

Comparative RNA-sequencing analysis reveals high complexity and heterogeneity of transcriptomic and immune profiles in hepatocellular carcinoma tumors of viral (HBV, HCV) and non-viral etiology

Supplementary data

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Supplementary Table 1. Patients` features

Variables	HBV group (n=8)	HCV group (n=8)	Non infection group (n=8)	<i>P</i> - Value
Age (mean \pm SD)	57 \pm 13	64 \pm 6	62 \pm 9	0.4251
Gender (n, %)				
Male % (n)	62.5% (5)	37.5% (3)	75% (6)	0.3012
Female % (n)	37.5% (3)	62.5% (5)	25% (2)	
Tumor size cm (mean \pm SD)	3.1 \pm 1.6	4.4 \pm 2.4	5.9 \pm 3.58	0.1257
Macrovascular invasion				
Yes	12.5 % (1)	25 % (2)	12.5 % (1)	0.7408
No	87.5 % (7)	75 % (6)	87.5 % (7)	
Microvascular invasion				
Yes	0%	25 % (2)	12.5 % (1)	0.3189
No	100% (8)	75 % (6)	87.5 % (7)	
Stages				
I % (n)	50 % (4)	50 % (4)	75 % (6)	0.3964
II % (n)	37.5 % (3)	37.5 % (3)	0% (0)	
III % (n)	12.5 % (1)	12.5 % (1)	25% (2)	
Overall Survival (months) (mean \pm SD)	37.63 \pm (13.87)	28.13 \pm (19.34)	30.88 \pm (13.89)	0.5846
PIVKA mAU/ml (mean \pm SD)	925.4 \pm 1419	6706 \pm 8295	11980 \pm 13042	0.0969
Serum AFP (ng/ml) (mean \pm SD)	198.6 \pm 412.5	833.3 \pm 812.1	134.5 \pm 349.9	0.0451

The *p* values are from the One-way ANOVA /Chi-square (and Fisher's exact) test; SD, standard deviation.

Supplementary Table 2. Primer sequences

Oligo name	Sequence
<i>COLEC10_F</i>	ATA-GCC-GTC-CTA-CCG-CTG-AA
<i>COLEC10_R</i>	TGA-TCT-CCC-ATA-TCA-CCC-AGT-TC
<i>HGF_F</i>	GCT-ATC-GGG-GTA-AAG-ACC-TAC-A
<i>HGF_R</i>	CGT-AGC-GTA-CCT-CTG-GAT-TGC
<i>CLEC1B_F</i>	GAC-AAC-CGG-AAC-ATT-GTG-GAG
<i>CLEC1B_R</i>	ACT-TCT-GGC-GAG-ATA-ATC-CGA
<i>CYP17A1_F</i>	TAT-GGC-CCC-ATC-TAT-TCG-GTT
<i>CYP17A1_R</i>	GCG-ATA-CCC-TTA-CGG-TTG-TTG
<i>HSF1_F</i>	CCA-TGA-AGC-ATG-AGA-ATG-AGG-C
<i>HSF1_R</i>	CTT-GTT-GAC-GAC-TTT-CTG-TTG-C
<i>BIRC5_F</i>	AGG-ACC-ACC-GCA-TCT-CTA-CAT
<i>BIRC5_R</i>	AAG-TCT-GGC-TCG-TTC-TCA-GTG
<i>HSP90AB1_F</i>	AGA-AAT-TGC-CCA-ACT-CAT-GTC-C
<i>HSP90AB1_R</i>	ATC-AAC-TCC-CGA-AGG-AAA-ATC-TC
<i>SLC22A1_F</i>	TGT-CAC-CGA-AAA-GCT-GAG-CC
<i>SLC22A1_R</i>	TCC-GTG-AAC-CAC-AGG-TAC-ATC
<i>HSPB1_F</i>	ACG-GTC-AAG-ACC-AAG-GAT-GG
<i>HSPB1_R</i>	AGC-GTG-TAT-TTC-CGC-GTG-A
<i>RNF187_F</i>	GTG-ATG-GAC-CGT-AGG-AAG-AAG-G
<i>RNF187_R</i>	GTG-ACC-TGA-ACC-GCT-CAG-TG
<i>FGFR4_F</i>	GAG-GGG-CCG-CCT-AGA-GAT-T
<i>FGFR4_R</i>	CAG-GAC-GAT-CAT-GGA-GCC-T

Supplementary Table 3. Data Common HBV & HCV

Crt. No.	Differentially expressed genes (DEGs)	Tumor group etiology		
		HBV log 2 (ratio)	HCV log 2 (ratio)	Non viral (non-B, non-C) log 2 (ratio)
Up-regulated genes				
1	MTNR1B	6.2	7.42	0
2	AFP	5.93	5.02	0
3	COL7A1;	5.43	7.24	0
4	RGSL1	4.85	3.72	0
5	PDE7B	4.83	5.75	0
6	FMO2	4.25	2.52	0
7	MDK	3.81	3.27	0
8	EGF	3.8	6.23	0
9	HAGLR	3.76	4.26	0
10	LDB2	3.72	4.57	0
11	EPS8L3	3.63	4.31	0
12	ANLN	3.53	5.62	0
13	KIF18B	3.48	5.65	0
14	CDC25C	3.4	4.85	0
15	CENPF	3.37	5.08	0
16	CPNE7	3.32	3.14	0
17	DEPDC1	3.31	5.64	0
18	EXO1	3.18	4.8	0
19	CYP7A1	3.03	3.12	0
20	MKI67	3.01	4.59	0
21	CDK1	2.98	4.35	0
22	CENPE	2.92	3.77	0
23	HMMR	2.91	3.92	0
24	C2orf48; RRM2	2.84	4.06	0
25	CCNB1	2.71	3.99	0
26	KCCAT333;	2.69	1.92	0
27	PRC1	2.64	3.61	0
28	TTC39A	2.63	3.37	0
29	SPP1	2.3	3.69	0
30	ARFGEF3	2.24	2.61	0
31	GREB1	2.21	1.84	0
32	NUSAP1	2.21	3.07	0
33	TPX2	2.15	3.6	0
34	SNAP25-AS1	1.93	1.88	0
35	GDNF-AS1	1.79	2.43	0
36	DPY19L2P2	1.78	1.58	0
Down-regulated genes				
1	MASP1	-1.66	-1.67	0
2	SERPINA11	-1.69	-2.1	0
3	C8B	-1.73	-2.27	0
4	NRG1	-1.76	-1.89	0

5	RCAN1	-1.83	-1.7	0
6	FOS	-1.86	-2.25	0
7	RND3	-1.9	-1.97	0
8	WDR17	-2	-1.78	0
9	NPR3	-2.08	-2.05	0
10	OLFML3	-2.26	-1.87	0
11	SEMA6D	-2.31	-2.57	0
12	TNXB	-2.31	-1.96	0
13	COL25A1	-2.36	-3.37	0
14	IGFBP3	-2.51	-1.99	0
15	STEAP4	-2.56	-2.72	0
16	CXCL12	-2.76	-2.97	0
17	PHACTR3	-2.76	-3.9	0
18	ANKRD18DP	-3.07	-3.23	0
19	DNASE1L3	-3.13	-2.87	0
20	HMGCLL1	-3.27	-4.07	0
21	CD5L	-3.41	-2.16	0
22	NDST3	-3.96	-4	0
23	NOL4	-4.35	-3.21	0

Supplementary Table 4. Data Common HBV& nonBnonC

Crt. No.	Differentially expressed genes (DEGs)	Tumor group etiology		
		HBV log 2 (ratio)	HCV log 2 (ratio)	Non viral (non-B, non-C) log 2 (ratio)
Up-regulated genes				
1	ODAM	6.14	0	9.05
2	CPLX2	5.32	0	10.41
3	SULT4A1	5.21	0	4.19
4	PAPPA2	5.02	0	3.13
5	FAM133A	4.7	0	5.22
6	MEOX2; MEOX2-AS1	4.17	0	3.55
7	NBPF22P	3.94	0	5.19
8	THBS4	3.91	0	2.58
9	GPC3	3.58	0	5.24
11	SMPX	3.14	0	4.03
12	NKD1	2.9	0	3.33
13	BRDTP1	2.3	0	3.19
14	RDM1	1.99	0	2.76
Down-regulated genes				
1	IL1RAPL2	-1.52	0	-2.18
2	VSIG4	-1.68	0	-2.18
3	MRC1	-1.76	0	-2.44

4	CYP2C8	-2.4	0	-2.68
5	SPP2	-2.51	0	-2.75
6	KCNJ16	-3.14	0	-3.2
7	MXD4	-3.47	0	-3.83
8	TDRD1	-4.33	0	-4.62
9	LRRC75A-AS1; SNORD49B	-4.62	0	4.58

Supplementary Table 5. Data Common HCV& nonBnonC

Crt. No.	Differentially expressed genes (DEGs)	Tumor group etiology		
		HBV log 2 (ratio)	HCV log 2 (ratio)	Non viral (non-B, non-C) log 2 (ratio)
Up-regulated genes				
1	GRINA	0	1.22	3.48
2	GLI4; ZFP41	0	1.35	3.74
3	TUBB	0	1.38	1.26
4	BSG	0	1.39	3.15
5	RNF187	0	1.45	2.35
6	SNRPB	0	1.46	2.04
7	PABPC1	0	1.48	1.93
8	HGS	0	1.52	2.13
9	MROH1	0	1.56	2.41
10	GLMP; TMEM79	0	1.68	1.98
11	PVT1	0	1.74	2.08
12	PRKDC	0	1.77	1.63
13	TMEM150B	0	1.79	3.31
14	ALDOA	0	1.83	2.97
15	MSTO1; STO2P	0	1.89	2.18
16	SCRIB	0	1.96	3.92
17	SQSTM1	0	1.99	2.24
18	TKT	0	2.07	3.3
19	SLC26A6	0	2.14	3.02
20	EZH2	0	2.22	2.57
21	NDRG1	0	2.3	2.08
22	ASPH	0	2.38	2.87
23	TXNRD1	0	2.38	2.44
24	COL5A3	0	2.4	3.27
25	CDRT1; TRIM16	0	2.45	3.99
26	HIST1H2AD; HIST1H3D	0	2.46	2.91
27	HMGA1	0	2.46	3.29
28	SRXN1	0	2.5	2.69
29	FBXW10; RIM16L	0	2.74	3.17
30	MCM4	0	2.91	2.3
31	LUCAT1	0	3.09	4.16

32	CABYR	0	3.12	4.94
33	ROBO1	0	3.2	2.06
34	HIST1H2AL; IST1H2BM; HIST1H2BN; HIST1H2BO; OR2B6		3.31	3.64
35	MCM2	0	3.47	2.7
36	RAD54L	0	3.61	3.29
37	RECQL4	0	3.65	4.71
38	SPINK5	0	4.47	3.2
39	HIST1H2AK; HIST1H2BL	0	3.78	4.89
40	TICRR	0	3.88	2.73
41	NQO1	0	3.93	4.14
42	DIAPH3	0	3.94	2.32
43	POLQ	0	4.0	2.35
44	PTPRQ	0	4.03	7.35
45	ZFPM2-AS1	0	4.03	3.48
46	HIST1H2AL	0	4.07	3.86
47	TLX1	0	4.07	3.09
48	FBXO43	0	4.22	2.9
49	SERINC2	0	4.37	5.48
50	CNTNAP4;	0	4.78	4.1
51	SNX29	0	4.87	5.28
52	AKR1B10; KR1B15	0	5.33	5.08
53	ALDH3A1	0	5.96	8.89
54	IGF2BP1	0	6.37	4.36
55	BAGE; BAGE3; BAGE4; BAGE5; TPTE	0	6.93	5.82
56	LSP1P3	0	7.33	5.94
57	RIMS2	0	7.46	5.29
58	SPINK4	0	10.18	13.45
59	ACTL8	0	11.23	9.12
Down-regulated genes				
1	PKHD1	0	-3.99	-2.76
2	LINC01093	0	-3.96	-3.19
3	GPM6A	0	-3.86	-3.22
4	ADGRB3	0	-3.85	-2.62
5	HHIP	0	-2.96	-2.57
6	CYP3A43	0	-2.94	-1.36
7	ATOH7	0	-2.79	-2.28
8	HBB; HBD	0	-2.79	-2.57
9	EPHA3	0	-2.73	-2.48
10	PDGFRA	0	-2.71	-3.16
11	C8A	0	-2.68	-1.44
12	ASIC5; TDO2	0	-2.66	-2.47
13	SOCS2	0	-2.5	-3.25
14	MMRN1	0	-2.48	-2.01
15	SLC7A2	0	-2.47	-1.99
16	JCHAIN	0	-2.45	-2.67

17	TDRD15	0	-1.99	-3.02
18	AMDHD1	0	-2.4	-1.73
19	HPX	0	-2.35	-1.8
20	NAT1; NAT2	0	-2.35	-2.41
21	MACC1	0	-2.33	-3.23
22	IL1RAP	0	-2.24	-1.89
23	PKHD1L1	0	-2.19	-2.19
24	SH3YL1	0	-2.19	-2.37
25	GLYATL1	0	-2.16	-2.06
26	SLC38A4	0	-2.05	-1.61
27	CYBRD1	0	-2.01	-1.77
28	DAB1	0	-1.99	-1.72
29	CYP2E1	0	-1.95	-1.77
30	APOF; STAT2	0	-1.91	-1.81
31	PLA2R1	0	-1.89	-1.75
32	A2M; PZP	0	-1.81	-1.73
33	ACAA2	0	-1.76	-1.64
34	SOCS2-AS1	0	-1.67	-1.63
35	PLG	0	-1.52	-1.75
36	PLSCR4	0	-1.52	-2.07
37	ID2	0	-1.47	-1.8

Supplementary Table 6. List of up and down-regulated genes in HBV related HCC

HBV unique upregulated in tumor	FC	HBV unique downregulated in tumor	FC
SCGB1D2	13.44	MEG8;MIR370;MIR411;MIR494;SNHG24;SNORD113-1;SNORD113-2;SNORD113-4;SNORD113-9;SNORD114-1;SNORD114-10;SNORD114-11;SNORD114-13;SNORD114-14;SNORD114-17;SNORD114-26;SNORD114-27;SNORD114-28;SNORD114-29;SNORD114-30;SNORD114-31;SNORD114-4;SNORD114-5;SNORD114-6;SNORD114-7;SNORD114-8	-5.25
DSCR8	11	CLEC1B	-5.11
PAGE4	9.58	FCN2	-4.9
ODAM;PRR27	9.41	LINC0001;PRSS55	-4.47
HOXC9	8.61	CRHBP	-4.14
SFTA1P	8.57	MIR10A	-4.06
CSN1S2BP	8.39	THSD7A	-3.79
MIR552	6.41	DSCAM	-3.63
BAGE;BAGE3;BAGE4;BAGE5	5.46	BBOX1	-3.54

PEG10	5.29
LOC101928775	5.24
LOC80078	4.98
MAGEA1	4.74
SPINK1	4.7
CTNNA2;LOC101927987	4.68
MIR4441	4.53
HOXA10;HOXA10-HOXA9;HOXA9	4.43
LOC100421746;PAGE5	4.21
MGAM2	3.74
ALG1L	3.45
LOC101928911;SPACA1	3.31
NOTUM	3.31
KIF4A	3.08
MIR325;MIR325HG	3.04
MIR4454	2.9
LGR5	2.81
IFI27	2.69
MGC32805;SNCAIP	2.58
FAM53A	2.5
SLC5A6	2.47
HOXA3	2.37
PTCHD4	2.28
EGFEM1P	2.28
MROH2A	2.25
ST8SIA3	2.21
LINC01010;LOC101928231;LOC101928304	2.19
LOC101927334	1.92
CDHR3	1.44
ATP6AP1L	1.38

HAO2;HSD3B2	-3.44
PLCXD3	-3.4
LRRC7	-3.28
GBA3;MIR548AJ2	-3.26
ADAMTS13	-3.16
ECM1	-3.12
CDH19	-3.09
FAM47E-STBD1	-3.06
KDM8	-2.81
DPT	-2.53
IL5RA	-2.45
NPY1R	-2.33
ALLC	-2.31
CCL19	-2.29
FGF14;FGF14-IT1	-2.2
KCNE1	-2.18
TDO2	-2.18
TPTE2	-2.16
XDH	-2.14
FCRL3	-2.13
KIAA1456	-2.12
HSD17B13	-2.11
FAM188B;INMT;INMT-FAM188B	-2.1
DTHD1	-2.09
MYO10	-2.02
CXCL2	-1.98
CPEB3	-1.95
IFNG-AS1;IL26	-1.92
CD163	-1.92
RASGEF1B	-1.92
FBP1	-1.87
EMBP1	-1.87
ANXA10	-1.82
PHLDA1	-1.79
LINC00548;LINC00598	-1.75
MT1L;MT2A	-1.71

MS4A6A	-1.69
LILRA6;LILRB2;LILRB3;LILRB5	-1.66
CCDC141;TTN	-1.63
CEP128;TSHR	-1.55
LOC101927156	-1.25

Supplementary Table 7. List of up and down-regulated genes in HCV related HCC

HCV unique upregulated in tumor	FC	HCV unique downregulated in tumor	FC
REG3A	10.59	CNTN3	-5.8
ANKRD33	10.38	GRIN2B	-5.73
LINC00162	9.68	FREM2	-5.63
TUBA3C	9.17	MIR378H	-5.62
MIR5007	8.83	TRPV6	-5.53
KHDC1L	8.48	FAM83F;LOC100130899	-5.36
ALX1	8.29	MUC6	-5.32
CYP2C9	8.14	CFTR	-5.26
FSTL5	8.05	SLC22A1	-3.12
LINC01142	7.54	MROH2B	-5.02
CLVS2	7.46	GABRB3	-5
CARD18	7.32	ACSM6;CYP2C8	-4.89
LINC00564	7.3	GABRP	-4.89
PRAME	7.3	SLC5A1	-4.75
CDH9	7.28	CXCL14	-4.57
MIR631	7.25	IGF2;INS;INS-IGF2	-4.5
OR8A1;OR8G1	7.22	GRHL2	-4.49
LOC101929645	7.2	GLS2	-4.36
LINC01419	7.14	VIPR1	-4.12
GALNT5	7.13	ADGRG7	-4.09
LINC00906;LOC102724958	7.01	PROM1	-4.09
NPSR1-AS1	6.95	LRRTM3	-4.06
LINC01611	6.91	CYP1A2	-3.98
LOC102723828	6.89	CTNNA3	-3.97
CD200R1	6.86	PWRN1;PWRN2;PWRN3	-3.96
LOC101929694	6.84	KCNN2	-3.93

LOC101927081	6.78
CNTNAP2	6.74
LOC102723968	6.63
LOC344887	6.56
CYTL1;LOC101928306	6.55
LOC101929584	6.43
TRIM71	6.36
MMP13	6.32
FEZF1-AS1	6.25
CSMD1	6.13
SKA1	6.13
GRM7-AS3	6.08
CDH7	6.05
ST8SIA6-AS1	5.96
CCDC144NL	5.89
ZIC4	5.88
MYBPC1	5.84
CASC20	5.76
ABCB5	5.57
C12orf56	5.56
NEK2	5.55
OSTN	5.54
BIRC5	5.52
TERT	5.5
DMP1	5.48
NPFFR2	5.45
PPP2R2C	5.44
XIRP2	5.41
LOC101927062	5.31
LINC00942	5.28
IBSP	5.26
LINC00002	5.2
CCDC169;CCDC169-SOHLH2;SOHLH2	5.16
KIF2C	5.12
PBK	5.12
HAVCR1	5.1

SYT9	-3.92
MFSD2A	-3.77
BMP10	-3.74
HAND2-AS1	-3.61
AJAP1	-3.55
ESRRG	-3.53
SHBG	-3.53
FENDRR	-3.51
AGBL4	-3.41
LOC100506869	-3.36
GNAO1	-3.3
OR5AK2;OR5AK4P	-3.3
BZRAP1;MIR142	-3.27
MIR1247	-3.26
SCN7A	-3.26
IDO2	-3.23
TIMD4	-3.21
CLSTN2	-3.12
FLJ22763	-3.12
MOGAT2	-3.05
NCAM1	-3.02
CYP2B6;CYP2B7P	-3.01
ASPG	-2.98
UROCI	-2.97
PCK1	-2.93
PGLYRP2	-2.92
BCHE	-2.91
FAM65C	-2.89
GSTA2	-2.82
ACSM3	-2.81
TNFRSF13B	-2.81
COL4A3	-2.73
FAM47E-STBD1;STBD1	-2.69
FAM129C	-2.62
LINC00924;LINC01197	-2.62
CYP2C18;CYP2C19;CYP2C9	-2.59

KIF20A	5.09
E2F7	5.08
CCNYL2	5.04
CNTN6	5.04
C21orf91	5.01
LINC00648	5.01
HMGA2	4.98
DLGAP5	4.97
NCAPG	4.94
GTSF1	4.9
CYP19A1	4.89
ROS1	4.87
CEP55	4.84
IGF2BP3	4.84
ERC2	4.82
TSPEAR	4.8
CDC45	4.76
TTK	4.71
UHRF1	4.68
GPR158	4.67
MATN3	4.66
SH3GL3	4.64
AXDND1	4.62
CDCA2	4.62
CKAP2L	4.62
SULT1C2	4.59
TRIP13	4.59
MCM10	4.57
XIRP1	4.57
ZNF444	4.57
CEACAM20	4.54
RGS13	4.54
WDR75	4.52
BUB1B;PAK6	4.52
LRFN5	4.46
SPTA1	4.45

LIFR-AS1	-2.57
GRAMD1C	-2.56
ANKRD55	-2.49
COL19A1	-2.49
NIPAL1	-2.49
UGT2B10;UGT2B28;UGT2B7	-2.49
LRRC4C	-2.48
HAL	-2.47
FCRL2	-2.45
CETP	-2.44
RDH16;ZBTB39	-2.43
RIC3	-2.42
GLYAT	-2.4
IGF1	2.61
TTR	-2.39
CYP3A4;CYP3A5;CYP3A7;CYP3A7-CYP3A51P	-2.38
HSD17B2	-2.28
FGB	-2.26
OR10J5	-2.25
IL1RL1	-2.24
C9;DAB2;FYB	-2.23
FGFR2	-2.22
NR4A1	-2.2
LOC200772	-2.19
FBLN5	-2.18
PLA2G5	-2.18
AZGP1	-2.17
FXYP1;FXYP7	-2.15
FAM110C	-2.13
PRELP	-2.12
AQP1;FAM188B;INMT;INMT-FAM188B	-2.09
ERRFI1	-2.03
RBMS3	-2.03
SPINT2	-1.96
TAT;ZNF19;ZNF23	-1.96
F11	-1.95

RPL10L	4.42
MIR4426	4.41
SLCO1C1	4.38
KIF14	4.36
TCN1	4.35
MKRN3	4.34
HIST1H3B	4.33
MUC15	4.33
CDKN3	4.32
PPP1R15B	4.3
GTSE1	4.29
GSDMC	4.28
BRSK2	4.23
CASC9	4.21
KIF23	4.13
RFX8	4.11
CACNA1E	4.1
LINC01060	4.1
MIR2052;MIR2052HG;PI15	4.1
MIR3144	4.1
POSTN	4.05
HHLA2	4.04
FAM111B	4.02
LINC00491	3.99
LINC01229	3.99
DUXAP8	3.98
CD200R1L	3.92
LINC01468	3.92
NRCAM	3.9
CALCR	3.86
NEIL3	3.81
SLC2A5	3.81
CDCA3	3.8
SLC28A2	3.8
ZFPM2	3.8
GPSM2	3.78

ALLC;COLEC11	-1.94
CPN1	-1.94
FCRL1	-1.94
GSTA1;GSTA3	-1.89
PTGIS	-1.86
SERPINF2	-1.86
GCH1	-1.85
FABP1	-1.83
LINC01197	-1.82
ADAMTS1	-1.81
ADAMTSL3	-1.81
ID1;MIR3193	-1.78
ITGA9	-1.77
MEF2C-AS1	-1.77
ADRA1B;LOC101927766	-1.76
COL14A1	-1.76
PANK1	-1.7
APOH	-1.69
OGDHL	-1.69
CYR61	-1.65
GADD45B	-1.64
LIPG	-1.63
SIK1	-1.63
SYNPO2	-1.63
C1R;C1RL	-1.57
AGXT	-1.55
MAT1A	-1.55
PEG3;ZIM2	-1.55
ACSL1	-1.53
ABAT	-1.51
BDH2	-1.51
DUSP1	-1.5
MPC1	-1.5
SLC27A2	-1.47
FGL1	-1.45
GABARAPL1	-1.41

TFAP2A	3.78
APCDD1L	3.76
EGFEM1P;LOC100507661	3.76
OSR2	3.76
EBF2	3.74
LOC613266	3.71
CRNDE	3.7
OR2AG1	3.7
PABPC4L	3.69
PYCR1	3.68
RIBC2	3.66
C5orf46	3.64
WDR62	3.61
ILDR2	3.57
HIST1H2AB	3.56
KIAA0101	3.55
PPP1R1B	3.53
GAD1	3.5
KIF11	3.49
PKIA-AS1	3.47
ZWINT	3.47
FXVD3	3.46
AURKA	3.41
LOC339862	3.41
MAEL	3.41
IL31RA	3.4
PRR19	3.4
RACGAP1	3.4
SMKR1;STRIP2	3.4
PRR11	3.39
TMEM74	3.39
TRPC3	3.39

SLC38A2	-1.41
DGAT2	-1.4
THBS1	-1.35
PPP1R3B	-1.34
IRF8	-1.33
MEG8;MIR370;SNHG24;SNORD113-1;SNORD113-2;SNORD113-4;SNORD113-5;SNORD113-6;SNORD114-1;SNORD114-10;SNORD114-14;SNORD114-17;SNORD114-20;SNORD114-21;SNORD114-23;SNORD114-28;SNORD114-30;SNORD114-31;SNORD114-4;SNORD114-5;SNORD114-6;SNORD114-7;SNORD114-8	-1.32
GOT1	-1.31
MUT	-1.3
MYOT	-1.28
ABCA10;ABCA5;ABCA6;ABCA8;ABCA9;PRO1804	-1.19
LINC00987;LOC101930452;LOC642846	-0.89

ADAM23	3.38
CENPM	3.36
LOC101929771	3.36
RMST	3.36
BRDT;EPHX4	3.35
HIST1H3J	3.34
OLFML2B	3.33
CD109	3.32
FOXN4	3.32
MEPE	3.25
ADAM12	3.24
UBE2U	3.23
LINC01301	3.21
E2F2	3.18
PARPBP	3.17
LRP1B	3.16
MSC	3.15
LOC101927592	3.14
HIST1H2BB	3.12
ECT2	3.1
NOX4	3.1
HIST1H3I	3.09
GDNF	3.08
LINGO1	3.08
MIR193A	3.08
PTHLH	3.06
TRPC7	3.06
SPHK1	3.05
SUSD4	3.05
HIST1H2AJ;HIST1H2AK	2.98
HIST1H2AG;HIST1H2AH;MIR3143	2.97
WNT5A	2.96
KPNA2	2.95
LINC01021	2.94
GJC1	2.93
DNAJC6	2.92

BBC3;MIR3191	2.91
RNF144A-AS1	2.9
WFDC21P	2.89
C6orf141	2.88
DUOX2	2.88
LOC101928858	2.87
STIL	2.87
CAPN9	2.86
PPFIA4	2.86
TCF19	2.86
LINC01594	2.84
CELSR3;MIR4793	2.83
DUXAP10;LINC01296	2.81
LOX	2.81
LOC440982;ZIC1	2.79
BCAT1	2.78
LINC01426	2.78
ZNF385D	2.78
SLC44A5	2.77
FCAMR	2.76
HELLS	2.74
HOXC4;HOXC5;HOXC6	2.74
C21orf58	2.69
TMEM232	2.69
BTNL8	2.66
LINC00470	2.62
CENPL	2.58
LOC441666	2.55
ARHGAP11B;LOC100288637	2.53
LOC654342	2.52
LOC101928622	2.51
C5orf45	2.5
FANCI	2.5
DNAH12	2.49
HIST1H2AE;HIST1H2BE;HIST1H2BF;HIST1H2BI	2.47
FAM78B	2.44

GPR35	2.44
ADAMTS14	2.43
CECR7	2.42
LMNB2	2.42
ACSM1	2.41
MGAM	2.4
PLCB1	2.4
ITGB3	2.38
UBD	2.38
DNAH8	2.37
LINC00535	2.33
FABP5	2.31
MAP2	2.31
GOLGA2P7;LOC642423	2.3
FIGNL2	2.28
INCENP	2.27
ADM	2.23
P4HA2	2.23
GAP43	2.22
LMNB1	2.22
TSPEAR;TSPEAR-AS1;TSPEAR-AS2	2.22
AURKB;LINC00324	2.21
BBS7;CCNA2	2.21
MTL5	2.21
TUBA1C	2.2
LOC100507195	2.14
ITGA5	2.12
HN1	2.11
BRIP1	2.1
HIST2H2BC;HIST2H2BE	2.09
MCM3	2.07
MCM6	2.06
SCARA3	2.06
SQLE;ZNF572	2.06
LINC01134	2.03
SMC4	2.02

CSTA	1.99
CDC25B;LOC101929125	1.97
KCNMB2;KCNMB2-AS1	1.97
PKM	1.94
CALCA	1.92
IL4I1;NUP62	1.91
SERPINH1	1.89
SPAG5	1.88
STIP1	1.87
CCT3	1.85
SLC29A4	1.85
FBXL8;HSF4	1.84
ENO1	1.83
MMP14;MRPL52	1.83
BRCA1	1.82
DTNA	1.81
EML6	1.79
GSDMD;ZC3H3	1.79
RRP12	1.78
SOGA1	1.78
LOC100288152;SLC9A3	1.76
ANXA2	1.75
ENAH	1.7
MIR3917;PAQR7;STMN1	1.68
VPS45	1.68
CKAP2	1.67
CKAP4	1.67
DLAT	1.67
GUCY1B2	1.65
LRRC37A8P;RDM1	1.65
H2AFZ	1.64
LINC01515	1.63
ADAMTS6	1.61
LAMC1	1.61
MCM8	1.61
MIR5195	1.61

TDRKH	1.61
NME1;NME1-NME2;NME2	1.59
HK1;HKDC1	1.56
XPOT	1.55
C1orf204;CFAP45;TAGLN2;VSIG8	1.53
LINC01572;PMFBP1	1.5
SCD	1.48
CHD1L	1.47
ACLY	1.46
ONECUT2	1.45
ITGA6	1.42
PSMD4	1.4
SAE1	1.39
TMEM64	1.38
TUBA1A;TUBA1B	1.38
CFL1	1.36
NPLOC4	1.33
LRRCS9	1.28
MIR3610;RAD21	1.28
CHEK1;STT3A	1.19
SSRP1	1.14

Supplementary Table 8. List of up and down-regulated genes in non-viral HCC

nonBnonC unique upregulated in tumor	FC
SLC22A12	12.56
GAGE2A	11.86
RPS17	11.66
HOXB13	9.89

nonBnonC unique downregulated in tumor	FC
MEG8;MIR370;SNHG24;SNORD113-1;SNORD113-2;SNORD113-4;SNORD113-5;SNORD113-6;SNORD113-7;SNORD113-9;SNORD114-1;SNORD114-10;SNORD114-11;SNORD114-14;SNORD114-17;SNORD114-2;SNORD114-20;SNORD114-21;SNORD114-23;SNORD114-24;SNORD114-26;SNORD114-27;SNORD114-28;SNORD114-3;SNORD114-30;SNORD114-31;SNORD114-4;SNORD114-5;SNORD114-6;SNORD114-7	-5.74
AP1B1;RFPL1	-5.12
ESRP1	-4.41
VTCN1	-4.35

GIF	9.72
LINC01242	9.46
GIP	9.09
MAGEB2	9.05
CELA3A	8.97
CSN1S2AP;ODAM	8.59
LINC01139	7.5
SNORD93	7.31
SLC6A2	6.91
FLNC	6.36
TGM3	6.35
CCDC136	6.1
LINC01322	6.06
CDH17	6.02
GRPR;MAGEB17	5.99
GP2	5.76
FER1L6	5.68
LOC101927948;LOC101927967	5.68
ENPP7P13	5.66
HSPB1	5.65
DCC	5.6
LOC101929645;LOC101929660	5.42
LDLRAD1	5.17
RHBG	5.12
VCX	4.95
ISX	4.91
LOC653712	4.8
CCDC124	4.71
L1CAM	4.57
ORAOV1	4.53
DIO2	4.51
MYO1A	4.46
CAMK2A	4.45
SP5	4.42

STK32A	-4.26
ATP13A4	-3.59
PTPRZ1	-3.58
BDKRB1;BDKRB2	-3.48
SLC14A1	-3.46
FLG-AS1	-3.41
FLG;HRNR	-3.34
ERP27	-3.3
GALNT3	-3.11
IPW;PWAR1;PWAR5;PWARSN;SNORD109B;SNORD116-10;SNORD116-16;SNORD116-17;SNORD116-18;SNORD116-21;SNORD116-22;SNORD116-23;SNORD116-26;SNORD116-4;SNORD116-6;SNORD116-7;SNRPN;SNURF	-3.04
FLRT2	-2.89
SULT1C4	-2.85
BMP5	-2.82
LINC00161	-2.79
TMEM156	-2.74
SAA2;SAA2-SAA4;SAA4	-2.73
LUM	-2.7
RGS2	-2.68
LRRC17	-2.66
CASC15	-2.57
SCART1	-2.57
RASSF8	-2.56
LINC00844	-2.55
MBOAT2	-2.55
KCNJ15	-2.53
MAPK10	-2.53
AKR1D1	-2.5
PTPN13	-2.46
RXFP1	-2.41
CLEC12A	-2.37
DDX26B	-2.37
OAT	-2.37
VNN1	-2.37
ANKRD18DP;LMLN-AS1	-2.33

CDH12	4.4
TERC	4.38
LINC01484	4.32
HIST1H2AH;MIR3143	4.29
ACHE	4.27
GCNT3	4.27
NECAB2;OSGIN1	4.23
PTP4A3	4.23
MLST8	4.19
AFAP1-AS1	4.17
MAGEC3	4.13
HIST1H4A	4.1
RHPN1	3.9
LINC01124;LOC101926913	3.84
SHANK2	3.83
SCUBE1	3.74
DFNB31	3.71
HSF1	3.67
TK1	3.63
CHTF18	3.61
AURKB	3.6
WNK4	3.6
CEP131	3.58
G6PD	3.57
CLVS1	3.56
LINC01108	3.56
ADCK5	3.54
FAM83H	3.52
SHARPIN	3.51
TONSL	3.51
ALDH1L1	3.49
GPAA1	3.44
SLC52A2	3.44
HIST1H2AM	3.43
KIFC2	3.43
GLUL;LINC00272;RGS1	3.41

BICC1	-2.32
MIR1273E	-2.31
LRAT;RBM46	-2.26
NNMT	-2.25
DACH1	-2.24
SPACA7	-2.23
ETNPPL	-2.2
CXCL8	-2.14
LECT2	-2.14
SLC25A36	-2.14
ANK3	-2.12
HTR2A;HTR2A-AS1	-2.12
ARHGAP15	-2.11
SLC8A1	-2.1
CP	-2.08
PRICKLE1	-2.07
SRGN	-2.05
F9	-2.04
MIR99AHG	-2.03
CD226	-2.02
DYNC2H1	-2.02
ASS1	-2.01
CCDC3	-2.01
ENDOD1	-1.98
LAMA2	-1.98
TC2N	-1.97
SPIRE1	-1.95
GBA3	-1.94
SLPI	-1.92
C6	-1.91
SLFN12	-1.91
ZFP1	-1.91
LOC101928304	-1.9
NR4A3	-1.88
FAM66C;FAM90A1	-1.87
IGFBP7	-1.87

AXIN2	3.39
ABHD1	3.37
PARP10	3.34
MDGA1	3.33
RPS16	3.32
SLC22A18	3.32
TP73	3.3
SLC6A9	3.26
COL1A1	3.24
CLSPN	3.23
LOC100506403;LOC101928269	3.22
RPLP1	3.22
LOC148709	3.21
MIR3917;STMN1	3.21
BCL2L12	3.17
MRPL4	3.17
CHRM3	3.14
ASPSR1	3.13
JOSD2	3.12
P2RY11;PPAN;PPAN-P2RY11	3.09
CELSR3;MIR4793;NCKIPSD	3.07
PKD1L2	3.04
KIAA1875	3.03
MOSPD3	3.02
PAK4	3
C19orf47	2.99
HGH1	2.98
ACSL6;MEIKIN	2.97
LINC01226	2.93
HIST1H2BF	2.92
SLCO5A1	2.92
LINC01604	2.91
TMEM201	2.9
MIR325HG	2.89
LOC101927136	2.87
CLCN7	2.85

SPATA6	-1.87
DLG2	-1.82
GSTZ1	-1.8
CREB5	-1.77
SAMSN1	-1.77
EPGN;MTHFD2L	-1.76
TRIM22	-1.76
CDC42EP3	-1.75
SYTL2	-1.74
TF	-1.74
ANXA1	-1.73
WDR72	-1.73
BMS1P21;MBL1P	-1.72
PKD4	-1.71
SCML4	-1.68
CYP4V2;KLKB1	-1.67
FSTL1;MIR198	-1.65
LRRK2	-1.65
UBXN8	-1.64
LST1	-1.63
PTPRC	-1.6
CRMP1;EVC	-1.59
ZNF211	-1.59
CPED1	-1.58
GYS2	-1.58
FGD4	-1.56
MBL2	-1.53
APOH;CEP112	-1.52
C5;TRAF1	-1.51
F2R	-1.51
GNB4	-1.51
APOL6	-1.46
FGG	-1.43
ADGRG6	-1.42
TCF4	-1.4
MAN1A1	-1.34

LINC00639	2.85
NCAPH	2.84
VPS28	2.83
CLK2;SCAMP3	2.81
MIB2	2.81
FGFR4	2.8
FOXP4	2.78
IKBKKG	2.75
ABCB8;ASIC3	2.74
SPPL2B	2.74
MROH6;NAPRT	2.73
NDOR1	2.73
ZNF517	2.73
GBA	2.72
RAD23A	2.72
IGSF8	2.7
GRN	2.69
PIF1	2.69
SMARCA4	2.69
ARF1	2.68
NUPR1	2.68
C14orf80	2.67
TCOF1	2.67
SNTG1	2.64
CHCHD10	2.63
ATAD3A;ATAD3B	2.62
EPHX1	2.62
RPL8;ZNF34;ZNF517	2.61
PIK3R2	2.6
GAS2L1	2.58
PKN1	2.57
PMVK	2.57
CCDC9	2.56

PHLDB2;PLCXD2	-1.33
GLUD1	-1.28
PSD3	-1.28
B2M	-1.27
PRDX4	-1.27
CD164	-1.25
ANKAR	-1.24
RPS15A	-1.18
RWDD3;TMEM56;TMEM56-RWDD3	-1.16
TSHR	-1.11
PCDHGA1;PCDHGA10;PCDHGA11;PCDHGA12;PCDHGA2;PCDHGA3;PCDHGA4;PCDHGA5;PCDHGA6;PCDHGA7;PCDHGA8;PCDHGA9;PCDHGB1;PCDHGB2;PCDHGB3;PCDHGB4;PCDHGB5;PCDHGB6;PCDHGB7;PCDHGC3;PCDHGC4;PCDHGC5	-0.95

LRRC14	2.56
CIZ1	2.53
MYH14	2.53
COPE	2.51
CTSD;IFITM10	2.5
TTL12	2.5
AP1M1	2.49
CLPTM1	2.49
CYHR1	2.49
LMNA	2.49
NRBP2;PUF60	2.47
BREA2;ZNF707	2.45
DBP	2.45
EPPK1;PLEC	2.45
LAMTOR2	2.45
TMEM74B	2.42
TM7SF2;VPS51	2.41
DLG5	2.4
EMD	2.4
PRKCSH	2.4
CLIP3;THAP8	2.39
MIR639;TECR	2.39
GUK1	2.38
IFRD2	2.38
NCLN	2.38
NDUFS6	2.38
ATP6V0D1	2.36
JRK	2.36
EPN1	2.35
FBXO31	2.34
RSPO2	2.34
HSPA1A;HSPA1B	2.33
MTMR11;SF3B4	2.33
VAR5	2.33
CTSA	2.31
SYNGR2	2.31

DCST2;LOC100505666	2.3
MAFG;SIRT7	2.29
MIR3672	2.29
NFKB2	2.29
TRIM55	2.29
ZC3H3	2.29
FAM3A	2.26
GDI1	2.25
RARA	2.25
C7orf50;COX19	2.24
FLNA	2.24
ATP13A2	2.23
DDX12P	2.23
FANCA	2.23
MAF1	2.21
SLC25A39	2.21
ZNF730	2.21
NDUFS8	2.2
MRPL38	2.19
MYO15B	2.19
RNPEPL1	2.17
ANAPC11	2.16
ASNA1	2.15
DNPH1	2.15
PLXNA1	2.15
NOTCH1	2.14
SLC4A2	2.14
TAF6	2.14
NDUFB7	2.13
PFDN6	2.13
WBP2	2.13
NIPAL2	2.12
PLXNB2	2.12
PQBP1	2.12
GPR137	2.11
CD74	2.1

GNB2	2.1
LSS	2.1
BCAR1	2.09
D2HGDH	2.09
TRAPPC9	2.09
ABHD4	2.08
SH3BP5L	2.08
TOR2A	2.08
EIF3K	2.07
ZSCAN31	2.07
ACTB	2.06
TRPM3	2.06
CDC42EP4	2.05
NCOA2	2.05
TMEM259	2.04
MYH9	2.03
RNH1	2.03
TSKU	2.03
MED15	2.01
ADHFE1;C8orf46;RRS1	1.99
ATP1A1	1.99
BAG3	1.98
GAA	1.98
FKBP5;LOC285847	1.97
RPP21;TRIM39;TRIM39-RPP21	1.96
ABCF1	1.95
IQCE	1.95
ACTN4	1.94
KDM4B	1.94
DRAP1	1.93
NINJ1	1.92
AGO2	1.91
SGK223	1.91
APOE	1.9
FDPS	1.9
MRPL28	1.9

NDUFA3	1.9
NPRL3	1.9
TMEM8A	1.9
COL18A1	1.89
H1FO	1.89
INPPL1	1.89
ETFB;VSIG10L	1.88
ICK	1.88
LOC100133315;ZNF705E	1.88
FAM20C	1.85
LMAN2	1.85
TWF2	1.85
ZBTB18	1.85
HIST1H2BJ;HIST1H2BK	1.84
ZNF513	1.84
MSH5;MSH5-SAPCD1;SAPCD1	1.83
AP3D1	1.82
09-Sep	1.81
NCL	1.81
NELFB	1.8
LGALS3BP	1.79
GSTT1	1.78
CTTN	1.77
DDX49	1.77
HNRNPA1;HNRNPA1P10	1.77
SEC13	1.76
ANKMY1	1.75
DPAGT1;H2AFX	1.75
HSP90AB1	1.75
MAPKAPK2	1.75
MIR4669;RXRA	1.75
UBA1	1.75
TRAP1	1.74
GTF2F1;PSPN	1.73
MSC-AS1	1.73
PTBP1	1.72

TALDO1	1.72
U2AF2	1.71
RPL18A	1.7
ATP6V1C1	1.69
FTL	1.68
RUVBL2	1.68
EEF1D	1.65
GPX4	1.65
LINC00189	1.65
FAAP20	1.64
DCAF7	1.63
MDH2	1.63
GPI;PDCD2L	1.62
BHLHE40	1.59
EIF4G1	1.59
TMED9	1.58
KRTCAP2	1.57
TTC13	1.57
RPS21	1.56
CYC1	1.55
CDC37;MIR1181	1.54
EIF3H	1.54
EEF2	1.51
HSPA5	1.51
CALM3	1.5
PARP1	1.5
TOMM20	1.5
ECH1	1.47
RPS2	1.46
EWSR1	1.44
HSP90AA1	1.44
DAP	1.43
ACTG1	1.42
ARIH1;MIR630	1.41
CDK11A;CDK11B	1.39
FTH1	1.39

BST2	1.37
P4HB	1.35
GAPDH	1.34
PTK2	1.34
SMC1A	1.33
PIIB	1.32
SEPHS2	1.25
NFE2L1	1.24
CASC19;CCAT1;PCAT2	1.2

Supplementary Table 9. List of regulatory genes in HCV related group

ABAT	CENPF	ERRF11	ITGA6	PRKDC
ACAA2	CENPL	EZH2	ITGA9	PSMD4
ACLY	CENPM	FASN	ITGB3	PYCR1
ACSL1	CFL1	FGFR2	KIF23	RACGAP1
ACSM1	CFTR	FOS	KIF2C	RECQL4
ACSM3	CHEK1	FOXO1	LAMA3	SERPINH1
ACSM6	COL14A1	FXR1	LAMC1	SHBG
ACTN2	COL19A1	FXR3	LMNB1	SKA1
ADRA1B	COL4A3	GABARAPL1	LMNB2	SLC27A2
AGXT	COL7A1	GAD1	MCM2	SLC38A2
AKR1B10	COLEC10	GLYAT	MCM3	SLC5A1
ALDH3A1	CXCL12	GLYATL1	MCM4	SMC4
ALDOA	CYP17A1	GNAO1	MCM6	SQSTM1
ALX1	CYP19A1	GOT1	MCM8	SSRP1
AURKA	CYP1A2	GREB1	MKI67	STIP1

AURKB	CYP2B6	GRIN2B	MOGAT2	TAT
BCHE	CYP2C18	GSTA1	NAT1	TFAP2A
BIRC5	CYP2C9	HGF	NEK2	THBS1
BRCA1	CYP2E1	HGS	NME1	TKT
BRIP1	CYP3A4	HMGA1	NQO1	TOP2A
BUB1B	CYP3A43	HSD17B2	OGDHL	TPX2
CACNA1E	DCN	IGF1	P4HA2	TRPC3
CCNB1	DGAT2	IGF2	PCK1	TRPV6
CCT3	DLAT	IGF2BP1	PDGFRA	TTR
CDC25B	DNAJC6	IGF2BP3	PKM	TUBA1A
CDC25C	DYNC1I1	IGFBP3	PLA2G5	TUBA1C
CDC45	EGF	IL4I1	PLG	TUBB
CDK1	EGR1	INCENP	PPFIA4	UBE2C
CENPE	ENO1	ITGA5	PRC1	ZWINT

Supplementary Table 10. List of regulatory genes in non-viral group

A2M	DLG2	HSPA5	RUVEL2
ACTB	DYNC1I1	IGF2BP1	SEC13
ACTG1	EEF1D	IGSF8	SLC6A2
ACTN2	EEF2	IKBKG	SLC8A1
AGO2	EGR1	INPPL1	SMARCA4
AKR1B10	EIF3H	LAMA3	SNRPB
ALDH3A1	EIF3K	LMNA	SQSTM1
ALDOA	EMD	MAFG	TALDO1
AP1B1	EPN1	MCM2	TCF4
AP1M1	EWSR1	MCM4	TK1
ARF1	EZH2	MYH9	TP73
ATP1A1	F2R	NCL	TRAP1
ATP6V0D1	FANCA	NFE2L1	TUBB
AURKB	FASN	NFKB2	TWF2
BAG3	FLNC	NQO1	U2AF2
BCAR1	FOXO1	OAT	UBA1
BSG	FTH1	PARP1	
C5	GAPDH	PIK3R2	

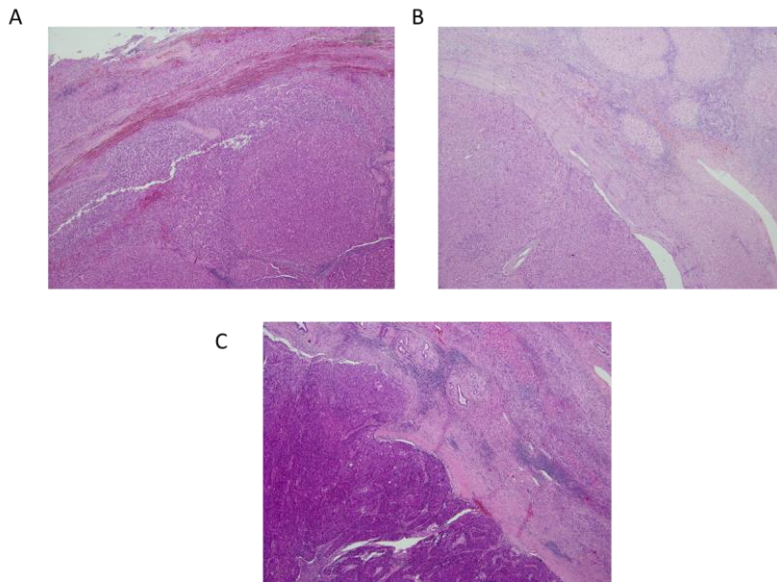
CAMK2A	GLUD1	PRKDC	
CDC37	GNB2	PTBP1	
CDK11A	GNB4	PTK2	
COL1A1	GSTT1	RARA	
COL5A3	HGF	RECQL4	
COPE	HGS	RPL18A	
CP	HMGA1	RPL8	
CTTN	HNRNPA1	RPLP1	
CXCL8	HSF1	RPS16	
CYP17A1	HSP90AA1	RPS17	
CYP2E1	HSP90AB1	RPS2	
DCAF7	HSPA1A	RPS21	

Supplementary Table 11. Clustering of immune gene data by ClueGO

ClueGOResults

Clusters	GOID	Term	Term Pvalue, Bonferroni step down
Cluster1	GO:0002280	monocyte activation involved in immune response	0.17470
Cluster1	GO:0002780	antibacterial peptide biosynthetic process	0.24500
Cluster1	GO:0010729	positive regulation of hydrogen peroxide biosynthetic process	0.38884
Cluster1	GO:0015204	urea transmembrane transporter activity	0.42971
Cluster1	GO:0015250	water channel activity	0.19817
Cluster1	GO:0015254	glycerol channel activity	0.41472
Cluster1	GO:0015911	long-chain fatty acid import across plasma membrane	0.42740
Cluster1	GO:0021930	cerebellar granule cell precursor proliferation	0.19817
Cluster1	GO:0042167	heme catabolic process	0.41027
Cluster1	GO:0042361	menaquinone catabolic process	0.30407
Cluster1	GO:0042376	phyloquinone catabolic process	0.30407
Cluster1	GO:0042822	pyridoxal phosphate metabolic process	0.30407
Cluster1	GO:0046951	ketone body biosynthetic process	0.38884
Cluster1	GO:0050051	leukotriene-B4 20-monoxygenase activity	0.35198
Cluster1	GO:0055062	phosphate ion homeostasis	0.10893
Cluster1	GO:0070295	renal water absorption	0.38884
Cluster1	GO:0090650	cellular response to oxygen-glucose deprivation	0.35198
Cluster1	GO:1904929	coreceptor activity involved in Wnt signaling pathway, planar cell polarity pathway	0.41472
Cluster1	GO:0021533	cell differentiation in hindbrain	0.13625
Cluster1	GO:0045649	regulation of macrophage differentiation	0.13625
Cluster1	GO:1901030	positive regulation of mitochondrial outer membrane permeabilization involved in apoptotic signaling pathway	0.04912
Cluster2	GO:0046631	alpha-beta T cell activation	0.00000
Cluster2	GO:0002503	peptide antigen assembly with MHC class II protein complex	0.07648
Cluster2	GO:0002507	tolerance induction	0.00163
Cluster2	GO:0002578	negative regulation of antigen processing and presentation	0.03229
Cluster2	GO:0002643	regulation of tolerance induction	0.00749
Cluster2	GO:0002666	positive regulation of T cell tolerance induction	0.03229
Cluster2	GO:0021879	forebrain neuron differentiation	0.05618
Cluster2	GO:0021902	commitment of neuronal cell to specific neuron type in forebrain	0.01579
Cluster2	GO:0031295	T cell costimulation	0.00023
Cluster2	GO:0032660	regulation of interleukin-17 production	0.04084
Cluster2	GO:0032663	regulation of interleukin-2 production	0.00141
Cluster2	GO:0032722	positive regulation of chemokine production	0.00257
Cluster2	GO:0032743	positive regulation of interleukin-2 production	0.03240
Cluster2	GO:0032753	positive regulation of interleukin-4 production	0.01783
Cluster2	GO:0033634	positive regulation of cell-cell adhesion mediated by integrin	0.01579
Cluster2	GO:0045058	T cell selection	0.00002
Cluster2	GO:0045061	thymic T cell selection	0.00031
Cluster2	GO:0045589	regulation of regulatory T cell differentiation	0.00189
Cluster2	GO:0045954	positive regulation of natural killer cell mediated cytotoxicity	0.15046
Cluster2	GO:0046633	alpha-beta T cell proliferation	0.05525
Cluster2	GO:0046635	positive regulation of alpha-beta T cell activation	0.00204
Cluster2	GO:0046641	positive regulation of alpha-beta T cell proliferation	0.01241
Cluster2	GO:0050854	regulation of antigen receptor-mediated signaling pathway	0.01643
Cluster2	GO:0051712	positive regulation of killing of cells of another organism	0.02683
Cluster2	GO:0070229	negative regulation of lymphocyte apoptotic process	0.03936
Cluster2	GO:0070232	regulation of T cell apoptotic process	0.04523
Cluster2	GO:0071639	positive regulation of monocyte chemotactic protein-1 production	0.05690
Cluster2	GO:2000318	positive regulation of T-helper 17 type immune response	0.07111
Cluster2	GO:2000514	regulation of CD4-positive, alpha-beta T cell activation	0.00301
Cluster2	GO:2000516	positive regulation of CD4-positive, alpha-beta T cell activation	0.04523
Cluster2	GO:0002228	natural killer cell mediated immunity	0.00000
Cluster2	GO:0002715	regulation of natural killer cell mediated immunity	0.00034
Cluster3	GO:0072178	nephric duct morphogenesis	0.05562
Cluster3	GO:0001631	cysteinyl leukotriene receptor activity	0.17470
Cluster3	GO:0002003	angiotensin maturation	0.41027
Cluster3	GO:0004875	complement receptor activity	0.38260
Cluster3	GO:0004914	interleukin-5 receptor activity	0.17470
Cluster3	GO:0030862	positive regulation of polarized epithelial cell differentiation	0.10401
Cluster3	GO:0039008	pronephric nephron tubule morphogenesis	0.10401
Cluster3	GO:0045725	positive regulation of glycogen biosynthetic process	0.26740
Cluster3	GO:0045959	negative regulation of complement activation, classical pathway	0.43391
Cluster3	GO:0048633	positive regulation of skeletal muscle tissue growth	0.38884
Cluster3	GO:0060720	spermatogonial cell proliferation	0.17470
Cluster3	GO:0070986	left/right axis specification	0.33646
Cluster3	GO:0071377	cellular response to glucagon stimulus	0.38260
Cluster3	GO:0090191	negative regulation of branching involved in ureteric bud morphogenesis	0.17470
Cluster3	GO:0090721	primary adaptive immune response involving T cells and B cells	0.10401
Cluster3	GO:1900025	negative regulation of substrate adhesion-dependent cell spreading	0.36998
Cluster3	GO:1905665	positive regulation of calcium ion import across plasma membrane	0.38260
Cluster3	GO:2000467	positive regulation of glycogen (starch) synthase activity	0.35198

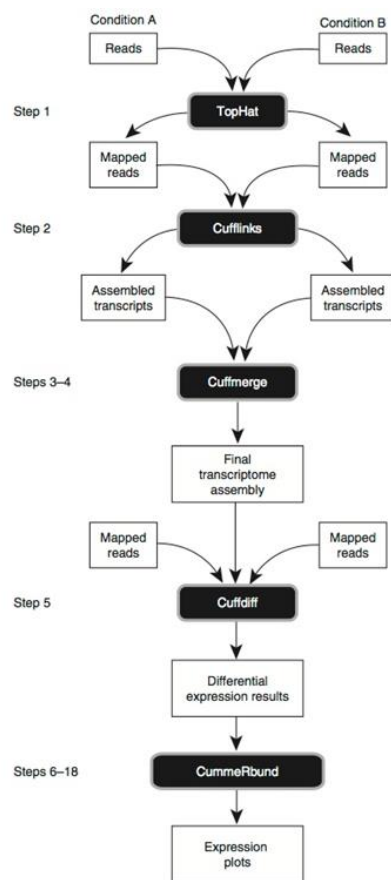
Supplementary Figure 1. Histology (hematoxylin-eosin staining) for the HCC patients (non-viral, HBV and HCV etiology)



A-Non-viral HCC; B- HBV HCC; C- HCV HCC (40X magnification)

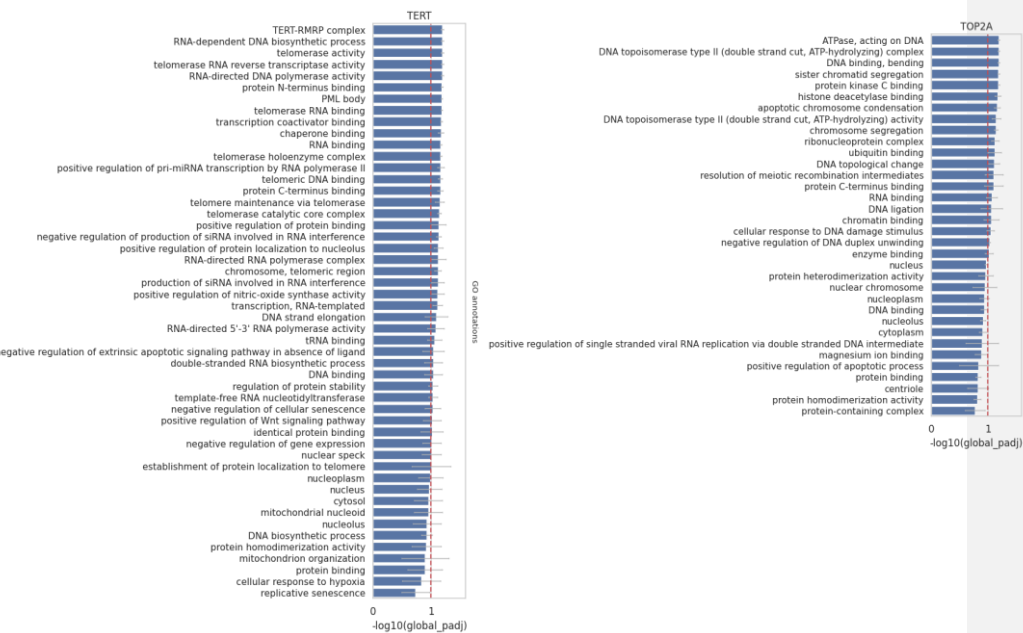
All patients enrolled in this study were diagnosed with HCC. Liver tumor samples were collected at the time of surgery. Histopathological parameters and tumor staging at diagnosis were determined (AJCC 7th ed.) and combined with surgical records and perioperative imaging. Tumor grading was performed according to the Edmondson–Steiner classification.

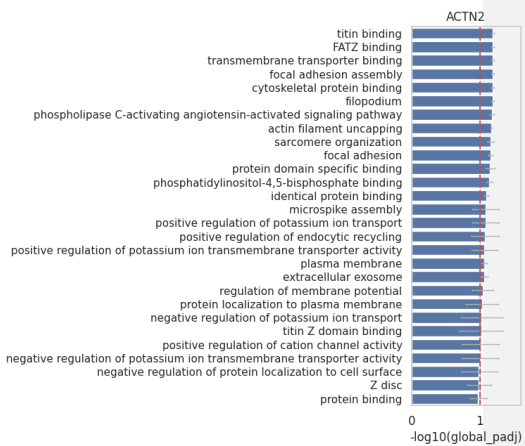
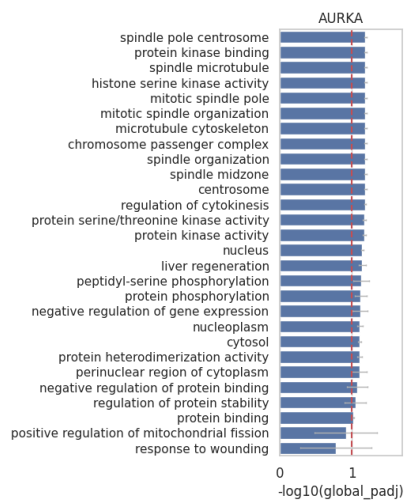
Supplementary Figure 2. Tuxedo pipeline

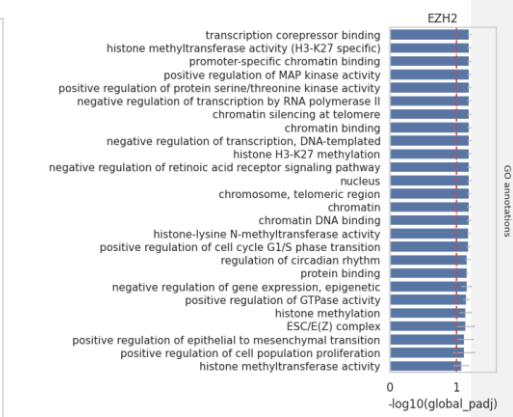
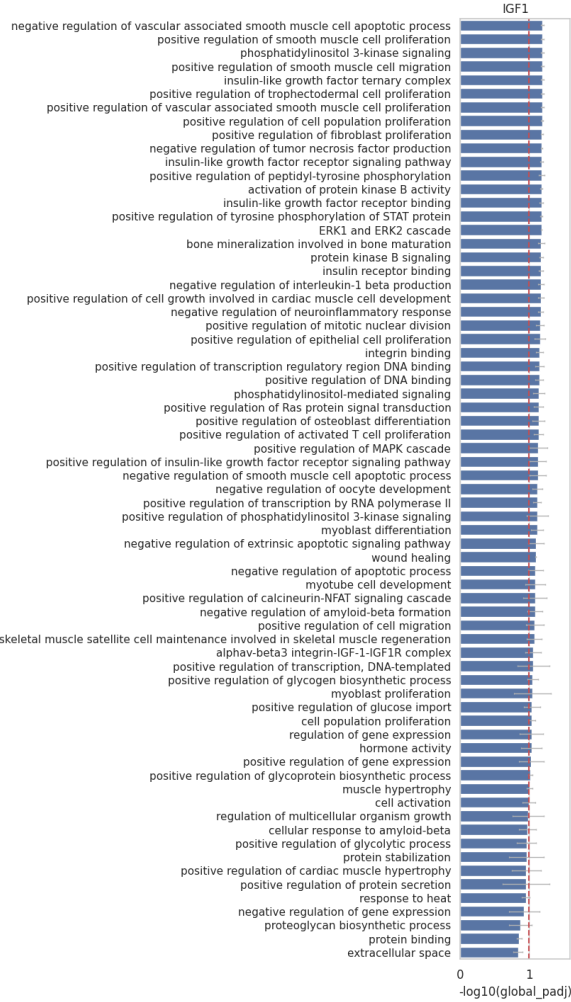


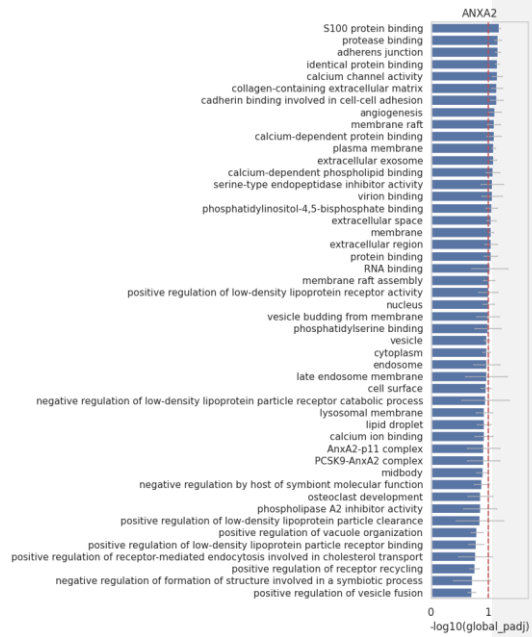
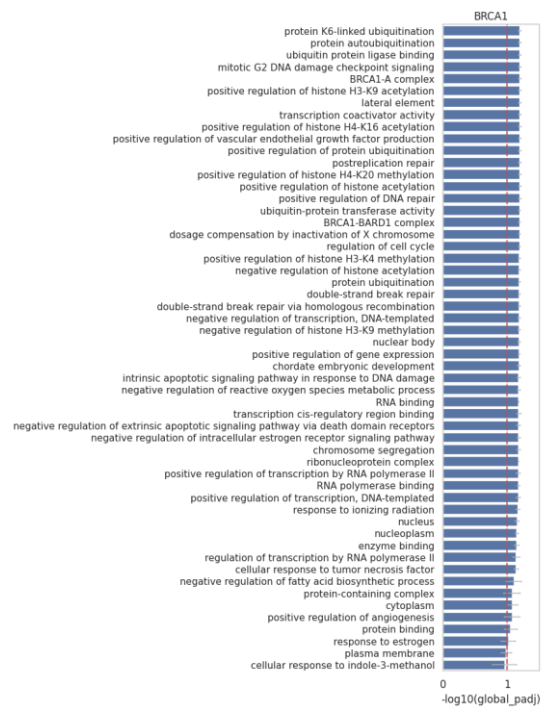
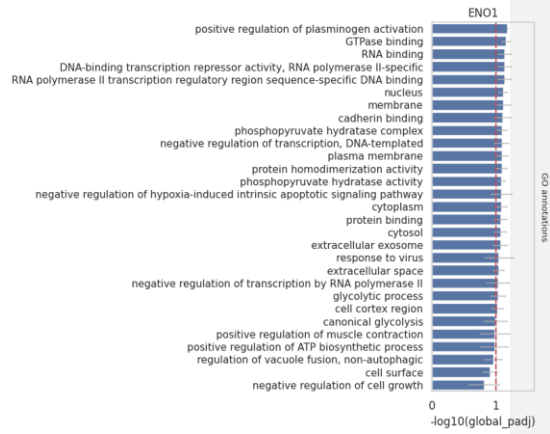
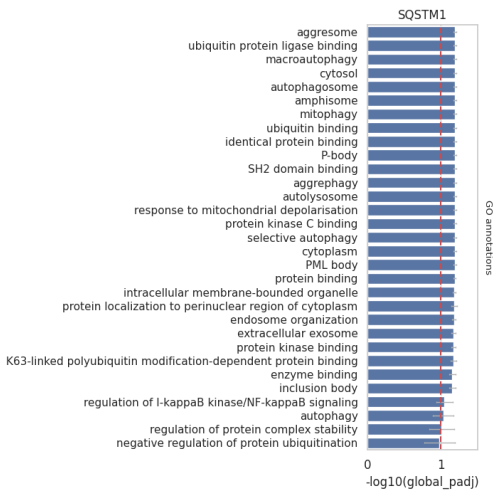
Supplementary Figure 3. HCV HUB and moonlighting genes enrichment

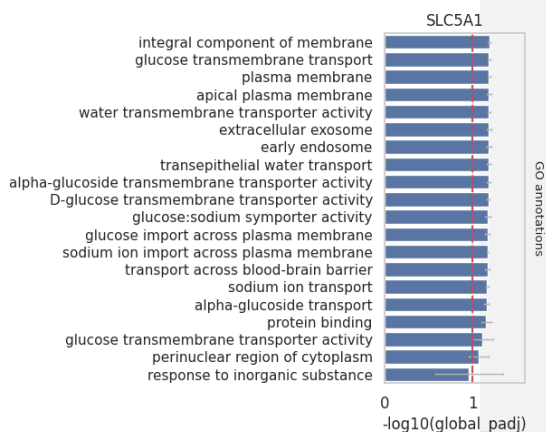
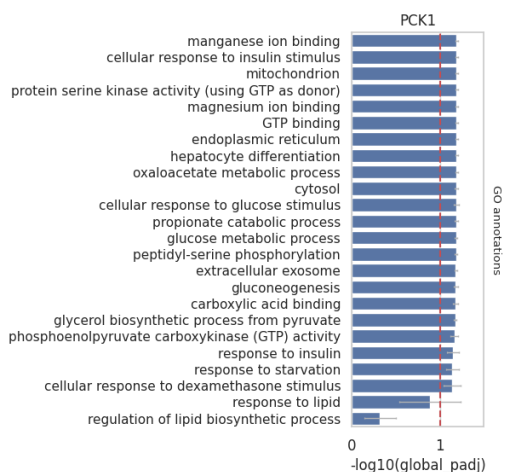
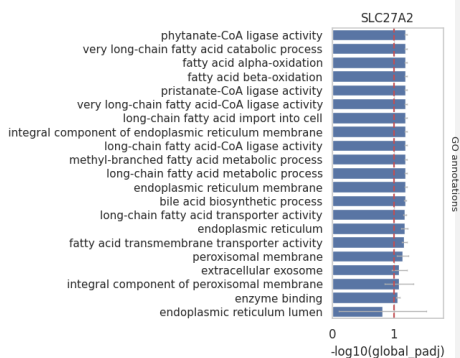
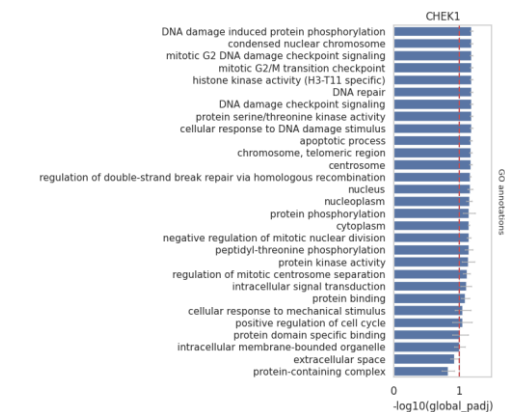
HCV HUB genes

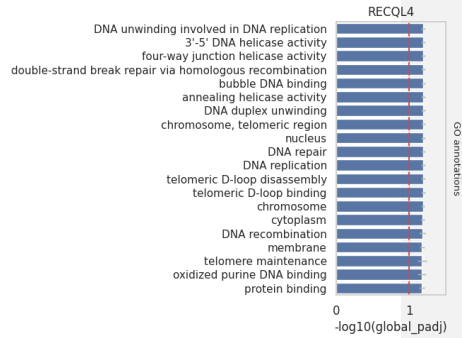
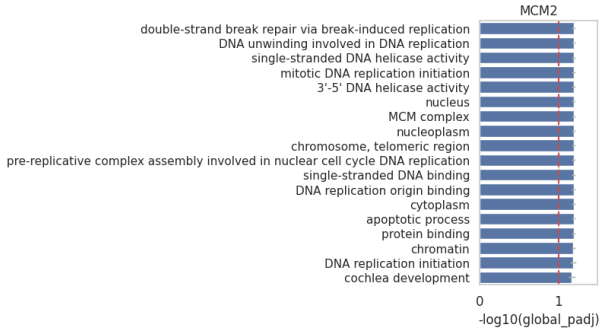
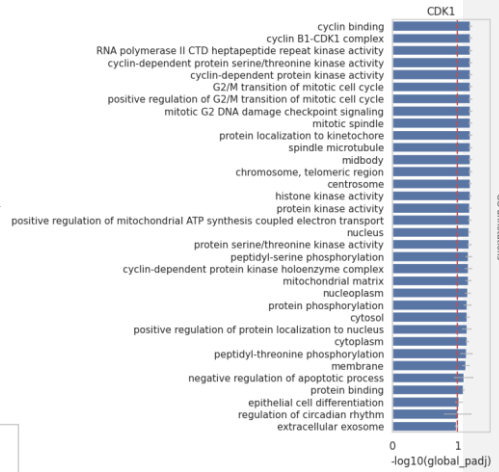
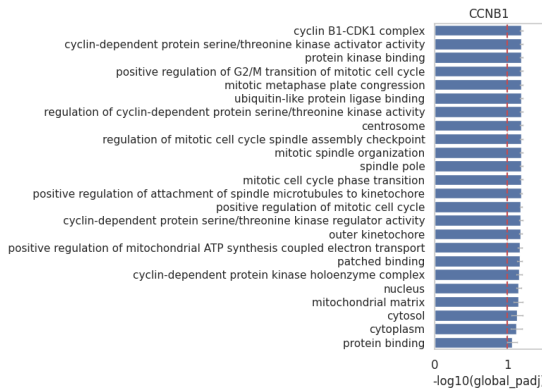
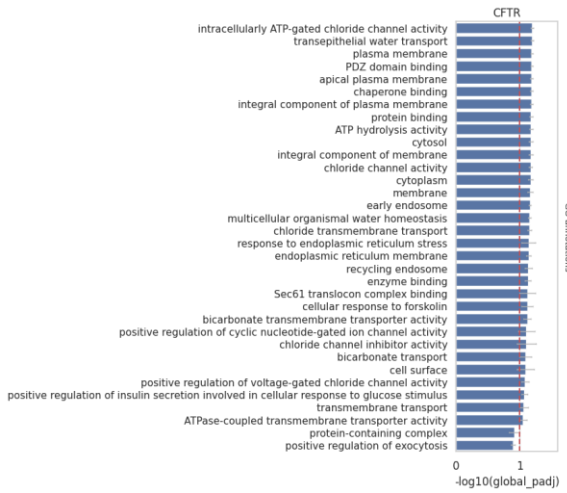


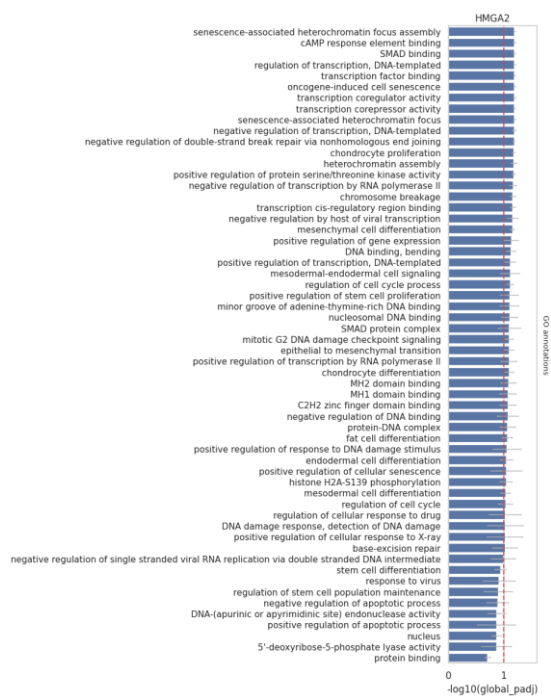


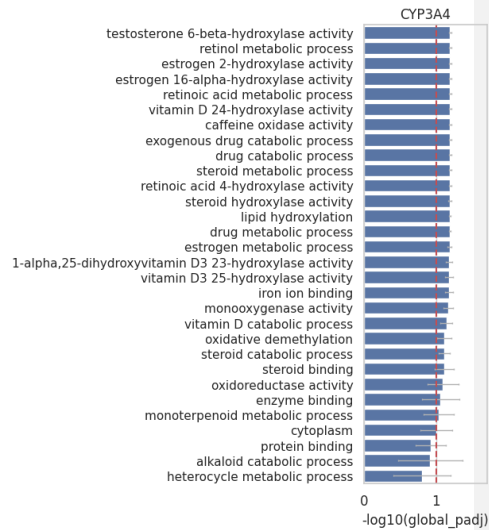
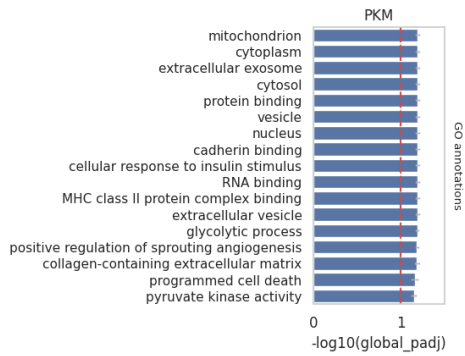




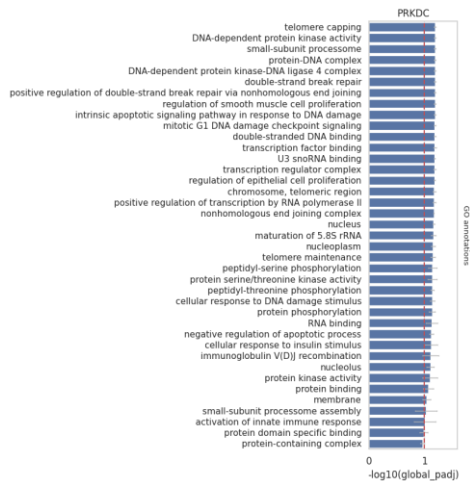
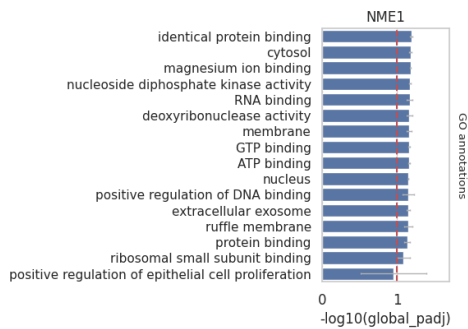
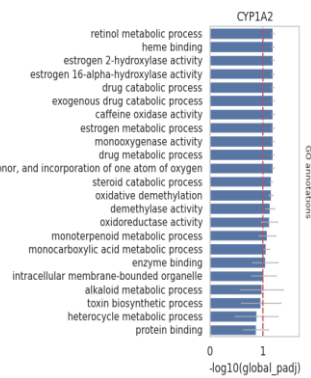




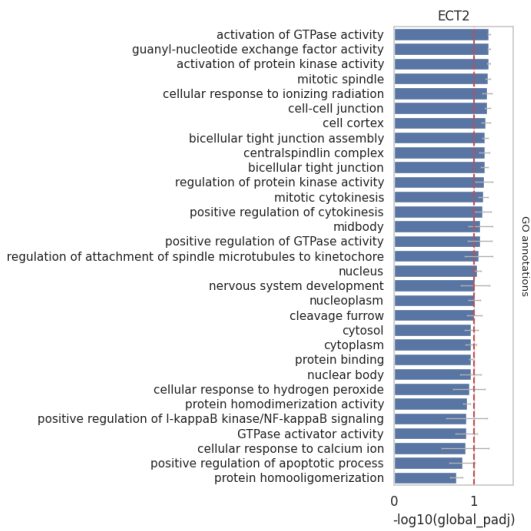




oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen, reduced flavin or flavoprotein as one donor, and incorporation of one atom of oxygen

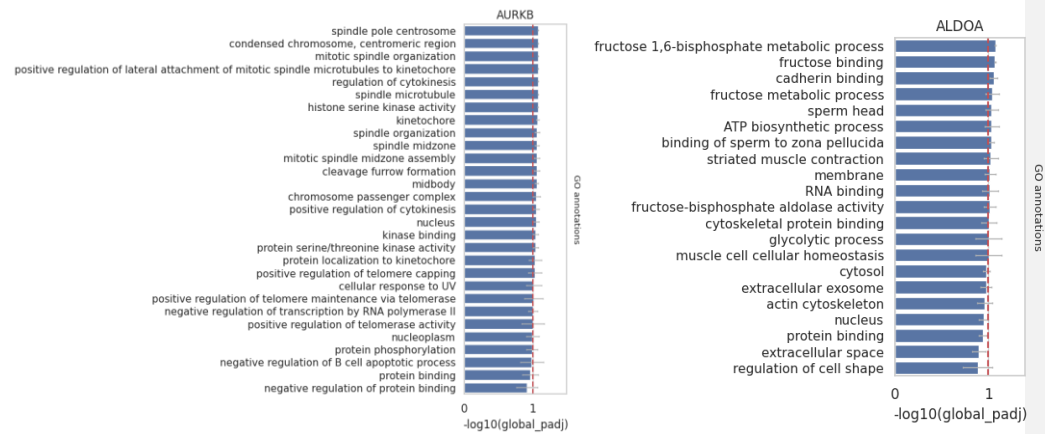


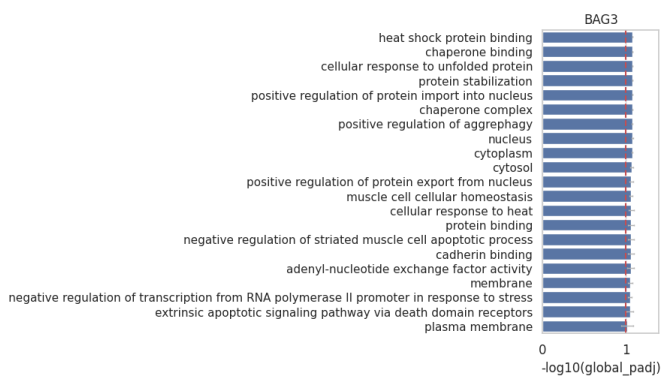
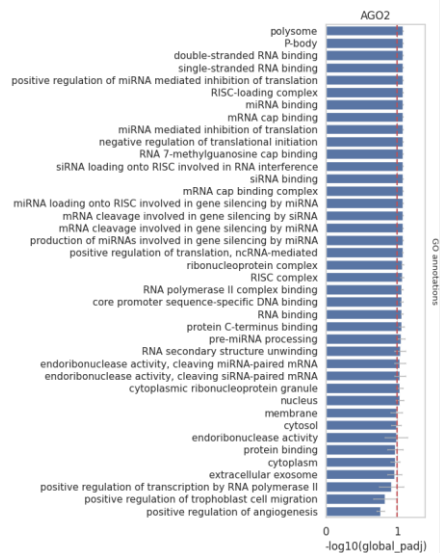
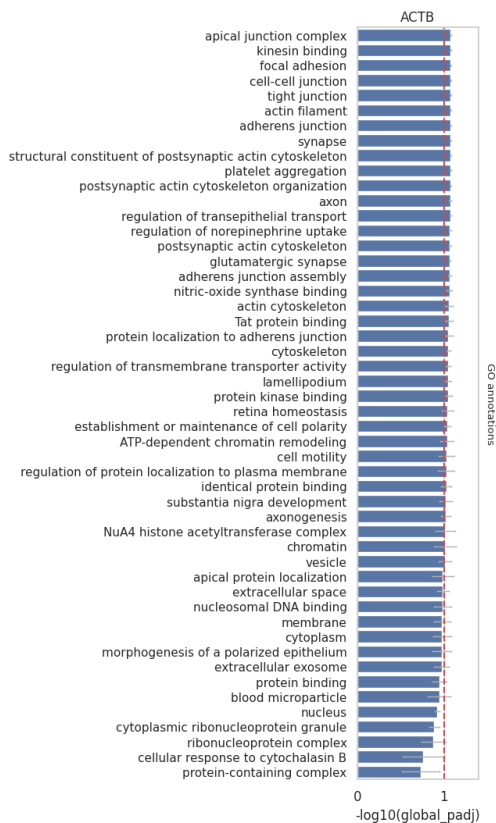
HCV Moonlightning gene

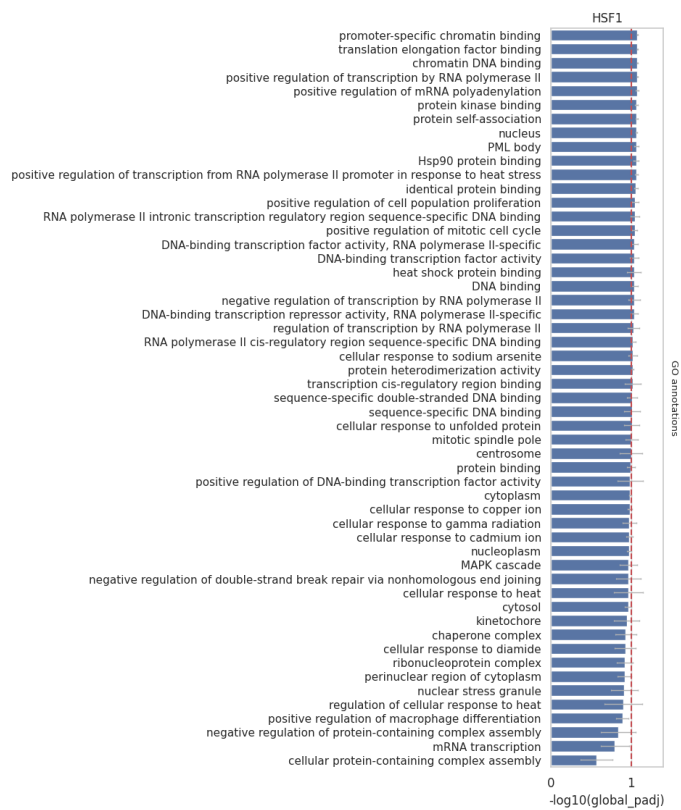


Supplementary Figure 4. nonBnonC HUB and moonlighting genes enrichment

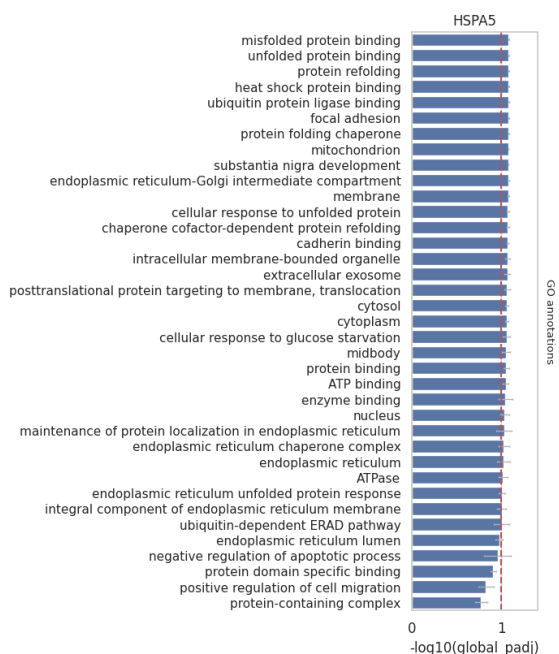
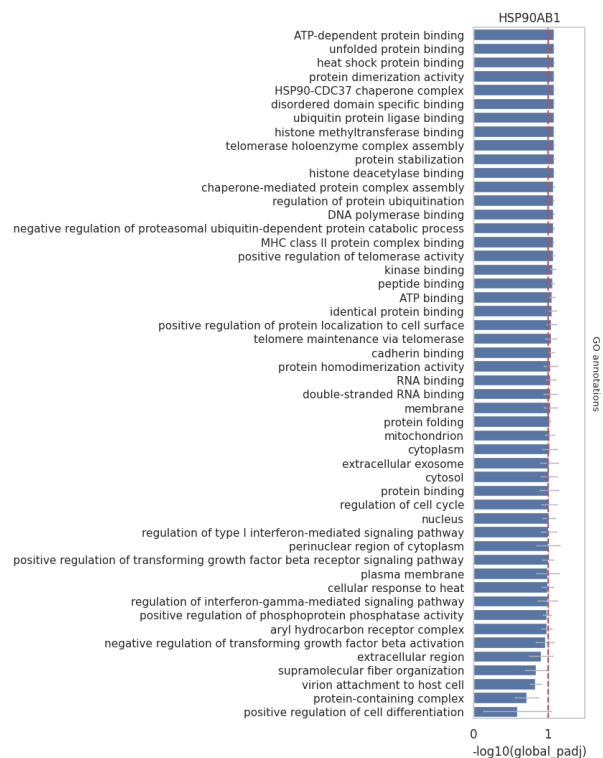
nonBnonC HUB genes

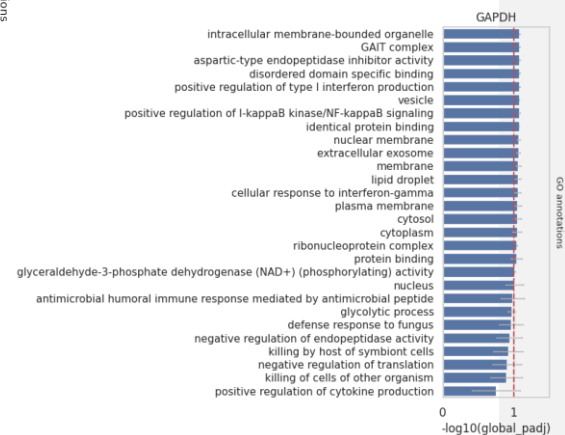
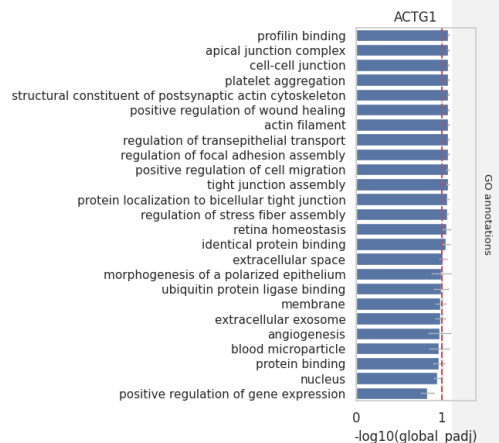
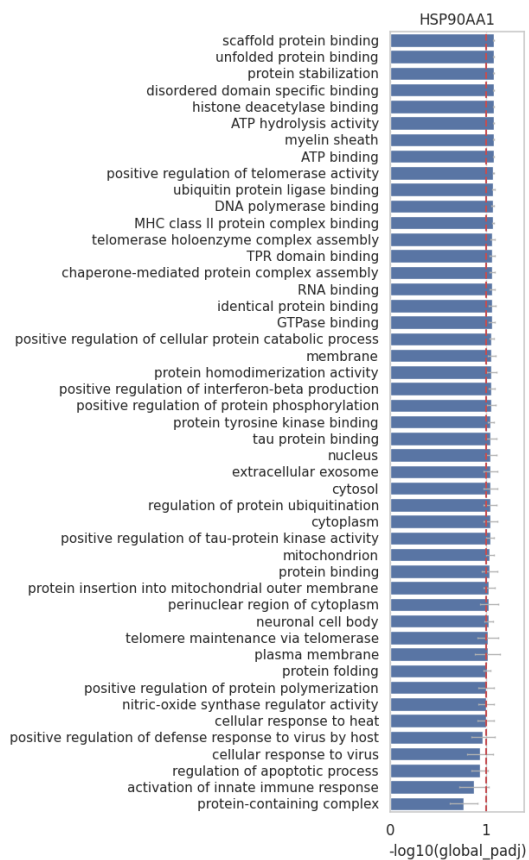


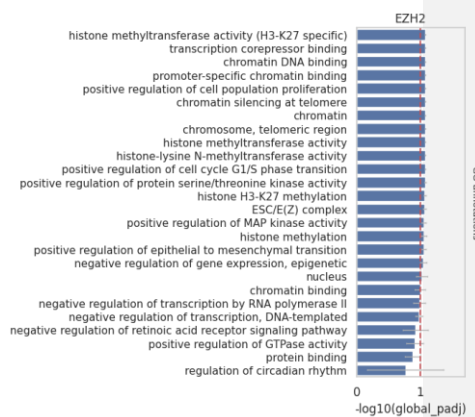
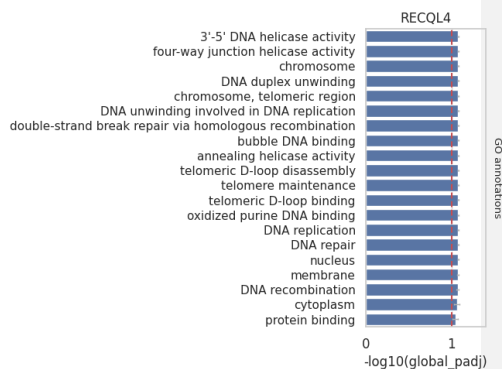
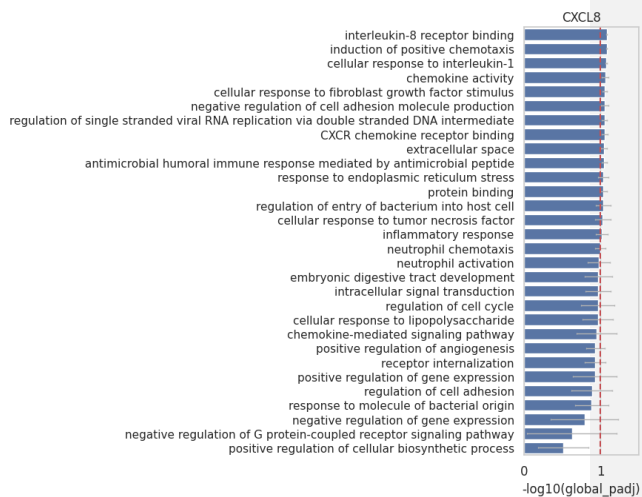
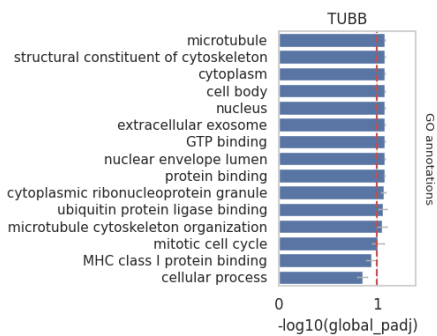


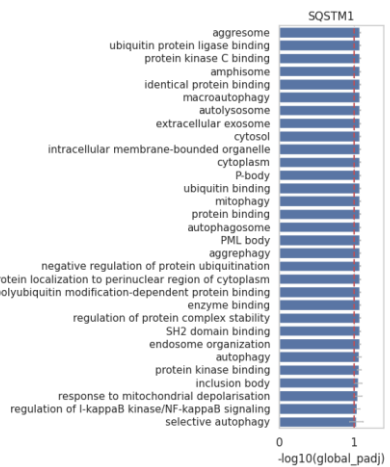
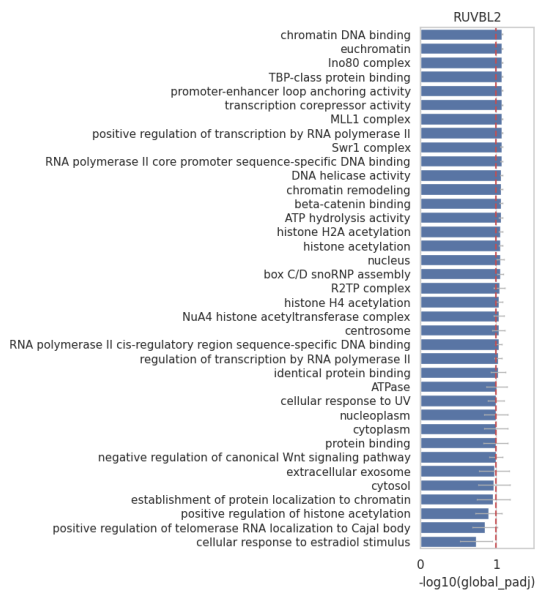
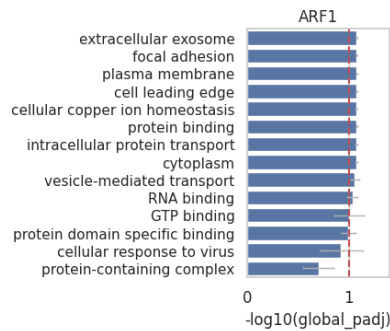
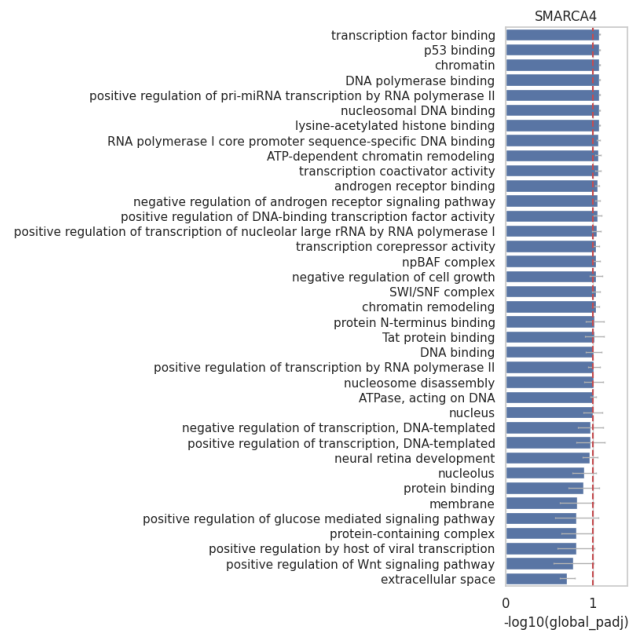


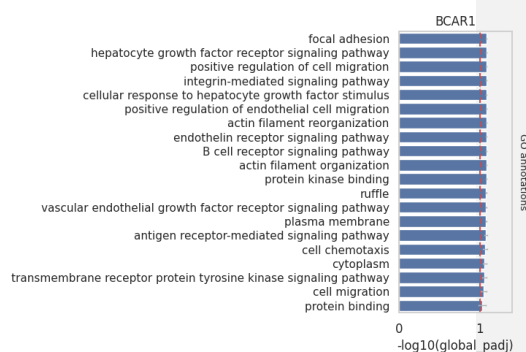
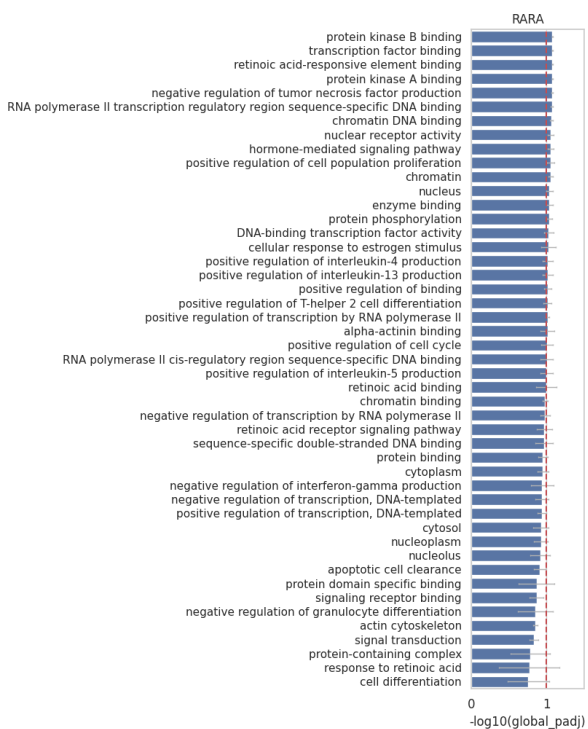


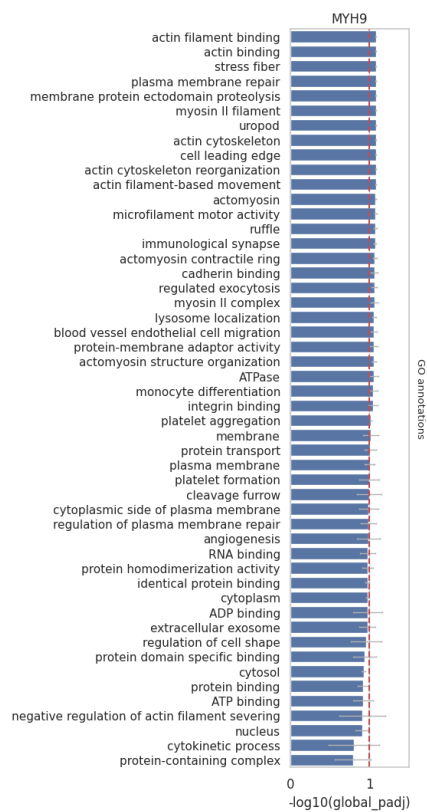
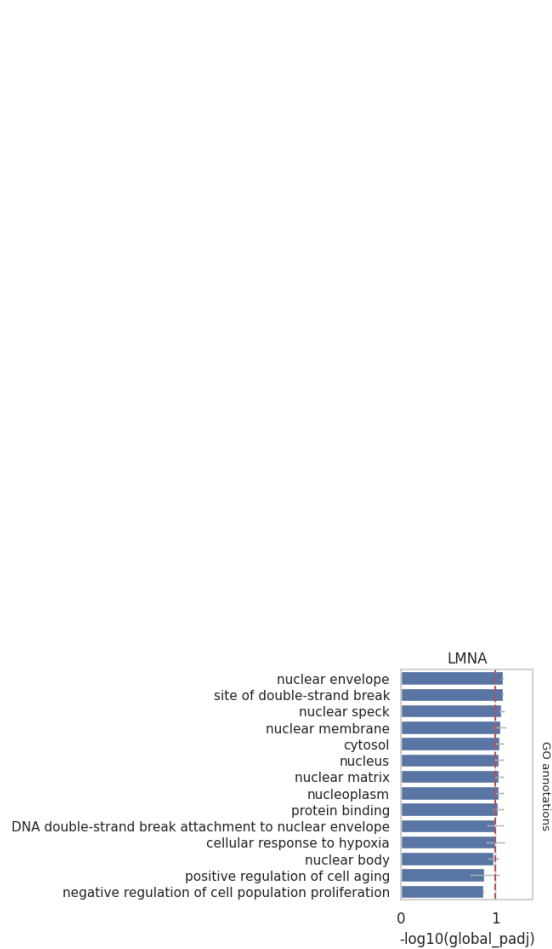


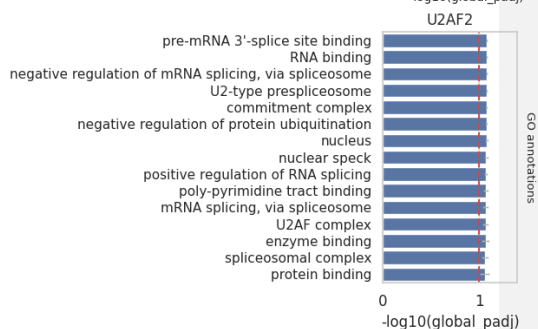
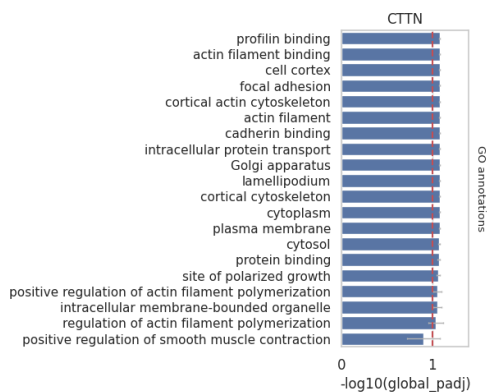
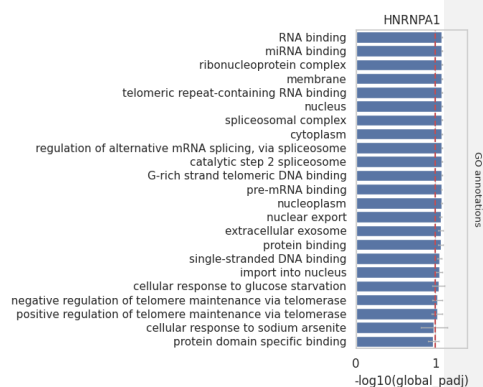
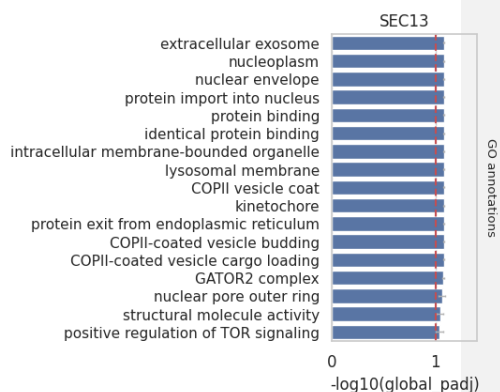
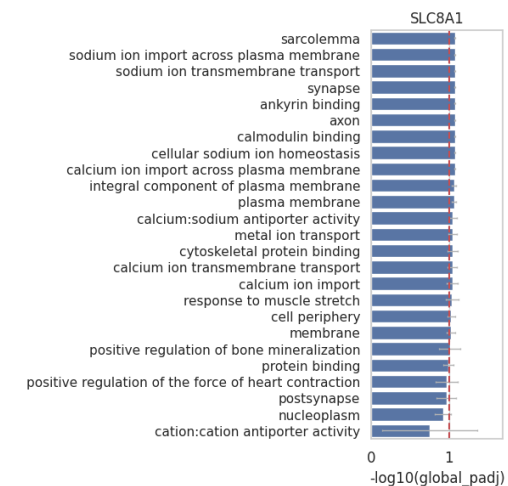


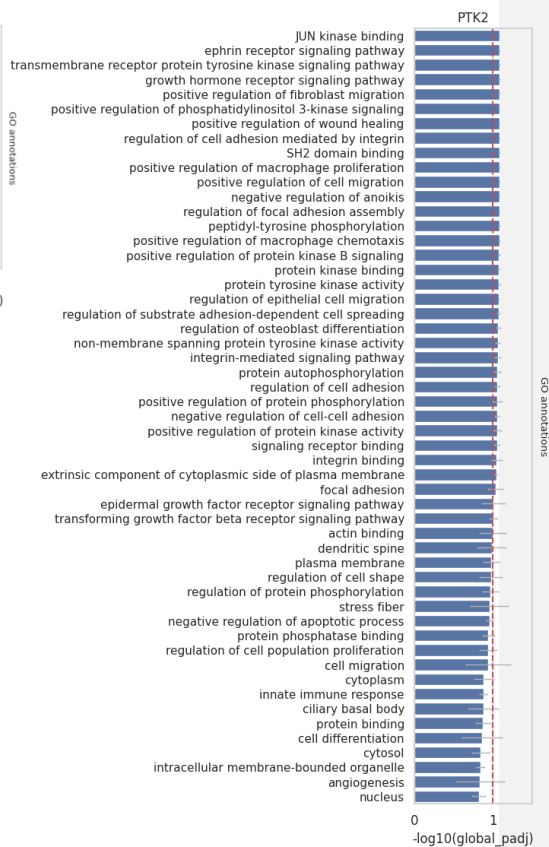
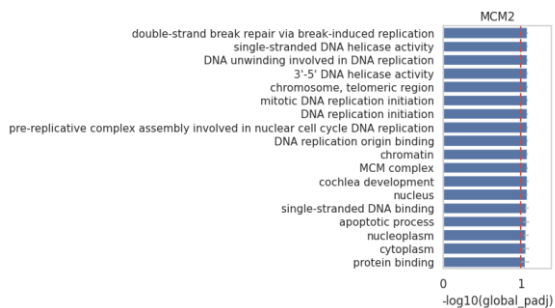
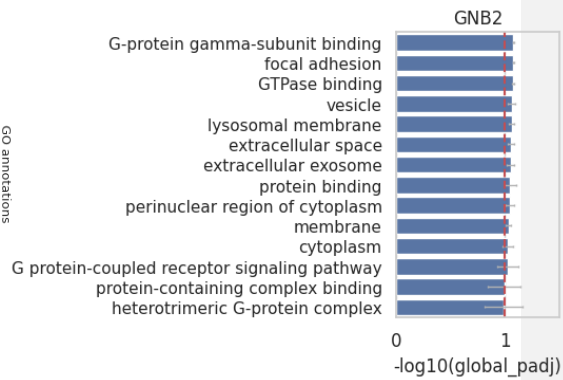
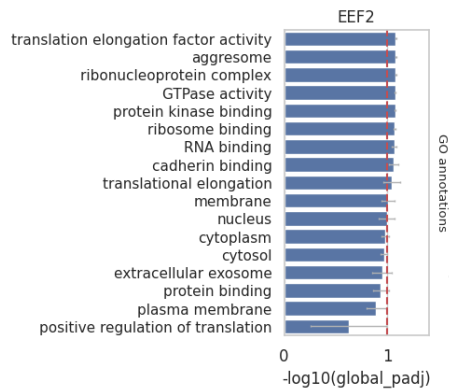


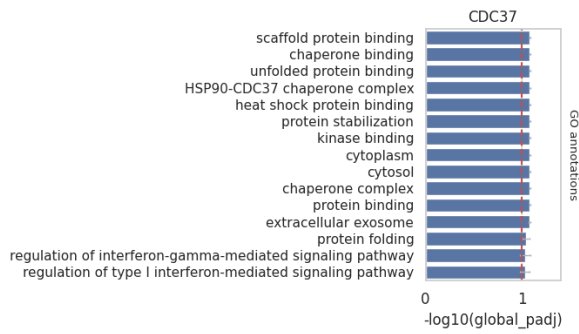




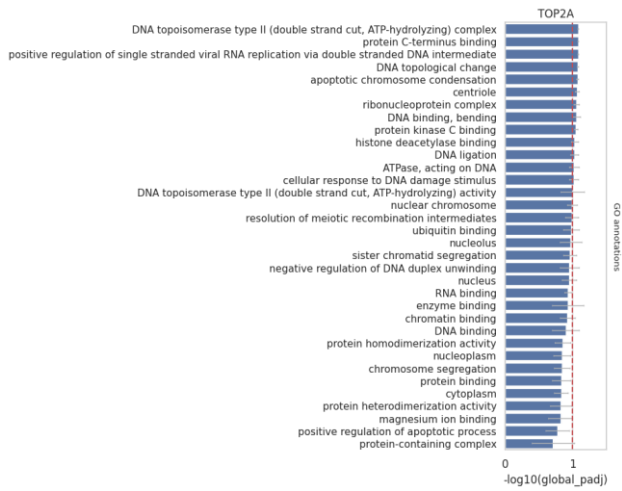


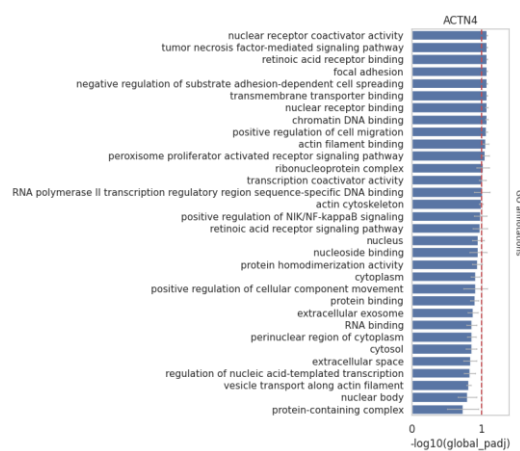


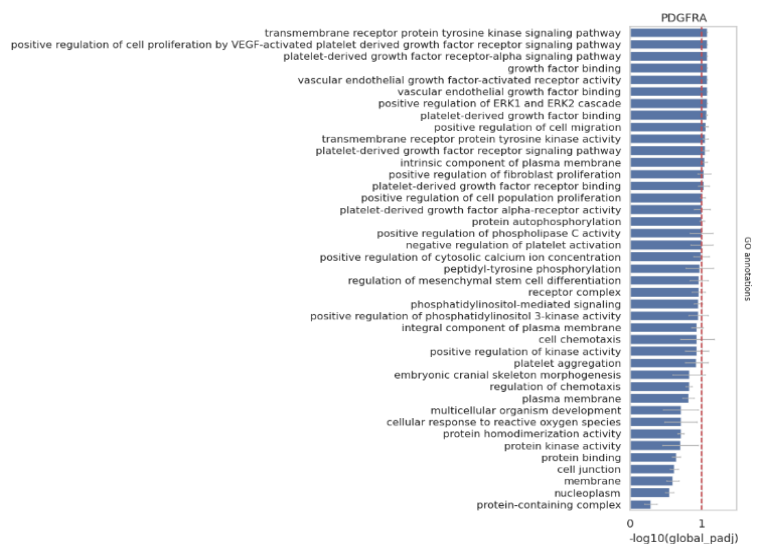




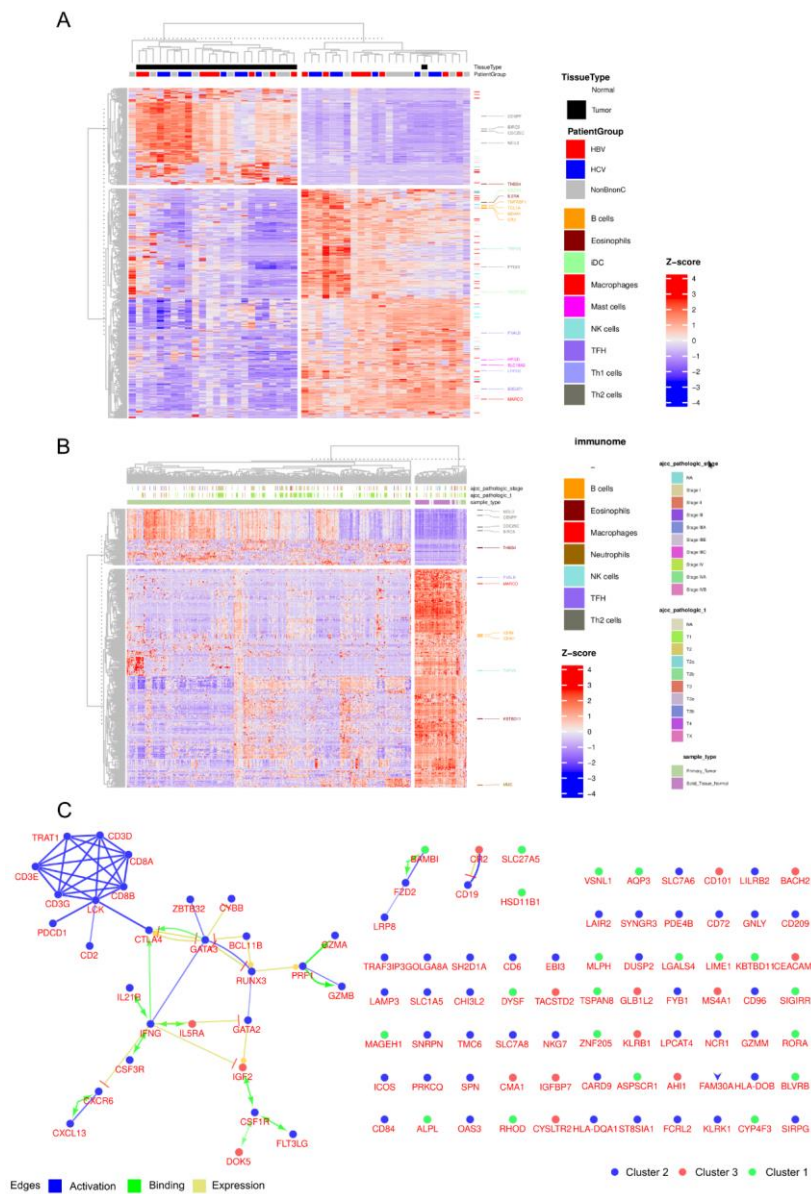
Non viral Moonlightning genes







Supplementary Figure 5. Immunome analysis in tumor tissues versus non-tumoral tissues and in TCGA cohort



The heatmap with genes differentially expressed in tumors compared to normal tissue samples from Bucuresti cohort (A) and TCGA cohort (B). Data was normalized and hierarchically clustered (Euclidean distance). Z-score spans between -4 (blue) and 4 (red). Immunome markers are highlighted. (A) Fold change >2.5 and adjusted pvalue <0.005. (B) Fold change >3, adjusted pvalue <0.001. (C) CluePedia scores for markers from Cluster 1 (green), Cluster 2 (blue) and Cluster 3 (red). Interactions are based on data from STRING (v11) database. Edges show activation (green), binding (blue), expression (yellow) scores.