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## **CYP2S1 is Negatively Regulated by Corticosteroids in Human Cell Lines.**

**Bebenek IG**, Solaimani P, Bui P, Hankinson O.

### **Abstract:**

Cytochrome P450s (CYPs) are monooxygenase proteins involved in the metabolism of both exogenous and endogenous compounds. CYP2S1 can metabolize eicosanoids in the absence of both NADPH and NADPH cytochrome P450 reductase, and can also activate the anticancer agent 1 AQ4N [1,4-bis{[2-(dimethylamino-N-oxide)ethyl]amino}-5,8-dihydroxy anthracene-9,10-dione]. CYP2S1 is mainly expressed in extrahepatic tissues such as the trachea, lung, stomach, small intestine, spleen, skin, breast, kidney and placenta. Furthermore, increased expression of CYP2S1 occurs in several tumors of epithelial origin, making the characterization of CYP2S1 regulation relevant to the treatment of disease. We report that the synthetic glucocorticoid receptor ligand dexamethasone (DEX) represses CYP2S1 expression. The ED(50) is between 1nM and 3nM and maximal repression is reached by 48h. Other corticosteroids are also effective at repressing CYP2S1. We show that repression by DEX is mediated by the glucocorticoid receptor and requires histone deacetylase activity.