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2008

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CYP4Z1 is a novel cytochrome P450 enzyme belonging to family 4. It is preferentially expressed in normal breast and neoplastic breast tissue, and located in the CYP4ABXZ gene cluster on chromosome 1. Three independent nuclear receptor pathways are known to be involved in the regulation of members of the CYP4 family, namely: the progesterone receptor (PGR); peroxisome proliferator activated receptor (PPARα); and the glucocorticoid receptor (GCR). In this study, we utilised an in vitro cell model to define the mechanisms regulating CYP4Z1 mRNA expression.

Two oestrogen receptor positive cell lines (T47D and ZR-75-1) were exposed to agonists of the PGR, PPARα or GCR for 21 hours. The effects of these agonists on CYP4Z1 mRNA were evaluated using semi-quantitative reverse transcriptase-polymerase chain reaction (RT-PCR). In addition, pre-treatment (30 min) with either actinomycin D or cyclohexamide provided a mechanism by which to evaluate whether CYP4Z1 induction is regulated at the transcriptional or translational level.

Our findings demonstrated a significant increase of CYP4Z1 mRNA in the T47D cells exposed to either the PGR ($p < 0.05$) or GCR ($p < 0.001$) agonist. However, in the ZR-75-1 cells CYP4Z1 mRNA expression was significantly increased on exposure to the GCR ($p < 0.01$) or PPARα ($p < 0.001$) agonist. Pre-treatment with actinomycin D prior to exposure to the PGR, GCR or PPARα agonist demonstrated a significant reduction ($p < 0.05$) in CYP4Z1 mRNA levels in both cell lines. However, pre-treatment with cycloheximide indicated no significant change - but warrants further investigation. Taken together, these results suggest that CYP4Z1 induction in T47D and ZR-75-1 is mediated through differential cell type specific regulatory mechanisms.