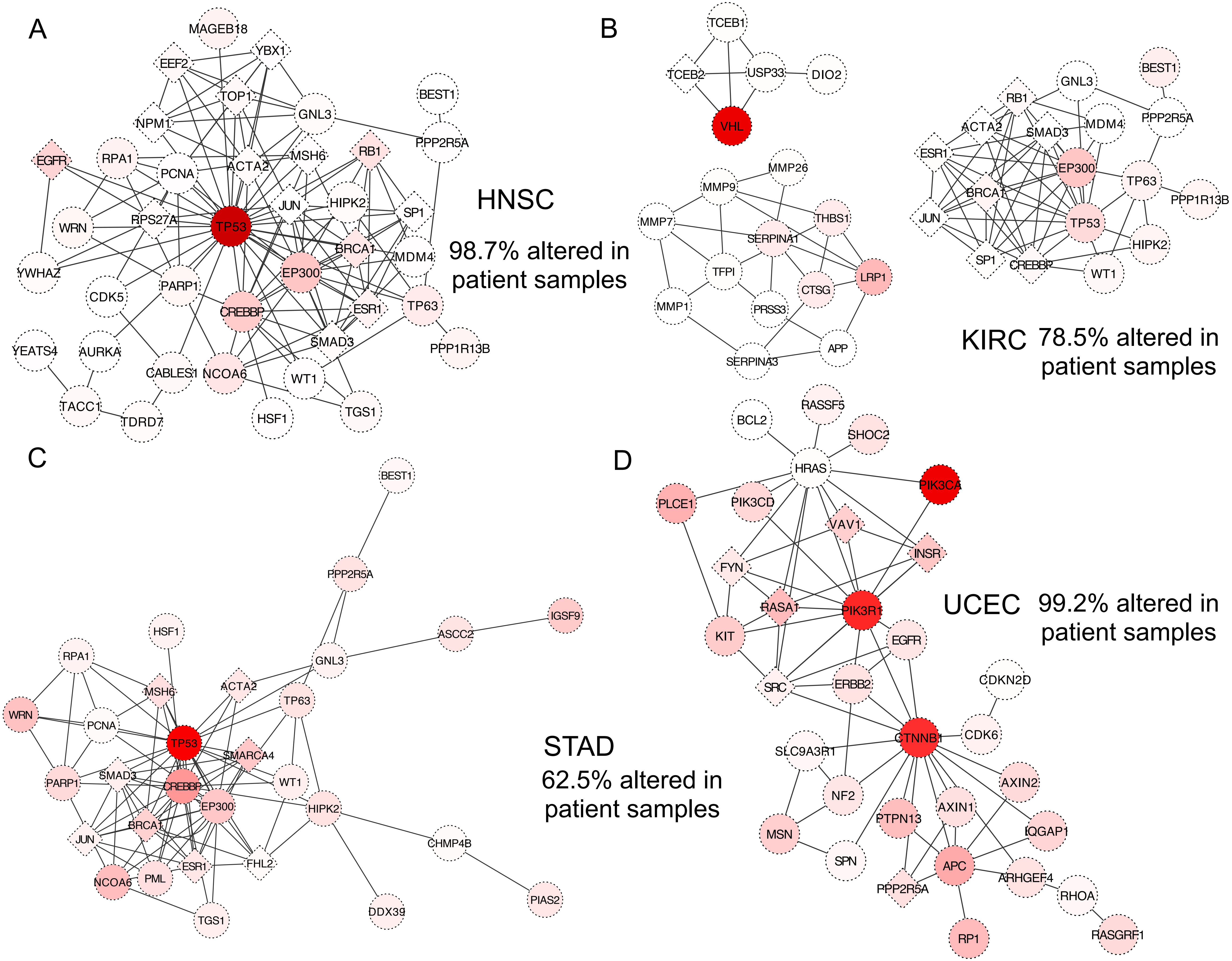
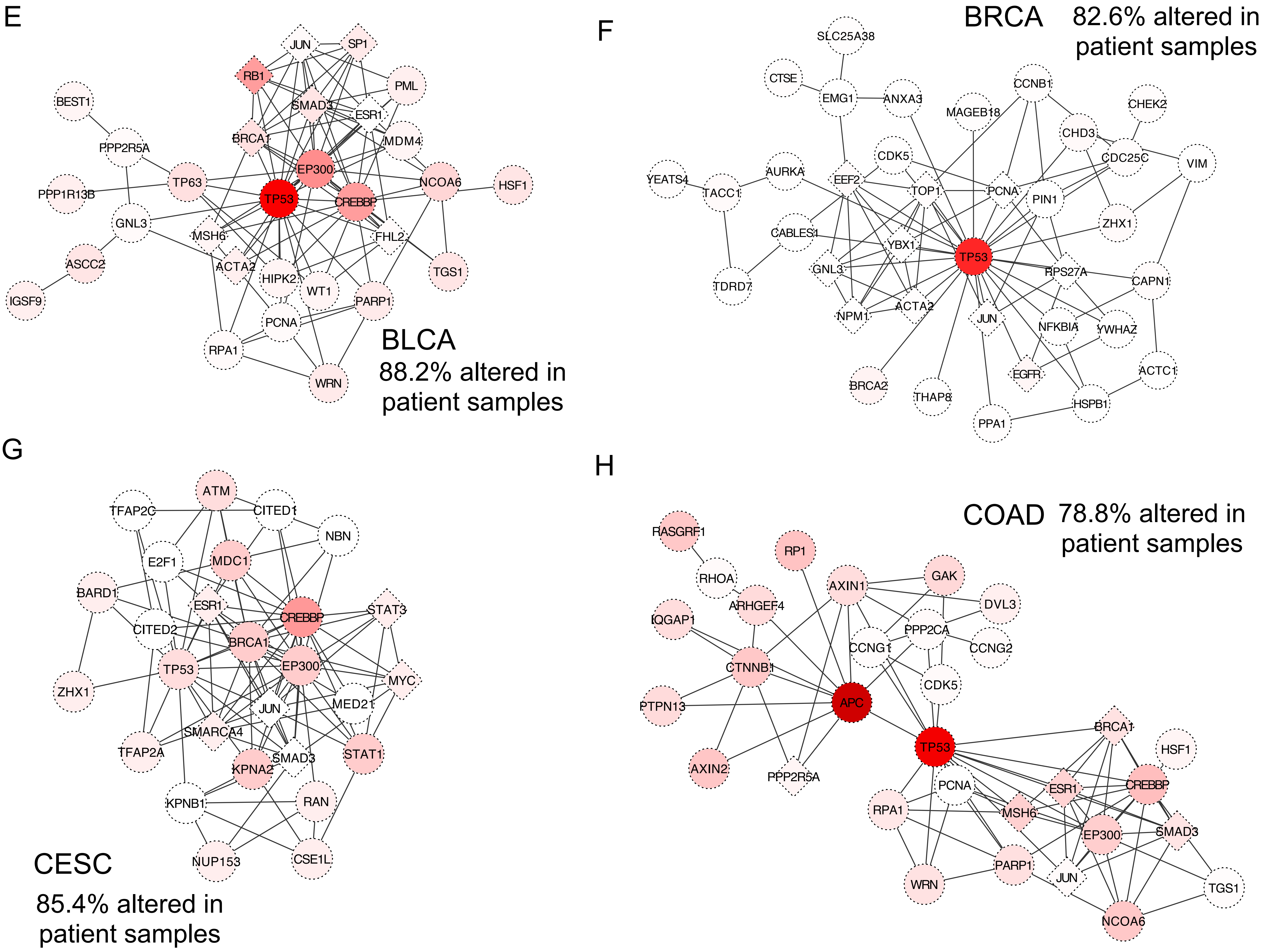
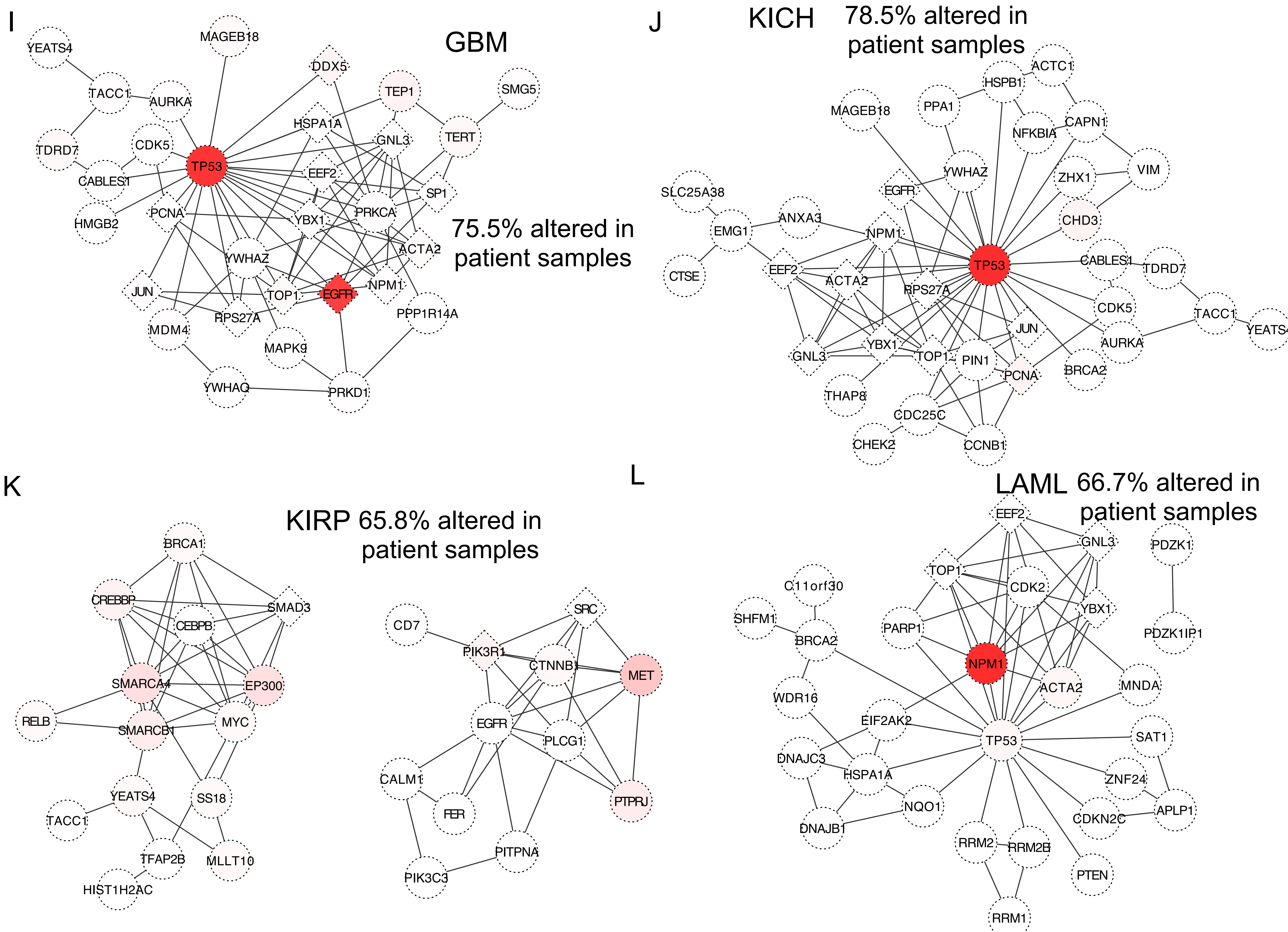
Supplementary Figure 1


A
HNSC
98.7% altered in patient samples
MAGEB18
YBX1
EEF2
TOP1
GNL3
BEST1
NPM1
PPP2R5A
EGFR
RPA1
PCNA
ACTA2
MSH6
RB1
JUN
HIPK2
SP1
WRN
RPS27A
TP53
BRCA1
MDM4
YWHAZ
EP300
CDK5
PARP1
TP63
CREBBP
ESR1
SMAD3
PPP1R13B
YEATS4
AURKA
CABLES1
NCOA6
WT1
TACC1
TDRD7
HSF1
TGS1
B
TCEB1
TCEB2
USP33
DIO2
VHL
MMP26
MMP9
MMP7
THBS1
SERPINA1
TFPI
LRP1
CTSG
MMP1
PRSS3
SERPINA3
APP
KIRC
78.5% altered in patient samples
BEST1
GNL3
RB1
ACTA2
SMAD3
MDM4
PPP2R5A
ESR1
EP300
TP63
PPP1R13B
BRCA1
JUN
TP53
HIPK2
SP1
CREBBP
WT1
C
STAD
62.5% altered in patient samples
BEST1
PPP2R5A
IGSF9
ASCC2
HSF1
RPA1
GNL3
MSH6
ACTA2
TP63
WRN
PCNA
TP53
SMARCA4
WT1
PARP1
SMAD3
CREBBP
EP300
HIPK2
BRCA1
JUN
CHMP4B
ESR1
FHL2
NCOA6
PML
TGS1
DDX39
PIAS2
D
UCEC
99.2% altered in patient samples
BCL2
RASSF5
SHOC2
HRAS
PIK3CA
PLCE1
PIK3CD
VAV1
INSR
FYN
RASA1
PIK3R1
KIT
EGFR
CDKN2D
SRC
ERBB2
CDK6
SLC9A3R1
CTNNB1
AXIN2
NF2
AXIN1
PTPN13
MSN
IQGAP1
SPN
APC
PPP2R5A
ARHGEF4
RHOA
RP1
RASGRF1


E
BLCA
88.2% altered in patient samples
TP53
EP300
CREBBP
RB1
JUN
SP1
SMAD3
ESR1
PML
MDM4
BRCA1
NCOA6
HSF1
TP63
BEST1
PPP2R5A
PPP1R13B
GNL3
MSH6
FHL2
ASCC2
IGSF9
ACTA2
HIPK2
WT1
TGS1
PARP1
PCNA
RPA1
WRN
F
BRCA
82.6% altered in patient samples
SLC25A38
CTSE
EMG1
ANXA3
CCNB1
MAGEB18
CHEK2
CHD3
CDC25C
VIM
CDK5
AURKA
YEATS4
TACC1
EEF2
TOP1
PCNA
PIN1
ZHX1
CABLES1
YBX1
TP53
GNL3
RPS27A
CAPN1
TDRD7
NPM1
ACTA2
JUN
NFKBIA
YWHAZ
EGFR
ACTC1
BRCA2
THAP8
HSPB1
PPA1
G
CESC
85.4% altered in patient samples
ATM
TFAP2C
CITED1
NBN
E2F1
MDC1
BARD1
ESR1
CREBBP
STAT3
CITED2
BRCA1
TP53
EP300
MYC
ZHX1
JUN
MED21
SMARCA4
TFAP2A
KPNA2
SMAD3
STAT1
KPNB1
RAN
NUP153
CSE1L
H
COAD
78.8% altered in patient samples
RASGRF1
RP1
RHOA
AXIN1
GAK
DVL3
ARHGEF4
IQGAP1
PPP2CA
CCNG1
CCNG2
CTNNB1
CDK5
PTPN13
APC
TP53
BRCA1
HSF1
AXIN2
PPP2R5A
PCNA
ESR1
CREBBP
RPA1
MSH6
EP300
SMAD3
PARP1
WRN
JUN
TGS1
NCOA6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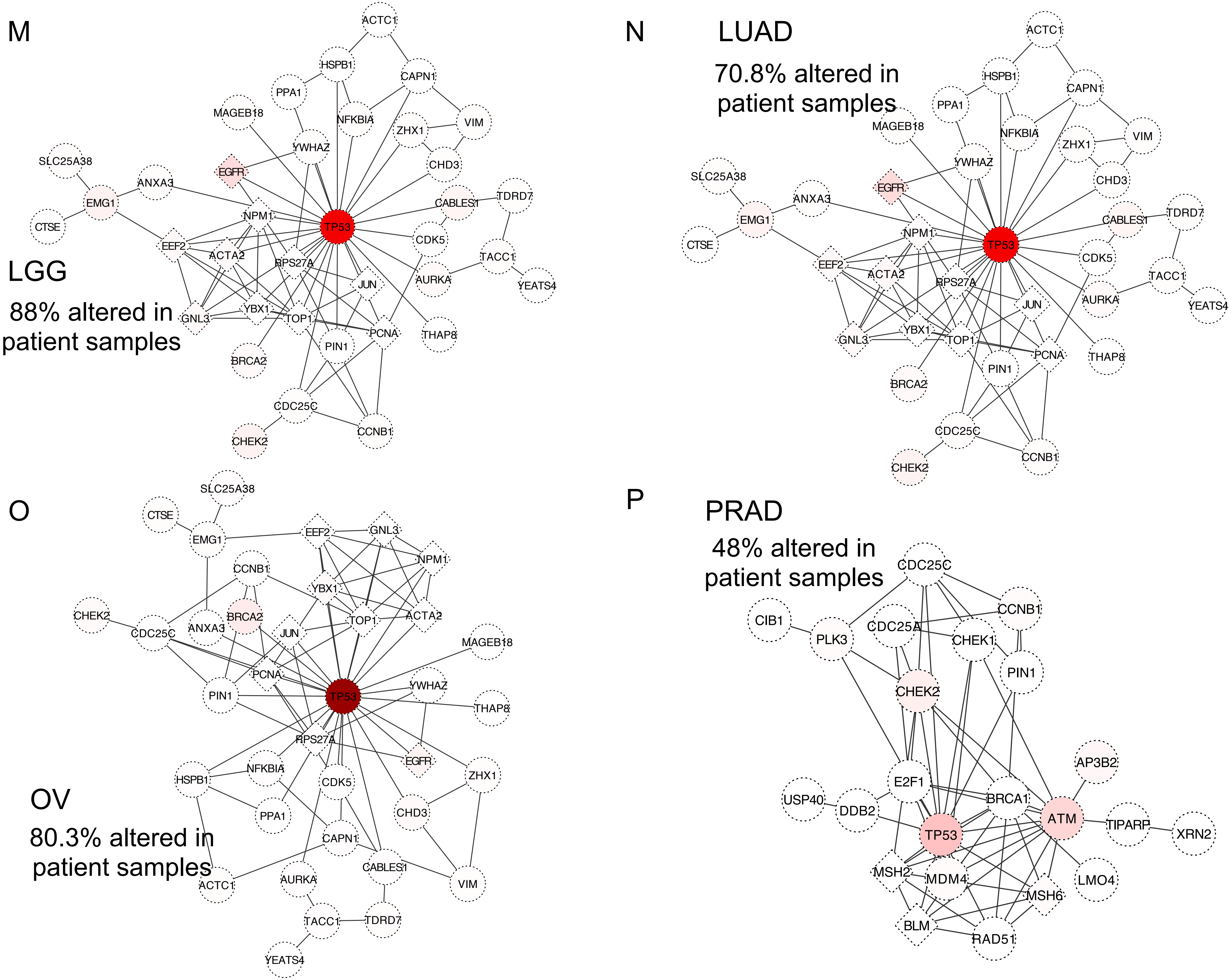
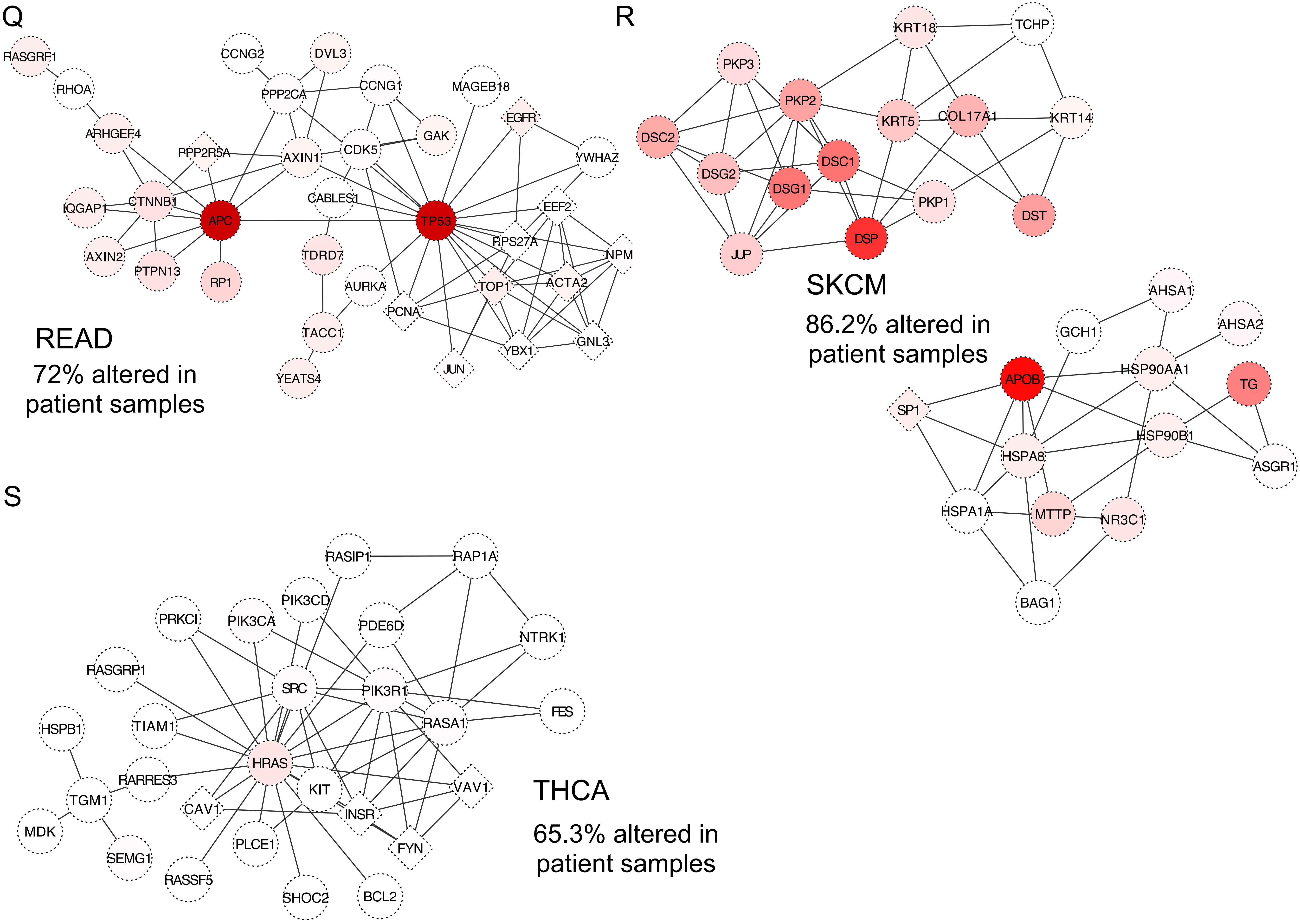
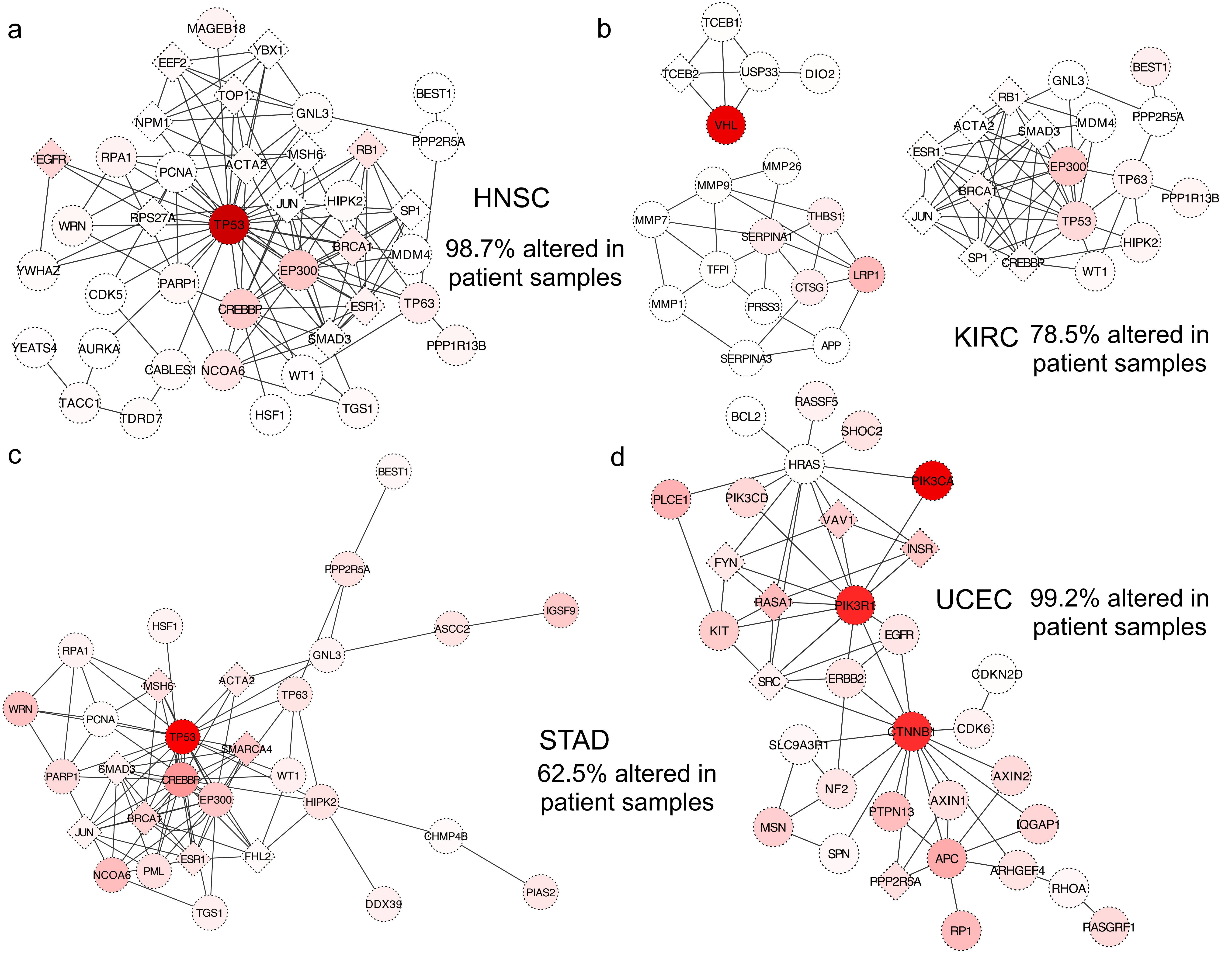
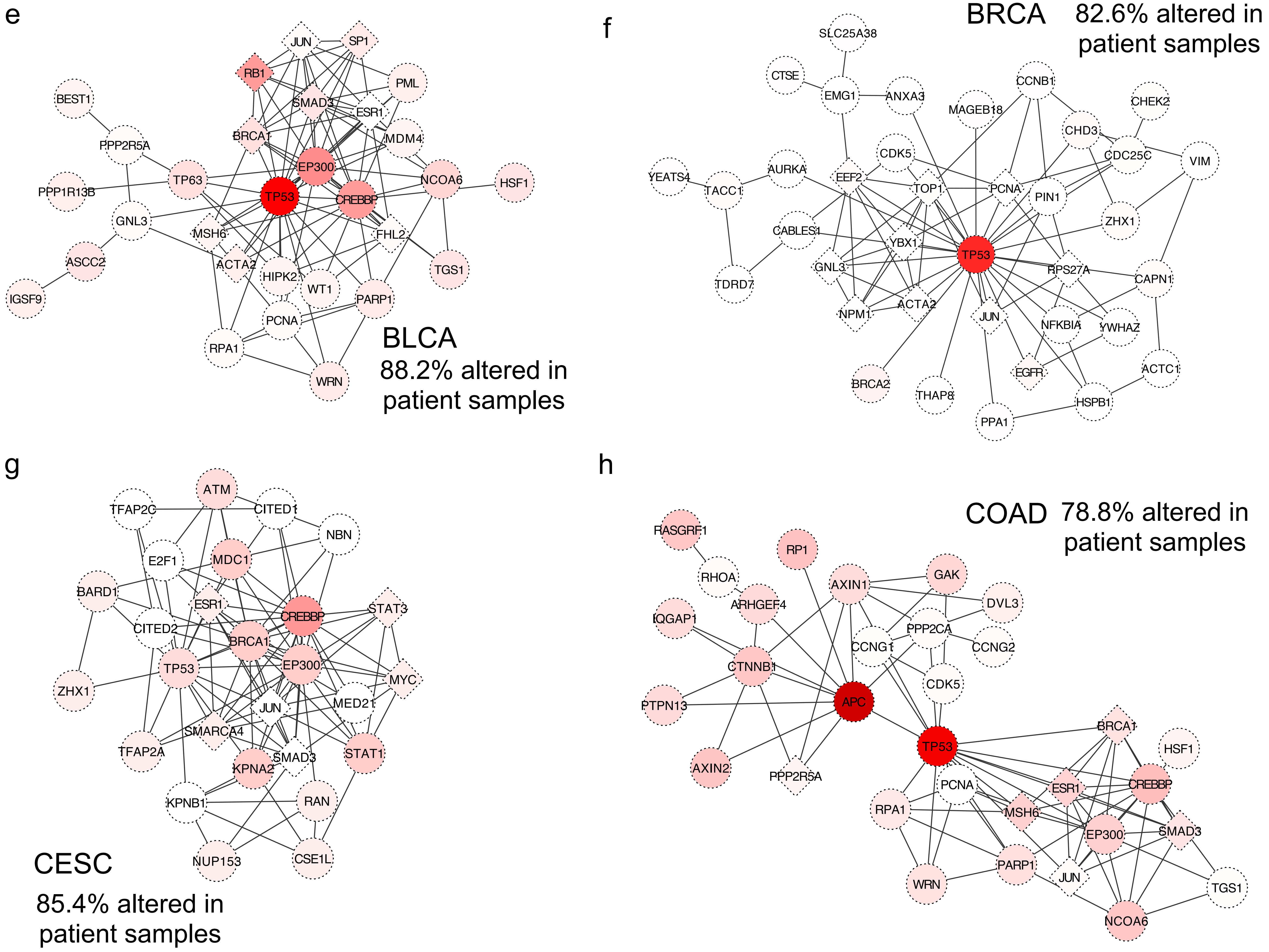
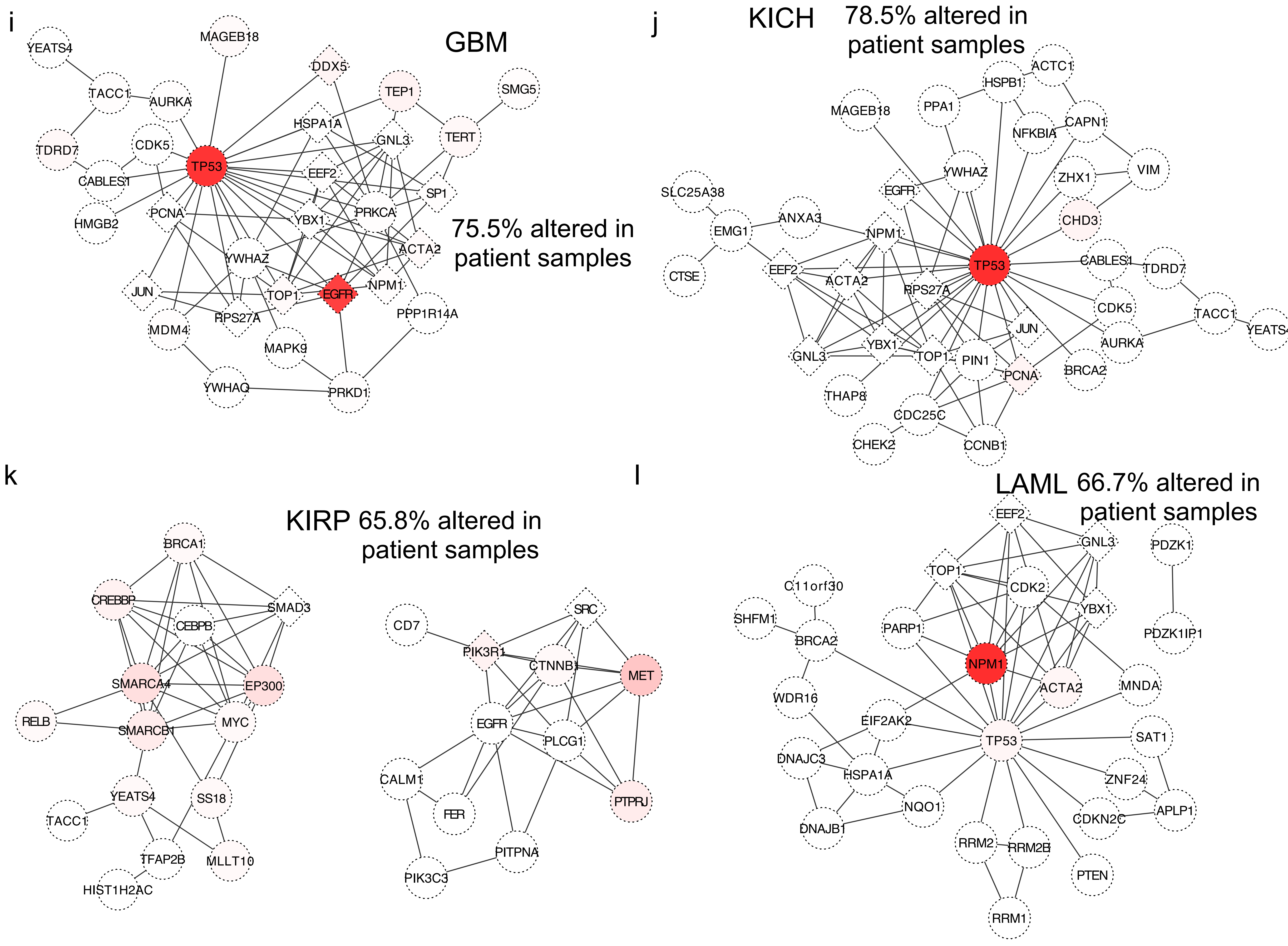
GBM
75.5% altered in patient samples
YEATS4
MAGEB18
DDX5
TEP1
SMG5
TACC1
AURKA
HSPA1A
GNL3
TERT
TDRD7
CDK5
TP53
EEF2
SP1
CABLES1
PRKCA
HMGB2
PCNA
YBX1
ACTA2
YWHAZ
JUN
TOP1
EGFR
NPM1
RPS27A
PPP1R14A
MDM4
MAPK9
YWHAQ
PRKD1
J
KICH
78.5% altered in patient samples
ACTC1
HSPB1
PPA1
MAGEB18
CAPN1
NFKBIA
YWHAZ
ZHX1
VIM
EGFR
SLC25A38
ANXA3
CHD3
EMG1
NPM1
TP53
CABLES1
TDRD7
CTSE
EEF2
ACTA2
RPS27A
CDK5
TACC1
YEATS4
JUN
YBX1
AURKA
GNL3
TOP1
PIN1
PCNA
BRCA2
THAP8
CDC25C
CHEK2
CCNB1
K
KIRP 65.8% altered in patient samples
BRCA1
CREBBP
SMAD3
CEBPB
SMARCA4
EP300
RELB
SMARCB1
MYC
YEATS4
SS18
TACC1
TFAP2B
MLLT10
HIST1H2AC
CD7
SRC
PIK3R1
CTNNB1
MET
EGFR
PLCG1
CALM1
FER
PTPRJ
PITPNA
PIK3C3
L
LAML 66.7% altered in patient samples
EEF2
GNL3
PDZK1
TOP1
C11orf30
CDK2
SHFM1
YBX1
BRCA2
PARP1
PDZK1IP1
NPM1
ACTA2
MNDA
WDR16
EIF2AK2
TP53
SAT1
DNAJC3
HSPA1A
ZNF24
NQO1
CDKN2C
APLP1
DNAJB1
RRM2
RRM2B
PTEN
RRM1


M
LGG
88% altered in patient samples
ACTC1
HSPB1
CAPN1
PPA1
MAGEB18
NFKBIA
ZHX1
VIM
YWHAZ
CHD3
SLC25A38
EGFR
ANXA3
CABLES1
TDRD7
EMG1
NPM1
TP53
CTSE
CDK5
EEF2
ACTA2
TACC1
RPS27A
AURKA
JUN
YEATS4
GNL3
YBX1
TOP1
PCNA
THAP8
PIN1
BRCA2
CDC25C
CCNB1
CHEK2
N
LUAD
70.8% altered in patient samples
ACTC1
HSPB1
CAPN1
PPA1
MAGEB18
NFKBIA
ZHX1
VIM
YWHAZ
CHD3
SLC25A38
EGFR
ANXA3
CABLES1
TDRD7
EMG1
NPM1
TP53
CTSE
CDK5
EEF2
ACTA2
TACC1
RPS27A
AURKA
JUN
YEATS4
GNL3
YBX1
TOP1
PCNA
THAP8
PIN1
BRCA2
CDC25C
CCNB1
CHEK2
O
OV
80.3% altered in patient samples
SLC25A38
CTSE
EMG1
EEF2
GNL3
NPM1
CCNB1
YBX1
CHEK2
CDC25C
ANXA3
BRCA2
JUN
TOP1
ACTA2
MAGEB18
PCNA
YWHAZ
PIN1
TP53
THAP8
RPS27A
EGFR
HSPB1
NFKBIA
CDK5
ZHX1
PPA1
CHD3
CAPN1
CABLES1
VIM
AURKA
ACTC1
TACC1
TDRD7
YEATS4
P
PRAD
48% altered in patient samples
CDC25C
CIB1
PLK3
CDC25A
CCNB1
CHEK1
PIN1
CHEK2
AP3B2
E2F1
BRCA1
USP40
DDB2
ATM
TIPARP
XRN2
TP53
MSH2
MDM4
MSH6
LMO4
BLM
RAD51


Q
RASGRF1
RHOA
ARHGEF4
CCNG2
DVL3
PPP2CA
CCNG1
MAGEB18
GAK
EGFR
YWHAZ
PPP2R5A
AXIN1
CDK5
CABLES1
IQGAP1
CTNNB1
APC
TP53
EEF2
RPS27A
NPM
AXIN2
PTPN13
RP1
TDRD7
AURKA
TOP1
ACTA2
PCNA
TACC1
YBX1
GNL3
JUN
YEATS4
READ
72% altered in
patient samples
R
KRT18
TCHP
PKP3
PKP2
KRT5
COL17A1
KRT14
DSC2
DSG2
DSC1
DSG1
PKP1
DST
DSP
JUP
SKCM
86.2% altered in
patient samples
AHSA1
GCH1
AHSA2
HSP90AA1
APOB
TG
SP1
HSP90B1
HSPA8
ASGR1
HSPA1A
MTTP
NR3C1
BAG1
S
RASIP1
RAP1A
PIK3CD
PRKCI
PIK3CA
PDE6D
NTRK1
RASGRP1
SRC
PIK3R1
FES
HSPB1
TIAM1
RASA1
HRAS
RARRES3
KIT
VAV1
TGM1
CAV1
INSR
MDK
PLCE1
FYN
SEMG1
RASSF5
SHOC2
BCL2
THCA
65.3% altered in
patient samples


a
HNSC
98.7% altered in patient samples
MAGEB18
YBX1
EEF2
TOP1
NPM1
GNL3
BEST1
PPP2R5A
EGFR
RPA1
PCNA
ACTA2
MSH6
RB1
JUN
HIPK2
SP1
WRN
RPS27A
TP53
BRCA1
MDM4
YWHAZ
EP300
CDK5
PARP1
CREBBP
ESR1
TP63
SMAD3
PPP1R13B
YEATS4
AURKA
CABLES1
NCOA6
WT1
TACC1
TDRD7
HSF1
TGS1
b
KIRC
78.5% altered in patient samples
TCEB1
TCEB2
USP33
DIO2
VHL
MMP26
MMP9
MMP7
THBS1
SERPINA1
TFPI
LRP1
CTSG
MMP1
PRSS3
APP
SERPINA3
BEST1
GNL3
RB1
PPP2R5A
ACTA2
SMAD3
MDM4
ESR1
EP300
TP63
PPP1R13B
BRCA1
JUN
TP53
HIPK2
SP1
CREBBP
WT1
c
STAD
62.5% altered in patient samples
BEST1
PPP2R5A
IGSF9
ASCC2
HSF1
GNL3
RPA1
ACTA2
MSH6
TP63
WRN
PCNA
TP53
SMARCA4
PARP1
SMAD3
CREBBP
WT1
EP300
HIPK2
BRCA1
JUN
CHMP4B
FHL2
ESR1
NCOA6
PML
PIAS2
TGS1
DDX39
d
UCEC
99.2% altered in patient samples
RASSF5
BCL2
SHOC2
HRAS
PIK3CA
PLCE1
PIK3CD
VAV1
INSR
FYN
RASA1
PIK3R1
KIT
EGFR
CDKN2D
SRC
ERBB2
CTNNB1
CDK6
SLC9A3R1
AXIN2
NF2
AXIN1
PTPN13
IQGAP1
MSN
SPN
APC
ARHGEF4
PPP2R5A
RHOA
RP1
RASGRF1


e
JUN
SP1
RB1
PML
BEST1
SMAD3
ESR1
BRCA1
MDM4
PPP2R5A
EP300
NCOA6
HSF1
TP63
TP53
CREBBP
PPP1R13B
GNL3
MSH6
FHL2
ASCC2
ACTA2
TGS1
HIPK2
WT1
IGSF9
PARP1
PCNA
RPA1
WRN
BLCA
88.2% altered in
patient samples
f
BRCA
82.6% altered in
patient samples
SLC25A38
CTSE
EMG1
ANXA3
CCNB1
MAGEB18
CHEK2
CHD3
CDK5
CDC25C
VIM
YEATS4
AURKA
EEF2
TOP1
PCNA
PIN1
TACC1
ZHX1
CABLES1
YBX1
TP53
GNL3
RPS27A
CAPN1
TDRD7
NPM1
ACTA2
JUN
NFKBIA
YWHAZ
ACTC1
EGFR
BRCA2
THAP8
HSPB1
PPA1
g
ATM
TFAP2C
CITED1
NBN
E2F1
MDC1
BARD1
ESR1
STAT3
CREBBP
CITED2
BRCA1
TP53
EP300
MYC
ZHX1
MED21
JUN
SMARCA4
TFAP2A
SMAD3
STAT1
KPNA2
KPNB1
RAN
NUP153
CSE1L
CESC
85.4% altered in
patient samples
h
COAD
78.8% altered in
patient samples
RASGRF1
RP1
RHOA
AXIN1
GAK
DVL3
ARHGEF4
IQGAP1
PPP2CA
CCNG1
CCNG2
CTNNB1
CDK5
PTPN13
APC
TP53
BRCA1
HSF1
AXIN2
PPP2R5A
PCNA
ESR1
CREBBP
RPA1
MSH6
EP300
SMAD3
PARP1
WRN
JUN
TGS1
NCOA6


i
GBM
75.5% altered in patient samples
YEATS4
MAGEB18
DDX5
TEP1
SMG5
TACC1
AURKA
HSPA1A
GNL3
TERT
TDRD7
CDK5
TP53
EEF2
SP1
CABLES1
PCNA
YBX1
PRKCA
HMGB2
ACTA2
YWHAZ
JUN
TOP1
EGFR
NPM1
PPP1R14A
MDM4
RPS27A
MAPK9
YWHAQ
PRKD1
j
KICH
78.5% altered in patient samples
ACTC1
HSPB1
PPA1
MAGEB18
CAPN1
NFKBIA
YWHAZ
ZHX1
VIM
EGFR
SLC25A38
CHD3
ANXA3
NPM1
EMG1
TP53
CABLES1
TDRD7
CTSE
EEF2
ACTA2
RPS27A
CDK5
TACC1
YEATS
JUN
YBX1
AURKA
GNL3
TOP1
PIN1
PCNA
BRCA2
THAP8
CDC25C
CHEK2
CCNB1
k
KIRP
65.8% altered in patient samples
BRCA1
CREBBP
SMAD3
CEBPB
SMARCA4
EP300
RELB
SMARCB1
MYC
YEATS4
SS18
TACC1
TFAP2B
MLLT10
HIST1H2AC
CD7
SRC
PIK3R1
CTNNB1
MET
EGFR
PLCG1
CALM1
FER
PTPRJ
PITPNA
PIK3C3
l
LAML
66.7% altered in patient samples
EEF2
GNL3
PDZK1
TOP1
C11orf30
CDK2
SHFM1
YBX1
PARP1
BRCA2
PDZK1IP1
NPM1
ACTA2
MNDA
WDR16
EIF2AK2
TP53
SAT1
DNAJC3
HSPA1A
ZNF24
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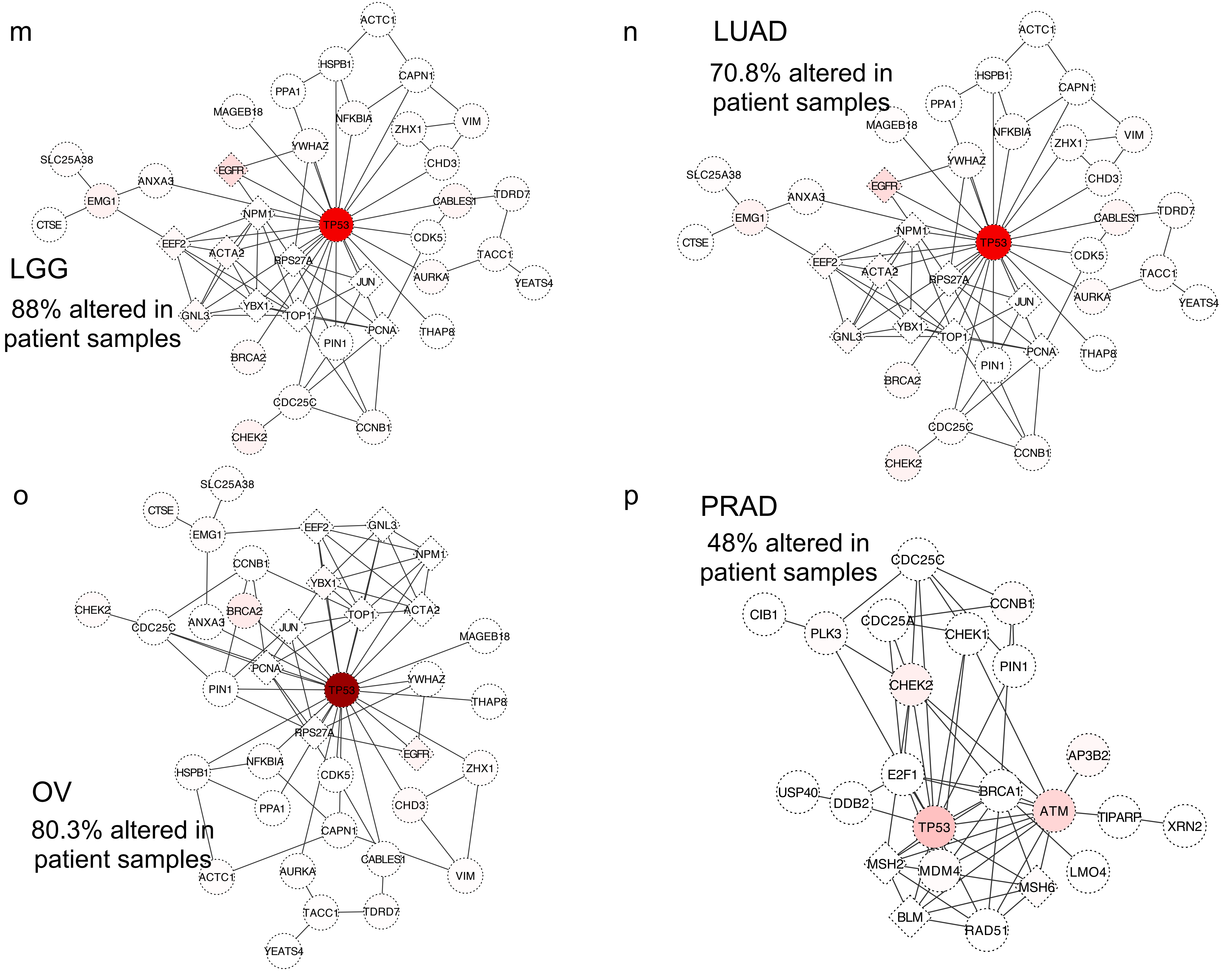
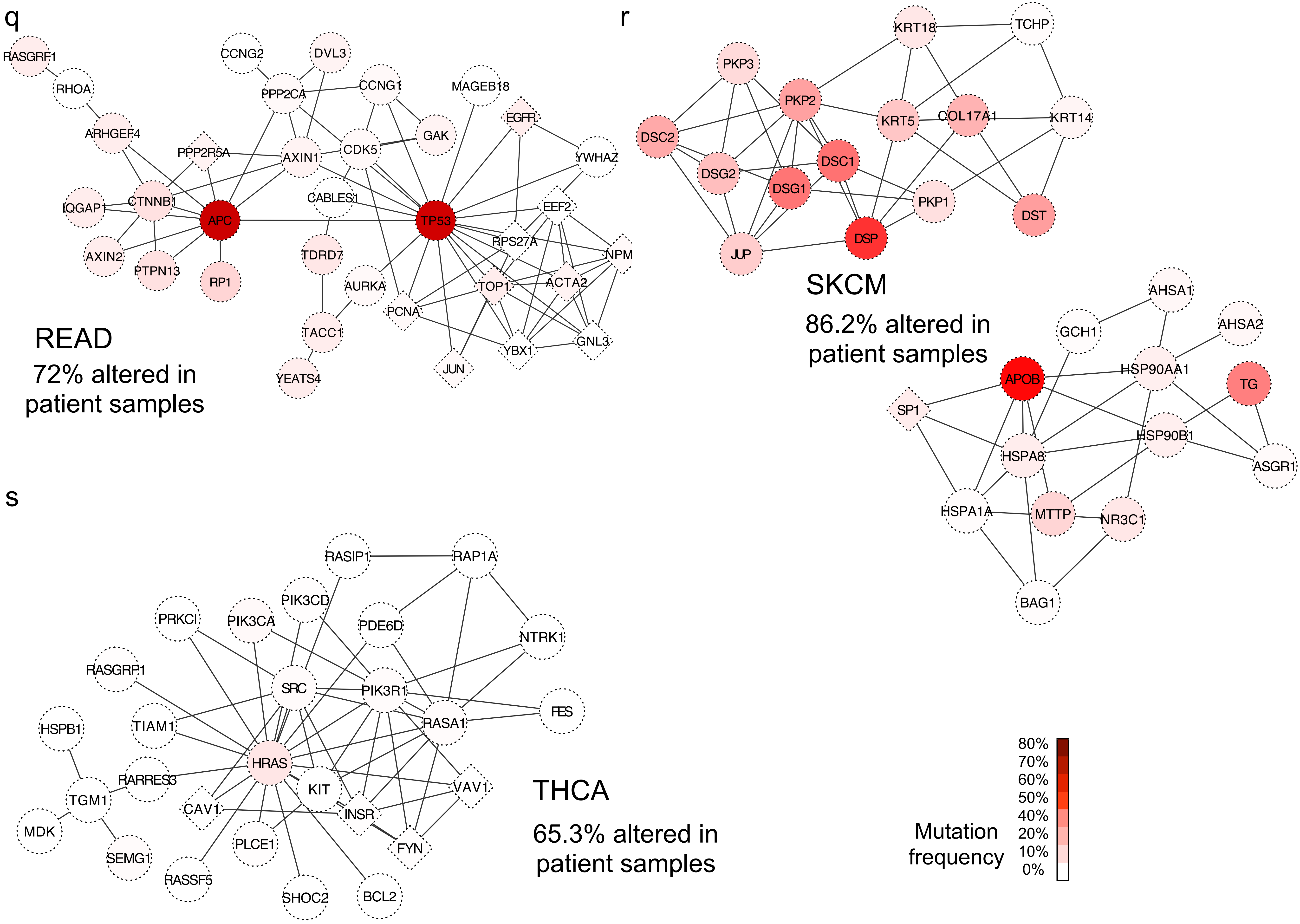
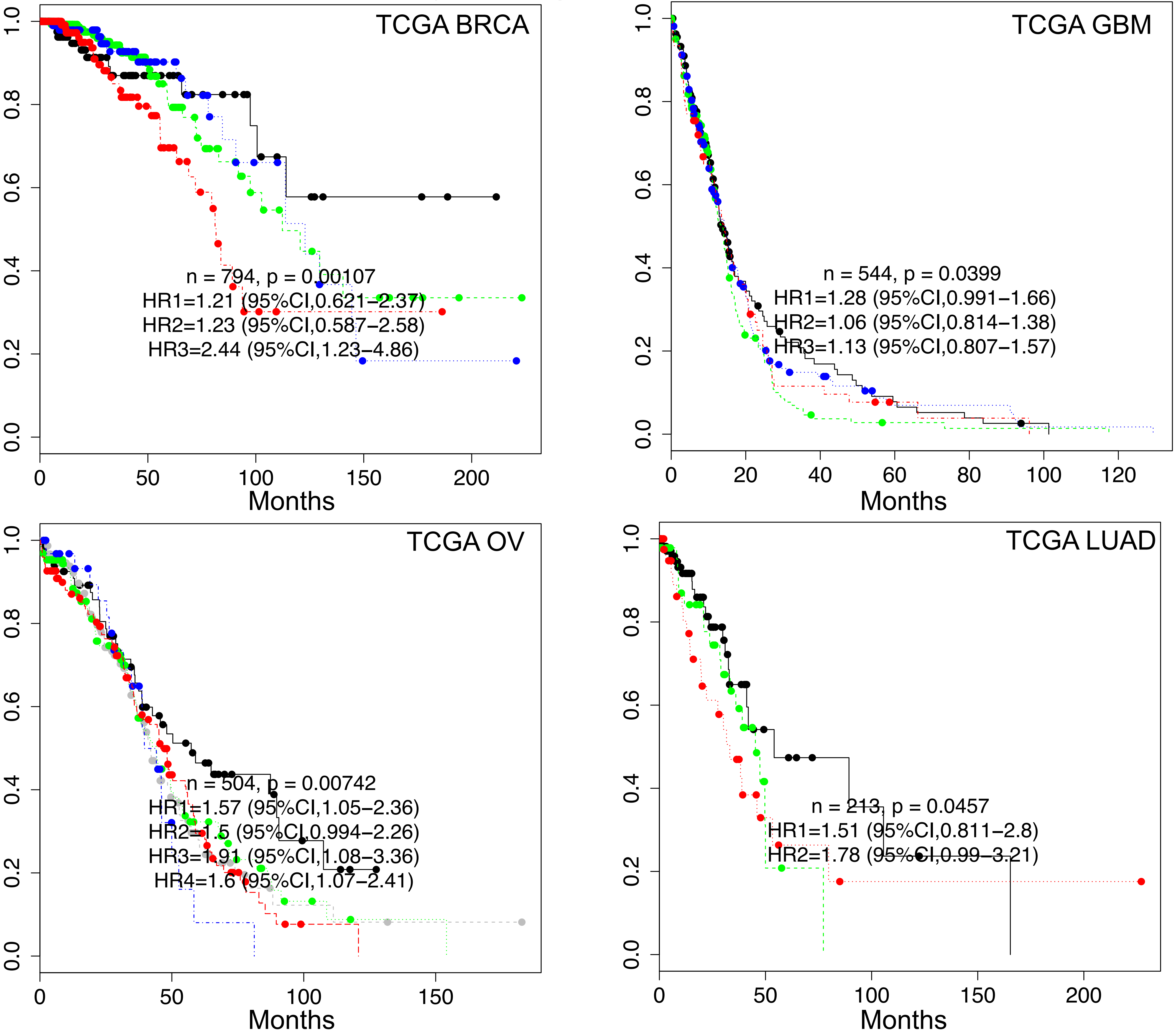
APLP1
DNAJB1
CDKN2C
RRM2
RRM2B
PTEN
RRM1

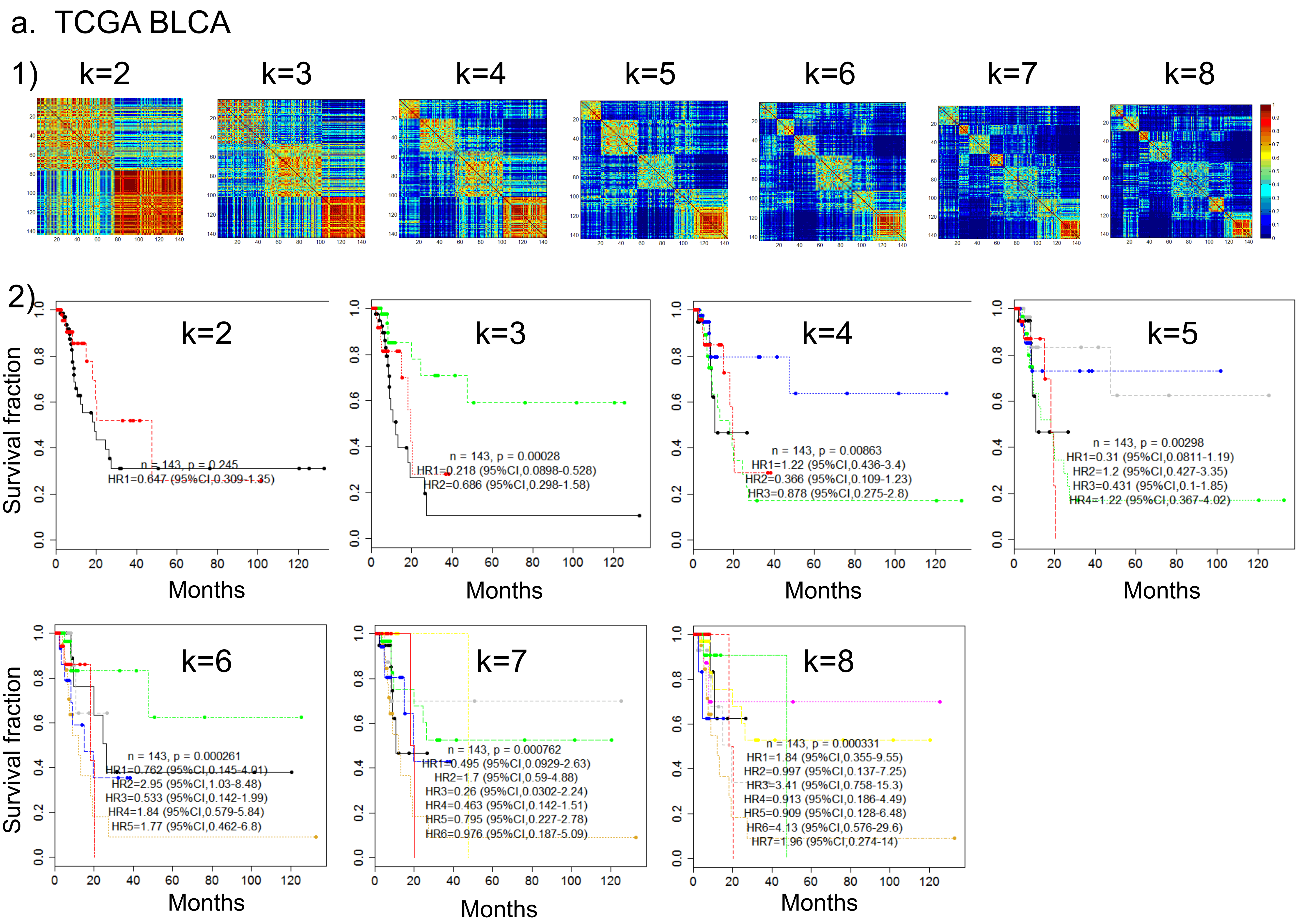

m
LGG
88% altered in patient samples
ACTC1
HSPB1
CAPN1
PPA1
NFKBIA
MAGEB18
ZHX1
VIM
YWHAZ
CHD3
SLC25A38
EGFR
ANXA3
CABLES1
TDRD7
EMG1
NPM1
TP53
CTSE
CDK5
EEF2
ACTA2
TACC1
RPS27A
AURKA
JUN
YEATS4
GNL3
YBX1
TOP1
PCNA
THAP8
PIN1
BRCA2
CDC25C
CCNB1
CHEK2
n
LUAD
70.8% altered in patient samples
ACTC1
HSPB1
CAPN1
PPA1
MAGEB18
NFKBIA
ZHX1
VIM
YWHAZ
CHD3
SLC25A38
EGFR
ANXA3
CABLES1
TDRD7
EMG1
NPM1
TP53
CTSE
CDK5
EEF2
ACTA2
TACC1
RPS27A
AURKA
JUN
YEATS4
GNL3
YBX1
TOP1
PCNA
THAP8
PIN1
BRCA2
CDC25C
CCNB1
CHEK2
o
OV
80.3% altered in patient samples
SLC25A38
CTSE
EMG1
EEF2
GNL3
NPM1
CCNB1
YBX1
TOP1
ACTA2
CHEK2
CDC25C
ANXA3
BRCA2
JUN
MAGEB18
PCNA
YWHAZ
PIN1
TP53
THAP8
RPS27A
EGFR
HSPB1
NFKBIA
CDK5
ZHX1
CHD3
PPA1
CAPN1
CABLES1
VIM
ACTC1
AURKA
TACC1
TDRD7
YEATS4
p
PRAD
48% altered in patient samples
CDC25C
CIB1
PLK3
CDC25A
CCNB1
CHEK1
PIN1
CHEK2
AP3B2
E2F1
USP40
DDB2
BRCA1
ATM
TIPARP
XRN2
TP53
MSH2
MDM4
MSH6
LMO4
BLM
RAD51


q
RASGRF1
RHOA
ARHGEF4
CCNG2
DVL3
PPP2CA
CCNG1
MAGEB18
GAK
EGFR
PPP2R5A
AXIN1
CDK5
YWHAZ
IQGAP1
CTNNB1
APC
CABLES1
TP53
EEF2
RPS27A
NPM
AXIN2
PTPN13
RP1
TDRD7
AURKA
TOP1
ACTA2
PCNA
TACC1
YBX1
GNL3
JUN
YEATS4
READ
72% altered in patient samples
r
KRT18
TCHP
PKP3
PKP2
KRT5
COL17A1
KRT14
DSC2
DSG2
DSC1
DSG1
PKP1
DST
JUP
DSP
SKCM
86.2% altered in patient samples
AHSA1
GCH1
AHSA2
HSP90AA1
APOB
TG
SP1
HSP90B1
HSPA8
ASGR1
HSPA1A
MTTP
NR3C1
BAG1
s
RASIP1
RAP1A
PIK3CD
PRKCI
PIK3CA
PDE6D
NTRK1
RASGRP1
SRC
PIK3R1
FES
HSPB1
TIAM1
RASA1
HRAS
RARRES3
KIT
VAV1
TGM1
CAV1
INSR
MDK
PLCE1
FYN
SEMG1
RASSF5
SHOC2
BCL2
THCA
65.3% altered in patient samples
Mutation frequency
80%
70%
60%
50%
40%
20%
10%
0%

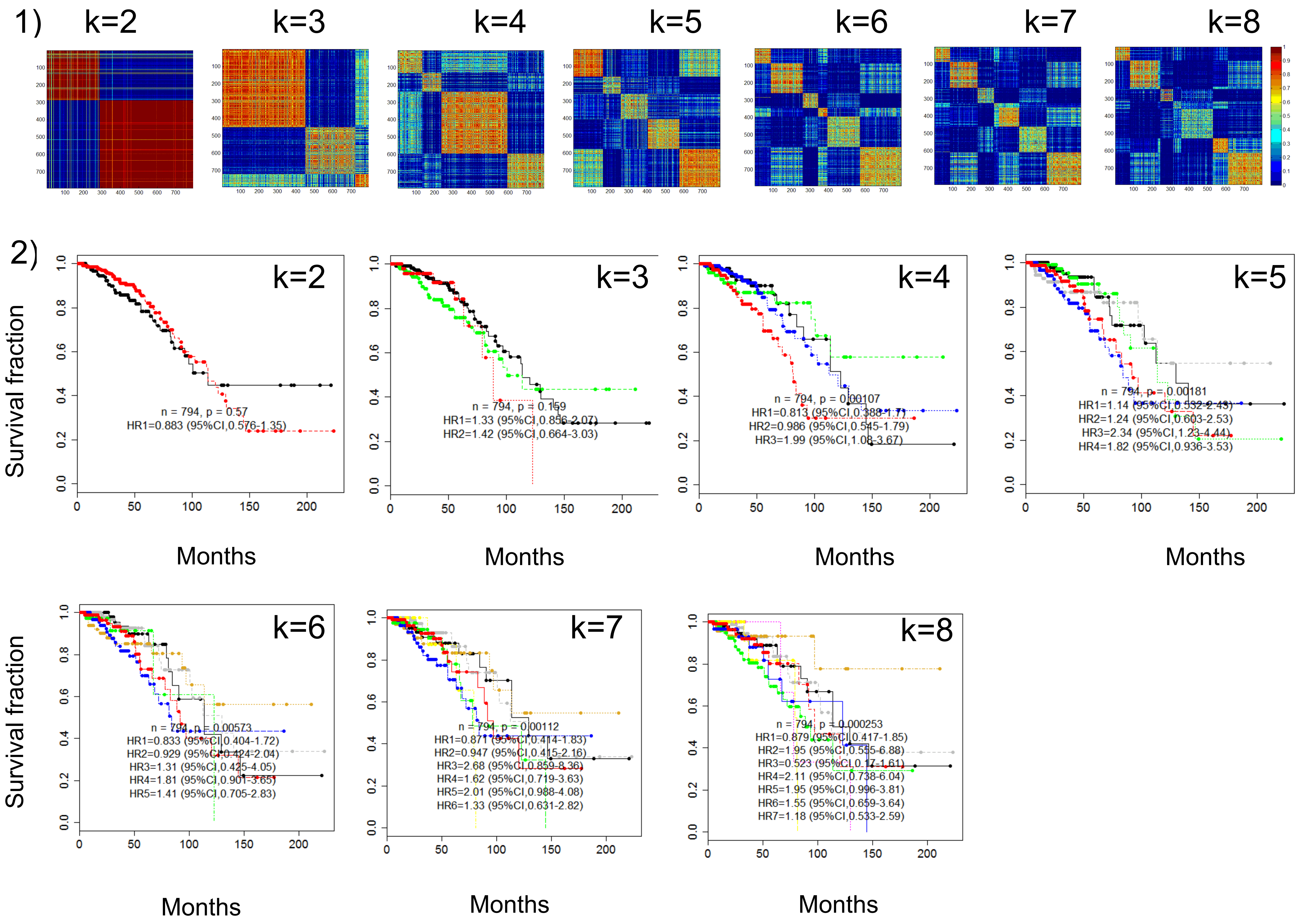
Supplementary Figure 2



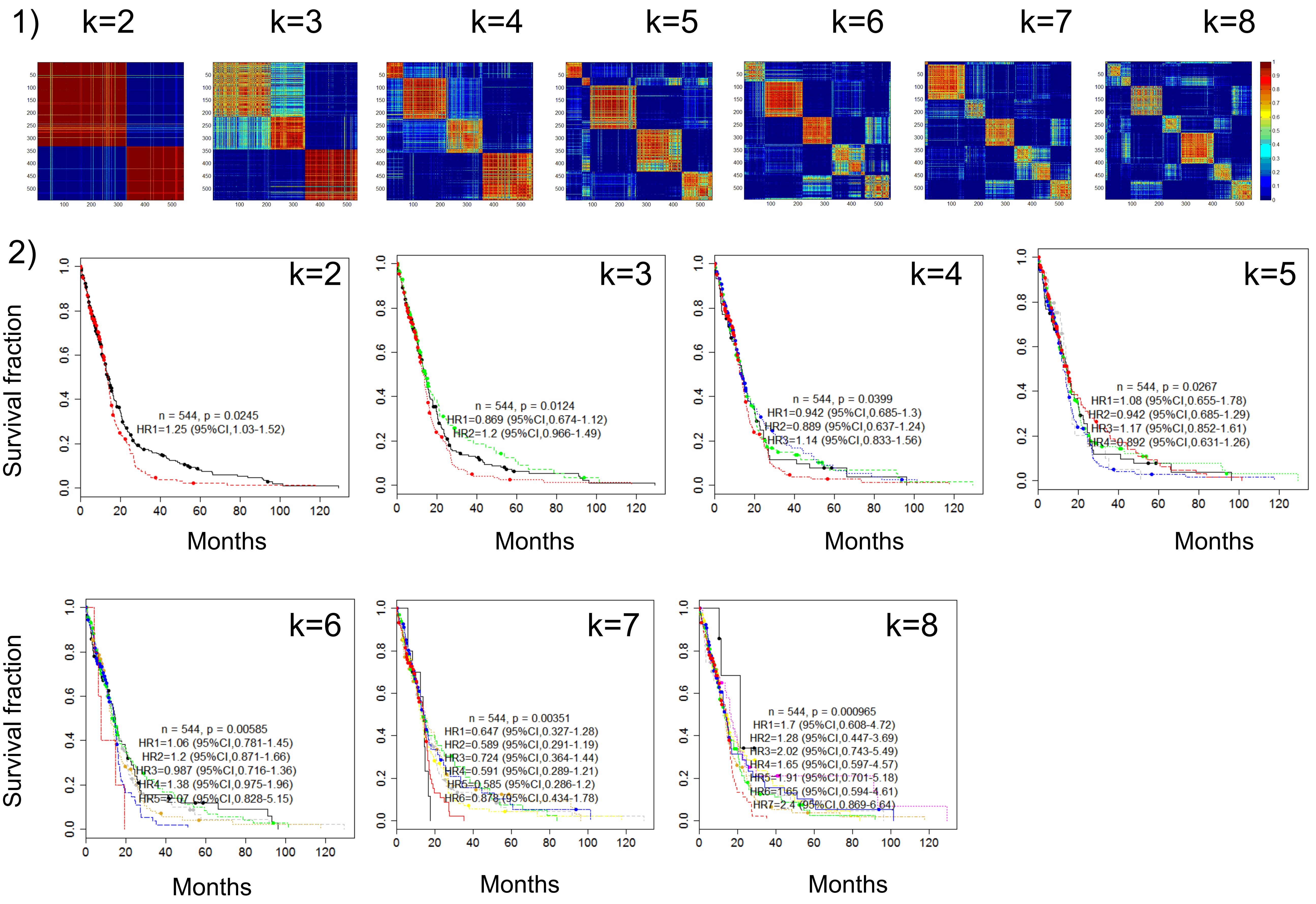
Supplementary Figure 3
KM plots


a. TCGA BLCA
1)
k=2
k=3
k=4
k=5
k=6
k=7
k=8
20
40
60
80
100
120
140
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
2)
Survival fraction
Months
0.0
0.2
0.4
0.6
0.8
1.0
0
20
40
60
80
100
120
k=2
n = 143, p = 0.245
HR1=0.647 (95%CI,0.309-1.35)
k=3
n = 143, p = 0.00028
HR1=0.218 (95%CI,0.0898-0.528)
HR2=0.686 (95%CI,0.298-1.58)
k=4
n = 143, p = 0.00863
HR1=1.22 (95%CI,0.436-3.4)
HR2=0.366 (95%CI,0.109-1.23)
HR3=0.878 (95%CI,0.275-2.8)
k=5
n = 143, p = 0.00298
HR1=0.31 (95%CI,0.0811-1.19)
HR2=1.2 (95%CI,0.427-3.35)
HR3=0.431 (95%CI,0.1-1.85)
HR4=1.22 (95%CI,0.367-4.02)
k=6
n = 143, p = 0.000261
HR1=0.762 (95%CI,0.145-4.01)
HR2=2.95 (95%CI,1.03-8.48)
HR3=0.533 (95%CI,0.142-1.99)
HR4=1.84 (95%CI,0.579-5.84)
HR5=1.77 (95%CI,0.462-6.8)
k=7
n = 143, p = 0.000762
HR1=0.495 (95%CI,0.0929-2.63)
HR2=1.7 (95%CI,0.59-4.88)
HR3=0.26 (95%CI,0.0302-2.24)
HR4=0.463 (95%CI,0.142-1.51)
HR5=0.795 (95%CI,0.227-2.78)
HR6=0.976 (95%CI,0.187-5.09)
k=8
n = 143, p = 0.000331
HR1=1.84 (95%CI,0.355-9.55)
HR2=0.997 (95%CI,0.137-7.25)
HR3=3.41 (95%CI,0.758-15.3)
HR4=0.913 (95%CI,0.186-4.49)
HR5=0.909 (95%CI,0.128-6.48)
HR6=4.13 (95%CI,0.576-29.6)
HR7=1.96 (95%CI,0.274-14)

b. TCGA BRCA

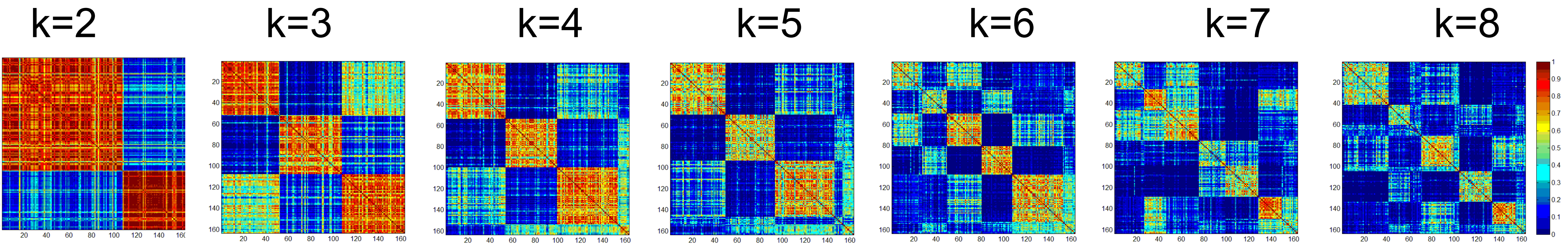

1)
k=2
k=3
k=4
k=5
k=6
k=7
k=8
100
200
300
400
500
600
700
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
2)
Survival fraction
Months
0.0
0.2
0.4
0.6
0.8
1.0
0
50
100
150
200
k=2
n = 794, p = 0.57
HR1=0.883 (95%CI,0.576-1.35)
k=3
n = 794, p = 0.159
HR1=1.33 (95%CI,0.856-2.07)
HR2=1.42 (95%CI,0.664-3.03)
k=4
n = 794, p = 0.00107
HR1=0.813 (95%CI,0.388-1.71)
HR2=0.986 (95%CI,0.545-1.79)
HR3=1.99 (95%CI,1.08-3.67)
k=5
n = 794, p = 0.00181
HR1=1.14 (95%CI,0.532-2.43)
HR2=1.24 (95%CI,0.603-2.53)
HR3=2.34 (95%CI,1.23-4.44)
HR4=1.82 (95%CI,0.936-3.53)
k=6
n = 794, p = 0.00573
HR1=0.833 (95%CI,0.404-1.72)
HR2=0.929 (95%CI,0.424-2.04)
HR3=1.31 (95%CI,0.425-4.05)
HR4=1.81 (95%CI,0.901-3.65)
HR5=1.41 (95%CI,0.705-2.83)
k=7
n = 794, p = 0.00112
HR1=0.871 (95%CI,0.414-1.83)
HR2=0.947 (95%CI,0.415-2.16)
HR3=2.68 (95%CI,0.859-8.36)
HR4=1.62 (95%CI,0.719-3.63)
HR5=2.01 (95%CI,0.988-4.08)
HR6=1.33 (95%CI,0.631-2.82)
k=8
n = 794, p = 0.000253
HR1=0.879 (95%CI,0.417-1.85)
HR2=1.95 (95%CI,0.555-6.88)
HR3=0.523 (95%CI,0.17-1.61)
HR4=2.11 (95%CI,0.738-6.04)
HR5=1.95 (95%CI,0.996-3.81)
HR6=1.55 (95%CI,0.659-3.64)
HR7=1.18 (95%CI,0.533-2.59)

c. TCGA GBM

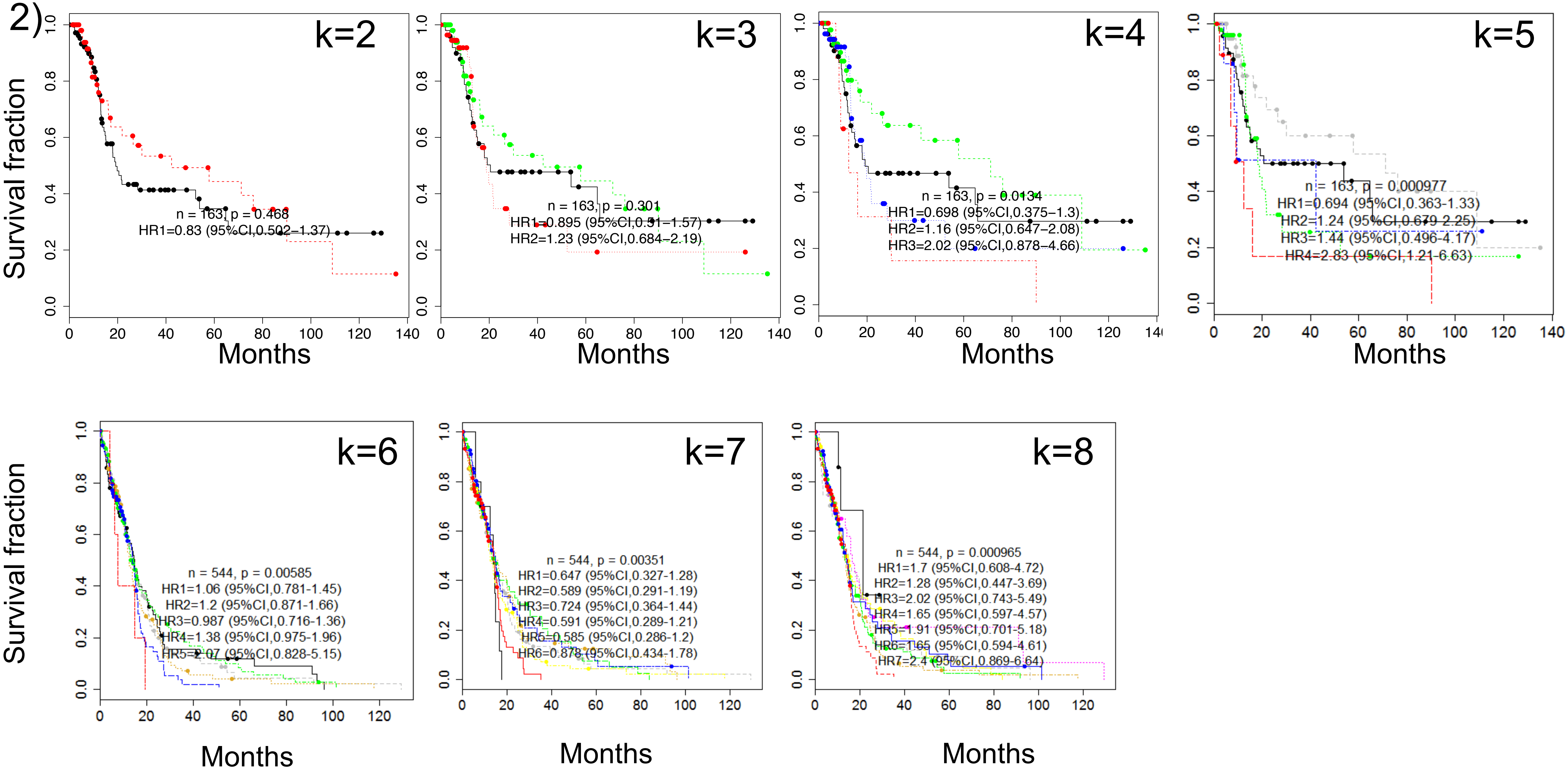

1)
k=2
k=3
k=4
k=5
k=6
k=7
k=8
50
100
150
200
250
300
350
400
450
500
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
2)
Survival fraction
Months
0.0
0.2
0.4
0.6
0.8
1.0
0
20
40
60
80
100
120
k=2
n = 544, p = 0.0245
HR1=1.25 (95%CI,1.03-1.52)
k=3
n = 544, p = 0.0124
HR1=0.869 (95%CI,0.674-1.12)
HR2=1.2 (95%CI,0.966-1.49)
k=4
n = 544, p = 0.0399
HR1=0.942 (95%CI,0.685-1.3)
HR2=0.889 (95%CI,0.637-1.24)
HR3=1.14 (95%CI,0.833-1.56)
k=5
n = 544, p = 0.0267
HR1=1.08 (95%CI,0.655-1.78)
HR2=0.942 (95%CI,0.685-1.29)
HR3=1.17 (95%CI,0.852-1.61)
HR4=0.892 (95%CI,0.631-1.26)
k=6
n = 544, p = 0.00585
HR1=1.06 (95%CI,0.781-1.45)
HR2=1.2 (95%CI,0.871-1.66)
HR3=0.987 (95%CI,0.716-1.36)
HR4=1.38 (95%CI,0.975-1.96)
HR5=2.07 (95%CI,0.828-5.15)
k=7
n = 544, p = 0.00351
HR1=0.647 (95%CI,0.327-1.28)
HR2=0.589 (95%CI,0.291-1.19)
HR3=0.724 (95%CI,0.364-1.44)
HR4=0.591 (95%CI,0.289-1.21)
HR5=0.585 (95%CI,0.286-1.2)
HR6=0.878 (95%CI,0.434-1.78)
k=8
n = 544, p = 0.000965
HR1=1.7 (95%CI,0.608-4.72)
HR2=1.28 (95%CI,0.447-3.69)
HR3=2.02 (95%CI,0.743-5.49)
HR4=1.65 (95%CI,0.597-4.57)
HR5=1.91 (95%CI,0.701-5.18)
HR6=1.65 (95%CI,0.594-4.61)
HR7=2.4 (95%CI,0.869-6.64)

d.TCGA HNSC

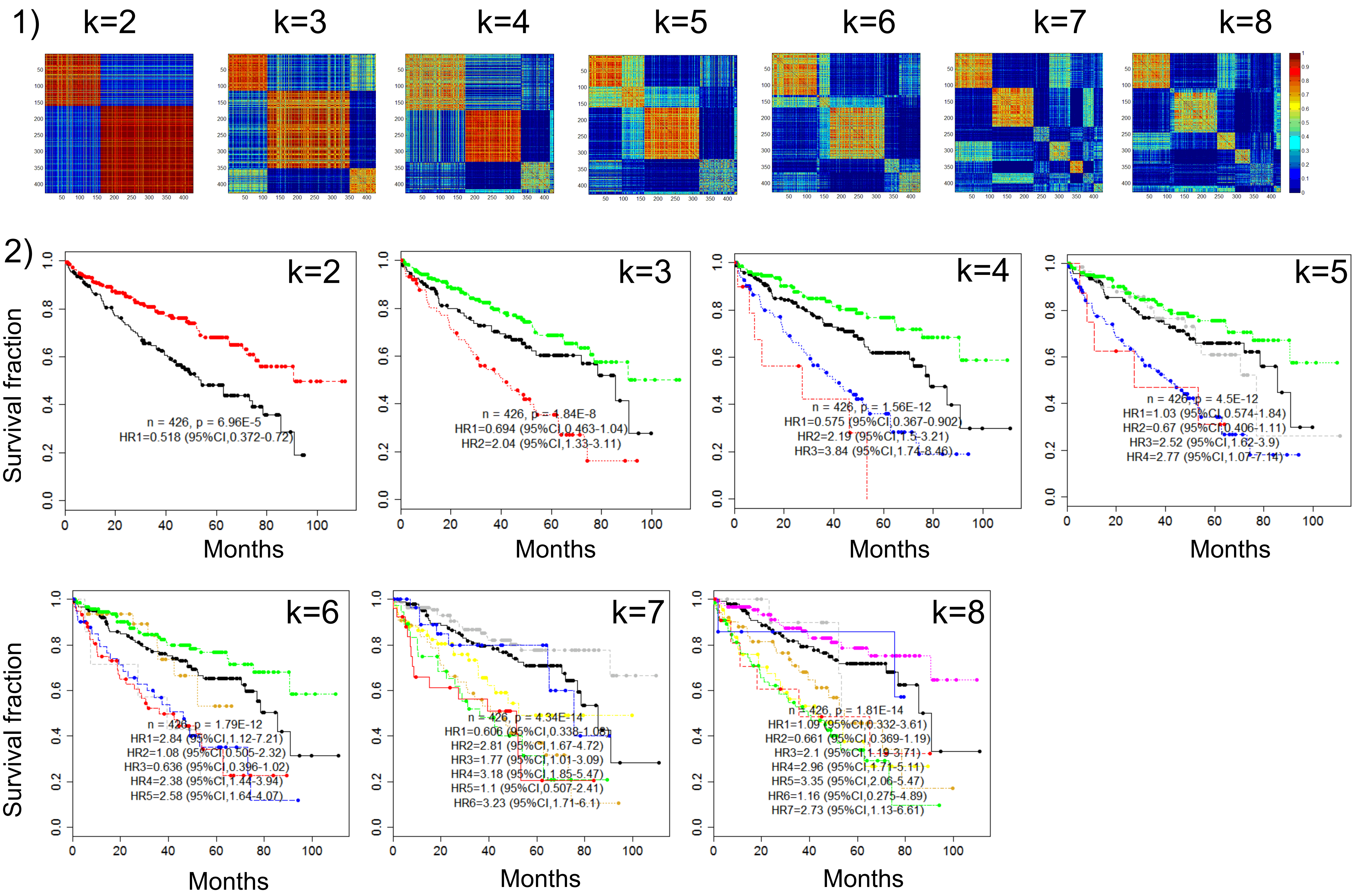
1)



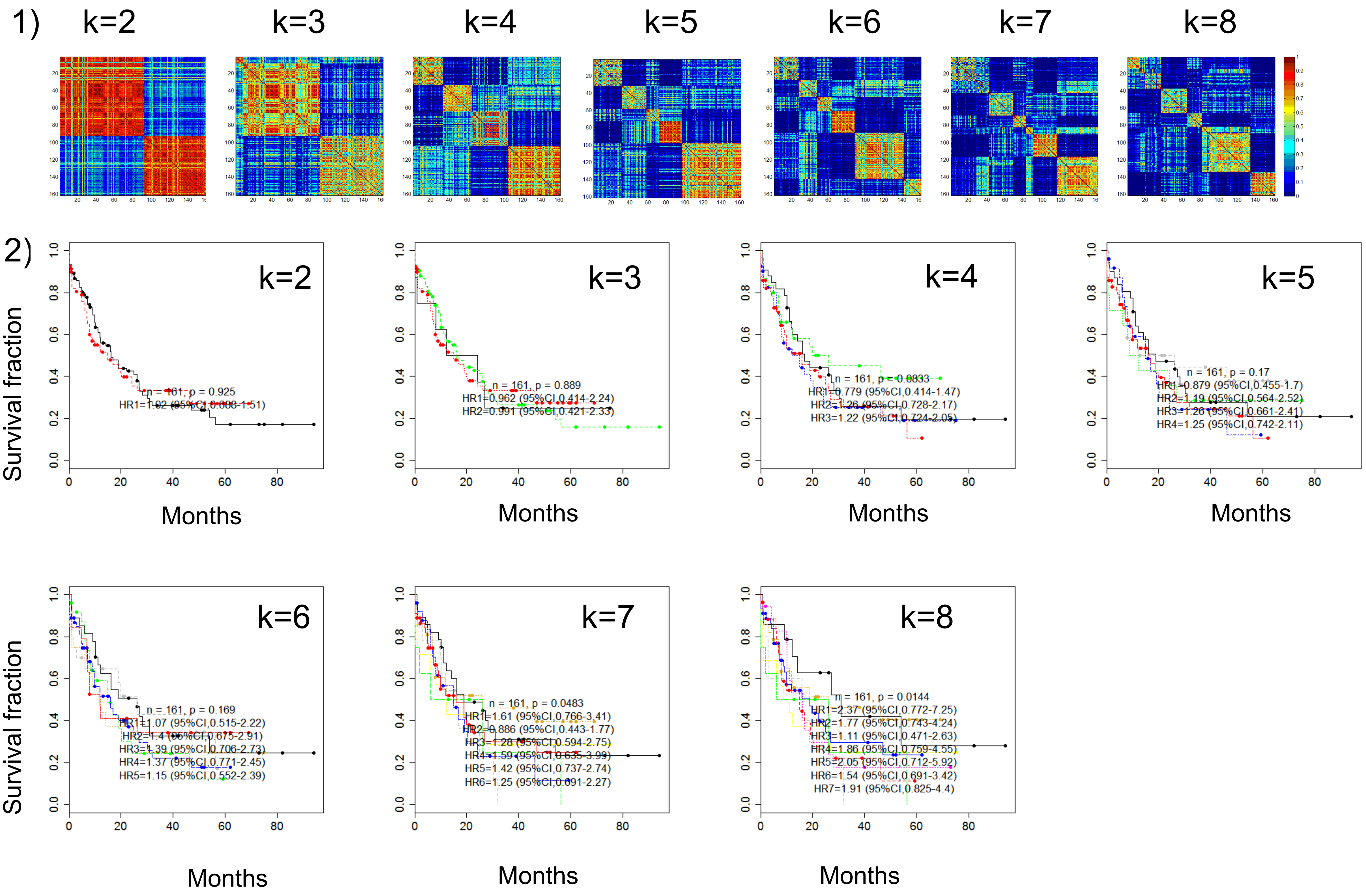
2)



e. TCGA KIRC

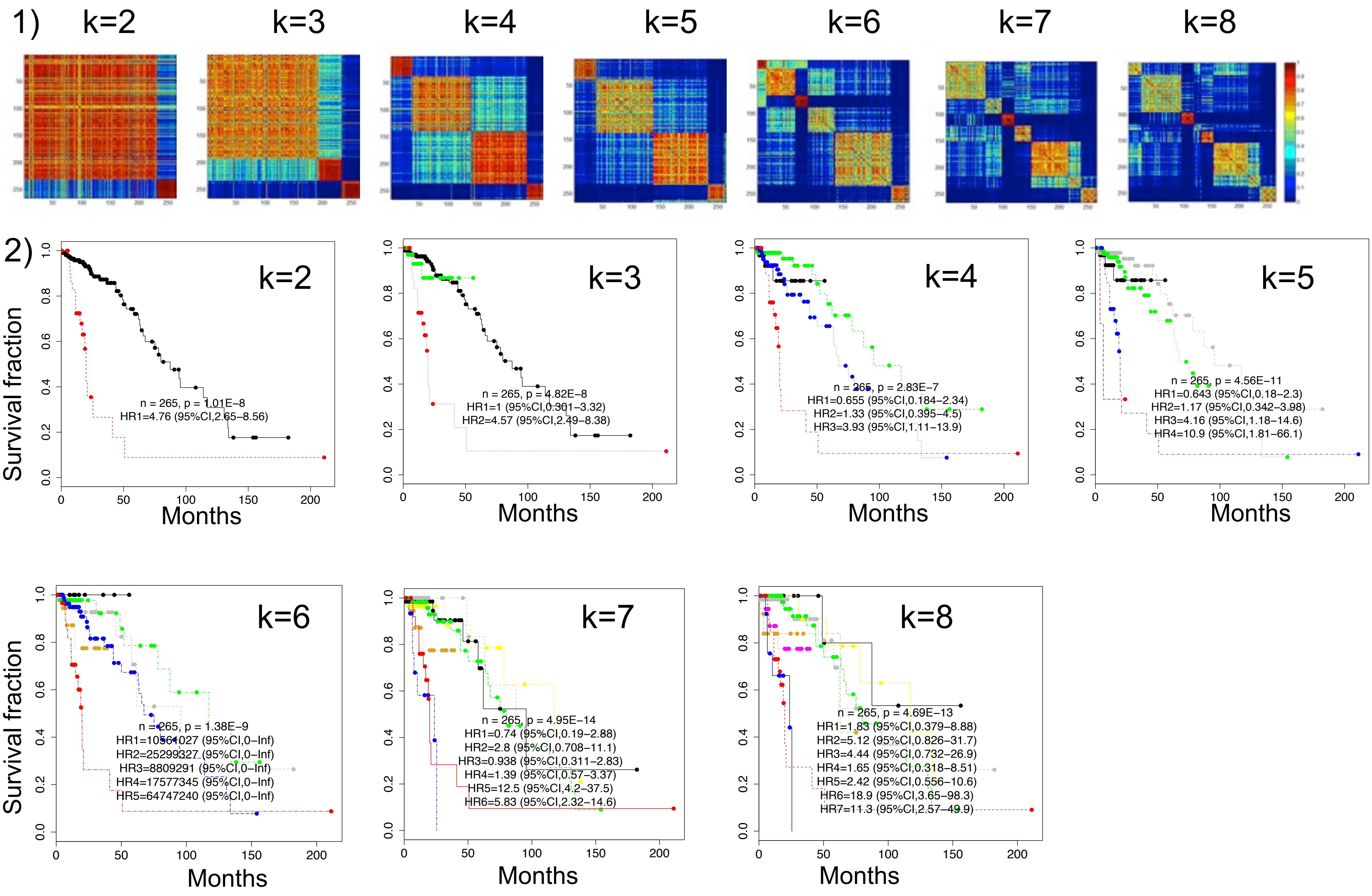

1)
k=2
k=3
k=4
k=5
k=6
k=7
k=8
2)
Survival fraction
Months
k=2
n = 426, p = 6.96E-5
HR1=0.518 (95%CI,0.372-0.72)
k=3
n = 426, p = 4.84E-8
HR1=0.694 (95%CI,0.463-1.04)
HR2=2.04 (95%CI,1.33-3.11)
k=4
n = 426, p = 1.56E-12
HR1=0.575 (95%CI,0.367-0.902)
HR2=2.19 (95%CI,1.5-3.21)
HR3=3.84 (95%CI,1.74-8.46)
k=5
n = 426, p = 4.5E-12
HR1=1.03 (95%CI,0.574-1.84)
HR2=0.67 (95%CI,0.406-1.11)
HR3=2.52 (95%CI,1.62-3.9)
HR4=2.77 (95%CI,1.07-7.14)
k=6
n = 426, p = 1.79E-12
HR1=2.84 (95%CI,1.12-7.21)
HR2=1.08 (95%CI,0.505-2.32)
HR3=0.636 (95%CI,0.396-1.02)
HR4=2.38 (95%CI,1.44-3.94)
HR5=2.58 (95%CI,1.64-4.07)
k=7
n = 426, p = 4.34E-14
HR1=0.606 (95%CI,0.338-1.08)
HR2=2.81 (95%CI,1.67-4.72)
HR3=1.77 (95%CI,1.01-3.09)
HR4=3.18 (95%CI,1.85-5.47)
HR5=1.1 (95%CI,0.507-2.41)
HR6=3.23 (95%CI,1.71-6.1)
k=8
n = 426, p = 1.81E-14
HR1=1.09 (95%CI,0.332-3.61)
HR2=0.661 (95%CI,0.369-1.19)
HR3=2.1 (95%CI,1.19-3.71)
HR4=2.96 (95%CI,1.71-5.11)
HR5=3.35 (95%CI,2.06-5.47)
HR6=1.16 (95%CI,0.275-4.89)
HR7=2.73 (95%CI,1.13-6.61)

f. TCGA LAML



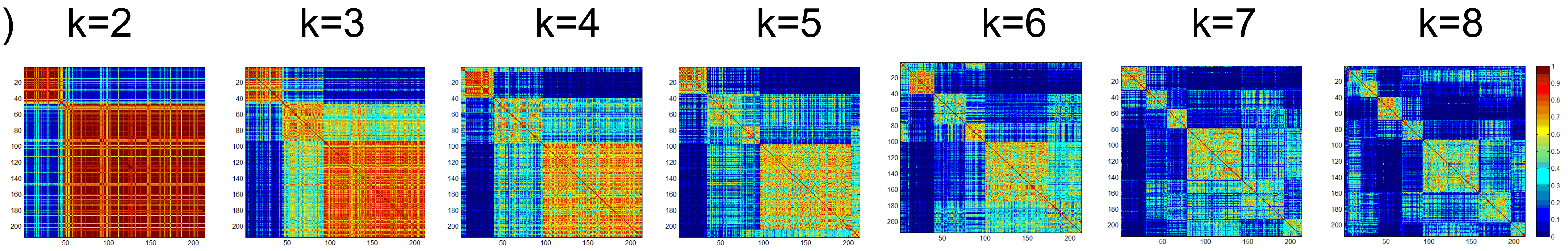
1)
k=2
k=3
k=4
k=5
k=6
k=7
k=8
2)
Survival fraction
Months
k=2
n = 161, p = 0.925
HR1=1.02 (95%CI,0.688-1.51)
k=3
n = 161, p = 0.889
HR1=0.962 (95%CI,0.414-2.24)
HR2=0.991 (95%CI,0.421-2.33)
k=4
n = 161, p = 0.0833
HR1=0.779 (95%CI,0.414-1.47)
HR2=1.26 (95%CI,0.728-2.17)
HR3=1.22 (95%CI,0.724-2.05)
k=5
n = 161, p = 0.17
HR1=0.879 (95%CI,0.455-1.7)
HR2=1.19 (95%CI,0.564-2.52)
HR3=1.26 (95%CI,0.661-2.41)
HR4=1.25 (95%CI,0.742-2.11)
k=6
n = 161, p = 0.169
HR1=1.07 (95%CI,0.515-2.22)
HR2=1.4 (95%CI,0.675-2.91)
HR3=1.39 (95%CI,0.706-2.73)
HR4=1.37 (95%CI,0.771-2.45)
HR5=1.15 (95%CI,0.552-2.39)
k=7
n = 161, p = 0.0483
HR1=1.61 (95%CI,0.766-3.41)
HR2=0.886 (95%CI,0.443-1.77)
HR3=1.28 (95%CI,0.594-2.75)
HR4=1.59 (95%CI,0.635-3.99)
HR5=1.42 (95%CI,0.737-2.74)
HR6=1.25 (95%CI,0.691-2.27)
k=8
n = 161, p = 0.0144
HR1=2.37 (95%CI,0.772-7.25)
HR2=1.77 (95%CI,0.743-4.24)
HR3=1.11 (95%CI,0.471-2.63)
HR4=1.86 (95%CI,0.759-4.55)
HR5=2.05 (95%CI,0.712-5.92)
HR6=1.54 (95%CI,0.691-3.42)
HR7=1.91 (95%CI,0.825-4.4)
0.0
0.2
0.4
0.6
0.8
1.0
0
20
40
60
80

g. TCGA LGG

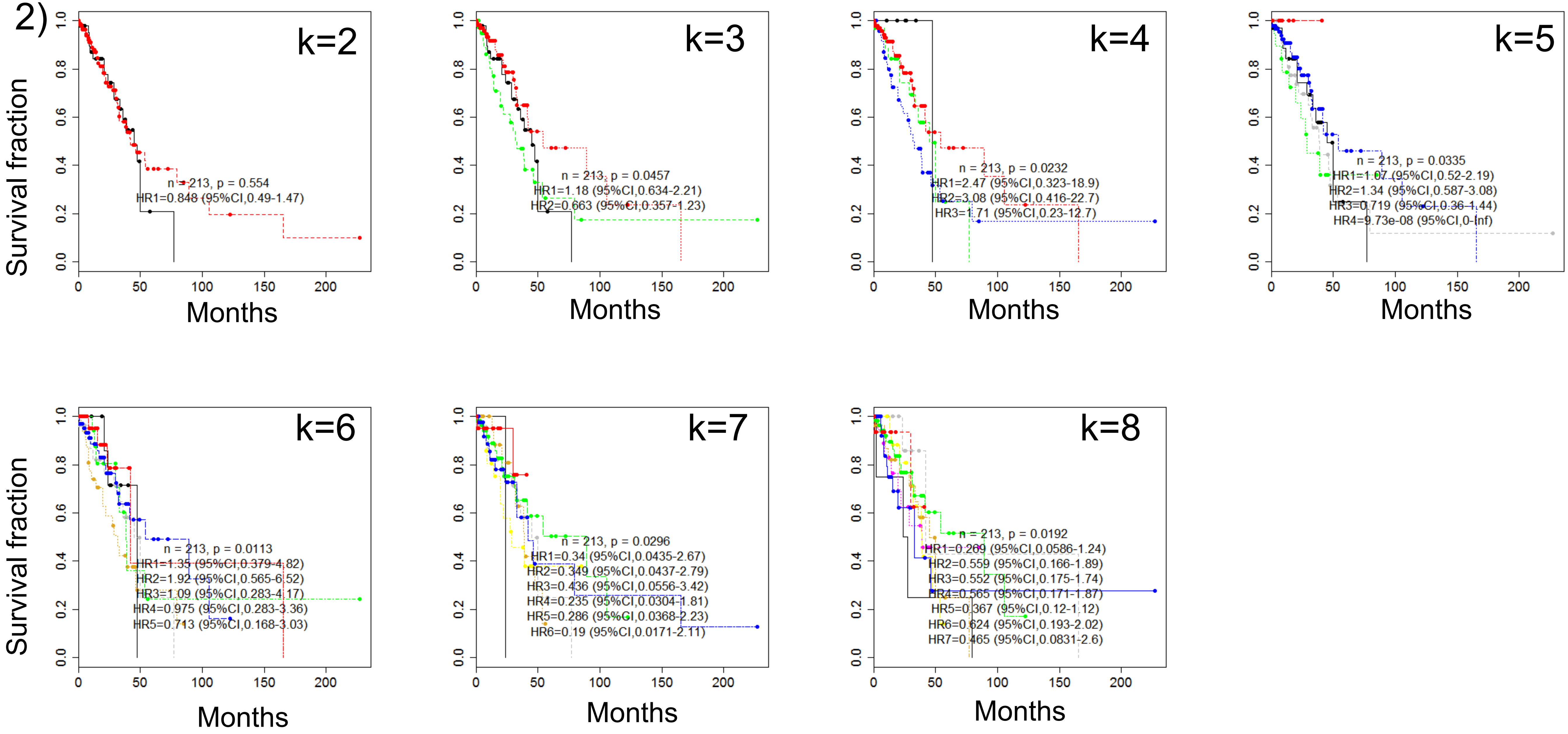

1)
k=2
k=3
k=4
k=5
k=6
k=7
k=8
2)
Survival fraction
Months
k=2
n = 265, p = 1.01E−8
HR1=4.76 (95%CI,2.65−8.56)
k=3
n = 265, p = 4.82E−8
HR1=1 (95%CI,0.301−3.32)
HR2=4.57 (95%CI,2.49−8.38)
k=4
n = 265, p = 2.83E−7
HR1=0.655 (95%CI,0.184−2.34)
HR2=1.33 (95%CI,0.395−4.5)
HR3=3.93 (95%CI,1.11−13.9)
k=5
n = 265, p = 4.56E−11
HR1=0.643 (95%CI,0.18−2.3)
HR2=1.17 (95%CI,0.342−3.98)
HR3=4.16 (95%CI,1.18−14.6)
HR4=10.9 (95%CI,1.81−66.1)
k=6
n = 265, p = 1.38E−9
HR1=10564027 (95%CI,0−Inf)
HR2=25299327 (95%CI,0−Inf)
HR3=8809291 (95%CI,0−Inf)
HR4=17577345 (95%CI,0−Inf)
HR5=64747240 (95%CI,0−Inf)
k=7
n = 265, p = 4.95E−14
HR1=0.74 (95%CI,0.19−2.88)
HR2=2.8 (95%CI,0.708−11.1)
HR3=0.938 (95%CI,0.311−2.83)
HR4=1.39 (95%CI,0.57−3.37)
HR5=12.5 (95%CI,4.2−37.5)
HR6=5.83 (95%CI,2.32−14.6)
k=8
n = 265, p = 4.69E−13
HR1=1.83 (95%CI,0.379−8.88)
HR2=5.12 (95%CI,0.826−31.7)
HR3=4.44 (95%CI,0.732−26.9)
HR4=1.65 (95%CI,0.318−8.51)
HR5=2.42 (95%CI,0.556−10.6)
HR6=18.9 (95%CI,3.65−98.3)
HR7=11.3 (95%CI,2.57−49.9)
0.0
0.2
0.4
0.6
0.8
1.0
0
50
100
150
200

h.TCGA LUAD

1)

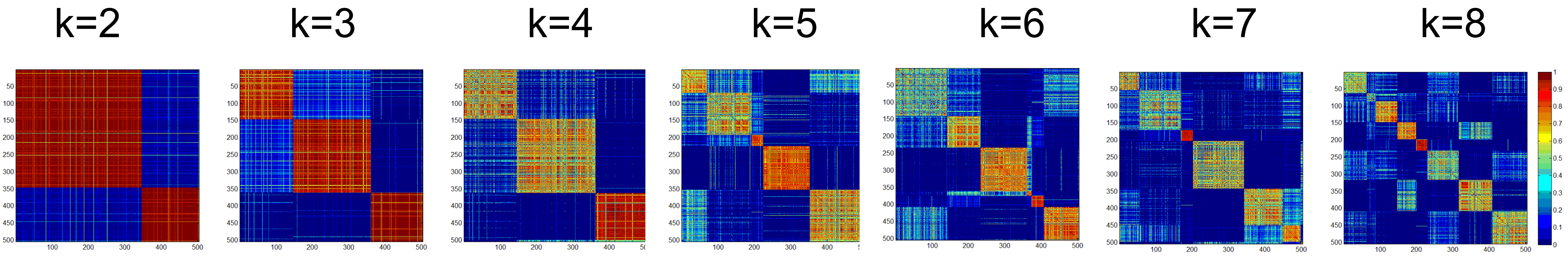


2)

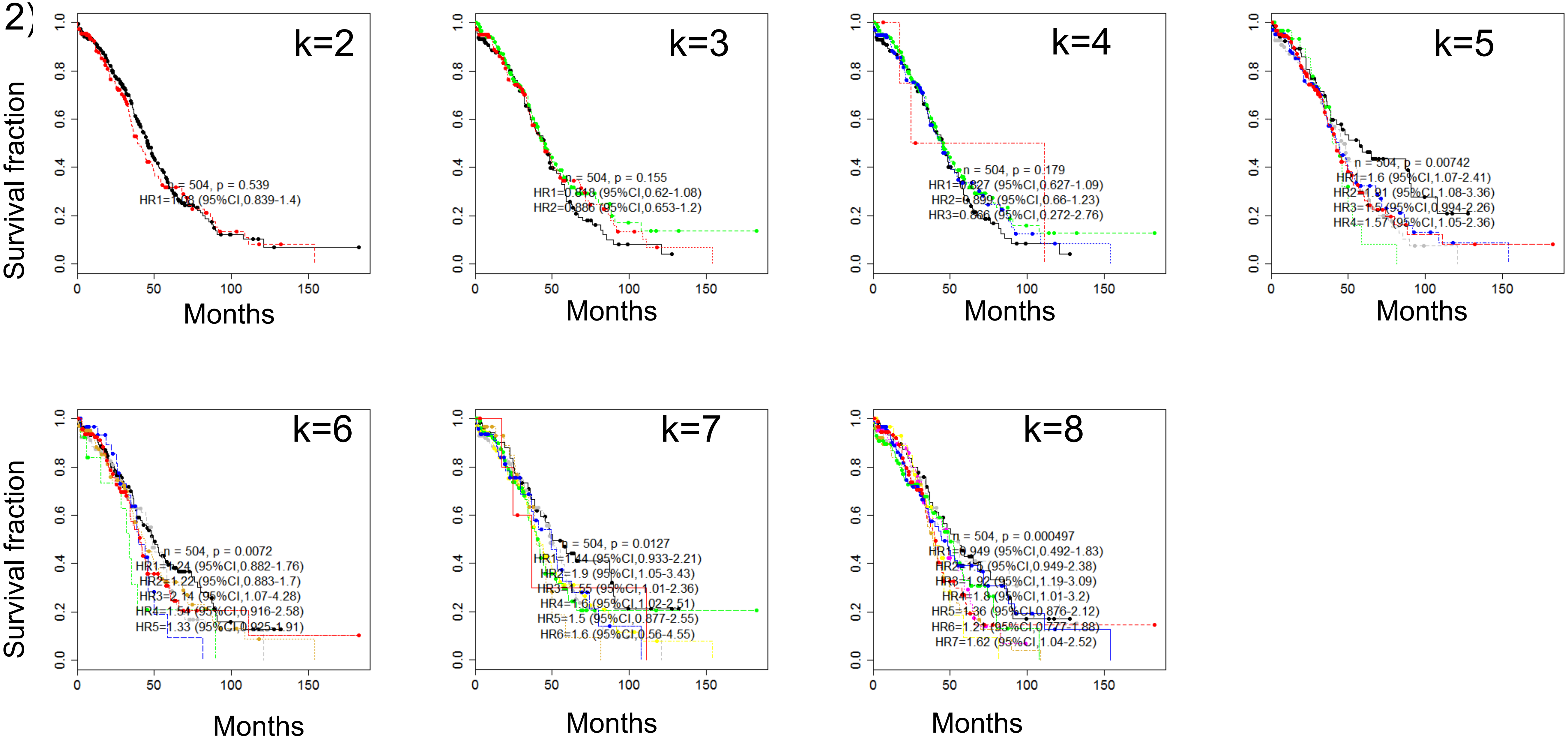


i. TCGA OV

1)

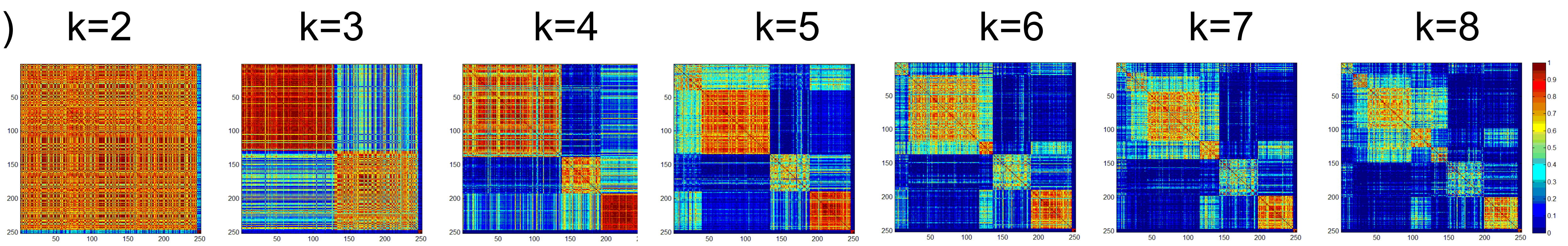

k=2
k=3
k=4
k=5
k=6
k=7
k=8
50
100
150
200
250
300
350
400
450
500
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1

2)

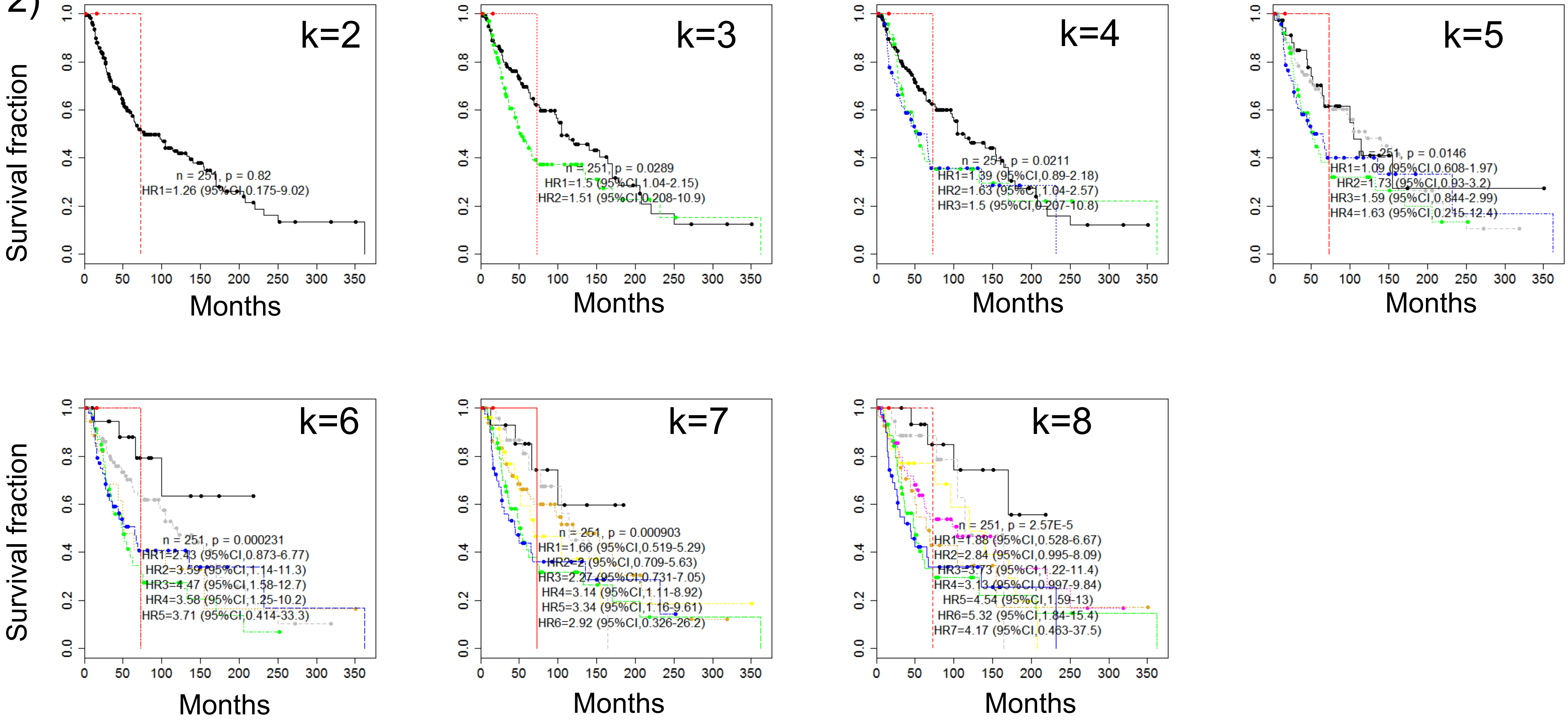

Survival fraction
k=2
n = 504, p = 0.539
HR1=1.08 (95%CI,0.839-1.4)
k=3
n = 504, p = 0.155
HR1=0.818 (95%CI,0.62-1.08)
HR2=0.886 (95%CI,0.653-1.2)
k=4
n = 504, p = 0.179
HR1=0.827 (95%CI,0.627-1.09)
HR2=0.899 (95%CI,0.66-1.23)
HR3=0.866 (95%CI,0.272-2.76)
k=5
n = 504, p = 0.00742
HR1=1.6 (95%CI,1.07-2.41)
HR2=1.91 (95%CI,1.08-3.36)
HR3=1.5 (95%CI,0.994-2.26)
HR4=1.57 (95%CI,1.05-2.36)
Months
k=6
n = 504, p = 0.0072
HR1=1.24 (95%CI,0.882-1.76)
HR2=1.22 (95%CI,0.883-1.7)
HR3=2.14 (95%CI,1.07-4.28)
HR4=1.54 (95%CI,0.916-2.58)
HR5=1.33 (95%CI,0.925-1.91)
k=7
n = 504, p = 0.0127
HR1=1.44 (95%CI,0.933-2.21)
HR2=1.9 (95%CI,1.05-3.43)
HR3=1.55 (95%CI,1.01-2.36)
HR4=1.6 (95%CI,1.02-2.51)
HR5=1.5 (95%CI,0.877-2.55)
HR6=1.6 (95%CI,0.56-4.55)
k=8
n = 504, p = 0.000497
HR1=0.949 (95%CI,0.492-1.83)
HR2=1.5 (95%CI,0.949-2.38)
HR3=1.92 (95%CI,1.19-3.09)
HR4=1.8 (95%CI,1.01-3.2)
HR5=1.36 (95%CI,0.876-2.12)
HR6=1.21 (95%CI,0.777-1.88)
HR7=1.62 (95%CI,1.04-2.52)
0.0
0.2
0.4
0.6
0.8
1.0
0
50
100
150
Months

j.TCGA SKCM

1)

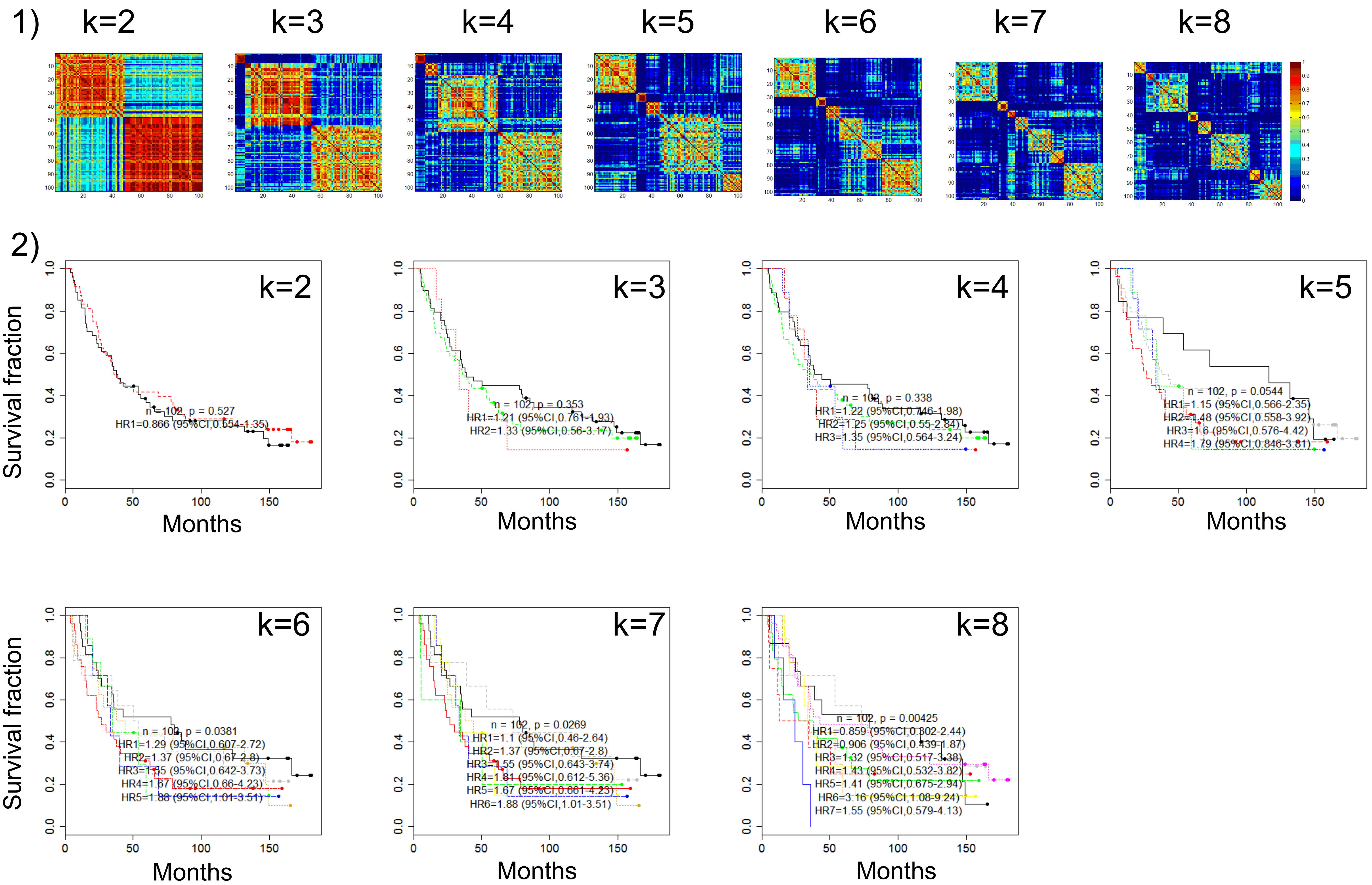


2)

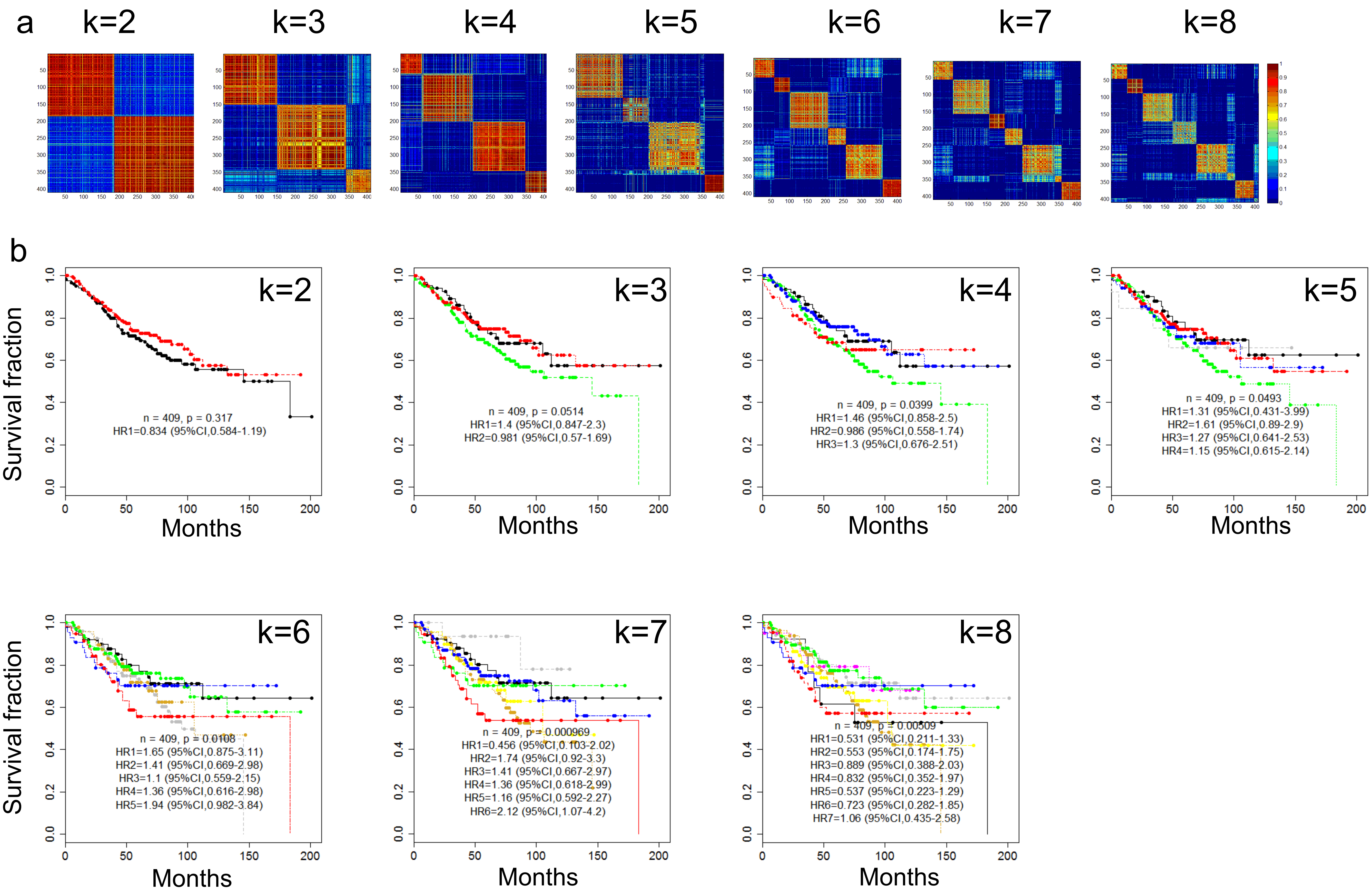


Supplementary Figure 4
Independent dataset

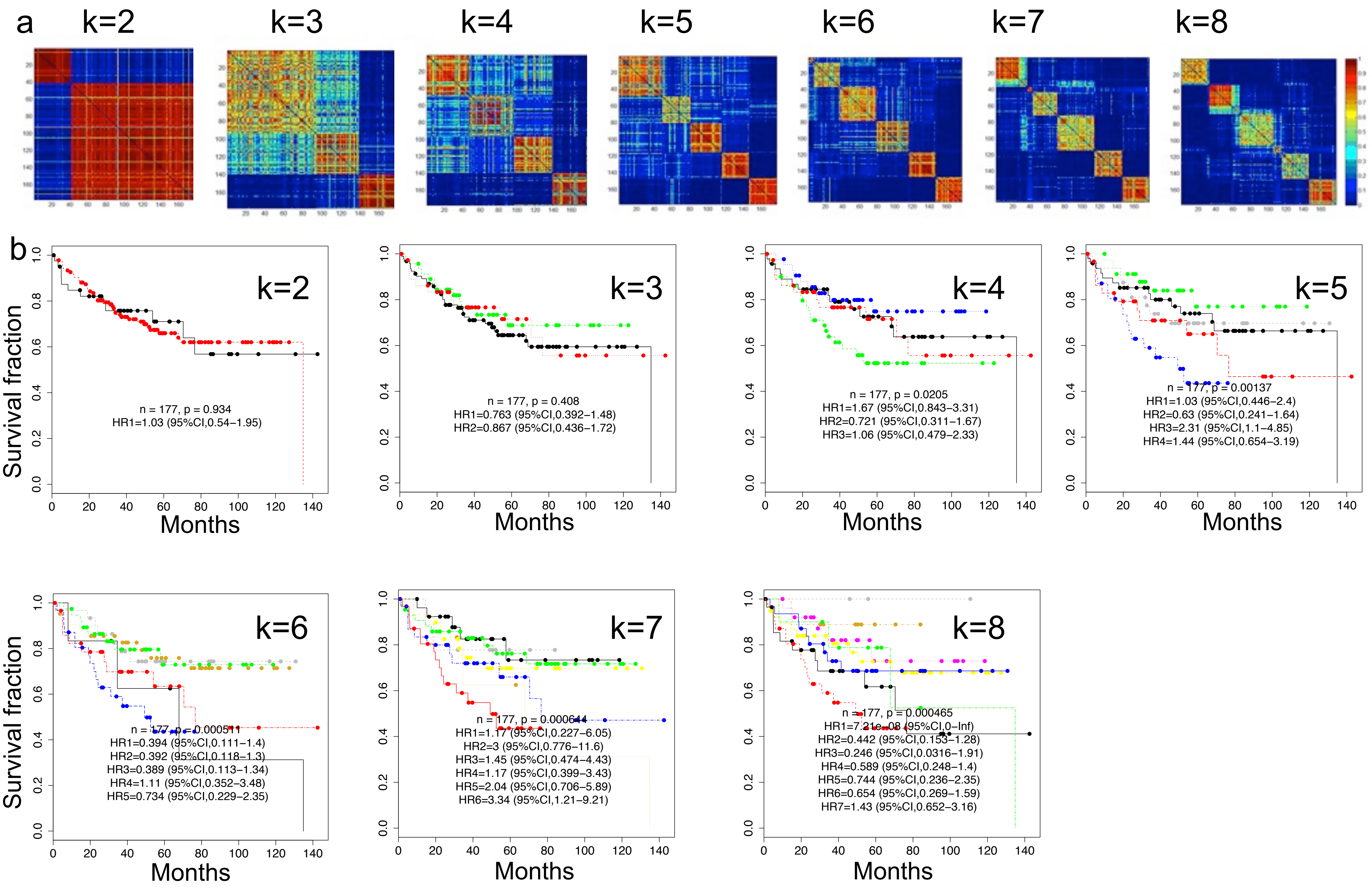
a. UTSW HNSC


1)
k=2
k=3
k=4
k=5
k=6
k=7
k=8
10
20
30
40
50
60
70
80
90
100
20
40
60
80
100
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
2)
Survival fraction
Months
0.0
0.2
0.4
0.6
0.8
1.0
0
50
100
150
k=2
n = 102, p = 0.527
HR1=0.866 (95%CI,0.554-1.35)
k=3
n = 102, p = 0.353
HR1=1.21 (95%CI,0.761-1.93)
HR2=1.33 (95%CI,0.56-3.17)
k=4
n = 102, p = 0.338
HR1=1.22 (95%CI,0.746-1.98)
HR2=1.25 (95%CI,0.55-2.84)
HR3=1.35 (95%CI,0.564-3.24)
k=5
n = 102, p = 0.0544
HR1=1.15 (95%CI,0.566-2.35)
HR2=1.48 (95%CI,0.558-3.92)
HR3=1.6 (95%CI,0.576-4.42)
HR4=1.79 (95%CI,0.846-3.81)
k=6
n = 102, p = 0.0381
HR1=1.29 (95%CI,0.607-2.72)
HR2=1.37 (95%CI,0.67-2.8)
HR3=1.55 (95%CI,0.642-3.73)
HR4=1.67 (95%CI,0.66-4.23)
HR5=1.88 (95%CI,1.01-3.51)
k=7
n = 102, p = 0.0269
HR1=1.1 (95%CI,0.46-2.64)
HR2=1.37 (95%CI,0.67-2.8)
HR3=1.55 (95%CI,0.643-3.74)
HR4=1.81 (95%CI,0.612-5.36)
HR5=1.67 (95%CI,0.661-4.23)
HR6=1.88 (95%CI,1.01-3.51)
k=8
n = 102, p = 0.00425
HR1=0.859 (95%CI,0.302-2.44)
HR2=0.906 (95%CI,0.439-1.87)
HR3=1.32 (95%CI,0.517-3.38)
HR4=1.43 (95%CI,0.532-3.82)
HR5=1.41 (95%CI,0.675-2.94)
HR6=3.16 (95%CI,1.08-9.24)
HR7=1.55 (95%CI,0.579-4.13)

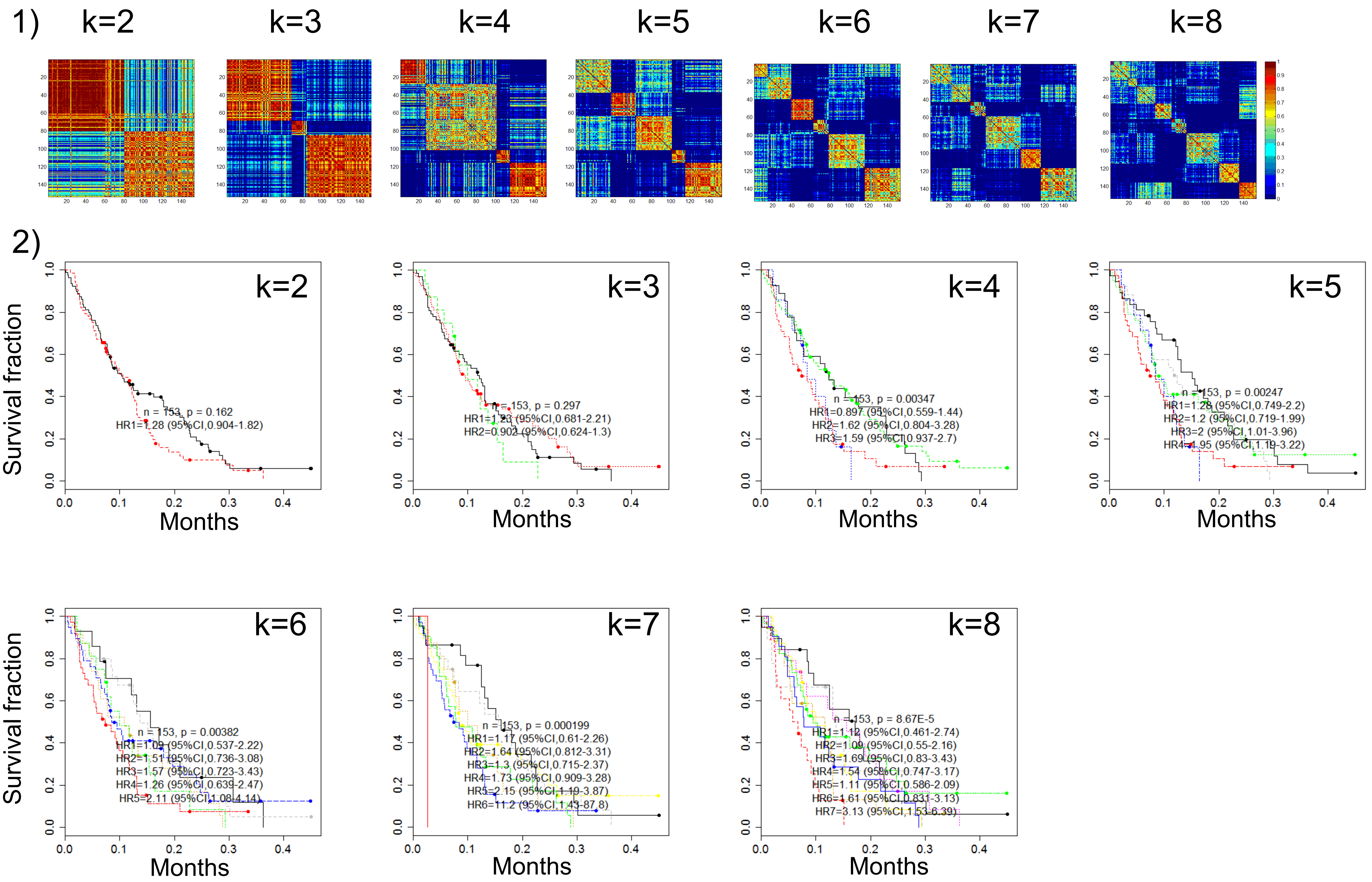
b.Colon cancer (GSE39582)



b.Colon cancer (GSE17538)

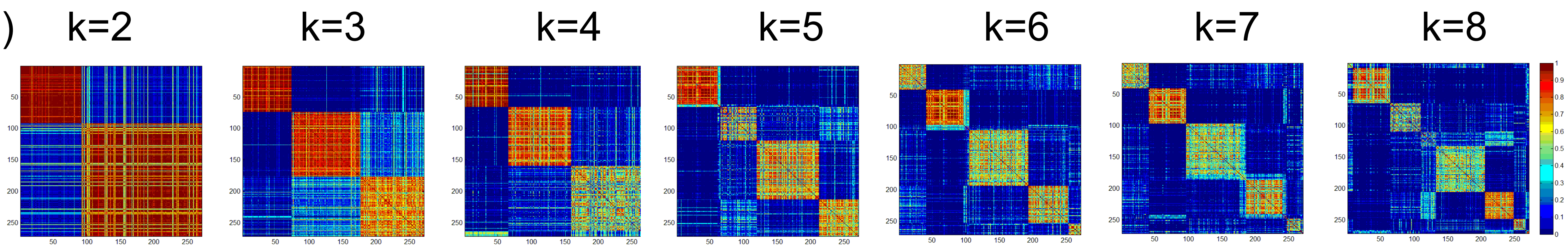


c. OV (Bonome et. al.,Cancer Research 2008,)

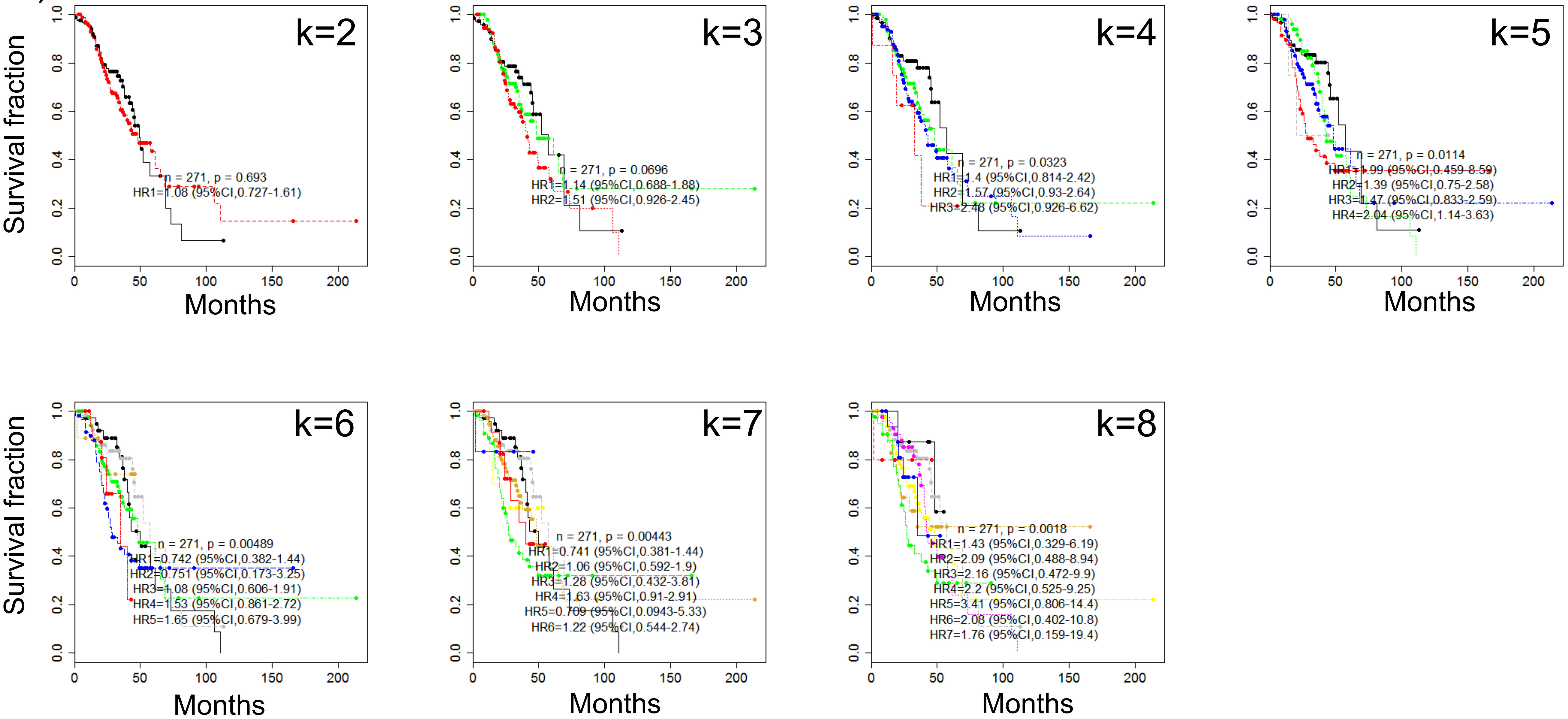


d. OV (Tothill et. al., Clinical Cancer Research, 2008)

1)

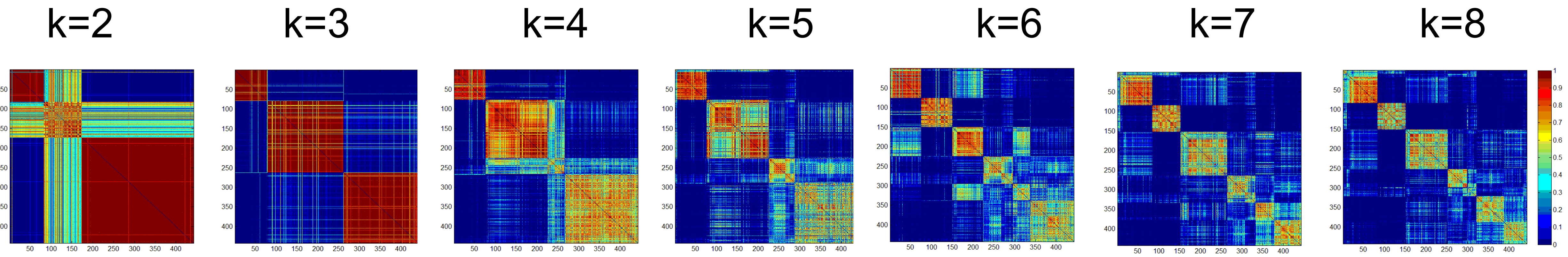


2)

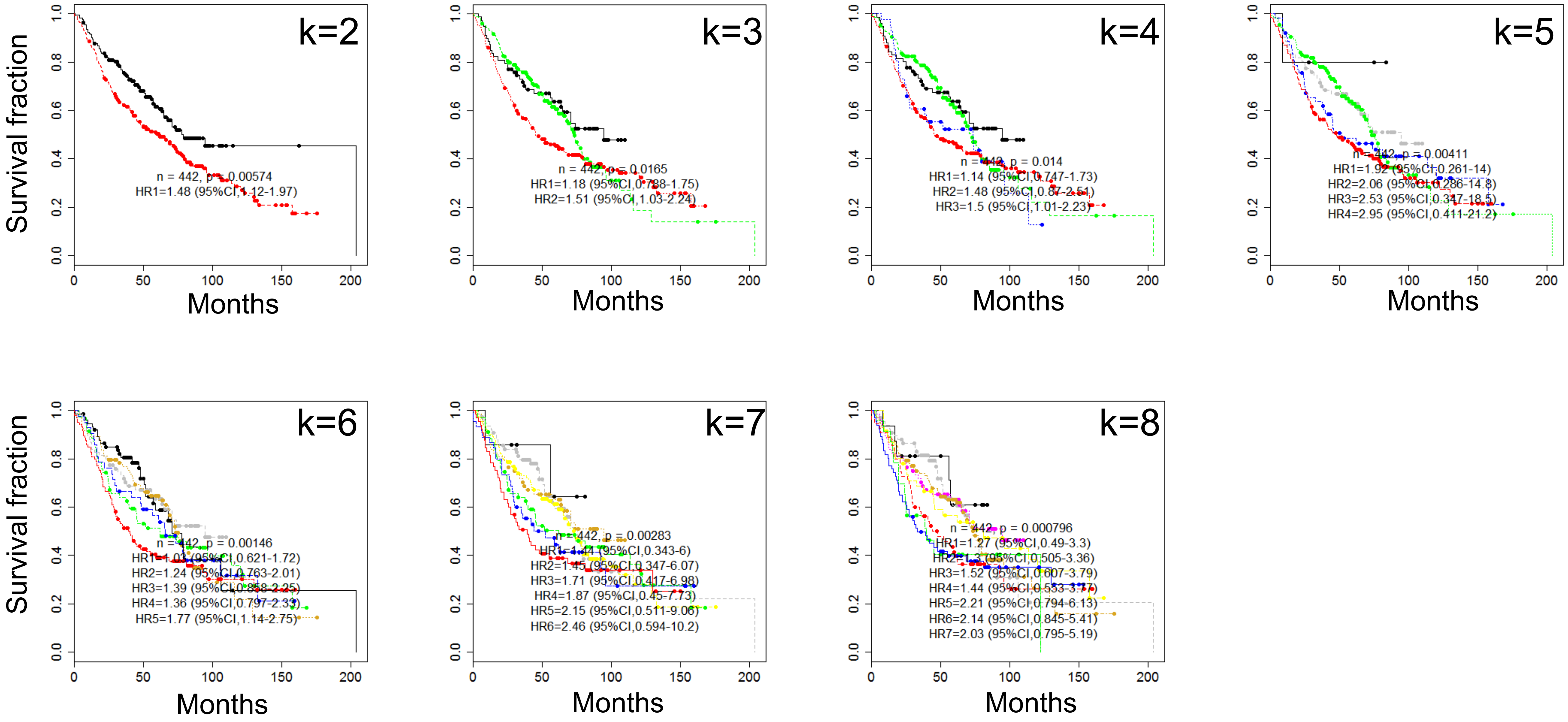


e. Lung adenocarcinoma (Shedden et. al., Nature Methods, 2008)

1)

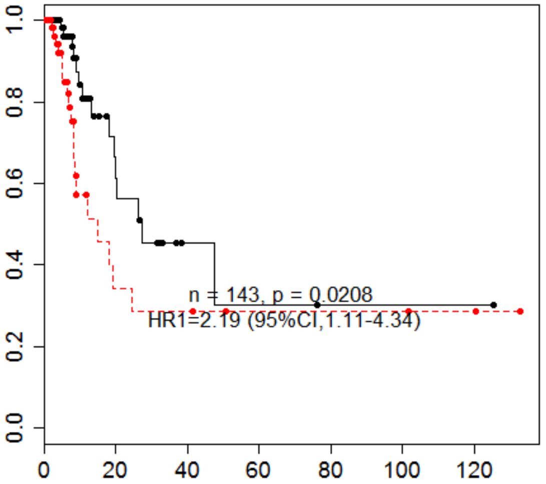


2)

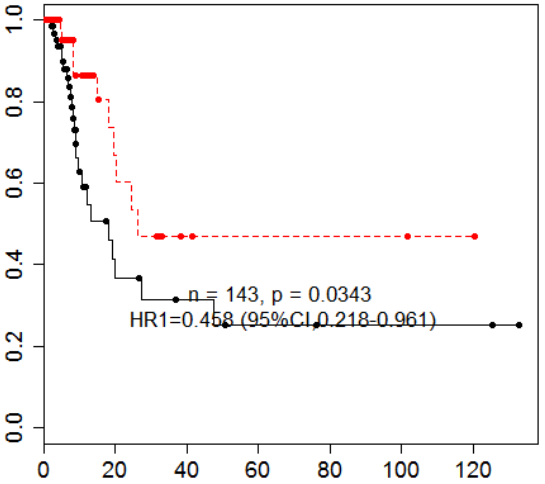


Supplementary Figure 5
Single gene analysis

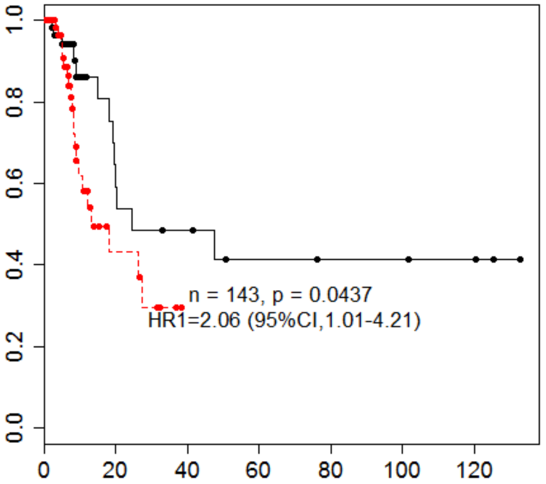
a. TCGA BLCA



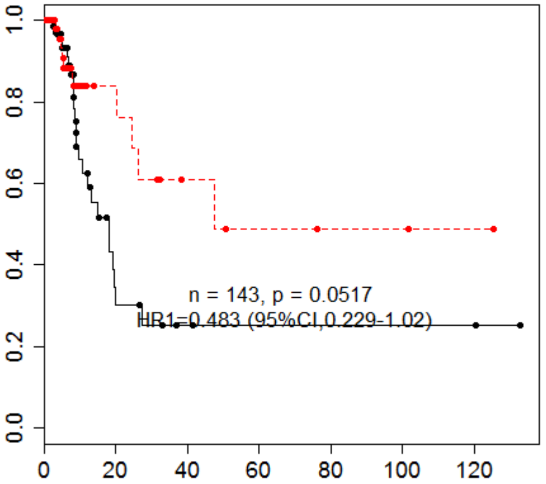
TP53



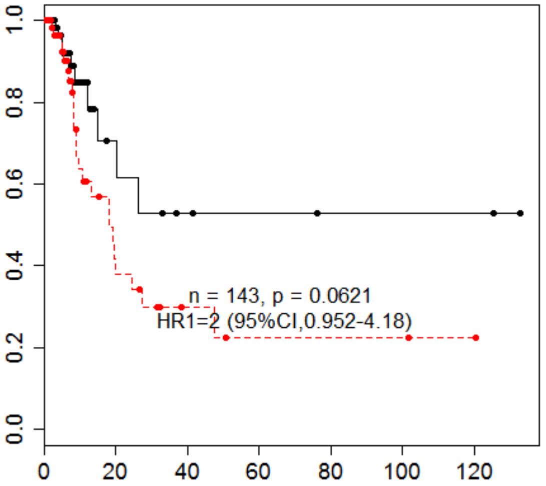
ASCC2



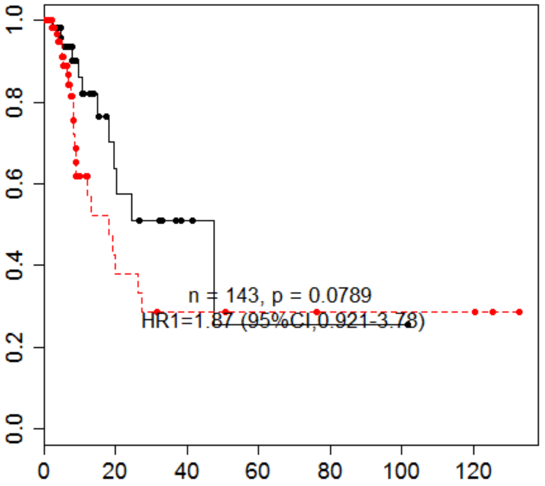
WRN



FHL2

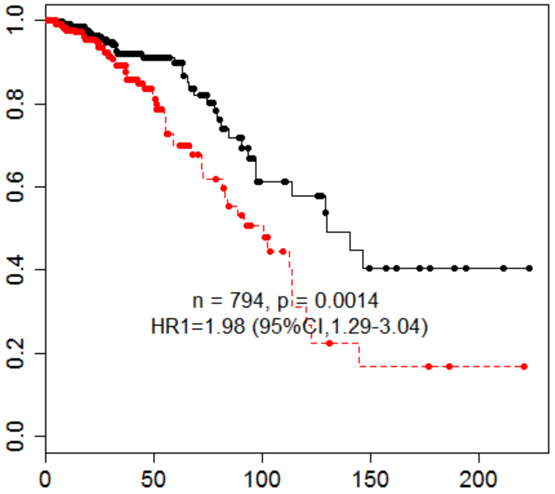


NCOA6

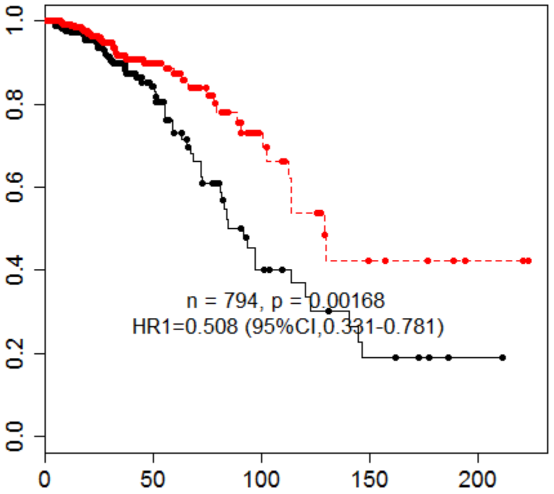


MSH6

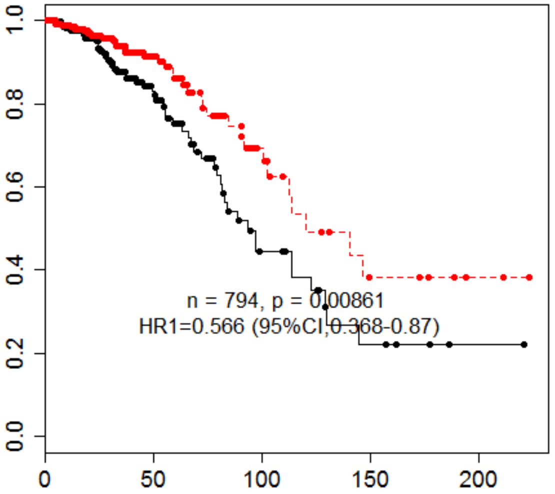
b. TCGA BRCA



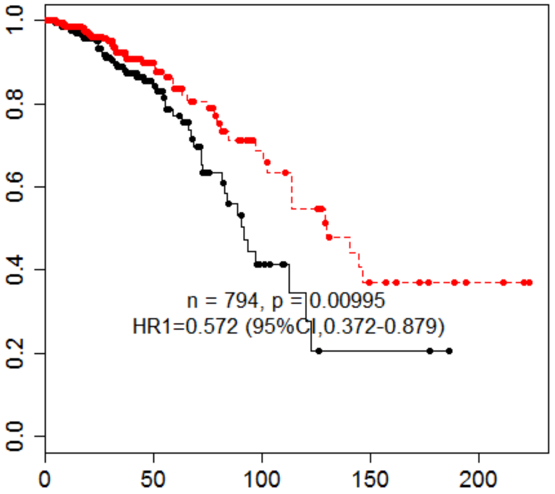
ZHX1



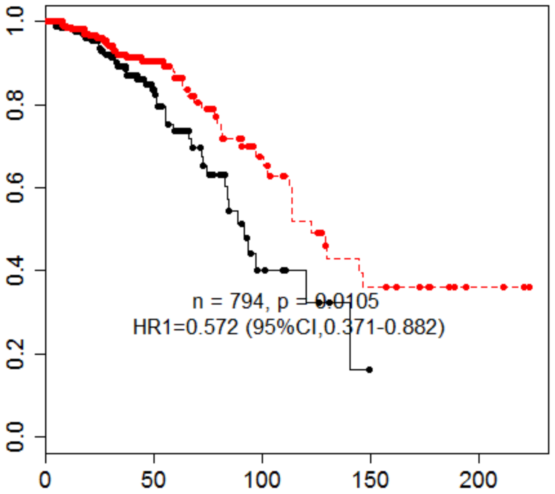
NFKBIA



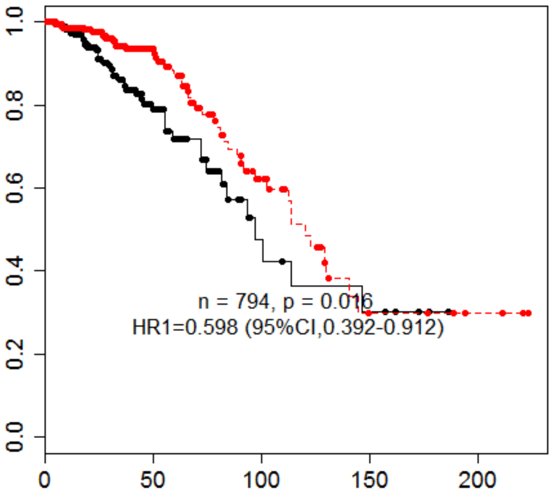
ACTA2



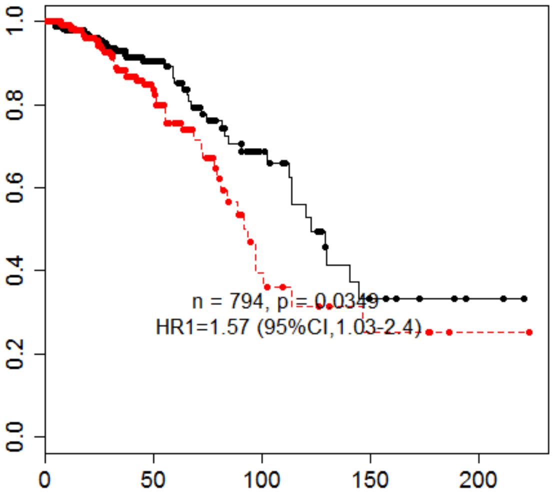
PIN1



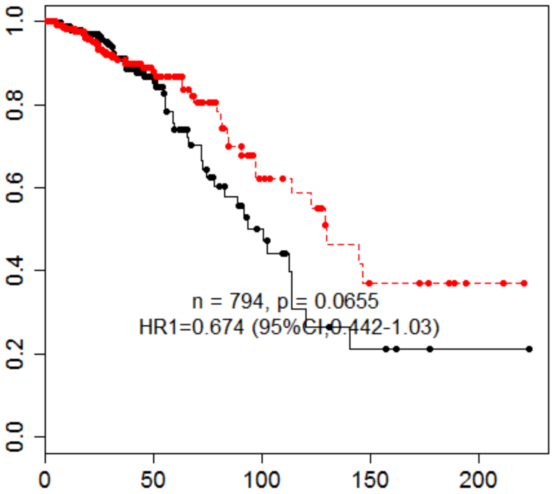
THAP8



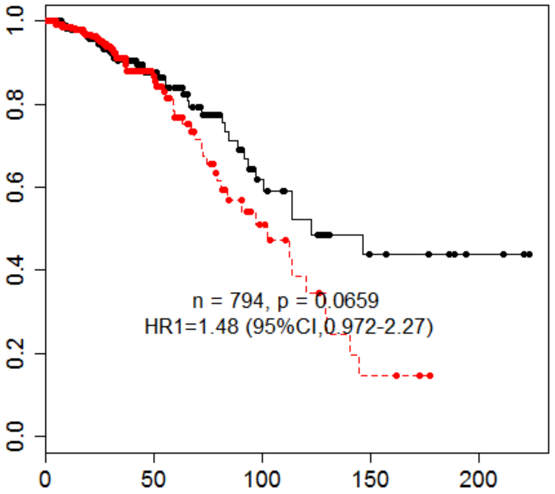
NAT6



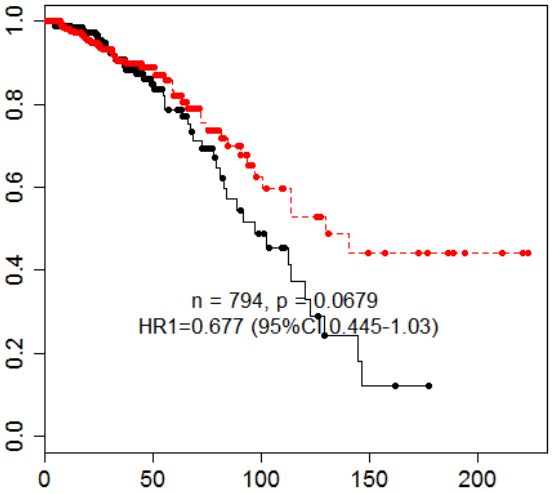
BRCA2



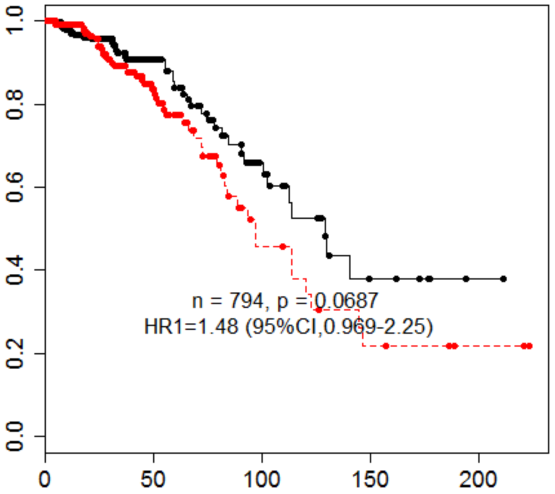
CDK5



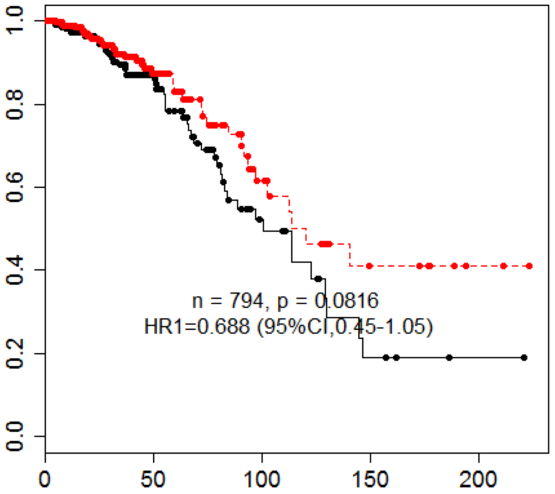
CHD3



YBX1

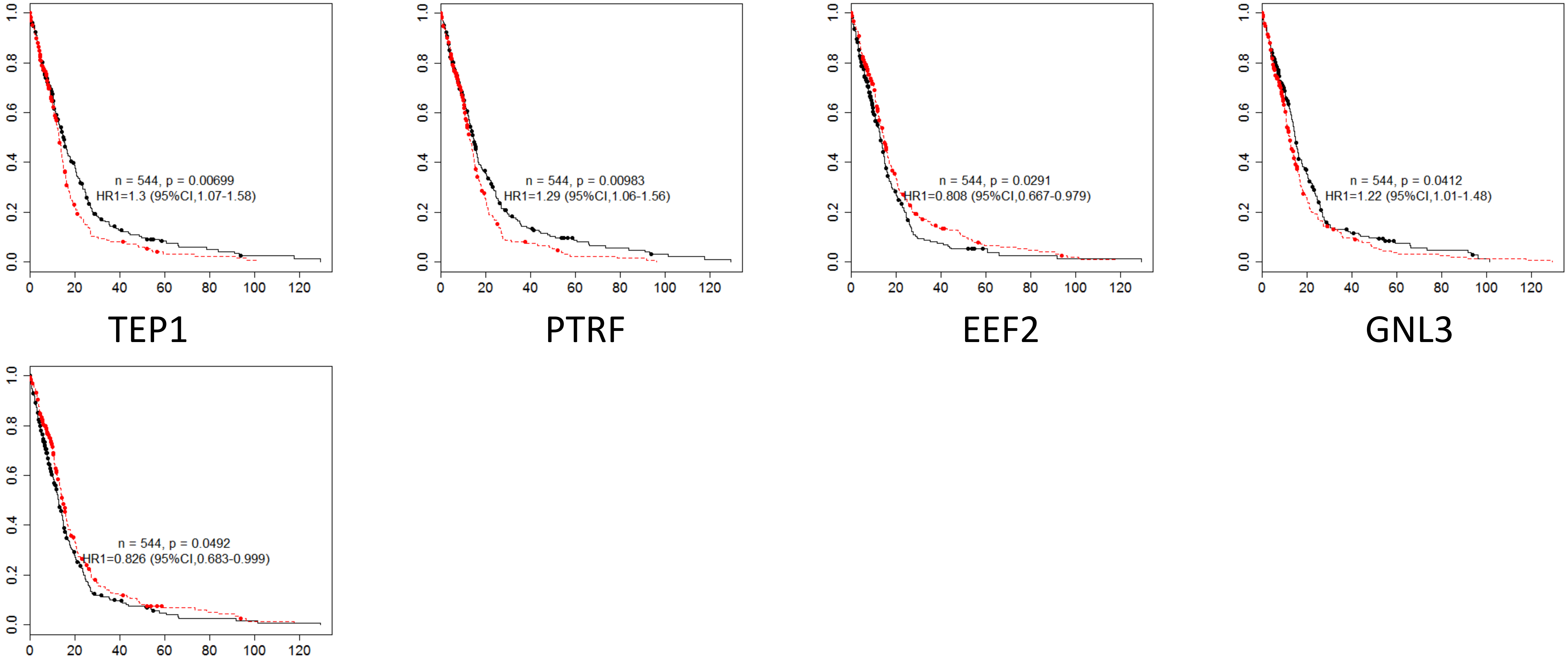


TDRD7



VIM

c. TCGA GBM



TEP1

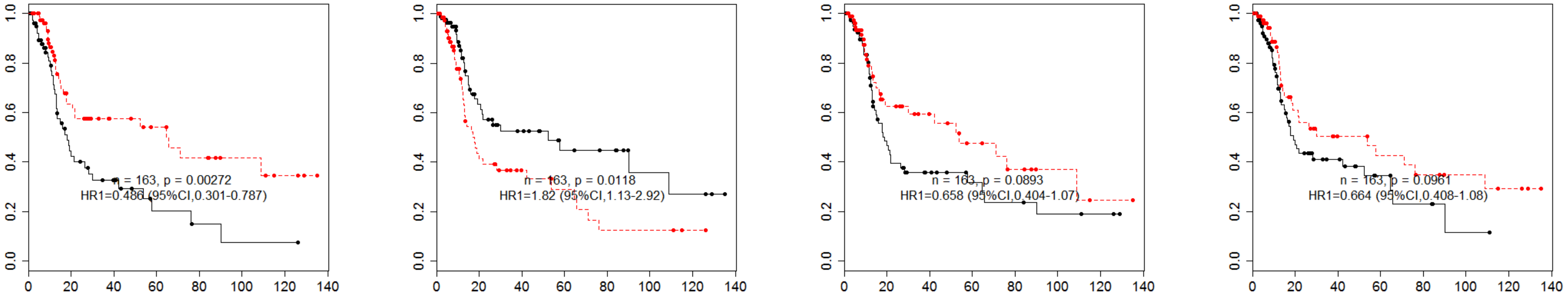
PTRF

EEF2

GNL3

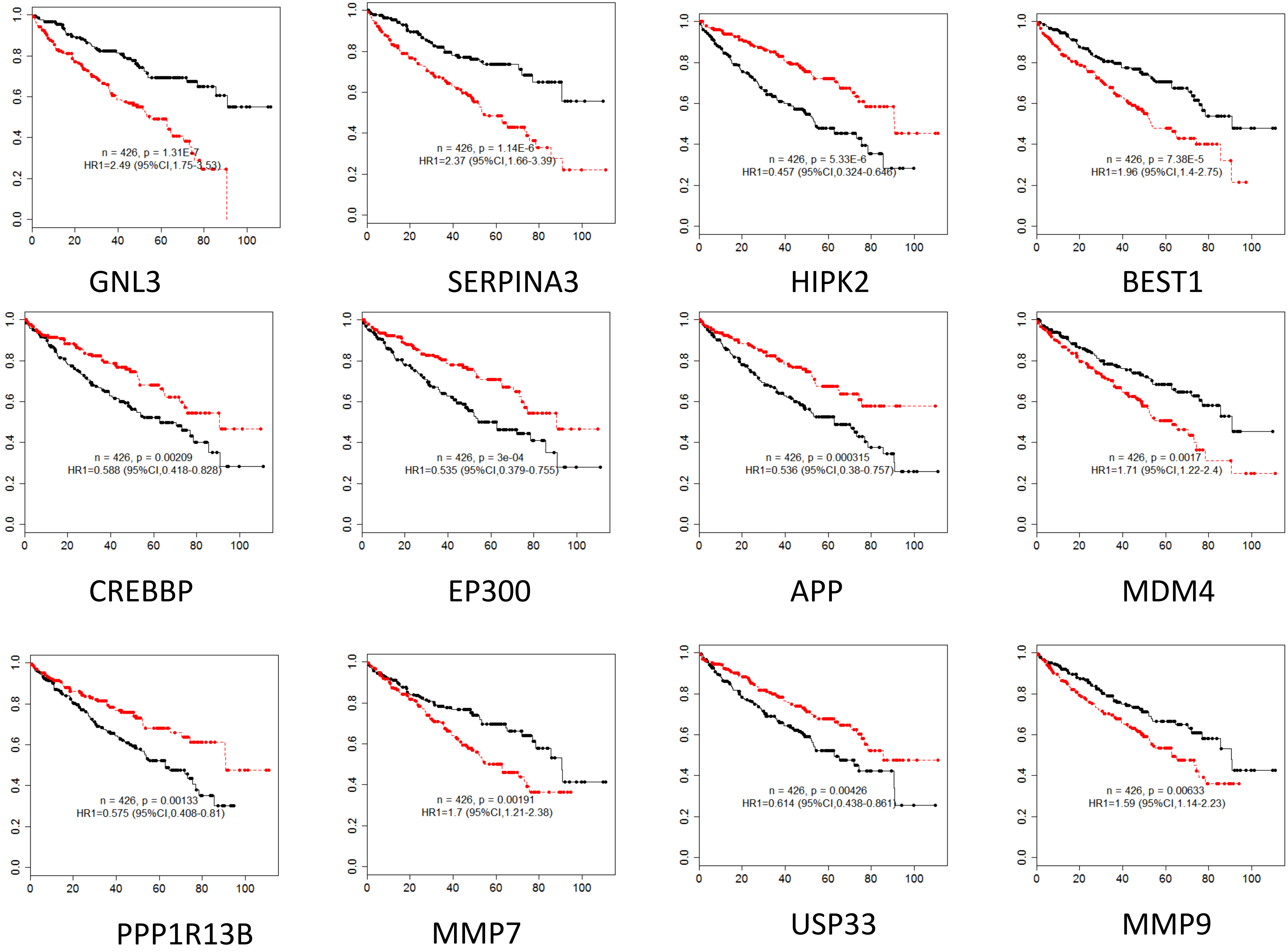
TOP1

d. TCGA HNSC



CABLES1 TOP1 EEF2 HIPK2

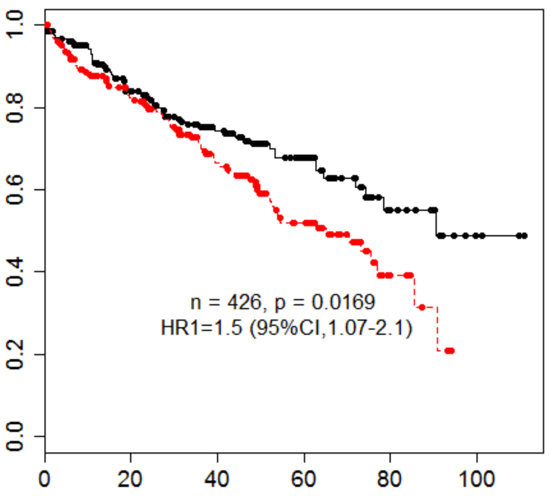
e. TCGA KIRC



GNL3 SERPINA3 HIPK2 BEST1

CREBBP EP300 APP MDM4

PPP1R13B MMP7 USP33 MMP9



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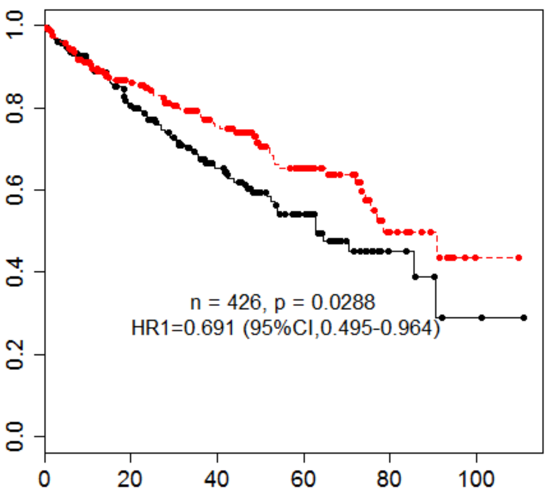
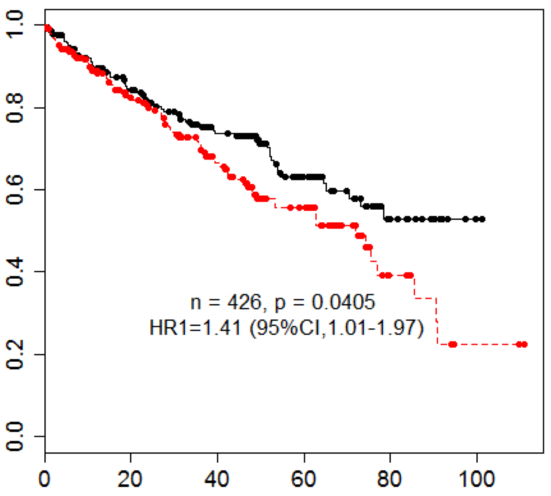
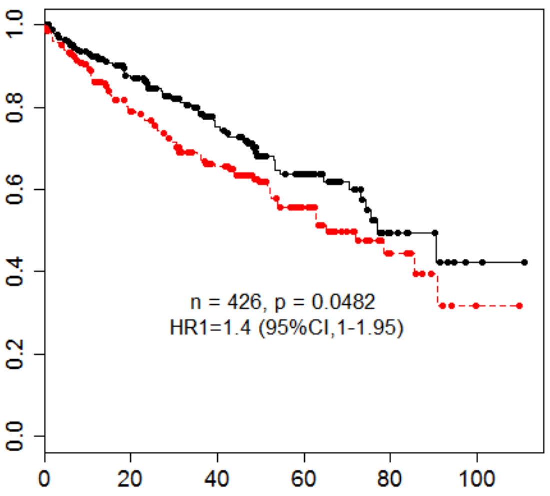


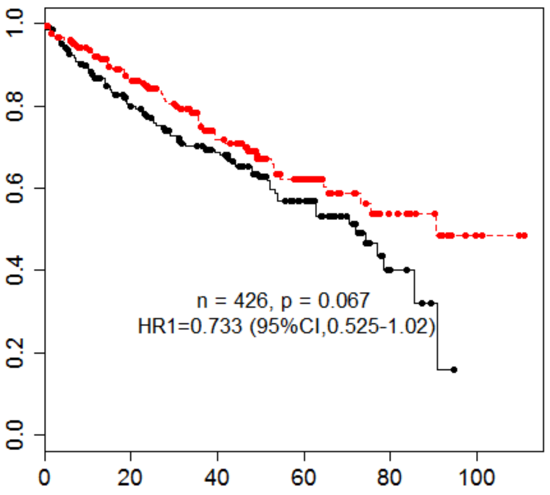
CTSG



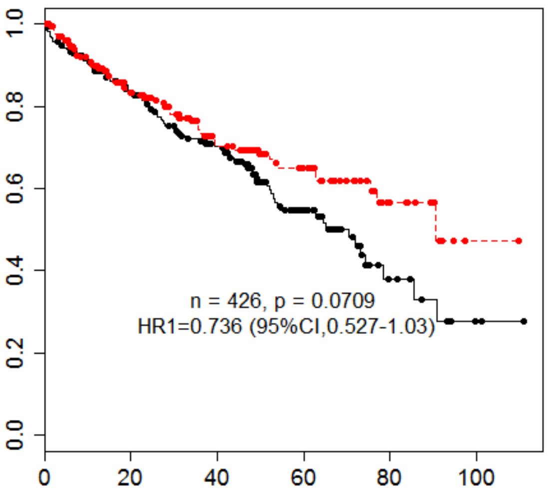
SERPINA1



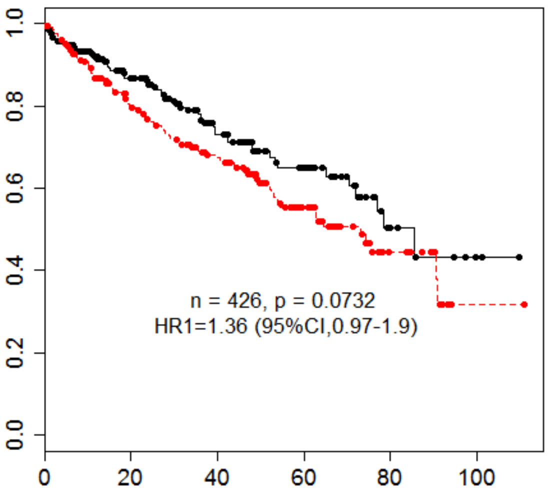
TCEB2



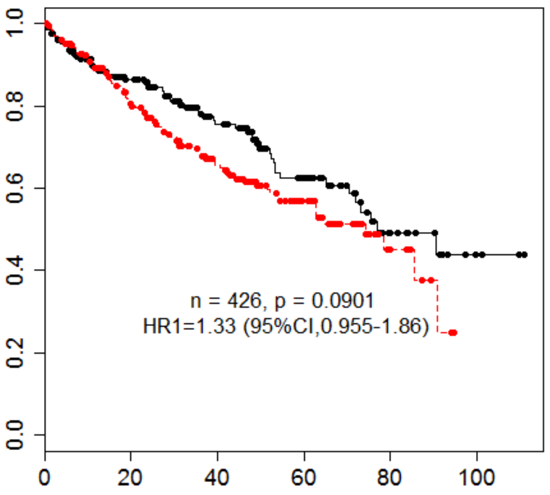
SP1



THBS1

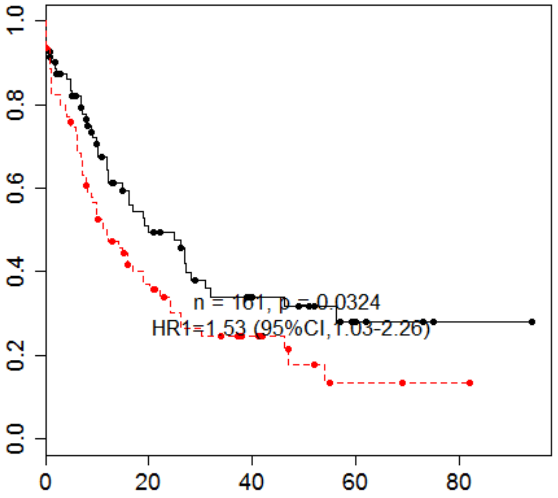


WT1

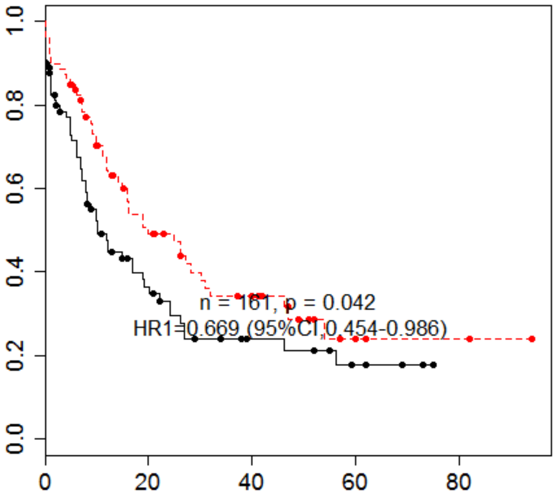


TCEB1

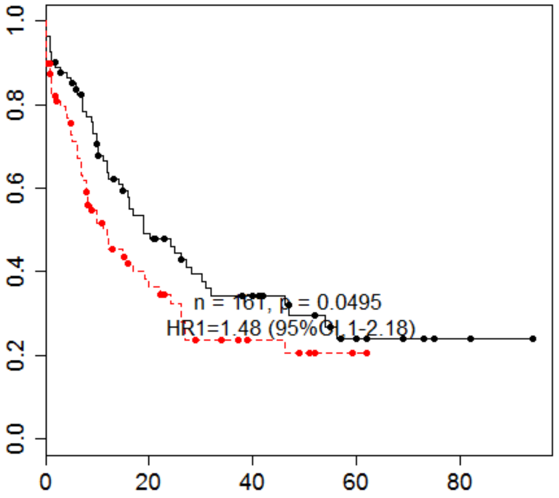
f. TCGA LAML



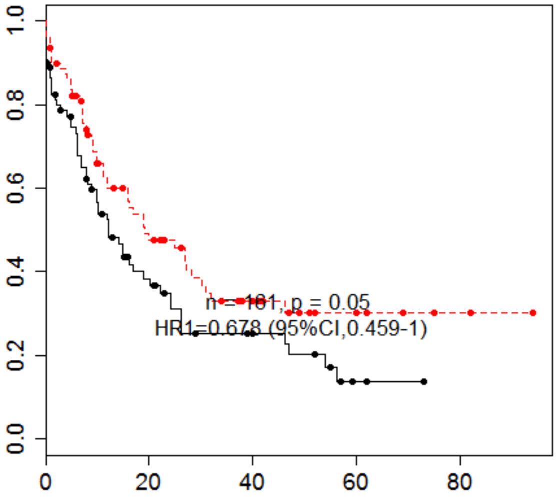
SHFM1



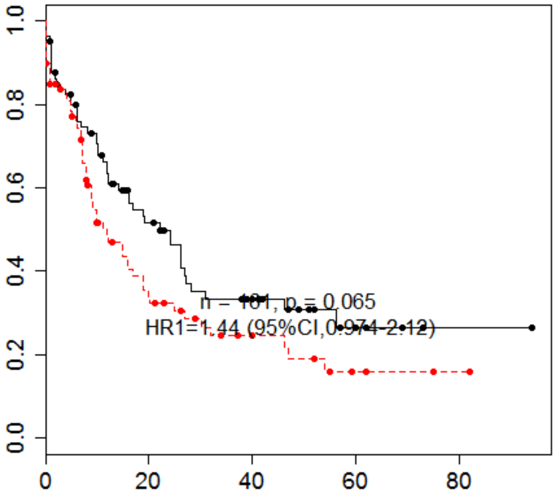
NPM1



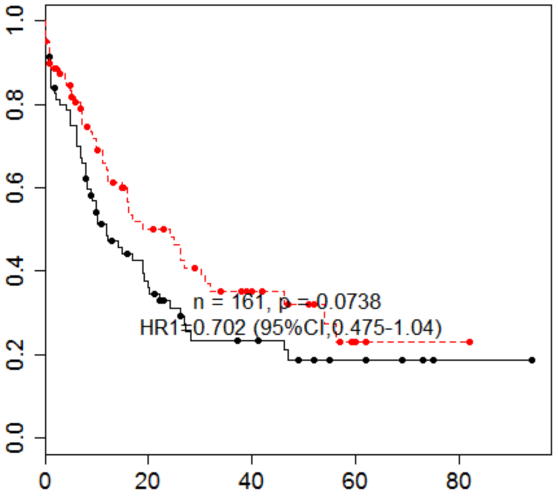
HSPA1A



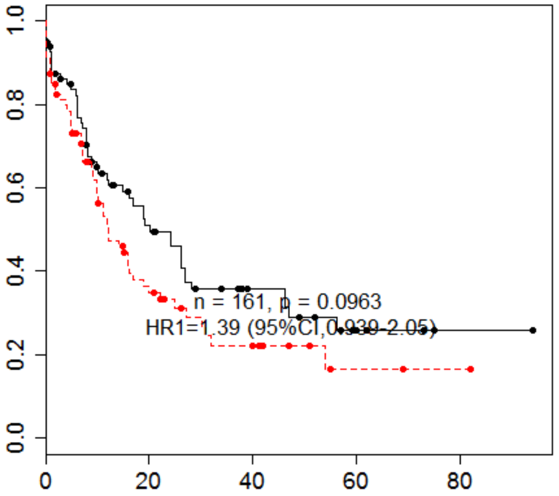
TP53



NQO1

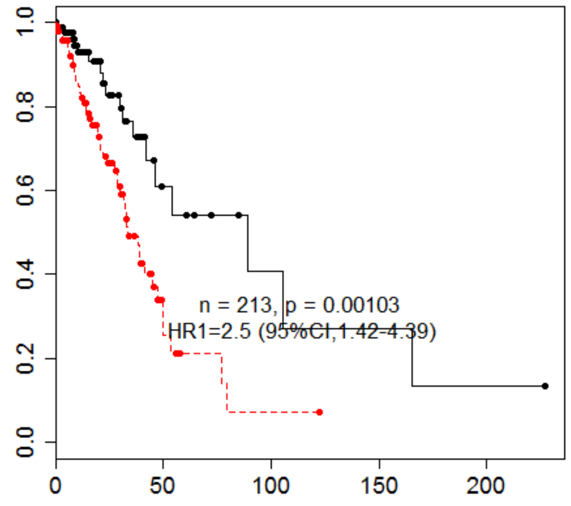


WDR16

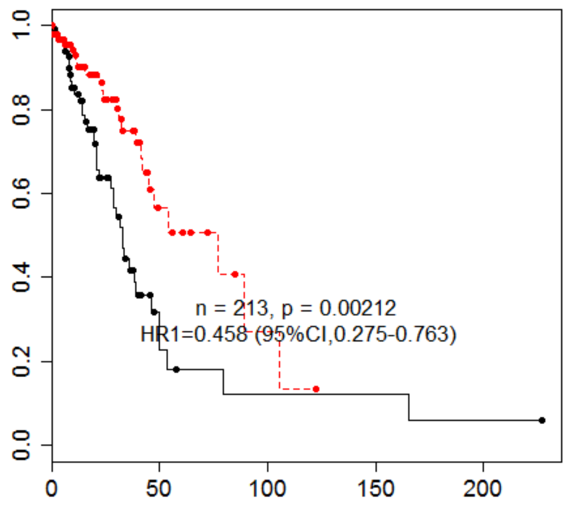


PARP1

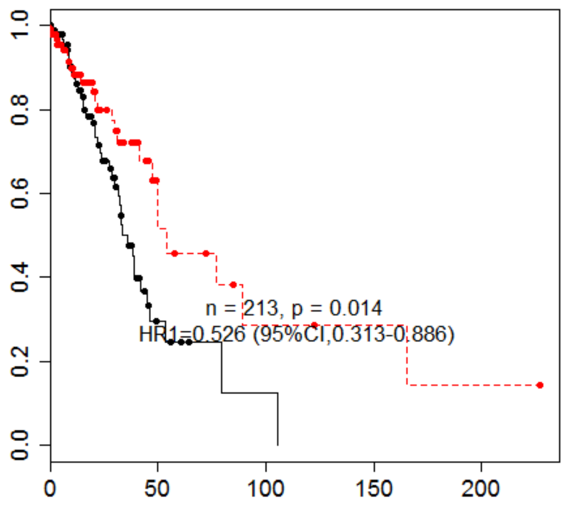
g. TCGA LUAD



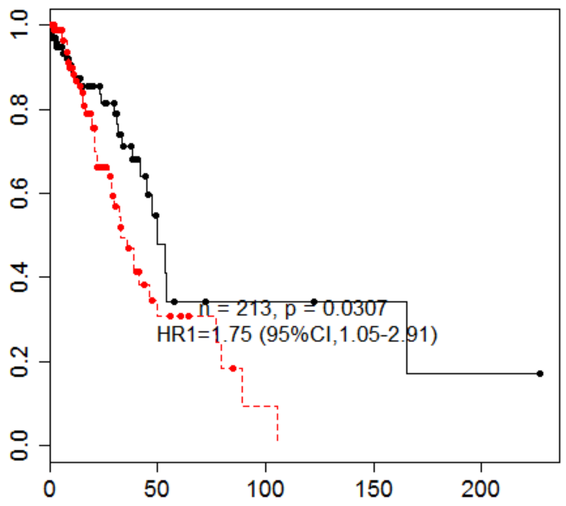
YBX1



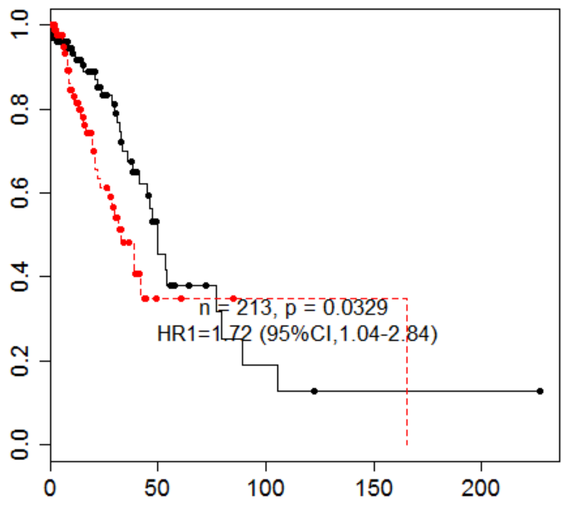
CABLES1



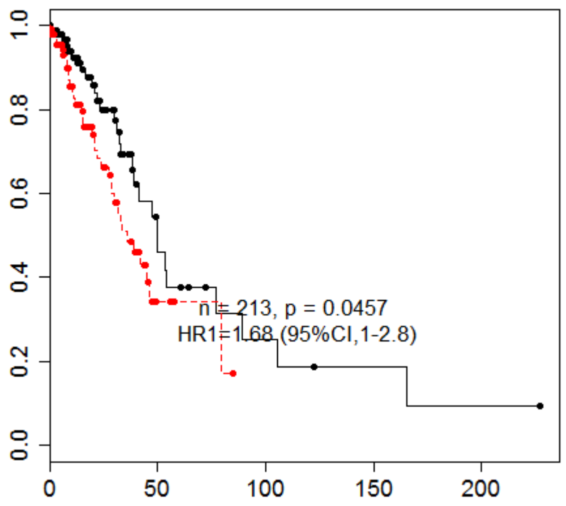
DDX5



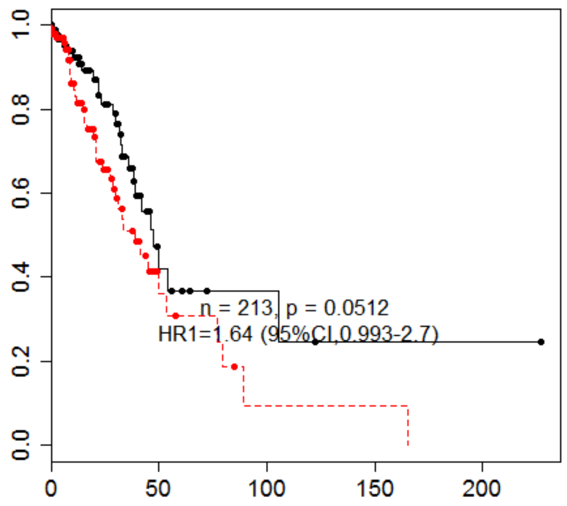
HSPA1A



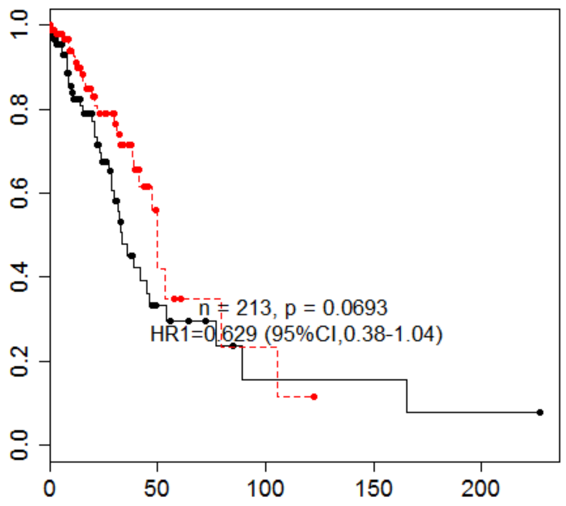
UPF3B



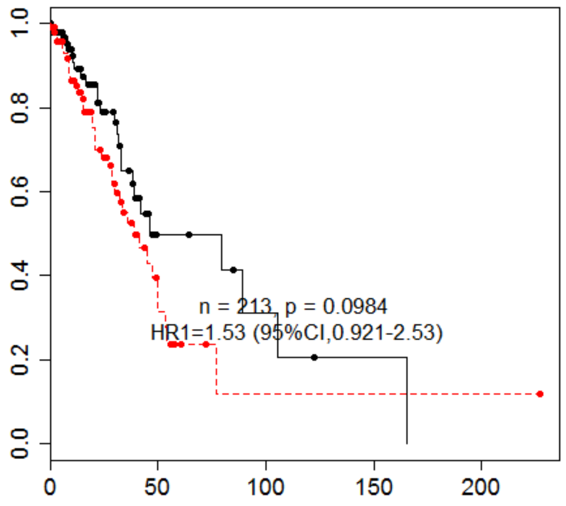
AURKA



YWHAZ

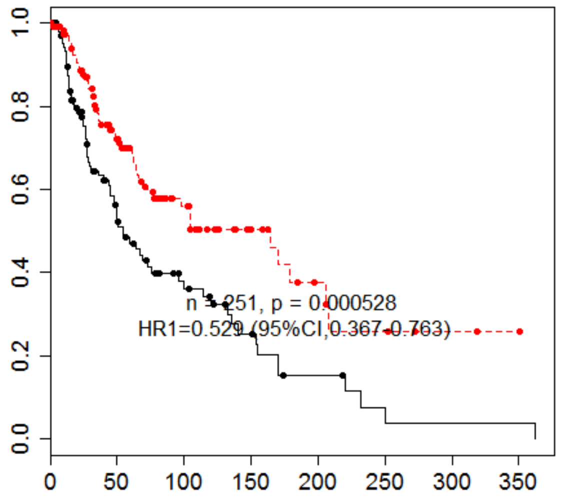


ACTC1

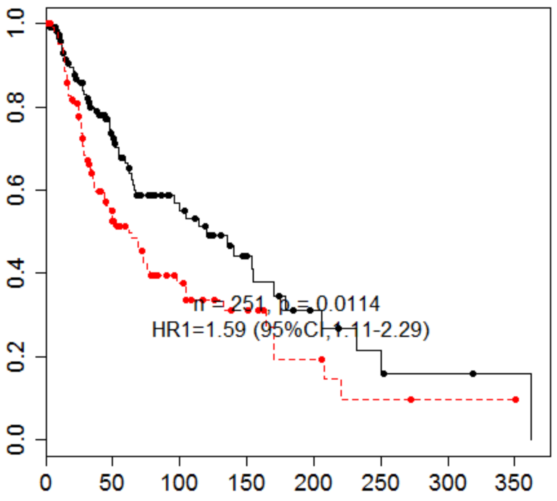


NPM1

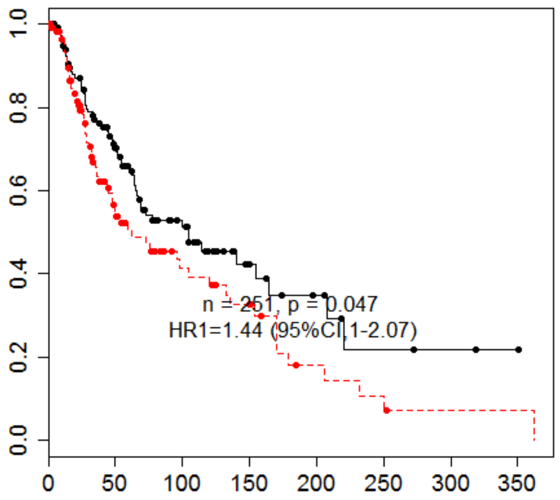
h.TCGA SKCM



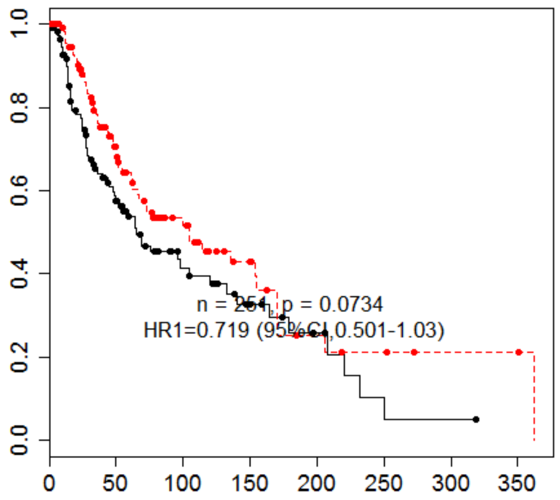
GCH1



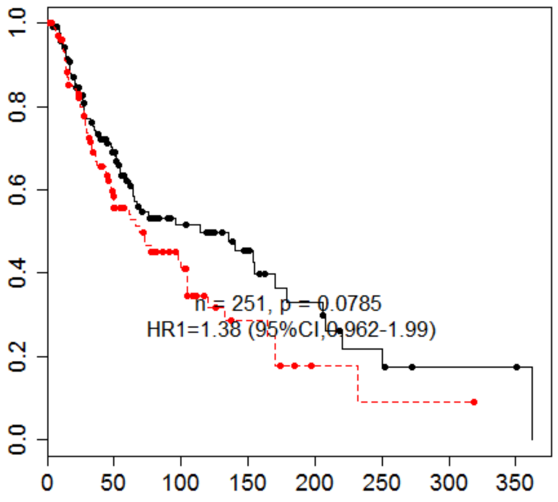
DSC1



AHSA1

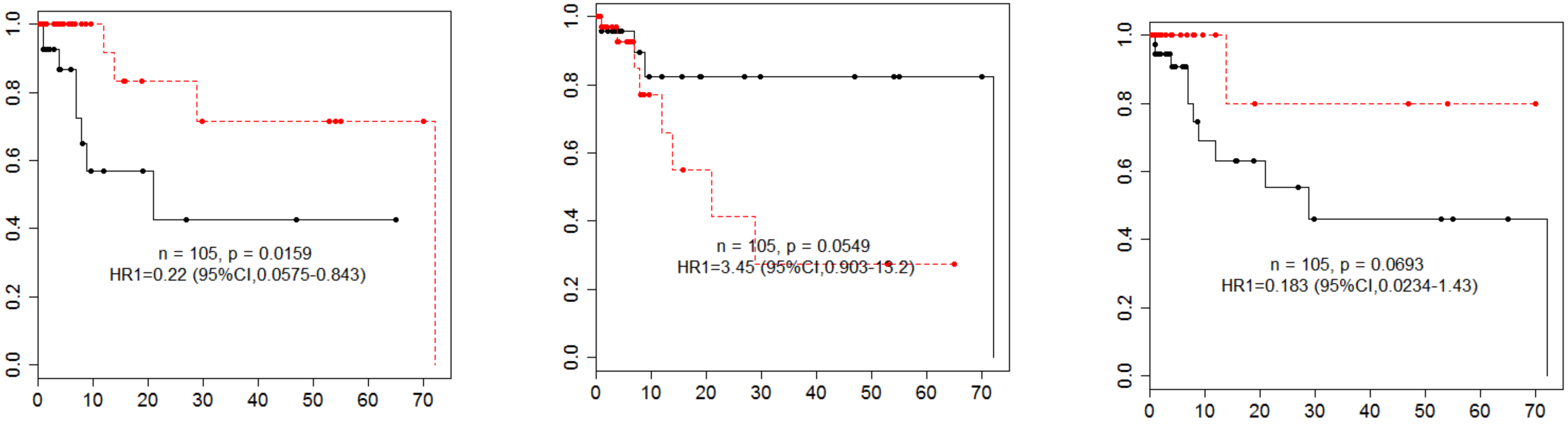


KRT18



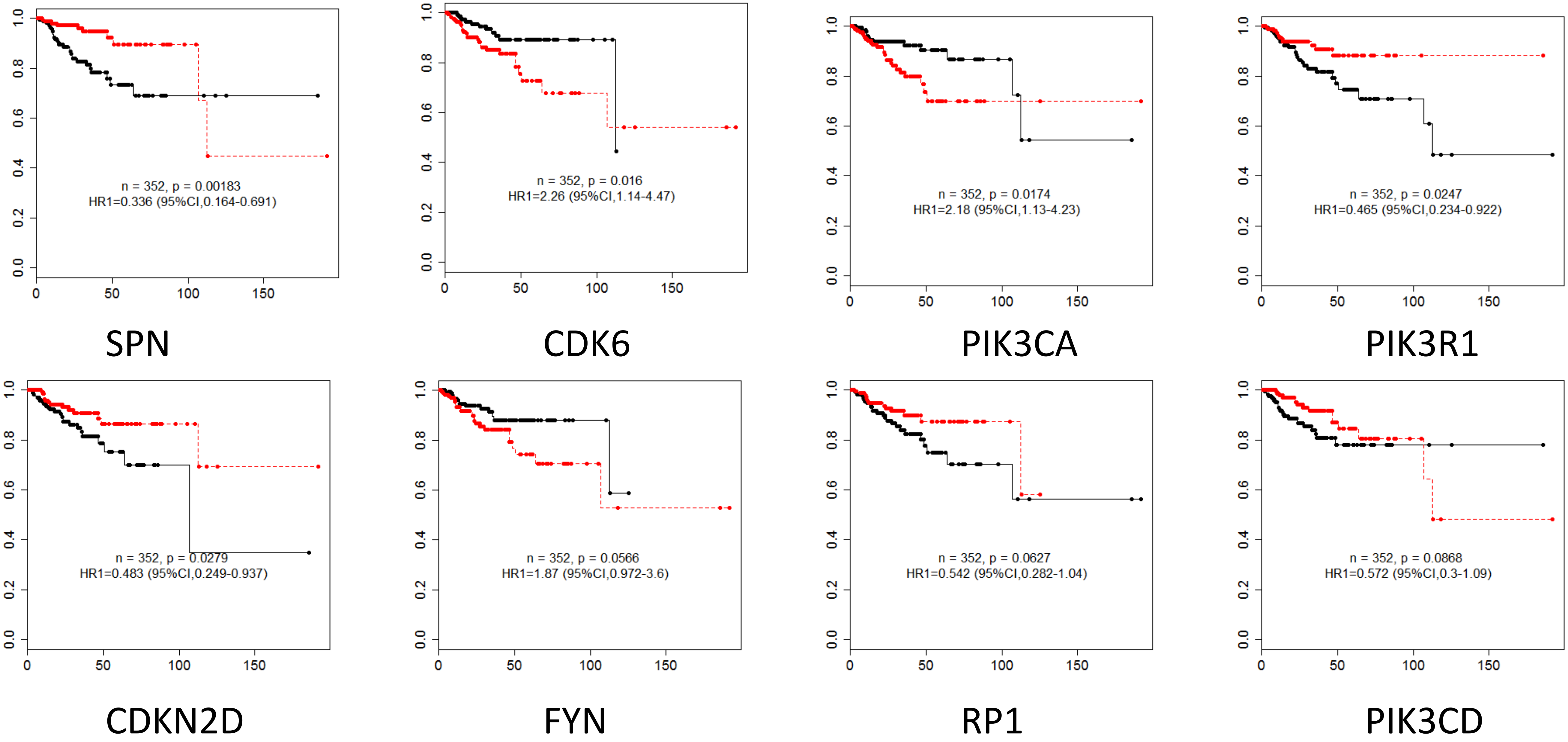
COL17A1

i. TCGA STAD



HSF1 ASCC2 ACTA2

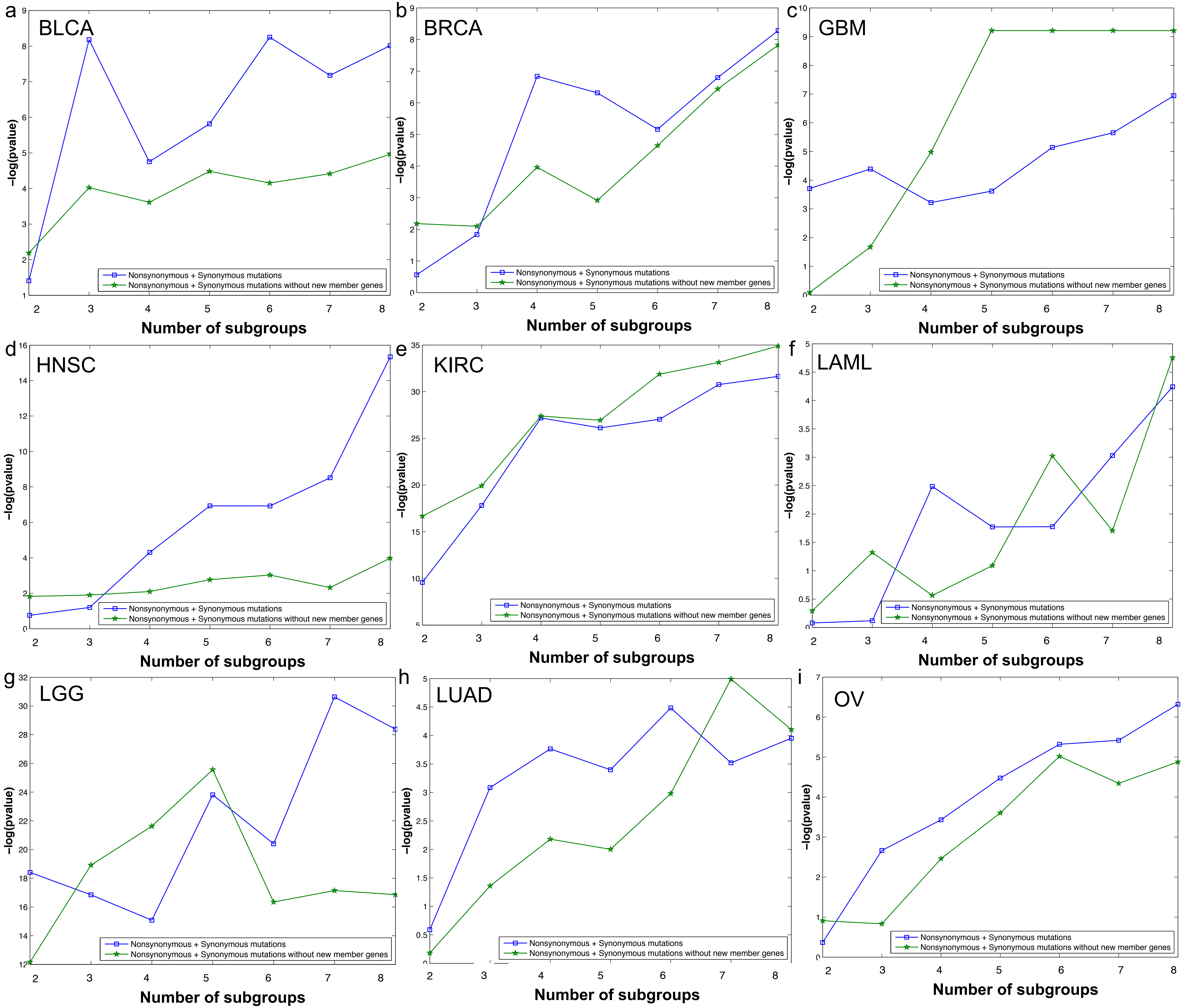
j. TCGA UCEC



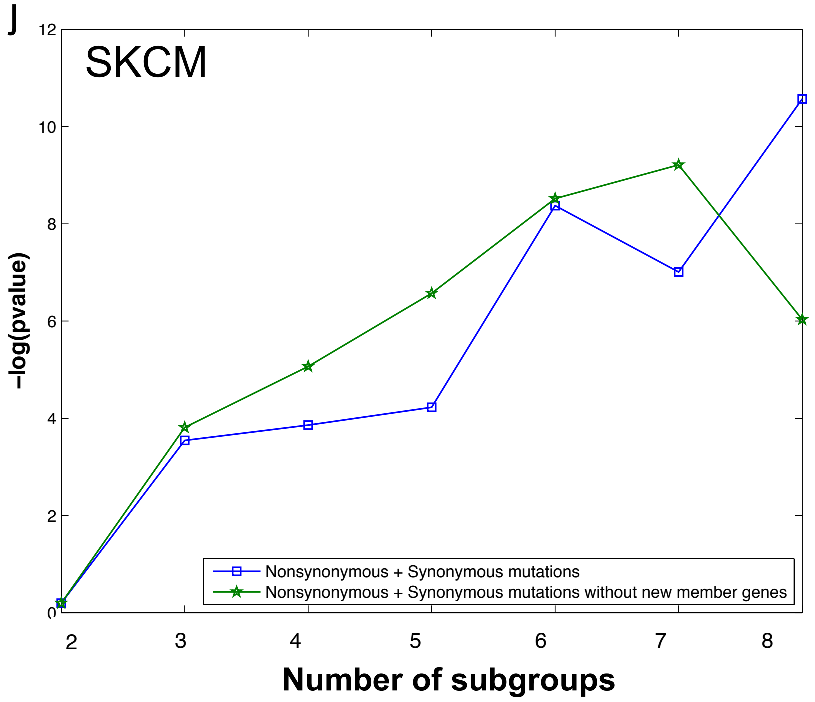
SPN CDK6 PIK3CA PIK3R1

CDKN2D FYN RP1 PIK3CD

Supplementary Figure 6
Patient stratification using original pathway annotations

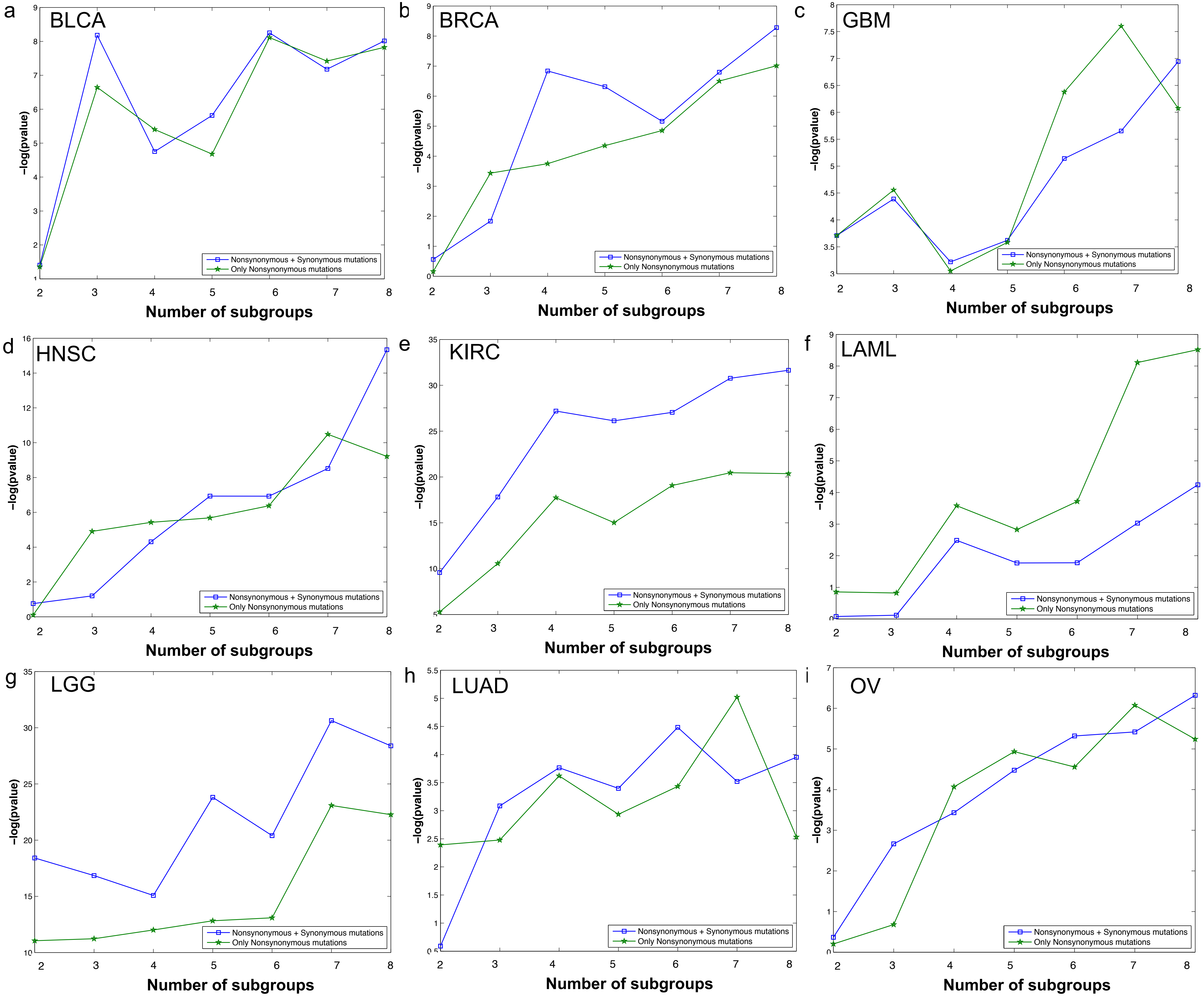

a
BLCA
−log(pvalue)
1 2 3 4 5 6 7 8 9
2 3 4 5 6 7 8
Number of subgroups
Nonsynonymous + Synonymous mutations
Nonsynonymous + Synonymous mutations without new member genes
b
BRCA
−log(pvalue)
0 1 2 3 4 5 6 7 8 9
2 3 4 5 6 7 8
Number of subgroups
Nonsynonymous + Synonymous mutations
Nonsynonymous + Synonymous mutations without new member genes
c
GBM
−log(pvalue)
0 1 2 3 4 5 6 7 8 9 10
2 3 4 5 6 7 8
Number of subgroups
Nonsynonymous + Synonymous mutations
Nonsynonymous + Synonymous mutations without new member genes
d
HNSC
−log(pvalue)
0 2 4 6 8 10 12 14 16
2 3 4 5 6 7 8
Number of subgroups
Nonsynonymous + Synonymous mutations
Nonsynonymous + Synonymous mutations without new member genes
e
KIRC
−log(pvalue)
5 10 15 20 25 30 35
2 3 4 5 6 7 8
Number of subgroups
Nonsynonymous + Synonymous mutations
Nonsynonymous + Synonymous mutations without new member genes
f
LAML
−log(pvalue)
0 0.5 1 1.5 2 2.5 3 3.5 4 4.5 5
2 3 4 5 6 7 8
Number of subgroups
Nonsynonymous + Synonymous mutations
Nonsynonymous + Synonymous mutations without new member genes
g
LGG
−log(pvalue)
12 14 16 18 20 22 24 26 28 30 32
2 3 4 5 6 7 8
Number of subgroups
Nonsynonymous + Synonymous mutations
Nonsynonymous + Synonymous mutations without new member genes
h
LUAD
−log(pvalue)
0 0.5 1 1.5 2 2.5 3 3.5 4 4.5 5
2 3 4 5 6 7 8
Number of subgroups
Nonsynonymous + Synonymous mutations
Nonsynonymous + Synonymous mutations without new member genes
i
OV
−log(pvalue)
0 1 2 3 4 5 6 7
2 3 4 5 6 7 8
Number of subgroups
Nonsynonymous + Synonymous mutations
Nonsynonymous + Synonymous mutations without new member genes

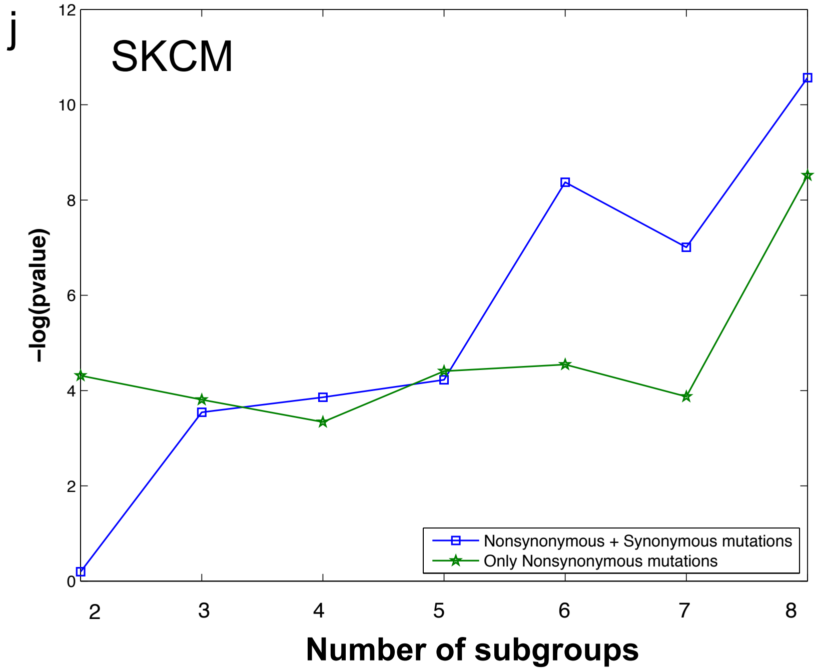
j


SKCM
-log(pvalue)
0
2
4
6
8
10
12
2
3
4
5
6
7
8
Number of subgroups
Nonsynonymous + Synonymous mutations
Nonsynonymous + Synonymous mutations without new member genes

Supplementary Figure 7

Patient stratification exclusively using non-synonymous mutation


a
BLCA
b
BRCA
c
GBM
d
HNSC
e
KIRC
f
LAML
g
LGG
h
LUAD
i
OV
−log(pvalue)
Number of subgroups
2
3
4
5
6
7
8
Nonsynonymous + Synonymous mutations
Only Nonsynonymous mutations


j
SKCM
-log(pvalue)
0
2
4
6
8
10
12
Number of subgroups
2
3
4
5
6
7
8
Nonsynonymous + Synonymous mutations
Only Nonsynonymous mutations