Global profiling of alternative RNA splicing events provides insights into molecular differences between various types of hepatocellular carcinoma.

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SUPPLEMENTAL DATA

Supplementary table 1 – Protein families encoded by transcripts that are differentially spliced in various types of HCC

	THBV/NNoV		THCV/NNoV		THBV&HCV/NNoV		TNoV/NNoV	
Protein classification	**Freq.**	**Percent.**	**Freq.**	**Percent.**	**Freq.**	**Percent.**	**Freq.**	**Percent.**
Extracellular matrix protein (PC00102)	29	1.5%	12	1.4%	1	0.6%	18	1.2%
Protease (PC00190)	50	2.5%	18	2.0%	5	3.0%	38	2.5%
Cytoskeletal protein (PC00085)	100	5.1%	53	6.0%	10	6.0%	88	5.7%
Transporter (PC00227)	105	5.3%	56	6.3%	7	4.2%	91	5.9%
Transmembrane receptor regulatory/adaptor protein (PC00226)	4	0.2%	3	0.3%	1	0.6%	4	0.3%
Transferase (PC00220)	159	8.0%	64	7.2%	11	6.6%	121	7.8%
Oxidoreductase (PC00176)	68	3.4%	27	3.1%	5	3.0%	60	3.9%
Lyase (PC00144)	27	1.4%	11	1.2%	2	1.2%	16	1.0%
Cell adhesion molecule (PC00069)	52	2.6%	20	2.3%	3	1.8%	44	2.9%
Ligase (PC00142)	54	2.7%	32	3.6%	7	4.2%	49	3.2%
Nucleic acid binding (PC00171)	225	11.4%	114	12.9%	18	10.8%	173	11.2%
Signaling molecule (PC00207)	101	5.1%	39	4.4%	11	6.6%	61	4.0%
Enzyme modulator (PC00095)	147	7.4%	74	8.4%	16	9.6%	103	6.7%
Calcium-binding protein (PC00060)	40	2.0%	19	2.2%	5	3.0%	31	2.0%
Defense/immunity protein (PC00090)	63	3.2%	24	2.7%	4	2.4%	49	3.2%
Hydrolase (PC00121)	187	9.5%	77	8.7%	15	9.0%	144	9.3%
Transfer/carrier protein (PC00219)	39	2.0%	22	2.5%	2	1.2%	34	2.2%
Membrane traffic protein (PC00150)	54	2.7%	22	2.5%	7	4.2%	36	2.3%
Phosphatase (PC00181)	45	2.3%	17	1.9%	3	1.8%	38	2.5%
Transcription factor (PC00218)	156	7.9%	67	7.6%	15	9.0%	128	8.3%
Chaperone (PC00072)	15	0.8%	2	0.2%	0	0.0%	4	0.3%
Cell junction protein (PC00070)	10	0.5%	9	1.0%	2	1.2%	10	0.6%
Surfactant (PC00212)	6	0.3%	4	0.5%	0	0.0%	4	0.3%
Structural protein (PC00211)	9	0.5%	5	0.6%	1	0.6%	9	0.6%
Receptor (PC00197)	132	6.7%	53	6.0%	8	4.8%	112	7.3%
Kinase (PC00137)	73	3.7%	32	3.6%	6	3.6%	61	4.0%
Storage protein (PC00210)	5	0.3%	1	0.1%	0	0.0%	4	0.3%
Isomerase (PC00135)	20	1.0%	5	0.6%	1	0.6%	11	0.7%
Splicing factor	23	1.16%	13	1.6%	2	1.2%	15	1.0%
Tumor suppressor	138	6.7%	63	3.0%	10	6.0%	109	7.1%
Oncogene	9	0.5%	4	0.5%	1	0.6%	5	0.3%

Supplementary table 2 - Bioinformatical prediction of functional changes caused by some of ASEs identified. (Negative delta-PSI means that the short isoform is favored and positive delta-PSI means that the long isoform is favored)

Gene	Delta PSI				Event type	Predicted residue variation (AA)	Predicted functional consequence
	THBV/NNoV	THCV/NNoV	THBV&HCV/NNoV	TNoV/NNoV			
A2M	-13,1	N/S	N/S	N/S	exon-skipping	-150	Loss of signal peptide, loss of part of MG2 domain
AAK1	-10,3	N/S	N/S	N/S	alternate-3p	-1	Unknown/No predicted functional change
ABCC10	-15,1	N/S	N/S	-17,0	alternate-3p	28	Gain of signal peptide
ACTA2	-22,2	N/S	N/S	N/S	exon-skipping	-45	Loss of part of actin domain
ACVRL1	-15,5	N/S	N/S	N/S	multiple-exon-skipping	-174	Loss of a transmembrane domain, loss of a TGFb domain, loss of a tyrosine kinase domain
ADCY5	16,2	N/S	N/S	N/S	exon-skipping	8	Unknown/No predicted functional change
ALDH1A3	-16,4	N/S	N/S	N/S	multiple-exon-skipping	-107	Loss of a part of aldehyde dehydrogenase domain
ALDH2	-12,1	N/S	N/S	N/S	exon-skipping	-47	Loss of a part of aldehyde dehydrogenase domain
AMDHD1	-18,4	N/S	N/S	N/S	exon-skipping	-109	Loss a part of aminohydrolase family domain
ANGPT1	21,1	22,7	N/S	N/S	alternate-5p	1	Unknown/No predicted functional change
ANKIB1	-11,6	N/S	N/S	N/S	exon-skipping	-731	Loss of all domains (ankyrin repeat, ankyrin repeat 5, IBR domain (a half ring finger domain))
ASPG	-21,8	-19,7	N/S	-21,5	exon-skipping	-18	Unknown/No predicted functional change
AXIN1	-10,9		N/S	N/S	exon-skipping	-36	Unknown/No predicted functional change
BUB1B	N/S	-24,6	N/S	-20,5	alternate-3p	513	Gain a protein kinase domain and complete a Mad3/bub1 domain
C16orf59	29,0	31,9	N/S	33,6	alternate-3p	43	Complete the DUF (domain of unknown function) incomplete in the short isoform protein
C5orf34	30,5	25,6	N/S	27,6	exon-skipping	441	Complete the DUF4524 (domain of unknown function) incomplete in the short isoform protein
CA13	15,9	16,1	N/S	12,1	exon-skipping	262 AA protein to no protein	Loss of the protein with a carbonic anhydrase domain du to NMD

CAND1	-15,7	N/S	N/S		alternate-5p+alternate-3p	-490	Loss of transmembrane domains
CENPL	-25,4	-29,8	-34,3	-29,4	exon-skipping	-46	Unknown/No predicted functional change
EHD3	-12,7	N/S	N/S	N/S	multiple-exon-skipping	-360	Loss of 2 NLS, loss a part of dynamin domain
EHF	37,8	N/S	N/S	35,2	exon-skipping	23	Unknown/No predicted functional change
GTPBP4	-22,6	N/S	N/S	N/S	exon-skipping	-116	Unknown/No predicted functional change
HADHA	-18,1	N/S	N/S	N/S	exon-skipping	-87	Loss of a part of the enoyl-CoA hydratase/isomerase domain
HAUS6	-17,0	N/S	N/S	N/S	alternate-3p	-35	Unknown/No predicted functional change
HBEGF	-13,0	N/S	N/S	N/S	exon-skipping+alternate-5p+alternate-3p	208 AA protein to no protein	Loss of the protein with an EGF-like domain du to the exclusion of the only exon coding for protein
HGF	-18,5	-17,6	N/S	-14,9	alternate-3p	-5	Unknown/No predicted functional change
IGFALS	N/S	10,1	N/S	N/S	alternate-3p	38	Gain of transmembrane domains
ITGB1	24,7	N/S	N/S	N/S	exon-skipping	3	Unknown/No predicted functional change
KIFC1	43,5	43,1	53,2	41,6	alternate-3p	8	Unknown/No predicted functional change
KMO	10,2	N/S	11,9	N/S	alternate-3p	27	Unknown/No predicted functional change
LRRC16B	31,4	35,5	N/S	35,7	exon-skipping	947	Change of cellular localisation and loss of a part of CARMIL CTERM domain
MARVELD2	N/S	-15,1	N/S	N/S	exon-skipping	-12	Unknown/No predicted functional change
MSS51	-10,3	N/S	N/S	N/S	alternate-3p	-221	Loss of a signal peptide, loss of a MYND finger domain
MT1G	-21,7	N/S	N/S	-13,8	alternate-3p	-1	Unknown/No predicted functional change
MXD3	39,5	34,2	42,7	35,3	intron-retention	195	Unknown/No predicted functional change
NFKB1	15,0	N/S	N/S	N/S	alternate-3p	1	Unknown/No predicted functional change
NOMO2	N/S	N/S	21,1	N/S	exon-skipping	167	Gain of a signal peptide
PANX2	10,1	N/S	N/S	N/S	exon-skipping	-134	Gain of innexin domain and of 2 transmembrane domains

PHF14	-12,1	-14,0	N/S	N/S	exon-skipping	-285	Unknown/No predicted functional change
PRPF4B	-34,5	-31,5	N/S	-27,0	alternate-5p+intron-retention	No protein to a 1007 AA protein	Gain of a tyrosine kinase protein (long isoform: NMD)
PTPN1	-22,0	N/S	N/S	N/S	exon-skipping	-73	Loss of a part of Y-phosphatase domain
RAB7A	-17,5	N/S	N/S	N/S	alternate-5p	-47	Loss of half the Ras domain
RARB	-12,1	N/S	N/S	N/S	alternate-5p	-112	Loss of a part of ZF-C4 domain (binding to DNA)
RINT1	-11,7	N/S	N/S	N/S	alternate-5p+alternate-3p+multiple-exon-skipping	-425	Loss of NLS and loss of a part of RINT1 TIP1 domain
SCRIB	-18,3	-16,8	N/S	-17,9	exon-skipping	-25	Unknown/No predicted functional change
SFMBT1	-10,1	N/S	N/S	N/S	exon-skipping	-96	Loss of SAM1 domain
SHQ1	-13,5	-14,2	N/S	-13,1	alternate-3p	89	Unknown/No predicted functional change
SLIT2	62,9	N/S	N/S	43,6	exon-skipping	8	Unknown/No predicted functional change
SPAG4	-27,2	N/S	-33,6	N/S	alternate-5p	-77	Unknown/No predicted functional change
SPINT2	N/S	-11,8	N/S	N/S	exon-skipping	-57	Loss of Kunitz domain (inhibition of proteases)
SUZ12	-12,7	N/S	N/S	N/S	exon-skipping	-23	Unknown/No predicted functional change
TPSB2	N/S	N/S	19,3	N/S	alternate-3p	152	Gain of signal peptide, gain of complete trypsin domain
VPS13A	-21,2	-16,2	-24,6	-18,0	exon-skipping	-39	Unknown/No predicted functional change
WASF2	-28,6	-14,5	N/S	-13,6	exon-skipping	-217	Loss of the WH2 motif
ZGRF1	15,5	17,4	N/S	14,3	exon-skipping	No protein to a 2104 AA protein	Gain of a protein with 2 AAA domains, a GRF zinc finger motif and a DUF2439 domain (short isoform: NMD)
ZNF35	12,3	N/S	N/S	N/S	exon-skipping	160	Cytoplasmic protein (short isoform) goes to non-cytoplasmic (long isoform)
ZNF445	-19,8	N/S	N/S	-20,2	alternate-5p	-12	Unknown/No predicted functional change
ZNF451	-15,6	N/S	N/S	N/S	exon-skipping	-48	Unknown/No predicted functional change
ZNF532	-14,5	-12,7	N/S	N/S	alternate-5p	-910	Unknown/No predicted functional change
ZNF552	-10,6	N/S	-16,4	-12,3	alternate-5p	4	Unknown/No predicted functional change

Supplementary table 3 – List of tumor suppressors for which AS is dysregulated in various types of HCC

THBV/NNoV

ABI2
ACHE
AFAP1L2
AGTR1
ALPL
ARID2
ARNTL
AXIN1
BARD1
BCL2L11
BIN1
BLNK
BRCA1
BRF1
BTK
CABLES1
CADM2
CASP8
CCAR1
CCNDBP1
CD44
CDK2
CEACAM1
CHEK1
CHEK2
CIZ1
CNDP2
CREM
CSMD1
CTCF
CTNNA3
CTNND1
CYLD
DDB2
DLG1
DMD
DNAJA3
DNMT3B
EEF1A1
EGR2
EHD3
EHF
EI24
EMP1
EPB41
ESR1
EZH1
EZH2
FAS
FLNA
FOXP1
GADD45A
GLS2
GPC3
GSN
GSTT1
GTPBP4
HPGD
HTATIP2
ING1
ING3
ING4
IRF3
ITGA7
ITGB1
KANK1
KDM8
KLF6
KMT2C
KRIT1
MAD1L1
MBD4
MFSD2A
MME
MT1G
MTSS1
MTUS1
NDRG2
NF1
NF2
NFKB1
NUMB
PANX2
PBRM1
PDCD4
PHACTR4
PLAGL1
PPARA
PPP2R1B
PTCH1
PTPN1
PTPN6
RAB7A
RAP1GAP
RARB
RASSF1
RBL2
RBM6
RBMX
RINT1
RNF111
RNH1
RPL10
RUNX3
SAFB
SAMD9L
SCRIB
SDHA
SEMA3B
SEPT4
SHQ1
SIRT2
SIRT3
SKP2
SLIT2
SMARCB1
SPOP
SRPX
STRADA
SUZ12
TBRG1
TCF3
TCF7L2
TES
TET2
TFPI2
THRB
TRIM35
TRIT1
TSC1
UHRF2
UVRAG
VEGFA
VEZT
VPS53
WWOX
XAF1
ZNF382

THCV/NNoV

AFAP1L2
BARD1
BIN1
BRCA1
CD44
CDKN2A
CEACAM1
CHEK1
CIZ1
COPS2
CREM
CSMD1
CTNNA3
DIABLO
DLG1
DNMT3B
DOK1
EMP1
ESR1
FLNA
GLS2
GPC3
GSN
HPGD
IGFALS
ING1
ING3
ING4
IRF3
ITGA7
KANK1
KDM8
KMT2C
KRIT1
MAD1L1
MLH1
MTSS1
NDRG2
NF1
NF2
NUMB
PBRM1
PPARA
PTPN6
RASSF4
RPL10
SAMD9L
SCRIB
SEPT4
SHQ1
SIRT3
SMARCB1
SPINT2
TBRG1
TCF3
TCF7L2
TP73
TRIT1
TSC2
VDR
VEGFA
VEZT
WNK2

THBV&HCV/NNoV

CASP8
CTNND1
FHIT
HACE1
ITGA7
KRIT1
LIMA1
NDRG2
NF2
TET2

TNoV/NNoV

ABI2
AFAP1L2
AGTR1
ALDH1A2
ALPL
ARNTL
BARD1
BCL2L11
BIN1
BLNK
BRCA1
BRF1
CADM2
CASP8
CCDC136
CCNDBP1
CD4
CD44
CDK2
CEACAM1
CHEK1
CIZ1
CREM
CSMD1
CTCFL
CTNNA3
CTNND1
CUX1
CYLD
DICER1
DLG1
DNMT3B
ECT2
EDA2R
EGR2
EHF
EI24
ESR1
EZH1
EZH2
FOXP1
GLS2
GPC3
GSN
GSTT1
HOPX
HPGD
IKZF1
IKZF2
ING1
ING4
IRF3
ITGA7
KDM8
KMT2C
KRIT1
LRP1B
MAD1L1
MFSD2A
MLH1
MT1G
MTSS1
MTUS1
NDRG2
NF2
NPAS2
NRCAM
NUMB
PARK2
PBRM1
PLAGL1
PLCB3
PML
PPARA
PRR5
PTCH1
PTPN6
RAP1GAP
RASSF1
RASSF4
RBM6
RNH1
RPL10
SCRIB
SEC14L2
SEMA3B
SEPT4
SHQ1
SIRT3
SLIT2
SMARCA4
SMARCB1
SRPX
STRADA
TBRG1
TCF3
TCF7L2
TFPI2
THRB
TRIT1
TSC1
VDR
VEGFA
VEZT
VPS53
WWOX
XAF1
ZMYND11
ZNF382

Supplementary table 4 - List of oncogenes for which AS is dysregulated in various types of HCC

THBV/NNoV	THCV/NNoV	THBV&HCV/NNoV	TNoV/NNoV
CBFB	ETS1	CBFB	AXL
DEK	KRAS		CBFB
ERBB2	MYH11		MDM2
ERG	TSC2		MYH11
ETS1			PML
KRAS			
MDM2			
MYH11			
TAL1			

Supplementary table 5 - List of kinases for which AS is dysregulated in various types of HCC

THBV/NNoV		THCV/NNoV	THBV&HCV/NNoV	TNoV/NNoV	
ALPK1	MAST4	AURKA	AURKB	AURKA	MPP1
AURKA	MELK	AURKB	CDK1	AURKB	MPP3
AURKB	MORN4	CAMK2D	PI4KAP1	BRSK2	MPP4
AURKC	MPP3	CDC42BPA	PIK3CB	CAMK2D	MVK
BRSK2	MVK	CDK1	RPS6KA4	CAMK2G	NEK2
BTK	NRBP2	CDK10	SLAMF7	CD244	NRBP2
CAMK2D	PANK1	CHKB		CDC42BPA	PAPSS2
CD244	PAPSS2	DGKZ		CDK1	PASK
CD84	PASK	DGUOK		CDK10	PI4KAP1
CDC42BPA	PFKM	DMPK		CDK2	PIK3CG
CDK1	PI4KAP1	FES		CDK4	PRPF4B
CDK10	PIK3CB	FYN		CDKL3	PRPS2
CDK14	PIP4K2C	GK5		CERKL	PTK7
CDK2	PIP5K1A	IP6K2		CHKB	RIPK2
CDK20	PRKDC	KHK		CLK3	SGK3
CDK4	PRPF4B	MAGIX		CLK4	SLAMF7
CDKL3	PRPS1	MAP3K6		CSNK1G1	SPHK2
CHKB	PRPS2	MORN1		DGKG	SRPK1
CIT	RIPK1	MORN4		DGKH	STK16
CMPK1	RIPK2	PAPSS2		DGKZ	TK2
DGKG	SGK1	PI4KAP1		DGUOK	TNK2
DGKZ	SGK3	PIK3CB		DSTYK	ULK3
DGUOK	SLAMF6	PRPF4B		FASTK	VRK2
EIF2AK2	SLAMF7	PTK6		FES	WNK4
FES	SPHK2	RIPK1		FGGY	
FYN	SRPK1	RPS6KA4		FYN	
GK5	STK16	SPHK2		GK5	
GNE	TANC1	STK16		IKBKB	
HCK	TESK2	ULK3		IP6K2	
IKBKB	TK2	WNK1		KHK	
IKBKE	TNK2	WNK2		KSR1	
IP6K2	ULK3	WNK4		MAP3K6	
KHK	VRK2			MAPK13	
KSR1	WNK1			MARK1	
MAGIX	WNK3			MAST4	
MAPK13	WNK4			MELK	
MARK3				MORN4	

Supplementary table 6 - List of transcription factors for which AS is dysregulated in various types of HCC

THBV/NNoV				THCV/NNoV		THBV&HCV/NNoV	TNoV/NNoV		
ARHGAP5	KBTBD4	RNH1	ZNF35	BCL11A	TCEA3	ARHGAP5	ARNTL	NCOR1	ZBTB24
ARNTL	KDM4A	RRN3	ZNF382	CARD8	TCF20	HDGFRP2	ATXN3	NFAT5	ZBTB38
ARNTL2	KDM5D	RUNX3	ZNF408	CCNL2	TCF3	KAT6A	BCL11A	NFATC4	ZBTB41
BCL11A	KRBOX4	SFMBT1	ZNF419	CNOT1	TFDP2	LIMA1	BRF1	NFE2	ZFP64
BRF1	LMO2	SMARCE1	ZNF445	CNOT8	TP73	MXD3	C3orf67	NFE2L2	ZMYM6
BTBD1	LRRC16B	SOX13	ZNF451	CREM	UBAC2	NLRC5	CARD8	NFIA	ZMYND11
C3orf67	LRRFIP2	SPOP	ZNF502	CRIP2	UTY	SMARCC2	CBFA2T2	NFYA	ZNF107
CAND1	MKL1	SREBF1	ZNF512	E2F7	VDR	SUPT20H	CCNL2	NFYC	ZNF138
CARD8	MLXIPL	STAT6	ZNF532	ETS1	XPNPEP3	TLE2	CDIP1	NLRC5	ZNF169
CBFA2T2	MORF4L2	SUPT20H	ZNF550	FHL2	YY1AP1	ZBTB24	CNOT8	NLRP6	ZNF195
CCNL2	MPND	TAF11	ZNF552	FOSB	ZBTB38	ZMYM1	CREB3L4	NPAS2	ZNF200
CDIP1	MSS51	TAF6	ZNF567	FOSL1	ZEB1	ZMYND8	CREM	NR1I3	ZNF233
CIITA	MXD3	TAL1	ZNF618	FOXM1	ZHX3	ZNF211	CRIP2	NR2C1	ZNF248
CLOCK	NCOA3	TBX3	ZNF707	GATA3	ZNF138	ZNF552	CTCFL	NR3C1	ZNF266
CNOT1	NCOR1	TCEA3	ZNF793	HDGFRP2	ZNF169	ZNF667	CUX1	PDLIM2	ZNF274
CNOT8	NFAT5	TCF20	ZNF85	HMGB2	ZNF195		E2F6	PDLIM5	ZNF285
CREM	NFATC3	TCF3	ZNF852	HNF1B	ZNF248		E2F7	PHC2	ZNF331
CRIP2	NFIA	TEAD2	ZSCAN2	HOXB6	ZNF532		EHF	PLAG1	ZNF346
CTCF	NFKB1	TFDP2		ING1	ZNF550		ELK1	PLAGL1	ZNF382
E2F6	NFYA	TFEB		ING4	ZNF559		FHL2	POGZ	ZNF408
E2F7	NLRC5	TFEC		IRF3	ZNF707		FOSB	PPARA	ZNF431
EHF	NLRP6	THRB		JMJD1C			FOSL1	PQBP1	ZNF445
ELF1	NR1D1	TLE2		KDM5D			FOXM1	PRDM16	ZNF446
ELK1	NR1I3	TOX4		LRRC16B			FOXP1	RARG	ZNF502
ERG	NR2C1	TRIM35		LRRFIP2			FOXP2	REST	ZNF512
ETS1	NR3C1	UBAC2		MARVELD2			GATA3	RNH1	ZNF527
FHL2	NR3C2	USF2		MLXIPL			HDGFRP2	RRN3	ZNF550
FOSB	PDDC1	UTY		MORF4L2			HMGB2	SMARCE1	ZNF552
FOSL1	PDLIM2	WIZ		MXD3			HOXB6	STAT6	ZNF582
FOXK2	PDLIM5	XPNPEP3		MYNN			IKZF1	SUPT20H	ZNF618
FOXM1	PEPD	YY1AP1		NCOA1			IKZF2	TAF6	ZNF707
FOXP1	PHC2	ZBTB24		NCOA3			ING1	TCEA3	ZNF738
GABPA	PHF14	ZBTB38		NCOR1			ING4	TCF12	ZNF79
GATA3	PLAG1	ZBTB41		NFYA			IRF3	TCF20	ZNF793
GCFC2	PLAGL1	ZEB1		NR1I3			IVNS1ABP	TCF3	ZNF821
GNE	POGZ	ZEB2		NR2C1			JMJD1C	TEAD2	ZSCAN2
HDGFRP2	PPARA	ZFP64		NR3C1			KDM5D	TEAD4	
HMGB2	PPARD	ZHX3		PHC2			LMO2	TFDP2	
HNF1B	PQBP1	ZNF107		PHF14			LRRC16B	THRB	
HOXB6	PRDM16	ZNF131		PLAG1			LRRFIP2	TLE2	
ING1	PRRC2B	ZNF195		POGZ			MKL1	UBAC2	
ING4	RARA	ZNF200		PPARA			MLXIPL	UTY	
IRF3	RARB	ZNF211		PQBP1			MORF4L2	VDR	
IRF6	RARG	ZNF233		PRRC2B			MPND	XPNPEP3	
IVNS1ABP	RBL2	ZNF248		PRRC2C			MXD3	YY1AP1	
JMJD1C	RELA	ZNF331		RRN3			NCOA3	ZBTB17	

Supplementary table 7 - List of genes for which AS is dysregulated in all types of HCC

ASEs misregulated in the four types of HCC

ACP1
ACSL4
ASPM
ATXN2L
AURKB
C1orf86
C5orf42
C6orf201
CARD14
CARKD
CCDC64
CD27-AS1
CDC45
CDK1
CDS2
CENPL
CEP164
CLN3
DHRS4L2
ENO3
FAM86C1
FDFT1
FETUB
FN1
GOLGA2
GPR116
HDGFRP2
HNRNPUL1
IL17RE
IL32
INCENP
ISYNA1
ITGA7
KIAA0895L
KIAA1324
KIFC1
KRIT1
MDK
MICU1
MSTO1
MXD3
NDRG2
NEB
NF2
NIPA2
OGFOD2
OSBPL6
PARPBP
PCYT2
PDE4DIP
PHF3
PI4KAP1
PIK3R3
PMM2
POLL
PORCN
RCC1
RGS3
SEC31B
SKA2
SLC2A6
SLC7A7
SORT1
ST3GAL3
STAU2
STK25
TAMM41
TJP2
VEGFB
VPS13A
WASH2P
WASH7P
ZFYVE19
ZNF655
ZNF692

Supplementary table 8 - List of genes uniquely dysregulated in HBV-associated HCC

ASEs misregulated in only THBV/NNoV

A2M
AAK1
ABCB7
ABCD3
ABHD10
ABI3BP
ACAD8
ACADSB
ACCS
ACHE
ACLY
ACMSD
ACSS2
ACTA2
ACTL6A
ACVRL1
ADAM10
ADAR
ADCY3
ADCY5
ADH6
ADPGK
AGPAT1
AGXT2L1
ALB
ALDH18A1
ALDH1A3
ALDH2
ALPK1
AMD1
AMDHD1
AMPD3
ANKHD1
ANKIB1
ANKRD19P
ANKS6
ANXA8
AOX1
AP1AR
BAZ2A
BBS4
BCL2L14
BCS1L
BDP1
BIVM
BRAP
BRWD3
BSDC1
BTBD1
BTK
C10orf118
C14orf159
C15orf39
C16orf62
C21orf58
C2CD5
C6orf106
CABLES1
CABYR
CACNA1H
CALCOCO2
CALD1
CAND1
CANX
CAP1
CAPN1
CBWD3
CCAR1
CCDC111
CCDC135
CCDC25
CCDC90B
CCM2
CCNG1
CCSER2
CD200
CD300A
CD34
CR2
CRYZ
CSDE1
CSF3R
CTCF
CTH
CTNNAL1
CWF19L2
CXorf38
CYBRD1
CYFIP2
CYP2B6
CYP2C8
CYP39A1
CYP4F2
DAO
DAXX
DAZAP2
DCAF7
DCDC5
DDB2
DEK
DET1
DGAT2
DGCR2
DHCR24
DHX36
DHX40
DHX58
DIAPH1
DIO1
DMD
DMGDH
DNAJA1
DNAJA3
DNAJC19
DNM2
DNPEP
DPP3
F7
F9
FADS6
FAM153A
FAM179B
FAM198A
FAM199X
FAM206A
FAM210A
FAM228A
FAM3C
FAM57A
FAM63B
FAM65C
FAS
FASTKD2
FBLN7
FBXL5
FBXO3
FGFR4
FKBP10
FKBP5
FKRP
FLJ00385
FLYWCH1
FLYWCH2
FNBP1L
FOLH1
FOPNL
FOXK2
FTSJ2
FUT6
FZD6
G3BP1
G6PC
G6PC3
GABPA
GABPB1
GADD45A
GUSBP4
HADHA
HAL
HAUS6
HBEGF
HCK
HEATR5A
HEATR5B
HECTD1
HECTD3
HERC4
HHAT
HINT3
HMGCS2
HNRNPC
HNRNPH3
HP1BP3
HSD11B1L
HSD17B4
HSD3B7
HSDL2
HSF4
HSPH1
HTATIP2
HYLS1
IAH1
IARS
IBTK
ICAM1
IDH3A
IDI1
IFNLR1
IGSF9
IKBKE
IL10RA
IL18RAP
IL6ST
INTS9
IREB2
LOC100506054
LOC155060
LOC619207
LOC654433
LRIF1
LRRC61
LSS
LTBP3
LUZP6
LYPLA1
LYSMD3
MAGT1
MAN2B2
MANEAL
MAP4
MAPKAP1
MARCH6
MARK3
MATN3
MAVS
MBD1
MBD4
MBNL3
MCCC1
MCCC2
MCOLN3
MEAF6
MEF2D
MEMO1
METTL23
METTL5
MFN1
MFSD12
MGAT4B
MGME1
MINK1
MIOS
MLIP
MLLT4
NKTR
NMRAL1
NOL11
NOVA1
NPEPPS
NPHP3
NR1D1
NR3C2
NRBF2
NRG3
NSG1
NUCB2
NUDT9
NUP50
NUP54
OGFOD1
OGT
ORC4
OXR1
P2RX4
P4HA2
PADI1
PAK4
PANK1
PANX2
PARP9
PCBP1-AS1
PCGF3
PCGF6
PCK1
PCK2
PCNX
PCNXL4
PCYOX1
PDCD1
PDCD4
PDDC1
PDE3B
PDE8B
POFUT2
POGK
POLB
POLDIP3
POLR2M
POLR3D
PPARD
PPIL2
PPM1E
PPP1R10
PPP1R8
PPP2R1A
PPP2R1B
PPP2R5D
PPP4R1
PRG4
PRKCSH
PRKDC
PRMT2
PRMT5
PRNP
PRPS1
PRSS8
PSMC1
PSMD3
PSME4
PTCD3
PTDSS1
PTPLAD1
PTPN1
PTPN21
PVRL4
PWWP2A
PYGL
RAB18
RAB2B
RAB5A
RAB5B
RAB6A
RSU1
RTN2
RTN3
RUNX3
SAFB
SAP130
SBF1
SBNO1
SCAND2P
SCARB1
SDC4
SDHA
SDHAP2
SEC23A
SEC23IP
SEC24D
SEC61A1
SECISBP2
SEMA5B
SENP6
SEPT10
SERPINF2
SETD4
SFMBT1
SFXN4
SGCD
SGCE
SGK1
SGSM3
SH3PXD2A
SHANK2
SIGLEC10
SIMC1
SIRT2
SKIV2L2
SKP2
SLAMF6
SLC13A5
SLC15A4
STEAP1B
STOM
STRAP
STT3A
STX16
STX5
SULF1
SUMF2
SUN1
SUN2
SURF4
SUV420H1
SUZ12
SWAP70
SYNE1
SYNJ2
SYP
TAF11
TAL1
TANC1
TARS
TBC1D4
TBRG4
TBX3
TCP11L1
TCTN3
TDRD9
TECPR2
TES
TESK2
TFEB
TFEC
TGM2
THEMIS
THSD7B
THTPA
TIMM10B
TLR2
TLR4
TSPO
TTC7A
TUFT1
TXN2
UACA
UBAP1
UBAP2L
UBE2K
UBL7
UBQLN4
UCHL5
UHRF2
USF2
USP15
USP36
UVRAG
VAC14
VAMP7
VASH2
VMP1
VNN2
VPS16
VPS26A
VPS41
VSIG4
VWF
WAC
WDR44
WDR6
WIPF2
WIZ
WNK3
WSB2
XIRP1
XPC
XRCC6
XRN2
YWHAE
ZBTB21

AP5M1
APH1A
API5
APMAP
APP
AQP3
AQP6
ARCN1
ARFGAP3
ARHGEF10L
ARID2
ARL5A
ARL6IP1
ARL8B
ARNTL2
ASB13
ASH2L
ASPH
ASPN
ASUN
ATG16L1
ATP2B2
ATP2B4
ATP2C1
ATP5SL
ATP6V1C1
ATP7B
ATP9B
AURKC
AXIN1
BACE1
CD68
CD84
CDC25B
CDK14
CDK20
CDS1
CECR2
CELF2
CERS2
CFHR4
CHD6
CHEK2
CHRD
CIDEC
CIITA
CIRH1A
CIT
CLASRP
CLOCK
CMPK1
CNDP2
CNPY3
CNTRL
COG3
COL18A1
COL1A2
COL6A6
COQ5
CORO1C
CPD
CPSF7
DRAM2
DSCR3
DUS3L
DUSP16
DYM
DYNC1LI1
DYNC2LI1
EBF4
ECD
EEF1A1
EFTUD2
EHD3
EIF2AK2
ELAC2
ELF1
ELN
EML4
ENOPH1
ENOX2
ENPP2
EOGT
EPB41
ERBB2
ERBB3
ERC1
ERG
ERMP1
ERVK13-1
ESYT2
F11R
F3
GCFC2
GDA
GDE1
GDI2
GEM
GEMIN7
GEMIN8
GFM2
GFOD2
GLE1
GLYATL1
GMPS
GNAS
GNB1
GNB5
GNE
GNL3
GNS
GOLGA5
GOLPH3L
GOT2
GPNMB
GPR137
GPR161
GPR180
GRAMD1B
GRB2
GSS
GSTO2
GTPBP4
GUCY1B3
IRF6
ITCH
ITFG3
ITGB1
IWS1
JKAMP
KBTBD4
KCNT2
KDM4A
KIAA0125
KIAA0232
KIAA1598
KIDINS220
KLF6
KLF7
KLHL12
KLHL2
KLRD1
KPNB1
KRBOX4
LAMP1
LASP1
LGMN
LILRB1
LILRB2
LILRB3
LILRB5
LIPC
LIPG
LMAN2L
LMBR1
MLPH
MME
MMP19
MMRN2
MNS1
MOB2
MON1B
MRC2
MROH7
MRPL3
MSS51
MST1P2
MTA1
MTF2
MTFR1
MTM1
MTMR14
MYD88
MYLIP
MYO9B
NAA60
NAE1
NARG2
NARS
NBEAL1
NCAPG2
NDC1
NDUFS5
NET1
NFATC3
NFKB1
PDGFC
PDHB
PDHX
PDXDC1
PDXDC2P
PDZK1
PEPD
PFKFB4
PFKM
PGGT1B
PGRMC1
PHACTR4
PI16
PIBF1
PIGA
PIGG
PIGT
PIK3R5
PIP4K2C
PIP5K1A
PLA2G1B
PLEKHH3
PLEKHO2
PLS3
PMPCA
PMS2CL
PMS2P5
PNPO
PODN
PODXL
POFUT1
RAB7A
RABEP1
RABGAP1
RAI2
RAP1B
RARA
RARB
RARS
RASSF6
RBBP5
RBL2
RBM23
RBM24
RBM42
RBM47
RBMX
RCBTB2
RDH16
RELA
RETSAT
RGPD1
RHPN2
RINT1
RMDN2
RNF111
RNF4
RNGTT
RPH3AL
RRAS2
RRM1
RSAD1
SLC17A1
SLC23A2
SLC25A13
SLC25A43
SLC27A2
SLC2A14
SLC2A2
SLC30A5
SLC35B2
SLC38A2
SLC38A7
SLC44A3
SLC7A9
SLC9A8
SLMAP
SMARCD1
SMEK1
SMIM8
SNAP23
SNTA1
SOX13
SPAG9
SPECC1L
SPOP
SPSB3
SRD5A1
SREBF1
SRP54
SRP72
SSFA2
ST6GAL1
TM9SF2
TMBIM1
TMEM116
TMEM136
TMEM161B
TMEM167B
TMEM170A
TMEM216
TMEM254
TMEM254-AS1
TMEM30A
TMEM44
TMEM63B
TMEM66
TMEM8A
TMPRSS4
TMTC1
TNKS1BP1
TOLLIP
TOP2B
TOR3A
TOX4
TPRG1L
TRAP1
TRAPPC11
TRAPPC6A
TRAPPC6B
TRIM35
TRIM41
TRIM5
TRPV3
ZC3H14
ZC3HC1
ZCCHC6
ZCWPW1
ZDHHC19
ZDHHC23
ZDHHC5
ZEB2
ZFYVE9
ZMAT5
ZNF131
ZNF302
ZNF326
ZNF35
ZNF410
ZNF415
ZNF419
ZNF451
ZNF567
ZNF839
ZNF85
ZNF852

Supplementary table 9 - List of genes uniquely dysregulated in HCV-associated HCC

ASEs misregulated in only THCV/NNoV

AASS
ANXA2
ATP6V0B
CACNB4
CCDC7
CD22
CDKN2A
CHRNA4
COPS2
DIABLO
DMPK
DNAJC18
DOK1
EFCAB1
EMR1
FAM83A-AS1
FBXO28
FCGR3A
FGFR1OP
FLJ39739
FUT10
GLT1D1
HNRNPH1
IGFALS
IL9R
INIP
JHDM1D
KAZN
KLHDC1
LINC00875
LOC388152
MAEL
MARS
MARVELD2
MORN1
MRPL55
MTHFSD
MYNN
N4BP2L1
NAALAD2
NCOA1
NEIL2
PHGDH
PHYHD1
PPP3CB
PRRC2C
PTK6
R3HDM2
RACGAP1
RYK
SAMD4A
SLC10A7
SMARCAD1
SNX5
SPINT2
SUSD1
TFPI
TGIF1
TP73
TROVE2
TSC2
WNK2
WNT2
ZNF106
ZNF30
ZNF559
ZNF568
ZNF638

Supplementary table 10 - List of genes uniquely dysregulated in HBV&HCV-associated HCC

ASEs misregulated in only THBV&HCV/NNoV

ALAD
ALOX12P2
ARHGAP44
ATP6V1H
C7orf63
CD28
CD8B
CNTNAP3
CYP21A2
DHX35
FAM135A
FAM13A
FHIT
FYB
GDPD5
GIGYF2
GNL1
GRB10
HACE1
KAT6A
KIFC3
KMT2E
LANCL1
LIMA1
LIN54
MCTP1
MIB2
NBPF10
NBPF8
NCEH1
NOMO2
NR2F1-AS1
ORAI2
PACSIN3
PMEPA1
RBMS1
RGN
RPL15
SMARCC2
SNRPN
SYBU
TCIRG1
TPSB2
TRABD2A
VANGL1
WDPCP
WEE2-AS1
XRCC1
ZCCHC7
ZFAT
ZMYM1
ZMYND8
ZNF182
ZNF667

Supplementary table 11 - List of genes uniquely dysregulated in virus-free HCC

ASEs misregulated in only TNoV/NNoV

AADAT
ACSF2
ACSL6
ADORA2A
AKAP17A
ALDH1A2
AMZ2
APOBEC3B
ARHGAP30
ARMC7
ATP13A4
ATRNL1
ATXN1
ATXN3
ATXN7L3
AXL
BBS1
BBX
BCAS1
BCL7B
BDKRB2
BPY2
BTBD7
BTNL8
BTRC
C12orf65
C1orf109
C1QTNF6
C21orf91
CADPS
CALML4
CAMK2G
CAPN12
CCDC136
CCDC149
CCDC91
CD320
CD4
CDAN1
CSNK1G1
CTCFL
CUL9
CUTC
CUX1
CWF19L1
CYB561D1
DCAF11
DCUN1D2
DDX11L1
DGKH
DICER1
DIO2
DIO3AS
DIP2A
DMAP1
DSTYK
ECT2
EDA2R
EPHA5
ERCC6L2
FAM213B
FAM21A
FAM227A
FAM92A1
FASTK
FBXL2
FGGY
FOXP2
FRMD1
FUZ
GALNT14
GALNT6
GAPVD1
GATS
GDAP1
GEMIN5
GEN1
GLIS3
JOSD2
KANSL1
KCNK17
KCNMB3
KIAA0391
KIAA0895
KIF20B
KLHL3
KLRF1
LGALS9
LIMCH1
LINC00910
LOC100287534
LOC400927
LOXL2
LOXL3
LRP1B
LRRC23
LRRC7
LRRK1
LRRN2
LUZP2
MARK1
MAZ
MCM2
MDH1B
MICAL2
MPC2
MPP1
MPP4
MRPL52
MS4A14
MSANTD2
MTCH1
NDUFAF7
NECAB2
NEK2
NFASC
NFATC4
PIK3CG
PLCB3
PLEKHS1
PML
POLR1B
PPCS
PPP2R2B
PRDX1
PROM1
PRR5
PSMD13
PSPH
PSTPIP1
PTK7
PTPN20A
PTPN20B
PTPRS
PYCR1
RAB37
RABL5
RAD51AP1
RAPGEF1
RAPGEF3
RBM14-RBM4
REPS1
RERG
REST
RGL4
RGS11
RIMBP2
RINL
RPGRIP1
RPL23AP7
RRAGC
RTEL1-TNFRSF6B
RUNDC3B
SCAMP4
SCARA5
SEC14L2
STAC3
STAG3L3
STARD3
SUV39H2
SVEP1
TBC1D17
TBCK
TCF12
TDP1
TEAD4
TESPA1
TIMD4
TM4SF19
TM7SF2
TMEM67
TNFRSF25
TOMM40L
TPK1
TREML1
TRIM39
TRPC4
TTLL3
TTLL7
TTYH1
UBE2J2
UBE2W
UNK
UPF3B
USP25
UXS1
VIPR2
VWA1
VWDE
WASF3
WASH1
WDR20
WDR81
WSCD1
ZBTB17

CDC25A
CEP97
CERKL
CFLAR
CHN1
CHRNA7
CIB2
CLCN7
CLEC4A
CLIP1
CLK3
CLK4
CNIH2
CNTN5
COL24A1
CPA5
CRCP
CREB3L4
CRYZL1
CSF2RA
CSF2RB
GPM6A
GRAP2
GUCY1B2
HDAC7
HDAC8
HELB
HERC2P3
HFE
HLA-G
HMCN1
HNRNPA1
HOPX
HPSE
ICA1
IGFLR1
IKZF1
IKZF2
IL34
INF2
ISCU
IYD
NFE2
NFE2L2
NFYC
NHSL2
NLGN4X
NPAS2
NRCAM
NXF3
ORAOV1
P2RX2
P4HA1
PAK3
PAOX
PAPD5
PARK2
PCDH18
PDCD1LG2
PDE10A
PGBD2
PGPEP1
PIFO
SENP7
SH2D1A
SIGMAR1
SLC12A4
SLC14A1
SLC25A12
SLC25A19
SLC26A3
SLC30A10
SLC35F6
SLC35G1
SLFN12
SMARCA4
SNAP91
SNCAIP
SNRPA1
SPATA9
SPDL1
SPEF2
SSPO
ST7L
ZDHHC15
ZMYM6
ZMYND11
ZNF266
ZNF274
ZNF285
ZNF334
ZNF346
ZNF431
ZNF446
ZNF454
ZNF527
ZNF534
ZNF582
ZNF738
ZNF79
ZNF791
ZNF821
ZNF823
ZSCAN25

SUPPLEMENTARY FIGURES

Figure S1. Characterization of splicing mysregulation in HCC. (A) Distribution of Delta PSI values in various types of HCC. **(B)** Distribution of multiple alternative splicing events (ASEs) in each gene for various types of HCC. **(C)** The splicing events lists for various types of HCC were filtered to keep only data with at least two replicates for both virus-induced HCC and virus-free healthy tissues (NNoV). Fold changes were then calculated between HCC and healthy tissues. Q-values (false-discovery rate) were calculated in order to take into account multiple statistical hypothesis testing, and results under 0.05 were considered significant. Events with a P-value of less than 0.05 were conserved. Events with expression levels higher than one TPM in at least one dataset were conserved.

Fig. S2. Characterization of ASEs that are modified in HBV- and HCVassociated HCC. (A) Gene ontology analysis for alternative splicing modifications in HBV- and HCV-associated HCC. The asterisk (*) indicates the other categories: Cellular process (GO: 0009987), cellular component organization or biogenesis (GO: 0071840), localization (GO: 0051179), locomotion (GO: 0040011) and multicellular organismal process (GO: 0032501). **(B)** Interaction network for cellular genes for which AS is modified in both HBV- and HCC-associated HCC. The network was determined by uploading the genes into STRING.

Figure S3. AS modifications in transcripts encoded by kinases and transcriptions factores in HBV- and HCV-associated HCC. (A) Alterations in the AS patterns of transcripts encoded by kinases in HBV- and HCV-associated HCC. Some transcripts have multiple ASEs that are modified. Red bars indicate negative Delta PSI values, and blue bars represent positive Delta PSI values. **(B)** Alterations in the AS patterns of transcripts encoded by transcription factors in HBV- and HCV-associated HCC.

Figure S4. Global profiling of ASE modifications in both HBV&HCVassociated HCC and virus-free-associated HCC. (A) Heatmap representation of ASEs (PSI values) for cellular transcripts in HBV&HCV-associated HCC. Data obtained from THBV&HCV (HBV&HCV-associated HCC) tissues are shown in purple and data obtained from heathy tissues (NNoV) are shown in green. **(B)** Heatmap representation of ASEs (PSI values) for cellular transcripts in virus-free HCC. Data obtained from virus-free-associated HCC tissues are shown in yellow and data obtained from heathy tissues (NNoV) are shown in green.

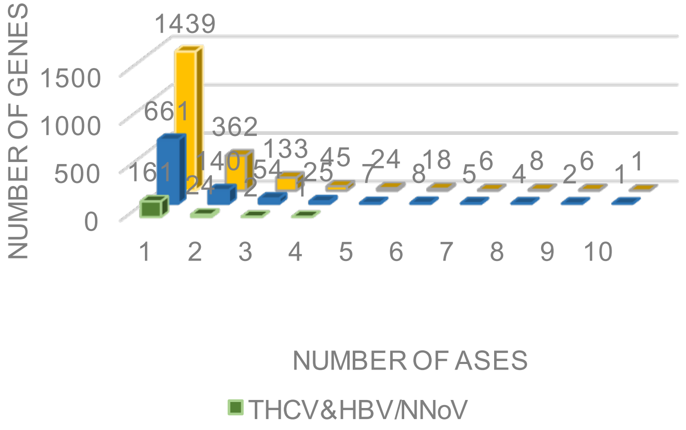
Figure S5. RNA splicing factors in HCC. Iris Graph representing the expression profile of splicing factors for **(A)** HCV-, **(B)** HBV&HCV-, and **(C)** virus-free HCC. Differences in gene expression levels are shown on a logarithmic color scale (Log2), from red (negative changes in expression) to blue (increase in gene expression). The expression of proteins involved in splicing modulated by more than 2-fold is indicated by an asterisk.

Fig. S6. Modifications to AS of 96 transcripts in response to knockdown of splicing factors with specific siRNAs. Using specific siRNAs, twelve splicing factors (listed on the right) were individually knocked-down in different cell lines to assess their implication in splicing of 96 differents transcripts (listed at the top). Individual knockdowns and ASEs are shown to indicate which knockdowns caused a shift in alternative splicing in various cell lines (PC-3, SKOV3, NIH:OVCAR-3, MDA-MB-231, MCF7). Each column represents a distinct knockdown performed with specific siRNAs. The changes in PSI values are displayed. The map represents the changes in PSI values in a color-coded scale. White areas indicate no shifts. Asterisks indicate transcripts for which AS was altered in HCV-associated HCC.

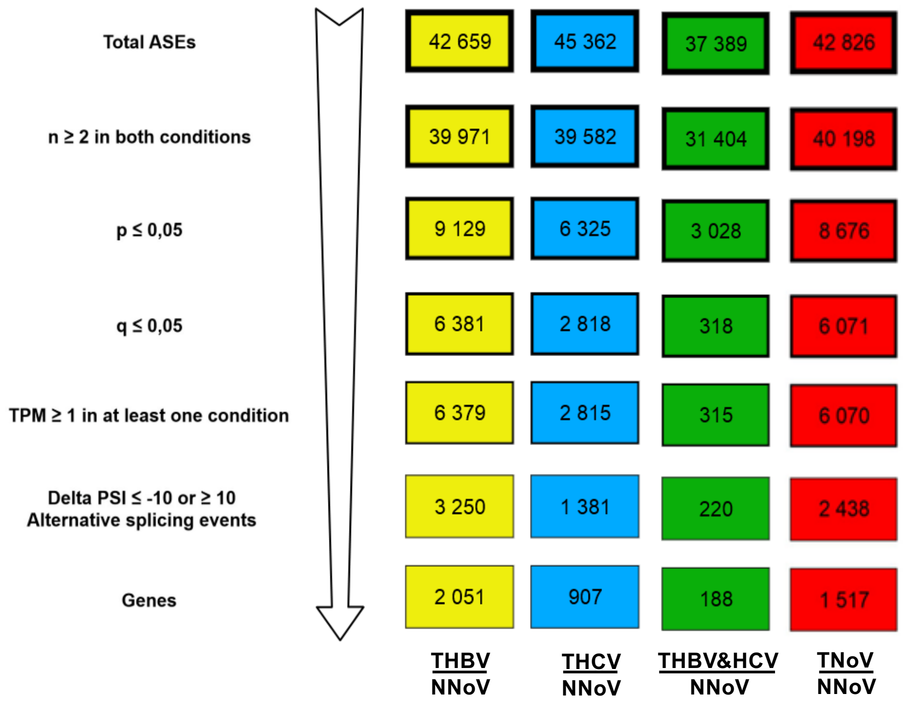
A

|ΔPSI|	THBV/NNoV	THCV/NNoV	THBV&HCV/NNoV	TNoV/NNoV
[10-20[	2190	844	61	1638
[20-30[	699	335	77	520
[30-40[	207	117	41	170
[40-50[	75	38	22	51
[50-60[	45	23	8	33
[60-70[	18	10	4	11
[70-80[	14	11	4	10
[80-90[	2	2	3	5
[90-100]	0	1	0	0

B



C



	THBV NNoV	THCV NNoV	THBV&HCV NNoV	TNoV NNoV
Total ASEs	42 659	45 362	37 389	42 826
n ≥ 2 in both conditions	39 971	39 582	31 404	40 198
p ≤ 0,05	9 129	6 325	3 028	8 676
q ≤ 0,05	6 381	2 818	318	6 071
TPM ≥ 1 in at least one condition	6 379	2 815	315	6 070
Delta PSI ≤ -10 or ≥ 10 Alternative splicing events	3 250	1 381	220	2 438
Genes	2 051	907	188	1 517

Fig. S1

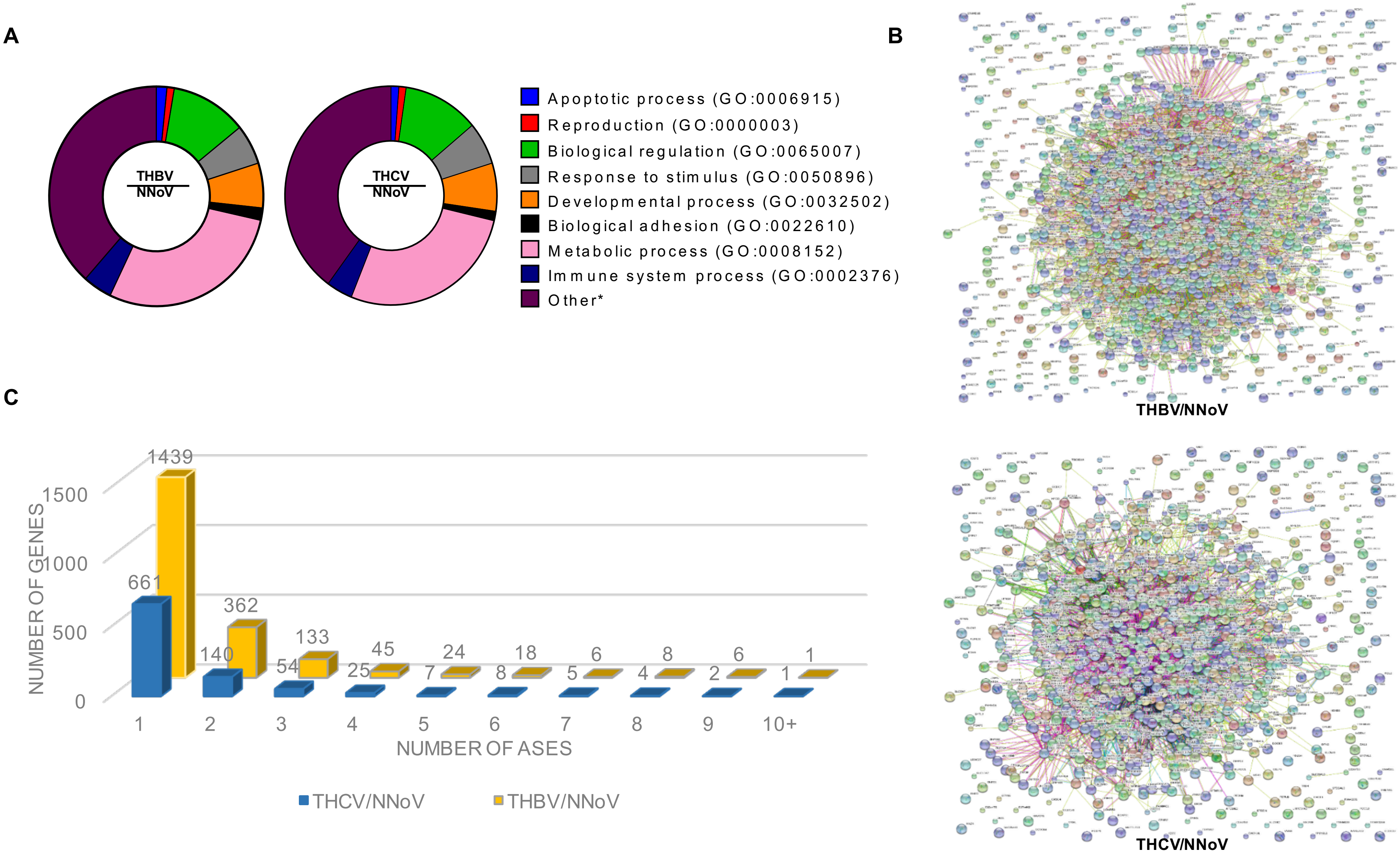

A
THBV
NNoV
THCV
NNoV
Apoptotic process (GO:0006915)
Reproduction (GO:0000003)
Biological regulation (GO:0065007)
Response to stimulus (GO:0050896)
Developmental process (GO:0032502)
Biological adhesion (GO:0022610)
Metabolic process (GO:0008152)
Immune system process (GO:0002376)
Other*
B
THBV/NNoV
THCV/NNoV
C
NUMBER OF GENES
0
500
1000
1500
1439
661
362
140
133
54
45
25
24
7
18
8
6
5
8
4
6
2
1
1
1
2
3
4
5
6
7
8
9
10+
NUMBER OF ASES
THCV/NNoV
THBV/NNoV

Fig. S2

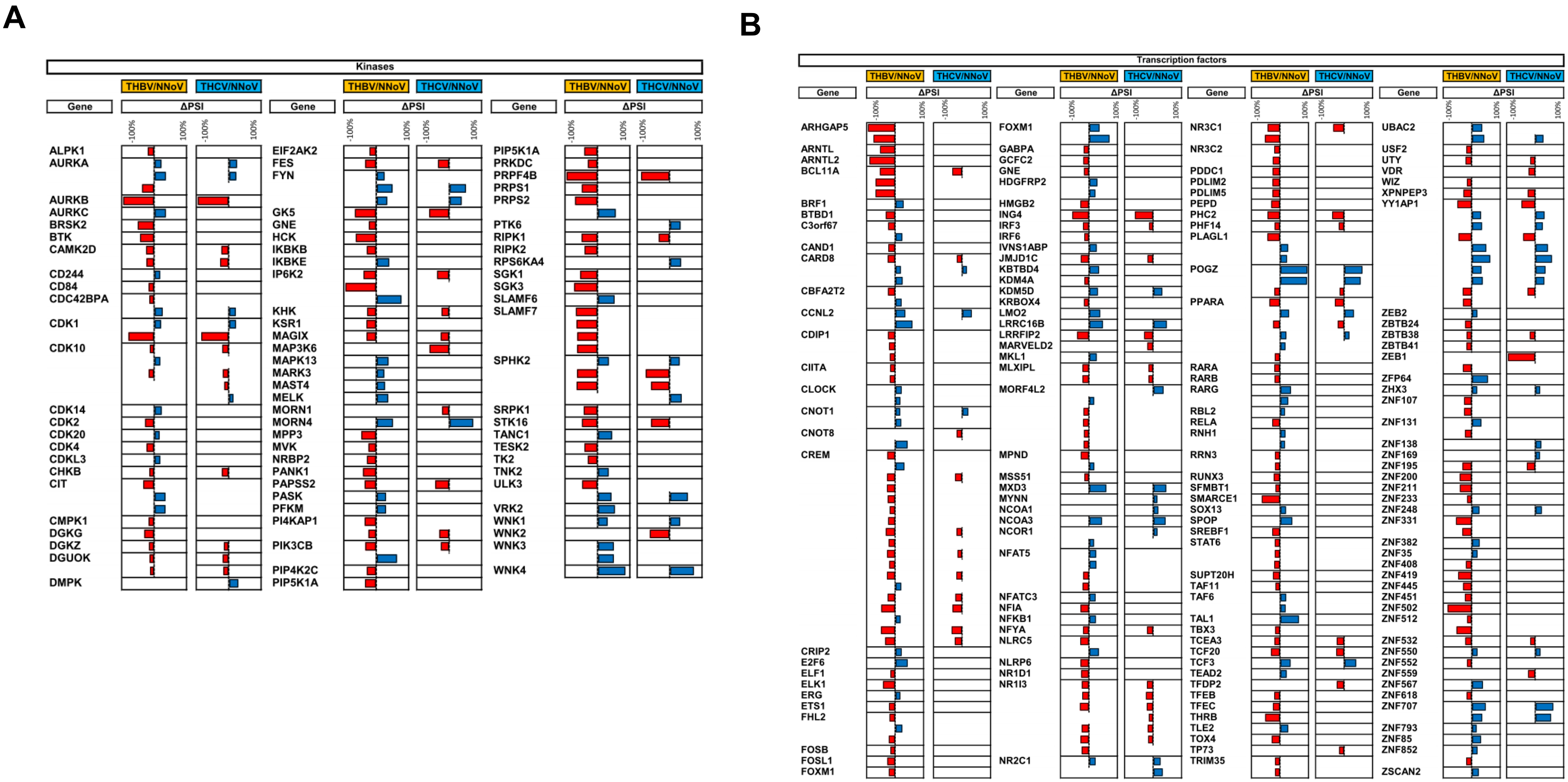

A
Kinases
THBV/NNoV
THCV/NNoV
Gene
ΔPSI
-100%
100%
ALPK1
AURKA
AURKB
AURKC
BRSK2
BTK
CAMK2D
CD244
CD84
CDC42BPA
CDK1
CDK10
CDK14
CDK2
CDK20
CDK4
CDKL3
CHKB
CIT
CMPK1
DGKG
DGKZ
DGUOK
DMPK
EIF2AK2
FES
FYN
GK5
GNE
HCK
IKBKB
IKBKE
IP6K2
KHK
KSR1
MAGIX
MAP3K6
MAPK13
MARK3
MAST4
MELK
MORN1
MORN4
MPP3
MVK
NRBP2
PANK1
PAPSS2
PASK
PFKM
PI4KAP1
PIK3CB
PIP4K2C
PIP5K1A
PIP5K1A
PRKDC
PRPF4B
PRPS1
PRPS2
PTK6
RIPK1
RIPK2
RPS6KA4
SGK1
SGK3
SLAMF6
SLAMF7
SPHK2
SRPK1
STK16
TANC1
TESK2
TK2
TNK2
ULK3
VRK2
WNK1
WNK2
WNK3
WNK4
B
Transcription factors
ARHGAP5
ARNTL
ARNTL2
BCL11A
BRF1
BTBD1
C3orf67
CAND1
CARD8
CBFA2T2
CCNL2
CDIP1
CIITA
CLOCK
CNOT1
CNOT8
CREM
CRIP2
E2F6
ELF1
ELK1
ERG
ETS1
FHL2
FOSB
FOSL1
FOXM1
FOXM1
GABPA
GCFC2
GNE
HDGFRP2
HMGB2
ING4
IRF3
IRF6
IVNS1ABP
JMJD1C
KBTBD4
KDM4A
KDM5D
KRBOX4
LMO2
LRRC16B
LRRFIP2
MARVELD2
MKL1
MLXIPL
MORF4L2
MPND
MSS51
MXD3
MYNN
NCOA1
NCOA3
NCOR1
NFAT5
NFATC3
NFIA
NFKB1
NFYA
NLRC5
NLRP6
NR1D1
NR1I3
NR2C1
NR3C1
NR3C2
PDDC1
PDLIM2
PDLIM5
PEPD
PHC2
PHF14
PLAGL1
POGZ
PPARA
RARA
RARB
RARG
RBL2
RELA
RNH1
RRN3
RUNX3
SFMBT1
SMARCE1
SOX13
SPOP
SREBF1
STAT6
SUPT20H
TAF11
TAF6
TAL1
TBX3
TCEA3
TCF20
TCF3
TEAD2
TFDP2
TFEB
TFEC
THRB
TLE2
TOX4
TP73
TRIM35
UBAC2
USF2
UTY
VDR
WIZ
XPNPEP3
YY1AP1
ZEB2
ZBTB24
ZBTB38
ZBTB41
ZEB1
ZFP64
ZHX3
ZNF107
ZNF131
ZNF138
ZNF169
ZNF195
ZNF200
ZNF211
ZNF233
ZNF248
ZNF331
ZNF382
ZNF35
ZNF408
ZNF419
ZNF445
ZNF451
ZNF502
ZNF512
ZNF532
ZNF550
ZNF552
ZNF559
ZNF567
ZNF618
ZNF707
ZNF793
ZNF85
ZNF852
ZSCAN2

Fig. S3

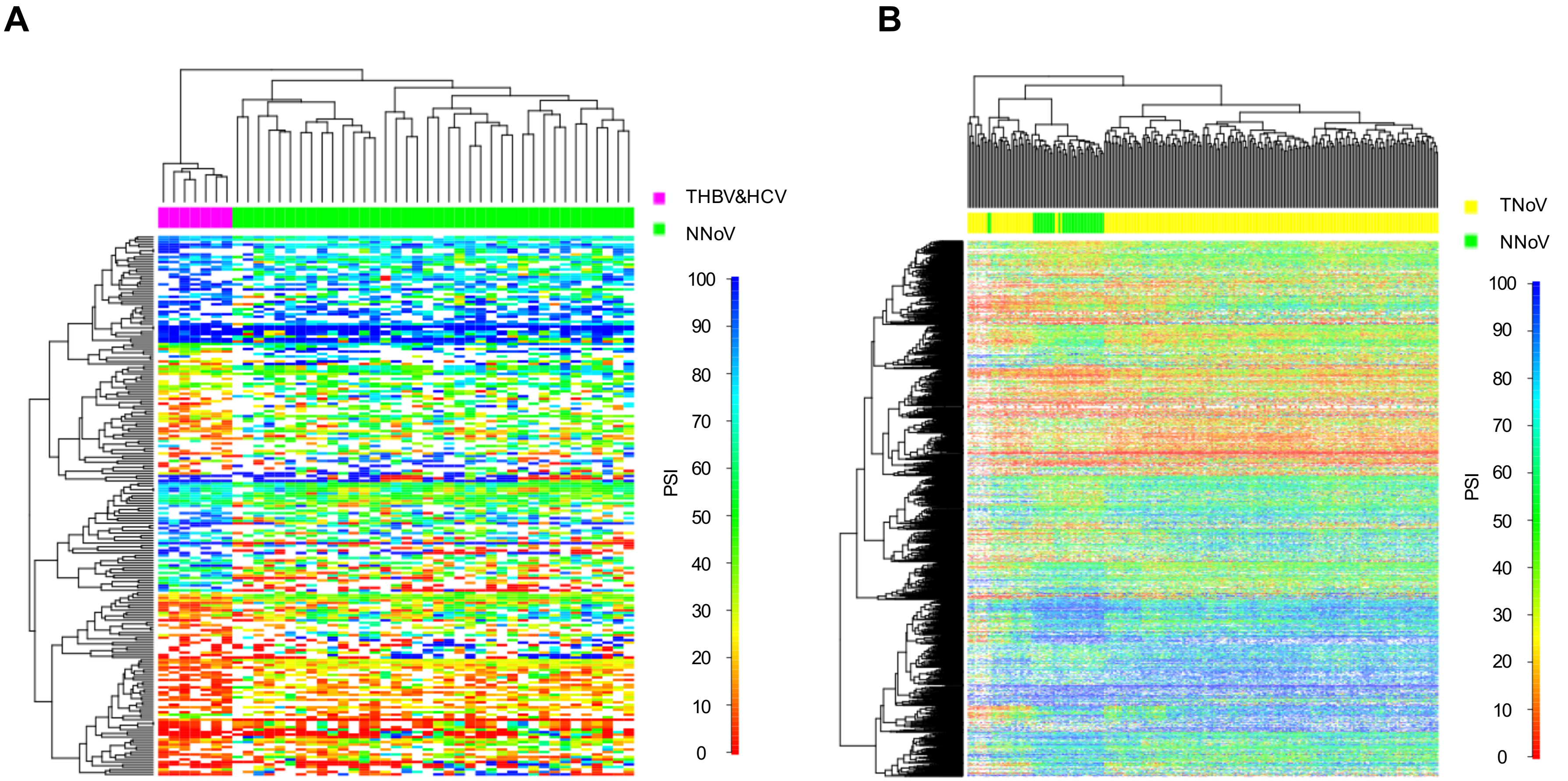

A
THBV&HCV
NNoV
100
90
80
70
60
50
40
30
20
10
0
PSI
B
TNoV
NNoV
100
90
80
70
60
50
40
30
20
10
0
PSI

Fig. S4

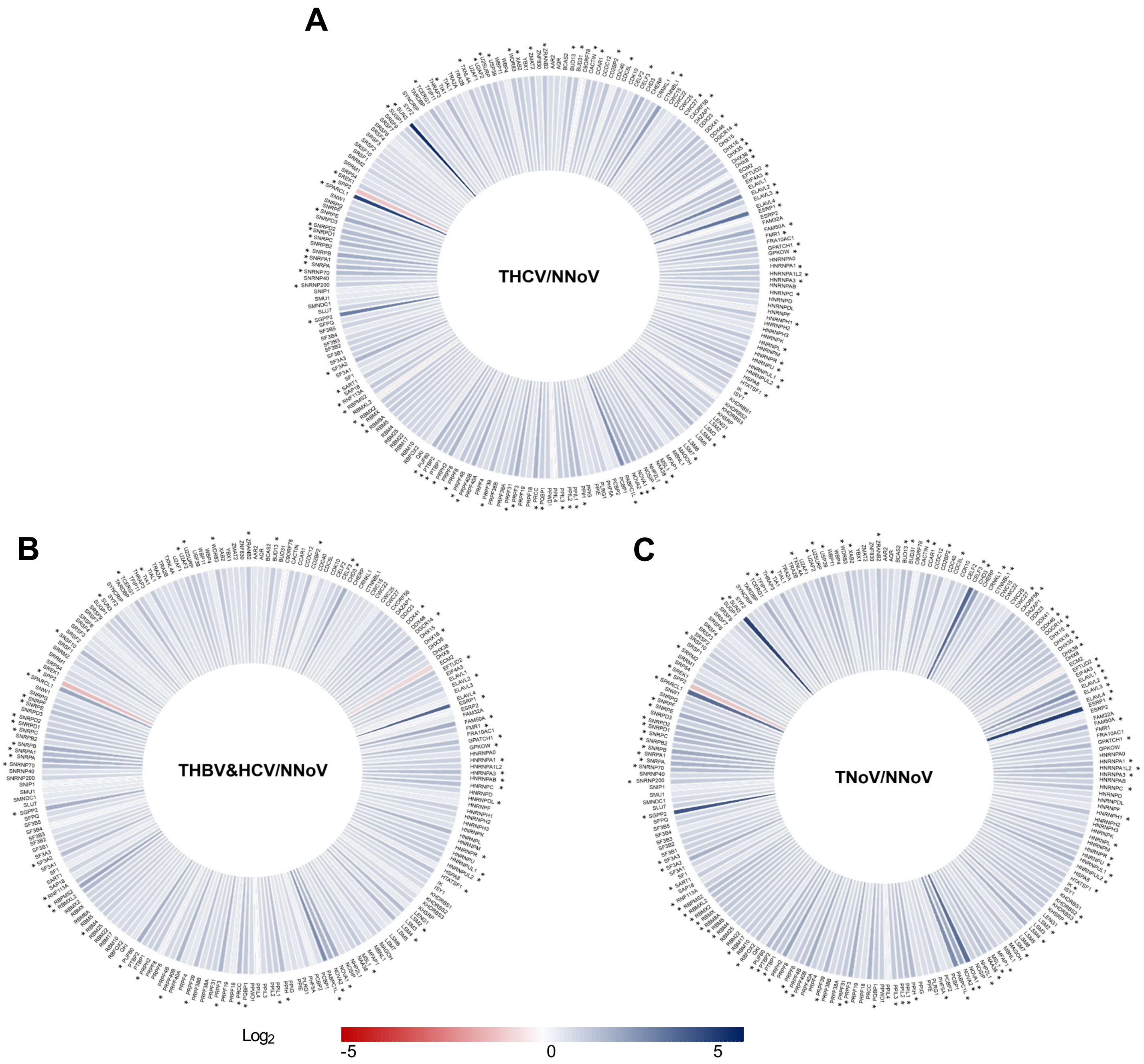


Fig. S5

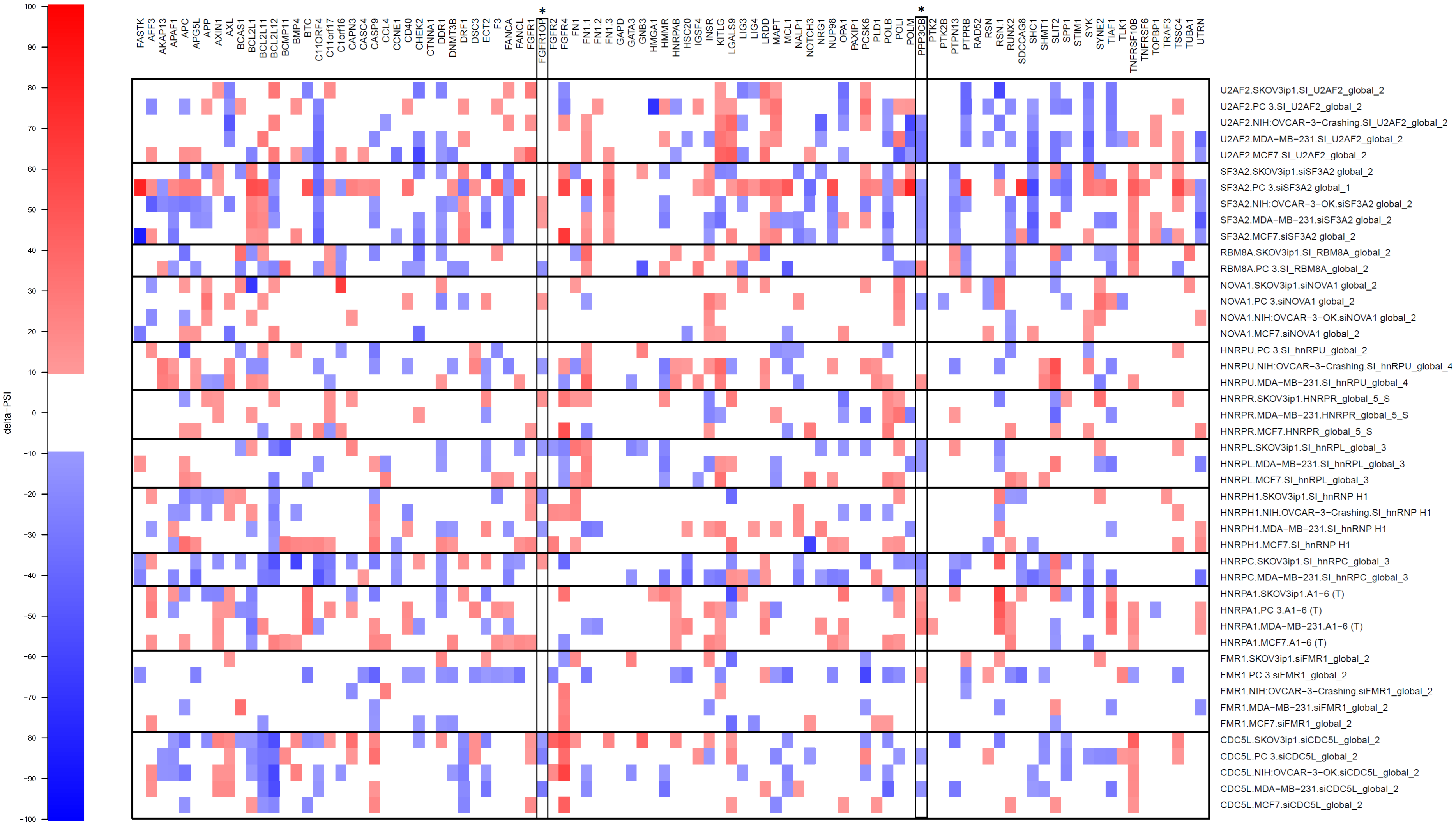

100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
delta−PSI
*
*
FASTK
AFF3
AKAP13
APAF1
APC
APG5L
APP
AXIN1
AXL
BCAS1
BCL2L1
BCL2L11
BCL2L12
BCMP11
BMP4
BTC
C11ORF4
C11orf17
C1orf16
CAPN3
CASC4
CASP9
CCL4
CCNE1
CD40
CHEK2
CTNNA1
DDR1
DNMT3B
DRF1
DSC3
ECT2
F3
FANCA
FANCL
FGFR1
FGFR1OP
FGFR2
FGFR4
FN1
FN1.1
FN1.2
FN1.3
GAPD
GATA3
GNB3
HMGA1
HMMR
HNRPAB
HSC20
IGSF4
INSR
KITLG
LGALS9
LIG3
LIG4
LRDD
MAPT
MCL1
NALP1
NOTCH3
NRG1
NUP98
OPA1
PAXIP1
PCSK6
PLD1
POLB
POLI
POLM
PPP3CB
PTK2
PTK2B
PTPN13
PTPRB
RAD52
RSN
RSN.1
RUNX2
SDCCAG8
SHC1
SHMT1
SLIT2
SPP1
STIM1
SYK
SYNE2
TIAF1
TLK1
TNFRSF10B
TNFRSF6
TOPBP1
TRAF3
TSSC4
TUBA1
UTRN
U2AF2.SKOV3ip1.SI_U2AF2_global_2
U2AF2.PC 3.SI_U2AF2_global_2
U2AF2.NIH:OVCAR−3−Crashing.SI_U2AF2_global_2
U2AF2.MDA−MB−231.SI_U2AF2_global_2
U2AF2.MCF7.SI_U2AF2_global_2
SF3A2.SKOV3ip1.siSF3A2 global_2
SF3A2.PC 3.siSF3A2 global_1
SF3A2.NIH:OVCAR−3−OK.siSF3A2 global_2
SF3A2.MDA−MB−231.siSF3A2 global_2
SF3A2.MCF7.siSF3A2 global_2
RBM8A.SKOV3ip1.SI_RBM8A_global_2
RBM8A.PC 3.SI_RBM8A_global_2
NOVA1.SKOV3ip1.siNOVA1 global_2
NOVA1.PC 3.siNOVA1 global_2
NOVA1.NIH:OVCAR−3−OK.siNOVA1 global_2
NOVA1.MCF7.siNOVA1 global_2
HNRPU.PC 3.SI_hnRPU_global_2
HNRPU.NIH:OVCAR−3−Crashing.SI_hnRPU_global_4
HNRPU.MDA−MB−231.SI_hnRPU_global_4
HNRPR.SKOV3ip1.HNRPR_global_5_S
HNRPR.MDA−MB−231.HNRPR_global_5_S
HNRPR.MCF7.HNRPR_global_5_S
HNRPL.SKOV3ip1.SI_hnRPL_global_3
HNRPL.MDA−MB−231.SI_hnRPL_global_3
HNRPL.MCF7.SI_hnRPL_global_3
HNRPH1.SKOV3ip1.SI_hnRNP H1
HNRPH1.NIH:OVCAR−3−Crashing.SI_hnRNP H1
HNRPH1.MDA−MB−231.SI_hnRNP H1
HNRPH1.MCF7.SI_hnRNP H1
HNRPC.SKOV3ip1.SI_hnRPC_global_3
HNRPC.MDA−MB−231.SI_hnRPC_global_3
HNRPA1.SKOV3ip1.A1−6 (T)
HNRPA1.PC 3.A1−6 (T)
HNRPA1.MDA−MB−231.A1−6 (T)
HNRPA1.MCF7.A1−6 (T)
FMR1.SKOV3ip1.siFMR1_global_2
FMR1.PC 3.siFMR1_global_2
FMR1.NIH:OVCAR−3−Crashing.siFMR1_global_2
FMR1.MDA−MB−231.siFMR1_global_2
FMR1.MCF7.siFMR1_global_2
CDC5L.SKOV3ip1.siCDC5L_global_2
CDC5L.PC 3.siCDC5L_global_2
CDC5L.NIH:OVCAR−3−OK.siCDC5L_global_2
CDC5L.MDA−MB−231.siCDC5L_global_2
CDC5L.MCF7.siCDC5L_global_2

Fig. S6