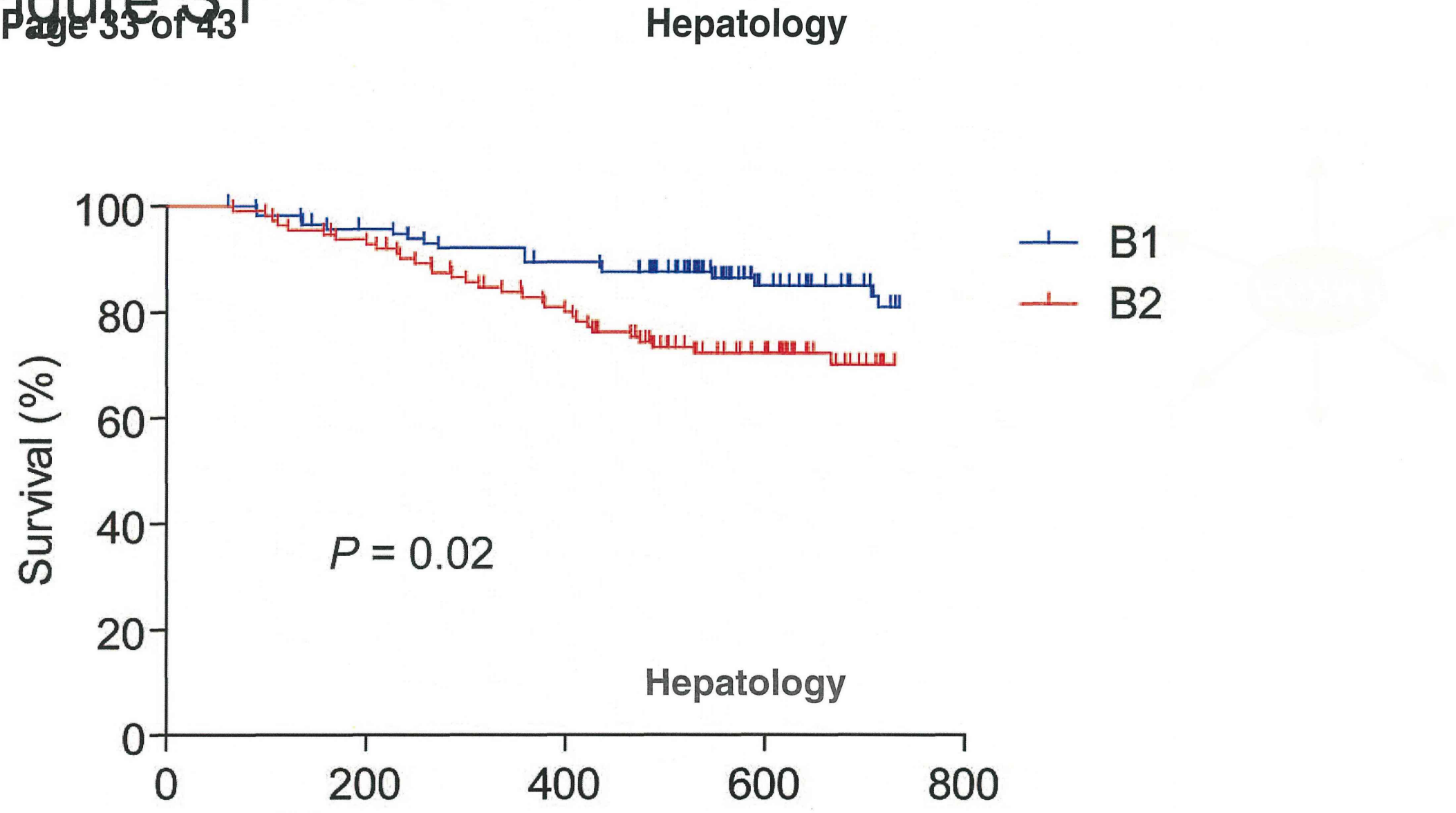
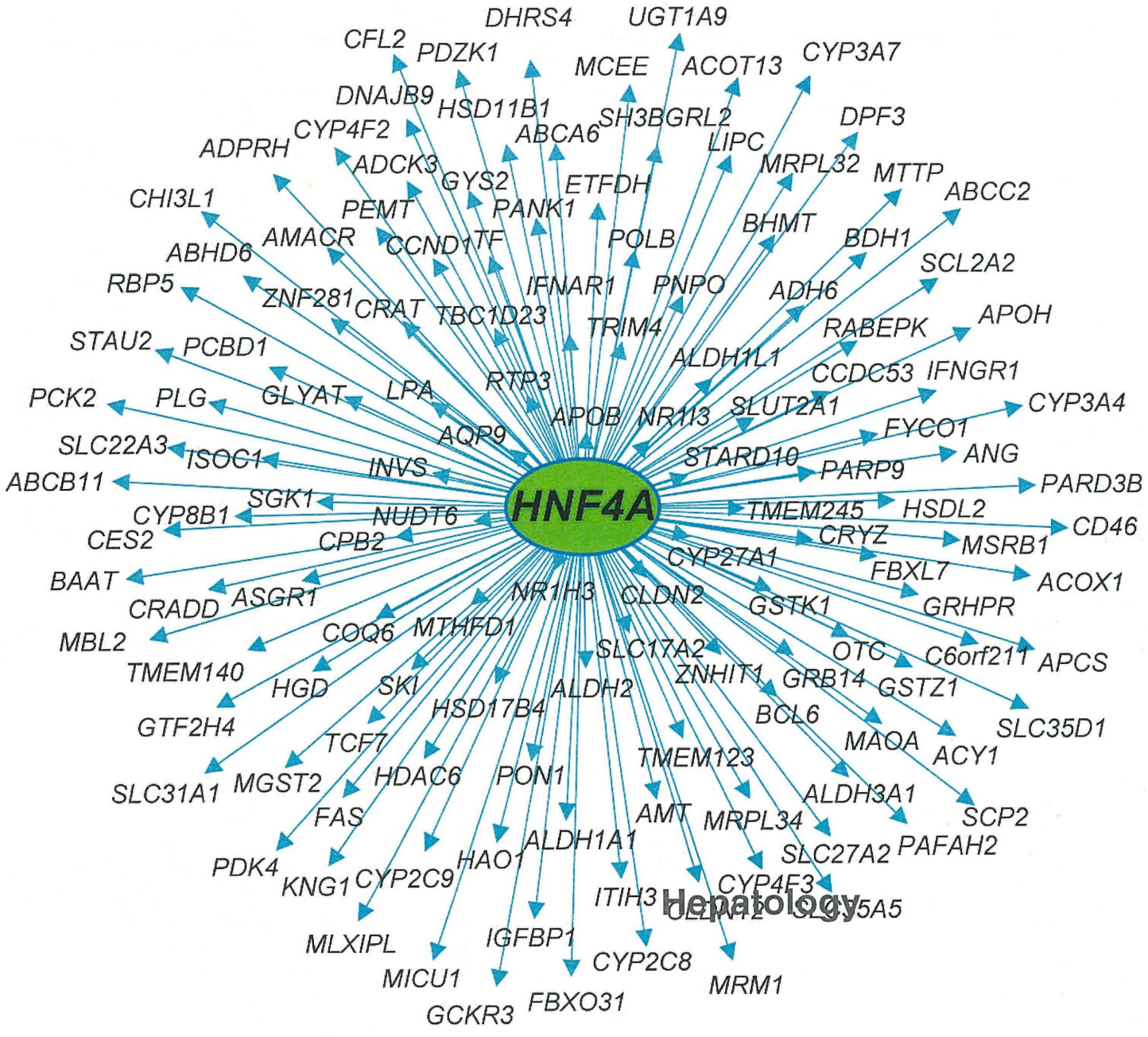
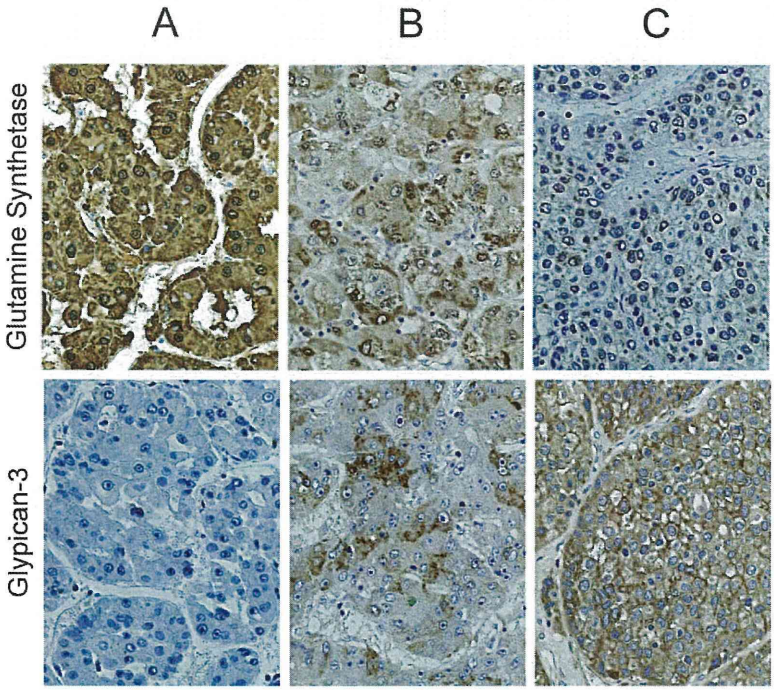
Figure S1


Hepatology
100
80
60
40
20
0
Survival (%)
P = 0.02
Hepatology
0
200
400
600
800
B1
B2


HNF4A
DHRS4
UGT1A9
CFL2
PDZK1
MCEE
ACOT13
CYP3A7
DNAJB9
HSD11B1
SH3BGRL2
DPF3
CYP4F2
ABCA6
LIPC
ADPRH
ADCK3
GYS2
ETFDH
MRPL32
MTTP
ABCC2
CHI3L1
PEMT
PANK1
BHMT
AMACR
CCND1
TF
POLB
BDH1
ABHD6
SCL2A2
RBP5
ZNF281
CRAT
TBC1D23
IFNAR1
PNPO
ADH6
APOH
STAU2
PCBD1
TRIM4
RABEPK
ALDH1L1
CCDC53
IFNGR1
PCK2
PLG
GLYAT
LPA
RTP3
APOB
NR1I3
SLUT2A1
CYP3A4
SLC22A3
ISOC1
AQP9
FYCO1
INVS
STARD10
PARP9
ANG
ABCB11
SGK1
PARD3B
CYP8B1
NUDT6
TMEM245
HSDL2
CES2
CPB2
CRYZ
MSRB1
CD46
BAAT
CYP27A1
FBXL7
ACOX1
CRADD
ASGR1
NR1H3
CLDN2
GSTK1
GRHPR
MBL2
COQ6
MTHFD1
OTC
C6orf211
APCS
TMEM140
SLC17A2
ZNHIT1
GRB14
GSTZ1
HGD
SKI
ALDH2
BCL6
GTF2H4
HSD17B4
MAOA
SLC35D1
TCF7
ACY1
TMEM123
SLC31A1
MGST2
HDAC6
PON1
ALDH3A1
AMT
MRPL34
SCP2
FAS
SLC27A2
PAFAH2
PDK4
ALDH1A1
HAO1
KNG1
CYP2C9
CYP4F3
ITIH3
MLXIPL
IGFBP1
CYP2C8
MICU1
MRM1
GCKR3
FBXO31
Hepatology
CDK1
STMN1
CENPA
FOXM1
PRC1
CDC25B

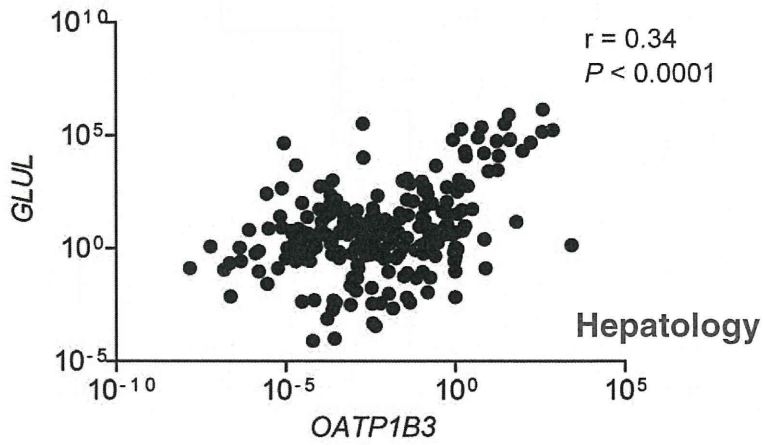
A



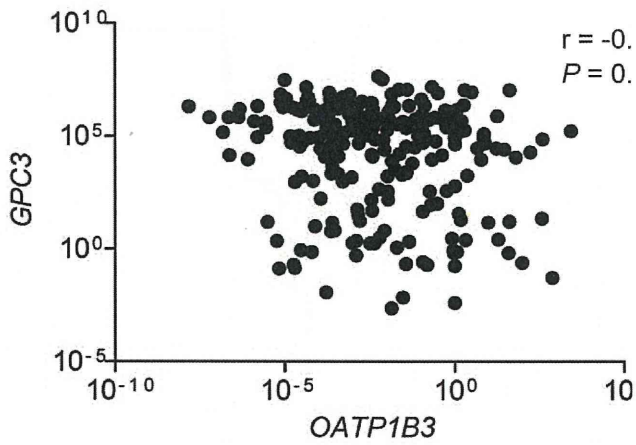
B

	A	B	C	*P*
Glutamine Synthetase				
High	9	25	12	
Low	0	15	9	0.06
Glypican-3				
High	3	18	16	
Low	6	22	5	0.03

C



D



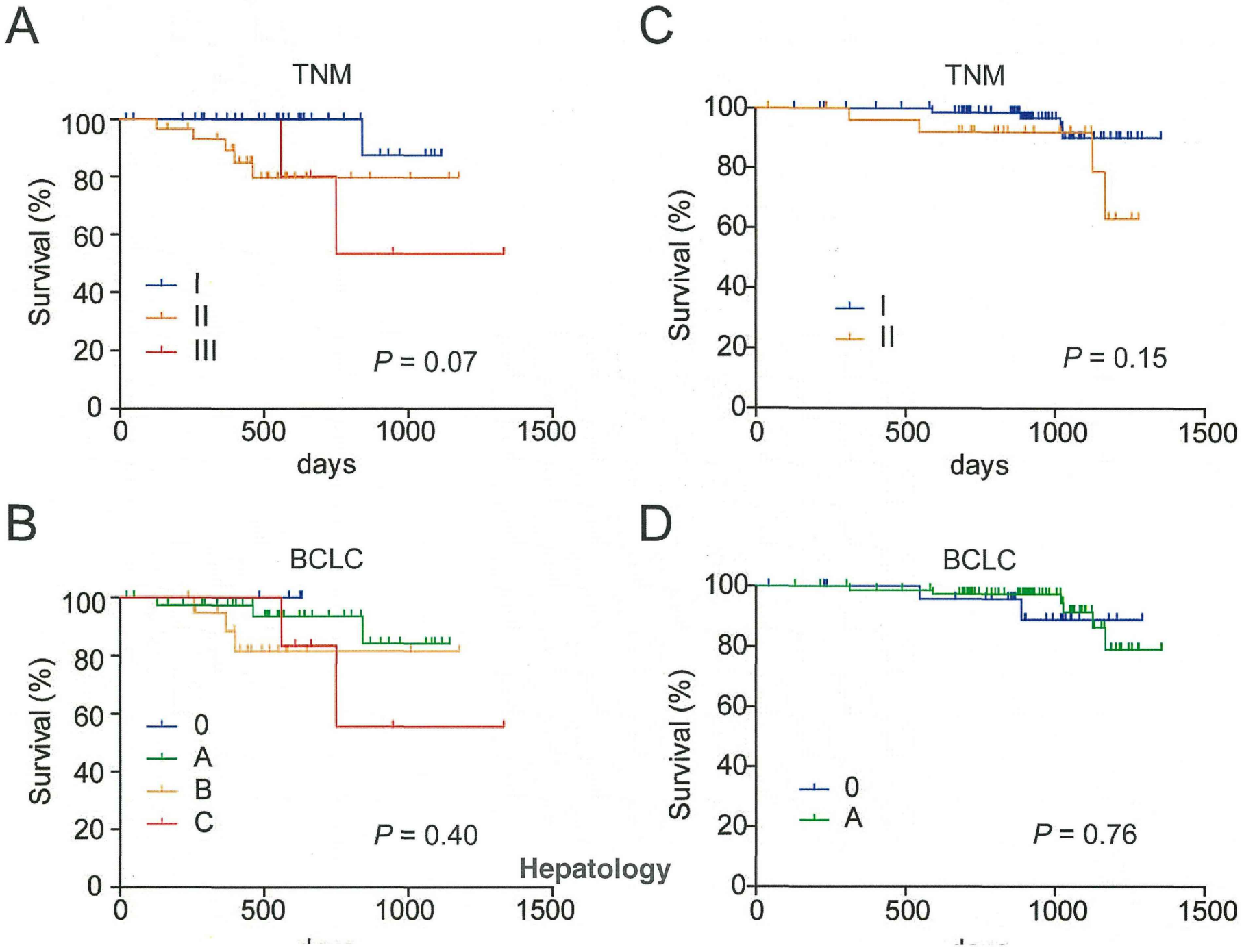

A
TNM
Survival (%)
100
80
60
40
20
0
I
II
III
P = 0.07
0
500
1000
1500
days
C
TNM
Survival (%)
I
II
P = 0.15
days
B
BCLC
Survival (%)
0
A
B
C
P = 0.40
Hepatology
D
BCLC
Survival (%)
0
A
P = 0.76

Figure S5

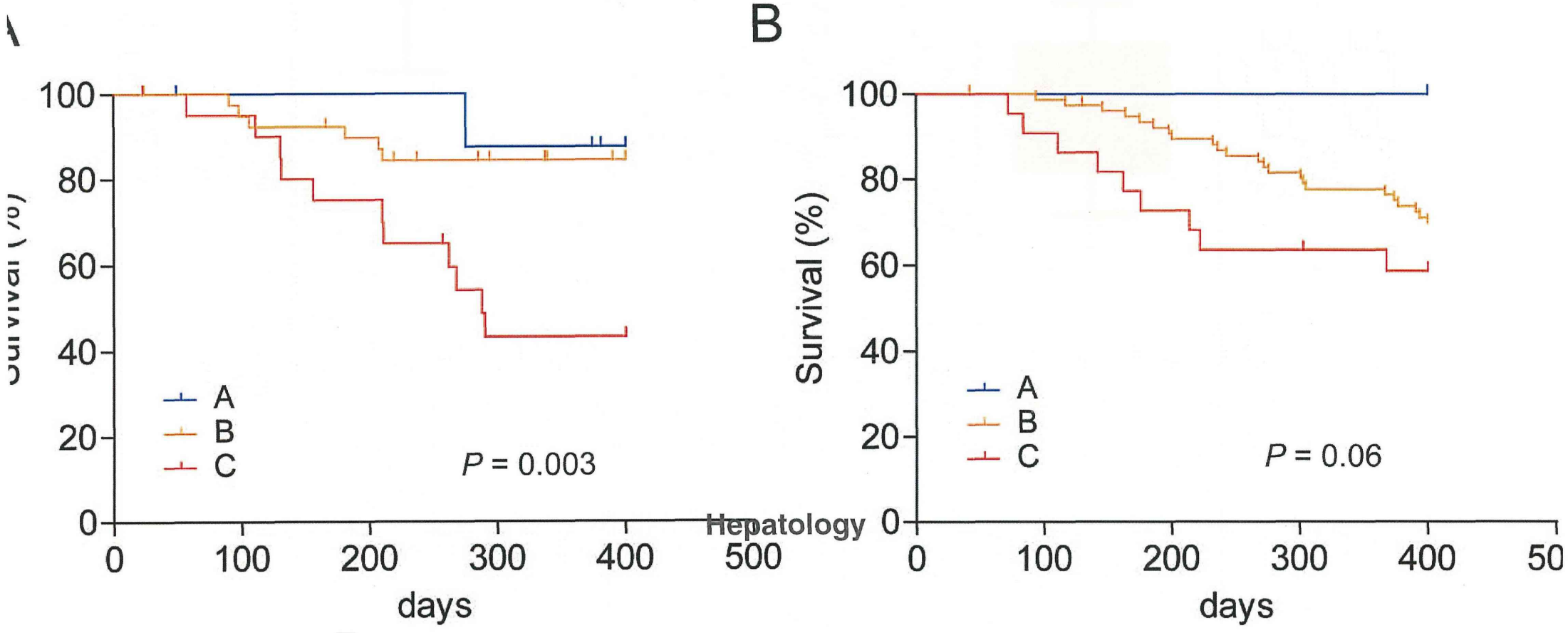
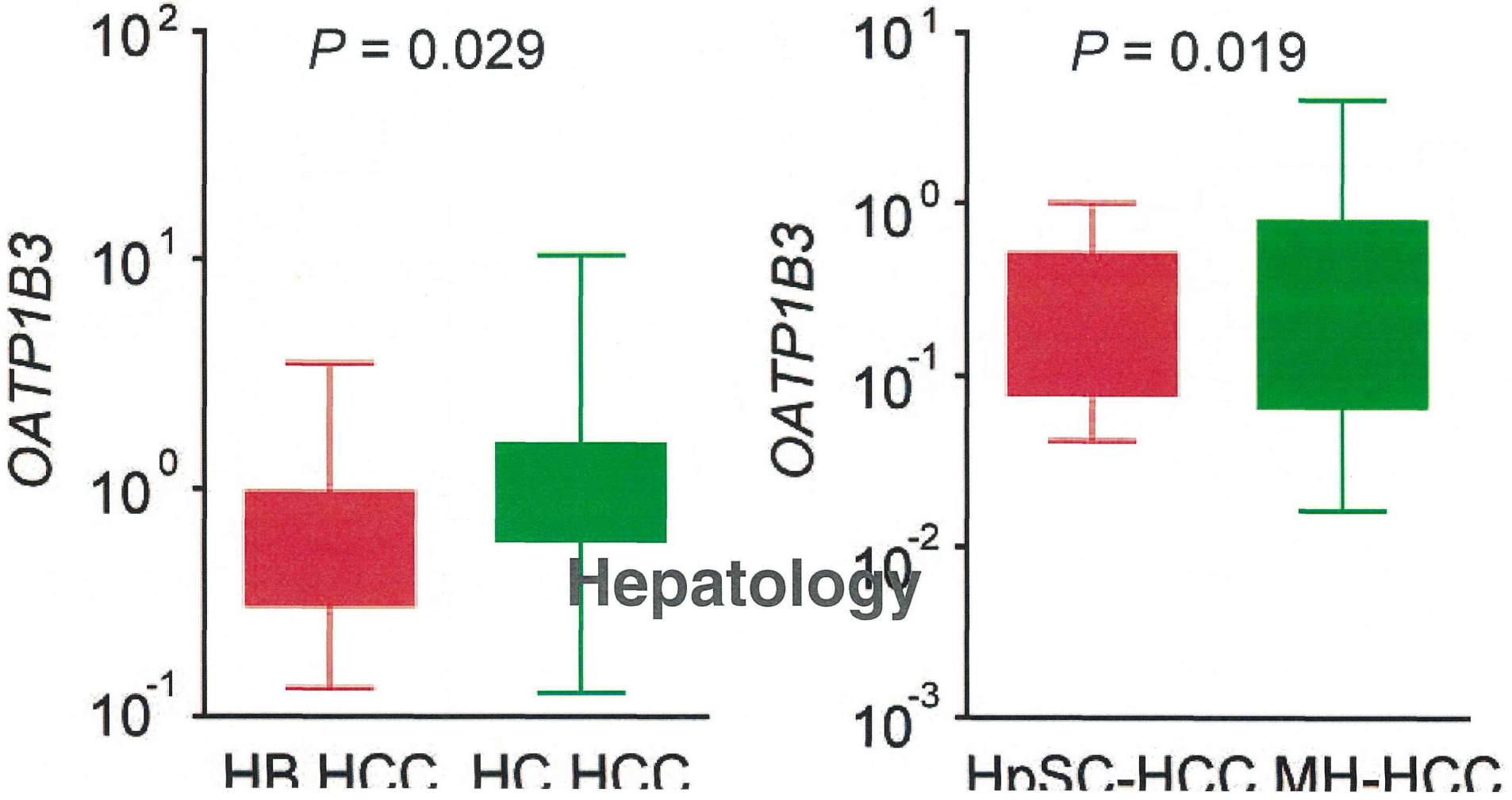

A
B
Survival (%)
100
80
60
40
20
0
0
100
200
300
400
500
days
A
B
C
P = 0.003
P = 0.06

Figure S6



Supplementary Materials

Supplementary Figure Legends

Figure S1 Overall survival curves of the 238 HCC cases analyzed by microarray and classified by the *OATP1B3* gene signature. HCC cases are clustered into 2 branches (B1 and B2) according to the *OATP1B3* gene signature and show different survival rates.

Figure S2 Interaction network analysis of transcription factors and their target genes activated in hyper- or hypo-intense HCCs. A total of 135 genes and 6 genes were identified as HNF4α (green node) and FOXM1 (orange node) target genes activated in hyper- or hypo-intense HCCs, respectively.

Figure S3 (A) Representative photomicrographs of IHC staining with anti-glutamine synthetase and anti-glypican-3 antibodies in class A, B, and C HCCs, according to the EOB-AFP classification. (B) Summary of glutamine synthetase and glypican-3 expression in class A, B, and C HCCs. (C, D) Scatter plot analyses of the microarray data from 238 HCCs.

Figure S4 Overall survival curves of Cohorts 1 (A, B) and 2 (C, D) according to TNM (A, C) and BCLC (B, D) stages. Most HCC patients included in this study were diagnosed with early-stage disease, and the prognosis of these patients was not separated by TNM and BCLC stages in either cohort.

Figure S5 Prognostic utility of the EOB-AFP classification. Recurrence-free survival curves of Cohorts 1 (A) and 2 (B) according to the EOB-AFP classification.

Figure S6 *OATP1B3* expression and HCC subtypes related to stem/maturation status. *OATP1B3* expression in HB HCC and HC HCC (left panel) and in HpSC-HCC and MH-HCC (right panel).

Supplementary Tables

Table S1 Performance of classifiers that predict serum AFP (20 ng/mL as the cut-off value) according to the *OATP1B3* gene signature.

Classifier	Correct classification (%)	*P*
CCP	72	<0.01
LDA	73	<0.01
1NN	65	0.01
3NN	66	0.01
NC	72	<0.01
SVM	71	0.04

Table S2 Performance of classifiers that predict serum AFP (100 ng/mL as the cut-off value) according to the *OATP1B3* gene signature.

Classifier	Correct classification (%)	*P*
CCP	73	<0.01
LDA	74	<0.01
1NN	69	0.01
3NN	74	<0.01
NC	72	<0.01
SVM	69	<0.01

Table S3 Performance of classifiers that predict serum AFP (300 ng/mL as the cut-off value) according to the *OATP1B3* gene signature.

Classifier	Correct classification (%)	*P*
CCP	71	<0.01
LDA	72	<0.01
1NN	73	0.02
3NN	74	0.02
NC	72	<0.01
SVM	63	<0.01

CCP, compound covariate predictor

LDA, diagonal linear discriminant analysis

1NN, 1-nearest neighbor

3NN, 3-nearest neighbors

NC, nearest centroid

SVM, support vector machines

Table S4 Characteristics of HCCs categorized by the EOB-AFP classification system in Cohort 1

Characteristics	Class A (n = 9)	Class B (n = 40)	Class C (n = 21)	*P**
Age (years, mean ± SE)	66.2 ± 3.6	66.1 ± 1.3	61.8 ± 2.1	0.21
Sex (male/female)	7/2	32/8	12/9	0.15
Etiology (HBV/HCV/other)	2/3/4	7/14/19	7/9/5	0.95
Liver cirrhosis (yes/no)	5/4	20/20	13/8	0.44
AFP (ng/mL, mean ± SE)	12.4 ± 1.9	23.9 ± 4.1	6,219 ± 2,297	<0.0001
Histologic grade†				
I–II	1	11	1	
II–III	8	22	16	
III–IV	0	7	4	0.11
Tumor size (cm, mean ± SE)	4.0 ± 0.9	4.5 ± 0.5	4.3 ± 0.6	0.94
Microscopic portal vein invasion (yes/no)	2/7	16/24	11/10	0.29
TNM classification (I/II/III)	6/2/1	20/19/1	9/9/3	0.32
BCLC stage (0/A/B/C)	0/7/1/1	2/22/15/1	2/8/7/4	0.17

*Kruskal-Wallis or c^2 test

†Edmondson-Steiner