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Cell Type-Dependent Modulation of Estrogen Response Element by Nuclear Receptors.

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This study examined the effects of nuclear receptors, CAR, SXR, and PPAR on the modulation of estrogen response elements in two human cell types, breast cancer cell lines and hepatoma cell line. Two different breast cancer cell lines, MCF-7 and MDA-MB-231 were cultured and effects of CAR, SXR, and PPAR on the ER-mediated transcriptional activation of a synthetic (4ERE)-tk-luciferase reporter gene were analyzed. In hepatoma cells, CAR significantly inhibited ER-mediated transactivation and SXR repressed modestly whereas the PPAR did not repress the ER-mediated transactivation of the synthetic ERE-containing promoter. In addition, CAR substantially inhibited ER-mediated transcriptional activity of an endogenous vitellogenin B1 promoter. Furthermore, treatment with an agonist of CAR, TCPOBOP, potentiated CAR-mediated transcriptional repression whereas an antagonist, androstenol, alleviated the repression effect. 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 PPAR slightly increased ER-mediated transactivation whereas in MDA-MB-231, CAR and PPAR but not SXR tend to increase the transactivation of the reporter gene. These results suggest that the modulatory effects of the nuclear receptors, CAR, SXR, and PPAR , on the estrogen response element were different in breast cancer cells from that of hepatoma cells. In conclusion, the transcriptional regulation of estrogen response element by estrogen can involve different cross-talk interaction between estrogen receptor and nuclear receptors depending on the estrogen target cells.