[P-64]

Low Abundance of Aryl Hydrocarbon Receptor and Cytochrome P4501A1 Deficiency Result in Irresponsiveness to Benzo[a]pyrene in Mouse Sertoli Cells

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The Sertoli cells have a critical role to differentiate the spermatogenic germ cells by the support of testosterone and follicle stimulating hormone in the testis. It has been reported that some endocrine disruptors such as pthalates (DEHP or MEHP) can destroy the Sertoli cells. In the present study, therefore the possible cytotoxical actions of benzo[a]pyrene (BaP) in Sertoli cell (TM4) have been investigated. BaP is associated with mutagenesis and carcinogenesis of some cells. BaP (0.01-100 μM) has been employed to the Sertoli cell culture. With any concentrations of BaP, the cells did not show cellular changes as determined by cell cycle analysis through flowcytometry. And this pattern was similar to BaP-7,8-dihydrodiol (BaP-diol; 0.1-1 μM) treatment but a relatively higher concentration of BaP-diol (5 μM) slightly tended to increase a cell death. In TM4 cells, we found that the endogeneous protein level of aryl hydrocarbon receptor (AhR) was extremely low, and that CYP1A1 expression was undetectable in trascriptional and translational levels. And also CYP1A1 activity monitored by ethoxyresorufin-o-deethylase assay was absent and remained unchanged after BaP challenge to the cells. In contrast, although p53 protein level was very high in the cells, its content was not altered during the treatment. However, BaP-7,8-dihydrodiol-9,10-epoxide treatment (0.1-1 μM), a terminally processed metabolite of BaP by CYP1A1, caused a significant cell death by caspase-dependent apoptotic fashion. Taken together, it is suggested that the irresponsiveness of TM4 (Sertoli cell) against BaP may be mainly due to low abundance of AhR and CYP1A1 deficiency in the cells.

Keyword : benzo[a]pyrene, Sertoli cell, AhR, CYP1A1