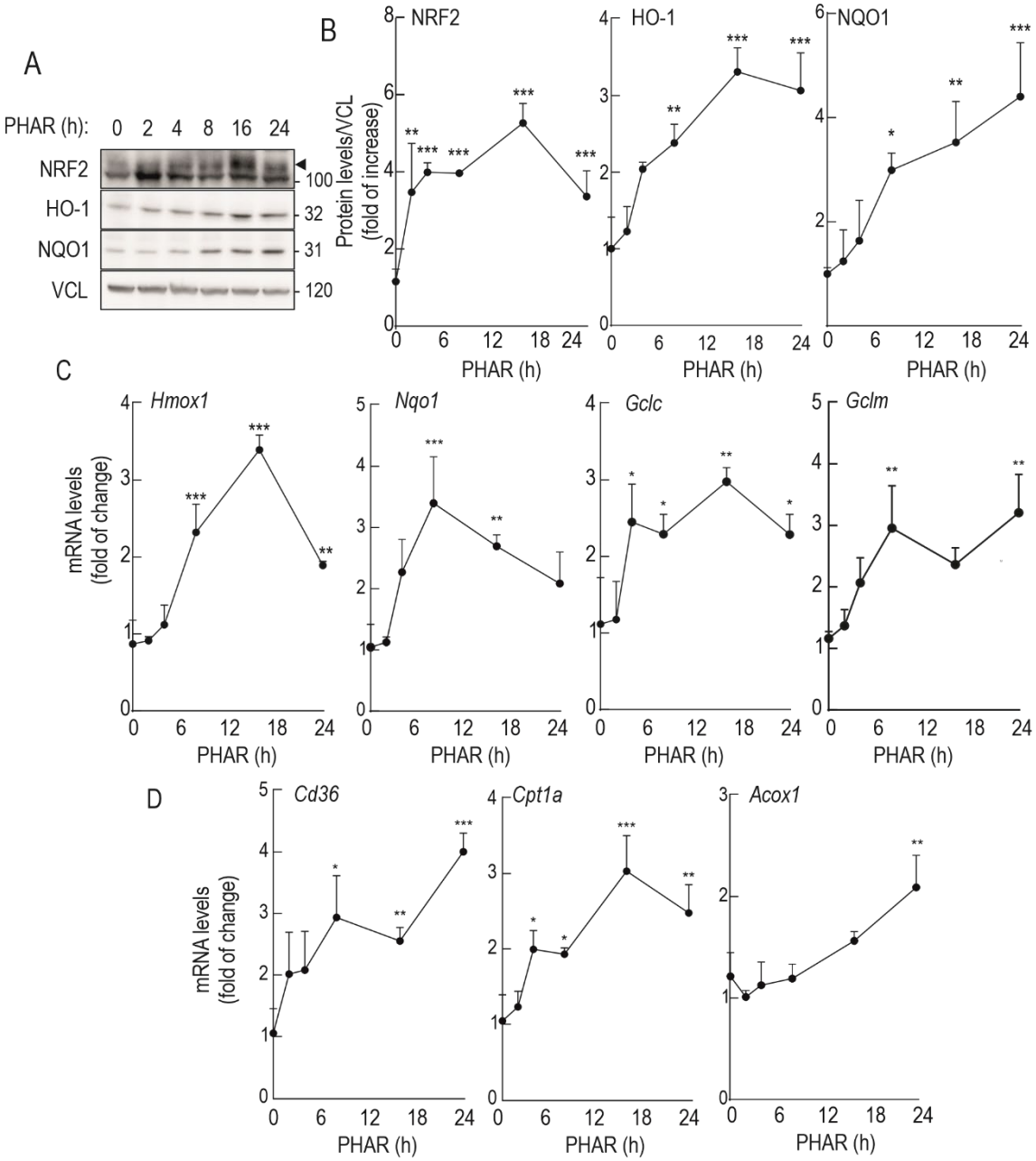
Supplemental Material

Gene product	Forward primer (5'-3')	Reverse primer (5'-3')
Hmox1	CACAGATGGCGTCACTTCGTC	GTGAGGACCCACTGGAGGAG
Nqo1	GGTAGCGGCTCCATGTACTC	CATCCTTCCAGGATCTGCAT
Gclc	TTACCGAGGCTACGTGTCAGAC	TATCGATGGTCAGGTCGATGTC
Gclm	AATCAGCCCCGATTTAGTCAGG	CCAGCGTGCAACTCCAAGGAC
Il1b	CTGGTGTGTGACGTTCCCATTA	CCGACAGCACGAGGCTTT
Tnf	CATCTTCTCAAAATTCGAGTGACAA	TGGGAGTAGACAAGGTACAACCC
Il6	CCTACCCCAATTTCCAATGCT	TATTTTCTGACCACAGTGAGGAATG
Il10	GTAGAAGTGATGCCCCAGGC	GGGGAGAAATCGATGACAGC
Il4	GTAGAAGTGATGCCCCAGGC	GGGGAGAAATCGATGACAGC
Ifng	ATGAACGCTACACACTGCATC	CCATCCTTTTGCCAGTTCCTC
Cpt1a	CTCCGCCTGAGCCATGAAG	CACCAGTGATGATGCCATTCT
Acox1	TCGAAGCCAGCGTTACGAG	TCGAAGCCAGCGTTACGAG
Cd36	AGATGACGTGGCAAAGAACAG	CCTTGGCTAGATAACGAACTCTG
Acaca	ATGGGCGGAATGGTCTCTTTC	TGGGGACCTTGTCTTCATCAT
Fasn	GGAGGTGGTGATAGCCGGTAT	TGGGTAATCCATAGAGCCCAG
Actb	TCCTTCCTGGGCATGGAG	AGGAGGAGCAATGATCTTGATCTT
Gapdh	CGACTTCAACAGCAACTCCCACTCTTCC	TGGGTGGTCCAGGGTTTCTTACTCCTT
Tbp	TGCACAGGAGCCAAGAGTGAA	CACATCACAGCTCCCCACCA

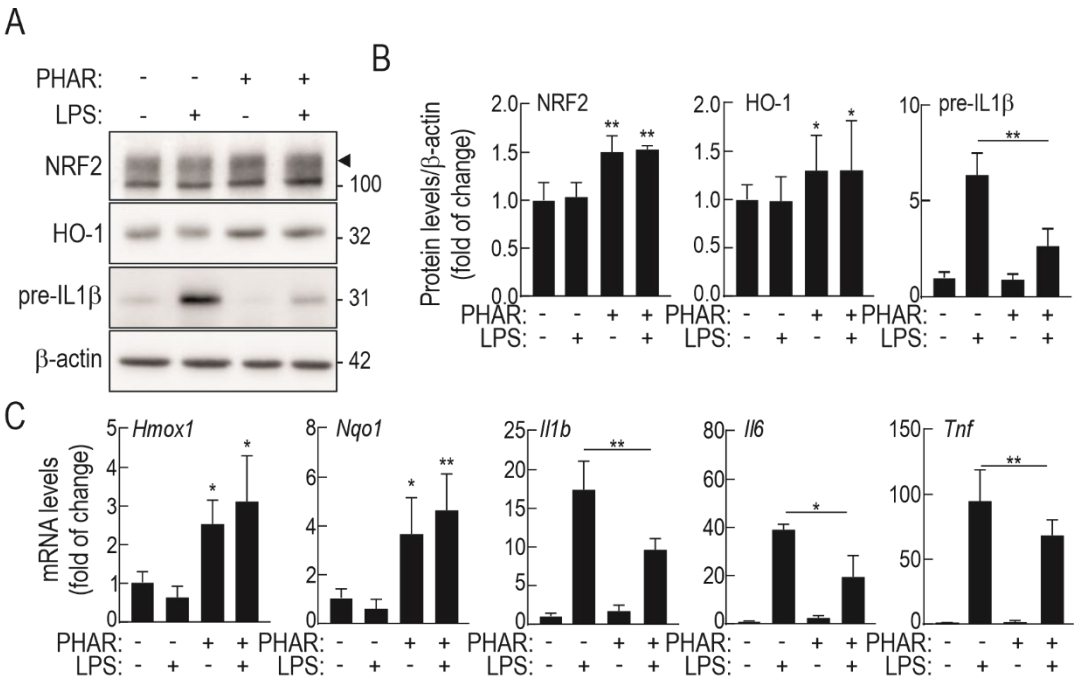
Supplemental Table 1. Mouse primers used for qRT-PCR.

Gene product	Forward primer (5'-3')	Reverse primer (5'-3')
HMOX1	TGCTCAACATCCAGCTCTTTGA	GCAGAATCTTGCACTTTGTTGC
ACTA2	GTGTTGCCCCTGAAGAGCAT	GCTGGGACATTGAAAGTCTCA
COL1A1	GAGGGCCAAGACGAAGACATC	CAGATCACGTCATCGCACAAC
ACTB	TCCTTCCTGGGCATGGAG	AGGAGGAGCAATGATCTTGATCTT
GAPDH	CTCTCTGCTCCTCCTGTTCGAC	TGAGCGATGTGGCTCGGCT
TBP	TGCACAGGAGCCAAGAGTGAA	CACATCACAGCTCCCCACCA

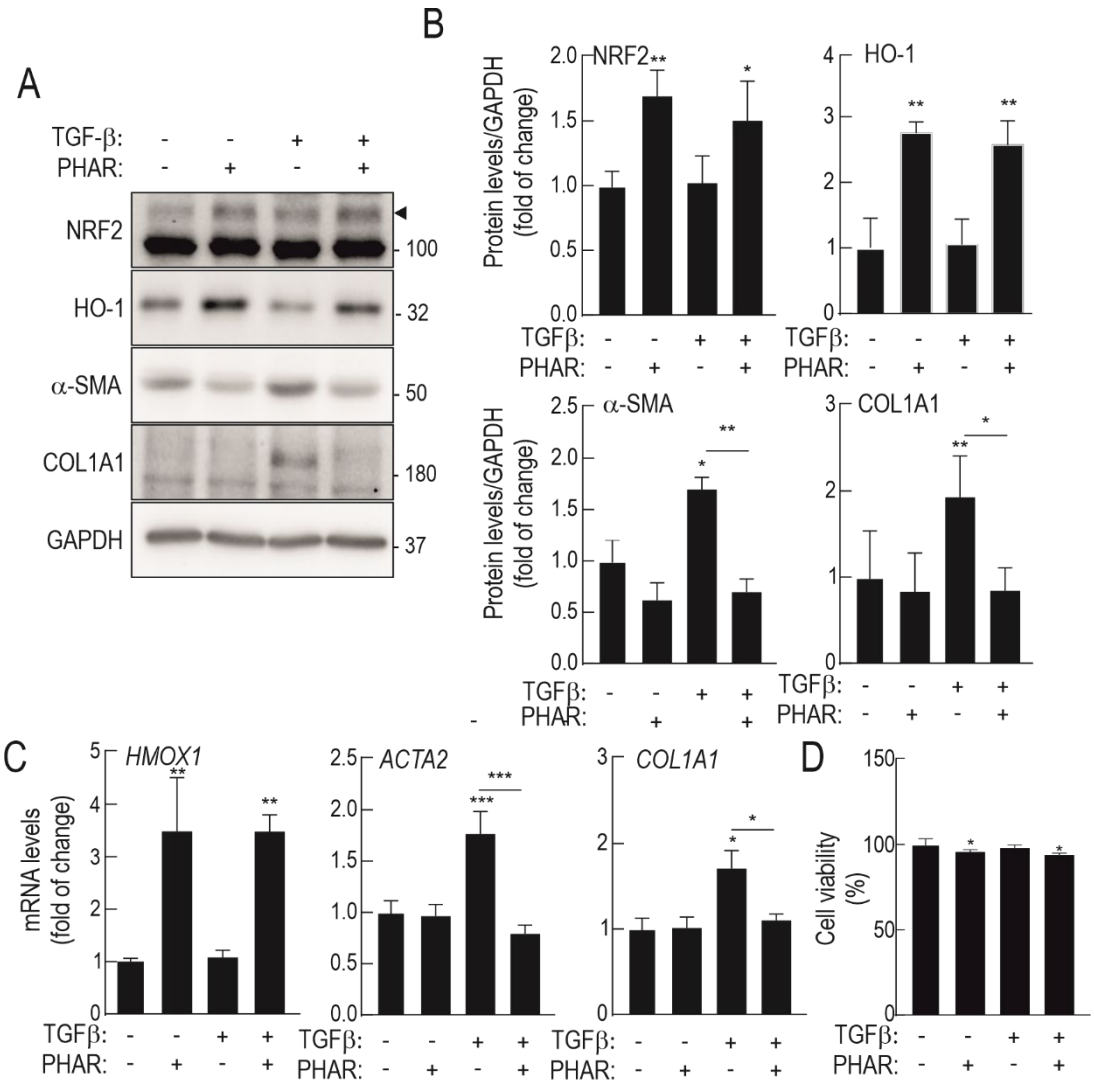
Supplemental Table 2. Human primers used for qRT-PCR of LX-2 cells.



Supplemental Figure 1. The transcriptional activity of NRF2 is stimulated by PHAR in hepatocytes and impacts on the regulation of lipid metabolism. Immortalized hepatocytes were treated with 10 μM of PHAR for indicated time periods. A, representative immunoblots of NRF2, HO-1, NQO1 and VCL as a loading control. Black arrow indicates NRF2 specific band. B, densitometric quantification of NRF2, HO-1 and NQO1 protein levels from representative immunoblots from A, expressed as a ratio of VCL. Data are mean ± S.D. (*n*=3). C-D, mRNA levels of *Hmox1*, *Nqo1*, *Gclc*, *Gclm*, *Cd36*, *Cpt1a* and *Acox1*, determined by qRT-PCR and normalized by the geometric mean of *Gapdh*, *Tbp,* and *Actb* levels. Data are mean ± S.D. (*n*=4). * p<0,5; **p<0,01; ***p<0.001 *vs* time 0 according to a one-way ANOVA followed by Bonferroni post-hoc test.



Supplemental Figure 2. PHAR reduces the inflammatory response in mouse Kupffer cells stimulated with LPS. Kupffer cells were pre-treated with 10 μM of PHAR for 8 h. Then, cells were treated with 100 ng/ml of LPS for 4h. A, representative immunoblots of NRF2, HO-1, pre-IL1β, and β-actin as a loading control. Black arrow indicates NRF2 specific band. B, densitometric analysis of NRF2, HO-1 and pre-IL1β protein levels from representative immunoblot from A, expressed as a ratio of β-actin. Data are mean ± S.D. (*n*=3). C, mRNA levels of *Hmox1, Nqo1, Il1b, Il6* and *Tnf* were determined by qRT-PCR and normalized by the geometric mean of *Gapdh*, *Tbp,* and *Actb* levels. Data are mean ± S.D. (*n*=4). *p<0.05; **p<0,01; ***p<0.001 *vs* vehicle or LPS according to a two-way ANOVA followed by Bonferroni post-hoc test.



Supplemental Figure 3. PHAR protects against TGF-β-induced fibrosis in LX-2 human stellate cells. LX2 cells maintained in low-serum were treated with 10 μM of PHAR or 5ng/ml of TGF-β for 16 h. A, representative immunoblots of NRF2, HO-1, α-SMA, COL1A1 and GAPDH as a loading control. Black arrow indicates NRF2 specific band. B, densitometric analysis of representative immunoblots from A, expressed as a ratio of GAPDH. Data are mean ± S.D. (*n*=3). C, mRNA levels of *HMOX1, ACTA2* and *COL1A1* were determined by qRT-PCR and normalized by the geometric mean of *GAPDH*, *TBP,* and *ACTB* levels. Data are mean ± S.D. (*n*=4). *p<0.05; **p<0,01; ***p<0.001 *vs.* vehicle or TGF-β according to a two-way ANOVA followed by Bonferroni post-hoc test. D, MTT assay was performed to assess cell viability of LX-2-treated cells. Data are mean ± S.D. (n=3). *p<0.05 *vs.* vehicle according to a two-way ANOVA followed by Bonferroni post-hoc test.