Supplemental Figure S1

Activating and inhibitory functions of WNT/β-catenin in the induction of cytochromes P450 by nuclear receptors in HepaRG cells

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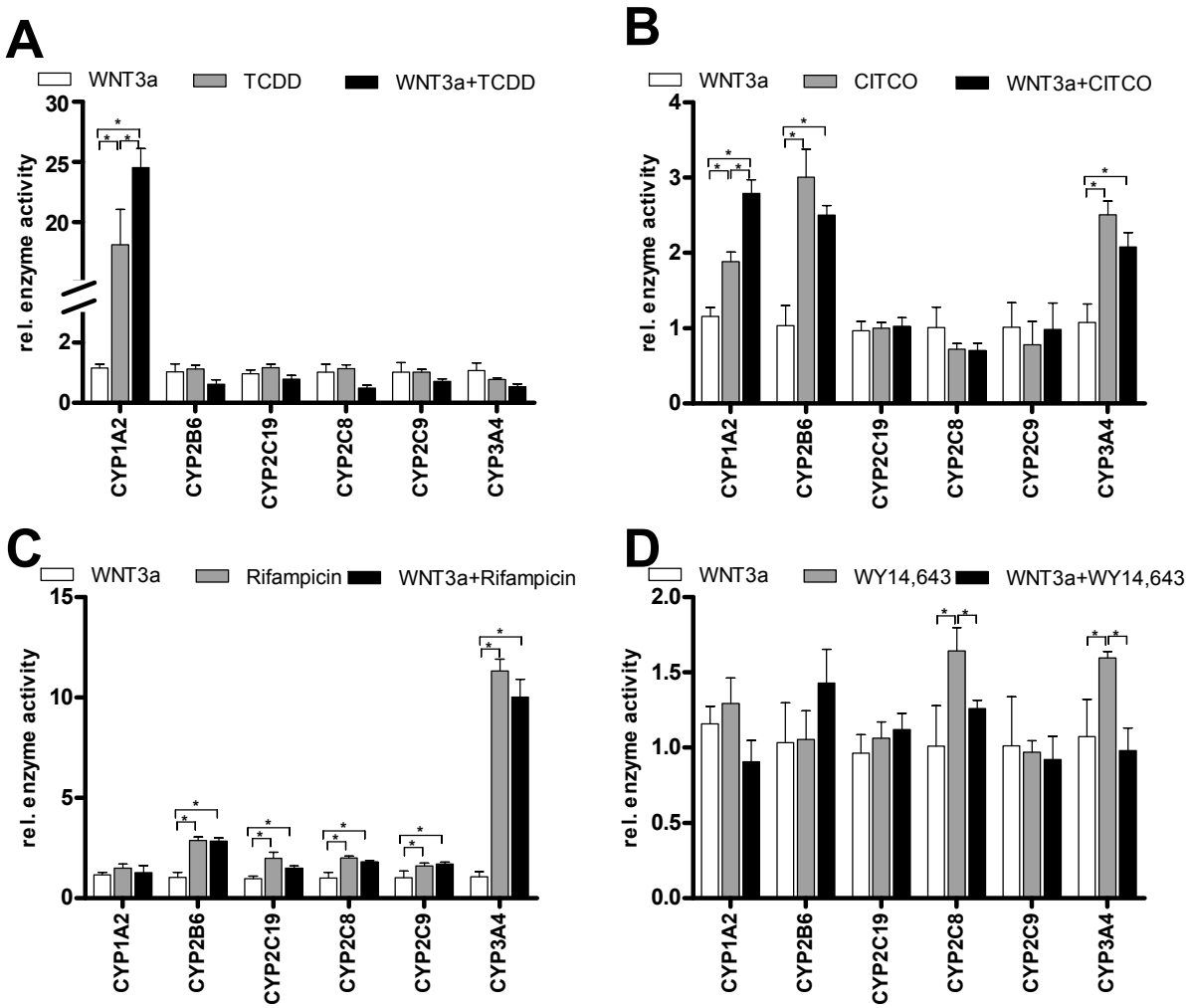

Supplemental Fig. S1. Activity of P450 enzymes during ligand-activated induction of nuclear receptors in combination WNT pathway activation. Enzyme activities measured by LC-MS/MS cocktail assay in the culture supernatants of HepaRG cells following WNT/β-catenin pathway activation (WNT3a, white bars) or treatment with 10nM of AhR agonist TCDD alone (A), 5µM of CAR agonist, CITCO (B), 10µM of PXR agonist, Rifampicin (C) or 100µM of PPARα agonist, WY14,643 (D) (corresponding light-grey bars on each panel) or in combination with WNT3a treatment (black bars on each panel). Activities measured: CYP1A2, phenacetin O-deethylation; CYP2B6, bupropion 4-hydroxylation; CYP2C8, amodiaquine N-desethylation; CYP2C9, tolbutamide 4'-hydroxylation; CYP2C19, S-mephenytoin 4'-hydroxylation; CYP2D6, propafenone 5-hydroxylation; CYP3A4, atorvastatin o-hydroxylation. Mean data of at least two independent experiments measured in triplicates are represented. Statistical significance for in comparison to vehicle is indicated by * ($p<0.05$, paired t-test).

Supplemental Figure S2

Activating and inhibitory functions of WNT/β-catenin in the induction of cytochromes P450 by nuclear receptors in HepaRG cells

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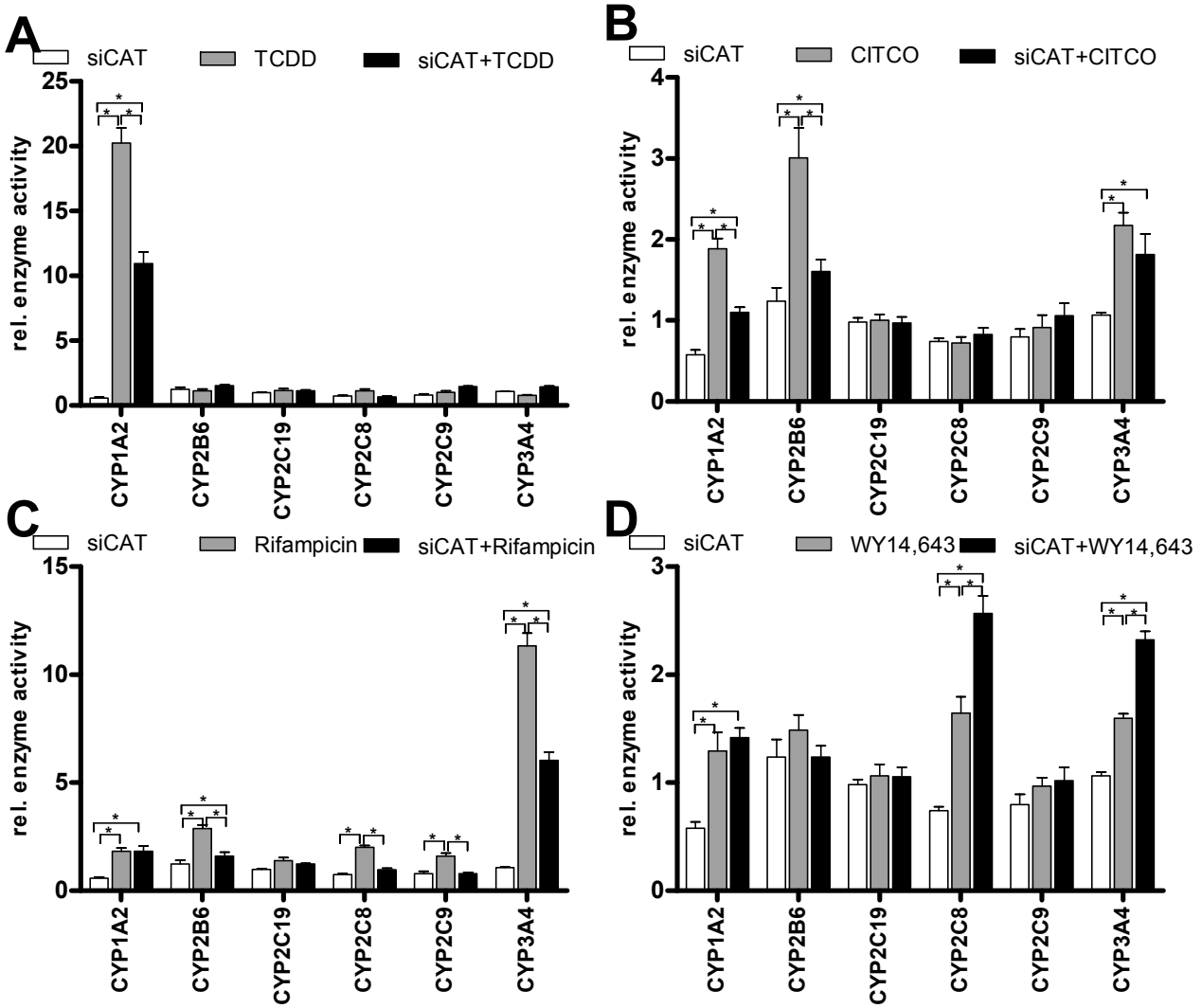

Supplemental Fig. S2. Activity of P450 enzymes during ligand-activated induction of nuclear receptors in combination with β-catenin knock-down. Enzyme activities measured by LC-MS/MS cocktail assay in the culture supernatants of HepaRG cells following b-catenin knock-down (siCAT, white bars) or treatment with 10nM of AhR agonist TCDD alone (A), 5μM of CAR agonist, CITCO (B), 10μM of PXR agonist, Rifampicin (C) or 100μM of PPARα agonist, WY14,643 (D) (corresponding light-grey bars on each panel) or in combination with siCAT treatment (black bars on each panel). Activities measured: CYP1A2, phenacetin O-deethylation; CYP2B6, bupropion 4-hydroxylation; CYP2C8, amodiaquine N-desethylation; CYP2C9, tolbutamide 4'-hydroxylation; CYP2C19, S-mephenytoin 4'-hydroxylation; CYP2D6, propafenone 5-hydroxylation; CYP3A4, atorvastatin o-hydroxylation. Mean data of at least two independent experiments measured in triplicates are represented. Statistical significance for in comparison to vehicle is indicated by * ($p<0.05$, paired t-test).