by BP. DNA mobility shift assay showed that E 2 had no effect on Ah receptor binding to xenobiotic responsive element, Ah receptor/Arnt heterodimer binding region in upstream sequence of CYP 1 A 1 and CYP 1 B 1. AIB 1, a transcriptional factor overexpressed in breast cancer, was transfected into HepG 2 cells. AIB 1 transfected HepG 2 cells reduced CYP 1 A 1 induction by BP. These results suggest that AIB 1 may involve Ah receptor mediated gene transcription and interaction with estrogen receptor.