Table S1 (related to Figures 1D and 3F). Pathology of human NASH liver samples.

ID	Age	Gender	Pathological diagnoses
1	68	Male	Non-alcoholic steatohepatitis; cirrhosis, mixed macronodular and micronodular type. Minimal inflammatory activity, with minimal or no ongoing steatosis. No evidence of hepatocyte dysplasia or malignancy.
2	56	Female	Type 2 Diabetes. Obesity. Advanced chronic liver disease (stage 4: "cirrhosis"). Marked fibrosis throughout the entire liver. The residual hepatocellular parenchyma shows abundant well-formed Mallory hyaline, consistent with advanced chronic liver disease from steatohepatitis.
3	53	Male	NASH. Cirrhosis. Mild steatosis and focal active steatohepatitis. Focal Mallory hyaline is identified.
4	67	Female	Cirrhosis, NASH. Active steatohepatitis, grade 2 of 3.
5	64	Female	NASH. Cirrhosis with steatohepatitis and moderate macrovesicular steatosis.
6	62	Female	Fatty liver. Cirrhosis. Cirrhosis with moderate macrovesicular steatosis (35%) and focal steatohepatitis, consistent with fatty liver disease.
7	43	Female	Fatty liver. Cirrhosis with focal steatosis and mild activity.
8	57	Female	NASH cirrhosis

Table S2 (related to Figure 2 and Figure S2). Primers used for *WWTR1* mutagenesis.

Primers	5'- Sequence -3'
S58A F	CCTGATgcgGGCTCGCACTCGC
S58A R	CTCCTTAAAG AAAGACTCCG GCAGGATCTT CT
S62A F	TCGCACgcgCGCCAGTCCAG
S62A R	GCCCGAATCA GGCTCCTTAA AGAAAGACTC C
S89A F	TCGCACgcgTCGCCCGCGTCC
S89A R	GCGGACATGC TGGGCACCC
S117A F	CAGCAGgccTACGACGTGACCGACG
S117A R	GCGGAGGTGC GCGTGCTGC
S311A F	GAGCAGgccACTGACAGTGGCCTG
S311A R	CCTCGAATGA TATGGCCCTC CATTGAGGAA AG

Note: lower case letters indicate the mutated nucleotide based on the sequence of WT human *WWTR1* mRNA.

Table S3 (related to all figures). siRNA and shRNA sequences used in this study.

Target Gene	siRNA or shRNA	siRNA Sense Sequences (5' to 3')
Btrc (β-TrCP)	siRNA	rGrArGrCrUrArArArUrUrGrUrGrArUrArCrCrUrUrCrCrUGT
Btrc (β-TrCP)	shRNA	GCGACATAGTTTACAGAGAAT
Lats2	siRNA	rArArGrArUrUrGrUrArUrUrUrArUrGrGrUrArArArArGrGAA
Rhoa	siRNA	rCrUrArCrCrArGrUrArUrUrUrArGrArArGrCrCrCrArArCrCAC
Rhoa	shRNA	GTCAAGCATTTCTGTCCAAAT
Itpr1 (IP3R1)	siRNA	rGrUrUrUrCrArUrCrUrGrCrArArGrCrUrArArUrArArArACA
Itpr2 (IP3R2)	siRNA	rGrCrUrUrUrGrArArGrUrArUrUrUrArCrGrCrCrCrArArCrCrACA
Itpr3 (IP3R3)	siRNA	rGrUrCrCrUrGrCrUrUrArGrUrArCrCrGrUrUrGrArArGrAGA
Prkaca (PKA)	siRNA	rGrGrArUrCrArGrUrUrUrGrArUrArGrArArUrCrArArGrACC
Gramd1b (ASTER-B)	siRNA	rGrGrCrGrUrUrUrCrUrCrUrGrArUrArUrCrArUrCrUrUrCCA
Gramd1b (ASTER-B)	shRNA	GATGAAGGACTCGCTTATCAA
Gramd1c (ASTER-C)	siRNA	rCrArArGrUrCrArCrUrGrGrArCrUrUrGrArArUrArArGrAAT
Gramd1c (ASTER-C)	shRNA	GGGAAAGAGATGAGAAGTTCT
Adcy10 (sAC)	siRNA	rGrArArArUrCrUrCrUrGrArCrGrArArUrGrArArGrArUrUCT
ADCY10 (human sAC)	siRNA	rCrArArUrCrArUrUrUrCrUrArArCrArUrGrUrCrArArArGAA
Cyp27a1	siRNA	rGrUrUrCrCrArGrArArCrUrCrArGrUrCrUrArUrArUrCrACT
Ch25h	siRNA	rArCrCrUrGrArUrUrUrCrUrGrArCrUrCrUrUrUrArArArUAA
Gnas	siRNA	rCrUrUrCrCrCrArCrCrUrGrArArUrUrCrUrArUrGrArGrCAT
Srebp2 (Srebf2)	siRNA	rArGrGrCrArArGrArCrUrGrArUrUrGrUrUrCrUrGrArGrCTG

Table S4 (Related to all figures). Primers used for qPCR.

Primers	Organism	5'- Sequence -3'
Hprt F	mouse	TCAGTCAACGGGGGACATAAA
Hprt R	mouse	GGGGCTGTACTGCTTAACCAG
HPRT F	human	CCTGGCGTCGTGATTAGTGAT
HPRT R	human	AGACGTTCAGTCCTGTCCATAA
Taz (*Wwtr1*) F	mouse	CATGGCGGAAAAAGATCCTCC
Taz (*Wwtr1*) R	mouse	GTCGGTCACGTCATAGGACTG
WWTR1 F	human	TCCCAGCCAAATCTCGTGATG
WWTR1 R	human	AGCGCATTGGGCATACTCAT
Tgfb1 F	mouse	CTCCCGTGGCTTCTAGTGC
Tgfb1 R	mouse	GCCTTAGTTTGGACAGGATCTG
Acta2 F	mouse	ATGCTCCCAGGGCTGTTTTCCCAT
Acta2 R	mouse	GTGGTGCCAGATCTTTTCCATGTCG
Btrc F	mouse	AAGACTGTAATAATGGCGAACCC
Btrc R	mouse	TCTCTTGGTTTATGCAAAGCCTG
Rhoa F	mouse	AGCTTGTGGTAAGACATGCTTG
Rhoa R	mouse	GTGTCCCATAAAGCCAACTCTAC
Col1a1 F	mouse	GCTCCTCTTAGGGGCCACT
Col1a1 R	mouse	CCACGTCTCACCATTGGGG
Col1a2 F	mouse	GTAACTTCGTGCCTAGCAACA
Col1a2 R	mouse	CCTTTGTCAGAATACTGAGCAGC
Col3a1 F	mouse	CTGTAACATGGAAACTGGGGAAA
Col3a1 R	mouse	CCATAGCTGAACTGAAAACCACC
Dpt F	mouse	TGGATGGGTGAATCTTAACCGC
Dpt R	mouse	TCAGAGCCTTCCTTCTTGCTA
Adgre1 (*F4/80,Emr1*) F	mouse	ACCACAATACCTACATGCACC
Adgre1 (*F4/80,Emr1*) R	mouse	AAGCAGGCGAGGAAAAGATAG
Tnfa F	mouse	CTTCTGTCTACTGAACTTCGGG
Tnfa R	mouse	CAGGCTTGTCACTCGAATTTTG
Mcp1 F	mouse	TTAAAAACCTGGATCGGAACCAA
Mcp1 R	mouse	GCATTAGCTTCAGATTTACGGGT
Ihh F	mouse	CTCTTGCCTACAAGCAGTTCA
Ihh R	mouse	CCGTGTTCTCCTCGTCCTT
Spp1 (Opn) F	mouse	CTGACCCATCTCAGAAGCAGAATCT
Spp1 (Opn) R	mouse	TCCATGTGGTCATGGCTTTCATTGG
Timp1 F	mouse	CTCAAAGACCTATAGTGCTGGC
Timp1 R	mouse	CAAAGTGACGGCTCTGGTAG
Last1 F	mouse	TGGTGACTCTGGGGATAAAGAA
Lats1 R	mouse	GGGAGTAACTCTGAATCCGAGAC
Lats2 F	mouse	GGACCCCAGGAATGAGCAG

Lats2 R	mouse	CCCTCGTAGTTTGCACCACC
Itpr1 F	mouse	CGTTTTGAGTTTGAAGGCGTTT
Itpr1 R	mouse	CATCTTGCGCCAATTCCCG
Itpr2 F	mouse	CCTCGCCTACCACATCACC
Itpr2 R	mouse	TCACCACTCTCACTATGTCGT
Itpr3 F	mouse	GGGCGCAGAACAACGAGAT
Itpr3 R	mouse	GAAGTTTTGCAGGTCACGGTT
Gnas F	mouse	CAGAGCCTCCATTGGGGTC
Gnas R	mouse	GCTTCTCGCTCAACTGGGG
Cyp27a1 F	mouse	CCAGGCACAGGAGAGTACG
Cyp27a1 R	mouse	GGGCAAGTGCAGCACATAG
Ch25h F	mouse	TGCTACAACGGTTCGGAGC
Ch25h R	mouse	AGAAGCCCACGTAAGTGATGAT
Prkaca F	mouse	AGATCGTCCTGACCTTTGAGT
Prkaca R	mouse	GGCAAAACCGAAGTCTGTCAC
Gramd1b F	mouse	ACACAATGGGCTACTGTGAGG
Gramd1b R	mouse	GGCTTGGTCTCGATGCTACT
Gramd1c F	mouse	AACAAAGATCAGGCCCACCG
Gramd1c R	mouse	AGTGAGCTCTTCAGCTGTTCC
Adcy10 F	mouse	TGCCAGTGGGATTGTCTTC
Adcy10 R	mouse	TGAGGCCCAAACACTGATAC
ADCY10 F	human	ACAAAGTGTACGACCTTCATGC
ADCY10 R	human	CGAAGCTCAGATAAATAGCCCTG

Hprt, hypoxanthine guanine phosphoribosyl transferase; *Taz* (*Wwtr*1), WW domain containing transcription regulator 1; *Tgfb1*, transforming growth factor, beta 1; *Acta2*, α-smooth muscle actin; *Btrc*, beta-transducin repeat containing protein; *Rhoa*, ras homolog family member A; *Col1a1*, collagen type I alpha 1; *Col1a2*, collagen type I alpha 2; *Col3a1*, collagen, type III, alpha 1; *Dpt*, dermatopontin; *Adgre1* (*F4/80*), adhesion G protein-coupled receptor E1; *Tnfa*, tumor necrosis factor-α ; *Mcp1*, monocyte chemoattractant protein-1; *Ihh*, Indian hedgehog; *Spp1*, secreted phosphoprotein 1; *Timp1*, tissue inhibitor of metalloproteinase 1; *Lats1,* large tumor suppressor; *Lats2,* large tumor suppressor 2; *Itpr1,* inositol 1,4,5-trisphosphate receptor 1; *Itpr2,* inositol 1,4,5-trisphosphate receptor 2; *Itpr3,* inositol 1,4,5-trisphosphate receptor 3; *Gnas,* GNAS (guanine nucleotide binding protein, alpha stimulating) complex locus; *Cyp27a1,* cytochrome P450 family 27 subfamily a polypeptide 1; *Ch25h,* cholesterol 25-hydroxylase; *Prkaca,* protein kinase, cAMP dependent, catalytic, alpha; *Gramd1b*, GRAM domain containing 1B; *Gramd1c*, GRAM domain containing 1C; Adcy10/ADCY10, adenylate cyclase 10.