

SUPPLEMENTARY FIGURE LEGENDS

Figure S1 Amino acid alignment of the human and the rabbit CYP4B1 enzyme

The ERR triad (blue) is the glutamine–arginine–arginine motif conserved in all cytochrome P450 sequences. C-ligand (orange) is the heme-binding cysteine residue. The meander region (brown) contains the conserved Pro-X-Arg motif.

Figure S2 Multiple sequence alignments of the amino acids in the meander region of several P450 enzymes

Figure S3 Analysis of single amino acid alterations in sections 1-3

Survival of HepG2 cells expressing h-P427 CYP4B1 proteins where 18 different amino acids from sections s1-s3 in the rabbit CYP4B1 enzyme were *singly* introduced into the human P427 CYP4B1 enzyme in 2.9, 9, 29, 90 and 290 μM 4-IPO by flow cytometry. For each construct the mean \pm SEM is shown from at least three experiments.

Figures S4 to S23 Graphical presentation of 95% family-wise confidence levels for the 4-IPO survival experiments by Tukey's HSD test

The horizontal lines plot confidence intervals for the pairwise difference of the means. The positions of the confidence intervals displays the direction and the magnitude of change. If the confidence interval between two experimental conditions where the cells are transduced with different vectors does not contain zero, then there is a significant difference between the two cell types. A confidence interval not crossing the vertical zero line indicates a greater difference between the two analyzed experimental conditions. For the statistical analysis, the difference between different transduced cells is only tested at a 4-IPO concentration of 90 μM , because this is the maximum 4-IPO plasma concentration that had been achieved in humans without major side-effects.