

**Supplemental Table 1: Patient demographics and quantification of intrahepatic HBV DNA****(n=99)**

Age	Mean $\pm$ SD	55 $\pm$ 10
Gender	Male	82 (83%)
	Female	17 (17%)
Race	Asian	85 (86%)
	Non-Asian	14 (14%)
HAI	Mean $\pm$ SD	3.8 $\pm$ 1.7
Ishak fibrosis stage	Mean $\pm$ SD	4.2 $\pm$ 1.5
ALT (Units/L)	Median, range	38 (11-328)
HCC Tumor Size (cm)	Mean $\pm$ SD	4.2 $\pm$ 3.5
	Median	3.0
Vascular invasion	Absent	12 (14%)
	Present	74 (86%)
Tumor differentiation	Well	11 (12%)
	Moderate	40 (46%)
	Poor	37 (42%)
AFP (ng/mL)	Median, range	51.9 (1.5-34020)
Serum HBV DNA	log <sub>10</sub> IU /ml (mean $\pm$ SD)	5.2 $\pm$ 5.7
	Detectable serum HBV DNA	37/75 (49%)

**Supplemental Table 2: Comparison of HBV DNA, cccDNA and replicative activity based on serum HBV DNA or serum HBeAg status. Only patients with serum HBV DNA or serum HBeAg status data available were included in this analysis.**

	Serum HBV DNA			Serum HBeAg status		
	Undetectable n=38	Detectable n=37	p	Negative n=51	Positive n=16	p
Male	32	30	0.8	44	12	0.4
Female	6	7		7	4	
Age	57 ± 11	59 ± 10	0.5	56 ± 9	48 ± 8	0.02
HAI grade	4.1 ± 1.9	4.3 ± 2.0	0.7	4.0 ± 1.8	4.0 ± 2.0	0.8
Ishak fibrosis stage	4.5 ± 1.4	3.9 ± 1.7	0.1	4.2 ± 1.6	4.4 ± 1.5	0.6
HCC tumor size	4.1 ± 2.9	5.6 ± 4.1	0.06	4.6 ± 3.6	3.4 ± 3.8	0.1
Vascular Invasion						
Absence	3	6	0.5	6	3	0.3
Presence	29	25		39	10	
Tumor differentiation						
Well	4	6	0.5	5	4	0.3
Moderate	17	18		21	6	
Poor	13	8		19	4	
AFP (ng/ml)	86.9 (3.8-8336)	53.1 (1.9-160000)	1	52.6 (2-34020)	46.4 (1.5-2319)	0.8
Serum HBV DNA (log <sub>10</sub> IU/ml)	0	3.3 (1.6-6.3)		0	3.6	0.1
HBV DNA (copies/cell)						
Tumor	0.009 (0-2.9)	0.08 (0-2.0)	0.7	0.04	0.09	0.8
Non-neoplastic liver	0.1 (0-1.6)	0.08 (0-8.0)	0.7	0.08	0.1	0.5
cccDNA (copies/cell)						
Tumor	0.00001 (0-0.2)	0.000002 (0-0.2)	0.4	0.0001 (0-2.7)	0.0002 (0-0.5)	0.7
Non-neoplastic liver	0.005 (0-0.4)	0.009 (0-0.6)	0.8	0.02 (0-0.4)	0.004 (0-0.8)	0.1
cccDNA/HBV DNA ratio						
Tumor	0.005 (0-12.4)	0.002 (0-0.2)	0.2	0.005 (0-24.6)	0.05 (0-0.6)	0.8
Non-neoplastic liver	0.06 (0-9.7)	0.08 (0-0.8)	0.7	0.1 (0-9.7)	0.03(0-7.5)	0.004
Death within 5 yrs	10	7	0.7	12	1	0.2
Recurrence within 5yrs	19	18	0.4	25	4	0.1

**Supplemental Table 3: Demographic comparisons according to replicative activity in either tumor or non-neoplastic liver (NT)**

	Replicative activity (Tumor)			Replicative activity (NT)		
	Low (n=43)	High (n=43)	p	Low (n=48)	High (n=48)	p
Male	34	38	0.4	38	43	0.3
Female	9	5		10	5	
Age (mean)	53 $\pm$ 10	56 $\pm$ 10	0.3	56 $\pm$ 11	54 $\pm$ 9	0.5
HAI grade (mean)	3.7 $\pm$ 1.9	3.8 $\pm$ 1.4	0.9	3.4 $\pm$ 1.2	4.1 $\pm$ 2.0	<b>0.04</b>
Ishak fibrosis stage	4.1 $\pm$ 1.6	4.4 $\pm$ 1.5	0.3	3.9 $\pm$ 1.6	4.7 $\pm$ 1.4	<b>0.01</b>
HCC tumor size (mean)	3.6 $\pm$ 3.1	4.5 $\pm$ 3.6	0.2	3.5 $\pm$ 2.5	4.6 $\pm$ 3.8	0.1
Vascular Invasion						
Absence	6	4	0.2	8	4	0.4
Presence	31	34		34	38	
Tumor differentiation						
Well	3	5	0.8	3	8	0.3
Moderate	17	16		20	19	
Poor	18	17		19	17	
AFP (median)	49.9	29.6	0.9	34.7	72.5	0.2
HBeAg status						
HBeAg-negative	22	27	0.2	28	23	<b>0.004</b>
HBeAg-positive	10	5		2	14	

**Supplemental Table 4: Demographics and HBV DNA of 21 patients for RNA-seq analysis**

	PID	Age	Race	Gender	Ishak stage	Tumor Size	NT HBV DNA	NT cccDNA	NT ccc /HBV ratio	HBV Genotype
1	P171	56	A	M	2	1.4	0.04	0.3	7.5	C
2	P170	57	A	M	1	2	0.2	0.3	1.5	B
3	P179	61	A	F	2	2.1	0.04	0.4	9.7	B
4	P157	34	A	F	1	2.5	0.7	0.8	1.1	C
5	P75	62	A	M	2	3	0.07	0.01	0.15	B
6	P158	49	NA	F	2	3.6	0.0015	0.0008	0.5	A
7	P131	57	A	M	2	4	0.06	0.02	0.3	B
8	P99	29	A	M	2	4.3	0.08	0.06	0.8	B
9	P106	60	A	M	2	4.5	0.001	0.000004	0.003	-
10	P161	63	A	M	0	4.8	0	0	N/A	-
11	P152	58	A	M	6	1.5	0.01	0.001	0.09	C
12	P62	49	A	F	6	1.6	0.05	0.04	0.8	C
13	P112	70	A	F	6	2	0.002	0.001	0.5	C
14	P6	55	A	F	6	2	0.3	0.1	0.3	C
15	P176	58	A	M	6	2.1	0.13	0.08	0.62	B
16	P49	59	A	M	6	2.5	0.8	0.0006	0.0008	C
17	P105	57	A	F	6	2.7	0.8	0.07	0.09	C
18	P140	75	A	M	6	3	0.06	0.03	0.4	C
19	P16	55	A	M	6	3	0.4	0.008	0.02	C
20	P138	49	A	M	6	3.1	0.02	0.001	0.07	-
21	P94	48	A	M	6	3.4	0.04	0.004	0.09	C

**Supplemental Table 5: List of genes that were associated with HBV replicative activity in non-neoplastic liver**

SNAPC5  
FAM186A  
KCNMB3  
FASTKD1  
CWH43  
DCAF4L1  
USF1  
RNF166  
C2CD4D  
CTSG  
LOC440434  
TBX19  
APOBEC3D  
IL2RB  
MLC1  
PRSS27  
SLC24A4  
TTLL3  
LOC286367  
VDAC3  
C1orf131  
C9orf139  
HNRNPH1  
GPR114  
RNF165  
EXTL2  
CRYBB3  
KCNH8  
PPHLN1  
ZNF587  
CELSR3  
NUP85  
TNFRSF25  
CHMP5  
FLRT1  
LRP2BP  
PHOSPHO1  
ZNF154  
C19orf18  
COG7  
LOC100131094

GNRHR  
LOC283174  
MYEF2  
PROSER1  
SLC18A2  
SUGT1  
TRIM38  
VILL  
CHN2  
ADO  
NRD1  
WDR27  
ALG13  
MINK1  
MLIP  
TIMMDC1  
ARAP3  
MITD1  
RAD9A  
TNFRSF19  
CACYPB  
SEC14L5  
IRF3  
MMP8  
NFE2L3  
TAF1C  
BCMO1  
MARK3  
LOC340544  
NCRNA00201  
TRIM11  
LRRC37A4  
NAPB  
NOSTRIN  
PPAP2A  
TRNT1  
C7orf53  
CNGA1  
DENND4B  
EXOC3L1  
FAM40A  
FANCG  
GNRH1

KIAA1967  
N6AMT1  
OBSCN  
CD207  
HAP1  
NCOA5  
NXF1  
RBM34  
RHOBTB1  
DKFZP686I15217  
FAM171A2  
LOC644961  
TTC21A  
TXK  
CLK2  
CROCCP3  
CYP21A1P  
DYNLL1  
FAM193B  
GTF2F2  
HAUS5  
MTMR9LP  
NFATC2IP  
NISCH  
PARVG  
SYCP2  
TRIP4  
ABCC10  
AHSA2  
ANKRD49  
DNASE1  
LMBR1L  
LUC7L3  
MKNK1  
SHISA9  
TKTL1  
VPS45  
ZBTB8OS  
ZNF337  
AGAP5  
AKAP8L  
ARGLU1  
EED

IGSF9B  
MATK  
PHC1  
PTCH2  
CCT6A  
LOC100132077  
NPL  
OGT  
PLXNB3  
PRPF38B  
SNRPA1  
TMUB2  
UFSP1  
VMAC  
WDR91  
WNK4  
ANKZF1  
CCDC36  
HDAC1  
INTS1  
LOC100130357  
NAA40  
NEK9  
PDE4C  
PSMA6  
SEC31B  
STAMBP  
AFG3L1P  
C2CD4C  
DDX26B  
DMTF1  
DZIP1L  
GPR88  
NBEAL2  
PDLIM7  
POMT2  
SLC10A3  
TUBGCP6  
VPS52  
ZNF345  
FBXW7  
MBD1  
RASAL1



SETD5  
ST18  
TUBA1C  
DNMT1  
LOC642852  
LYSMD4  
PRPF39  
RIOK2  
TBRG1  
TDRD6  
ZNF10  
AIF1L  
ARHGEF1  
ATG16L1  
AXIN2  
BCAM  
DIDO1  
GTF2H4  
GTPBP5  
IL23A  
LENG8  
LOC100216546  
LUC7L  
MATN3  
NRF1  
NUDT19  
ORAOV1  
RUSC1-AS1  
TYK2  
USP48  
C7orf44  
CDK11A  
ERCC3  
LOC338799  
NEURL4  
POLR3E  
RARS  
SPOP  
ZNF101  
ADPGK  
ATG4B  
C12orf75  
CRYGS

FRG1  
FXVD2  
GAB3  
LOC100507062  
LPCAT4  
MALAT1  
MS4A2  
NECAP1  
RTCD1  
TARSL2  
TRAF2  
ZNF266  
ZNF75A  
ZNF862  
AHSA1  
ARHGAP9  
C3orf33  
HCG26  
LOC283624  
MCTS1  
NTSR1  
PMS2P3  
QSOX2  
SAFB2  
SPDYE5  
SREK1  
TTC1  
TXNDC9  
WTIP  
ZNF767  
ZNF830  
CCNL2  
DCAF5  
EML5  
FLJ31306  
FLJ42393  
HSPB9  
LOC401233  
MCART6  
NAGK  
REG1A  
SNX11  
SRSF2

TCF3  
TNFAIP2  
TRIM7  
ZNF44  
ADCY4  
ARHGEF10  
DYNC1LI2  
GORASP1  
LTF  
MAP3K10  
NT5DC2  
PTRHD1  
SETMAR  
SPDEF  
ZNF142  
ZNF169  
ZNF814  
CDRT1  
DMPK  
DOK3  
F5  
LOC100131434  
NCBP2  
OSBPL2  
PNISR  
RPL32P3  
SLC35A1  
TRIM52  
UIMC1  
ZNF580  
C1orf159  
HCG18  
HRNR  
ING2  
MFSD10  
NAT9  
NLRP1  
NR2C1  
PCGF3  
PNN  
PRRT2  
RCN3  
RPL23AP64

TMC8  
TMEM44  
UBXN2B  
USH1C  
ZNF860  
AKAP17A  
ARPC5L  
ATXN2L  
DPP9  
DTX3  
EFTUD2  
GALNT3  
GDPD3  
KIAA0907  
KIAA1310  
LECT2  
LOC554206  
LOC84856  
PALM3  
PARD6G  
PRSS21  
SAMD3  
SEMA3G  
SLMO1  
TMC7  
USP39  
ARHGEF25  
C19orf77  
CCDC137  
COG4  
DPH1  
HDAC7  
IMPDH1  
NCDN  
NDUFA8  
PPT2-EGFL8  
PRDM11  
SSB  
STK11IP  
TMEM216  
ZDHHC7  
AHI1  
ANAPC4

BTF3L4  
CD160  
CD34  
CHRNA2  
CLASRP  
CWC25  
DEF6  
EWSR1  
FOXK1  
GNN  
LY6G5B  
MDH1B  
MXRA8  
NSMCE2  
PANK4  
SNRNP40  
SOX12  
TRIM39  
WDR60  
WDR85  
YPEL5  
ZNF212  
ZNF781  
ATG16L2  
BHLHA15  
CCR2  
CYP1B1-AS1  
DDX55  
FUK  
ICAM3  
KIAA0895L  
LRRC14  
MAPK13  
NAIP  
PIAS3  
RBM6  
SNHG1  
SRP19  
SYTL1  
TTC13  
C22orf29  
CCDC50  
ERMN

GCFC1  
GK5  
GTPBP3  
LEPREL4  
LOC100129387  
LTB4R  
MAPK8IP3  
NKG7  
SRRM5  
STK32C  
SUGP2  
TESC  
TIAF1  
UBA7  
WDR52  
ZCCHC8  
ZNF346  
ZNF436  
ZNF605  
BCAT2  
C14orf182  
C5orf56  
CCDC76  
CCDC84  
CDAN1  
COL6A4P2  
DARS  
FREM2  
KIAA1530  
LOC100506469  
LOC440104  
LOC729513  
NOL8  
PSME1  
PTGDR  
STAT2  
TBCC  
TH  
TRIM28  
UTP6  
WDR73  
ZSWIM1  
BANP

BST2  
DBF4B  
DPCD  
FAM13AOS  
ILF3  
KLF8  
LOC100507489  
MSTO2P  
SRSF11  
UNC13D  
ZNF785  
AGAP6  
AK5  
C2CD2L  
C6orf203  
CNTD1  
CTC1  
DPY30  
ELMOD3  
ESRP1  
GRIPAP1  
INPPL1  
IP6K2  
KIAA1841  
LOC100507424  
MKX  
N4BP2L2  
PCNT  
PHF1  
POLE4  
RBM17  
RBM39  
RBM5  
SPIN3  
STARD5  
TCIRG1  
WHSC1  
ZNF707  
ARHGAP4  
C9orf172  
CCDC66  
CXXC1  
CXorf56

FBXL19  
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HAPLN4  
HIP1R  
KCNQ1OT1  
LOC283922  
MAEA  
MDM4  
MXD3  
PLD4  
PLRG1  
PSMA3  
PYGO2  
SGK494  
SLC35E3  
ABCC5  
ARID3B  
C16orf48  
CAPS  
CLCN7  
DUS3L  
GPATCH3  
IKBKB  
MADD  
PAAF1  
PRKCDBP  
SNRPA  
SPATS2  
STK36  
TIA1  
TP73-AS1  
TPSB2  
UAP1L1  
VPS37C  
CACNB1  
CDH6  
CXorf23  
DDX19B  
DIP2A  
DNLZ  
DUSP22  
ETV4  
EXOC3



EXOSC3  
LOC100131193  
LOC253039  
LOC643037  
LRCH4  
METTL21D  
NMI  
NUPL2  
PRAM1  
RAGE  
SETD6  
TMC4  
ARL6IP6  
C3orf62  
C8orf77  
CENPO  
CHRNA10  
CLIC3  
CSPP1  
CTHRC1  
EFCAB4A  
GIGYF1  
HNRNPA2B1  
HSD17B12  
LOC100128288  
LOC100507321  
LOC401320  
MORC2  
NRG4  
PIGG  
PLEKHG5  
PMS2CL  
SCARF1  
SCN3A  
SDR39U1  
SIN3B  
SPIRE2  
TCERG1  
THOC1  
USP20  
ZNF655  
APLP1  
C14orf149

C6orf47  
CCT4  
CLEC2D  
GGA3  
HOMER3  
KIAA0556  
KRI1  
LOC100130231  
LOC100133445  
MYO19  
MYOM1  
OXTR  
PDZD4  
PSTK  
RBM23  
REXO2  
SRSF4  
TMEM184A  
TRIM27  
ZBTB12  
ZNFX1-AS1  
ANAPC2  
ASB16  
C14orf142  
CNOT10  
COPS6  
DDX51  
FAM136A  
FAM83F  
FSD1  
HECTD3  
IMPG2  
JMJD7  
KCND2  
KLC1  
LOC100506123  
MTRF1  
MTRNR2L9  
PPP1R13B  
QRICH1  
RBP1  
SFSWAP  
USP45

VASH2  
ZNF276  
AMMECR1L  
ANKRD10  
C9orf173  
CCDC77  
CD247  
KCTD15  
LOC100272228  
MAP3K4  
MRPS25  
PABPC4L  
PPBP  
PPP2R2B  
RASA4  
RBM25  
SLC22A5  
SRP14  
TTLL5  
ZNF738

**Supplemental Table 6: list of genes that correlated with Ishak fibrosis stage**

C11orf80  
MYO7B  
LOC283070  
TBCD  
TASP1  
TP53I3  
IQCE  
DTNA  
SRD5A1  
PGBD1  
TECPR1  
CASP8  
RPS6KA4  
AGRN  
S100A14  
NIPAL3  
LFNG  
EDA2R  
TRIM22  
CAPN2  
PHLDA3  
EMB  
ITIH1  
EFCAB4B  
RFX5  
C15orf58  
ABCA2  
TBC1D1  
EHBP1L1  
JAG2  
ANXA2  
CAPG  
LOC100506776  
RALGPS1  
GLIS2  
NPW  
CD151  
ITM2C  
ADSL  
SERPINA7  
FLJ41484  
MR1

DTD1  
BAX  
KDEL3  
PDGFRB  
SNX1  
ITGB5  
LRSAM1  
ATG9B  
KANK1  
VBP1  
PYGB  
DYNLT1  
TNFSF13B  
LOC100507055  
DDR1  
CHI3L1  
ITGA7  
HMG1  
HECW1  
ZMAT3  
KIAA1797  
RASSF3  
FAS  
B3GNT9  
ABCA7  
SOBP  
GSS  
CDH16  
C15orf52  
SNX20  
ABCB9  
CYP4F22  
CYGB  
ACLY  
SPN  
CDC25B  
IL10RB  
DOCK6  
SEMA4F  
RNF213  
CNPY4  
CHAF1B  
ACBD6

LOC100506746

UXS1

AGAP2

TMPRSS13

PCBP4

SLC16A10

PRKX

FASN

MICA

GRK6

6-Sep

RBM45

SPATA21

GALNTL4

RPIA

APOBEC3C

VWF

VPS45

MIF4GD

KIAA1522

ABCA10

PANK1

FCHO1

MOGAT3

FDXR

APOBEC3H

LPHN1

ELOVL1

HAR1A

LAT2

ATP2A3

HMGCS2

FAM43A

PGS1

CD59

CENPK

ZNF101

IFT74

SAAL1

OXCT1

TMED3

MCCC2

SNX11

ZNF195  
ASPA  
CHCHD6  
SKA2  
LYL1  
HDGFRP3  
EML2  
RNASE1  
SNPH  
DCDC2  
CAMK1D  
TMCO4  
ZDHHC24  
HMHA1  
SEPN1  
PVRIG  
SLFN12L  
IL3RA  
CHD3  
GRAMD1B  
CRADD  
ADD1  
C1orf186  
FBXL2  
RAB11FIP4  
MAN1B1  
TMEM92  
ACMSD  
PPP1R13L  
LINGO1  
PQLC3  
LYZ  
MRAP2  
LOC374443  
PLCH2  
SPINT2  
SV2A  
SLC12A7  
PIK3R6  
CHPF2  
BAIAP3  
CCDC64  
CENPH

PIIP5K1  
RNF152  
RORA  
LNX1  
PCGF2  
HMGN4  
APOF  
SMPD2  
BPGM  
FKBP1B  
EXOC7  
UGT1A3  
CAMK2G  
DDB2  
LLGL1  
AMPD3  
PLD4  
ARPC5  
CD6  
FAM3B  
EXO1  
C17orf62  
LOC388692  
SLFN13  
HPS1  
C7orf31  
FBXL16  
PIK3C2G  
ANXA4  
TBC1D10C  
LPPR2  
DGCR2  
RNF207  
BCAS4  
KIAA0664  
NTS  
C1orf93  
DCTN1  
FTSJD2  
BBC3  
OPTN  
HELLS  
ST14



BST2  
SH2D3A  
BCRP2  
ZNF200  
MPPED1  
CCR2  
FANCD2  
TKT  
SDHD  
RABIF  
FEZ2  
ADAMTSL2  
RNASEH2A  
NLRC3  
MYO5A  
SERPING1  
MAT1A  
LY9  
S100A4  
CDH23  
RPS27L  
ARHGAP27  
TMC7  
SMYD3  
CDO1  
FAM155A  
ITGAM  
LOC100505576  
EPCAM  
FANCI  
ADM2  
LOC399753  
SLX4  
FAM129B  
NOTUM  
SCUBE1  
NLGN3  
GABRP  
AQP1  
LCMT1  
SOX9  
FZD2  
C5orf39

ANXA2P2  
FANCB  
TRIOBP  
RASAL3  
RHOBTB2  
WIPF3  
FCHSD1  
LOC729799  
PHLPP1  
ZNF683  
SEMA7A  
C15orf38  
SNAP25  
PLSCR4  
CIDEB  
TRAFD1  
NOD2  
CCDC88B  
MTHFD1L  
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VAV2  
TAT  
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OLFM2  
LIG1  
SPINT1  
CACNA2D3  
HABP4  
SKA1  
SCP2  
GJD3  
SH3KBP1  
TCTN2  
CD63  
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ARHGAP22  
RPL39L  
SPON2  
TRAF2  
DGCR11  
MXI1  
ARPC1B  
RBBP7

KCNK6  
NUDT1  
INTS9  
ODZ4  
BAIAP2L1  
SMARCE1  
GAL3ST4  
CD58  
DERL3  
PRDM8  
PCNXL3  
C9orf6  
KIF21B  
PKN1  
TEP1  
ARHGEF16  
EPHB2  
C5orf20  
C17orf49  
DAB2IP  
STAT5A  
LASP1  
CASP10  
PVT1  
POLH  
LRRN4  
ALDH3B1  
TMCC2  
GGPS1  
KIAA0664L3  
CHFR  
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C7orf29  
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HLA-DQA2  
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CACNA1D  
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POLD1  
BTN3A1  
MEI1  
PROCR

SLA2  
C15orf57  
PPP1R9B  
XPNPEP1  
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ERMN  
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NSMAF  
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IQSEC2

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SEMA3G  
DEF6  
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GYS2  
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ANKH  
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LUM  
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CTHRC1  
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TSPAN4  
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ZNF346  
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TLR5  
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TRPM4  
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SYT7  
STK17B

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GPBAR1  
GALNT6  
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LIN9



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GJA4  
MGRN1  
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EPDR1  
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FAT1  
PACS1  
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GPR132  
TGFB1  
TACC3  
SNTB1  
ZNF607  
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DDX26B  
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NLRP6  
LAMC3  
CENPJ

HDAC6  
GRAP2  
SYNGAP1  
MEP1A  
PRMT2  
STX7  
RHOF  
RASGRP4  
TCF7  
PIGU  
ANKS6  
MYEF2  
CD3E  
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SULT1C2  
MAGED1  
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RARG  
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GINS1  
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WNT2B  
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DBNDD1  
CSTB  
VSIG10  
ORAI2  
TMC8  
MICB  
ENTPD6

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SEMA4D  
HHAT  
HTT  
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DKK3  
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PLCG1  
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CIITA  
OSBPL7  
PLCD1  
ITIH5  
PAPLN  
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ACADSB  
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TIAM2  
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CASP2  
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RBCK1  
HRCT1  
GNMT  
HSF5  
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SUMF2  
CD3D  
RNASE6  
MTL5  
BICC1  
DKK2  
PAQR4  
CARD9  
SDK2  
ZNF587  
VRK1  
VOPP1

EXOSC9  
APIP  
NELF  
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CLEC4C  
CROCC  
GNB1  
TIFAB  
GLYR1  
HVCN1  
SIPA1L2  
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TMSB4X  
NR1D2  
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S1PR4  
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CGREF1  
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LOC100506190  
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OSCAR  
GRIN2D  
MAGED2  
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DLG3  
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ZNF469  
IL21R  
SERPINB1  
C9orf131  
GNAI3  
KIAA1530

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RARS  
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VASH2  
FAM176B  
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INPP4A  
GPR160  
EME2  
PTPN7  
GTDC1  
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ISM1  
CTC1  
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TMSB10  
RLTPR  
CBX6  
TRIM21  
SEL1L3  
AP1S3  
MFNG  
AEN  
BAK1  
AZI1  
HEATR8-TTC4  
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LOC100506844  
ATF6B  
MAPK3  
MCM3  
CLEC4A  
VDR  
PCSK7  
PTTG1  
CD2  
RCAN3  
GABRE  
SIDT1  
CERS5  
ITGA3  
VEPH1  
SOX2OT

WBP5  
CDR2L  
TFF3  
HIF1AN  
POF1B  
GPX7  
C7orf50  
SEZ6L2  
C19orf10  
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CPA3  
C5orf34  
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STBD1  
CD79B  
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NAAA  
B4GALNT3  
GGT6  
SULF2  
SNCG  
NAT8B  
YKT6  
MDK  
TULP4  
C18orf10  
PBX4  
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PIGG  
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TRIM45  
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LOC100132077  
LOC150197  
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BHLHE41  
NLRP1



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MLLT6  
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ENOPH1  
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SARNP  
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GINS2  
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CLIC6  
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GMIP  
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ZNF669  
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ADAMTS10  
SPTB  
HECTD1  
AGTRAP  
SIT1  
QTRTD1  
TMEM56  
NUDT18  
GLRX3  
SLC25A30  
MS4A2  
AOX1  
AATK  
AGBL4  
ZBTB12  
RMI2  
P2RY6  
MOSC2  
FAM110A  
ABAT  
HKDC1  
CCR5  
TRAF3  
HEXA  
RFC2  
C9orf167  
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IKBIP  
TNFAIP8L2  
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C16orf3  
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GATA5  
BACE2  
NLRP11  
CLDN10  
GPSM3  
EVPLL

NAIP  
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LAT  
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HAUS2  
    9-Sep  
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MRAS  
TINF2  
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PDZK1IP1  
CDCA4  
MCU  
HS1BP3  
PALMD  
RECQL4  
CCDC23  
CHIC1  
ARHGEF1  
CFL1  
ADAP1  
CLEC14A  
SASH3  
SRA1  
NEU1  
ARF3  
APOBEC3F  
ADORA1  
AMDHD1  
KCNC3  
NES  
TTN  
INPP5D  
LGALS3  
IGFBP7  
CCL5  
SLC27A2  
CD19  
TRIM6  
OIP5  
TMEM156  
RUSC2

JPH4  
NQO1  
SECTM1  
RNF114  
DUOX1  
TCL1A  
APBB3  
CHST2  
ZNF93  
RGS12  
MPV17  
USP18  
COTL1  
LACC1  
DUSP4  
OSBPL1A  
CD40LG  
EHF  
PDE9A  
SOX18  
LEPRE1  
FUCA2  
TRPM2  
CHST10  
KCNQ3  
TAP1  
CDC20  
CYB561D1  
KIF18A  
ACSS1  
SYT12  
FAM96A  
RASA3  
DNAJC22  
CST7  
SAE1  
RNF157  
CD248  
ENO2  
CD163L1  
IRS2  
CBS  
MYO1F

PLXNC1  
PDZD2  
LPAR5  
PCYOX1L  
HOGA1  
CENPE  
DDX25  
FBLN2  
C7orf70  
ITGB1BP1  
AKNA  
CLEC17A  
ALOX5AP  
SCD  
CD247  
ESRRG  
SLC27A1  
HNRNPR  
RNF144B  
CCR7  
PTRF  
PIIF  
JAK3  
CCDC112  
MLLT1  
CLIP3  
XYLT2  
ALS2CL  
PPAP2C  
SFRP5  
CNBP  
TRIP13  
PRKACA  
SAMD9  
SPA17  
LOC401431  
KLF2  
PAK6  
SALL4  
TNK2  
TMEM165  
ME1  
SYT11

DKFZp779M0652

SAMD3

COL23A1

SLC35A4

GIT2

NBEAL2

SCML4

TNFAIP8

C12orf4

SP100

GOLGA7

LOC439990

CD3G

MXRA8

MMS22L

TBC1D10B

FMNL3

PRKCB

PROCA1

MS4A14

S100A11

CD79A

CD48

CCDC85B

WIPF1

PRKCQ

ANKRD11

TC2N

KIAA0226

RASSF5

DTL

ADCY6

BLOC1S2

SMG6

2-Mar

ARSK

CUBN

FAM40B

ENTPD2

LDB1

PIK3R2

SPIB

PPIH

CUL7  
GM2A  
SLC5A4  
MOCS1  
KIAA0556  
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HTR2B  
ZBED3  
FMNL1  
GDPD4  
GPR88  
C9orf103  
OSBPL3  
TAGLN2  
EPHX3  
CCNB2  
ABR  
CCDC8  
CSGALNACT1  
COL4A3  
FIBP  
FBLIM1  
PPP1R2  
PPP2R5A  
ITPR3  
XPO6  
CARD11  
KIAA1704  
MAPK11  
S100A6  
ITPKA  
AGL  
WAS  
CCDC57  
LY86  
SPNS1  
GPX8  
XRCC4  
STARD3NL  
GIPC1  
C1orf183  
ACYP1  
PARD3B

MMS19  
FAM49B  
REEP4  
PCK1  
CXorf36  
HCCS  
TAP2  
LOC283663  
LOC284749  
C10orf54  
LAIR1  
C9orf139  
TSNARE1  
SDHAP2  
C1orf131  
CYP2B6  
NPTN  
SPATA18  
C19orf52  
GCNT4  
CCDC136  
C6orf1  
OPA3



**Supplemental Table 7:** Liver cancer-related function enrichment of differentially expressed genes associated with liver fibrosis.

CHIANG_LIVER_CANCER_SUBCLASS_PROLIFERATION_UP	1.81114e-09
HOSHIDA_LIVER_CANCER_SUBCLASS_S1	7.35499e-10
WOO_LIVER_CANCER_RECURRENCE_UP	3.32133e-06

**Supplemental Table 8:** 26 common genes that were associated with both viral replicative activity and Ishak fibrosis stage.

ABCC10  
APLP1  
ARHGAP4  
ARHGAP9  
CCR2  
CD34  
CDH6  
CTHRC1  
DDX26B  
DEF6  
DMPK  
ERMN  
ESRP1  
ETV4  
MYEF2  
NT5DC2  
PLD4  
SEMA3G  
STK32C  
SUGT1  
TMC4  
TRAF2  
ZNF101  
ZNF860