Supplementary Results

Interaction between CYP4F2, CYP4F11 and CYP4F12

We used MetaCore™ to put *CYP4F2*, *CYP4F11* and *CYP4F12* into a cellular context to evaluate the significance of gene networks that these three genes participate in and to identify regulatory cascades that lead to or from these genes. Supplementary Figure 3 highlights the network interactions of nuclear transcriptional factors relating to the gene expression of *CYP4F2*, *CYP4F11* and *CYP4F12*. Several nuclear transcription factors including pregnane X receptor (PXR), aryl hydrocarbon receptor (AHR), activator protein 1(AP-1), peroxisome proliferator-activated receptor (PPAR) alpha, sterol regulatory element-binding protein 1 (SREBP-1), retinoid X receptor (RXR) and retinoic acid receptor (RAR) are known to be involved in the metabolism and clearance of diverse endogenous and exogenous compounds as well as gene activation (Pavek and Dvorak 2008; Zhou et al., 2009).

Supplementary Discussion

Interaction between CYP4F2, CYP4F11 and CYP4F12

Our network analysis shows that the regulation of *CYP4F2*, *CYP4F11* and *CYP4F12* expression is co-ordinated via numerous nuclear transcription factors including AP-1, RXR, RAR and SREBP, which are also known to be involved in the regulation of a number of other P450 isoforms (Rushmore and Kong 2002; Roth et al., 2008). This is consistent with data from various cell lines: AP-1 and RXR have been shown to regulate *CYP4F11* expression (Wang et al., 2010) in human keratinocyte-derived HaCaT cells; RXR stimulated whilst RAR repressed *CYP4F2* expression in the HepG2 cell line (Zhang et al., 2000; Zhang and Hardwick 2000); SREBP mediated the induction of *CYP4F2* expression by statins in primary human hepatocytes and HepG2 cells (Hsu et al., 2007); and PXR has been shown to regulate *CYP4F2* expression in healthy human lymphocytes (Siest et al., 2008) and *CYP4F12* expression in primary human hepatocytes (Hariparsad et al., 2009). Further work is required to further assess the cross-regulation of the *CYP4F* genes.

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