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IN HUMAN BREAST CANCER MCF-7 CELLS, ESTROGEN INVOLVES IN *CYPIA1* GENE EXPRESSION.

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Cytochrome P450 enzymes have been intensively investigated in hepatic tissues and several mammalian cell lines. Compared to most studies about cytochrome P450 isozymes in liver in vivo and hepatic cell lines in vitro, the study of cytochrome P450IA1 in human breast cancer cells could be very important to understand the mechanism of the regulation of CYPIA1 gene expression and cell growth. MCF-7 human breast cencer cells are well characterized to study estrogen and antiestrogen action due to the fact that they contain high level of estrogen receptor and have biological markers characterized. And also MCF-7 cells express high level of arylhydrocarbon hydroxylase activity and human cytochrome P450IA1 cDNA was cloned from MCF-7 cells. Ah receptor was characterized in many breast cancer cell lines and polycyclic aromatic hydrocarbon such as 3-MC induced the expression of CYPIA1 gene and cytochrome P450- dependent monooxygenase activity. We undertook a study to examine the effect of estrogens and other chemicals on the regulation of human CYPIA1 gene expression in MCF-7 cells via RTPCR analysis, that might help us to understand the mechanism of the regulation of CYPIA1 gene expression and MCF-7 cell growth. Expression vector containing the functional 5'-regulatory region of human CYPIA1 fused to the CAT reporter gene was transfected into estrogen receptor positive MCF-7 cells or estrogen receptor negative MDA-MB-231 cells. After these cells were treated with various chemicals, RTPCR was carried out to measure both CYPIA1 mRNA and CAT mRNA levels. InM 3-MC increased in both P450 and CAT mRNA levels over those of control by two folds in MCF-7 cells but does not in MDA-MB-231 cells. Estrogen or tamoxifen or retinoic acid or chrysin decreased in both P450 and CAT mRNA levels that were induced by 3-MC in MCF-7 when each chemical was administered with 3-MC concomitantly. These results suggested that the level of CYPIA1 gene expression is modulated with estrogen-related molecules and make it possible to speculate that ER is related to CYPIA1 gene expression and cell growth in breast cancer cells. [Supported by grants from the Korean Ministry of Education]