Figure S1. Alterations and expression of hub genes in 360 patients with hepatocellular carcinoma from the cBioPortal database. (A) OncoPrint schematic of the alterations in HDAC2, HDAC3, SHC1, RAC1, IGF1R and CBL occurred in 7, 11, 21, 12, 11 and 6% of cases, respectively. (B) Expression heatmap of the hub genes. Blue indicates downregulation and red indicates upregulation. HDAC, histone deacetylate; SHC1, SHC-transforming protein 1; RAC1, Ras-related protein Rac1; IGF1R, insulin like growth factor 1 receptor; CBL, E3 ubiquitin-protein ligase CBL.

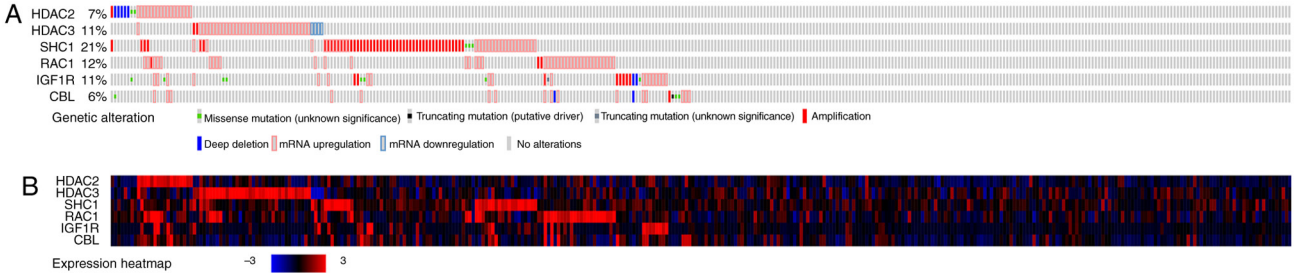

Figure S2. OS curves of 360 HCC cases with or without alterations of hub genes from the cBioPortal database. OS curve of HCC cases based on (A) HDAC2 alteration (log rank P=0.0213), (B) HDAC3 alteration (log rank P=0.373), (C) SHC1 alteration (log rank P=6.153x10^{-3}), (D) RAC1 alteration (log rank P=0.0144), (E) IGF1R alteration (log rank P=0.474) and (F) CBL alteration (log rank P=0.298). OS, overall survival; HCC, hepatocellular carcinoma; HDAC, histone deacetylate; SHC1, SHC-transforming protein 1; RAC1, Ras-related protein Rac1; IGF1R, insulin like growth factor 1 receptor; CBL, E3 ubiquitin-protein ligase CBL.

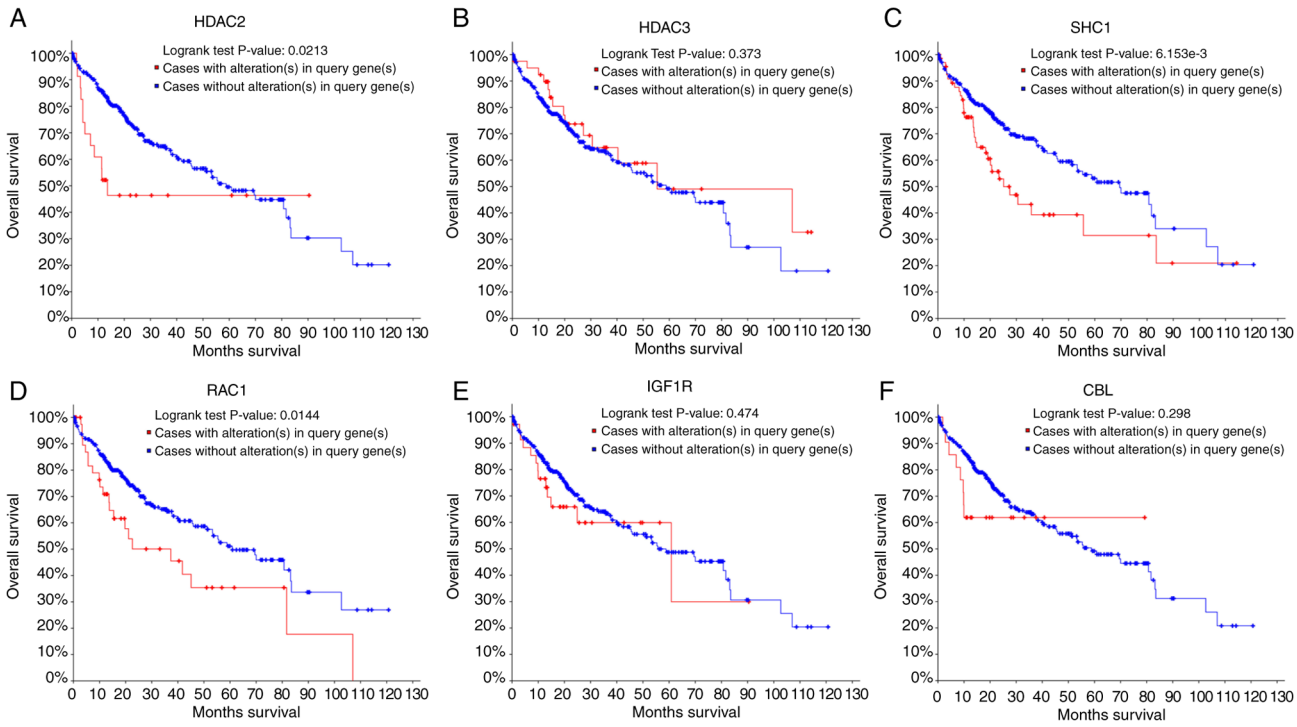

Figure S3. DFS curves of 360 HCC cases with or without alterations of hub genes. DFS curves for HCC cases based on (A) HDAC2 alteration (log rank P=6.488x10^{-3}), (B) HDAC3 alteration (log rank P=0.709), (C) SHC1 alteration (log rank P=0.0347), (D) RAC1 alteration (log rank P=0.516), (E) IGF1R alteration (log rank P=6.991x10^{-3}) and (F) CBL alteration (log rank P=0.0827). DFS, disease-free survival; HDAC, histone deacetylate; SHC1, SHC-transforming protein 1; RAC1, Ras-related protein Rac1; IGF1R, insulin like growth factor 1 receptor; CBL, E3 ubiquitin-protein ligase CBL.

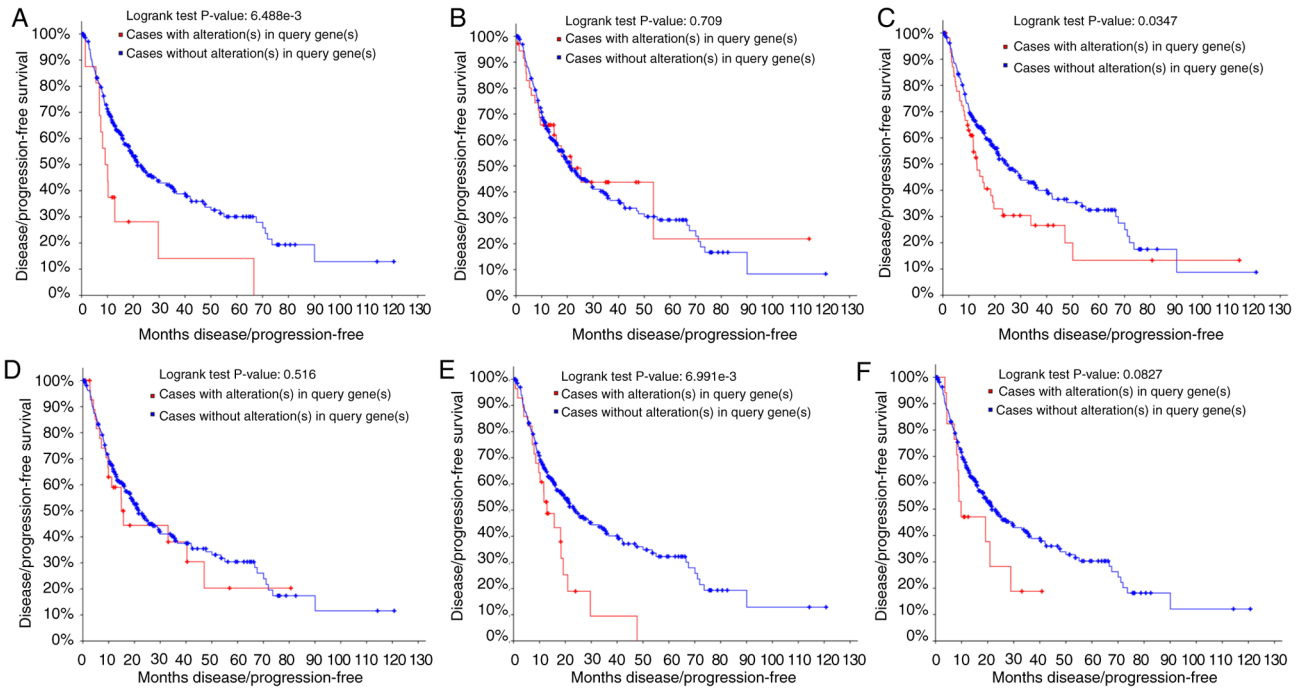

Figure S4. Splicing events of 2 hub genes. (A) Alternative splicing of SHC1-7856-AA was significantly decreased in HCC (P<0.0001). In the code SHC1-7856-AA, SHC1 is the gene symbol, 7856 denotes the order number of the splicing event in the dataset and AA indicates the type of splicing. (B) Alternative splicing of RAC1-78720-ES was significantly increased (P=0.0253) in HCC. AA, alternative acceptor; ES, exon skipping; SHC1, SHC-transforming protein 1; RAC1, Ras-related protein Rac1; HCC, hepatocellular carcinoma.

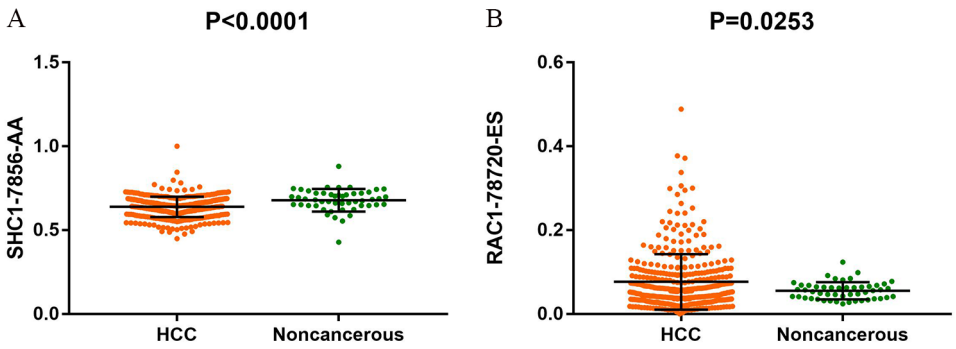

Table SI. Candidate hub genes of microRNA-100-5p.

Gene	Gene entrez ID
AACS	65985
ABCC5	10057
ACAP2	23527
ACBD3	64746
ACKR3	57007
ACOT11	26027
ADAM19	8728
ADAMTS5	11096
ADCY1	107
AGO2	27161
AGPAT4	56895
ALG13	79868
AMMECR1	9949
ANKRD28	23243
ANKRD49	54851
ANKRD52	283373
ANTXR1	84168
AP1AR	55435
AP1S3	130340
API5	8539
ARID3A	1820
ARID3B	10620
ASH2L	9070
ATP11C	286410
ATP2B4	493
ATP6AP1	537
BAG5	9529
BAZ2A	11176
BBX	56987
BCAT1	586
BEND6	221336
BMP2	650
BMPR2	659
BRD3	8019
BTBD9	114781
C10orf25	220979
C14orf28	122525
C1orf115	79762
C20orf166	128826
C20orf194	25943
C5orf22	55322
C7orf26	79034
C9orf170	401535
CACNA1I	8911
CACNG7	59284
CAMTA1	23261
CAND2	23066
CASZ1	54897
CBL	867
CCDC113	29070
CCDC124	115098
CCDC134	79879
CD274	29126
CD93	22918
CDC25A	993
CDH6	1004
CDS2	8760
CEP104	9731
CEP170B	283638

Table SI. Continued.

Gene	Gene entrez ID
CEP85	64793
CHST3	9469
CIRBP	1153
CLCN6	1185
CLDN11	5010
CLDN4	1364
CLYBL	171425
COG5	10466
COL4A3BP	10087
COPS7B	64708
COQ2	27235
CPNE5	57699
CROCC	9696
CTDSP2	10106
CTDSPL	10217
CUX1	1523
CWC25	54883
CXCL16	58191
CYP20A1	57404
CYP26B1	56603
CYP2W1	54905
CYYR1	116159
DDX26B	203522
DESI2	51029
DFFB	1677
DGCR2	9993
DHRS13	147015
DLG5	9231
DNAJB7	150353
DNAJC11	55735
DNAJC5	80331
DNASE2	1777
DPY19L3	147991
DUSP4	1846
E2F2	1870
E2F7	144455
EDC3	80153
EFNB2	1948
ELFN2	114794
ELOVL6	79071
EMR2	30817
EPB41L1	2036
EPC2	26122
EPDR1	54749
ERGIC1	57222
F11R	50848
FAIM2	23017
FAM105B	90268
FAM110D	79927
FAM115C	285966
FAM126B	285172
FAM129A	116496
FAM163A	148753
FAM49A	81553
FAM63B	54629
FAM64A	54478
FARP1	10160
FGF11	2256
FGFR3	2261

Table SI. Continued.

Gene	Gene entrez ID
FKBP5	2289
FOXA1	3169
FOXH1	8928
FOXJ3	22887
FOXO3	2309
FRAT1	10023
FRMD1	79981
FRMD7	90167
FSTL4	23105
FZD1	8321
FZD5	7855
FZD7	8324
FZD8	8325
GABRA2	2555
GALNT11	63917
GATAD2B	57459
GDE1	51573
GDF11	10220
GET4	51608
GFM1	85476
GMDS	2762
GMEB2	26205
GMPS	8833
GNAO1	2775
GNL3L	54552
GNS	2799
GOLGA3	2802
GPR180	160897
GPR26	2849
GPR55	9290
GPRC5B	51704
GRM6	2916
GTF3C1	2975
HCAR3	8843
HDAC2	3066
HDAC3	8841
HDHD2	84064
HDLBP	3069
HES7	84667
HIP1	3092
HIPK2	28996
HIPK3	10114
HLA-DOA	3111
HLCS	3141
HN1L	90861
HOXA1	3198
HOXC5	3222
HS1BP3	64342
HS3ST2	9956
HS3ST3B1	9953
HS6ST1	9394
HSD17B13	345275
HSD3B7	80270
HSP90B1	7184
HSPA12B	116835
ICMT	23463
IFIT2	3433
IFIT3	3437
IGF1R	3480

Table SI. Continued.

Gene	Gene entrez ID
IKZF4	64375
IL22RA1	58985
IMPDH1	3614
INPP4A	3631
INPP5E	56623
INSM1	3642
IRAK3	11213
IREB2	3658
JPH3	57338
KBTBD11	9920
KBTBD8	84541
KCNA7	3743
KCNJ11	3767
KCTD15	79047
KDM6B	23135
KIAA0430	9665
KIAA0754	643314
KLF8	11279
KMO	8564
KMT2D	8085
LAMA5	3911
LDOC1L	84247
LHFPL2	10184
LIF	3976
LOC101928125	101928125
LPP	4026
LPPR4	9890
LRRC8B	23507
LRRFIP2	9209
LRRN1	57633
LURAP1	541468
MAN2A2	4122
MAPRE2	10982
MASP1	5648
MBD3	53615
MBNL1	4154
MBTD1	54799
MCC	4163
MFHAS1	9258
MPP3	4356
MTF1	4520
MTMR3	8897
MTOR	2475
MYCBP	26292
MYCBPAP	84073
MYH10	4628
MYLK4	340156
N4BP3	23138
NARFL	64428
NCMAP	400746
NCS1	23413
NDST1	3340
NDUFA10	4705
NEBL	10529
NEFM	4741
NIP7	51388
NIPBL	25836
NKAIN1	79570
NKTR	4820

Table SI. Continued.

Gene	Gene entrez ID
NLRC3	197358
NLRP2	55655
NOTCH1	4851
NOX4	50507
NPC1	4864
NPR3	4883
NR1I3	9970
NR6A1	2649
NT5DC3	51559
NTSR1	4923
NUDT19	390916
NUP188	23511
NUP62CL	54830
NXF1	10482
ONECUT2	9480
OSBP2	23762
OSBPL2	9885
OTC	5009
OTUD3	23252
P2RX1	5023
PACSIN1	29993
PAPD7	11044
PATE2	399967
PAX2	5076
PCDH7	5099
PCSK9	255738
PDLIM2	64236
PDLIM4	8572
PDXK	8566
PEX19	5824
PEX5L	51555
PGR	5241
PHC3	80012
PHOX2B	8929
PI15	51050
PIK3IP1	113791
PKNOX1	5316
PLCL2	23228
PLXDC1	57125
PLXNA1	5361
PNLIPRP3	119548
PODXL	5420
POLE	5426
POLR2J2	246721
POLR2J3	548644
PPARGC1B	133522
PPFIA3	8541
PPIF	10105
PPM1H	57460
PPP1R3F	89801
PPP1R7	5510
PPP2R3B	28227
PPP3CA	5530
PRDM1	639
PRDM2	7799
PREX1	57580
PRKAB2	5565
PRPH2	5961
PTGES	9536

Table SI. Continued.

Gene	Gene entrez ID
PTPN11	5781
PTPRN2	5799
PWP2	5822
RAB3B	5865
RAC1	5879
RAP1B	5908
RAPH1	65059
RASA2	5922
RASA3	22821
RASGRP3	25780
RASSF4	83937
RASSF6	166824
RAVER2	55225
RBFA	79863
RBM19	9904
RBM22	55696
RCBTB1	55213
RELB	5971
RHBDL3	162494
RHEBL1	121268
RMDN1	51115
RMND5A	64795
RNF144B	255488
RNF213	57674
RPTOR	57521
RRAGD	58528
RRN3	54700
SAE1	10055
SAP30BP	29115
SASH3	54440
SCNN1A	6337
SCNN1G	6340
SEMA4G	57715
SEMA6A	57556
SETD1B	23067
SETX	23064
SGCB	6443
SGCD	6444
SGPL1	8879
SH3BP4	23677
SHC1	6464
SIRT7	51547
SKI	6497
SLC12A2	6558
SLC14A1	6563
SLC18A1	6570
SLC25A38	54977
SLC26A7	115111
SLC27A4	10999
SLC35F1	222553
SLC39A1	27173
SLC44A1	23446
SLC8A2	6543
SMAD7	4092
SMARCA4	6597
SMARCA5	8467
SMARCD1	6602
SMC1A	8243
SMEK2	57223

Table SI. Continued.

Gene	Gene entrez ID
SMPDL3B	27293
SNX9	51429
SORL1	6653
SOX1	6656
SPAG6	9576
SPEN	23013
SPN	6693
SRCIN1	80725
SRMS	6725
SRRM3	222183
SRSF3	6428
SSTR1	6751
ST5	6764
ST6GALNAC4	27090
STAT5B	6777
STK17B	9262
STK24	8428
STK35	140901
STMN3	50861
SUDS3	64426
SULF1	23213
SV2B	9899
SYP	6855
TAOK1	57551
TARDBP	23435
TBC1D16	125058
TBKBP1	9755
TENM1	10178
TFCP2L1	29842
THAP2	83591
THAP6	152815
TIGD6	81789
TIMM10B	26515
TMC2	117532
TMEM135	65084
TMEM236	653567
TMEM30A	55754
TMEM87B	84910
TMPRSS13	84000
TNFAIP8L1	126282
TNNI3K	51086
TRIB1	10221
TRIB2	28951
TRIM2	23321
TRIM41	90933
TSPAN11	441631
TSPAN14	81619
TSPYL2	64061
TSPYL4	23270
TTC1	7265
TTC22	55001
TTC30A	92104
TTC38	55020
TTC39A	22996
TTLL7	79739
TTYH3	80727
U2SURP	23350
UBE4A	9354
UGCG	7357

Table SI. Continued.

Gene	Gene entrez ID
UHRF1BP1	54887
USP12	219333
USP51	158880
VENTX	27287
VLDLR	7436
VNN1	8876
WDFY3	23001
WWC3	55841
XPNPEP3	63929
XXYLT1	152002
YIPF6	286451
ZADH2	284273
ZBTB4	57659
ZBTB7A	51341
ZCCHC12	170261
ZDHHC18	84243
ZFAT	57623
ZFX	7543
ZFYVE19	84936
ZFYVE20	64145
ZNF106	64397
ZNF19	7567
ZNF197	10168
ZNF317	57693
ZNF483	158399
ZNF554	115196
ZNF595	152687
ZNF618	114991
ZNF704	619279
ZNF75A	7627
ZNF786	136051
ZNF845	91664
ZNRF2	223082
ZZEF1	23140