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Transcriptional Activity of Estrogen Receptor is Differentially Influenced by Different Xenobiotic Nuclear Receptors between Human Breast Cancer Cells and Hepatoma Cells

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The purpose of this study was to examine the effects of xenobiotic nuclear receptors, CAR, SXR, and PPARγ on the transcriptional activity of estrogen receptor in human breast cancer cell lines and compare with those in human hepatoma cell line. Two different breast cancer cell lines, MCF-7 and MDA-MB-231 were cultured and effects of CAR, SXR, and PPARγon the ER-mediated transcriptional activation of synthetic (4ERE)-tk-luciferase reporter gene were analyzed. Consistent with the previous report, CAR significantly inhibited ER-mediated transactivation and SXR repressed modestly whereas the PPARγ did not repress the ER-mediated transactivation. However, in breast cancer cells neither of the xenobiotic receptors repressed the ER-mediated transactivation. Instead, they tend to increase the transactivation depending on the cell type and xenobiotic nuclear receptors. In MCF-7, SXR but not CAR or PPARγ slightly increased ER-mediated transactivation whereas in MDA-MB-231, CAR and PPARγ but not SXR tend to increase the transactivation of the reporter gene. These results indicate that the effects of ER cross-talk by the CAR, SXR, and PPARγ, are different in breast cancer cells from hepatoma cells. In conclusion, the transcriptional regulation by estrogen can involve different cross-talk interaction between estrogen receptor and xenobiotic nuclear receptors depending on the estrogen target cells.