Supplemental Document 1: Detailed description methods Microarray analysis

Total RNA was extracted from frozen liver tissue in combination with homogenization using a modified TRIzol reagent-based phenol extraction method described by Chomczynski and Sacchi (1). Tissue samples were initially transferred to disruption Teflon vessels, containing a disruption ball, and 500 µL TRIzol reagent (Invitrogen/Life Technologies, Karlsruhe, Germany) were added. Subsequently the complete system was pre-cooled in liquid N_2 and inserted into a bead mill dismembrator (Braun, Melsungen, Germany), where sample disruption was carried out at 2600 rpm for 2 min. Another 500 µl TRIzol reagent were added to the frozen tissue powder. After thawing 1 ml total volume of total RNA-containing TRIzol solution was further processed. Following final RNA preparation, RNA was DNase-treated (RNase-Free DNase Set, Qiagen, Hilden, Germany) and further purified using the RNA Clean-Up and Concentration Micro Kit (Norgen, Biotech Corp., Thorold, ON, Canada). RNA concentrations and purity were measured using a ND-8000 spectrophotometer (Thermo Fisher Scientific Inc., Wilmington, DE, USA). RNA integrity was validated by means of lab-on-a-chip capillary electrophoresis technology using an Agilent 2100 Bioanalyzer (Agilent Technologies, Santa Clara, CA, USA). Only RNA samples with an RNA integrity number (RIN) $\geq$ 8.4, 260/280 nm $\geq$ 2.0, 260/230 nm $\geq$ 1.9 were used for microarray analyses.

Purified total RNA samples were subjected to transcriptome analysis using GeneChip Mouse Gene 1.0 ST Arrays (Affymetrix Inc., Santa Clara, CA, USA). Expression profiling was done at the level of single RNA samples (for each group n = 3), which means that for each treatment or control group n = 3 arrays were used. RNA samples of different animals were not pooled. Target preparation and hybridization were performed according to the manufacturer's instructions using the Ambion® WT Expression Kit (Ambion/Life Technologies, Karlsruhe, Germany) combined with the GeneChip® WT Terminal Labeling and Controls Kit (GeneAtlas® WT Expression Kit

User Manual, Affymetrix Inc.). For each sample, 200 ng of total RNA were reverse transcribed into cDNA. After completed *in vitro* transcription, the resulting cRNA was purified and its concentration determined using a ND-8000 spectrophotometer (Thermo Fisher Scientific Inc.). Subsequently, 12 µg of cRNA were used for reverse transcription into first-strand cDNA, followed by cRNA hydrolysis and purification of single-stranded cDNA (ssDNA). After ssDNA quantification using a ND-8000 spectrophotometer (Thermo Fisher Scientific Inc.), 5.5 µg ssDNA were used for fragmentation and subsequent terminal labeling. Efficiency of fragmentation was checked by gel electrophoretic separation using an Agilent 2100 Bioanalyzer (Agilent Technologies). Fragmented and labeled target DNA was filled into array cartridges and hybridization was carried out at 45 °C for 17 h in a hybridization oven. Subsequently, arrays were washed and stained with streptavidin–phycoerythrin using the standard fluidics protocol for Fluidics Station 450 (Affymetrix Inc.) and scanned with a GeneChip Scanner 3000 (Affymetrix Inc.).

Quality assessment of hybridizations was monitored by inspection of scan images and by carefully reviewing exo- and endogenous controls using the Expression Console software (Affymetrix Inc.). For all processed arrays, the available control parameters passed the default threshold tests and all arrays were considered to be of good quality. Microarray data analysis was performed using the Rosetta Resolver® software system for gene expression data analysis (Rosetta Bio software, Seattle, WA, USA). Briefly, normalized intensity signals were calculated by processing the Affymetrix CEL files using the Affymetrix Rosetta intensity data summarization. Samples were analyzed based on fold change calculations and signal statistics after direct comparison of different samples. Genes exhibiting significantly different expression on the mRNA level were identified using the following cut-off criteria: one-way analysis of variance with subsequent Benjamini and Hochberg false discovery rate multiple-testing

correction on pair-wise comparisons (ANOVA, $p \leq 0.05$), signal correction statistics (Ratio Builder software, $p \leq 0.05$) and fold change ≥ 1.5-fold.

1. Chomczynski P, Sacchi N 1987 Single-step method of RNA isolation by acid guanidinium thiocyanate-phenol-chloroform extraction. Analytical biochemistry **162**:156-159.