Supplementary information

Inactivating mutations of the chromatin remodeling gene *ARID2* in hepatocellular carcinoma

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Supplementary Methods

Preparation of clinical samples

Fresh-frozen surgically resected tumor and matched normal adjacent tissues were obtained from patients treated at the Johns Hopkins Hospital, Cancer Institute and Hospital of Chinese Academy of Medical Sciences and Peking Union Medical College and University Medical Center Utrecht under Institutional Review Board protocols. Tumor tissue was analyzed by frozen section to assess neoplastic cellularity. Tumors were macrodissected to remove residual normal tissue and enhance neoplastic cellularity, as confirmed by multiple frozen sections. Normal tissue was also analyzed by frozen section to confirm the presence of only non-neoplastic tissue.

Preparation of Illumina genomic DNA libraries

Genomic DNA libraries were prepared following Illumina's (Illumina, San Diego, CA) suggested protocol with the following modifications. (**1**) 3 micrograms (µg) of genomic DNA from tumor or normal cells in 100 microliters (µl) of TE was fragmented in a Covaris sonicator (Covaris, Woburn, MA) to a size of 100-500 bp. DNA was purified with a PCR purification kit (Cat # 28104, Qiagen, Valencia, CA) and eluted in 35 µl of elution buffer included in the kit. (**2**) Purified, fragmented DNA was mixed with 40 µl of H_2O, 10 µl of 10 x T4 ligase buffer with 10 mM ATP, 4 µl of 10 mM dNTP, 5 µl of T4 DNA polymerase, 1 µl of Klenow Polymerase, and 5 µl of T4 polynucleotide Kinase. All reagents used for this step and those described below were from New England Biolabs (NEB, Ipswich, MA) unless otherwise specified. The 100 µl end-repair mixture was incubated at 20°C for 30 min, purified by a PCR purification kit (Cat # 28104, Qiagen) and eluted with 32 µl of elution buffer (EB). (**3**) To A-tail, all 32 µl of end-repaired DNA was mixed with 5 µl of 10 x Buffer (NEB buffer 2), 10 µl of 1 mM dATP and 3 µl of Klenow (exo-). The 50 µl mixture was incubated at 37°C for 30 min before DNA was purified with a MinElute PCR purification kit (Cat # 28004, Qiagen). Purified DNA was eluted with 12.5 µl of 70°C EB and obtained with 10 µl of EB. (**4**) For adaptor ligation, 10 µl of A-tailed DNA was mixed with 10 µl of PE-adaptor (Illumina), 25 µl of 2x Rapid ligase buffer and 5 µl of Rapid Ligase. The ligation mixture was incubated at room temperature (RT) or 20°C for 15 min. (**5**) To purify adaptor- ligated DNA, 50 µl of ligation mixture from step (4) was mixed with 200 µl of NT buffer from NucleoSpin Extract II kit (cat# 636972, Clontech, Mountain View, CA) and loaded into NucleoSpin column. The column was centrifuged at 14000 g in a desktop centrifuge for 1 min, washed once with 600 µl of wash buffer (NT3 from Clontech), and centrifuged again for 2 min to dry completely. DNA was eluted in 50 µl elution buffer included in the kit. (**6**) To obtain an amplified library, ten PCRs of 25 µl each were set up, each including 13.25 µl of H_2O, 5 µl of 5 x Phusion HF buffer, 0.5 µl of a dNTP mix containing 10 mM of each dNTP, 0.5 µl of Illumina PE primer #1, 0.5 µl of Illumina PE primer #2, 0.25 µl of Hotstart Phusion polymerase, and 5 µl of the DNA from step (5). The PCR program used was: 98°C 1 minute; 6 cycles of 98°C for 20 seconds, 65°C for 30 seconds, 72oC for 30 seconds; and 72oC for 5 min. To purify the PCR product, 250 µl PCR mixture (from the ten PCR reactions) was mixed with 500 µl NT buffer from a NucleoSpin Extract II kit and purified as described in step (5). Library DNA was eluted with 70°C-warm elution buffer and the DNA concentration was estimated by absorption at 260 nm.

Exome and targeted subgenomic DNA capture

Human exome capture was performed following a protocol from Agilent's SureSelect Paired-End Version 2.0 Human Exome Kit (Agilent, Santa Clara, CA) with the following modifications.

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(1) A hybridization mixture was prepared containing 25 µl of SureSelect Hyb # 1, 1 µl of SureSelect Hyb # 2, 10 µl of SureSelect Hyb # 3, and 13 µl of SureSelect Hyb # 4. **(2)** 3.4 µl (0.5 µg) of the PE-library DNA described above, 2.5 µl of SureSelect Block #1, 2.5 µl of SureSelect Block #2 and 0.6 µl of Block #3; was loaded into one well in a 384-well Diamond PCR plate (cat# AB-1111, Thermo-Scientific, Lafayette, CO), sealed with microAmp clear adhesive film (cat# 4306311; ABI, Carlsbad, CA) and placed in GeneAmp PCR system 9700 thermocycler (Life Sciences Inc., Carlsbad CA) for 5 minutes at 95°C, then held at 65°C (with the heated lid on). **(3)** 25-30 µl of hybridization buffer from step (1) was heated for at least 5 minutes at 65°C in another sealed plate with heated lid on. **(4)** 5 µl of SureSelect Oligo Capture Library, 1 µl of nuclease-free water, and 1 µl of diluted RNase Block (prepared by diluting RNase Block 1: 1 with nuclease-free water) were mixed and heated at 65^oC for 2 minutes in another sealed 384-well plate. **(5)** While keeping all reactions at 65°C, 13 µl of Hybridization Buffer from Step (3) was added to the 7 µl of the SureSelect Capture Library Mix from Step (4) and then the entire contents (9 µl) of the library from Step (2). The mixture was slowly pipetted up and down 8 to 10 times. **(6)** The 384-well plate was sealed tightly and the hybridization mixture was incubated for 24 hours at 65°C with a heated lid.

After hybridization, five steps were performed to recover and amplify captured DNA library: **(1)** Magnetic beads for recovering captured DNA: 50 µl of Dynal MyOne Streptavidin C1 magnetic beads (Cat # 650.02, Invitrogen Dynal, AS Oslo, Norway) was placed in a 1.5 ml microfuge tube and vigorously resuspended on a vortex mixer. Beads were washed three times by adding 200 µl of SureSelect Binding buffer, mixing on a vortex for five seconds and then removing the supernatant after placing the tubes in a Dynal magnetic separator. After the third wash, beads were resuspended in 200 µl of SureSelect Binding buffer. **(2)** To bind captured DNA, the entire hybridization mixture described above (29 µl) was transferred directly from the thermocycler to the bead solution and mixed gently; the hybridization mix /bead solution was incubated an Eppendorf thermomixer at 850rpm for 30 minutes at room temperature. **(3)** To wash the beads, the supernatant was removed from beads after applying a Dynal magnetic separator and the beads was resuspended in 500 µl SureSelect Wash Buffer #1 by mixing on vortex mixer for 5 seconds and incubated for 15 minutes at room temperature. Wash Buffer#1 was then removed from beads after magnetic separation. The beads were further washed three times, each with 500 µl pre-warmed SureSelect Wash Buffer #2 after incubation at 65°C for 10 minutes. After the final wash, SureSelect Wash Buffer #2 was completely removed. **(4)** To elute captured DNA, the beads were suspended in 50 µl SureSelect Elution Buffer, vortex-mixed and incubated for 10 minutes at room temperature. The supernatant was removed after magnetic separation, collected in a new 1.5 ml microcentrifuge tube, and mixed with 50 µl of SureSelect Neutralization Buffer. DNA was purified with a Qiagen MinElute column and eluted in 17 µl of 70^oC EB to obtain 15 µl of captured DNA library. **(5)** The captured DNA library was amplified in the following way: 15 PCR reactions each containing 9.5 µl of H_2O, 3 µl of 5 x Phusion HF buffer, 0.3 µl of 10 mM dNTP, 0.75 µl of DMSO, 0.15 µl of Illumina PE primer #1, 0.15µl of Illumina PE primer #2, 0.15 µl of Hotstart Phusion polymerase, and 1 µl of captured exome library were set up. The PCR program used was: 98^oC for 30 seconds; 14 cycles of 98^oC for 10 seconds, 65^oC for 30 seconds, 72^oC for 30 seconds; and 72^oC for 5 min. To purify PCR products, 225µl PCR mixture (from 15 PCR reactions) was mixed with 450 µl NT buffer from NucleoSpin Extract II kit and purified as described above. The final library DNA was eluted with 30 µl of 70^oC elution buffer and DNA concentration was estimated by OD260 measurement.

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Somatic mutation identification by massively parallel sequencing
Captured DNA libraries were sequenced with the Illumina GAIIx Genome Analyzer, yielding 150 (2 X 75) base pairs from the final library fragments. Sequencing reads were analyzed and aligned to human genome hg18 with the Eland algorithm in CASAVA 1.6 software (Illumina). A mismatched base was identified as a mutation only when (i) it was identified by more than three distinct tags; (ii) the number of distinct tags containing a particular mismatched base was at least 15% of the total distinct tags; and (iii) it was not present in >0.5% of the tags in the matched normal sample. SNP search databases included
http://www.ncbi.nlm.nih.gov/projects/SNP/ and http://browser.1000genomes.org/index.html.

Evaluation of genes in additional tumors and matched normal controls.
For the *ARID2, CTNNB1, TP53, DMXL1* and *NLRP1* genes that were mutated in at least 2 tumors in the discovery screen, the coding region was sequenced in two validation sets, comprising additional 129 hepatocellular carcinoma tumors and matched controls. PCR amplification and Sanger sequencing were performed following protocols described previously[1] using the primers listed in supplementary table 4.

Statistics

Two-tailed *P* values were calculated using Fisher's exact test.

References

S1.   Sjoblom, T. et al. The consensus coding sequences of human breast and colorectal cancers. *Science* 314, 268-74 (2006).

Supplementary Figure 1
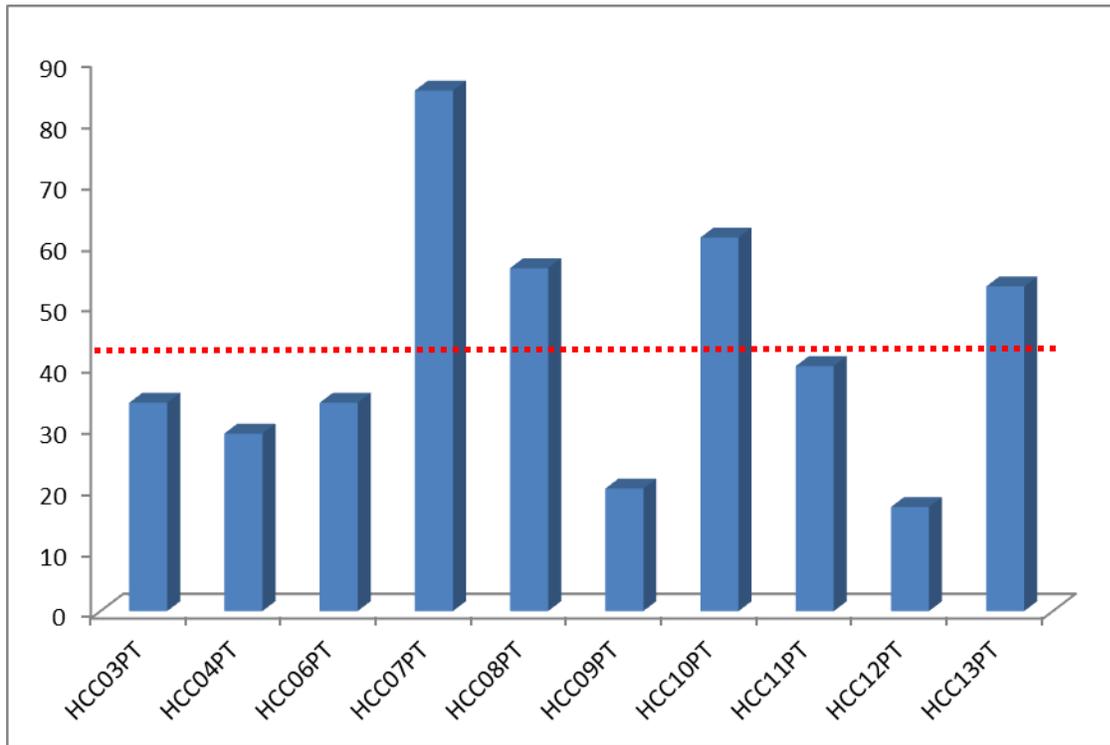
Supplementary Figure 1: Number of non-synonymous somatic mutations identified through exome sequencing of 10 HCV-associated HCCs. Dotted line indicated the mean, 42.9 non-synonymous somatic mutations per HCC tumor.

Supplementary Figure 2

a

ARID2
HCC05PT
g.chr12, 44410093G>A
c.IVS93-1G>A, splice site

ARID2
HCC07PT
g.chr12, 44517604G>T
p. E393X

ARID2
HCC21PT
g.chr12, 44530611delC
frameshift

b

ARID2

ARID   LXXLL   RFX   ZnF
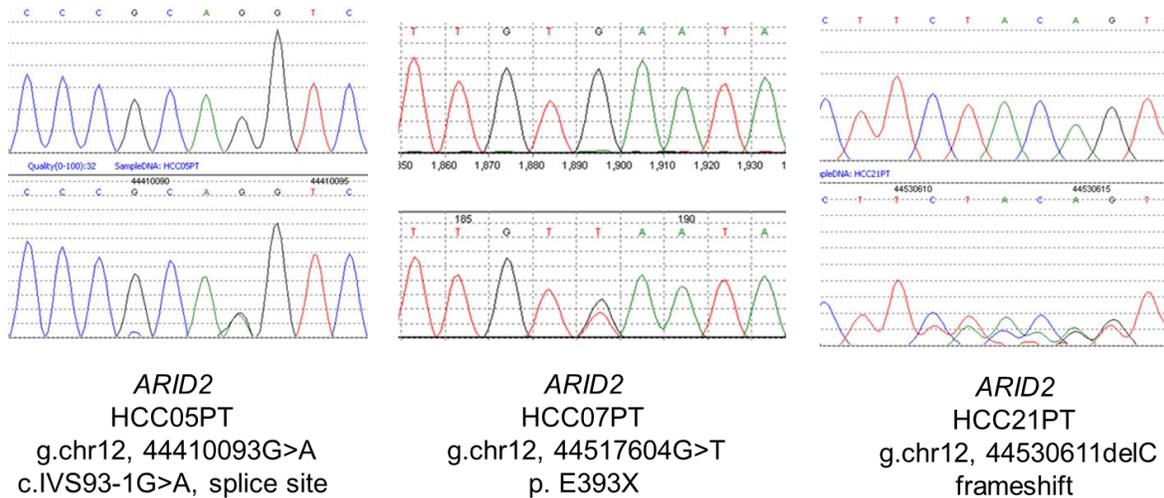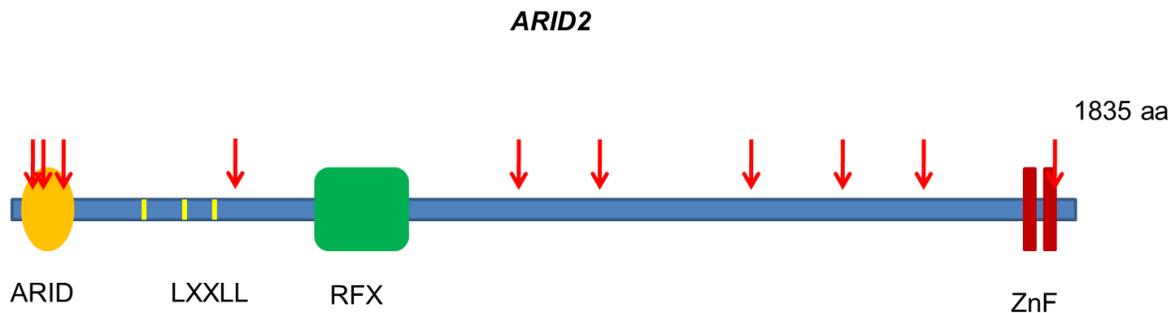
Supplementary Figure 2: Somatic mutations in the *ARID2* gene. a. Examples of sequence chromatograms showing inactivating somatic mutations of *ARID2* in HCC tumors (lower panels) but not in matched normal control samples (upper panels). b. Somatic mutations identified in the *ARID2* gene. Truncating mutations are indicated by red arrows. ARID, AT-rich interaction domain; LXXLL, Leu-Xaa-Xaa-Leu-Leu motif; RFX, RFX-like DNA binding motif; ZnF, C2H2 Zinc Fingers.

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Supplementary Table 1. Clinical characteristics of hepatocellular carcinoma samples used in the discovery screen

Sample	Age	Sex	Self-reported Ethnicity	Geographic location	Etiology	Stage	Source of tumor DNA	Histological type	Source of matched normal DNA
HCC03T	67	Male	White	United States	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC04T	46	Male	White	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC06T	59	Female	White	United States	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC07T	59	Male	Black	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC08T	51	Female	White	United States	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC09T	56	Female	Black	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC10T	56	Male	White	United States	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC11T	60	Male	Black	United States	HCV	T3b	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC12T	61	Female	White	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC13T	56	Male	Black	United States	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver

Supplementary Table 2. Summary of sequence analysis of hepatocellular carcinomas in the discovery screen

Sample	Sample type	Bases in target region	Bases sequenced (after quality filtering)	Bases mapped to genome	Bases mapped to targeted region	Average # of reads per targeted base	Targeted bases with at least 10 reads (%)	Known SNPs identified in targeted region
HCC03N	Normal	37,806,033	13,471,487,250	11,479,098,450	4,934,096,276	128.0	95.7%	21,265
HCC03T	Primary tumor	37,806,033	12,150,135,150	10,280,356,725	4,297,274,742	106.7	95.3%	21,146
HCC04N	Normal	37,806,033	11,657,716,350	9,867,968,925	4,289,350,945	111.1	95.5%	19,363
HCC04T	Primary tumor	37,806,033	13,162,622,850	11,330,038,200	4,894,120,601	123.0	96.1%	19,373
HCC06N	Normal	37,806,033	7,977,985,350	6,876,156,150	2,999,128,839	78.8	93.9%	19,611
HCC06T	Primary tumor	37,806,033	7,061,294,700	6,114,484,125	2,642,547,690	68.4	92.9%	19,334
HCC07N	Normal	37,806,033	7,073,294,550	6,054,591,600	2,634,280,037	69.3	93.1%	21,348
HCC07T	Primary tumor	37,806,033	8,219,748,750	7,050,607,500	3,036,867,954	78.4	94.1%	21,349
HCC08N	Normal	37,806,033	10,833,485,250	9,318,566,250	4,208,008,785	109.9	94.9%	19,619
HCC08T	Primary tumor	37,806,033	9,666,538,050	8,371,581,900	3,644,699,213	92.9	94.7%	19,504
HCC09N	Normal	37,806,033	9,755,729,250	8,183,036,250	3,524,782,995	91.3	94.3%	21,434
HCC09T	Primary tumor	37,806,033	11,109,517,050	9,373,906,125	4,001,761,649	99.5	95.1%	21,459
HCC10N	Normal	37,806,033	12,103,302,300	10,467,227,175	4,710,373,502	122.8	95.6%	19,619
HCC10T	Primary tumor	37,806,033	5,956,198,050	5,142,645,450	2,210,413,571	57.1	91.5%	19,293
HCC11N	Normal	37,806,033	11,595,139,200	9,980,277,900	3,893,912,617	101.7	95.6%	21,456
HCC11T	Primary tumor	37,806,033	12,791,470,800	11,124,790,500	4,536,645,518	114.1	95.2%	21,360
HCC12N	Normal	37,806,033	12,767,426,775	11,179,805,025	4,434,897,498	115.1	95.8%	19,476
HCC12T	Primary tumor	37,806,033	16,577,510,850	12,889,029,150	4,938,244,630	117.6	94.8%	19,339
HCC13N	Normal	37,806,033	8,932,602,600	7,743,654,150	3,193,377,937	83.3	94.7%	21,456
HCC13T	Primary tumor	37,806,033	10,900,646,700	9,335,411,400	4,038,932,281	100.4	95.5%	21,126
Average		37,806,033	10,688,192,591	9,108,161,648	3,853,185,864	98	94.7%	20,397

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Supplementary Table 3. Non-synonymous somatic mutations identified in ten HCV-associated HCCs in the discovery screen

Gene Symbol	Gene ID	Tumor Samples	Nucleotide (genomic)*	Amino acid (protein)	Mutation Type	Visual confirmation
CHD5	ENSG00000116254	HCC08T	g.chr1: 6126541T>C	p. R658G	Missense	Yes
GPR153	ENSG00000158292	HCC03T	g.chr1: 6237231G>A	p. R108C	Missense	Yes
SLC45A1	ENSG00000162426	HCC07T	g.chr1: 8320588A>G	p. M575V	Missense	Yes
RERE	ENSG00000142599	HCC13T	g.chr1: 8477799C>A	p. A339S	Missense	Yes
UBR4	ENSG00000127481	HCC10T	g.chr1: 19396310C>A	p. L310F	Missense	Yes
KIF17	ENSG00000117245	HCC11T	g.chr1: 20887010C>A	p. V466L	Missense	Yes
SPOCD1	ENSG00000134668	HCC09T	g.chr1: 32053496C>T	p. G9D	Missense	Yes
TRIT1	ENSG00000043514	HCC11T	g.chr1: 40086327C>A	p. D245Y	Missense	Yes
PTPRF	ENSG00000142949	HCC10T	g.chr1: 43841783C>T	p. T817I	Missense	Yes
RAD54L	ENSG00000085999	HCC03T	g.chr1: 46499630G>C	p. V293L	Missense	Yes
PRPF38A	ENSG00000134748	HCC11T	g.chr1: 52646843T>A	p. L102Q	Missense	Yes
LRRIQ3	ENSG00000162620	HCC07T	g.chr1: 74280133G>A	p. P357L	Missense	Yes
LPHN2	ENSG00000117114	HCC13T	g.chr1: 82229247G>T	p. D1348Y	Missense	Yes
AMY2A	ENSG00000196318	HCC07T	g.chr1: 103963742A>T	p. E186V	Missense	Yes
CSF1	ENSG00000184371	HCC08T	g.chr1: 110268112G>T	p. R449L	Missense	Yes
VANGL1	ENSG00000173218	HCC13T	g.chr1: 116029605C>A	p. N416K	Missense	Yes
IGSF3	ENSG00000143061	HCC10T	g.chr1: 116960444C>T	p. E68K	Missense	Yes
CD2	ENSG00000116824	HCC03T	g.chr1: 117104591A>T	p. T143S	Missense	Yes
TTF2	ENSG00000116830	HCC03T	g.chr1: 117419846G>T	p. D373Y	Missense	Yes
HIST2H3D	ENSG00000183598	HCC10T	g.chr1: 148051779T>A	p. K28X	Nonsense	Yes
PGLYRP3	ENSG00000159527	HCC03T	g.chr1: 151543028C>G	p. R153T	Missense	Yes
S100A3	ENSG00000188015	HCC10T	g.chr1: 151787461A>T	p. L42Q	Missense	Yes
TMEM79	ENSG00000163472	HCC08T	g.chr1: 154522815G>A	p. V300M	Missense	Yes
OR10R2	ENSG00000198965	HCC08T	g.chr1: 156717154C>A	p. S288Y	Missense	Yes
MNDA	ENSG00000163563	HCC04T	g.chr1: 157080438C>A	p. P158T	Missense	Yes
DUSP27	ENSG00000198842	HCC03T	g.chr1: 165363653delG	fs	Indel	Yes
SERPINC1	ENSG00000117601	HCC10T	g.chr1: 172146517T>C	p. K254E	Missense	Yes
TNN	ENSG00000120332	HCC12T	g.chr1: 173315304G>A	p. G208R	Missense	Yes
FAM5B	ENSG00000198797	HCC13T	g.chr1: 175465795C>T	p. P54S	Missense	Yes
DHX9	ENSG00000135829	HCC07T	g.chr1: 181113898G>T	p. C773F	Missense	Yes
RGL1	ENSG00000143344	HCC07T	g.chr1: 181977938A>T	p. E8V	Missense	Yes
TPR	ENSG00000047410	HCC12T	g.chr1: 184594299T>A	p. Q499L	Missense	Yes
LHX9	ENSG00000143355	HCC13T	g.chr1: 196155765C>T	p. A72V	Missense	Yes
CAMSAP1L1	ENSG00000118200	HCC09T	g.chr1: 199084022G>A	p. C501Y	Missense	Yes
CAMSAP1L1	ENSG00000118200	HCC10T	g.chr1: 199085516A>G	p. D999G	Missense	Yes
SYT2	ENSG00000143858	HCC09T	g.chr1: 200841410C>G	p. E38D	Missense	Yes
TMCC2	ENSG00000133069	HCC11T	g.chr1: 203477391T>C	p. S115P	Missense	Yes
SLC45A3	ENSG00000158715	HCC07T	g.chr1: 203897722A>G	p. S372P	Missense	Yes
PTPN14	ENSG00000152104	HCC07T	g.chr1: 212616239C>A	p. E951D	Missense	Yes
PTPN14	ENSG00000152104	HCC07T	g.chr1: 212616240T>A	p. E951V	Missense	Yes
SUSD4	ENSG00000143502	HCC06T	g.chr1: 221504717G>T	p. P201Q	Missense	Yes
ITPKB	ENSG00000143772	HCC13T	g.chr1: 224991020C>G	p. V255L	Missense	Yes
OR2T4	ENSG00000196944	HCC06T	g.chr1: 246591615A>G	p. N37S	Missense	Yes
TUBAL3	ENSG00000178462	HCC09T	g.chr10: 5425865T>C	p. Y319C	Missense	Yes
PLXDC2	ENSG00000120594	HCC11T	g.chr10: 20146074C>G	p. F20L	Missense	Yes
SLC18A3	ENSG00000187714	HCC07T	g.chr10: 50489703C>T	p. P304L	Missense	Yes
SGMS1	ENSG00000198964	HCC06T	g.chr10: 51773591C>A	p. S97I	Missense	Yes
MYPN	ENSG00000138347	HCC09T	g.chr10: 69629218G>C	p. E1125Q	Missense	Yes

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HK1	ENSG00000156515	HCC08T	g.chr10: 70799287C>T	p. T263I	Missense	Yes
PLCE1	ENSG00000138193	HCC08T	g.chr10: 95781743G>A	p. S317N	Missense	Yes
COX15	ENSG00000014919	HCC07T	g.chr10: 101479441C>T	p. S44N	Missense	Yes
ABCC2	ENSG00000023839	HCC08T	g.chr10: 101559927A>G	p. D621G	Missense	Yes
COL17A1	ENSG00000065618	HCC09T	g.chr10: 105810007C>T	p. S334N	Missense	Yes
PNLIPRP1	ENSG00000187021	HCC07T	g.chr10: 118354904G>T	p. G397C	Missense	Yes
PPP2R2D	ENSG00000175470	HCC07T	g.chr10: 133611260G>A	p. E126K	Missense	Yes
SIGIRR	ENSG00000185187	HCC13T	g.chr11: 397098G>A	p. A231V	Missense	Yes
HRAS	ENSG00000174775	HCC09T	g.chr11: 523874T>A	p. Q61L	Missense	Yes
MRGPRE	ENSG00000184350	HCC11T	g.chr11: 3205905C>A	p. G233V	Missense	Yes
ART1	ENSG00000129744	HCC07T	g.chr11: 3637474A>G	p. Y50C	Missense	Yes
STIM1	ENSG00000167323	HCC08T	g.chr11: 3945445A>G	p. D76G	Missense	Yes
OR52N5	ENSG00000181009	HCC11T	g.chr11: 5755509T>C	p. K311R	Missense	Yes
ST5	ENSG00000166444	HCC07T	g.chr11: 8708425C>T	p. A330T	Missense	Yes
SAA4	ENSG00000148965	HCC06T	g.chr11: 18214049T>C	p. M1V	Missense	Yes
MRGPRX2	ENSG00000183695	HCC04T	g.chr11: 19034104C>T	p. R141H	Missense	Yes
OR4C12	ENSG00000221954	HCC08T	g.chr11: 49959956A>T	p. L220M	Missense	Yes
OR5AP2	ENSG00000172464	HCC07T	g.chr11: 56166000T>C	p. I164M	Missense	Yes
FAM111B	ENSG00000189057	HCC07T	g.chr11: 58648985A>G	p. H280R	Missense	Yes
OR10V1	ENSG00000172289	HCC04T	g.chr11: 59237796C>A	p. M33I	Missense	Yes
FADS2	ENSG00000134824	HCC08T	g.chr11: 61387047A>G	p. I304V	Missense	Yes
RAB3IL1	ENSG00000167994	HCC04T	g.chr11: 61426573C>A	p. G306W	Missense	Yes
CDC42BPG	ENSG00000171219	HCC08T	g.chr11: 64359467C>A	p. R627S	Missense	Yes
IGHMBP2	ENSG00000132740	HCC13T	g.chr11: 68460880G>A	p. A786T	Missense	Yes
P4HA3	ENSG00000149380	HCC07T	g.chr11: 73674959C>T	p. D299N	Missense	Yes
SERPINH1	ENSG00000149257	HCC13T	g.chr11: 74957448A>G (Homo)	p. H216R	Missense	Yes
C11orf30	ENSG00000158636	HCC07T	g.chr11: 75934715T>A	p. I1167K	Missense	Yes
RAB30	ENSG00000137502	HCC13T	g.chr11: 82370959G>A	p. L170F	Missense	Yes
PICALM	ENSG00000073921	HCC13T	g.chr11: 85420301T>C (Homo)	p. Y44C	Missense	Yes
GRIA4	ENSG00000152578	HCC09T	g.chr11: 105300351T>A	p. I498N	Missense	Yes
CCDC84	ENSG00000186166	HCC07T	g.chr11: 118387189C>T	p. R167W	Missense	Yes
GRIK4	ENSG00000149403	HCC09T	g.chr11: 120358073G>T	p. G815V	Missense	Yes
TECTA	ENSG00000109927	HCC03T	g.chr11: 120505630G>A	p. S814N	Missense	Yes
SORL1	ENSG00000137642	HCC10T	g.chr11: 120950229A>G	p. Y1136C	Missense	Yes
KCNA5	ENSG00000130037	HCC06T	g.chr12: 5024323G>A	p. R250Q	Missense	Yes
CLEC7A	ENSG00000172243	HCC03T	g.chr12: 10171277T>G	p. X78Y	Missense	Yes
CAPZA3	ENSG00000177938	HCC13T	g.chr12: 18782614G>T	p. E49X	Nonsense	Yes
SLCO1C1	ENSG00000139155	HCC11T	g.chr12: 20781339C>A	p. L472I	Missense	Yes
SYT10	ENSG00000110975	HCC13T	g.chr12: 33470355G>T	p. P165H	Missense	Yes
PRICKLE1	ENSG00000139174	HCC13T	g.chr12: 41139917C>G	p. K819N	Missense	Yes
ARID2	ENSG00000189079	HCC07T	g.chr12: 44517604G>T	p. E393X	Nonsense	Yes
ARID2	ENSG00000189079	HCC08T	g.chr12: 44531120C>T	p. Q983X	Nonsense	Yes
RPAP3	ENSG00000005175	HCC11T	g.chr12: 46350389G>C	p. L432V	Missense	Yes
TUBA1C	ENSG00000167553	HCC10T	g.chr12: 47952394G>A	p. R156H	Missense	Yes
KRT82	ENSG00000161850	HCC10T	g.chr12: 51083941T>G	p. K144T	Missense	Yes
KRT6A	ENSG00000205420	HCC13T	g.chr12: 51173161C>A	p. G27W	Missense	Yes
KRT8	ENSG00000170421	HCC12T	g.chr12: 51584942A>C	p. S31A	Missense	Yes
SOAT2	ENSG00000167780	HCC13T	g.chr12: 51798981G>A	p. A302T	Missense	Yes
HOXC9	ENSG00000180806	HCC13T	g.chr12: 52680535C>A	p. P99Q	Missense	Yes
KIF5A	ENSG00000155980	HCC08T	g.chr12: 56262667T>C	p. I1003T	Missense	Yes
LRIG3	ENSG00000139263	HCC08T	g.chr12: 57568487T>C	p. K280E	Missense	Yes
MIR1279	MI0006426	HCC12T	g.chr12: 67953253T>G	p. I5L	Missense	Yes
KCNC2	ENSG00000166006	HCC11T	g.chr12: 73730709C>A	p. W448L	Missense	Yes
ACSS3	ENSG00000111058	HCC08T	g.chr12: 80149024G>T	p. K524N	Missense	Yes
ALX1	ENSG00000180318	HCC07T	g.chr12: 84219151A>T	p. T250S	Missense	Yes
TMTC3	ENSG00000139324	HCC13T	g.chr12: 87113266T>G	p. I818M	Missense	Yes
DCN	ENSG00000011465	HCC10T	g.chr12: 90071099T>C	IVS4-2	Splice site	Yes
ACAD10	ENSG00000111271	HCC06T	g.chr12: 110624390A>T	p. K77X	Nonsense	Yes
NAA25	ENSG00000111300	HCC07T	g.chr12: 110951728A>T	p. L970Q	Missense	Yes
DDX55	ENSG00000111364	HCC12T	g.chr12: 122667082A>G	p. Y343C	Missense	Yes

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ATP6V0A2	ENSG00000185344	HCC07T	g.chr12: 122808438A>G	p. Q826R	Missense	Yes
TMEM132B	ENSG00000139364	HCC03T	g.chr12: 124704258A>C	p. E762D	Missense	Yes
TMEM132D	ENSG00000151952	HCC07T	g.chr12: 128135044C>T	p. E534K	Missense	Yes
MIPEP	ENSG00000027001	HCC06T	g.chr13: 23282024T>C	p. K565E	Missense	Yes
HTR2A	ENSG00000102468	HCC10T	g.chr13: 46307631G>A	p. T253I	Missense	Yes
KPNA3	ENSG00000102753	HCC04T	g.chr13: 49174584T>C	p. E469G	Missense	Yes
TMTC4	ENSG00000125247	HCC04T	g.chr13: 100092555C>G	p. G218R	Missense	Yes
NALCN	ENSG00000102452	HCC12T	g.chr13: 100595163T>A	p. Q642L	Missense	Yes
TMCO3	ENSG00000150403	HCC08T	g.chr13: 113198225G>A	p. V110I	Missense	Yes
OR4N2	ENSG00000176294	HCC07T	g.chr14: 19366042A>G	p. M199V	Missense	Yes
OR4K5	ENSG00000176281	HCC04T	g.chr14: 19458759G>C	p. D52H	Missense	Yes
OSGEP	ENSG00000092094	HCC11T	g.chr14: 19985436G>A	p. S318F	Missense	Yes
NDRG2	ENSG00000165795	HCC04T	g.chr14: 20557155G>A	p. R241X	Nonsense	Yes
MMP14	ENSG00000157227	HCC07T	g.chr14: 22385034T>A	p. H565Q	Missense	Yes
EFS	ENSG00000100842	HCC08T	g.chr14: 22897975C>T	p. A401T	Missense	Yes
MYH6	ENSG00000197616	HCC03T	g.chr14: 22929455C>T	p. R1128H	Missense	Yes
LRRC16B	ENSG00000186648	HCC06T	g.chr14: 23600611G>C	p. E790D	Missense	Yes
LRFN5	ENSG00000165379	HCC04T	g.chr14: 41425810G>T	p. V78L	Missense	Yes
C14orf106	ENSG00000129534	HCC06T	g.chr14: 44762886A>G	p. L885S	Missense	Yes
WDR89	ENSG00000140006	HCC10T	g.chr14: 63136379T>C	p. H12R	Missense	Yes
GPHN	ENSG00000171723	HCC04T	g.chr14: 66658784C>G	p. T562S	Missense	Yes
ZFP36L1	ENSG00000185650	HCC11T	g.chr14: 68326506G>A	p. R172C	Missense	Yes
SFRS5	ENSG00000100650	HCC11T	g.chr14: 69305146T>C	IVS2+2	Splice site	Yes
PTPN21	ENSG00000070778	HCC10T	g.chr14: 88044082A>G	p. L129S	Missense	Yes
ATG2B	ENSG00000066739	HCC11T	g.chr14: 95841804T>A	p. K1536N	Missense	Yes
HSP90AA1	ENSG00000080824	HCC13T	g.chr14: 101619890T>G	p. N566T	Missense	Yes
GPR176	ENSG00000166073	HCC03T	g.chr15: 37880741G>C	p. P478A	Missense	Yes
C15orf23	ENSG00000128944	HCC10T	g.chr15: 38471505G>A	p. E271K	Missense	Yes
PLA2G4F	ENSG00000168907	HCC11T	g.chr15: 40221647T>C	p. I793V	Missense	Yes
DMXL2	ENSG00000104093	HCC03T	g.chr15: 49565693G>A	p. S1784L	Missense	Yes
GCOM1	ENSG00000137878	HCC07T	g.chr15: 55711991A>G	p. Y249C	Missense	Yes
ZWILCH	ENSG00000174442	HCC10T	g.chr15: 64626046C>T	p. T584I	Missense	Yes
GOLGA6A	ENSG00000159289	HCC09T	g.chr15: 72154035T>C	p. Q403R	Missense	Yes
CSPG4	ENSG00000173546	HCC13T	g.chr15: 73769127G>A	p. A445V	Missense	Yes
ACSBG1	ENSG00000103740	HCC04T	g.chr15: 76262178C>T	p. W223X	Nonsense	Yes
CASKIN1	ENSG00000167971	HCC07T	g.chr16: 2171795A>G	p. L589P	Missense	Yes
ZC3H7A	ENSG00000122299	HCC06T	g.chr16: 11772152C>G	p. E366Q	Missense	Yes
PDXDC1	ENSG00000179889	HCC11T	g.chr16: 15003205A>C	p. Q78P	Missense	Yes
NOMO2	ENSG00000185164	HCC10T	g.chr16: 18443327A>C (homo)	p. F648C	Missense	Yes
NOMO2	ENSG00000185164	HCC10T	g.chr16: 18443348C>G	p. C641S	Missense	Yes
NOMO2	ENSG00000185164	HCC10T	g.chr16: 18446438G>C	p. Q606E	Missense	Yes
C16orf62	ENSG00000103544	HCC13T	g.chr16: 19618443G>A	p. R922K	Missense	Yes
DNAH3	ENSG00000158486	HCC08T	g.chr16: 20950080A>G	p. Y1743H	Missense	Yes
PRKCB	ENSG00000166501	HCC11T	g.chr16: 24110005G>A	p. E606K	Missense	Yes
TNRC6A	ENSG00000090905	HCC03T	g.chr16: 24741715G>T	p. R1798L	Missense	Yes
SRCAP	ENSG00000080603	HCC08T	g.chr16: 30632042C>T	p. P715S	Missense	Yes
CDH8	ENSG00000150394	HCC11T	g.chr16: 60492584C>A	p. G183C	Missense	Yes
NFATC3	ENSG00000072736	HCC13T	g.chr16: 66714443G>T	p. D386Y	Missense	Yes
SF3B3	ENSG00000189091	HCC10T	g.chr16: 69133169G>T	p. Q388H	Missense	Yes
BCAR1	ENSG00000050820	HCC13T	g.chr16: 73826522C>A	p. Q592H	Missense	Yes
CYBA	ENSG00000051523	HCC11T	g.chr16: 87244916G>A	p. Q3X	Nonsense	Yes
MYO1C	ENSG00000197879	HCC10T	g.chr17: 1318130T>C	p. Y933C	Missense	Yes
VMO1	ENSG00000182853	HCC10T	g.chr17: 4635398C>A	p. X203L	Missense	Yes
NLRP1	ENSG00000091592	HCC07T	g.chr17: 5376933C>T	p. D1077N	Missense	Yes
NLRP1	ENSG00000091592	HCC03T	g.chr17: 5402995T>G	p. K582T	Missense	Yes
ACAP1	ENSG00000072818	HCC10T	g.chr17: 7190492A>G	p. D322G	Missense	Yes
TP53	ENSG00000141510	HCC06T	g.chr17: 7514728G>A	p. R342X	Nonsense	Yes
TP53	ENSG00000141510	HCC11T	g.chr17: 7519270delC	fs	Indel	Yes
TP53	ENSG00000141510	HCC13T	g.chr17: 7520144_7520145dupG	fs	Indel	Yes
FAM18B	ENSG00000171928	HCC07T	g.chr17: 18642943G>A	p. A142T	Missense	Yes

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ALDH3A2	ENSG00000072210	HCC12T	g.chr17: 19495585A>C	p. Y96S	Missense	Yes
NF1	ENSG00000196712	HCC10T	g.chr17: 26583846A>G	p. Y1106C	Missense	Yes
RAD51L3	ENSG00000185379	HCC03T	g.chr17: 30470720C>A	p. C9F	Missense	Yes
TBC1D3F	ENSG00000185128	HCC09T	g.chr17: 33361565C>T	p. A65V	Missense	Yes
PLXDC1	ENSG00000161381	HCC13T	g.chr17: 34549503T>A	p. Q62L	Missense	Yes
PPP1R1B	ENSG00000131771	HCC07T	g.chr17: 35039328delC	fs	Indel	Yes
CCDC56	ENSG00000183978	HCC10T	g.chr17: 38203713T>C	IVS1-2	Splice site	Yes
MPP2	ENSG00000108852	HCC12T	g.chr17: 39316098T>A	p. Q101L	Missense	Yes
GJC1	ENSG00000182963	HCC07T	g.chr17: 40238573C>G	p. E47Q	Missense	Yes
GFAP	ENSG00000131095	HCC06T	g.chr17: 40347974C>T	p. R136Q	Missense	Yes
NGFR	ENSG00000064300	HCC09T	g.chr17: 44945087G>A	p. G334D	Missense	Yes
COL1A1	ENSG00000108821	HCC13T	g.chr17: 45621265C>A	p. E1015X	Nonsense	Yes
TMEM92	ENSG00000167105	HCC13T	g.chr17: 45706871G>A	p. A4T	Missense	Yes
TEX14	ENSG00000121101	HCC10T	g.chr17: 54031703C>T	p. E668K	Missense	Yes
GDPD1	ENSG00000153982	HCC13T	g.chr17: 54666675G>T	p. Q61H	Missense	Yes
MED13	ENSG00000108510	HCC04T	g.chr17: 57414458T>C	p. N1230D	Missense	Yes
MARCH101	ENSG00000173838	HCC10T	g.chr17: 58191056A>T	p. I85N	Missense	Yes
LRRC37A3	ENSG00000176809	HCC03T	g.chr17: 60286293G>T	p. T1478N	Missense	Yes
SLC39A11	ENSG00000133195	HCC11T	g.chr17: 68156565C>A	p. D301Y	Missense	Yes
ITGB4	ENSG00000132470	HCC03T	g.chr17: 71258716C>T	p. A1241V	Missense	Yes
FOXJ1	ENSG00000129654	HCC12T	g.chr17: 71645721C>T	p. G192R	Missense	Yes
NPTX1	ENSG00000171246	HCC07T	g.chr17: 76059407T>C	p. D367G	Missense	Yes
GNAL	ENSG00000141404	HCC08T	g.chr18: 11679804T>C	p. L81P	Missense	Yes
KIAA1012	ENSG00000153339	HCC06T	g.chr18: 27701400A>C	p. I809S	Missense	Yes
MOCOS	ENSG00000075643	HCC07T	g.chr18: 32029238G>T	p. A55S	Missense	Yes
PIK3C3	ENSG00000078142	HCC04T	g.chr18: 37796490A>C	p. D99A	Missense	Yes
SMAD2	ENSG00000175387	HCC13T	g.chr18: 43625724C>T	p. W422X	Nonsense	Yes
SERPINB2	ENSG00000197632	HCC10T	g.chr18: 59715396A>G	p. N127S	Missense	Yes
ADNP2	ENSG00000101544	HCC13T	g.chr18: 75995053A>G	p. K256E	Missense	Yes
ZNF554	ENSG00000172006	HCC10T	g.chr19: 2785327C>T	p. S365F	Missense	Yes
KDM4B	ENSG00000127663	HCC13T	g.chr19: 4990959A>G	p. Q85R	Missense	Yes
TNFSF14	ENSG00000125735	HCC04T	g.chr19: 6621079A>G	p. M1T	Missense	Yes
C19orf45	ENSG00000198723	HCC07T	g.chr19: 7476211T>A	p. Y248N	Missense	Yes
OR7G3	ENSG00000170920	HCC11T	g.chr19: 9097917delG	fs	Indel	Yes
SMARCA4	ENSG00000127616	HCC06T	g.chr19: 11029977C>T	p. R1491X	Nonsense	Yes
OR10H3	ENSG00000171936	HCC07T	g.chr19: 15713894C>T	p. P231L	Missense	Yes
CYP4F2	ENSG00000186115	HCC04T	g.chr19: 15861343C>T	p. V270I	Missense	Yes
GDF15	ENSG00000130513	HCC07T	g.chr19: 18358084G>A	p. A29T	Missense	Yes
NPHS1	ENSG00000161270	HCC10T	g.chr19: 41014469C>T	p. A1068T	Missense	Yes
APLP1	ENSG00000105290	HCC04T	g.chr19: 41054613C>T	p. R229W	Missense	Yes
RYR1	ENSG00000196218	HCC08T	g.chr19: 43668646G>C	p. Q1837H	Missense	Yes
NCCRP1	ENSG00000188505	HCC08T	g.chr19: 44380680A>T	IVS2-2	Splice site	Yes
C19orf61	ENSG00000105771	HCC10T	g.chr19: 48928994C>T	p. G447E	Missense	Yes
APOC2	ENSG00000213044	HCC13T	g.chr19: 50143911A>G	p. N57D	Missense	Yes
SYMPK	ENSG00000125755	HCC10T	g.chr19: 51039203C>T	p. G258S	Missense	Yes
CGB1	ENSG00000204748	HCC13T	g.chr19: 54230696G>T	p. R151S	Missense	Yes
SIGLEC9	ENSG00000129450	HCC04T	g.chr19: 56322099T>C	p. V250A	Missense	Yes
SIGLEC6	ENSG00000105492	HCC10T	g.chr19: 56725930C>A	p. G164W	Missense	Yes
LILRA1	ENSG00000104974	HCC13T	g.chr19: 59798508C>A	p. H164N	Missense	Yes
NLRP2	ENSG00000022556	HCC07T	g.chr19: 60186248G>A	p. G457D	Missense	Yes
EPS8L1	ENSG00000131037	HCC08T	g.chr19: 60285459G>A	p. R332Q	Missense	Yes
EPS8L1	ENSG00000131037	HCC04T	g.chr19: 60286815C>T	p. A459V	Missense	Yes
SOX11	ENSG00000176887	HCC07T	g.chr2: 5750567A>T	p. K88I	Missense	Yes
LPIN1	ENSG00000134324	HCC13T	g.chr2: 11837167G>T	p. G265V	Missense	Yes
APOB	ENSG00000084674	HCC08T	g.chr2: 21086461T>C	p. I2262V	Missense	Yes
FNDC4	ENSG00000115226	HCC07T	g.chr2: 27571020_27571021dupG	fs	Indel	Yes
FNDC4	ENSG00000115226	HCC07T	g.chr2: 27571029A>G	p. S8P	Missense	Yes
ATP6V1B1	ENSG00000116039	HCC11T	g.chr2: 71040670G>A	p. G180D	Missense	Yes
C2orf65	ENSG00000159374	HCC13T	g.chr2: 74639466G>A	p. P493L	Missense	Yes
POLR1A	ENSG00000068654	HCC08T	g.chr2: 86158860G>T	p. S382Y	Missense	Yes

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AFF3	ENSG00000144218	HCC07T	g.chr2: 99541776T>C	p. Y1118C	Missense	Yes
MERTK	ENSG00000153208	HCC10T	g.chr2: 112468363A>G	p. N454S	Missense	Yes
HS6ST1	ENSG00000136720	HCC06T	g.chr2: 128792267A>C	p. V114G	Missense	Yes
MGAT5	ENSG00000152127	HCC12T	g.chr2: 134896877A>T	p. I571F	Missense	Yes
RAB3GAP1	ENSG00000115839	HCC13T	g.chr2: 135627797G>T	p. E724X	Nonsense	Yes
LRP1B	ENSG00000168702	HCC08T	g.chr2: 141382094C>T	p. W1114X	Nonsense	Yes
KYNU	ENSG00000115919	HCC11T	g.chr2: 143516184A>G	p. I457M	Missense	Yes
ACVR2A	ENSG00000121989	HCC09T	g.chr2: 148319248T>A	IVS1+2	Splice site	Yes
RIF1	ENSG00000080345	HCC08T	g.chr2: 151981620T>G	p. H154Q	Missense	Yes
DPP4	ENSG00000197635	HCC03T	g.chr2: 162638203C>A	p. A16S	Missense	Yes
TLK1	ENSG00000198586	HCC10T	g.chr2: 171593144T>C	p. Y396C	Missense	Yes
EVX2	ENSG00000174279	HCC10T	g.chr2: 176653701T>C	p. T271A	Missense	Yes
NFE2L2	ENSG00000222043	HCC13T	g.chr2: 177807047C>G	p. E82Q	Missense	Yes
PDE11A	ENSG00000128655	HCC10T	g.chr2: 178677297A>G	p. I47T	Missense	Yes
TTN	ENSG00000155657	HCC07T	g.chr2: 179349360C>T	p. G1826S	Missense	Yes
TMEFF2	ENSG00000144339	HCC10T	g.chr2: 192630665T>G	p. D174A	Missense	Yes
NBEAL1	ENSG00000144426	HCC07T	g.chr2: 203770268A>T	IVS20-2	Splice site	Yes
PECR	ENSG00000115425	HCC07T	g.chr2: 216654653T>G	p. Q19H	Missense	Yes
SCG2	ENSG00000171951	HCC07T	g.chr2: 224170576G>A	p. Q557X	Nonsense	Yes
ALPP	ENSG00000163283	HCC12T	g.chr2: 232952486A>T	p. H110L	Missense	Yes
UGT1A6	ENSG00000167165	HCC08T	g.chr2: 234255680T>C	p. F120L	Missense	Yes
SLC4A11	ENSG00000088836	HCC11T	g.chr20: 3157797C>G	p. M670I	Missense	Yes
SIGLEC1	ENSG00000088827	HCC10T	g.chr20: 3627917T>A	p. Y573F	Missense	Yes
PLCB1	ENSG00000182621	HCC07T	g.chr20: 8557019C>T	p. P109S	Missense	Yes
PLCB1	ENSG00000182621	HCC07T	g.chr20: 8557020C>G	p. P109R	Missense	Yes
C20orf103	ENSG00000125869	HCC11T	g.chr20: 9444767C>T	p. L120F	Missense	Yes
SLC24A3	ENSG00000185052	HCC06T	g.chr20: 19514102G>T	p. G176C	Missense	Yes
INSM1	ENSG00000173404	HCC06T	g.chr20: 20297225C>T	p. P105L	Missense	Yes
CST2	ENSG00000170369	HCC13T	g.chr20: 23755236C>T	p. W21X	Nonsense	Yes
ASXL1	ENSG00000171456	HCC08T	g.chr20: 30487750G>T	p. E1192X	Nonsense	Yes
SNTA1	ENSG00000101400	HCC11T	g.chr20: 31461770A>C	p. S357A	Missense	Yes
ACTR5	ENSG00000101442	HCC10T	g.chr20: 36814273C>T	p. P231S	Missense	Yes
WFDC9	ENSG00000180205	HCC07T	g.chr20: 43670851A>G	p. I35T	Missense	Yes
SLC12A5	ENSG00000124140	HCC06T	g.chr20: 44113845A>G	p. N769S	Missense	Yes
ZNFX1	ENSG00000124201	HCC03T	g.chr20: 47297239T>C	p. N1910S	Missense	Yes
PRIC285	ENSG00000130589	HCC07T	g.chr20: 61661104T>C	p. Q2630R	Missense	Yes
LIME1	ENSG00000203896	HCC08T	g.chr20: 61840051C>T	p. Q114X	Nonsense	Yes
IFNAR1	ENSG00000142166	HCC08T	g.chr21: 33629744A>G	p. I41V	Missense	Yes
PKNOX1	ENSG00000160199	HCC03T	g.chr21: 43303266G>A	p. E72K	Missense	Yes
COL6A2	ENSG00000142173	HCC07T	g.chr21: 46356327C>A	p. T41N	Missense	Yes
CLDN5	ENSG00000184113	HCC08T	g.chr22: 17891651G>A	p. A43V	Missense	Yes
VPREB1	ENSG00000169575	HCC08T	g.chr22: 20929519A>T	p. R70X	Nonsense	Yes
CABIN1	ENSG00000099991	HCC11T	g.chr22: 22786518G>C	p. V511L	Missense	Yes
ADORA2A	ENSG00000128271	HCC07T	g.chr22: 23167391G>C	p. K391N	Missense	Yes
TFIP11	ENSG00000100109	HCC08T	g.chr22: 25225410A>T	p. L330H	Missense	Yes
EWSR1	ENSG00000182944	HCC10T	g.chr22: 28024807G>C	p. G501A	Missense	Yes
SFI1	ENSG00000198089	HCC03T	g.chr22: 30332322T>G	p. L688X	Nonsense	Yes
SAMM50	ENSG00000100347	HCC10T	g.chr22: 42717522C>T	p. R423C	Missense	Yes
KCNH8	ENSG00000183960	HCC04T	g.chr3: 19473420T>C	p. F661S	Missense	Yes
XYLB	ENSG00000093217	HCC10T	g.chr3: 38429470C>T	p. Q525X	Nonsense	Yes
CTNNB1	ENSG00000168036	HCC08T	g.chr3: 41241102A>G	p. D32G	Missense	Yes
CTNNB1	ENSG00000168036	HCC07T	g.chr3: 41241108G>T	p. G34V	Missense	Yes
CTNNB1	ENSG00000168036	HCC03T	g.chr3: 41241108G>T	p. G34V	Missense	Yes
CTNNB1	ENSG00000168036	HCC10T	g.chr3: 41241114A>C	p. H36P	Missense	Yes
CTNNB1	ENSG00000168036	HCC07T	g.chr3: 41241140T>C	p. S45P	Missense	Yes
PTH1R	ENSG00000160801	HCC08T	g.chr3: 46915231C>G	p. F238L	Missense	Yes
SCAP	ENSG00000114650	HCC12T	g.chr3: 47445142T>A	p. Y92F	Missense	Yes
WDR6	ENSG00000178252	HCC11T	g.chr3: 49024476G>T	p. A169S	Missense	Yes
MAPKAPK3	ENSG00000114738	HCC08T	g.chr3: 50658635G>C	p. K255N	Missense	Yes
PRICKLE2	ENSG00000163637	HCC11T	g.chr3: 64060194C>T	p. S703N	Missense	Yes

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EPHA3	ENSG00000044524	HCC07T	g.chr3: 89563026G>C	p. G725R	Missense	Yes
CBLB	ENSG00000114423	HCC11T	g.chr3: 106903987G>A	p. P534S	Missense	Yes
CCDC80	ENSG00000091986	HCC07T	g.chr3: 113840898C>T	p. R182K	Missense	Yes
SIDT1	ENSG00000072858	HCC13T	g.chr3: 114794570T>A	p. F344I	Missense	Yes
IGSF11	ENSG00000144847	HCC10T	g.chr3: 120131752T>C	p. Q37R	Missense	Yes
KTELC1	ENSG00000163389	HCC13T	g.chr3: 120693071G>T	p. V328L	Missense	Yes
GOLGB1	ENSG00000173230	HCC04T	g.chr3: 122895716T>G	p. E2110A	Missense	Yes
SEC61A1	ENSG00000058262	HCC10T	g.chr3: 129271142A>T	p. I460F	Missense	Yes
RAB43	ENSG00000172780	HCC07T	g.chr3: 130296671C>G	p. R79P	Missense	Yes
XRN1	ENSG00000114127	HCC10T	g.chr3: 143620139T>C	p. N415D	Missense	Yes
AADACL2	ENSG00000197953	HCC09T	g.chr3: 152957614G>T	p. V228L	Missense	Yes
MECOM	ENSG00000085276	HCC04T	g.chr3: 170316507C>A	p. G428V	Missense	Yes
DVL3	ENSG00000161202	HCC07T	g.chr3: 185364798A>T	p. D94V	Missense	Yes
PSMD2	ENSG00000175166	HCC11T	g.chr3: 185506409C>G	p. L567V	Missense	Yes
TMEM44	ENSG00000145014	HCC07T	g.chr3: 195812971C>T	p. S327N	Missense	Yes
ZDHHC19	ENSG00000163958	HCC07T	g.chr3: 197419825A>C	p. F138V	Missense	Yes
OTOP1	ENSG00000163982	HCC07T	g.chr4: 4250663T>C	p. I267V	Missense	Yes
DHX15	ENSG00000109606	HCC08T	g.chr4: 24187026T>C	p. I149V	Missense	Yes
FIP1L1	ENSG00000145216	HCC07T	g.chr4: 53940152A>G	p. E45G	Missense	Yes
STAP1	ENSG00000035720	HCC11T	g.chr4: 68123717T>A	p. I71K	Missense	Yes
EPGN	ENSG00000182585	HCC10T	g.chr4: 75397646C>T	p. T92I	Missense	Yes
PRKG2	ENSG00000138669	HCC07T	g.chr4: 82311896T>A	p. N239Y	Missense	Yes
IL21	ENSG00000138684	HCC04T	g.chr4: 123761517G>A	p. R34C	Missense	Yes
FAT4	ENSG00000196159	HCC07T	g.chr4: 126590252T>A	p. Y2877X	Nonsense	Yes
PCDH10	ENSG00000138650	HCC12T	g.chr4: 134293182C>A	p. H813N	Missense	Yes
RXFP1	ENSG00000171509	HCC07T	g.chr4: 159789169A>T	p. S609C	Missense	Yes
RXFP1	ENSG00000171509	HCC07T	g.chr4: 159789170G>A	p. S609N	Missense	Yes
RAPGEF2	ENSG00000109756	HCC08T	g.chr4: 160470611A>G	p. K273R	Missense	Yes
TRIM61	ENSG00000183439	HCC03T	g.chr4: 166110258C>T	p. C116Y	Missense	Yes
DDX60	ENSG00000137628	HCC08T	g.chr4: 169465862G>A	p. S45L	Missense	Yes
CEP72	ENSG00000112877	HCC10T	g.chr5: 690839A>G	p. D371G	Missense	Yes
ZDHHC11	ENSG00000188818	HCC13T	g.chr5: 886915G>T	p. A303D	Missense	Yes
FASTKD3	ENSG00000124279	HCC03T	g.chr5: 7919906T>C	p. K431E	Missense	Yes
MTRR	ENSG00000124275	HCC07T	g.chr5: 7945940G>T	p. G518C	Missense	Yes
SLC1A3	ENSG00000079215	HCC13T	g.chr5: 36716292A>G	p. E378G	Missense	Yes
NIPBL	ENSG00000164190	HCC10T	g.chr5: 37039124C>T	p. S1258L	Missense	Yes
ITGA2	ENSG00000164171	HCC08T	g.chr5: 52413282T>A	p. L1048X	Nonsense	Yes
MRPS36	ENSG00000134056	HCC08T	g.chr5: 68557939C>T	p. P21S	Missense	Yes
MARVELD2	ENSG00000152939	HCC10T	g.chr5: 68751179A>G	p. I71V	Missense	Yes
OCLN	ENSG00000197822	HCC03T	g.chr5: 68840800G>A	p. A43T	Missense	Yes
ZFYVE16	ENSG00000039319	HCC09T	g.chr5: 79774737A>C	p. N820T	Missense	Yes
MBLAC2	ENSG00000176055	HCC07T	g.chr5: 89793099G>A	p. Q161X	Nonsense	Yes
NUDT12	ENSG00000112874	HCC08T	g.chr5: 102914553T>C	p. K433E	Missense	Yes
DMXL1	ENSG00000172869	HCC13T	g.chr5: 118435231T>C	p. I23T	Missense	Yes
DMXL1	ENSG00000172869	HCC07T	g.chr5: 118497683T>A	p. V722D	Missense	Yes
SLC27A6	ENSG00000113396	HCC07T	g.chr5: 128329875A>G	p. K49R	Missense	Yes
C5orf20	ENSG00000251380	HCC09T	g.chr5: 134813195T>A	p. M112L	Missense	Yes
NEUROG1	ENSG00000181965	HCC06T	g.chr5: 134898861T>C	p. Y140C	Missense	Yes
PCDHA5	ENSG00000204965	HCC12T	g.chr5: 140181674G>A	p. V44I	Missense	Yes
PCDHB8	ENSG00000120322	HCC07T	g.chr5: 140538950G>A	p. C384Y	Missense	Yes
PCDHB15	ENSG00000113248	HCC07T	g.chr5: 140607294C>T	p. T655I	Missense	Yes
AFAP1L1	ENSG00000157510	HCC10T	g.chr5: 148675930G>A	p. A380T	Missense	Yes
DOCK2	ENSG00000134516	HCC07T	g.chr5: 169407149T>C	p. Y1342H	Missense	Yes
ZFP2	ENSG00000198939	HCC08T	g.chr5: 178291309A>G	p. Y130C	Missense	Yes
EXOC2	ENSG00000112685	HCC10T	g.chr6: 509087T>C	p. I579V	Missense	Yes
HIVEP1	ENSG00000095951	HCC03T	g.chr6: 12230520A>T	p. I836F	Missense	Yes
HIST1H1E	ENSG00000168298	HCC06T	g.chr6: 26264833G>T	p. R79L	Missense	Yes
OR12D3	ENSG00000112462	HCC08T	g.chr6: 29431291T>C	p. I221V	Missense	Yes
NCR3	ENSG00000204475	HCC12T	g.chr6: 31665700G>A	p. R76C	Missense	Yes
RDBP	ENSG00000204356	HCC10T	g.chr6: 32030103A>C	p. F280V	Missense	Yes

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ITPR3	ENSG00000096433	HCC04T	g.chr6: 33741619T>A	p. V480E	Missense	Yes
GRM4	ENSG00000124493	HCC13T	g.chr6: 34208926C>T	p. C109Y	Missense	Yes
CDKN1A	ENSG00000124762	HCC08T	g.chr6: 36760061_36760062dupG	fs	Indel	Yes
MOCS1	ENSG00000124615	HCC06T	g.chr6: 39985628G>A	p. A344V	Missense	Yes
CUL7	ENSG00000044090	HCC10T	g.chr6: 43122625T>A	p. I790F	Missense	Yes
MIR113B	MI0000822	HCC09T	g.chr6: 52121744G>C	p. G22A	Missense	Yes
BAI3	ENSG00000135298	HCC13T	g.chr6: 70099594T>G	p. L1054R	Missense	Yes
FUT9	ENSG00000172461	HCC06T	g.chr6: 96758526C>A	p. Y258X	Nonsense	Yes
C6orf58	ENSG00000184530	HCC06T	g.chr6: 127940076C>T	p. S18F	Missense	Yes
MAP3K4	ENSG00000085511	HCC13T	g.chr6: 161390966C>T	p. R558C	Missense	Yes
THBS2	ENSG00000186340	HCC07T	g.chr6: 169371699C>T	p. D718N	Missense	Yes
PHF10	ENSG00000130024	HCC03T	g.chr6: 169856818G>A	p. R159X	Nonsense	Yes
CHST12	ENSG00000136213	HCC03T	g.chr7: 2439939G>T	p. W380L	Missense	Yes
EVX1	ENSG00000106038	HCC11T	g.chr7: 27252091A>C	p. H249P	Missense	Yes
CREB5	ENSG00000146592	HCC13T	g.chr7: 28576646A>G	p. I144V	Missense	Yes
SUN3	ENSG00000164744	HCC04T	g.chr7: 48035051T>C	p. K4E	Missense	Yes
HGF	ENSG00000019991	HCC08T	g.chr7: 81210655T>C	p. Y272C	Missense	Yes
TFR2	ENSG00000106327	HCC06T	g.chr7: 100064904C>T	p. R433K	Missense	Yes
TRIP6	ENSG00000087077	HCC09T	g.chr7: 100306227A>C	p. T309P	Missense	Yes
POT1	ENSG00000128513	HCC08T	g.chr7: 124319565T>C	p. K39E	Missense	Yes
ZNF467	ENSG00000181444	HCC08T	g.chr7: 149093941G>A	p. R195C	Missense	Yes
ZNF775	ENSG00000196456	HCC07T	g.chr7: 149724792G>T	p. S97I	Missense	Yes
CRYGN	ENSG00000127377	HCC11T	g.chr7: 150766203C>A	p. D28Y	Missense	Yes
USP17L2	ENSG00000223443	HCC06T	g.chr8: 12033009C>T	p. A224T	Missense	Yes
C8orf41	ENSG00000129696	HCC06T	g.chr8: 33480861G>T	p. H354Q	Missense	Yes
BRF2	ENSG00000104221	HCC06T	g.chr8: 37821582A>G	p. W282R	Missense	Yes
SFRP1	ENSG00000104332	HCC07T	g.chr8: 41241905T>G	p. K295Q	Missense	Yes
POLB	ENSG00000070501	HCC07T	g.chr8: 42346592A>G	p. N281S	Missense	Yes
DNAJC5B	ENSG00000147570	HCC12T	g.chr8: 67174804A>C	p. Y195S	Missense	Yes
MMP16	ENSG00000156103	HCC04T	g.chr8: 89278611G>A	p. P58L	Missense	Yes
COX6C	ENSG00000164919	HCC03T	g.chr8: 100973359T>C	p. M23V	Missense	Yes
UBR5	ENSG00000104517	HCC06T	g.chr8: 103367857C>T	p. A1708T	Missense	Yes
RIMS2	ENSG00000176406	HCC11T	g.chr8: 104966929T>A	p. V117E	Missense	Yes
FER1L6	ENSG00000214814	HCC07T	g.chr8: 125163810A>G	p. K1441E	Missense	Yes
FAM135B	ENSG00000147724	HCC07T	g.chr8: 139232971C>G	p. E977Q	Missense	Yes
DMRT2	ENSG00000173253	HCC10T	g.chr9: 1047119A>G	p. N511S	Missense	Yes
BNC2	ENSG00000173068	HCC06T	g.chr9: 16409126T>C	p. Y1054C	Missense	Yes
IFNA10	ENSG00000186803	HCC13T	g.chr9: 21196972C>G	p. G42A	Missense	Yes
CNTNAP3	ENSG00000106714	HCC08T	g.chr9: 39078510G>C	p. L1044V	Missense	Yes
CNTNAP3	ENSG00000106714	HCC08T	g.chr9: 39078517C>A	p. M1041I	Missense	Yes
ANKRD20A4	ENSG00000172014	HCC08T	g.chr9: 68680931G>A	p. V207I	Missense	Yes
FAM189A2	ENSG00000135063	HCC07T	g.chr9: 71188462T>A	p. Y197X	Nonsense	Yes
TRPM6	ENSG00000119121	HCC03T	g.chr9: 76626450G>A	p. A322V	Missense	Yes
C9orf47	ENSG00000186354	HCC06T	g.chr9: 90795783T>A	p. I18N	Missense	Yes
FBP1	ENSG00000165140	HCC10T	g.chr9: 96412059T>C	p. M178V	Missense	Yes
COL15A1	ENSG00000204291	HCC09T	g.chr9: 100789457C>A	p. P237T	Missense	Yes
TGFBR1	ENSG00000106799	HCC07T	g.chr9: 100939960A>C	IVS3-2	Splice site	Yes
AKNA	ENSG00000106948	HCC13T	g.chr9: 116163989C>T	p. R647H	Missense	Yes
DENND1A	ENSG00000119522	HCC13T	g.chr9: 125184403C>T	p. R720H	Missense	Yes
SPTAN1	ENSG00000197694	HCC03T	g.chr9: 130428645T>A	p. L2140H	Missense	Yes
SETX	ENSG00000107290	HCC11T	g.chr9: 134193940A>T	p. S956T	Missense	Yes
DBH	ENSG00000123454	HCC06T	g.chr9: 135511512A>G	p. Y494C	Missense	Yes
ABCA2	ENSG00000107331	HCC08T	g.chr9: 139029954T>C	p. K1170E	Missense	Yes
NHS	ENSG00000188158	HCC04T	g.chrX: 17304298C>A	p. A166E	Missense	Yes
PHEX	ENSG00000102174	HCC12T	g.chrX: 22155619C>A	p. N680K	Missense	Yes
MAGEB6	ENSG00000176746	HCC08T	g.chrX: 26122731C>T	p. P283S	Missense	Yes
MAOA	ENSG00000189221	HCC06T	g.chrX: 43476914A>C	p. E327A	Missense	Yes
RBM10	ENSG00000182872	HCC04T	g.chrX: 46915548G>A	p. A127T	Missense	Yes
SHROOM4	ENSG00000158352	HCC11T	g.chrX: 50393976G>T	p. L613M	Missense	Yes
FOXR2	ENSG00000189299	HCC06T	g.chrX: 55667047C>A	p. P60T	Missense	Yes

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SLC7A3	ENSG00000165349	HCC04T	g.chrX: 70064476G>A	p. Q314X	Nonsense	Yes
OGT	ENSG00000147162	HCC07T	g.chrX: 70672822A>T	p. D36V	Missense	Yes
PHKA1	ENSG00000067177	HCC07T	g.chrX: 71747709C>T	p. R807K	Missense	Yes
KIAA2022	ENSG00000050030	HCC10T	g.chrX: 73877047G>T	p. P1357H	Missense	Yes
GPR174	ENSG00000147138	HCC10T	g.chrX: 78313440T>C	p. C94R	Missense	Yes
FAM46D	ENSG00000174016	HCC11T	g.chrX: 79585830C>A	p. P379Q	Missense	Yes
CYLC1	ENSG00000183035	HCC03T	g.chrX: 83015343A>G	p. K324R	Missense	Yes
ZNF711	ENSG00000147180	HCC08T	g.chrX: 84406046A>G	p. I244M	Missense	Yes
CPXCR1	ENSG00000147183	HCC07T	g.chrX: 87895524G>T	p. M151I	Missense	Yes
NOX1	ENSG00000007952	HCC06T	g.chrX: 100003863G>C	p. R253G	Missense	Yes
RGAG1	ENSG00000181110	HCC10T	g.chrX: 109582840G>T	p. R780M	Missense	Yes
ODZ1	ENSG00000009694	HCC08T	g.chrX: 123925105T>G	p. Q60P	Missense	Yes
BCORL1	ENSG00000085185	HCC03T	g.chrX: 128982675C>A	p. T1159N	Missense	Yes
IGSF1	ENSG00000147255	HCC07T	g.chrX: 130244197G>T	p. T383N	Missense	Yes
MAGEC3	ENSG00000165509	HCC09T	g.chrX: 140810991C>A	p. P368Q	Missense	Yes
MTM1	ENSG00000171100	HCC10T	g.chrX: 149577111A>G	p. I405V	Missense	Yes
PASD1	ENSG00000166049	HCC04T	g.chrX: 150567775T>C	p. M221T	Missense	Yes
FAM58A	ENSG00000147382	HCC11T	g.chrX: 152513291G>A	p. R111C	Missense	Yes
F8	ENSG00000185010	HCC03T	g.chrX: 153847985G>T	p. A394D	Missense	Yes
TSPY1	ENSG00000168757	HCC13T	g.chrY: 6174373G>T	p. V22L	Missense	Yes
TSPY2	ENSG00000168757	HCC13T	g.chrY: 6174373G>T	p. V22L	Missense	Yes

*Coordinates refer to the human reference genome hg18 release (NCBI 36.1, March 2006).

Supplementary Table 4. Somatic mutations in *CTNNB1, TP53, ARID2, DMXL1* and *NLRP1* in human hepatocellular carcinomas

Sample	Gene	Transcript Accession	Nucleotide (genomic)*	Amino acid (protein)	Mutation type
HCC07T	*ARID2*	ENST00000334344	g.chr12: 44517604G>T	p.E393X	Nonsense
HCC08T	*ARID2*	ENST00000334344	g.chr12: 44531120C>T	p.Q983X	Nonsense
HCC05T	*ARID2*	ENST00000334344	g.chr12: 44410093G>A	Splice site	Splice site
HCC15T	*ARID2*	ENST00000334344	g.chr12: 44409960_44409961dupA	fs	Indel
HCC21T	*ARID2*	ENST00000334344	g.chr12: 44530611delC	fs	Indel
HCC200T	*ARID2*	ENST00000334344	g.chr12: 44411280delA	fs	Indel
HCC366T	*ARID2*	ENST00000334344	g.chr12: 44573689G>T	p.E1761X	Nonsense
HCC202T	*ARID2*	ENST00000334344	g.chr12: 44532238delA	fs	Indel
HCC202T	*ARID2*	ENST00000334344	g.chr12: 44532586_44532592delACATTCT	fs	Indel
HCC47T	*ARID2*	ENST00000334344	g.chr12: 44532926_44532929delGTAC	fs	Indel
HCC07T	*DMXL1*	ENST00000311085	g.chr5: 118497683T>A	p.V722D	Missense
HCC13T	*DMXL1*	ENST00000311085	g.chr5: 118435231T>C	p.I23T	Missense
HCC203T	*DMXL1*	ENST00000311085	g.chr5: 118507471C>T	p.Q805X	Nonsense
HCC204T	*DMXL1*	ENST00000311085	g.chr5: 118468783A>T	p.S99C	Missense
HCC205T	*DMXL1*	ENST00000311085	g.chr5: 118534664A>T	p.E2093D	Missense
HCC206T	*DMXL1*	ENST00000311085	g.chr5: 118492942_118492944delAGA	in-frame del	Indel
HCC03T	*NLRP1*	ENST00000269280	g.chr17: 5402995T>G	p.K582T	Missense
HCC07T	*NLRP1*	ENST00000269280	g.chr17: 5376933C>T	p.D1077N	Missense
HCC207T	*NLRP1*	ENST00000269280	g.chr17: 5403147C>T	p.M531I	Missense
HCC207T	*NLRP1*	ENST00000269280	g.chr17: 5403146G>T	p.Q532K	Missense
HCC208T	*NLRP1*	ENST00000269280	g.chr17: 5383537T>A	p.Q931L	Missense
HCC03T	*CTNNB1*	ENST00000405570	g.chr3: 41241108G>T	p.G34V	Missense
HCC07T	*CTNNB1*	ENST00000405570	g.chr3: 41241140T>C	p.S45P	Missense
HCC07T	*CTNNB1*	ENST00000405570	g.chr3: 41241108G>T	p.G34V	Missense
HCC08T	*CTNNB1*	ENST00000405570	g.chr3: 41241102A>G	p.D32G	Missense
HCC10T	*CTNNB1*	ENST00000405570	g.chr3: 41241114A>C	p.H36P	Missense
HCC209T	*CTNNB1*	ENST00000405570	g.chr3: 41241107G>A	p.G34R	Missense
HCC210T	*CTNNB1*	ENST00000405570	g.chr3: 41241108G>A	p.G34E	Missense
HCC211T	*CTNNB1*	ENST00000405570	g.chr3: 41241101G>T	p.D32Y	Missense
HCC203T	*CTNNB1*	ENST00000405570	g.chr3: 41241129C>T	p.T41I	Missense
HCC212T	*CTNNB1*	ENST00000405570	g.chr3: 41241102A>T	p.D32V	Missense
HCC213T	*CTNNB1*	ENST00000405570	g.chr3: 41241141C>T	p.S45F	Missense
HCC214T	*CTNNB1*	ENST00000405570	g.chr3: 41241128A>G	p.T41A	Missense
HCC215T	*CTNNB1*	ENST00000405570	g.chr3: 41241140T>C	p.S45P	Missense
HCC05T	*CTNNB1*	ENST00000405570	g.chr3: 41241102A>G	p.D32G	Missense
HCC15T	*CTNNB1*	ENST00000405570	g.chr3: 41241101G>C	p.D32H	Missense
HCC24T	*CTNNB1*	ENST00000405570	g.chr3: 41249915T>A	p.N387K	Missense
HCC26T	*CTNNB1*	ENST00000405570	g.chr3: 41241128A>G	p.T41A	Missense
HCC200T	*CTNNB1*	ENST00000405570	g.chr3: 41241114A>C	p.H36P	Missense
HCC165T	*CTNNB1*	ENST00000405570	g.chr3: 41241140T>C	p.S45P	Missense
HCC507T	*CTNNB1*	ENST00000405570	g.chr3: 41241116T>C	p.S37P	Missense
HCC50T	*CTNNB1*	ENST00000405570	g.chr3: 41241140T>C	p.S45P	Missense
HCC556T	*CTNNB1*	ENST00000405570	g.chr3: 41241141C>T	p.S45F	Missense
HCC567T	*CTNNB1*	ENST00000405570	g.chr3: 41241105C>T	p.S33F	Missense
HCC219T	*CTNNB1*	ENST00000405570	g.chr3: 41241105C>G	p.S33C	Missense
HCC202T	*CTNNB1*	ENST00000405570	g.chr3: 41243770A>T	p.K335I	Missense
HCC220T	*CTNNB1*	ENST00000405570	g.chr3: 41241129C>T	p.T41I	Missense
HCC221T	*CTNNB1*	ENST00000405570	g.chr3: 41241117_41241149 delCTGGTGCCACTACCACAGCTCCTTCTCTGAGTG	in-frame del	Indel
HCC222T	*CTNNB1*	ENST00000405570	g.chr3: 41241140T>C	p.S45P	Missense
HCC223T	*CTNNB1*	ENST00000405570	g.chr3: 41241128A>G	p.T41A	Missense
HCC06T	*TP53*	ENST00000269305	g.chr17: 7514728G>A	p. R343X	Nonsense
HCC11T	*TP53*	ENST00000269305	g.chr17: 7519270delC	fs	Indel

HCC13T	*TP53*	ENST00000269305	g.chr17: 7520144_7520145insG	fs	Indel
HCC209T	*TP53*	ENST00000269305	g.chr17: 7520317T>A	Splice site	Splice site
HCC210T	*TP53*	ENST00000269305	g.chr17: 7518294A>C	p.C238G	missense
HCC211T	*TP53*	ENST00000269305	g.chr17: 7517846G>A	p.R273C	missense
HCC224T	*TP53*	ENST00000269305	g.chr17: 7519095C>T	Splice site	Splice site
HCC225T	*TP53*	ENST00000269305	g.chr17: 7517842A>G	p.V274A	missense
HCC226T	*TP53*	ENST00000269305	g.chr17: 7517852C>A	p.E271X	Nonsense
HCC227T	*TP53*	ENST00000269305	g.chr17: 7520424C>T	Splice site	Splice site
HCC228T	*TP53*	ENST00000269305	g.chr17: 7517653T>A	Splice site	Splice site
HCC229T	*TP53*	ENST00000269305	g.chr17: 7517845C>T	p.R273H	missense
HCC230T	*TP53*	ENST00000269305	g.chr17: 7519094A>T	Splice site	Splice site
HCC231T	*TP53*	ENST00000269305	g.chr17: 7519251C>T	p.C135Y	missense
HCC207T	*TP53*	ENST00000269305	g.chr17: 7519135T>A	p.R174W	missense
HCC232T	*TP53*	ENST00000269305	g.chr17: 7517866C>A	p.G266V	missense
HCC233T	*TP53*	ENST00000269305	g.chr17: 7518996T>G	p.H193P	missense
HCC234T	*TP53*	ENST00000269305	g.chr17: 7518334C>T	Splice site	Splice site
HCC204T	*TP53*	ENST00000269305	g.chr17: 7520063delC	fs	Indel
HCC235T	*TP53*	ENST00000269305	g.chr17: 7517849C>T	p.V272M	missense
HCC370T	*TP53*	ENST00000269305	g.chr17: 7518252_7518254delGGA	in-frame del	indel
HCC416T	*TP53*	ENST00000269305	g.chr17: 7517839C>A	p.C275F	missense
HCC46T	*TP53*	ENST00000269305	g.chr17: 7518275_7518276insGG	fs	Indel
HCC477T	*TP53*	ENST00000269305	g.chr17: 7519114G>A	p.R181C	missense
HCC477T	*TP53*	ENST00000269305	g.chr17: 7518936C>T	p.R213Q	missense
HCC482T	*TP53*	ENST00000269305	g.chr17: 7518259C>A (homo)	p.R249S	missense
HCC554T	*TP53*	ENST00000269305	g.chr17: 7519233C>T	p.C141Y	missense
HCC241T	*TP53*	ENST00000269305	g.chr17: 7519128C>A	p.C176F	missense
HCC242T	*TP53*	ENST00000269305	g.chr17: 7517809T>A	p.E285V	missense
HCC243T	*TP53*	ENST00000269305	g.chr17: 7518272C>A	p.G245V	missense
HCC244T	*TP53*	ENST00000269305	g.chr17: 7517608_7517609insTTC	in-frame ins	Indel
HCC254T	*TP53*	ENST00000269305	g.chr17: 7517845C>T	p.R273H	missense
HCC246T	*TP53*	ENST00000269305	g.chr17: 7517863delC	fs	Indel
HCC247T	*TP53*	ENST00000269305	g.chr17: 7518259C>A	p.R249S	missense
HCC248T	*TP53*	ENST00000269305	g.chr17: 7519186C>A (homo)	p.V157F	missense
HCC221T	*TP53*	ENST00000269305	g.chr17: 7517809T>C	p.E285G	missense
HCC249T	*TP53*	ENST00000269305	g.chr17: 7519217C>T	p.W146X	Nonsense
HCC250T	*TP53*	ENST00000269305	g.chr17: 7520210C>A	p.E68X	Nonsense
HCC251T	*TP53*	ENST00000269305	g.chr17: 7514742C>T	p.R337H	missense
HCC44T	*TP53*	ENST00000269305	g.chr17: 7518259C>A	p.R249S	missense

*Coordinates refer to the human reference genome hg18 release (NCBI 36.1, March 2006).

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Supplementary Table 5. Primers used for PCR amplification and sequencing

Gene Symbol	Transcript IDs	Coding Exon Number	Genomic Region of Interest[*]	M13 PCR primer sequence[†]	PCR primer sequence
ARID2	ENST00000334344	1	chr12: 44409883-44409982	CTCTGGTAGGAAGCGCTGG	GGTGTAGAGACCGTGAAGATCC
ARID2	ENST00000334344	2	chr12: 44410090-44410191	AGGGACTCGCTTTCCTGG	CCAGCGAGAGGGAAATACAAA
ARID2	ENST00000334344	3	chr12: 44411263-44411368	TACCGATCGATCCGAAACAC	CTGTTTGGTGTGCAAGGTTTG
ARID2	ENST00000334344	4	chr12: 44491464-44491605	TGTGCAAAGGAAGGGACTAAC	TTGCATTGAGTTTATCTGCGG
ARID2	ENST00000334344	5	chr12: 44497716-44497942	GCTGTGTTCTGTATTCAAGGGA	AGCAATCGTCTCAACTCAGGA
ARID2	ENST00000334344	6	chr12: 44501466-44501541	AAATGAAAGCCAGTGTGGAGTAA	TTGTTGGCTTAGCTGCATGT
ARID2	ENST00000334344	7	chr12: 44516635-44516709	AGCCACCATACCTAGCCTGTG	CACTGCAATCTGAAGTACCCG
ARID2	ENST00000334344	8	chr12: 44516787-44517045	TCTGACAGAAACAAGTCTCATGG	GCCATTTCTGAATTTAAAGCATC
ARID2	ENST00000334344	9	chr12: 44517367-44517471	AACGTTATGCAACATTGTCCTG	GCAGCACATCAGGTAAAGTGAG
ARID2	ENST00000334344	10	chr12: 44517544-44517761	TCATCTGATGTTTCATACTGTTACAAA	GGAAACAAGTATGCCTGAGGA
ARID2	ENST00000334344	11	chr12: 44519375-44519550	CCAAATTCCACTTTGGCCTAC	ATGTGTTCACCAGTGATGGC
ARID2	ENST00000334344	12	chr12: 44526902-44526991	TTCTGGATGTCTGTAGAATACATTTCC	GCCTGGTATGATATGTGCTCC
ARID2	ENST00000334344	13	chr12: 44528882-44529024	ATTGCCTCCACATGGCTTTAG	CCTCCACCACACTATAACCTATCC
ARID2	ENST00000334344	14	chr12: 44529626-44529830	TCTTTGCTTTCCATCCTTGC	GAAGATTGGTTGGCAACAGG
ARID2	ENST00000334344	15	chr12: 44530082-44530142	TCCTGATGTATCTCCTGCTCC	AAAGACATTTGTGTTGCAGTCAG
ARID2	ENST00000334344	15	chr12: 44530143-44530354	GAGTGCCTGAAGGGATCTGTC	TTTCAGAGGACTCCTGTTGCC
ARID2	ENST00000334344	15	chr12: 44530355-44530637	CTGTGGCACAAACTGTTTCAA	GACTTGGGACACCAGCAATAG
ARID2	ENST00000334344	15	chr12: 44530638-44530920	GTAATTCCACAGCAGTCTTCCATT	TGGCTGGTGCATAAGTTTGAC
ARID2	ENST00000334344	15	chr12: 44530921-44531203	CTATTGCTGGTGTCCCAAGTC	TTACCACCTGGTGTTGAAGGA
ARID2	ENST00000334344	15	chr12: 44531204-44531489	TGCTGGGCTATTTGAGATCAGT	TCTTCCAGCTGGTCAGACAGT
ARID2	ENST00000334344	15	chr12: 44531490-44531732	GAAACGTGGTCCTTCAACACC	GGAAGTCCAACTCCTGTCTGC
ARID2	ENST00000334344	15	chr12: 44531733-44531900	TGAGTTCTGTTTCCCAGATGC	CCATAACAGTTGTGCCAAATACG
ARID2	ENST00000334344	15	chr12: 44531901-44532069	TGAGTTCTGTTTCCCAGATGC	GAACGCAGACAGGAGTTAG
ARID2	ENST00000334344	15	chr12: 44532070-44532333	AGGAAGCAAAGGAAGCAACAG	CACTAAATTGCTGTGTTGCCG
ARID2	ENST00000334344	15	chr12: 44532334-44532662	TCCTGCGACTGTTTCCCTATC	AGGTGAGAATGGAGCATCTGG
ARID2	ENST00000334344	15	chr12: 44532663-44532818	GCCCAAGTGTAGTTGTCTCACC	ATAACTTACCTGCGGGACCAC
ARID2	ENST00000334344	15	chr12: 44532819-44532950	AGGACAGGTTGGATACAAGTGAG	TTCGGTCTACAAATGGCACAG
ARID2	ENST00000334344	16	chr12: 44540847-44541003	TCGCTAAAGTTAGTGGTTCTAAAGG	CAATGTGGTATTACCTTCGTGG
ARID2	ENST00000334344	17	chr12: 44571826-44571972	AAGCAAGAGAATGGCGACGTC	TGATTCCACTTGGAAATATAAGCAG
ARID2	ENST00000334344	18	chr12: 44572057-44572150	ATGCAGCAACTGAACATGGAG	ATTGCTGGTTCATGGCAGAG
ARID2	ENST00000334344	19	chr12: 44573466-44573597	CTCACCTGCGACCACATTC	GGCAGGGTGGTCATAGTTGTC
ARID2	ENST00000334344	20	chr12: 44573676-44573775	TGGCCTGACCTAGGCATAAAC	GCATGCCTTGAAACCCTTATC
ARID2	ENST00000334344	21	chr12: 44584980-44585132	ACGAAGCTTCCTCTCAGCATC	ATGCTTCCCTCTCTTCCTGC
CTNNB1	ENST00000405570	1	chr3: 41240560-41240580	GCCTGACAAGTAAGCAGGGAG	AGACCATGAGGTCTGCGTTTC
CTNNB1	ENST00000405570	2	chr3: 41241017-41241252	TCCACAGTTCAGCATTTACCTAAG	AAATATTTCAATGGGTCATATCACAG
CTNNB1	ENST00000405570	3	chr3: 41241445-41241706	TGCAGCCTTATTAACCACCAC	CCTTACTGAAAGTCAGAATGCAG
CTNNB1	ENST00000405570	4	chr3: 41241825-41242071	ACGAGGACCAGGTAAGCAATG	ATCCACTGGTGAACTGGGAAG
CTNNB1	ENST00000405570	5	chr3: 41242151-41242360	AGAAACCATTCCCACAACCC	GGCCATCTTTAAGTCTGGAGG
CTNNB1	ENST00000405570	6	chr3: 41243699-41243851	TCTTGGCTGCAAACTGAATAGG	GCAAGCTGGCTGAAATTCTTG
CTNNB1	ENST00000405570	7	chr3: 41249832-41249943	CAGAAGGACACCTCCTAAGGC	AAGGAGACCTTCCATCCCTTC
CTNNB1	ENST00000405570	8	chr3: 41250020-41250366	GTAAACTGGTGCCATGGGAAT	CAGCCATCCAACAGCTAGAGA
CTNNB1	ENST00000405570	9	chr3: 41250630-41250796	AGGAAGTATGGCTGCGATAGG	GAAAGAAGTTCAGGATCCTTTGG
CTNNB1	ENST00000405570	10	chr3: 41252215-41252342	TGGAATCCTTCTTCCTTCCTG	GTGAAATGTGAAATCTCCTCCC
CTNNB1	ENST00000405570	11	chr3: 41252840-41252998	GCAGCTGCATATGTCGCTAAG	AATTGGGAATGTTTGCACCAC
CTNNB1	ENST00000405570	12	chr3: 41253079-41253208	AAGGAACCAAAGCCTTTAGCAG	AGGGAAACATCAATGCAAATG
CTNNB1	ENST00000405570	13	chr3: 41254507-41254575	GAGCAAACCGGCTCTTCTG	GCCTGGCAGCACATAATAGG
CTNNB1	ENST00000405570	14	chr3: 41255625-41255841	ACCACTCCCACCCTACCAAC	CTTTGGATGCCCTAACCTCAG
TP53	ENST00000269305	1	chr17: 7513648-7513737	CCATCTTGATTTGAATTCCCG	ATTGCAAGCAAGGGTTCAAAG
TP53	ENST00000269305	2	chr17: 7514648-7514762	AGCTGCCTTTGACCATGAAG	ATTGCACCATTGCACTCCC
TP53	ENST00000359597	1	chr17: 7517346-7517386	AGTTTATCAGGAAGTAACACCATCG	CAAAGACAATGGCTCCTGGTT
TP53	ENST00000269305	3	chr17: 7517574-7517655	GGAGCACTAAGCGAGGTAAGC	TTGTCTTTGAGGCATCACTGC
TP53	ENST00000269305	4	chr17: 7517740-7517884	TTGGGCAGTGCTAGGAAAGAG	GTTGGGAGTAGATGGAGCCTG
TP53	ENST00000269305	5	chr17: 7518220-7518337	AGAAATCGGTAAGAGGTGGGC	CATCCTTGGCTAACGGTGAAAC
TP53	ENST00000269305	6	chr17: 7518898-7519018	CTGCTCAGATAGCGATGGTG	AGGCCCTTAGCCTCTGTAAGC
TP53	ENST00000269305	7	chr17: 7519092-7519283	GGGCCAGACCTAAGAGCAATC	AAGCTCCTGAGGTGTAGACGC
TP53	ENST00000269305	8	chr17: 7520033-7520319	GAGGAATCCCAAAGTTCCAAAC	ACGTTCTGGTAAGGACAAGGG
TP53	ENST00000269305	9	chr17: 7520421-7520450	CAGTCAGATCCTAGCGTCGAG	AAATCATCCATTGCTTGGGAC
TP53	ENST00000269305	10	chr17: 7520560-7520641	AGGGTTGGAAGTGTCTCATGC	AGCCCAACCCTTGTCCTTAC
DMXL1	ENST00000311085	1	chr5: 118435160-118435254	GGAAGGAGGGAGGGAAGC	CCTTAGTTCTCAAGGGCCAGG
DMXL1	ENST00000311085	2	chr5: 118461569-118461702	TCTTTGAAACAAAGCCAAGTCTC	GGTAAGGGAAATAGTGCCAAATG
DMXL1	ENST00000311085	3	chr5: 118465525-118465604	CATTCTTAAGCATCAGTGAATGAAA	CAACAATTCATTGGCACAATTT
DMXL1	ENST00000311085	4	chr5: 118468770-118468856	CACACCCAGCAGAAGTGAAATAC	TTGACCACCAGTTATGGATATTCTC
DMXL1	ENST00000311085	5	chr5: 118473741-118473881	TTTGTAGAACACGGGAAATAGAGA	AAATACAGCCTTCTCCTCCGT
DMXL1	ENST00000311085	6	chr5: 118478065-118478139	CACAAAGATGTGGGTGTGAAAC	TTAGACGGGCATAGTGGTGTG
DMXL1	ENST00000311085	7	chr5: 118479748-118479934	GGCTCAGAAGTCCTGTAACTATGG	TCTGTGCTCAACGTCTCTTCC
DMXL1	ENST00000311085	8	chr5: 118482405-118482602	TTTCTTCATTGGTACCTTAGTTGG	TTCAGCCAAGTCAAATGTAATCA
DMXL1	ENST00000311085	9	chr5: 118484561-118484737	GGCTAAGACAGTCACCTCCAAT	GGATTAAGAGAACAGCCAGGTACTTT
DMXL1	ENST00000311085	10	chr5: 118492801-118493021	CCATGTTTGGATCATGTCATTG	TGAAAGAGAAGGACTTTCAGGC

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Gene	Transcript	Exon	Coordinates*	Forward primer†	Reverse primer†
DMXL1	ENST00000311085	11	chr5: 118496722-118496983	GCTATCCAGAAGCTCGGTAATTC	TGGAATTCTGGAAACAAAGGAC
DMXL1	ENST00000311085	12	chr5: 118497084-118497259	GCTAGTTTGGCATGTGGATTG	GCCACTGATTCAGAGAACCATC
DMXL1	ENST00000311085	12	chr5: 118497260-118497618	CTGGGTATAAGAGTGGGCAGC	TGCCTGTACCAAGAATGTTGAC
DMXL1	ENST00000311085	12	chr5: 118497619-118497776	GGCTACAAAGCATGCACTAGG	GGACACCAGATGTTGATAACCC
DMXL1	ENST00000311085	13	chr5: 118497858-118497987	GGCTGCCCACTCTTATACCC	CTTTCAAAGAGTGAAAGAAATGGTT
DMXL1	ENST00000311085	14	chr5: 118507431-118507528	GGACTATATTTAGGCCCACTTGAA	CAATAACCATGGATGAGGAACC
DMXL1	ENST00000311085	15	chr5: 118508126-118508236	CCATACGCTTACGTTCTGCTG	CCAATTCATCTTTATTAACTGCCTAA
DMXL1	ENST00000311085	16	chr5: 118510427-118510554	ACTTGTGTTTGAAGCCTTAGGTAAA	GAATGGCTTTAAGAAATATGTCCC
DMXL1	ENST00000311085	17	chr5: 118510839-118511068	AGCCATTCTCATTAAATGGTGATA	TTTCCATTTCTAGTTCTGTGTGGA
DMXL1	ENST00000311085	18	chr5: 118512329-118512575	AAACATACAGCCAAGATGCCC	GAATTGTCTGCTCAAGGACCC
DMXL1	ENST00000311085	18	chr5: 118512576-118512920	AAATGCCAGGGTTTCCTTACC	AGATGGAGAATCTGCCACGTC
DMXL1	ENST00000311085	18	chr5: 118512921-118513127	CCATATCCACTGAAGGATCGAA	CATATCCTGACTGTAGGAATTGGA
DMXL1	ENST00000311085	18	chr5: 118513128-118513334	GCAATGCACTTAACAAGATGGG	GGTAAGGAAACCCTGGCATTT
DMXL1	ENST00000311085	18	chr5: 118513335-118513648	AGTGGCCAGAAAGAACCTGAG	ACTGCATTCGATCCTTCAGTG
DMXL1	ENST00000311085	18	chr5: 118513649-118513961	TTACCTTGGCTTCTGTCTCGG	CTTGGTAAAGTTCGGAGAGCC
DMXL1	ENST00000311085	18	chr5: 118513962-118514019	CAAGCATCATCCCACCTCAG	TGGAGCAGATGTCTTTGATGG
DMXL1	ENST00000311085	19	chr5: 118515519-118515634	TCTCCAGTATGTTTCTTCATTAACTCC	AAGAATGTTATATGCCTATATTGGGTG
DMXL1	ENST00000311085	20	chr5: 118528097-118528274	GGCAGAGAAGATATGAAATGCC	ACAGTGGAATTTGCCATAAGC
DMXL1	ENST00000311085	21	chr5: 118528773-118528878	ATGGATATGTGCCAGCCTTTC	CCTCATCAGGTTTCTTCCACTC
DMXL1	ENST00000311085	22	chr5: 118530206-118530379	TTTGGCCTTGTGTTATTTCCA	AAGTTATGAACTGGCAGATGTTCTA
DMXL1	ENST00000311085	23	chr5: 118531193-118531462	AGACCATGAATTCAATTTGTTTG	TTGTTTCTTATCCTTCTTTGCTAATTT
DMXL1	ENST00000311085	24	chr5: 118533780-118533969	CCTTGCATCCAACTTTAATGG	ATGTGTTGTTGTCTCTTCAGTGC
DMXL1	ENST00000311085	24	chr5: 118533970-118534159	TGAAACACAACACTTGGTTGG	TTTCCACACATATGAGCCTAACA
DMXL1	ENST00000311085	24	chr5: 118534160-118534672	TCCATTAAAGTTGGATGCAAGG	TTTGGTGAGGCAAATCTTCAG
DMXL1	ENST00000311085	24	chr5: 118534673-118534878	AGCTTTCCCTAAAGCAACCG	TGCATTTGGCAGAAATGAAG
DMXL1	ENST00000311085	25	chr5: 118535368-118535567	TTGAAATGCTGACTTCTTCACATC	GGAATCAACATAAACTTGGCAATG
DMXL1	ENST00000311085	26	chr5: 118538851-118538935	AGGGTTTGAGATTCATCTGCC	GGAAATAGTTCATGAAGGCAAAG
DMXL1	ENST00000311085	27	chr5: 118540947-118541082	ACTGTAATTCAGAATGAGTGGTGAA	TTTCTCATTTGTACTTATTCTGTCCC
DMXL1	ENST00000311085	28	chr5: 118541586-118541842	AGAAGAAAGATATCCGTATTTGGG	TCAGTGACAGCTATGTTTGTTTGTC
DMXL1	ENST00000311085	29	chr5: 118553298-118553484	GTGCTTATTTGTAGTTAACCTTAGCTCTTA	TGGAATGTAGCCTGATACTAATGAAA
DMXL1	ENST00000311085	30	chr5: 118557418-118557568	TGGAGCAAGATCTGTGAGGAA	TGGCTGCTAAATTTCATGATTTC
DMXL1	ENST00000311085	31	chr5: 118559961-118560054	TCAGGTTGATTCCTGATAGTGG	CGGATACATTTACAGATGGTTGG
DMXL1	ENST00000311085	32	chr5: 118561345-118561554	CACTCCAGCCCGGATGAC	CACCTTGCACATCTTCCCTG
DMXL1	ENST00000311085	33	chr5: 118566909-118567034	TTGCCTATGTTTATGATACGTGTTT	TGGCACCAAGGAATTGTTATC
DMXL1	ENST00000311085	34	chr5: 118580491-118580585	CCAGATTGCAATTTAAGGAACTG	ATGCAAGTACTAATTGATAGATTGGC
DMXL1	ENST00000311085	35	chr5: 118584062-118584191	CATAAACGTATCTCCAAACTGAAGC	TTATTTAAAGCTCTTGCCACCC
DMXL1	ENST00000311085	36	chr5: 118584530-118584679	TTAAATCATCCTTTATCCATTAACCTAGA	TTGAGGTATGAGGTCATTGTGTG
DMXL1	ENST00000311085	37	chr5: 118588299-118588367	AAAGGTTCCCACACATTTCTT	GATCCTAGTCAGTAATGCCCAAA
DMXL1	ENST00000311085	38	chr5: 118596930-118597065	TGCTCCTATCGTATTTGAGGATG	ACTACTACCCACGGAGCTGTTC
DMXL1	ENST00000311085	39	chr5: 118600912-118601012	GCAAAGTGACTGAGAACACAGG	GGTGTCACACTGAGGGTAAGG
DMXL1	ENST00000311085	40	chr5: 118602579-118602678	CAGAGGATTTAAGAAAGCCAGAAAC	GGGCAGGAGATGACACTTTC
DMXL1	ENST00000311085	41	chr5: 118604009-118604069	CTTTCAAATCCTGCCATCCTG	CAAGATTCCACCACTGCATTC
DMXL1	ENST00000311085	42	chr5: 118607949-118608174	GCAATTAGCACTGCTGACTACAAA	CACCCAGTTTGTTTCCCATCT
DMXL1	ENST00000311085	43	chr5: 118610585-118610817	TCAGTGCATCAAGGGCAAAG	TACCTTAGGTGGTCTGCCTGC
NLRP1	ENST00000262467	1	chr17: 5345854-5345920	TGGTTACAGCGTTTCAGCATC	CCTCACCTAAGCCCATTTCTC
NLRP1	ENST00000269280	1	chr17: 5358794-5359121	GAGGGATGCAGAGATGAGAGAG	GATGGCAACTTGTTTGCAGAG
NLRP1	ENST00000269280	2	chr17: 5359513-5359565	TCCCTTCCTTTCTCTCTTCCC	CTCTAAGGACCCTTCCAGCTC
NLRP1	ENST00000269280	3	chr17: 5361786-5361935	TGTGTCCTCATCCTTCTGTGG	GTGCCCAGCTCCTTCATTG
NLRP1	ENST00000269280	4	chr17: 5364921-5365060	AAACACACAGATGCACCATCC	CCTCGATTTATCCTGTCCCTG
NLRP1	ENST00000269280	5	chr17: 5365564-5365834	CAAGAGCGAAACTCTGTCTCAA	CTGTACAAGAGGCCCATCCTT
NLRP1	ENST00000269280	6	chr17: 5374521-5374752	TAAGGAAGCCACAACACCCTC	TGAAGCCACTGTACCGTATCC
NLRP1	ENST00000269280	7	chr17: 5376862-5377032	CCCTTACAGTGCAGCCATAGG	CCAGTGGTGAGTGTGAGTTGG
NLRP1	ENST00000262467	7	chr17: 5377332-5377432	GAGCTCAAACAATCCTCCCAC	GTGTGTCTGCAGCTTCTGCTC
NLRP1	ENST00000269280	9	chr17: 5377937-5378036	TTTAGTGGGAATGTCATGTGGAC	CCATAGACGTTCTGGAGAGGG
NLRP1	ENST00000269280	10	chr17: 5380891-5380988	AGGTGACAGGTCCCAGGATTC	GACAAGTGCACCTCACTCTGG
NLRP1	ENST00000269280	11	chr17: 5383455-5383633	AAGGCCACAGATGCTGAGAAG	TGGTAAGAAACTTGGGTTGGC
NLRP1	ENST00000269280	12	chr17: 5385897-5386075	GAGATCCTGTAGGCTCCTCCC	ATGGTTGCTTATGGGTGTCTG
NLRP1	ENST00000269280	13	chr17: 5397426-5397604	ACAAAGACAAATCCCTCAGCC	GCTGGTCAGTACTGGAGATGG
NLRP1	ENST00000269280	14	chr17: 5402379-5402668	TGTCTTGGAGGATGAGAAGGG	GGAGACCCTGATCCTTTAGCC
NLRP1	ENST00000269280	14	chr17: 5402669-5403018	ACTTCCAAGACCACCACAACC	CCATCACTTGTGTCAGGAACG
NLRP1	ENST00000269280	14	chr17: 5403019-5403392	CAAGAAGGTGGAGATGATGGC	TGGTGTAGATGAGCCAGGATG
NLRP1	ENST00000269280	14	chr17: 5403393-5403722	AGCTGGCCTGATTATGTGGAA	ATTCCTTCCTGCTGGACTCAG
NLRP1	ENST00000269280	14	chr17: 5403723-5404091	AGACTCACCACCTTGGACTGG	GCAGTGTGTGGCTTGGAGTAG
NLRP1	ENST00000269280	15	chr17: 5425899-5426110	CTTAGCCTGCCAACCTGGTC	GACCCATCTCTCAGGACTGTTG
NLRP1	ENST00000269280	16	chr17: 5426710-5426894	AGGAGACCAGCTCAGTTCCC	CCATGCACAGACATGATCCTC
NLRP1	ENST00000269280	17	chr17: 5427727-5428005	AAGAGACGGTAAGAGCCAAGG	AGGGAGGGCTCAGTGGTG

*Coordinates refer to the human reference genome hg18 release (NCBI 36.1, March 2006).

†M13 denotes the universal sequencing primer 5'-GTAAAACGACGGCCAGT-3'.

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Supplementary Table 6. Clinical characteristics of 23 patients with HCV-associated hepatocellular carcinoma used in the first prevalence screen

Sample	Age	Sex	Self-reported ethnicity	Geographic location	Etiology	Stage	Source of tumor DNA	Histological type	Source of matched normal DNA
HCC05T	62	Female	Black	United States	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC14T	60	Male	Black	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC15T	46	Male	White	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC16T	51	Male	Black	United States	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC17T	51	Male	White	United States	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC18T	75	Male	White	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC19T	56	Male	White	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC20T	55	Male	Black	United States	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC21T	70	Female	Hispanic	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC22T	65	Male	White	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC23T	67	Male	White	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC24T	66	Male	Arabic	United States	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC25T	65	Male	White	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC26T	56	Male	White	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC27T	52	Female	White	United States	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC28T	65	Female	White	United States	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC29T	73	Male	White	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC30T	73	Female	Asian	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC44T	70	Female	Not available	Netherlands	HCV	Not available	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC45T	49	Female	Not available	Netherlands	HCV	Not available	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC47T	53	Male	Not available	Netherlands	HCV	Not available	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC252T	55	Female	Black	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC253T	61	Male	White	United States	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver

Supplementary Table 7. Clinical characteristics of 106 patients with hepatocellular carcinomas used in the second prevalence screen

Sample	Age	Sex	Self-reported ethnicity	Geographic location	Etiology	Stage	Source of tumor DNA	Histological type	Source of matched normal DNA
HCC41T	67	Male	not available	Netherlands	HBV	Not available	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC42T	55	Male	not available	Netherlands	HBV	Not available	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC43T	64	Male	not available	Netherlands	HBV	Not available	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC46T	54	Male	not available	Netherlands	HBV	Not available	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC48T	48	Male	not available	Netherlands	HBV	Not available	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC235T	77	Female	White	United States	No known underlying liver disease	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC200T	60	Female	White	United States	Cryptogenic cirrhosis	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC276T	63	Male	Asian	United States	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC255T	80	Male	White	United States	No known underlying liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC16T	25	Female	White	United States	HCC arising in hepatic adenoma	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC165T	59	Male	White	United States	No known underlying liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC50T	70	Male	White	United States	No known underlying liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC187T	54	Male	White	United States	Cryptogenic cirrhosis	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC300T	60	Male	White	United States	Alcohol, Alpha-1-antitrypsin deficiency	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC158T	59	Female	Asian	United States	HBV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC140T	53	Male	White	United States	Cryptogenic cirrhosis	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC245T	54	Female	Black	United States	Cryptogenic cirrhosis	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC64T	63	Male	Black	United States	Alcohol	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC1T	55	Male	White	United States	No known underlying liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC46T	71	Male	White	United States	No known underlying liver disease, mild steatosis	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC38T	65	Male	Black	United States	HBV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC366T	62	Male	White	United States	Alcohol	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC368T	33	Female	White	United States	HCC arising in hepatic adenoma	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC370T	50	Female	Black	United States	No known underlying liver disease	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC388T	47	Female	White	United States	No known underlying liver disease	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC467T	19	Female	Black	United States	No known underlying liver disease	T3A	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC412T	45	Female	White	United States	No known underlying liver disease	t1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC413T	48	Female	White	United States	HCC arising in hepatic adenoma	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC416T	76	Male	Asian	United States	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC505T	69	Male	Asian	United States	No known underlying liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC484T	74	Male	White	United States	No known underlying liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC448T	37	Male	Black	United States	HBV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC471T	53	Male	White	United States	Alpha-1-antitrypsin deficiency	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC477T	46	Male	Asian	United States	HBV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC482T	65	Female	Asian	United States	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC492T	48	Female	White	United States	HCC arising in hepatic adenoma	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC507T	60	Male	White	United States	No known underlying liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC521T	64	Female	White	United States	No known underlying liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC524T	52	Male	Asian	United States	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC553T	74	Female	White	United States	No known underlying liver disease	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC554T	63	Female	White	United States	No known underlying liver disease	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC556T	69	Male	White	United States	No known underlying liver disease	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC571T	73	Male	Asian	United States	HBV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC567T	76	Male	White	United States	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC568T	64	Male	White	United States	No known underlying liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC219T	58	Male	Asian	China	Cirrhosis, alcohol	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC205T	66	Male	Asian	China	Cirrhosis	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC256T	62	Male	Asian	China	Cirrhosis	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC257T	47	Female	Asian	China	Cirrhosis	T3a	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC209T	63	Male	Asian	China	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC210T	64	Male	Asian	China	HBV, HCV	T3a	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC211T	56	Male	Asian	China	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC224T	72	Male	Asian	China	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC258T	74	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC202T	68	Male	Asian	China	HBV	T3	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC259T	44	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC241T	52	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC203T	76	Male	Asian	China	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC212T	73	Male	Asian	China	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC242T	45	Male	Asian	China	HBV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC260T	61	Male	Asian	China	No underlining liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC261T	50	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC243T	46	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC262T	29	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC263T	63	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC264T	74	Male	Asian	China	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC213T	52	Male	Asian	China	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC265T	70	Female	Asian	China	HBV	T3	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC244T	50	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC225T	57	Female	Asian	China	HBV, HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC266T	48	Female	Asian	China	HBV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC254T	59	Male	Asian	China	Cirrhosis, alcohol	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC226T	68	Female	Asian	China	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC214T	59	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver

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HCC206T	74	Female	Asian	China	No underlining liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC227T	83	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC228T	61	Male	Asian	China	HBV	T3a	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC267T	53	Male	Asian	China	HBV	T3a	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC229T	60	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC220T	75	Male	Asian	China	No underlining liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC230T	48	Male	Asian	China	HBV	T3a	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC215T	60	Male	Asian	China	HBV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC231T	47	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC207T	53	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC268T	69	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC269T	56	Female	Asian	China	HBV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC208T	65	Female	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC246T	74	Male	Asian	China	No underlining liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC232T	58	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC233T	69	Female	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC270T	61	Female	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC271T	55	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC247T	36	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC272T	37	Female	Asian	China	HBV	T3a	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC248T	53	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC221T	52	Male	Asian	China	HBV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC249T	55	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC273T	52	Female	Asian	China	Mild cirrhosis	T3a	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC234T	77	Male	Asian	China	HCV	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC222T	72	Male	Asian	China	No underlining liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC223T	71	Male	Asian	China	Mild cirrhosis	T2	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC250T	47	Male	Asian	China	No underlining liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC274T	53	Male	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC251T	54	Male	Asian	China	No underlining liver disease	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC275T	48	Female	Asian	China	HBV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver
HCC204T	71	Male	Asian	China	HCV	T1	Primary tumor	Hepatocellular carcinoma	non-neoplastic liver

Supplementary Table 8. Comparison of five mutated genes, *TP53, CTNNB1*, *ARID2*, *DMXL1* and *NLRP1* in human hepatocellular carcinomas from different geographic locations

Geographic locations	Total cases	*TP53* mutations	*CTNNB1* mutations	*ARID2* mutations	*DMXL1* mutations	*NLRP1* mutations
United States and Europe	78	11 (14.1%)	14 (17.9%)	8 (10.3%)	2 (2.6%)	2 (2.6%)
China	61	28 (45.9%$^\$$)	14 (23.0%)	1 (1.6%)	4 (6.6%)	2 (3.3%)

$^\$$ Prevalence of *TP53* mutations in United States and Europe vs China, P<0.0001