

Supporting Information

Integrative ‘-omics’ analysis in primary human hepatocytes unravels persistent mechanisms of cyclosporine A-induced cholestasis

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Table S1 All the DMGs, DEGS and DE-miRs after 3 days (T3) and 5 days (T5) of daily treatment of PHH with 30 μ M of CsA and also after 8 days (T8, 3 days of washout upon the 5 days of daily exposure with 30 μ M of CsA).

DMGs, differentially methylated genes; DEGs, differentially expressed genes; DE-miRs, differentially expressed microRNAs; PHH, primary human hepatocytes; CsA, cyclosporine A.

Table S2 Results of the ‘enriched pathway-based sets’ of the 1353 DEGs (576 upregulated DEGs and 777 downregulated DEGs) after the exposure of PHH for 3 days daily to 30 μ M CsA. DEGs, differentially expressed genes; PHH, primary human hepatocytes; CsA, cyclosporine A.

Table S3 Results of the ‘enriched pathway-based sets’ of the 1481 DEGs (743 upregulated DEGs and 738 downregulated DEGs) after the exposure of PHH for 5 days daily to 30 μ M CsA. DEGs, differentially expressed genes; PHH, primary human hepatocytes; CsA, cyclosporine A.

Table S4 Results of the ‘enriched pathway-based sets’ of the 1638 DEGs (789 upregulated DEGs and 849 downregulated DEGs) after the exposure of PHH for 5 days daily to 30 μ M CsA followed by a washout of 3 days.

DEGs, differentially expressed genes; PHH, primary human hepatocytes; CsA, cyclosporine A.

Table S5 Results of the ‘enriched pathway-based sets’ of the 828 DEGs (354 upregulated DEGs and 474 downregulated DEGs, see Figure 1C and 1D) which were persistently changed in the same direction after the exposure of PHH for 3 and 5 days daily to 30 μ M CsA (Day 3 and Day

5, respectively) and after the washout of 3 days upon the 5 days daily treatment with 30 μ M CsA (Day 8, WO).

DEGs, differentially expressed genes; PHH, primary human hepatocytes; CsA, cyclosporine A; WO, washout.

Table S6 Results of the ‘enriched pathway-based sets’ of the 476 DMGs (222 hypermethylated DMGs and 254 hypomethylated DMGs) after the exposure of PHH for 3 days daily to 30 μ M CsA.

DMGs, differentially methylated genes; PHH, primary human hepatocytes; CsA, cyclosporine A.

Table S7 Persistent upregulated (A) and downregulated (B) DEGs after 5 days daily exposure of PHH with 30 μ M CsA followed by a 3 day washout period which were changed in the same direction in the in vivo data. Results of the ‘enriched pathway-based sets’ (C) of the 29 persistently changed DEGs in the in vitro data which change in the same direction in the in vivo data (10 upregulated DEGs and 19 downregulated DEGs).

DEGs, differentially expressed genes; PHH, primary human hepatocytes; CsA, cyclosporine A.

Figure S1 Venn diagram of persistent upregulated and downregulated DEGs and DE-miRs-TG after 3 and 5 days daily exposure of PHH with 30 μ M CsA and 5 days daily exposure of PHH with 30 μ M CsA followed by a 3 day washout period.

DEGs, differentially expressed genes; DE-miRs-TG, differentially expressed microRNAs target genes; PHH, primary human hepatocytes; CsA, cyclosporine A.