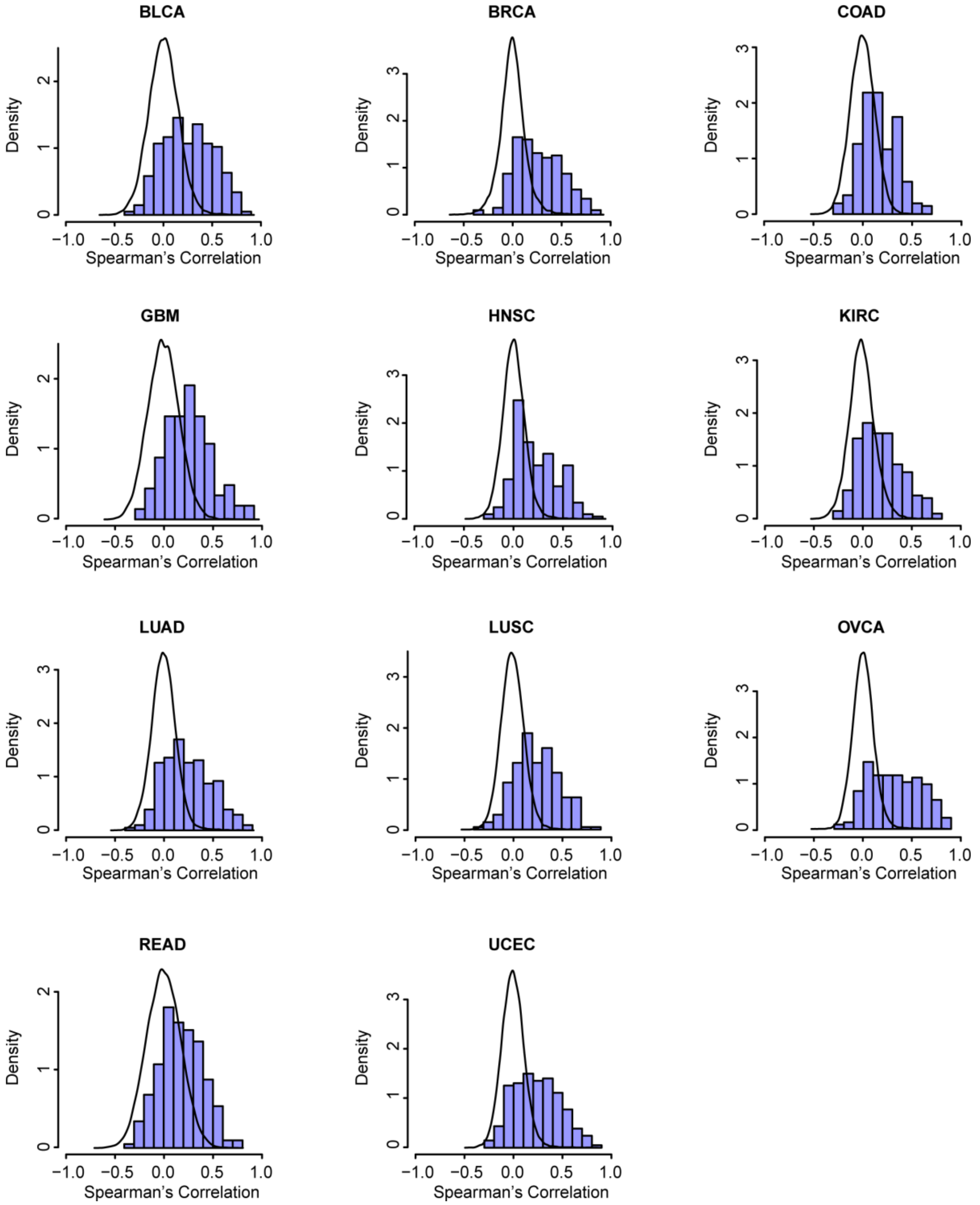
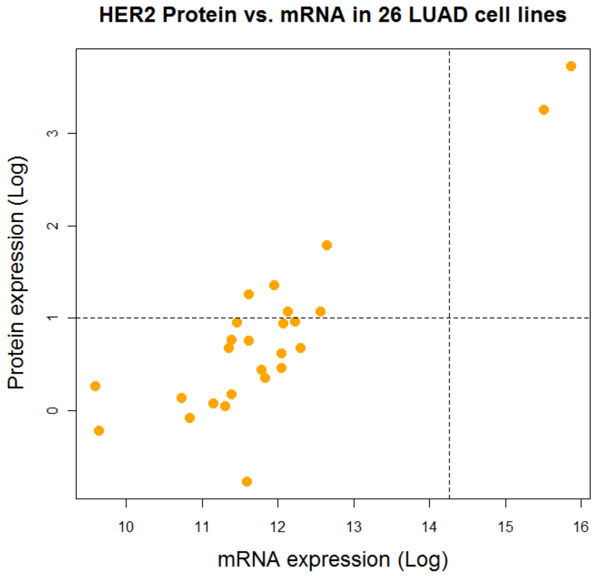
Supplementary Figures

Supplementary Figure 1: Correlation between protein and mRNA



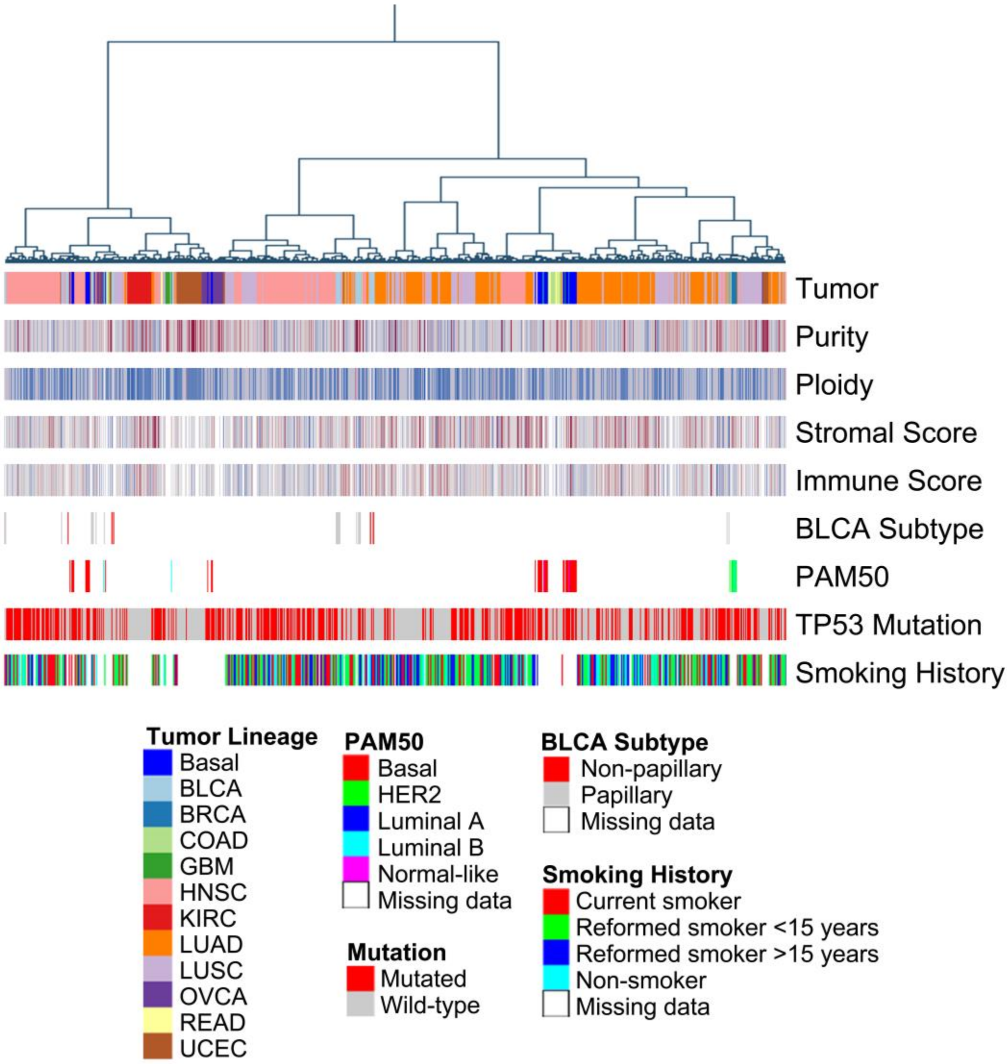
Eleven histograms of Spearman's correlation (ρ) in 206 pairs of proteins and matched mRNA across all tumor lineages. The black curve represents the background of ρ using 28,960 random pairs of (matched or unmatched) proteins and mRNA in the same dataset. Tumor lineage is indicated above each histogram.

Supplementary Figure 2: Dotplot showing relative HER2 protein and ERRB2 mRNA expression levels in 26 LUAD cell lines[1]



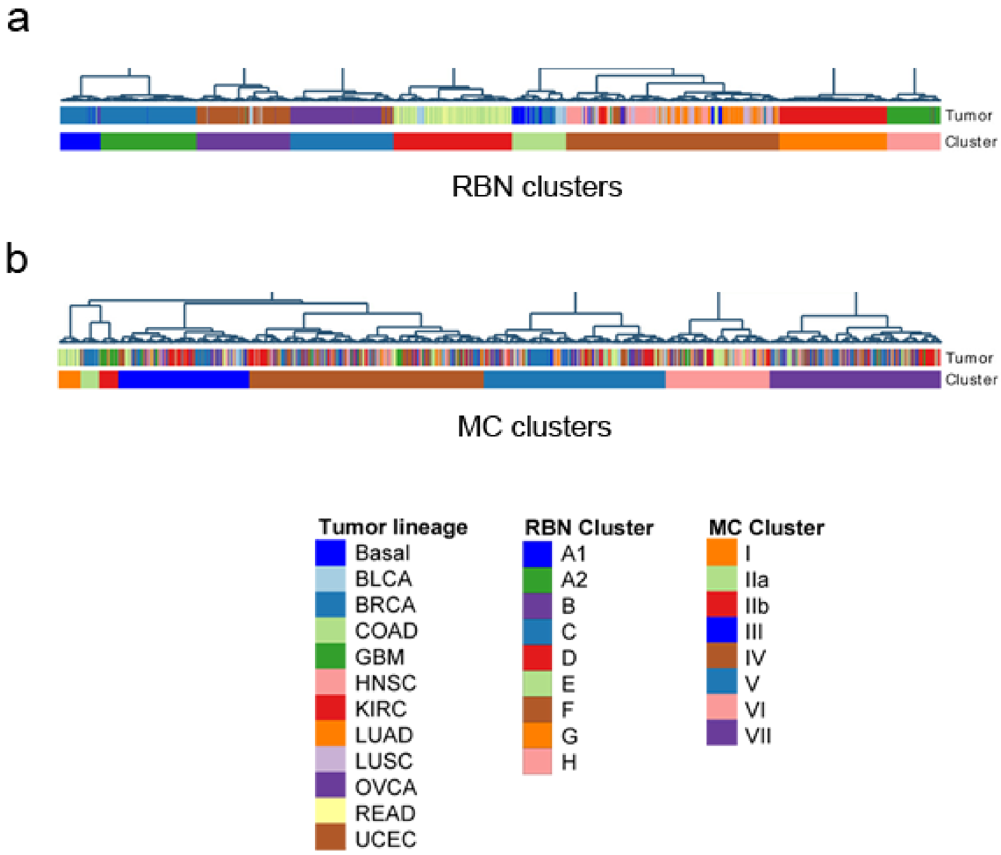
The cutoffs used in Fig. 1 of 14.26 for mRNA and 1.0 for protein are shown by the vertical and horizontal dashed lines, respectively. The thresholds were chosen based on breast cancer HER2 positive samples. Using the same cutoffs, more cell lines are identified as HER2 positive by protein (7 cell lines) than by mRNA (2 cell lines). Spearman's correlation (ρ) is 0.77 between mRNA and protein expressions. Supplementary Table 1 shows the actual values and cell line names.

Supplementary Figure 3: Smoking history and TP53 mutation status of samples in cluster_F



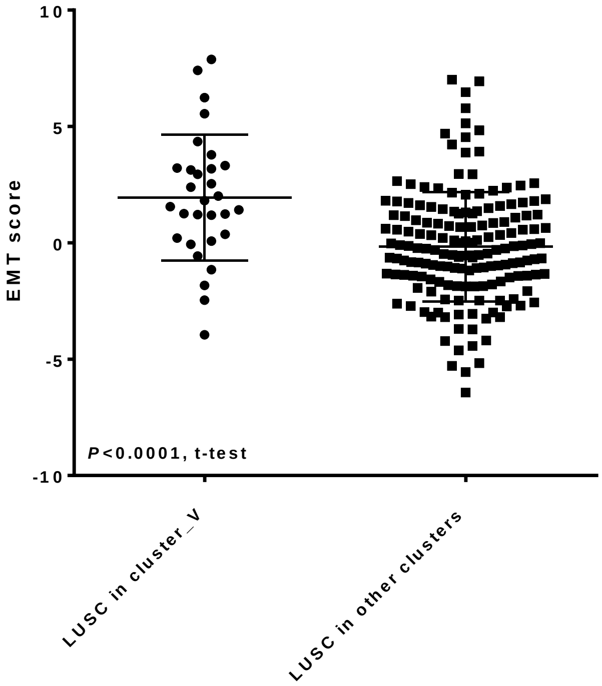
Zoomed-in view of cluster_F. Horizontally, samples are arranged as shown in the overall RBN heatmap (Fig. 2a). Smoking history and TP53 mutation status as well as a number of molecular/clinical variables are highlighted.

Supplementary Figure 4: Zoomed-in views of RBN and MC clusters showing association with tumor types



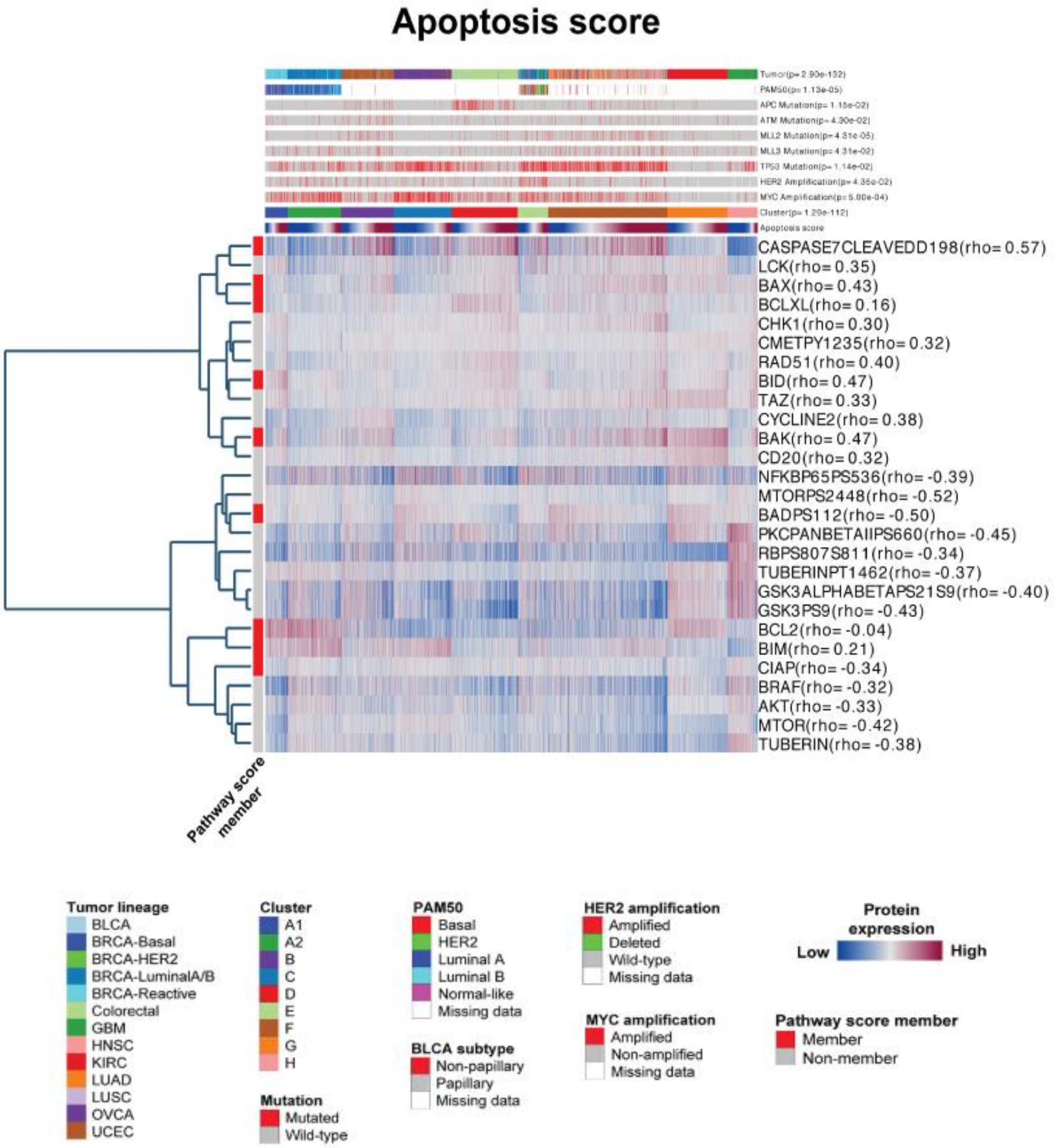
(a) Zoomed-in view of RBN clusters, showing good correspondence between the clusters and the tumor lineages. (b) Zoomed-in view of MC clusters, showing that the tumor lineages are distributed across the clusters. Virtually no cluster is dominant by a single tumor type (except the three left-most clusters as explained in the legend for Supplementary Table 7).

Supplementary Figure 5: LUSC EMT score in MC cluster_V vs. other clusters

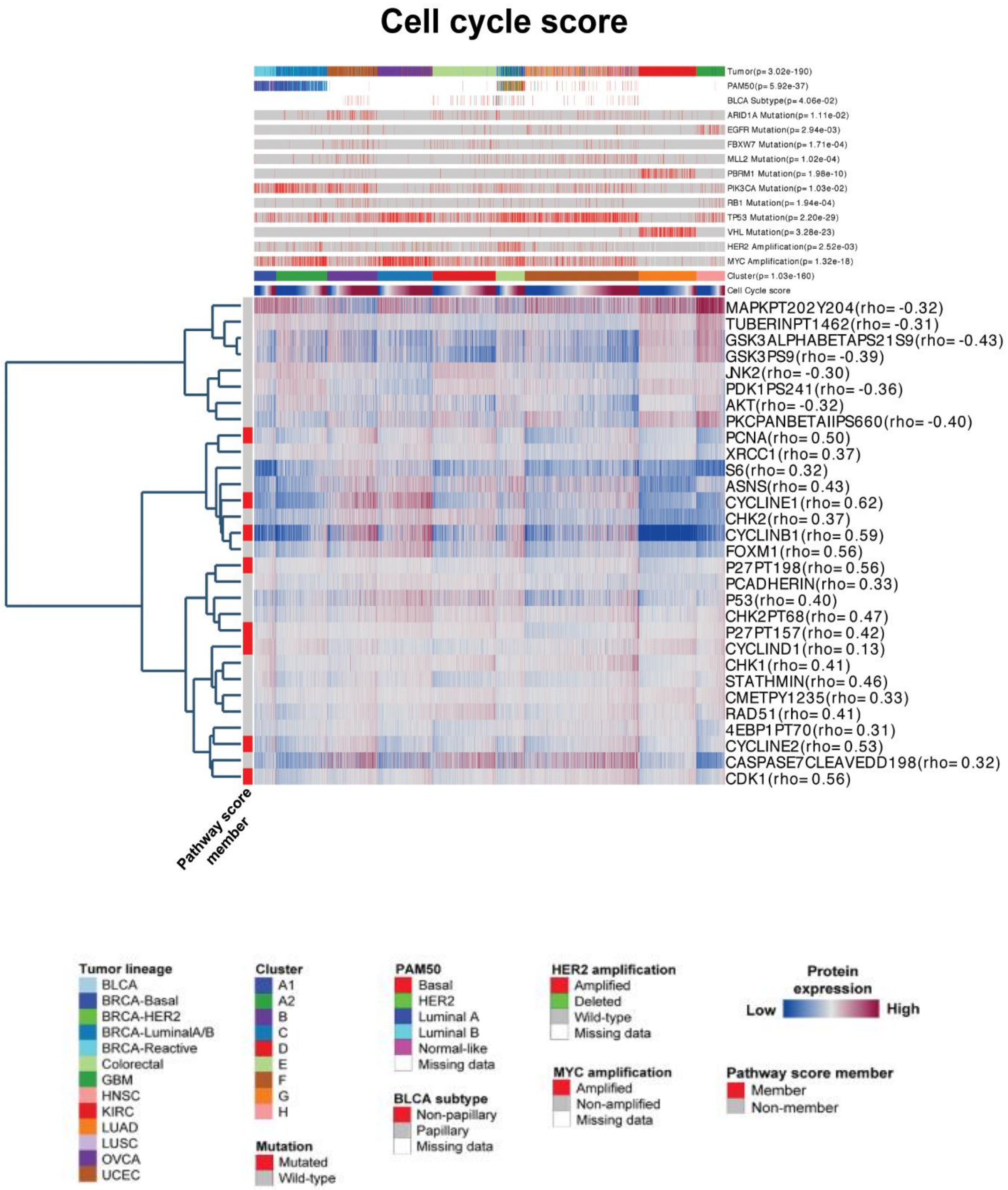


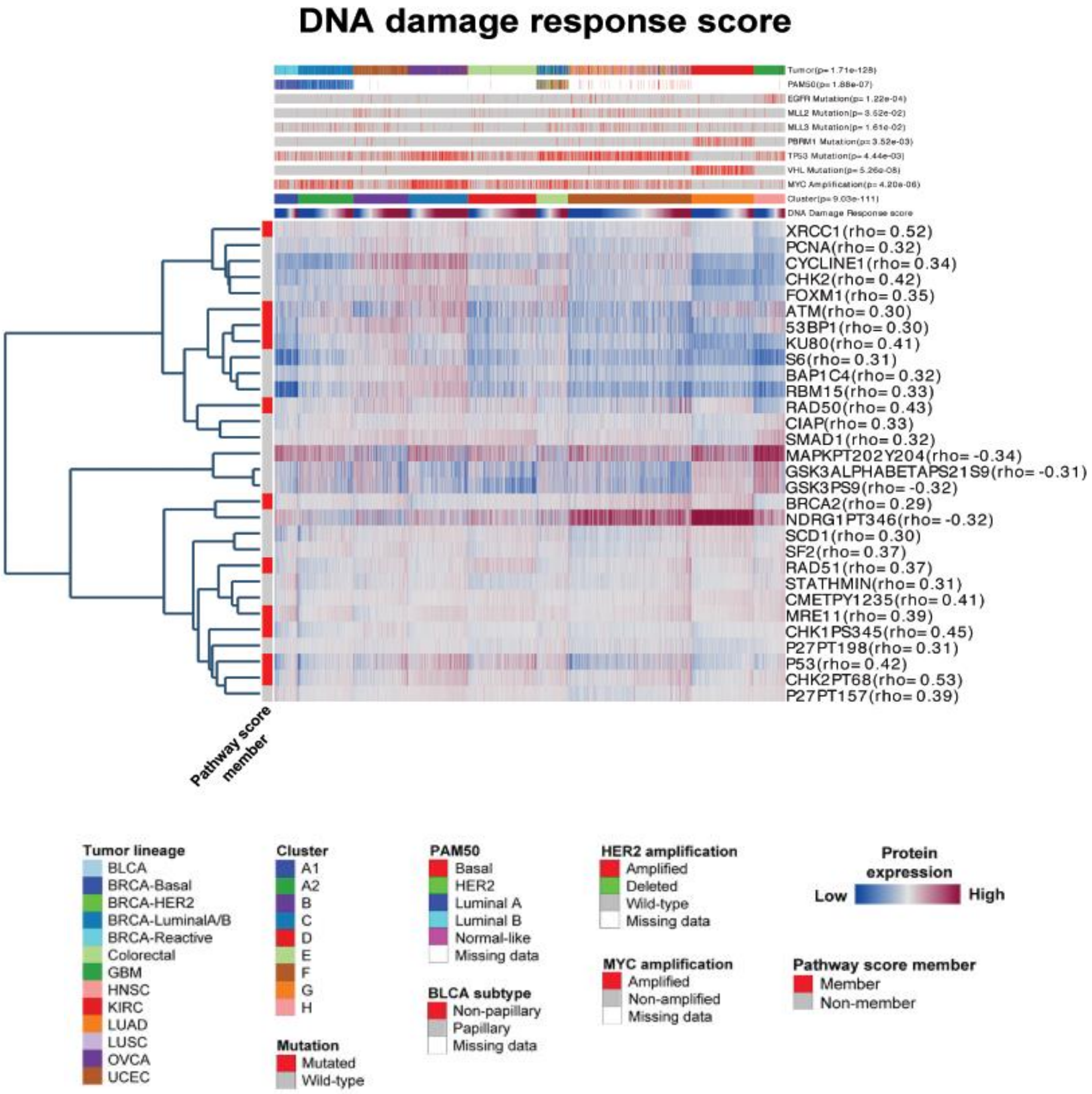
Dotplot shows the EMT score of each LUSC sample in cluster_V and in other clusters in the MC dataset. The lines indicate the mean ±S.D. of EMT score. t-test shows that the LUSC samples in cluster_V have a higher EMT signature than other LUSC samples (*P*< 0.0001, t-test).

Supplementary Figure 6: Heatmaps showing pathway members and associated proteins and molecular/ clinical variables with pathway scores (RBN dataset by cluster)

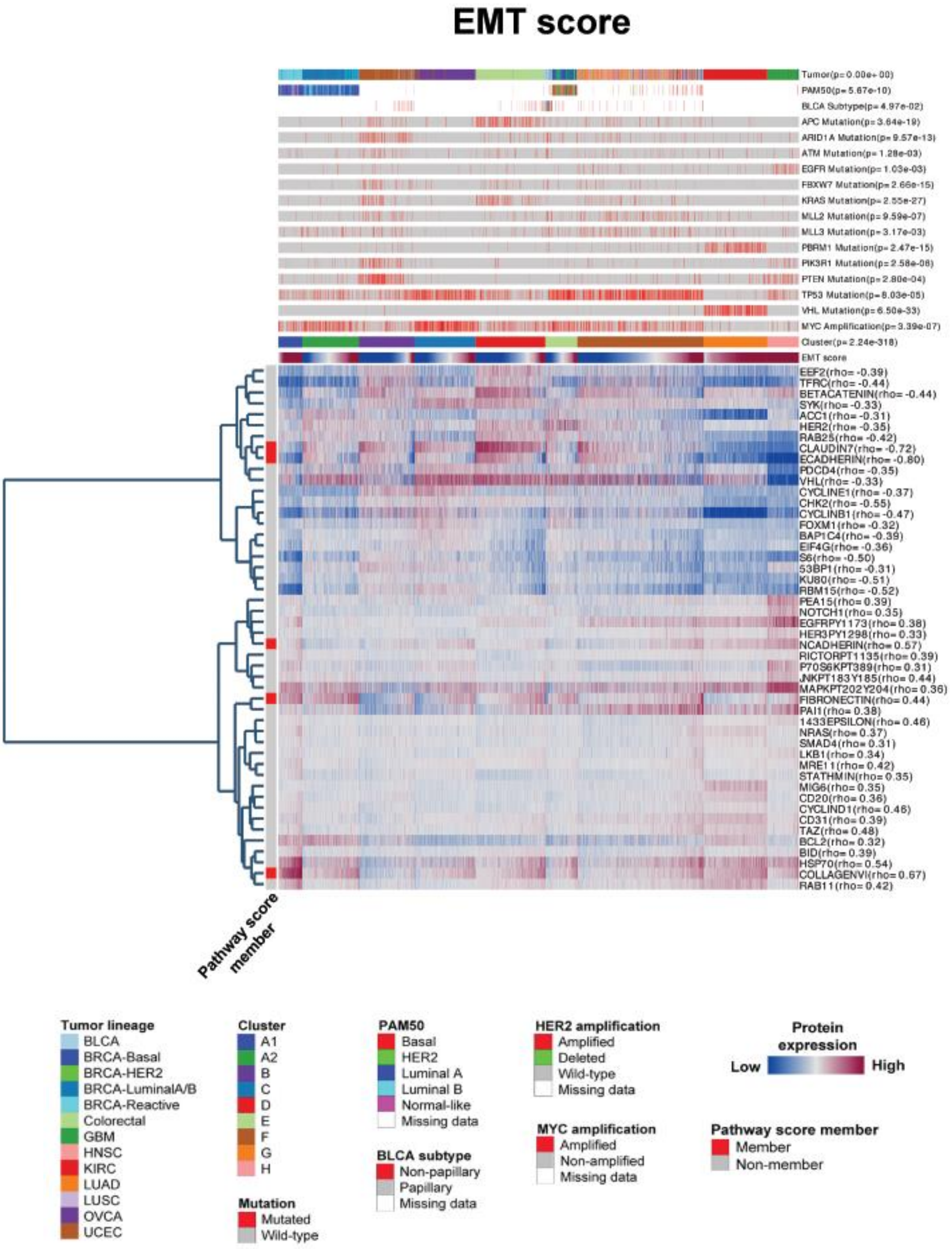


The pathways included are (in consecutive order) Apoptosis, Cell cycle, DNA damage response, EMT, Hormone_a, Hormone_b, PI3K/Akt, Ras/MAPK, RTK and TSC/mTOR. Heatmaps depict the protein levels of the pathway members and proteins with a high correlation (*ρ*>0.3/ *ρ*<-0.3, Spearman's correlation) to the pathway score. Annotation bars (selected from Fig. 2) are included if statistically associated with the pathway score (*P*-values <0.05, Kruskal-Wallis test). Pathway members are marked in red on the left hand side. High-resolution images of the heatmap can be found online (http://bioinformatics.mdanderson.org/main/TCGA/Pancan11/RPPA).


Cell cycle score



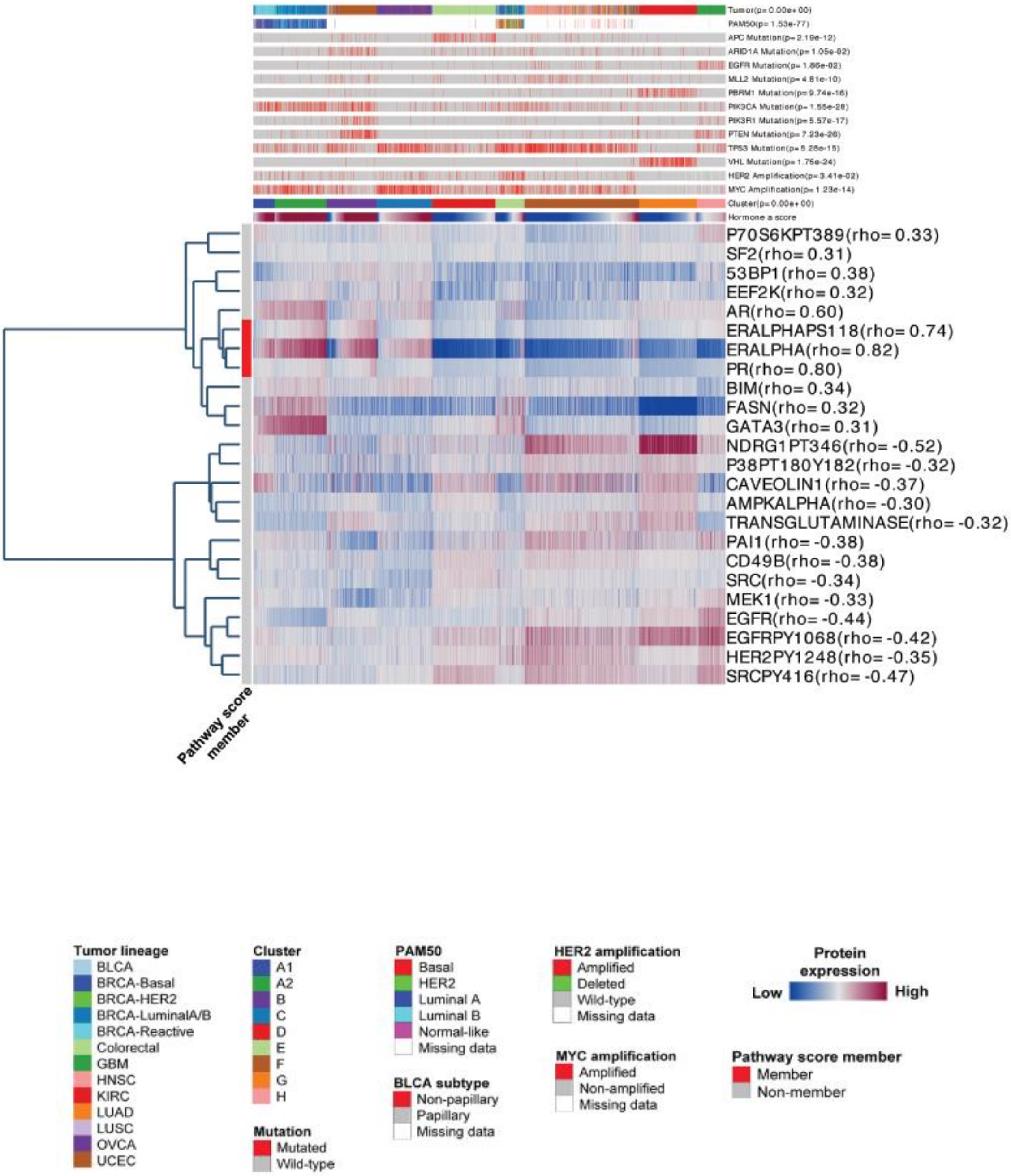
DNA damage response score

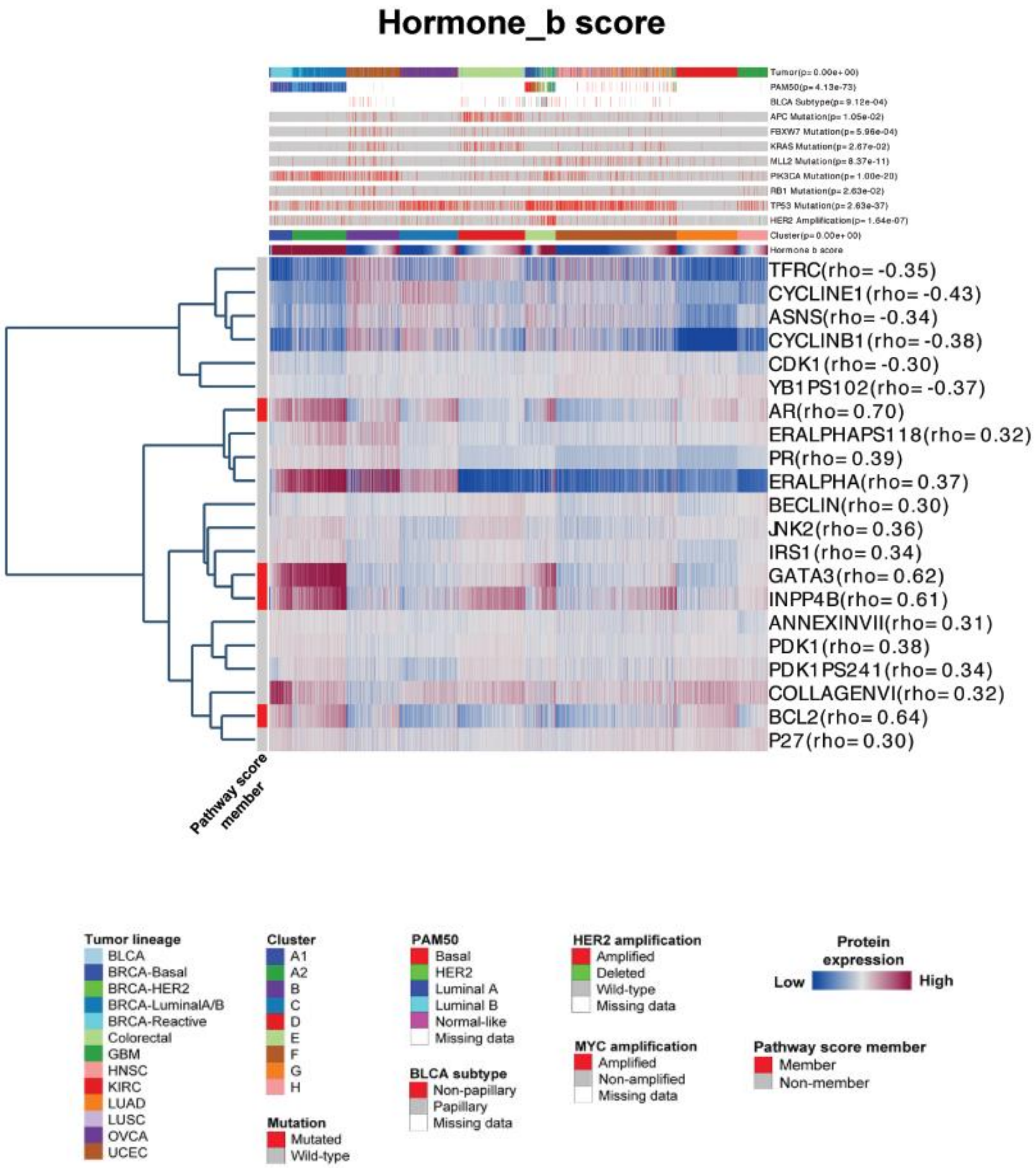


EMT score

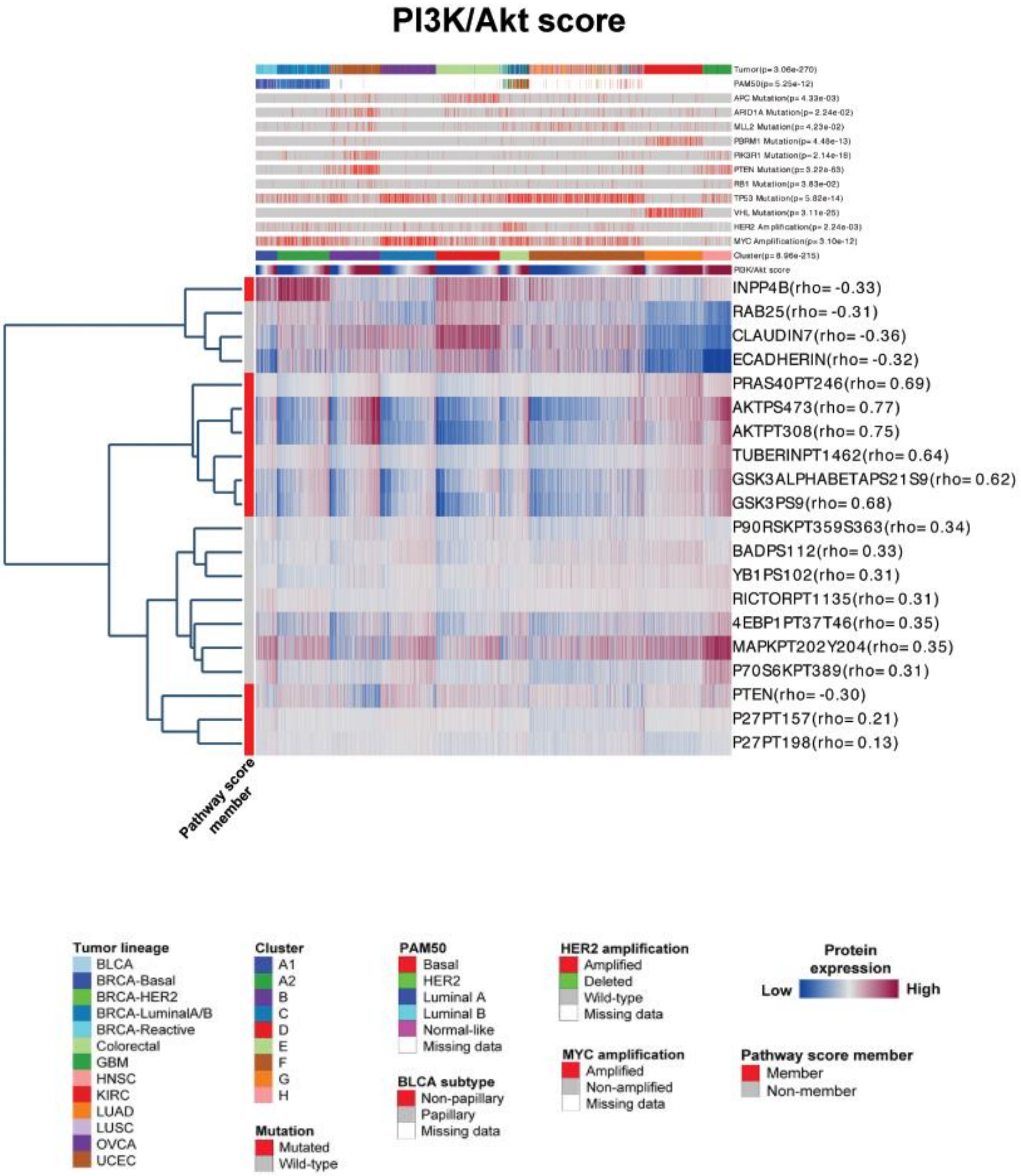
Tumor(p=0.00e+00)
PAM50(p=5.67e-10)
BLCA Subtype(p=4.97e-02)
APC Mutation(p=3.64e-19)
ARID1A Mutation(p=9.57e-13)
ATM Mutation(p=1.28e-03)
EGFR Mutation(p=1.03e-03)
FBXW7 Mutation(p=2.66e-15)
KRAS Mutation(p=2.55e-27)
MLL2 Mutation(p=9.59e-07)
MLL3 Mutation(p=3.17e-03)
PBRM1 Mutation(p=2.47e-15)
PIK3R1 Mutation(p=2.58e-08)
PTEN Mutation(p=2.80e-04)
TP53 Mutation(p=8.03e-05)
VHL Mutation(p=6.50e-33)
MYC Amplification(p=3.39e-07)
Cluster(p=2.24e-318)
EMT score
EEF2(rho=-0.39)
TFRC(rho=-0.44)
BETACATENIN(rho=-0.44)
SYK(rho=-0.33)
ACC1(rho=-0.31)
HER2(rho=-0.35)
RAB25(rho=-0.42)
CLAUDIN7(rho=-0.72)
ECADHERIN(rho=-0.80)
PDCD4(rho=-0.35)
VHL(rho=-0.33)
CYCLINE1(rho=-0.37)
CHK2(rho=-0.55)
CYCLINB1(rho=-0.47)
FOXM1(rho=-0.32)
BAP1C4(rho=-0.39)
EIF4G(rho=-0.36)
S6(rho=-0.50)
53BP1(rho=-0.31)
KU80(rho=-0.51)
RBM15(rho=-0.52)
PEA15(rho=0.39)
NOTCH1(rho=0.35)
EGFRPY1173(rho=0.38)
HER3PY1298(rho=0.33)
NCADHERIN(rho=0.57)
RICTORPT1135(rho=0.39)
P70S6KPT389(rho=0.31)
JNKPT183Y185(rho=0.44)
MAPKPT202Y204(rho=0.36)
FIBRONECTIN(rho=0.44)
PAI1(rho=0.38)
1433EPSILON(rho=0.46)
NRAS(rho=0.37)
SMAD4(rho=0.31)
LKB1(rho=0.34)
MRE11(rho=0.42)
STATHMIN(rho=0.35)
MIG6(rho=0.35)
CD20(rho=0.36)
CYCLIND1(rho=0.46)
CD31(rho=0.39)
TAZ(rho=0.48)
BCL2(rho=0.32)
BID(rho=0.39)
HSP70(rho=0.54)
COLLAGENVI(rho=0.67)
RAB11(rho=0.42)
Pathway score member
Tumor lineage
BLCA
BRCA-Basal
BRCA-HER2
BRCA-LuminalA/B
BRCA-Reactive
Colorectal
GBM
HNSC
KIRC
LUAD
LUSC
OVCA
UCEC
Cluster
A1
A2
B
C
D
E
F
G
H
Mutation
Mutated
Wild-type
PAM50
Basal
HER2
Luminal A
Luminal B
Normal-like
Missing data
BLCA subtype
Non-papillary
Papillary
Missing data
HER2 amplification
Amplified
Deleted
Wild-type
Missing data
MYC amplification
Amplified
Non-amplified
Missing data
Protein expression
Low
High
Pathway score member
Member
Non-member

Hormone_a score

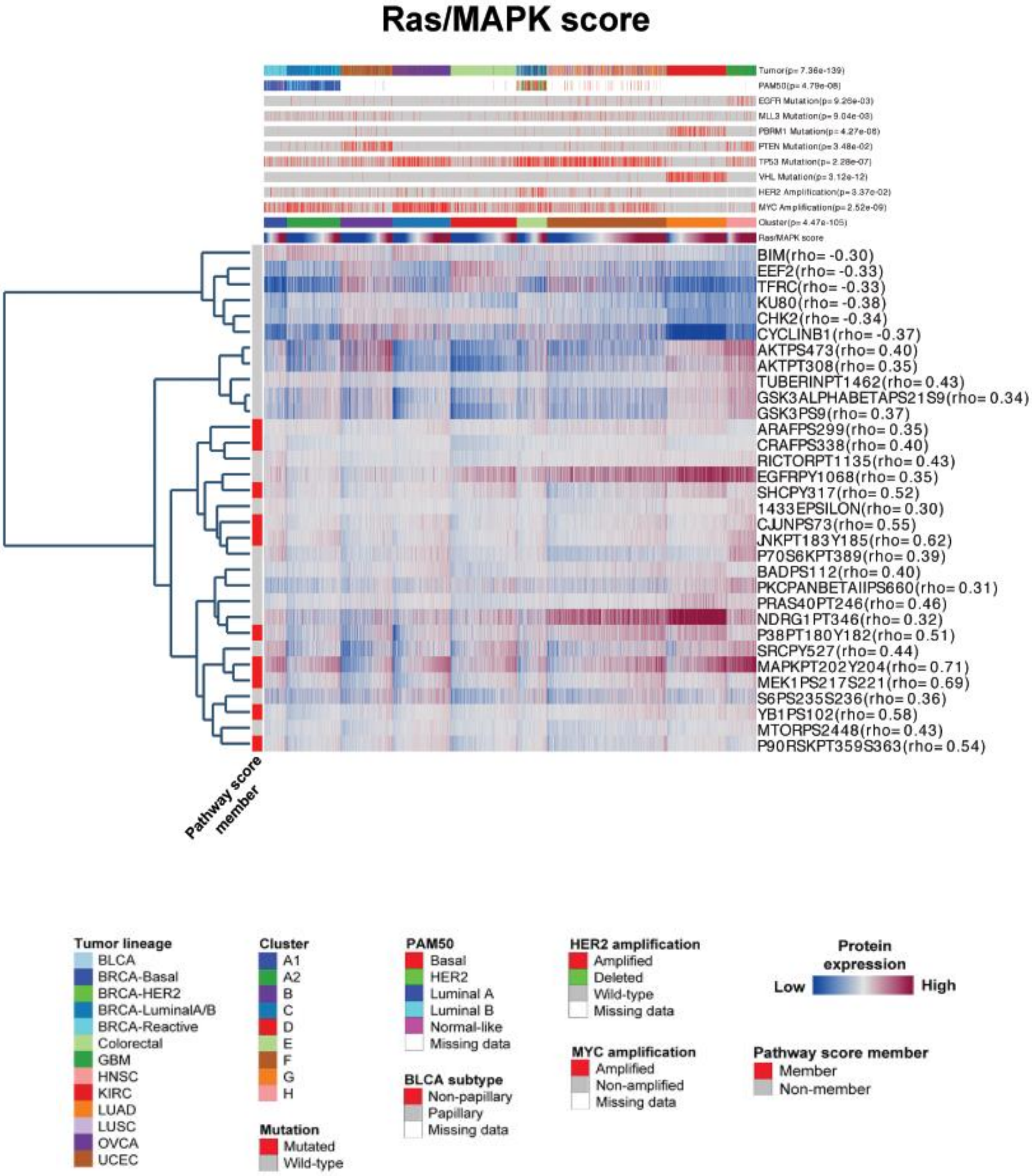




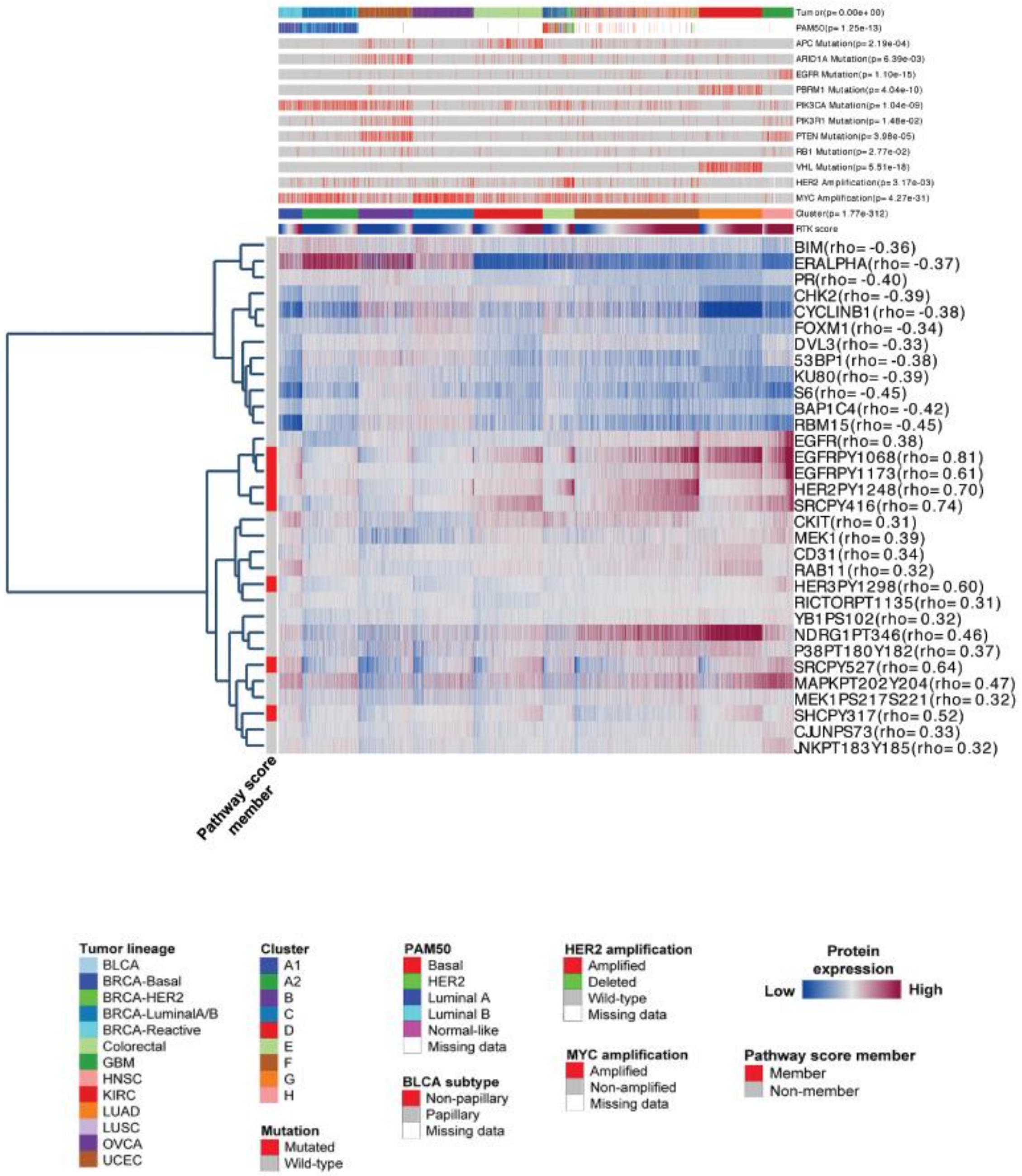
Hormone_b score

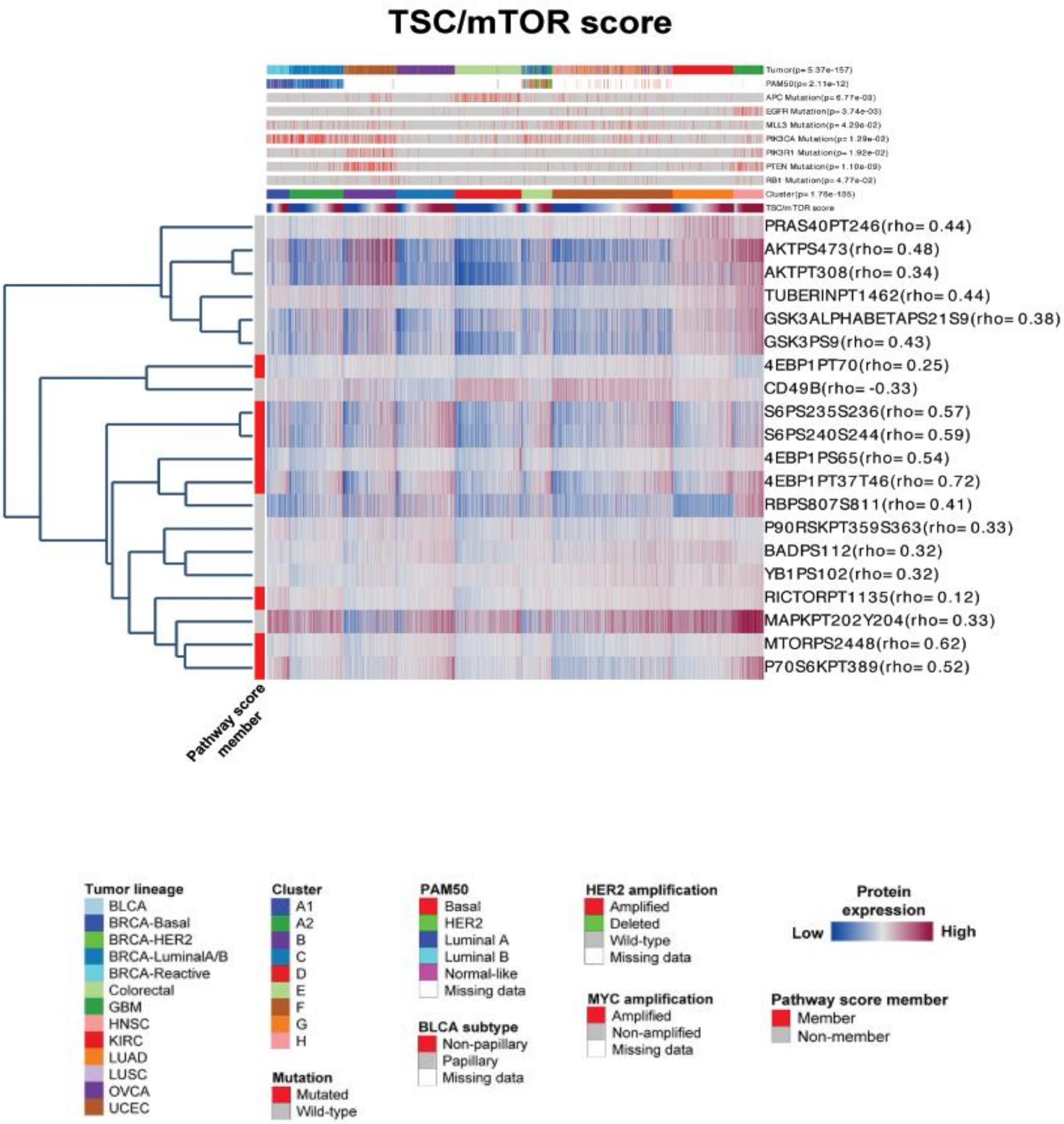


PI3K/Akt score

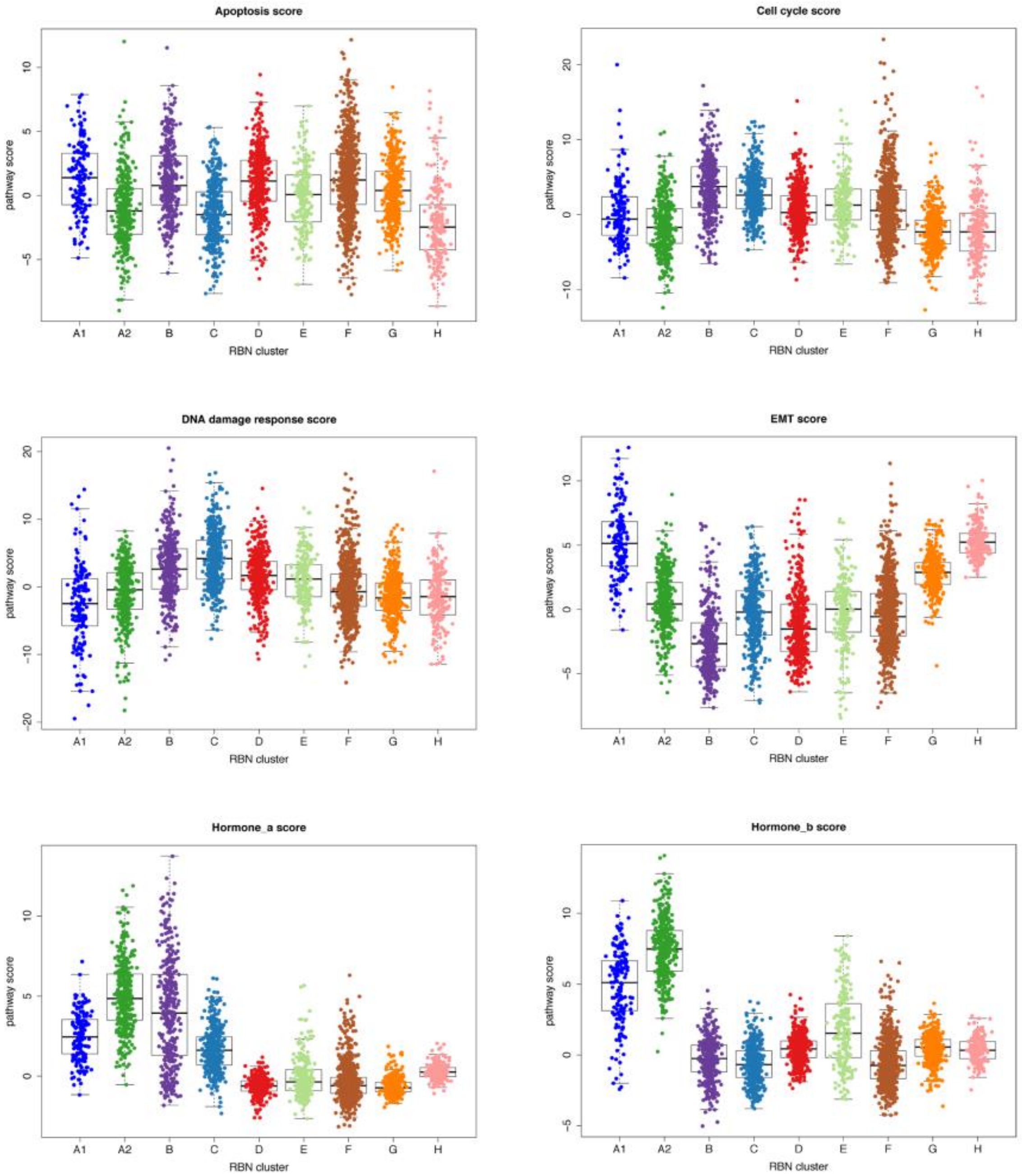

Ras/MAPK score
Tumor(p= 7.36e-139)
PAM50(p= 4.79e-08)
EGFR Mutation(p= 9.26e-03)
MLL3 Mutation(p= 9.04e-03)
PBRM1 Mutation(p= 4.27e-08)
PTEN Mutation(p= 3.48e-02)
TP53 Mutation(p= 2.28e-07)
VHL Mutation(p= 3.12e-12)
HER2 Amplification(p= 3.37e-02)
MYC Amplification(p= 2.52e-09)
Cluster(p= 4.47e-105)
Ras/MAPK score
BIM(rho= -0.30)
EEF2(rho= -0.33)
TFRC(rho= -0.33)
KU80(rho= -0.38)
CHK2(rho= -0.34)
CYCLINB1(rho= -0.37)
AKTPS473(rho= 0.40)
AKTPT308(rho= 0.35)
TUBERINPT1462(rho= 0.43)
GSK3ALPHABETAPS21S9(rho= 0.34)
GSK3PS9(rho= 0.37)
ARAFPS299(rho= 0.35)
CRAFPS338(rho= 0.40)
RICTORPT1135(rho= 0.43)
EGFRPY1068(rho= 0.35)
SHCPY317(rho= 0.52)
1433EPSILON(rho= 0.30)
CJUNPS73(rho= 0.55)
JNKPT183Y185(rho= 0.62)
P70S6KPT389(rho= 0.39)
BADPS112(rho= 0.40)
PKCPANBETAIIPS660(rho= 0.31)
PRAS40PT246(rho= 0.46)
NDRG1PT346(rho= 0.32)
P38PT180Y182(rho= 0.51)
SRCPY527(rho= 0.44)
MAPKPT202Y204(rho= 0.71)
MEK1PS217S221(rho= 0.69)
S6PS235S236(rho= 0.36)
YB1PS102(rho= 0.58)
MTORPS2448(rho= 0.43)
P90RSKPT359S363(rho= 0.54)
Pathway score member
Tumor lineage
BLCA
BRCA-Basal
BRCA-HER2
BRCA-LuminalA/B
BRCA-Reactive
Colorectal
GBM
HNSC
KIRC
LUAD
LUSC
OVCA
UCEC
Cluster
A1
A2
B
C
D
E
F
G
H
Mutation
Mutated
Wild-type
PAM50
Basal
HER2
Luminal A
Luminal B
Normal-like
Missing data
BLCA subtype
Non-papillary
Papillary
Missing data
HER2 amplification
Amplified
Deleted
Wild-type
Missing data
MYC amplification
Amplified
Non-amplified
Missing data
Protein expression
Low
High
Pathway score member
Member
Non-member

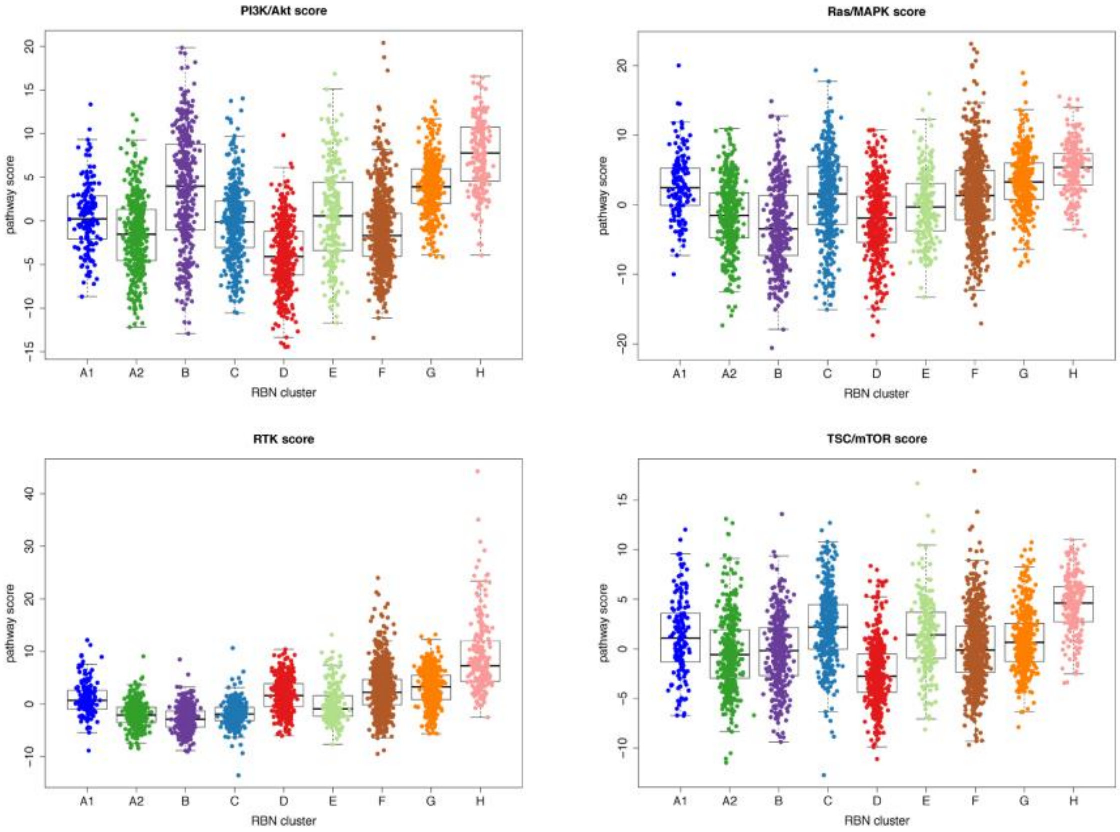
RTK score


Tumor(p=0.00e+00)
PAM50(p=1.25e-13)
APC Mutation(p=2.19e-04)
ARID1A Mutation(p=6.39e-03)
EGFR Mutation(p=1.10e-15)
PBRM1 Mutation(p=4.04e-10)
PIK3CA Mutation(p=1.04e-09)
PIK3R1 Mutation(p=1.48e-02)
PTEN Mutation(p=3.98e-05)
RB1 Mutation(p=2.77e-02)
VHL Mutation(p=5.51e-18)
HER2 Amplification(p=3.17e-03)
MYC Amplification(p=4.27e-31)
Cluster(p=1.77e-312)
RTK score
BIM(rho=-0.36)
ERALPHA(rho=-0.37)
PR(rho=-0.40)
CHK2(rho=-0.39)
CYCLINB1(rho=-0.38)
FOXM1(rho=-0.34)
DVL3(rho=-0.33)
53BP1(rho=-0.38)
KU80(rho=-0.39)
S6(rho=-0.45)
BAP1C4(rho=-0.42)
RBM15(rho=-0.45)
EGFR(rho=0.38)
EGFRPY1068(rho=0.81)
EGFRPY1173(rho=0.61)
HER2PY1248(rho=0.70)
SRCPY416(rho=0.74)
CKIT(rho=0.31)
MEK1(rho=0.39)
CD31(rho=0.34)
RAB11(rho=0.32)
HER3PY1298(rho=0.60)
RICTORPT1135(rho=0.31)
YB1PS102(rho=0.32)
NDRG1PT346(rho=0.46)
P38PT180Y182(rho=0.37)
SRCPY527(rho=0.64)
MAPKPT202Y204(rho=0.47)
MEK1PS217S221(rho=0.32)
SHCPY317(rho=0.52)
CJUNPS73(rho=0.33)
JNKPT183Y185(rho=0.32)
Pathway score member
Tumor lineage
BLCA
BRCA-Basal
BRCA-HER2
BRCA-LuminalA/B
BRCA-Reactive
Colorectal
GBM
HNSC
KIRC
LUAD
LUSC
OVCA
UCEC
Cluster
A1
A2
B
C
D
E
F
G
H
Mutation
Mutated
Wild-type
PAM50
Basal
HER2
Luminal A
Luminal B
Normal-like
Missing data
BLCA subtype
Non-papillary
Papillary
Missing data
HER2 amplification
Amplified
Deleted
Wild-type
Missing data
MYC amplification
Amplified
Non-amplified
Missing data
Protein expression
Low
High
Pathway score member
Member
Non-member


TSC/mTOR score
Tumor(p=5.37e-157)
PAM50(p=2.11e-12)
APC Mutation(p=6.77e-03)
EGFR Mutation(p=3.74e-03)
MLL3 Mutation(p=4.29e-02)
PIK3CA Mutation(p=1.29e-02)
PIK3R1 Mutation(p=1.92e-02)
PTEN Mutation(p=1.10e-09)
RB1 Mutation(p=4.77e-02)
Cluster(p=1.76e-135)
TSC/mTOR score
PRAS40PT246(rho=0.44)
AKTPS473(rho=0.48)
AKTPT308(rho=0.34)
TUBERINPT1462(rho=0.44)
GSK3ALPHABETAPS21S9(rho=0.38)
GSK3PS9(rho=0.43)
4EBP1PT70(rho=0.25)
CD49B(rho=-0.33)
S6PS235S236(rho=0.57)
S6PS240S244(rho=0.59)
4EBP1PS65(rho=0.54)
4EBP1PT37T46(rho=0.72)
RBPS807S811(rho=0.41)
P90RSKPT359S363(rho=0.33)
BADPS112(rho=0.32)
YB1PS102(rho=0.32)
RICTORPT1135(rho=0.12)
MAPKPT202Y204(rho=0.33)
MTORPS2448(rho=0.62)
P70S6KPT389(rho=0.52)
Pathway score member
Tumor lineage
BLCA
BRCA-Basal
BRCA-HER2
BRCA-LuminalA/B
BRCA-Reactive
Colorectal
GBM
HNSC
KIRC
LUAD
LUSC
OVCA
UCEC
Cluster
A1
A2
B
C
D
E
F
G
H
Mutation
Mutated
Wild-type
PAM50
Basal
HER2
Luminal A
Luminal B
Normal-like
Missing data
BLCA subtype
Non-papillary
Papillary
Missing data
HER2 amplification
Amplified
Deleted
Wild-type
Missing data
MYC amplification
Amplified
Non-amplified
Missing data
Protein expression
Low
High
Pathway score member
Member
Non-member

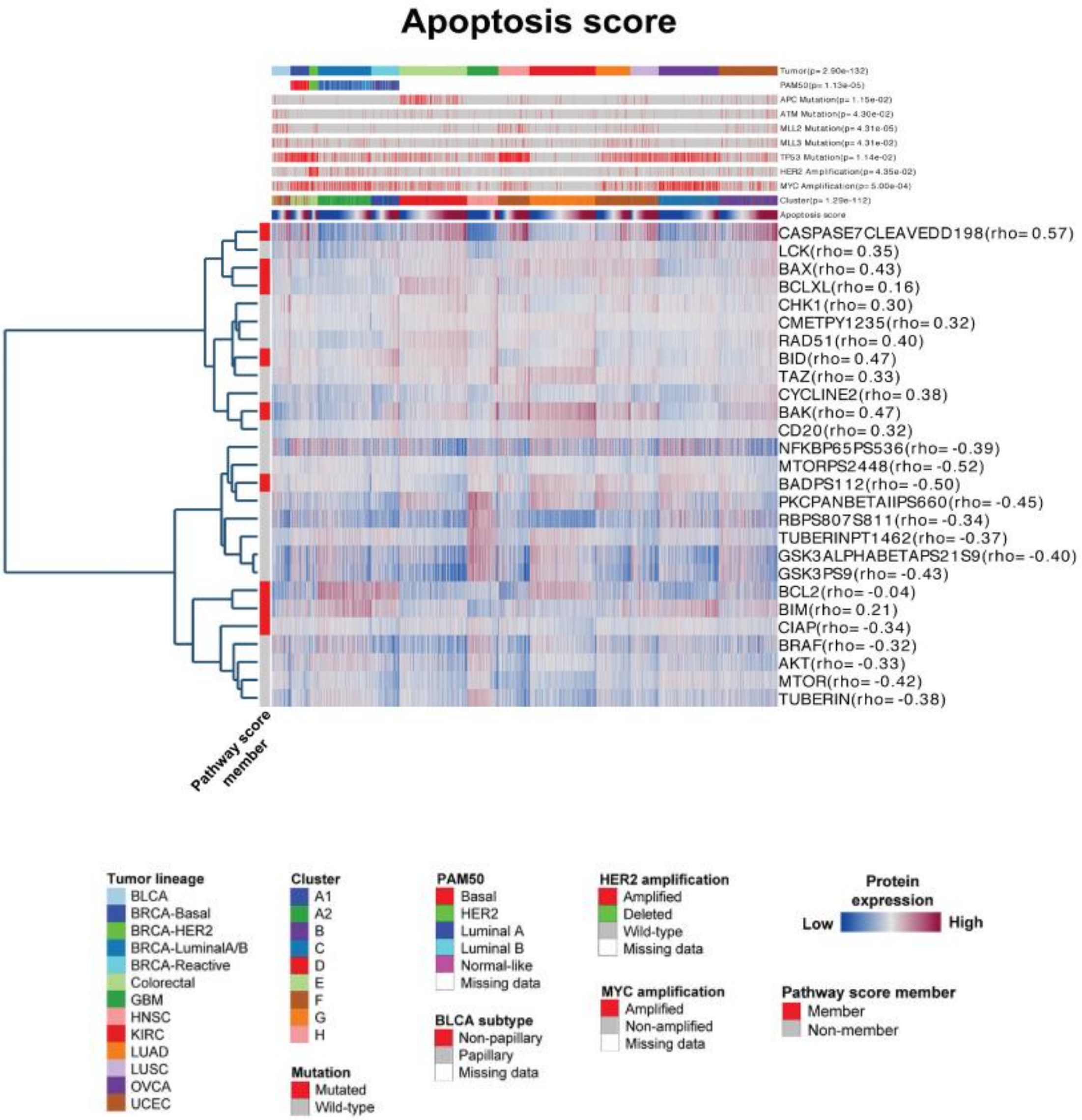
Supplementary Figure 7: Dotplots showing pathway scores across RBN clusters



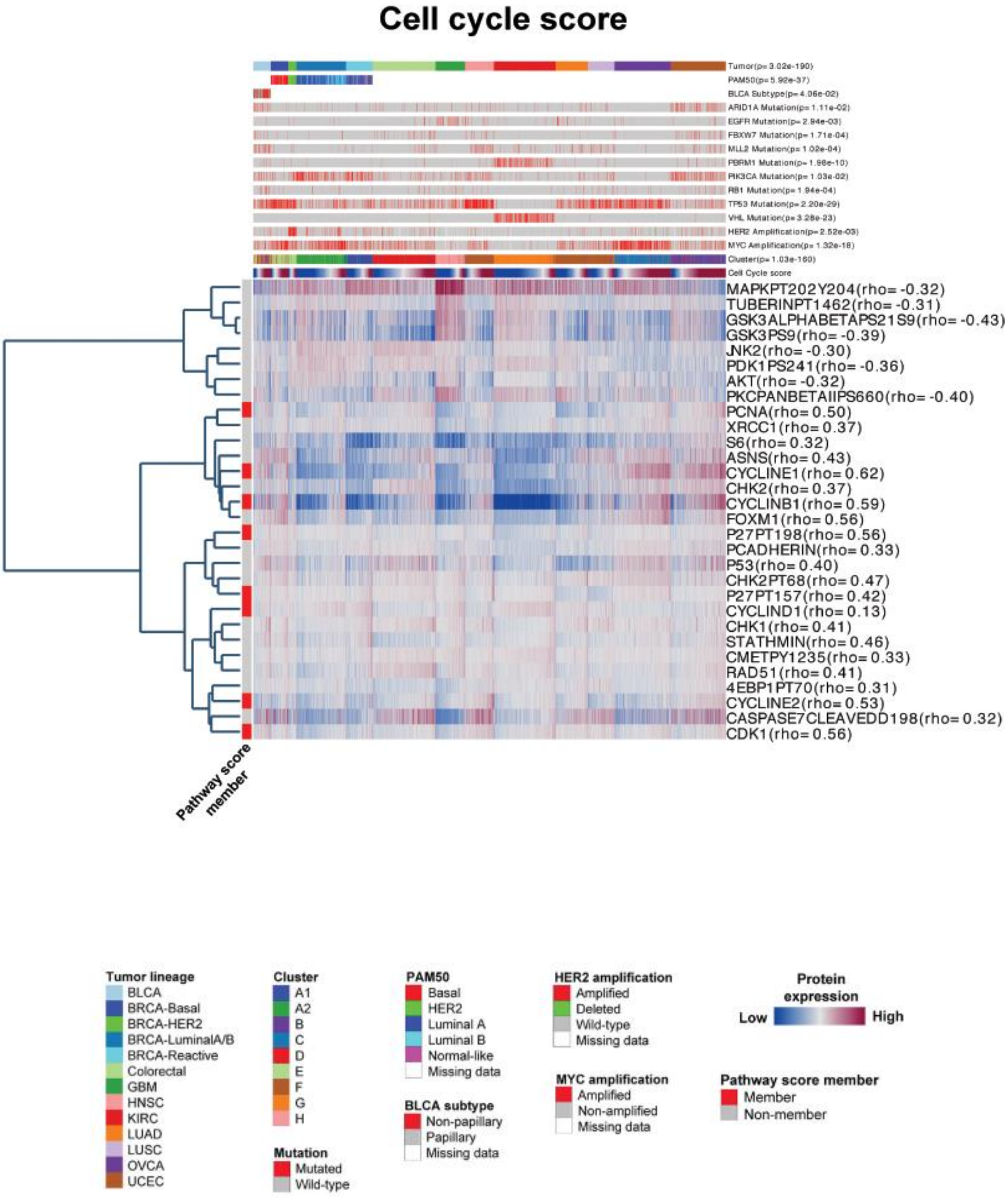


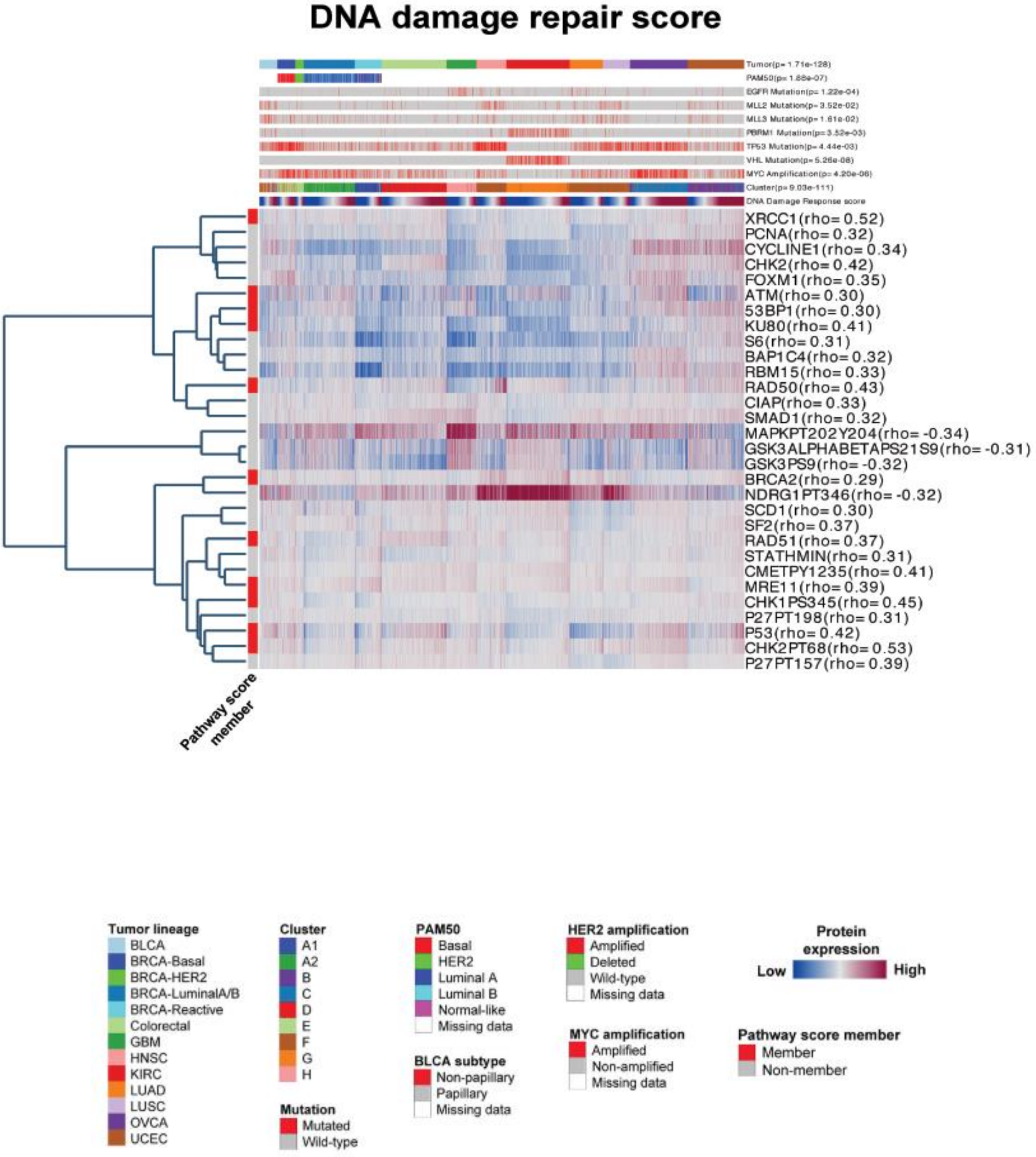
Pathway score of each sample, across RBN clusters, is shown in the dotplots. Each dot represents pathway score of a sample.

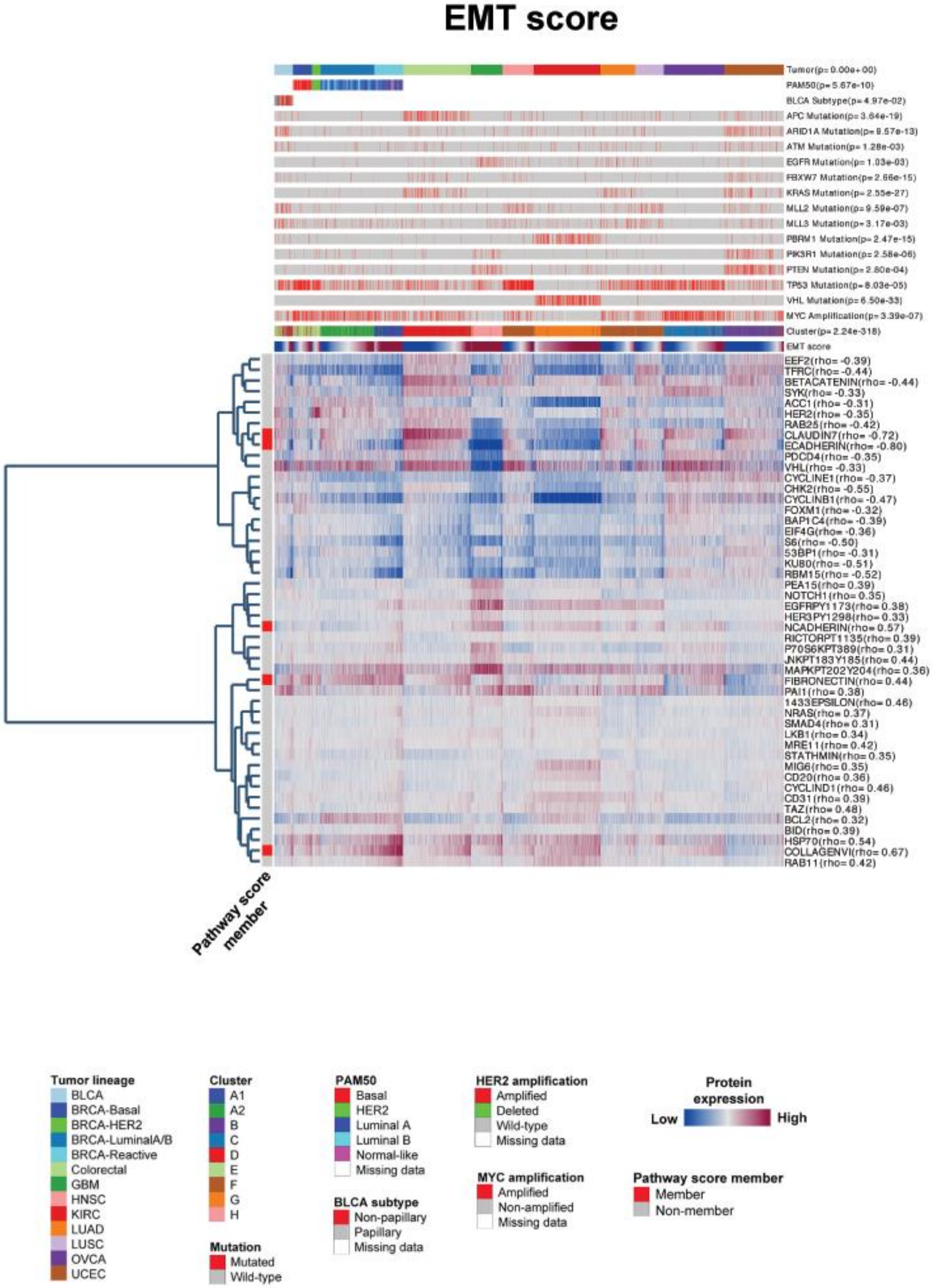
Supplementary Figure 8: Heatmaps showing pathway members and associated proteins and molecular/ clinical variables with pathway scores (RBN dataset by tumor lineage)

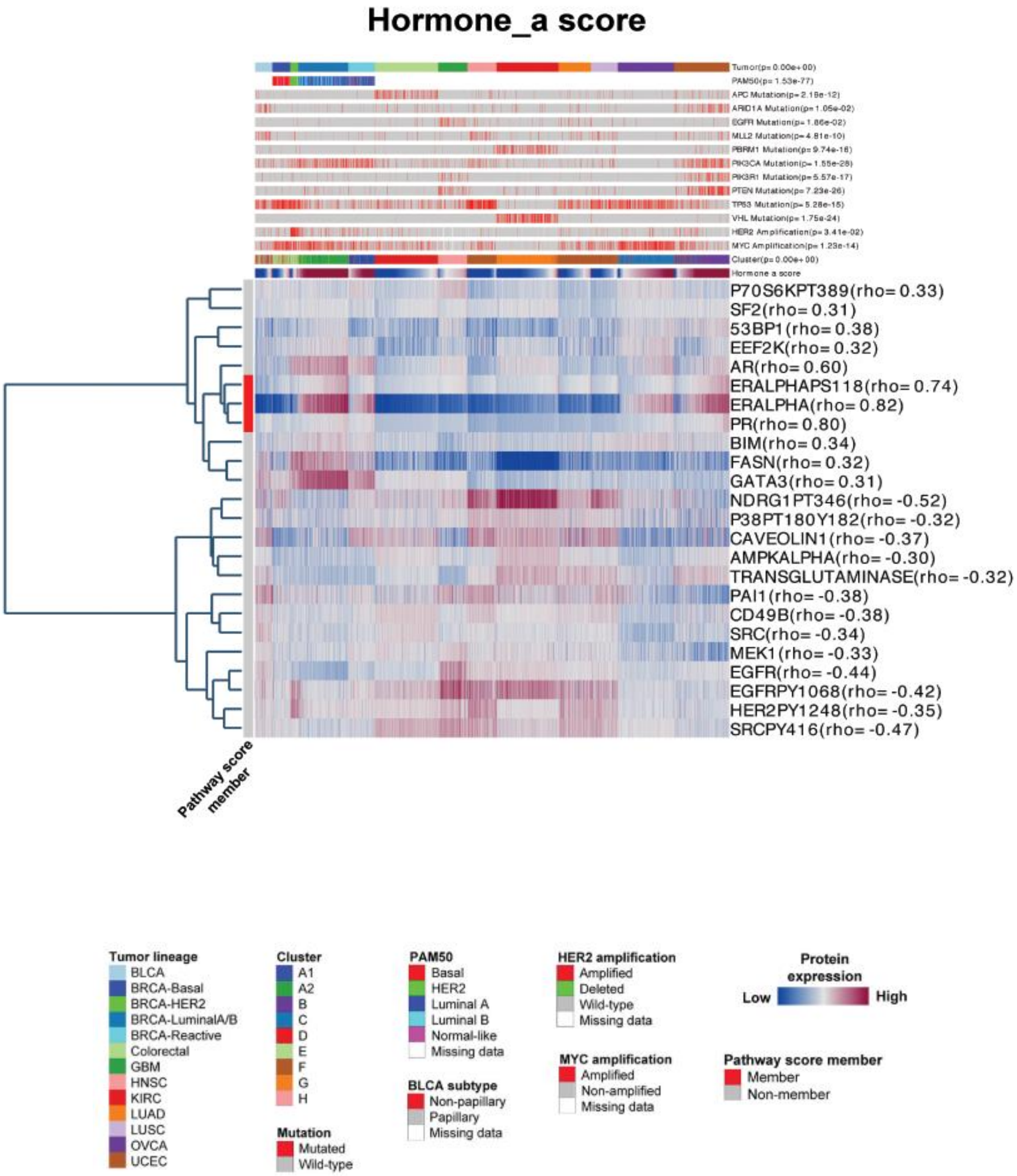


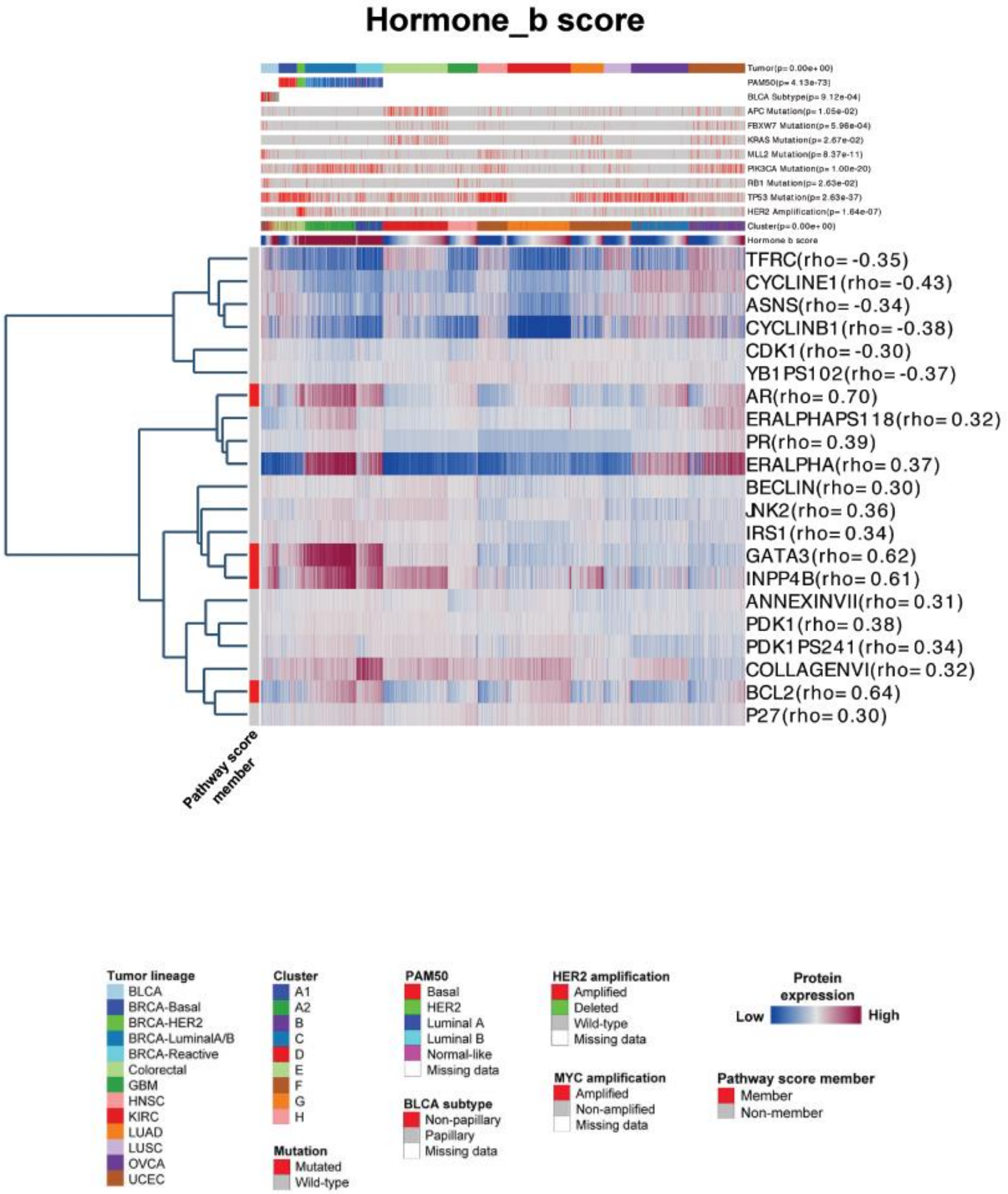
The pathways included are (in alphabetical order) Apoptosis, Cell cycle, DNA damage response, EMT, Hormone_a, Hormone_b, PI3K/Akt, Ras/MAPK, RTK and TSC/mTOR. Heatmaps depict the protein levels of the pathway members and proteins with a high correlation (ρ>0.3/ ρ<-0.3, Spearman's correlation) to the pathway score. Annotation bars (selected from Fig. 2) are included if statistically associated with the pathway score (*P*-values <0.05, Kruskal-Wallis test). Pathway members are marked in red on the left hand side. High-resolution images of the heatmap can be found online (http://bioinformatics.mdanderson.org/main/TCGA/Pancan11/RPPA).

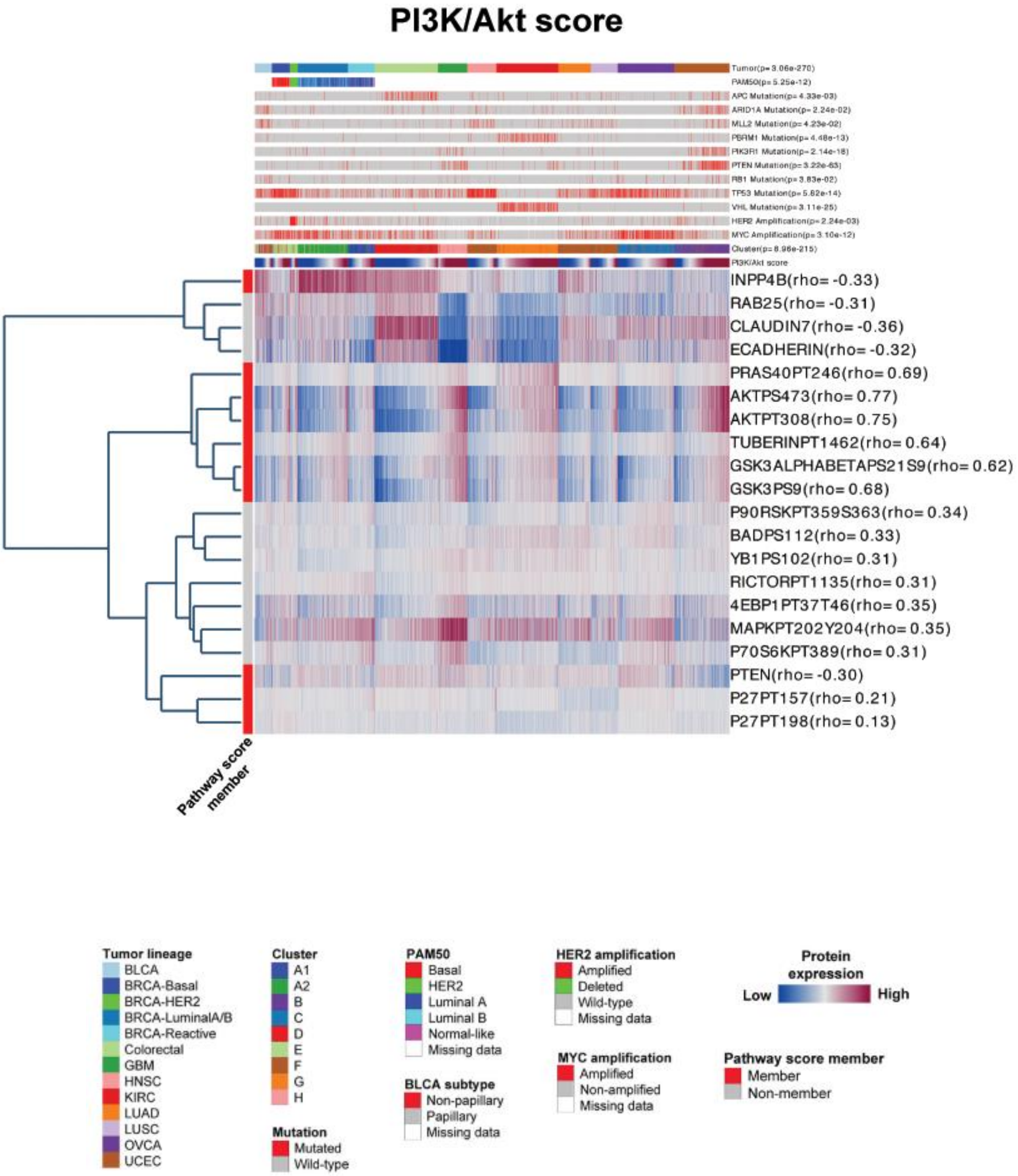

Cell cycle score
Tumor(p= 3.02e-190)
PAM50(p= 5.92e-37)
BLCA Subtype(p= 4.06e-02)
ARID1A Mutation(p= 1.11e-02)
EGFR Mutation(p= 2.94e-03)
FBXW7 Mutation(p= 1.71e-04)
MLL2 Mutation(p= 1.02e-04)
PBRM1 Mutation(p= 1.98e-10)
PIK3CA Mutation(p= 1.03e-02)
RB1 Mutation(p= 1.94e-04)
TP53 Mutation(p= 2.20e-29)
VHL Mutation(p= 3.28e-23)
HER2 Amplification(p= 2.52e-03)
MYC Amplification(p= 1.32e-18)
Cluster(p= 1.03e-160)
Cell Cycle score
MAPKPT202Y204(rho= -0.32)
TUBERINPT1462(rho= -0.31)
GSK3ALPHABETAPS21S9(rho= -0.43)
GSK3PS9(rho= -0.39)
JNK2(rho= -0.30)
PDK1PS241(rho= -0.36)
AKT(rho= -0.32)
PKCPANBETAIIPS660(rho= -0.40)
PCNA(rho= 0.50)
XRCC1(rho= 0.37)
S6(rho= 0.32)
ASNS(rho= 0.43)
CYCLINE1(rho= 0.62)
CHK2(rho= 0.37)
CYCLINB1(rho= 0.59)
FOXM1(rho= 0.56)
P27PT198(rho= 0.56)
PCADHERIN(rho= 0.33)
P53(rho= 0.40)
CHK2PT68(rho= 0.47)
P27PT157(rho= 0.42)
CYCLIND1(rho= 0.13)
CHK1(rho= 0.41)
STATHMIN(rho= 0.46)
CMETPY1235(rho= 0.33)
RAD51(rho= 0.41)
4EBP1PT70(rho= 0.31)
CYCLINE2(rho= 0.53)
CASPASE7CLEAVEDD198(rho= 0.32)
CDK1(rho= 0.56)
Pathway score member
Tumor lineage
BLCA
BRCA-Basal
BRCA-HER2
BRCA-LuminalA/B
BRCA-Reactive
Colorectal
GBM
HNSC
KIRC
LUAD
LUSC
OVCA
UCEC
Cluster
A1
A2
B
C
D
E
F
G
H
Mutation
Mutated
Wild-type
PAM50
Basal
HER2
Luminal A
Luminal B
Normal-like
Missing data
BLCA subtype
Non-papillary
Papillary
Missing data
HER2 amplification
Amplified
Deleted
Wild-type
Missing data
MYC amplification
Amplified
Non-amplified
Missing data
Protein expression
Low
High
Pathway score member
Member
Non-member

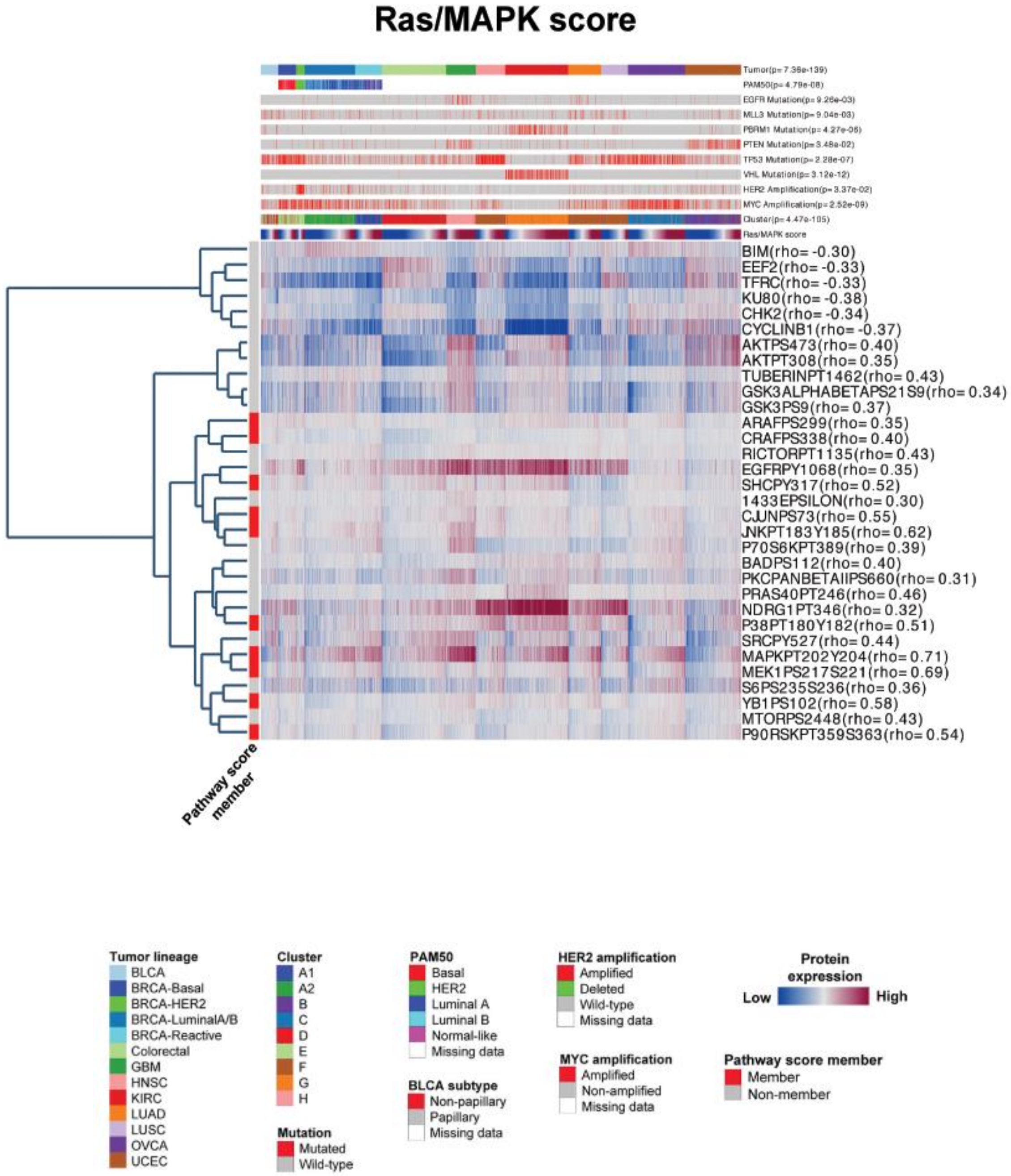

DNA damage repair score
Tumor(p= 1.71e-128)
PAM50(p= 1.88e-07)
EGFR Mutation(p= 1.22e-04)
MLL2 Mutation(p= 3.52e-02)
MLL3 Mutation(p= 1.61e-02)
PBRM1 Mutation(p= 3.52e-03)
TP53 Mutation(p= 4.44e-03)
VHL Mutation(p= 5.26e-08)
MYC Amplification(p= 4.20e-06)
Cluster(p= 9.03e-111)
DNA Damage Response score
XRCC1(rho= 0.52)
PCNA(rho= 0.32)
CYCLINE1(rho= 0.34)
CHK2(rho= 0.42)
FOXM1(rho= 0.35)
ATM(rho= 0.30)
53BP1(rho= 0.30)
KU80(rho= 0.41)
S6(rho= 0.31)
BAP1C4(rho= 0.32)
RBM15(rho= 0.33)
RAD50(rho= 0.43)
CIAP(rho= 0.33)
SMAD1(rho= 0.32)
MAPKPT202Y204(rho= -0.34)
GSK3ALPHABETAPS21S9(rho= -0.31)
GSK3PS9(rho= -0.32)
BRCA2(rho= 0.29)
NDRG1PT346(rho= -0.32)
SCD1(rho= 0.30)
SF2(rho= 0.37)
RAD51(rho= 0.37)
STATHMIN(rho= 0.31)
CMETPY1235(rho= 0.41)
MRE11(rho= 0.39)
CHK1PS345(rho= 0.45)
P27PT198(rho= 0.31)
P53(rho= 0.42)
CHK2PT68(rho= 0.53)
P27PT157(rho= 0.39)
Pathway score member
Tumor lineage
BLCA
BRCA-Basal
BRCA-HER2
BRCA-LuminalA/B
BRCA-Reactive
Colorectal
GBM
HNSC
KIRC
LUAD
LUSC
OVCA
UCEC
Cluster
A1
A2
B
C
D
E
F
G
H
Mutation
Mutated
Wild-type
PAM50
Basal
HER2
Luminal A
Luminal B
Normal-like
Missing data
BLCA subtype
Non-papillary
Papillary
Missing data
HER2 amplification
Amplified
Deleted
Wild-type
Missing data
MYC amplification
Amplified
Non-amplified
Missing data
Protein expression
Low
High
Pathway score member
Member
Non-member

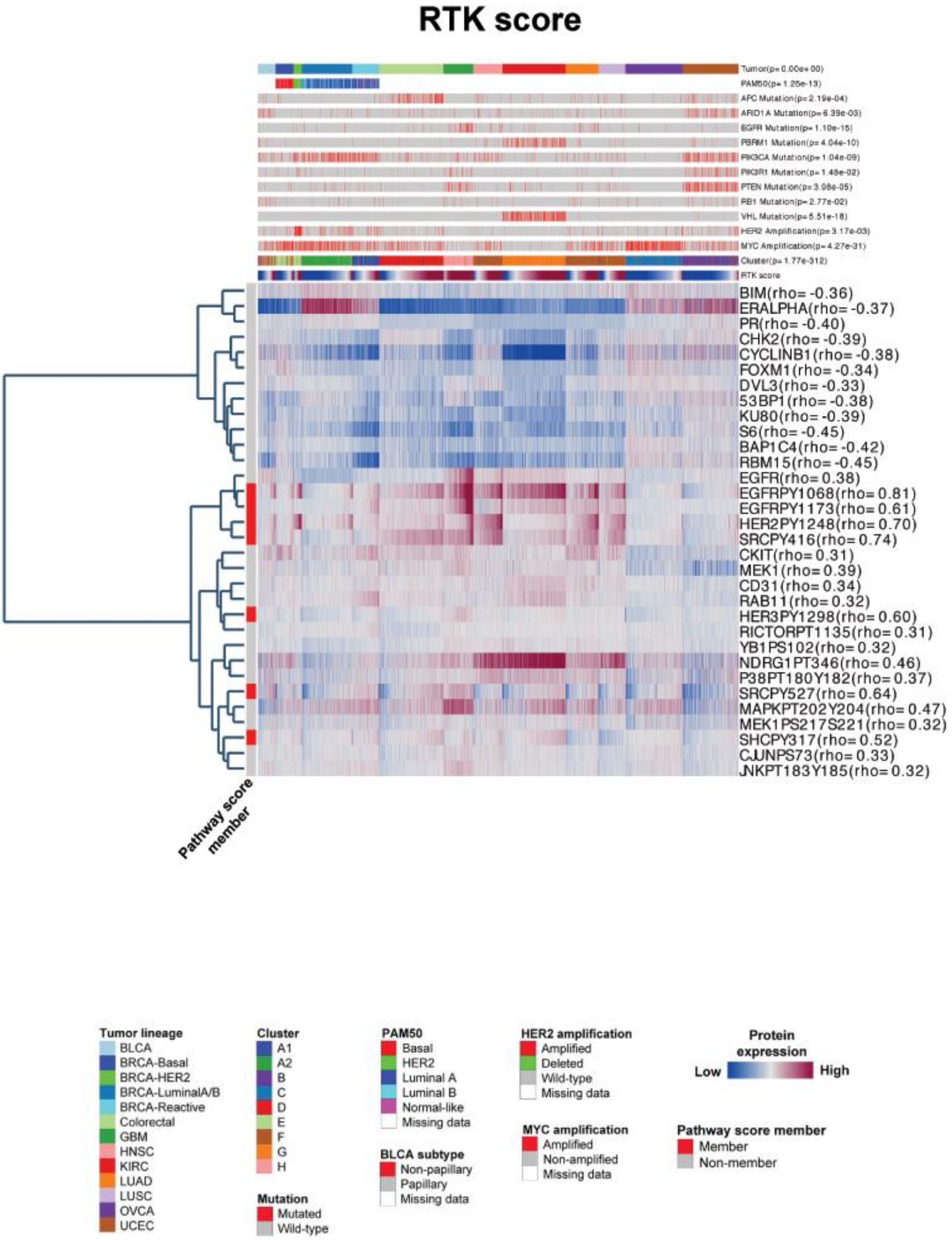

EMT score
Tumor(p= 0.00e+00)
PAM50(p= 5.67e-10)
BLCA Subtype(p= 4.97e-02)
APC Mutation(p= 3.64e-19)
ARID1A Mutation(p= 9.57e-13)
ATM Mutation(p= 1.28e-03)
EGFR Mutation(p= 1.03e-03)
FBXW7 Mutation(p= 2.66e-15)
KRAS Mutation(p= 2.55e-27)
MLL2 Mutation(p= 9.59e-07)
MLL3 Mutation(p= 3.17e-03)
PBRM1 Mutation(p= 2.47e-15)
PIK3R1 Mutation(p= 2.58e-06)
PTEN Mutation(p= 2.80e-04)
TP53 Mutation(p= 8.03e-05)
VHL Mutation(p= 6.50e-33)
MYC Amplification(p= 3.39e-07)
Cluster(p= 2.24e-318)
EMT score
EEF2(rho= -0.39)
TFRC(rho= -0.44)
BETACATENIN(rho= -0.44)
SYK(rho= -0.33)
ACC1(rho= -0.31)
HER2(rho= -0.35)
RAB25(rho= -0.42)
CLAUDIN7(rho= -0.72)
ECADHERIN(rho= -0.80)
PDCD4(rho= -0.35)
VHL(rho= -0.33)
CYCLINE1(rho= -0.37)
CHK2(rho= -0.55)
CYCLINB1(rho= -0.47)
FOXM1(rho= -0.32)
BAP1C4(rho= -0.39)
EIF4G(rho= -0.36)
S6(rho= -0.50)
53BP1(rho= -0.31)
KU80(rho= -0.51)
RBM15(rho= -0.52)
PEA15(rho= 0.39)
NOTCH1(rho= 0.35)
EGFRPY1173(rho= 0.38)
HER3PY1298(rho= 0.33)
NCADHERIN(rho= 0.57)
RICTORPT1135(rho= 0.39)
P70S6KPT389(rho= 0.31)
JNKPT183Y185(rho= 0.44)
MAPKPT202Y204(rho= 0.36)
FIBRONECTIN(rho= 0.44)
PAI1(rho= 0.38)
1433EPSILON(rho= 0.46)
NRAS(rho= 0.37)
SMAD4(rho= 0.31)
LKB1(rho= 0.34)
MRE11(rho= 0.42)
STATHMIN(rho= 0.35)
MIG6(rho= 0.35)
CD20(rho= 0.36)
CYCLIND1(rho= 0.46)
CD31(rho= 0.39)
TAZ(rho= 0.48)
BCL2(rho= 0.32)
BID(rho= 0.39)
HSP70(rho= 0.54)
COLLAGENVI(rho= 0.67)
RAB11(rho= 0.42)
Pathway score member
Tumor lineage
BLCA
BRCA-Basal
BRCA-HER2
BRCA-LuminalA/B
BRCA-Reactive
Colorectal
GBM
HNSC
KIRC
LUAD
LUSC
OVCA
UCEC
Cluster
A1
A2
B
C
D
E
F
G
H
Mutation
Mutated
Wild-type
PAM50
Basal
HER2
Luminal A
Luminal B
Normal-like
Missing data
BLCA subtype
Non-papillary
Papillary
Missing data
HER2 amplification
Amplified
Deleted
Wild-type
Missing data
MYC amplification
Amplified
Non-amplified
Missing data
Protein expression
Low
High
Pathway score member
Member
Non-member

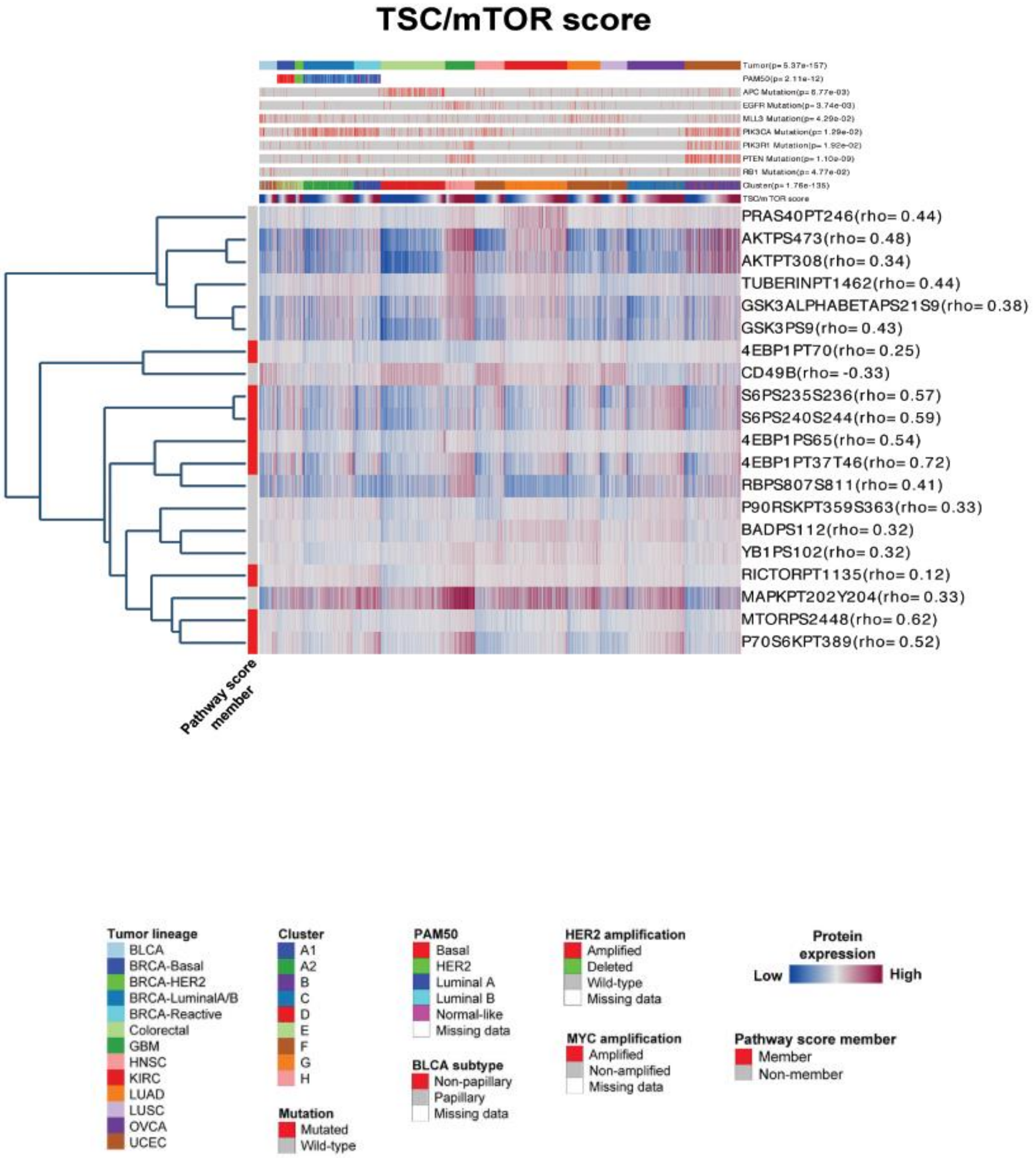

Hormone_a score
Tumor(p= 0.00e+00)
PAM50(p= 1.53e-77)
APC Mutation(p= 2.19e-12)
ARID1A Mutation(p= 1.05e-02)
EGFR Mutation(p= 1.86e-02)
MLL2 Mutation(p= 4.81e-10)
PBRM1 Mutation(p= 9.74e-16)
PIK3CA Mutation(p= 1.55e-28)
PIK3R1 Mutation(p= 5.57e-17)
PTEN Mutation(p= 7.23e-26)
TP53 Mutation(p= 5.28e-15)
VHL Mutation(p= 1.75e-24)
HER2 Amplification(p= 3.41e-02)
MYC Amplification(p= 1.23e-14)
Cluster(p= 0.00e+00)
Hormone a score
P70S6KPT389(rho= 0.33)
SF2(rho= 0.31)
53BP1(rho= 0.38)
EEF2K(rho= 0.32)
AR(rho= 0.60)
ERALPHAPS118(rho= 0.74)
ERALPHA(rho= 0.82)
PR(rho= 0.80)
BIM(rho= 0.34)
FASN(rho= 0.32)
GATA3(rho= 0.31)
NDRG1PT346(rho= -0.52)
P38PT180Y182(rho= -0.32)
CAVEOLIN1(rho= -0.37)
AMPKALPHA(rho= -0.30)
TRANSGLUTAMINASE(rho= -0.32)
PAI1(rho= -0.38)
CD49B(rho= -0.38)
SRC(rho= -0.34)
MEK1(rho= -0.33)
EGFR(rho= -0.44)
EGFRPY1068(rho= -0.42)
HER2PY1248(rho= -0.35)
SRCPY416(rho= -0.47)
Pathway score member
Tumor lineage
BLCA
BRCA-Basal
BRCA-HER2
BRCA-LuminalA/B
BRCA-Reactive
Colorectal
GBM
HNSC
KIRC
LUAD
LUSC
OVCA
UCEC
Cluster
A1
A2
B
C
D
E
F
G
H
Mutation
Mutated
Wild-type
PAM50
Basal
HER2
Luminal A
Luminal B
Normal-like
Missing data
BLCA subtype
Non-papillary
Papillary
Missing data
HER2 amplification
Amplified
Deleted
Wild-type
Missing data
MYC amplification
Amplified
Non-amplified
Missing data
Protein expression
Low
High
Pathway score member
Member
Non-member


Hormone_b score
Tumor(p=0.00e+00)
PAM50(p=4.13e-73)
BLCA Subtype(p=9.12e-04)
APC Mutation(p=1.05e-02)
FBXW7 Mutation(p=5.96e-04)
KRAS Mutation(p=2.67e-02)
MLL2 Mutation(p=8.37e-11)
PIK3CA Mutation(p=1.00e-20)
RB1 Mutation(p=2.63e-02)
TP53 Mutation(p=2.63e-37)
HER2 Amplification(p=1.64e-07)
Cluster(p=0.00e+00)
Hormone b score
TFRC(rho=-0.35)
CYCLINE1(rho=-0.43)
ASNS(rho=-0.34)
CYCLINB1(rho=-0.38)
CDK1(rho=-0.30)
YB1PS102(rho=-0.37)
AR(rho=0.70)
ERALPHAPS118(rho=0.32)
PR(rho=0.39)
ERALPHA(rho=0.37)
BECLIN(rho=0.30)
JNK2(rho=0.36)
IRS1(rho=0.34)
GATA3(rho=0.62)
INPP4B(rho=0.61)
ANNEXINVII(rho=0.31)
PDK1(rho=0.38)
PDK1PS241(rho=0.34)
COLLAGENVI(rho=0.32)
BCL2(rho=0.64)
P27(rho=0.30)
Pathway score member
Tumor lineage
BLCA
BRCA-Basal
BRCA-HER2
BRCA-LuminalA/B
BRCA-Reactive
Colorectal
GBM
HNSC
KIRC
LUAD
LUSC
OVCA
UCEC
Cluster
A1
A2
B
C
D
E
F
G
H
Mutation
Mutated
Wild-type
PAM50
Basal
HER2
Luminal A
Luminal B
Normal-like
Missing data
BLCA subtype
Non-papillary
Papillary
Missing data
HER2 amplification
Amplified
Deleted
Wild-type
Missing data
MYC amplification
Amplified
Non-amplified
Missing data
Protein expression
Low
High
Pathway score member
Member
Non-member

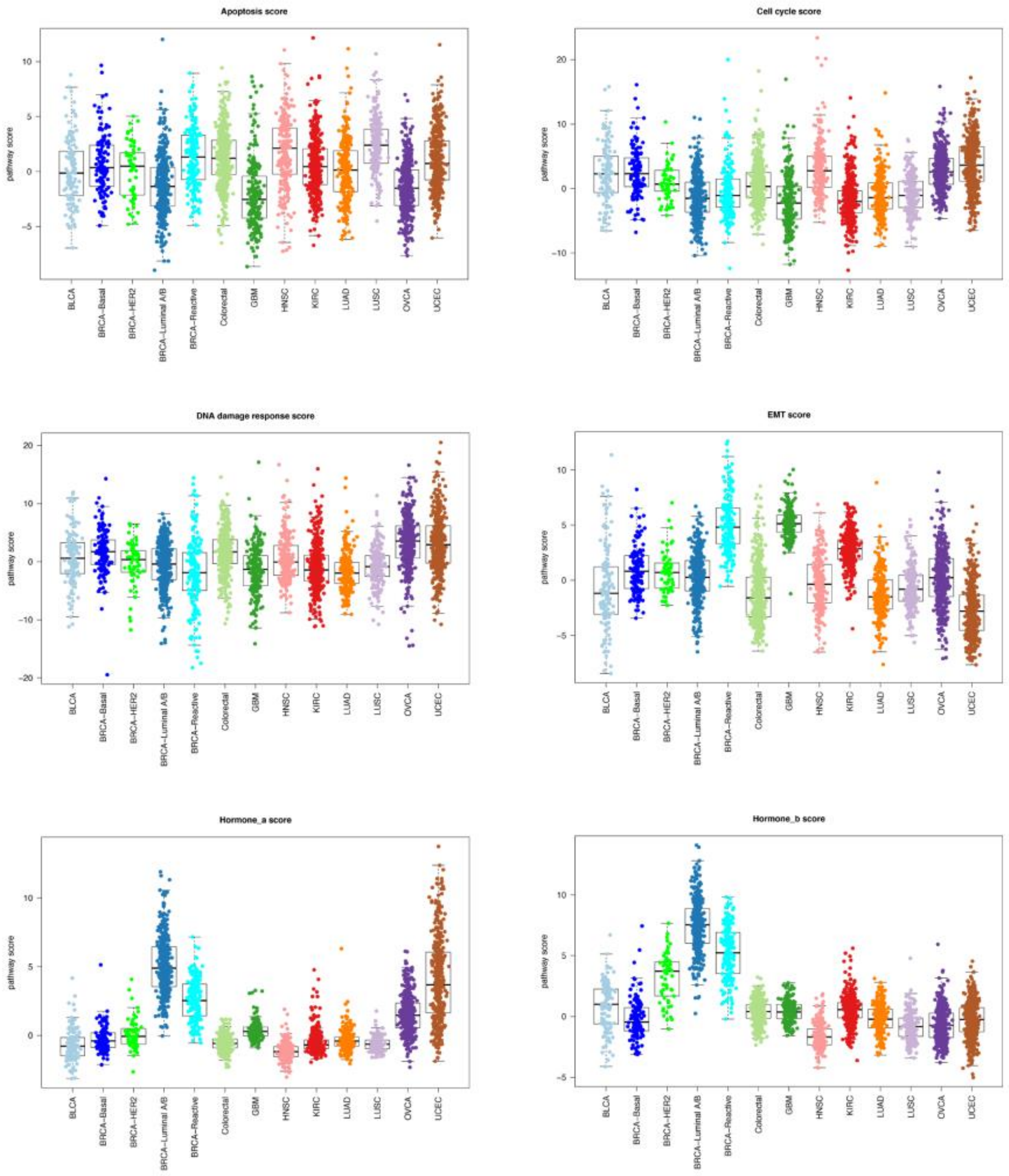

PI3K/Akt score
Tumor(p= 3.06e-270)
PAM50(p= 5.25e-12)
APC Mutation(p= 4.33e-03)
ARID1A Mutation(p= 2.24e-02)
MLL2 Mutation(p= 4.23e-02)
PBRM1 Mutation(p= 4.48e-13)
PIK3R1 Mutation(p= 2.14e-18)
PTEN Mutation(p= 3.22e-63)
RB1 Mutation(p= 3.83e-02)
TP53 Mutation(p= 5.82e-14)
VHL Mutation(p= 3.11e-25)
HER2 Amplification(p= 2.24e-03)
MYC Amplification(p= 3.10e-12)
Cluster(p= 8.96e-215)
PI3K/Akt score
INPP4B(rho= -0.33)
RAB25(rho= -0.31)
CLAUDIN7(rho= -0.36)
ECADHERIN(rho= -0.32)
PRAS40PT246(rho= 0.69)
AKTPS473(rho= 0.77)
AKTPT308(rho= 0.75)
TUBERINPT1462(rho= 0.64)
GSK3ALPHABETAPS21S9(rho= 0.62)
GSK3PS9(rho= 0.68)
P90RSKPT359S363(rho= 0.34)
BADPS112(rho= 0.33)
YB1PS102(rho= 0.31)
RICTORPT1135(rho= 0.31)
4EBP1PT37T46(rho= 0.35)
MAPKPT202Y204(rho= 0.35)
P70S6KPT389(rho= 0.31)
PTEN(rho= -0.30)
P27PT157(rho= 0.21)
P27PT198(rho= 0.13)
Pathway score member
Tumor lineage
BLCA
BRCA-Basal
BRCA-HER2
BRCA-LuminalA/B
BRCA-Reactive
Colorectal
GBM
HNSC
KIRC
LUAD
LUSC
OVCA
UCEC
Cluster
A1
A2
B
C
D
E
F
G
H
Mutation
Mutated
Wild-type
PAM50
Basal
HER2
Luminal A
Luminal B
Normal-like
Missing data
BLCA subtype
Non-papillary
Papillary
Missing data
HER2 amplification
Amplified
Deleted
Wild-type
Missing data
MYC amplification
Amplified
Non-amplified
Missing data
Protein expression
Low
High
Pathway score member
Member
Non-member

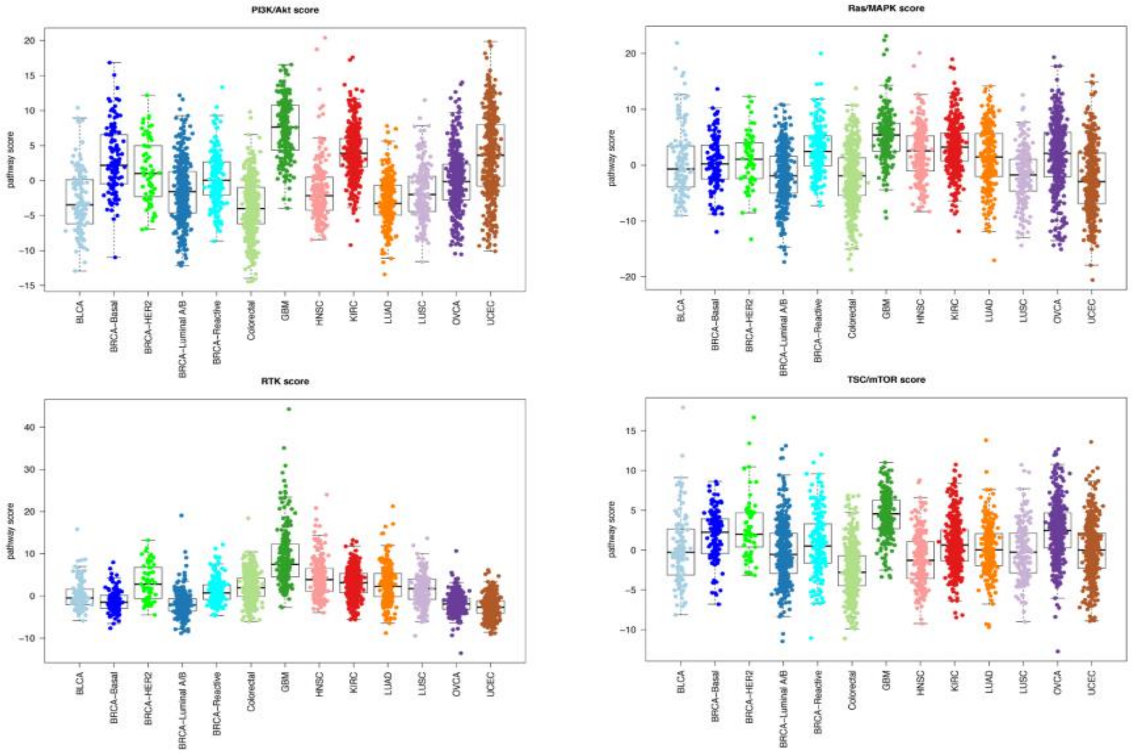

Ras/MAPK score
Tumor(p=7.36e-139)
PAM50(p=4.79e-08)
EGFR Mutation(p=9.26e-03)
MLL3 Mutation(p=9.04e-03)
PBRM1 Mutation(p=4.27e-06)
PTEN Mutation(p=3.48e-02)
TP53 Mutation(p=2.28e-07)
VHL Mutation(p=3.12e-12)
HER2 Amplification(p=3.37e-02)
MYC Amplification(p=2.52e-09)
Cluster(p=4.47e-105)
Ras/MAPK score
BIM(rho= -0.30)
EEF2(rho= -0.33)
TFRC(rho= -0.33)
KU80(rho= -0.38)
CHK2(rho= -0.34)
CYCLINB1(rho= -0.37)
AKTPS473(rho= 0.40)
AKTPT308(rho= 0.35)
TUBERINPT1462(rho= 0.43)
GSK3ALPHABETAPS21S9(rho= 0.34)
GSK3PS9(rho= 0.37)
ARAFPS299(rho= 0.35)
CRAFPS338(rho= 0.40)
RICTORPT1135(rho= 0.43)
EGFRPY1068(rho= 0.35)
SHCPY317(rho= 0.52)
1433EPSILON(rho= 0.30)
CJUNPS73(rho= 0.55)
JNKPT183Y185(rho= 0.62)
P70S6KPT389(rho= 0.39)
BADPS112(rho= 0.40)
PKCPANBETAIIPS660(rho= 0.31)
PRAS40PT246(rho= 0.46)
NDRG1PT346(rho= 0.32)
P38PT180Y182(rho= 0.51)
SRCPY527(rho= 0.44)
MAPKPT202Y204(rho= 0.71)
MEK1PS217S221(rho= 0.69)
S6PS235S236(rho= 0.36)
YB1PS102(rho= 0.58)
MTORPS2448(rho= 0.43)
P90RSKPT359S363(rho= 0.54)
Pathway score member
Tumor lineage
BLCA
BRCA-Basal
BRCA-HER2
BRCA-LuminalA/B
BRCA-Reactive
Colorectal
GBM
HNSC
KIRC
LUAD
LUSC
OVCA
UCEC
Cluster
A1
A2
B
C
D
E
F
G
H
Mutation
Mutated
Wild-type
PAM50
Basal
HER2
Luminal A
Luminal B
Normal-like
Missing data
BLCA subtype
Non-papillary
Papillary
Missing data
HER2 amplification
Amplified
Deleted
Wild-type
Missing data
MYC amplification
Amplified
Non-amplified
Missing data
Protein expression
Low
High
Pathway score member
Member
Non-member

RTK score
Tumor(p=0.00e+00)
PAM50(p=1.25e-13)
APC Mutation(p=2.19e-04)
ARID1A Mutation(p=6.39e-03)
EGFR Mutation(p=1.10e-15)
PBRM1 Mutation(p=4.04e-10)
PIK3CA Mutation(p=1.04e-09)
PIK3R1 Mutation(p=1.46e-02)
PTEN Mutation(p=3.98e-05)
RB1 Mutation(p=2.77e-02)
VHL Mutation(p=5.51e-18)
HER2 Amplification(p=3.17e-03)
MYC Amplification(p=4.27e-31)
Cluster(p=1.77e-312)
RTK score
BIM(rho=-0.36)
ERALPHA(rho=-0.37)
PR(rho=-0.40)
CHK2(rho=-0.39)
CYCLINB1(rho=-0.38)
FOXM1(rho=-0.34)
DVL3(rho=-0.33)
53BP1(rho=-0.38)
KU80(rho=-0.39)
S6(rho=-0.45)
BAP1C4(rho=-0.42)
RBM15(rho=-0.45)
EGFR(rho=0.38)
EGFRPY1068(rho=0.81)
EGFRPY1173(rho=0.61)
HER2PY1248(rho=0.70)
SRCPY416(rho=0.74)
CKIT(rho=0.31)
MEK1(rho=0.39)
CD31(rho=0.34)
RAB11(rho=0.32)
HER3PY1298(rho=0.60)
RICTORPT1135(rho=0.31)
YB1PS102(rho=0.32)
NDRG1PT346(rho=0.46)
P38PT180Y182(rho=0.37)
SRCPY527(rho=0.64)
MAPKPT202Y204(rho=0.47)
MEK1PS217S221(rho=0.32)
SHCPY317(rho=0.52)
CJUNPS73(rho=0.33)
JNKPT183Y185(rho=0.32)
Pathway score member
Tumor lineage
BLCA
BRCA-Basal
BRCA-HER2
BRCA-LuminalA/B
BRCA-Reactive
Colorectal
GBM
HNSC
KIRC
LUAD
LUSC
OVCA
UCEC
Cluster
A1
A2
B
C
D
E
F
G
H
Mutation
Mutated
Wild-type
PAM50
Basal
HER2
Luminal A
Luminal B
Normal-like
Missing data
BLCA subtype
Non-papillary
Papillary
Missing data
HER2 amplification
Amplified
Deleted
Wild-type
Missing data
MYC amplification
Amplified
Non-amplified
Missing data
Protein expression
Low
High
Pathway score member
Member
Non-member


TSC/mTOR score
Tumor(p= 5.37e-157)
PAM50(p= 2.11e-12)
APC Mutation(p= 6.77e-03)
EGFR Mutation(p= 3.74e-03)
MLL3 Mutation(p= 4.29e-02)
PIK3CA Mutation(p= 1.29e-02)
PIK3R1 Mutation(p= 1.92e-02)
PTEN Mutation(p= 1.10e-09)
RB1 Mutation(p= 4.77e-02)
Cluster(p= 1.76e-135)
TSC/mTOR score
PRAS40PT246(rho= 0.44)
AKTPS473(rho= 0.48)
AKTPT308(rho= 0.34)
TUBERINPT1462(rho= 0.44)
GSK3ALPHABETAPS21S9(rho= 0.38)
GSK3PS9(rho= 0.43)
4EBP1PT70(rho= 0.25)
CD49B(rho= -0.33)
S6PS235S236(rho= 0.57)
S6PS240S244(rho= 0.59)
4EBP1PS65(rho= 0.54)
4EBP1PT37T46(rho= 0.72)
RBPS807S811(rho= 0.41)
P90RSKPT359S363(rho= 0.33)
BADPS112(rho= 0.32)
YB1PS102(rho= 0.32)
RICTORPT1135(rho= 0.12)
MAPKPT202Y204(rho= 0.33)
MTORPS2448(rho= 0.62)
P70S6KPT389(rho= 0.52)
Pathway score member
Tumor lineage
BLCA
BRCA-Basal
BRCA-HER2
BRCA-LuminalA/B
BRCA-Reactive
Colorectal
GBM
HNSC
KIRC
LUAD
LUSC
OVCA
UCEC
Cluster
A1
A2
B
C
D
E
F
G
H
Mutation
Mutated
Wild-type
PAM50
Basal
HER2
Luminal A
Luminal B
Normal-like
Missing data
BLCA subtype
Non-papillary
Papillary
Missing data
HER2 amplification
Amplified
Deleted
Wild-type
Missing data
MYC amplification
Amplified
Non-amplified
Missing data
Protein expression
Low
High
Pathway score member
Member
Non-member

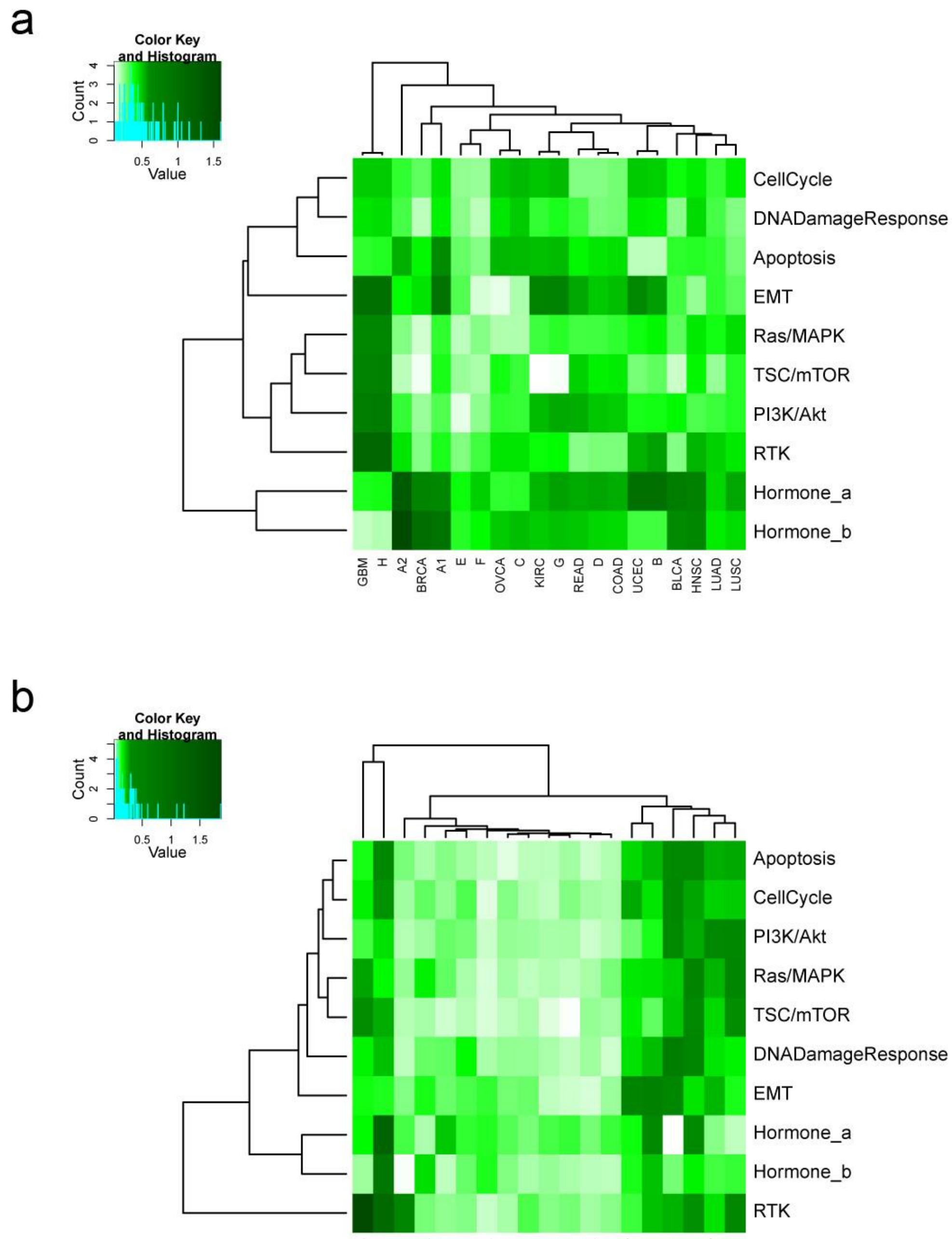
Supplementary Figure 9: Dotplots showing pathway scores (RBN dataset) across tumor lineages





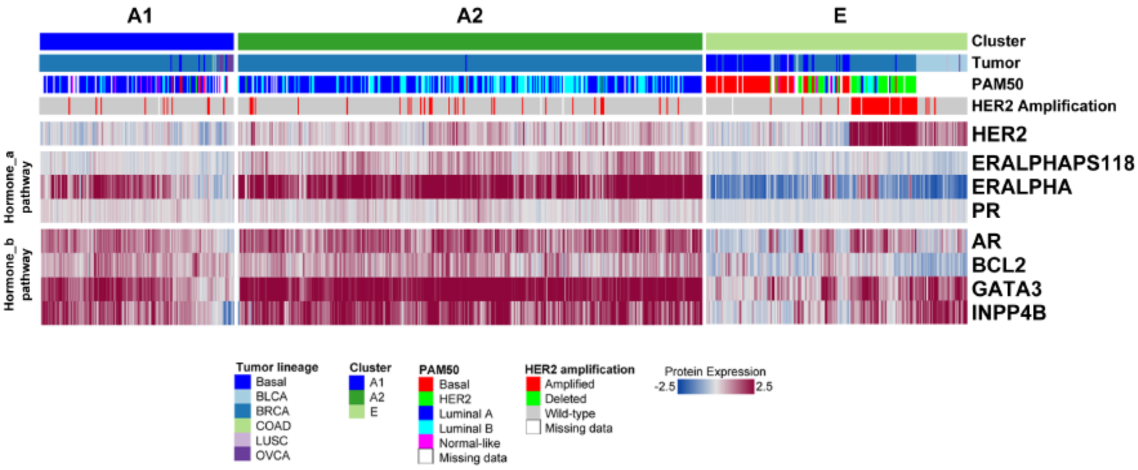
Pathway score of each sample, across RBN clusters, is shown in the dotplots. Each dot represents pathway score of a sample.

Supplementary Figure 10: Heatmaps depicting differential pathway activity (sign independent absolute values) for tumor lineages and protein clusters based on the (a) RBN and (b) MC datasets



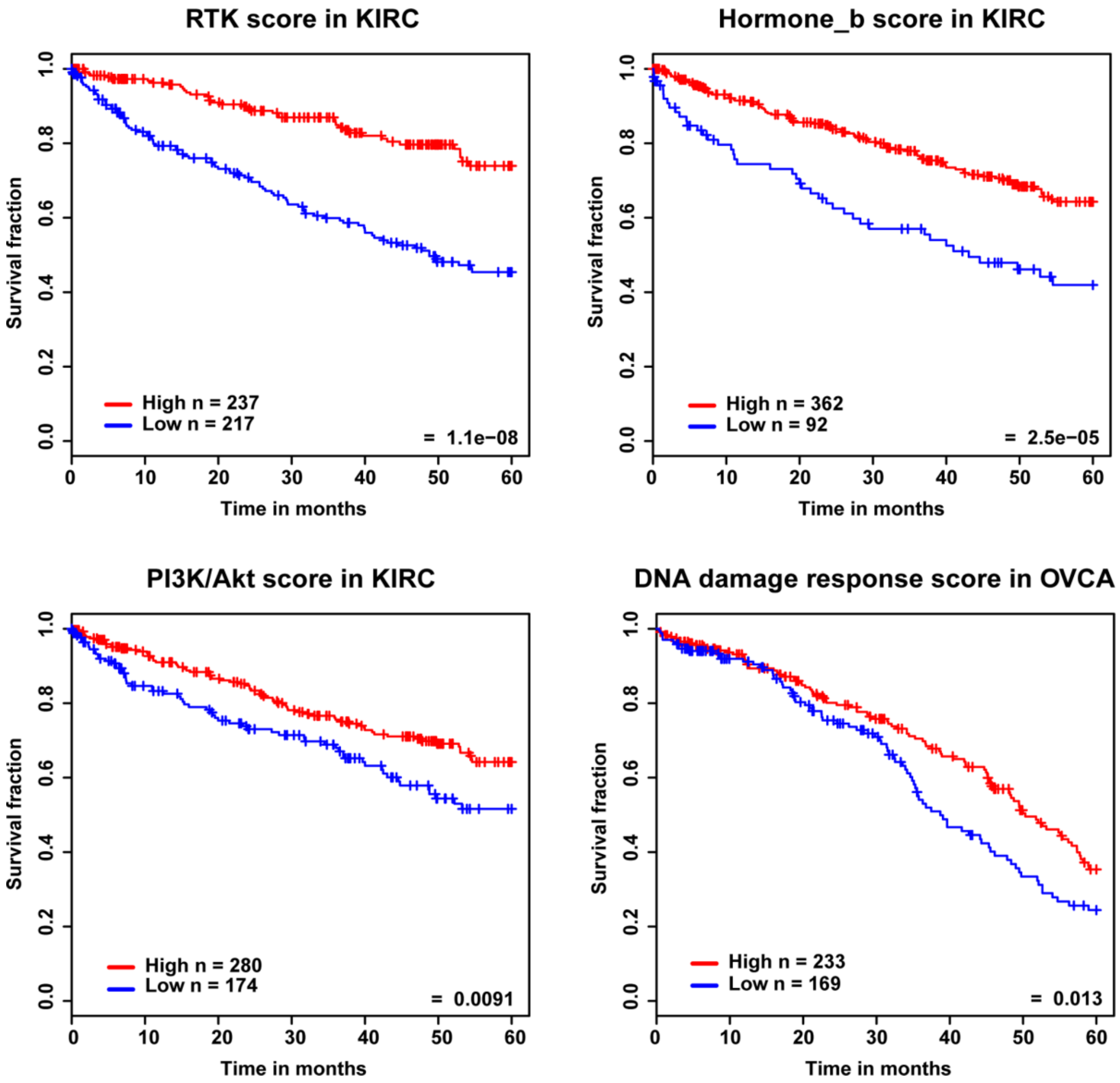
The heatmaps show unsupervised hierarchical clustering on both axes. After scaling the data to mean zero globally, for each pathway and cluster or disease type, the average absolute protein level over the pathway proteins was calculated. This differential pathway activity indicates the deviation in a given cluster or disease type of this pathway from its mean expression, irrespective of activation or suppression, and can thus be seen as a proxy for pathway differentiation. White color means no change, whereas dark green color means a large change from the mean.

Supplementary Figure 11: Zoomed-in views of RBN heatmap showing hormone_a and hormone_b in clusters_A1, _A2 and _E



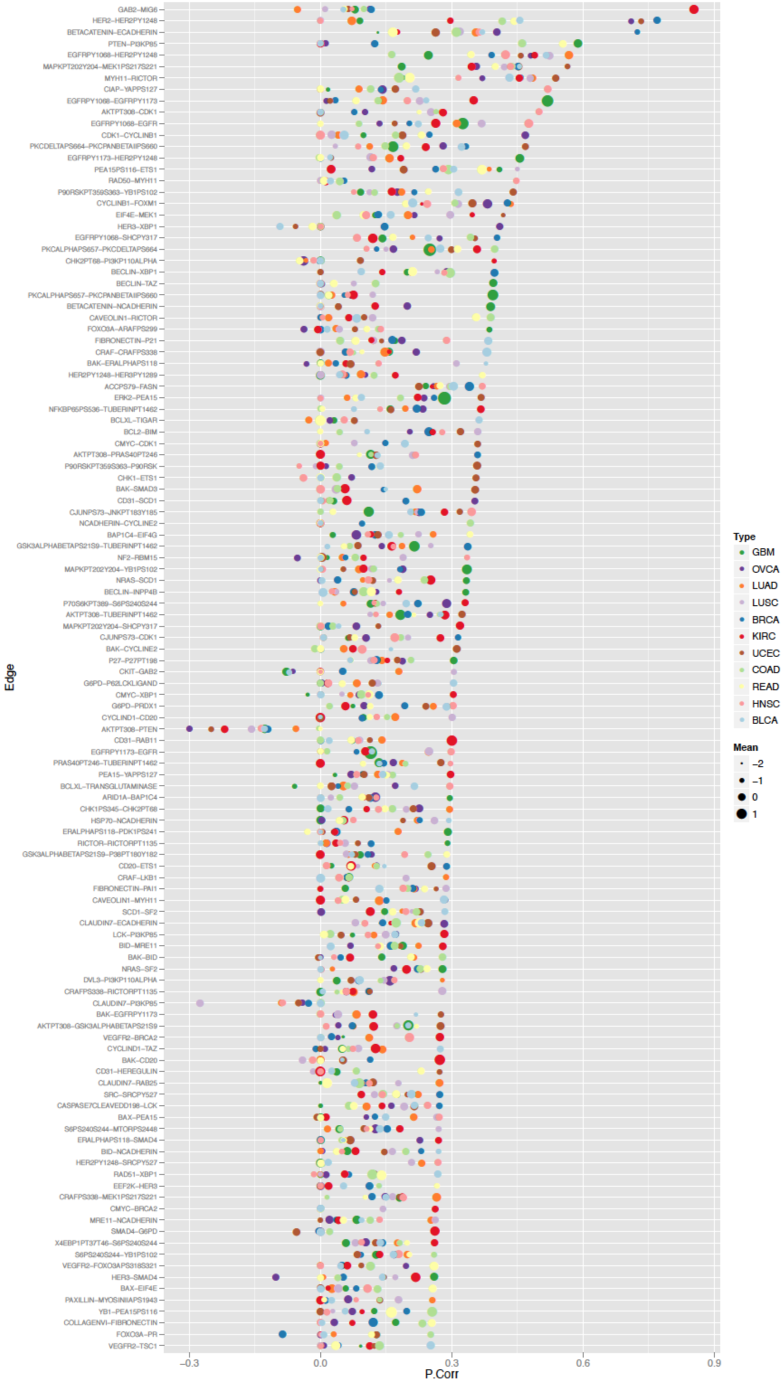
Heatmap shows the protein level of members in hormone_a and hormone_b in cluster_A1, _A2 and _E, underscoring that HER2-positive breast cancers, whether ER-positive or -negative, demonstrated elevated levels of GATA3, INPP4B, and AR suggestive of active downstream hormonal signaling despite low levels of ER, pER and PR.

Supplementary Figure 12: Pathways related to patient outcome



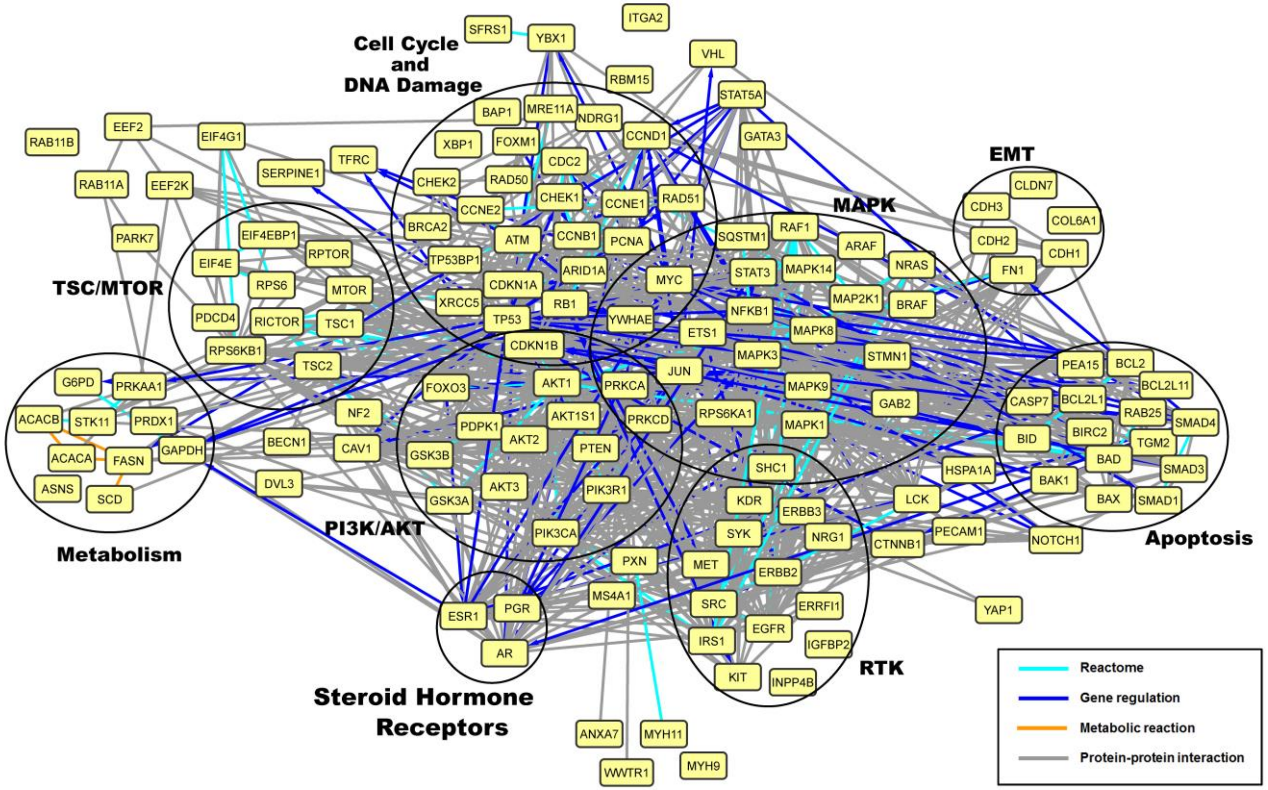
Kaplan-Meier survival curves showing overall survival per tumor lineage, based on the four pathways that validated in the test set of the formal training/test set analysis (by optimized cutoff) and showed marked associations with survival (RTK score in KIRC; hormone_b score in KIRC; PI3K in KIRC and DNA damage response in OVCA). *P*-values are calculated by log-rank test. For pathway score members and calculation of the pathway score, Supplementary Table 13 and Method.

Supplementary Figure 13: Visualization of the absolute partial correlation of the protein-protein links in the network



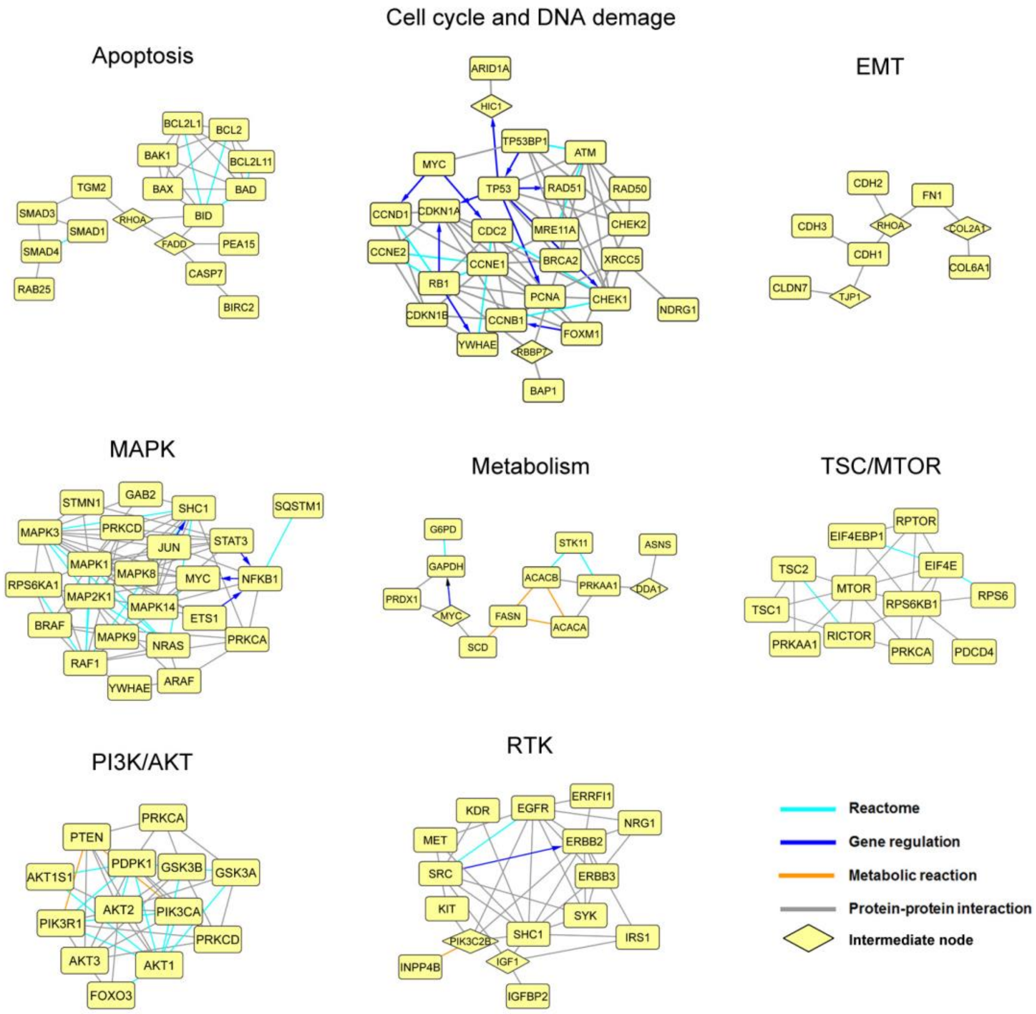
Each row represents a protein-protein link (with at least 0.25 absolute partial correlation in one tumor lineage) shown in Fig. 6. The x-axis shows the absolute partial correlation. The color and size of the circles shows the tumor lineage and mean expression (relative to the global mean) of the lowest expressed protein out of the two proteins from the link, respectively. High-resolution figure is available at http://bioinformatics.mdanderson.org/main/TCGA/Pancan11/RPPA.

Supplementary Figure 14: Visualization of pathways coverage by RPPA



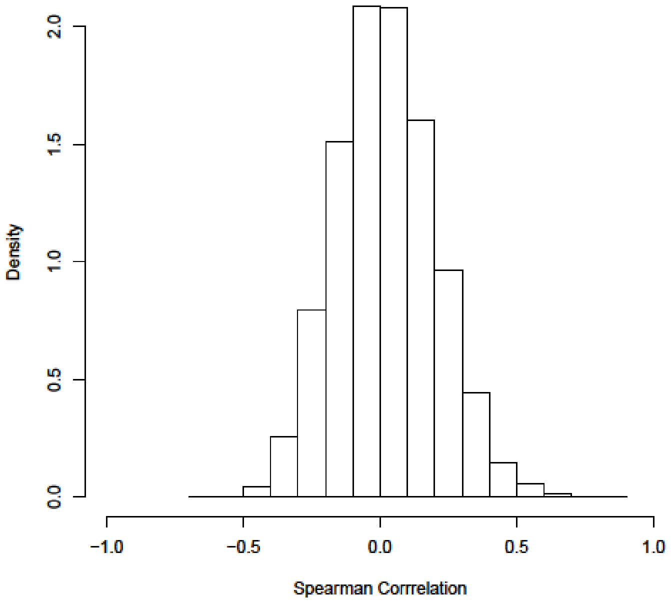
a. Antibody names were converted to gene names for input into Netwalker. Interaction information was obtained using prior knowledge from multiple databases (for detailed info, Komurov *et al*[2]. Nodes were assigned to specific pathways based on the KEGG pathway database. Interaction information was obtained from Netwalker as described previously[2]. Once generated, networks were exported for visualization in cytoscape[3].

Supplementary Figure 14: Visualization of pathways coverage by RPPA (continued)



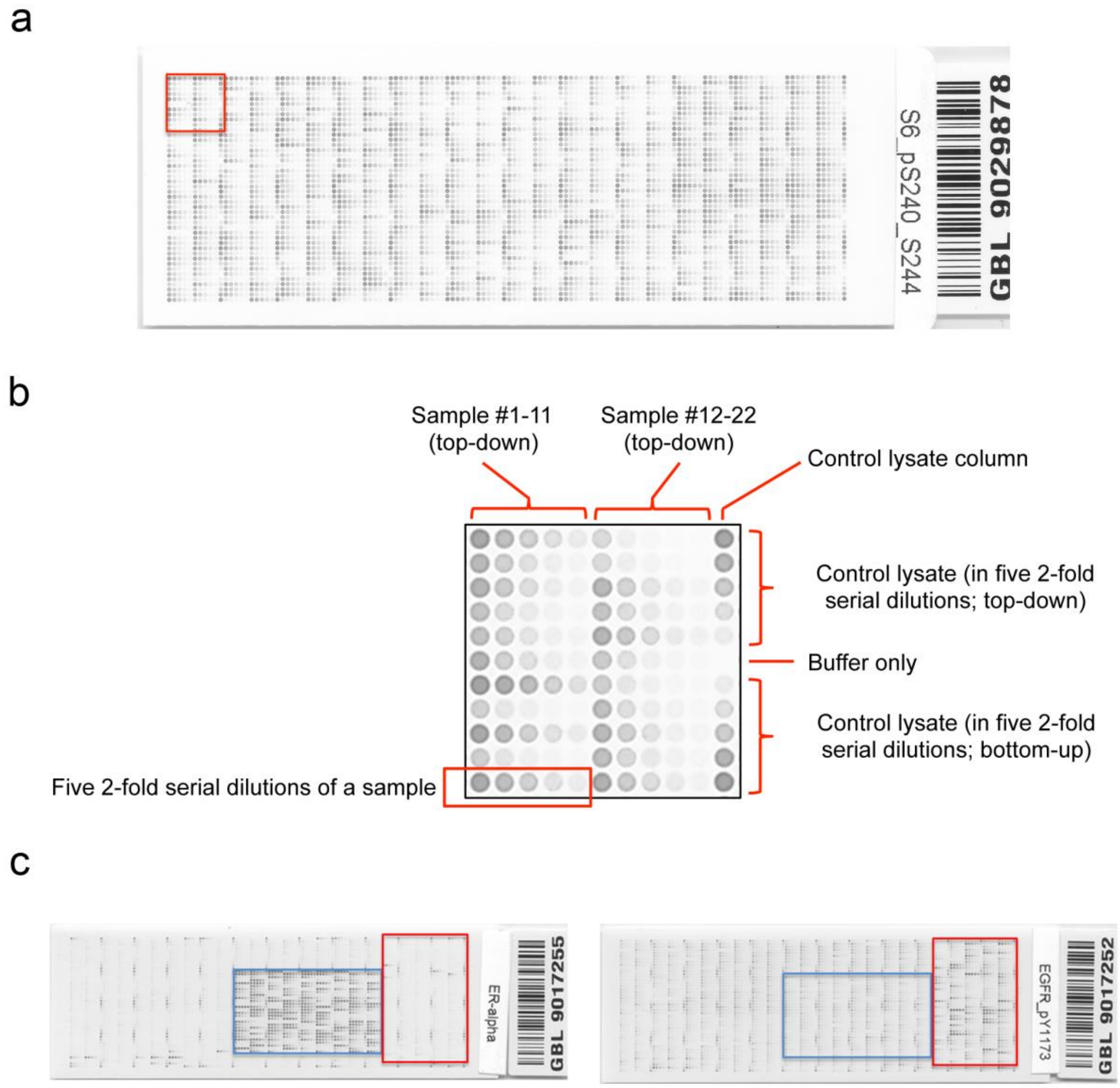
b. Zoomed-in views of pathways of interest. To visualize maximum connectivity of the pathway, intermediate nodes were added using the Netwalker gene connector function.

Supplementary Figure 15: Redundancy in RPPA antibodies



Histogram of Spearman’s correlation (*ρ*) of each protein with all the other proteins in the pan-cancer dataset. The mean (expected) *ρ* for the distribution is 0.02.

Supplementary Figure 16: Representative image of RPPA slide



a. Image of a developed RPPA slide stained by phosphorylated S6 (S240/S244) antibody. Each spot represent a sample or control lysate (in different dilutions). An 11x11 grid is highlighted in a red box. Each slide contains 12x4 (total 48) 11x11 grids.

b. Zoomed-in view of an 11x11 grid showing the standard orientation of the samples and control lysate. Each grid contains 22 samples and 1 control lysate. Each sample is represented by 5 spots with 2-fold serial dilution as indicated. Samples are arranged, top-down, in first 10 columns. The last column contains duplicates of control lysate in 2-fold serial dilution. One spot of buffer only is printed in the center of last column.

c. Two representative RPPA images showing distant signal patterns of 2 tumor types. RPPA slides stained by ER-alpha (right) and phosphorylated EGFR (Y1137) (left) are shown. BRCA samples are highlighted by blue box, while GBM samples are highlighted by red box.

Supplementary Tables

Supplementary Table 1: Relative HER2 protein and ERRB2 mRNA expression levels in 26 lung adenocarcinoma (LUAD) cell lines

LUAD Cell Line	HER2 Protein	ERBB2 mRNA
CALU3	3.73	15.87
CALU6	-0.22	9.63
H1355	0.08	11.14
H1395	0.05	11.30
H1437	0.68	12.30
H1648	0.46	12.05
H1650	0.96	12.23
H1666	1.36	11.95
H1693	1.79	12.64
H1819	3.25	15.51
H1975	0.44	11.78
H1993	0.68	11.35
H2009	0.62	12.04
H2073	0.26	9.59
H2087	-0.08	10.83
H2126	1.07	12.56
H2347	0.94	12.07
H322	1.26	11.61
H358	0.95	11.46
H820	0.35	11.83
HCC1833	-0.77	11.59
HCC193	0.77	11.39
HCC2279	0.14	10.73
HCC4006	0.18	11.38
HCC515	0.76	11.61
HCC78	1.07	12.13

The first column contains the cell line name. The highlighted cells contain values above the threshold of 1.0 for protein and 14.26 for mRNA (same as those used in Fig. 1). The corresponding plot is shown in Supplementary Figure 2. More cell lines are identified as HER2 positive by protein (7 cell lines) than by mRNA (2 cell lines).

Supplementary Table 2: Top 25 Protein discriminators for RBN clusters

Discriminators for cluster_A1		
Protein	**Fold change (Log)**	**adj. *P*-value**
COLLAGENVI	1.60	1.26E-264
GATA3	1.08	1.11E-151
RBM15	-1.13	1.57E-133
RAB11	0.65	1.88E-124
BETACATENIN	-1.27	1.30E-87
S6	-0.80	1.26E-86
BCL2	0.79	3.28E-76
SYK	-0.87	1.48E-71
HSP70	1.11	2.98E-71
GAPDH	-1.75	9.33E-67
ACETYLATUBULIN.LYS40.	-1.18	6.31E-64
ERALPHA	1.22	2.05E-61
BID	0.36	1.75E-60
FASN	1.06	7.85E-60
NF2	-0.45	9.17E-58
TRFC	-1.11	2.15E-51
PR	0.29	4.76E-48
CAVEOLIN1	1.17	8.70E-48
ERK2	-0.53	5.97E-47
MTOR	-0.34	1.27E-44
AR	0.64	3.02E-44
GSK3ALPHABETA	-0.28	4.95E-43
CYCLIND1	0.27	8.72E-43
FIBRONECTIN	0.72	1.33E-42
BRAF	-0.59	3.86E-40

Discriminators for cluster_A2		
Protein	**Fold change (Log)**	**adj. *P*-value**
GATA3	2.46	0.00E+00
ERALPHA	2.87	0.00E+00
FASN	1.78	0.00E+00
AR	1.22	1.22E-291
INPP4B	1.48	5.29E-248
ERALPHAPS118	0.60	3.50E-179
EGFR	-0.71	5.12E-162
PKCALPHAPS657	-0.70	2.96E-159
BCL2	0.78	2.94E-151
PKCALPHA	-0.73	1.09E-146
PR	0.34	1.48E-140
ACC1	0.73	9.05E-97
BIM	0.51	7.05E-92
NDRG1PT346	-1.02	3.04E-90
NCADHERIN	-0.43	4.27E-88
CYCLINE1	-0.57	1.01E-80
VEGFR2	0.55	4.40E-79
SRCPY416	-0.57	7.50E-79
NOTCH1	-0.27	1.35E-71
YB1PS102	-0.24	3.68E-71
PDK1PS241	0.30	9.81E-69
YAP	-0.30	4.99E-66
IRS1	0.28	1.63E-62
FIBRONECTIN	0.58	3.47E-60
BRAF	-0.59	3.86E-40

Discriminators for cluster_B		
Protein	**Fold change (Log)**	**adj. *P*-value**
COLLAGENVI	-0.93	1.54E-199
GATA3	-0.85	1.58E-193
ERALPHA	1.44	1.07E-167
S6	0.73	4.50E-147
CYCLINE1	0.79	5.11E-143
PR	0.34	2.83E-134
ERALPHAPS118	0.51	6.87E-134
TRFC	1.21	3.45E-124
KU80	0.51	1.10E-115
MEK1	-0.58	1.14E-115
CYCLINB1	1.01	1.31E-112
RBM15	0.68	1.73E-107
FIBRONECTIN	-0.80	2.60E-106
CHK2	0.47	5.54E-101
X53BP1	0.59	6.48E-97
MAPKPT202Y204	-0.90	2.57E-87
AKTPT308	0.81	1.10E-84
RAB11	-0.35	6.03E-83
HSP70	-0.81	3.43E-82
EEF2	0.66	1.46E-80
SRCPY527	-0.67	3.23E-76
NDRG1PT346	-0.90	2.30E-70
TRANSGLUTAMINASE	0.57	5.14E-70
MRE11	-0.19	9.36E-68
CYCLINE2	0.33	3.39E-65

Discriminators for cluster_C		
Protein	**Fold change (Log)**	**adj. *P*-value**
CYCLINE1	1.05	3.52E-253
GATA3	-0.84	8.58E-207
RBM15	0.90	9.20E-189
BAP1C4	0.57	1.39E-186
FOXM1	0.61	2.67E-153
CHK2	0.52	8.64E-132
PDK1PS241	-0.41	1.08E-130
SYK	0.76	1.97E-122
GAB2	0.74	1.86E-121
CYCLINB1	0.99	2.66E-117
SRC	-0.46	1.85E-115
DVL3	0.41	3.64E-113
IGFBP2	1.10	1.54E-106
CKIT	-0.63	3.63E-103
CD49B	-0.43	4.39E-96
BCL2	-0.59	1.67E-95
RAB11	-0.35	1.18E-86
ERALPHA	0.95	2.56E-85
VHL	1.28	3.36E-85
PDCD4	0.71	2.66E-84
CHK2PT68	0.28	1.09E-76
JNK2	-0.33	5.13E-76
CMYC	0.50	2.11E-75
AMPKALPHA	-0.36	2.20E-75
INPP4B	-0.74	1.81E-74

Discriminators for cluster_D		
Protein	**Fold change (Log)**	**adj. *P*-value**
TIGAR	0.93	0.00E+00
CLAUDIN7	1.67	0.00E+00
ERALPHA	-1.66	7.73E-255
MYH11	2.33	7.17E-199
EEF2	0.95	3.64E-185
PEA15PS116	1.25	2.00E-160
RICTOR	1.18	2.76E-160
RAB25	0.80	1.03E-151
SRC	0.49	1.56E-145
AKTPT308	-0.99	1.43E-144
BCLXL	0.39	2.02E-139
ECADHERIN	1.15	1.07E-135
YB1	0.46	4.84E-120
AR	-0.67	1.53E-119
AMPKPT172	0.68	2.77E-115
CD49B	0.44	4.47E-114
TRFC	1.03	6.01E-111
CHK2	0.44	4.50E-109
RICTORPT1135	-0.22	4.30E-107
P90RSK	0.37	1.81E-106
SYK	0.66	8.23E-106
XBP1	0.33	1.09E-100
BETACATENIN	0.84	6.63E-100
SRCPY416	0.59	3.64E-99
CRAFPS338	-0.18	6.38E-97

Discriminators for cluster_E		
Protein	**Fold change (Log)**	**adj. *P*-value**
FASN	1.33	1.24E-117
ERALPHA	-1.19	4.64E-75
GATA3	0.63	1.36E-71
HER2	0.80	1.76E-57
FOXM1	0.46	4.63E-52
S6	0.50	2.48E-46
NCADHERIN	-0.40	8.95E-46
ACC1	0.61	2.10E-42
CYCLINB1	0.71	2.27E-36
PEA15	-0.32	7.77E-35
PKCALPHAPS657	-0.40	1.29E-34
IGFBP2	-0.81	1.57E-34
RAB25	0.51	2.08E-34
MYH11	-1.25	4.94E-33
DJ1	-0.29	2.20E-32
ASNS	0.48	9.33E-32
ERALPHAPS118	-0.30	9.33E-32
CAVEOLIN1	-0.82	1.26E-31
ACCPS79	0.46	4.98E-31
SMAD3	-0.24	7.55E-30
AMPKALPHA	-0.29	1.49E-29
PKCALPHA	-0.40	2.14E-29
EGFRPY1173	-0.53	5.75E-27
CD20	-0.17	1.03E-26
MAPKPT202Y204	-0.62	1.13E-26

Discriminators for cluster_F		
Protein	**Fold change (Log)**	**adj. *P*-value**
GATA3	-0.70	2.56E-244
AR	-0.72	4.75E-205
ERALPHA	-1.15	9.85E-202
PR	-0.26	5.03E-151
YAP	0.34	4.77E-148
HER2PY1248	0.68	8.03E-144
SRCPY416	0.57	7.36E-142
P70S6KPT389	-0.37	1.85E-129
CD49B	0.38	1.35E-128
NDRG1PT346	0.85	8.02E-116
GAB2	-0.53	1.67E-112
TUBERINPT1462	-0.29	1.68E-102
ERK2	-0.40	3.02E-102
CDK1	0.22	3.85E-96
PAI1	0.66	2.23E-90
CAVEOLIN1	0.79	1.47E-87
TRANSGLUTAMINASE	0.46	3.50E-87
RAPTOR	-0.26	3.47E-86
PI3KP110ALPHA	-0.24	1.89E-83
SMAD3	0.23	5.31E-82
PKCDELTAPS664	-0.17	4.31E-77
BRCA2	0.20	2.13E-76
STAT5ALPHA	-0.45	4.14E-76
ECADHERIN	0.66	8.63E-75
BAX	0.25	2.47E-74

Discriminators for cluster_G		
Protein	**Fold change (Log)**	**adj. *P*-value**
NDRG1PT346	3.31	0.00E+00
MIG6	0.72	0.00E+00
FASN	-2.06	0.00E+00
CYCLINB1	-1.88	0.00E+00
AMPKALPHA	0.86	0.00E+00
ACC1	-1.37	0.00E+00
GATA3	-0.98	6.33E-275
CD20	0.44	1.78E-266
GAPDH	2.36	1.13E-254
TRANSGLUTAMINASE	1.06	1.90E-241
ACCPS79	-0.94	3.43E-208
CHK2	-0.64	1.31E-200
PR	-0.39	1.37E-190
CLAUDIN7	-1.19	2.57E-168
RAB11	0.49	2.82E-164
CD31	0.44	7.06E-161
PI3KP110ALPHA	-0.45	3.31E-157
BAK	0.66	9.56E-153
SMAD1	-0.38	2.54E-149
CRAF	-0.33	1.53E-144
DVL3	-0.45	1.42E-135
PRAS40PT246	0.42	6.62E-127
MYH11	1.87	7.03E-126
ASNS	-0.73	6.56E-121
ERK2	0.57	7.71E-120

Discriminators for cluster_H		
Protein	**Fold change (Log)**	**adj. *P*-value**
PKCDELTAPS664	0.77	0.00E+00
ERK2	1.36	0.00E+00
ACETYLATUBULIN.LYS40.	2.51	0.00E+00
EGFR	1.35	0.00E+00
EGFRPY1173	1.93	4.41E-283
NOTCH1	0.75	1.22E-280
PKCALPHAPS657	1.22	3.19E-266
PKCALPHA	1.34	5.12E-266
PEA15	0.97	7.44E-265
ECADHERIN	-2.17	4.08E-228
MYOSINIIAPS1943	-0.84	1.13E-221
HER3PY1298	0.49	2.84E-186
VHL	-2.62	2.42E-184
P70S6KPT389	0.77	2.30E-177
NCADHERIN	0.80	5.95E-170
TUBERINPT1462	0.67	5.95E-168
PDCD4	-1.37	1.60E-163
JNKPT183Y185	0.56	4.70E-159
EGFRPY1068	2.22	6.04E-159
SRCPY416	1.07	1.67E-158
VEGFR2	-1.02	1.51E-155
MAPKPT202Y204	1.56	1.17E-151
CLAUDIN7	-1.50	7.27E-147
RAB25	-1.06	1.80E-137
CMYC	-0.89	1.54E-127

Top 25 protein discriminators (according to adjusted *P*-value (Benjamini Hochberg)) of each RBN clusters are listed. Positive values (highlighted in red) in Fold change (Log) column indicate a fold change increase, in log scale, of the protein level of particular protein comparing to that in all other clusters by LIMMA analysis, while negative values indicate fold change decrease. Full list is available at http://bioinformatics.mdanderson.org/main/TCGA/Pancan11/RPPA.

Supplementary Table 3: Top 25 RNA discriminators for RBN clusters

RBN clusters								
A1	A2	B	C	D	E	F	G	H
ANKRD30A	GATA3	RPL13AP20	EEF1A1P9	CLCA1	PSME4	SCEL	ACSM2A	PMP2
GATA3	TBC1D9	RPSAP9	APOA1	CDX1	GRHL1	GRIK3	ACSM2B	AP1M2
TBC1D9	SLC39A6	RPS26P11	SOX17	NOX1	PVRL4	FAM83A	SLC17A3	KRT18
SLC39A6	ANKRD30A	HNRNPA1L2	KLHL14	PHGR1	GATA3	SFN	AGXT2	OLIG2
RABEP1	RABEP1	NCRNA00182	CLDN16	FABP1	TFAP2C	FOXE1	SLC22A2	KRT8
ZNF552	ZNF552	LOC100133161	MEIS1	MEP1A	HKDC1	FGFBP1	NAT8	HEPACAM
LMX1B	ESR1	FTHL3	LRRTM1	REG4	ESRP1	IL1F5	GLYAT	PRSS8
ADIPOQ	WWP1	RPL21	ZNF503	REG3A	GRHL2	TMPRSS11E2	UGT2A3	GFAP
SCGB2A2	XBP1	SOX17	RBM38	CDH17	ELF5	B3GNT5	SLC28A1	ARHGEF5
XBP1	LMX1B	LOC100132287	PRKCI	CDX2	GGCT	SERPINB3	CUBN	SPINT1
WWP1	NAT1	POTEE	BCAM	KRT20	GAL3ST1	GPR87	SLC17A4	GRB7
ABCC11	TRPS1	PGAM4	NPR1	GPA33	SLC5A6	MALL	BHMT	NCAN
ESR1	HKDC1	LOC100133331	PAX8	SPINK4	GTPBP4	LAMP3	ENPEP	BAIAP2L1
HKDC1	PSAT1	LOC100132247	CLDN6	ZG16	CDC42SE1	SFTPB	FXYD2	EVPL
TRPS1	KIAA1467	MSX1	LYPD1	MUC17	F11R	LAMB3	GRHL2	RIPK4
PIP	C6orf211	STX18	WT1	SLC26A3	CST3	ROS1	SLC6A13	C1orf61
SPOPL	GFRA1	RPL36A	KCNK15	RPSAP9	MASP1	KLF5	SLC22A12	DSG2
GFRA1	FOXA1	LIMS3	FTHL3	LGALS4	KRT7	SFTPA1	SLC3A1	HOOK1
SCUBE2	SPOPL	FLJ45445	MUC16	DEFA6	RAB25	GBP6	ESRP1	CLDN4
AMN	GSTP1	LOC613037	C14orf4	HNF4A	ALDH3B2	BAIAP2L1	SLC13A1	SPINT2
PRLR	MYB	DLX5	UPK3B	RPL13AP20	SMARCD2	GNA15	SLC22A11	EPCAM
CILP	MAGED2	RPL39	NR2F6	RPS26P11	VGLL1	KRT6A	IGSF9	ELF3
NAT1	PRLR	LOC80154	HDAC7	QKI	HBA1	SPRR1B	EPB41L4B	FAM83H
TFAP2B	AMN	LIMS3	HSPB1P1	MUC2	PAX8	PERP	ACAD11	APC2
PDCD4	ABCC11	SBDS	C15orf39	RPL21	CLEC18B	LAD1	EPN3	ESRP1

Top 25 RNA discriminators (according to adjusted *P*-value (Benjamini Hochberg)) of each RBN clusters are listed. Discriminators with positive fold change are highlighted in red, while discriminators with negative fold change are highlighted in green. Full list is available at http://bioinformatics.mdanderson.org/main/TCGA/Pancan11/RPPA.

Supplementary Table 4: Top 25 miRNA discriminators for RBN clusters

RBN clusters								
A1	A2	B	C	D	E	F	G	H
hsa.mir.190b	hsa.mir.190b	hsa.mir.9	hsa.mir.21	hsa.mir.552	hsa.mir.141	hsa.mir.944	hsa.mir.200c	hsa.mir.214
hsa.mir.210	hsa.mir.378	hsa.mir.141	hsa.mir.142	hsa.mir.194	hsa.mir.934	hsa.mir.10b	hsa.mir.141	hsa.mir.574
hsa.mir.505	hsa.mir.342	hsa.mir.139	hsa.mir.374a	hsa.mir.192	hsa.mir.3677	hsa.mir.27b	hsa.mir.122	hsa.mir.212
hsa.mir.135b	hsa.mir.141	hsa.mir.449a	hsa.mir.101	hsa.mir.2355	hsa.mir.96	hsa.mir.2355	hsa.mir.183	hsa.mir.766
hsa.mir.502	hsa.mir.182	hsa.mir.429	hsa.mir.29b	hsa.mir.215	hsa.mir.3613	hsa.mir.223	hsa.mir.204	hsa.mir.376a
hsa.mir.197	hsa.mir.135b	hsa.mir.135b	hsa.mir.542	hsa.mir.3613	hsa.mir.2355	hsa.mir.191	hsa.mir.375	hsa.mir.132
hsa.mir.501	hsa.mir.505	hsa.mir.200a	hsa.mir.19b	hsa.mir.3607	hsa.mir.182	hsa.mir.24	hsa.mir.30a	hsa.mir.127
hsa.mir.30a	hsa.mir.375	hsa.mir.196b	hsa.mir.22	hsa.mir.205	hsa.mir.3127	hsa.mir.21	hsa.mir.205	hsa.mir.137
hsa.mir.532	hsa.mir.30a	hsa.mir.449c	hsa.mir.126	hsa.mir.99b	hsa.mir.374a	hsa.mir.203	hsa.mir.1270	hsa.mir.134
hsa.mir.182	hsa.mir.3127	hsa.mir.3613	hsa.mir.32	hsa.mir.125a	hsa.mir.200c	hsa.mir.99b	hsa.mir.126	hsa.mir.654
hsa.mir.378	hsa.mir.502	hsa.mir.449b	hsa.mir.424	hsa.mir.3065	hsa.mir.183	hsa.mir.27a	hsa.mir.182	hsa.mir.370
hsa.mir.877	hsa.mir.221	hsa.mir.3200	hsa.mir.197	hsa.let.7c	hsa.mir.19b	hsa.mir.125a	hsa.mir.127	hsa.mir.323
hsa.mir.222	hsa.mir.3607	hsa.mir.96	hsa.mir.92b	hsa.mir.3647	hsa.mir.205	hsa.mir.190b	hsa.mir.194	hsa.mir.432
hsa.mir.423	hsa.mir.532	hsa.mir.550a	hsa.mir.15a	hsa.mir.328	hsa.mir.98	hsa.mir.452	hsa.mir.192	hsa.mir.376b
hsa.mir.130b	hsa.mir.224	hsa.mir.106b	hsa.mir.590	hsa.mir.3127	hsa.mir.106b	hsa.mir.22	hsa.mir.96	hsa.mir.744
hsa.mir.1307	hsa.mir.452	hsa.mir.500a	hsa.mir.30e	hsa.mir.193a	hsa.mir.32	hsa.mir.152	hsa.mir.149	hsa.mir.197
hsa.mir.92a	hsa.mir.92a	hsa.mir.500b	hsa.mir.92a	hsa.mir.99a	hsa.mir.590	hsa.mir.3065	hsa.mir.190	hsa.mir.200a
hsa.mir.577	hsa.mir.204	hsa.mir.135a	hsa.mir.2355	hsa.mir.3653	hsa.mir.185	hsa.mir.141	hsa.mir.653	hsa.mir.485
hsa.mir.15b	hsa.mir.29c	hsa.let.7g	hsa.mir.29c	hsa.mir.1301	hsa.mir.21	hsa.mir.221	hsa.mir.382	hsa.mir.502
hsa.mir.184	hsa.mir.96	hsa.mir.335	hsa.mir.1226	hsa.mir.584	hsa.mir.429	hsa.mir.30c	hsa.mir.200b	hsa.mir.324
hsa.mir.455	hsa.mir.197	hsa.mir.200b	hsa.mir.195	hsa.mir.342	hsa.mir.3647	hsa.mir.328	hsa.mir.654	hsa.mir.221
hsa.mir.188	hsa.mir.577	hsa.mir.130b	hsa.mir.582	hsa.mir.3677	hsa.mir.30e	hsa.mir.511	hsa.mir.203	hsa.mir.222
hsa.mir.362	hsa.mir.27b	hsa.mir.3615	hsa.mir.152	hsa.mir.365	hsa.mir.142	hsa.mir.3130	hsa.mir.425	hsa.mir.200b
hsa.mir.942	hsa.mir.222	hsa.mir.18a	hsa.mir.200c	hsa.mir.378c	hsa.mir.204	hsa.mir.29c	hsa.mir.379	hsa.mir.329
hsa.mir.324	hsa.mir.140	hsa.mir.19b	hsa.mir.374b	hsa.mir.7	hsa.mir.19a	hsa.mir.185	hsa.mir.130b	hsa.mir.487b

Top 25 miRNA discriminators (according to adjusted *P*-value (Benjamini Hochberg)) of each RBN clusters are listed. Discriminators with positive fold change are highlighted in red, while discriminators with negative fold change are highlighted in green. Full list is available at http://bioinformatics.mdanderson.org/main/TCGA/Pancan11/RPPA.

Supplementary Table 5: Top 25 Mutation discriminators for RBN clusters

RBN clusters								
A1	A2	B	C	D	E	F	G	H
CDH1	GATA3	PTEN	TP53	APC	TP53	TP53	VHL	EGFR
PIK3CA	TP53	CTNNB1	PIK3CA	KRAS	VHL	CSMD3	TP53	PTEN
TP53	PIK3CA	PIK3R1	VHL	TCF7L2	PTEN	LRP1B	PBRM1	VHL
VHL	VHL	ARID1A	PBRM1	SMAD4	KRAS	TTN	PIK3CA	APC
TTN	CSMD3	PIK3CA	PTEN	FBXW7	CSMD3	CDKN2A	BAP1	CSMD3
MUC17	TTN	CTCF	MUC16	NRAS	MAP3K1	USH2A	MUC4	LRP1B
ARID1A	APC	RPL22	TTN	ACVR2A	PKHD1	FAM135B	KRAS	PIK3R1
CSMD3	PBRM1	ARID5B	ARID1A	TGFBR2	ZNF804A	NOTCH1	CSMD3	PBRM1
GPR98	LRP1B	WDFY4	MLL2	EVC2	NPAP1	ZFHX4	RYR2	ODZ1
PTEN	MAP3K1	ZFHX3	FRG1B	VHL	DPP10	MUC16	APC	KRAS
MAP3K1	USH2A	CSDE1	PCDH11X	SEC63	COL5A1	RYR2	ZFHX4	CDH10
DNAH9	DNAH5	WDR87	FLG	KIAA1804	FAT2	VHL	SETD2	FMN2
ANK2	KRAS	FBXW7	MLL3	PRDM2	CDH18	FAT1	TTN	FBXW7
APC	PLEC	GIGYF2	CDKN2A	PTEN	ASTN2	CDH10	MUC16	FAT4
PCDH15	FBN2	MDN1	SDK1	AXIN2	CDH10	PCLO	FLG	CSMD1
MUC16	CDKN2A	LRRFIP1	FAT4	FAT4	KDR	KEAP1	GATA3	PIK3CA
SI	FRAS1	TAF1	SPTA1	TECTA	COL3A1	ZNF804A	FAT1	GPR112
CSMD2	ZNF804A	RGPD3	SYNE1	FAT2	RP1	MLL2	PTPRD	BIRC6
HRNR	PCDH15	PPIG	CTNND2	ATP10A	PAPPA	ZNF536	PIK3R1	GATA3
FBN2	MUC16	NUP98	NOTCH1	DNMT1	APC	XIRP2	BAI3	FAT1
FAT1	SYNE1	SMG1	MUC4	SACS	N4BP2	COL11A1	LRP1B	TP53
SETD2	CDH10	MKI67	PCLO	GRIK3	NLRP5	SI	RB1	KEL
MLL2	FLG	GOLGA4	KRAS	SMAD2	ATP8A2	PCDH11X	CDH10	TNR
PBRM1	ADAMTS12	GEN1	TCHH	HYDIN	ZNFX1	NAV3	SPTA1	ZNF804B
LRP1	MUC17	MUC5B	CTNNA2	COL6A3	GRID1	PAPPA2	RELN	BAI3

Top 25 mutation discriminators (according to information gain) of each RBN clusters are listed. Mutations enriched in cluster are highlighted in red, while mutations depleted in cluster are highlighted in green. Full list is available at http://bioinformatics.mdanderson.org/main/TCGA/Pancan11/RPPA.

Supplementary Table 6: Top 25 co-mutations in cluster_F specified for TP53 wild-type and mutation

Cases with co-mutation (n, (%))	n=79 TP53 wild-type	n=83 TP53 mutated
CSMD3	9 (11%)	36 (43%)
LRP1B	7 (9%)	31 (37%)
TTN	7 (9%)	51 (61%)
CDKN2A	0 (0%)	18 (22%)
USH2A	2 (3%)	15 (18%)
FAM135B	4 (5%)	15 (18%)
NOTCH1	5 (6%)	15 (18%)
ZFHX4	3 (4%)	19 (23%)
MUC16	8 (10%)	26 (31%)
RYR2	6 (8%)	25 (30%)
FAT1	1 (1%)	20 (24%)
CDH10	1 (1%)	7 (8%)
PCLO	5 (6%)	24 (29%)
KEAP1	3 (4%)	7 (8%)
ZNF804A	2 (3%)	11 (13%)
MLL2	7 (9%)	12 (14%)
ZNF536	3 (4%)	13 (16%)
XIRP2	2 (3%)	12 (14%)
COL11A1	0 (0%)	10 (12%)
SI	1 (1%)	10 (12%)
PCDH11X	3 (4%)	10 (12%)
NAV3	0 (0%)	15 (18%)
PAPPA2	1 (1%)	13 (16%)

Supplementary Table 7: Correspondence between RBN protein clusters and mRNA clusters

	RPPA RBN Cluster	A1	A2	B	C	D	E	F	G	H
mRNA Cluster	Dominant Tissues	BRCA (130)	BRCA (359)	UCEC (252), BLCA (17)	OVCA (182), UCEC (23)	COAD (124), READ (52), BLCA (27)	BRCA (151), BLCA (40)	LUAD (228), HNSC (204), LUSC (165), BRCA (47), BLCA (27), KIRC (26), UCEC (25), OVCA (14), COAD (5)	KIRC (407)	GBM (72)
1	BLCA (65)	0	0	1	0	18	38	11	0	0
4	HNSC (205), LUSC (144), BLCA (34), LUAD (6)	0	0	14	0	6	3	367	0	0
6	GBM (72)	0	1	8	1	0	2	4	0	72
7	BRCA (573)	124	358	1	0	2	78	11	0	0
8	BRCA (116)	6	0	1	0	1	72	36	0	1
9	KIRC (432)	0	0	0	0	0	0	25	407	0
10	LUAD (220), LUSC (13)	0	0	5	0	0	0	228	0	0
11	UCEC (291)	0	0	244	23	0	0	24	0	0
15	COAD (131), READ (55)	0	0	6	1	176	0	8	0	0
16	OVCA (200)	1	0	4	180	0	0	14	0	1

Contingency table showing how many samples fall in a given RBN protein cluster (columns) vs. mRNA cluster (rows). mRNA clusters were obtained from Hoadley et al (personal communication). Only samples that are common between the mRNA and protein datasets are considered. mRNA clusters with too few common samples are not shown. Numbers >=10 are highlighted. Most of the protein clusters predominantly correspond to a single mRNA cluster, as one would expect. However, interestingly, mRNA clusters are derived from a pool of about 20,000 genes, whereas only 181 proteins and phosphoproteins are used to derive the protein clusters. Such a level of agreement seems to validate the protein data, as well as the choice of proteins. Notable exceptions are cluster_E and F. Cluster_E brings together breast basal and HER2 samples with some bladder samples that have high HER2. Cluster_F has a squamous-like signature with HNSC, LUSC and LUAD being dominant tissues. LUAD is a separate cluster in mRNA.

Supplementary Table 8: Cross-tabulation of how samples fall within RBN vs. MC clusters

		RBN Clusters								
		A1	A2	B	C	D	E	F	G	H
MC Clusters	I	0	2	0	0	84	1	0	0	0
	IIa	0	2	0	6	0	50	14	0	0
	IIb	0	0	0	0	0	1	13	1	61
	III	0	105	31	96	48	46	104	65	20
	IV	1	91	132	122	71	61	230	136	77
	V	142	34	76	67	128	8	144	107	8
	VI	5	15	24	22	75	3	201	40	24
	VII	10	130	106	94	60	43	134	75	21

The table shows that most of the MC clusters don’t correspond to a single dominant RBN cluster, but are spread out across several RBN clusters. That shows that the two clustering approaches are different and they reveal different insights, which are mentioned in the main text. Notable exceptions include: (i) MC cluster_I, which has a dominant colorectal signature (corresponding to RBN cluster_D) due to the proteins phospho-PEA15, YB1, and ETS1, (ii) MC cluster_IIa, which has a dominant HER2 signature (corresponding to RBN cluster_E), (iii) MC cluster_IIb, which has a dominant EGFR signature, corresponding to GBM (RBN cluster_H), and (iv) RBN cluster_A1, which has a dominant breast reactive signature (corresponding to MC cluster_V). However, even in those exceptions, a one-to-one correspondence doesn’t quite exist because the reverse relationship doesn’t hold; e.g. even though MC cluster_I predominantly has COAD/READ samples from RBN cluster_D, RBN cluster_D does not predominantly have samples from MC cluster_I. It has many more samples in common with MC cluster_V.

Supplementary Table 9: Top 25 Protein discriminators for MC clusters

Discriminators for cluster_I		
Protein	**Fold change (Log)**	**adj. *P*-value**
PEA15PS116	3.42	0.00E+00
YB1	0.88	5.63E-112
EEF2	1.11	1.67E-74
ETS1	0.93	3.95E-68
EGFRPY1173	-0.66	8.18E-34
NRAS	-0.29	5.65E-25
CMETPY1235	-0.18	5.72E-22
X1433EPSILON	-0.19	9.12E-22
SF2	-0.23	4.11E-20
STATHMIN	-0.23	2.24E-19
SMAD4	-0.20	1.94E-18
ARAFPS299	-0.24	1.37E-17
SCD1	-0.26	1.68E-16
FOXO3A	-0.20	2.27E-15
EGFRPY1068	-0.75	6.43E-15
CRAFPS338	-0.13	9.86E-15
ERK2	0.38	6.94E-14
BETACATENIN	0.57	6.94E-14
CD31	-0.24	6.94E-14
HER2PY1248	-0.39	6.94E-14
HER3PY1298	-0.18	1.09E-13
RBM15	0.42	2.09E-13
RICTORPT1135	-0.15	4.65E-13
P53	-0.39	6.82E-13
MRE11	-0.15	1.16E-12

Discriminators for cluster_IIa		
Protein	**Fold change (Log)**	**adj. *P*-value**
HER2	2.59	1.72E-289
HER2PY1248	2.04	2.52E-251
ERALPHA	-1.76	1.64E-58
EGFRPY1068	1.25	6.04E-33
BCL2	-0.73	6.33E-32
GATA3	-0.63	2.02E-23
HER3PY1298	0.24	1.14E-19
EGFRPY1173	-0.49	2.87E-16
PR	-0.22	6.23E-15
FASN	0.69	8.08E-14
DJ1	-0.31	6.93E-13
PEA15PS116	-0.54	9.07E-11
P70S6K	0.28	5.69E-10
P27	-0.23	2.01E-09
ERALPHAPS118	-0.27	7.23E-09
BIM	-0.31	2.12E-08
CYCLINB1	0.51	3.14E-08
SHCPY317	0.21	3.64E-07
ASNS	0.35	8.53E-07
ACCPS79	0.32	3.34E-06
COLLAGENVI	-0.29	7.97E-06
S6PS240S244	0.34	8.41E-06
SCD1	0.16	8.41E-06
CAVEOLIN1	-0.50	1.31E-05
XRCC1	-0.14	2.58E-05

Discriminators for cluster_IIb		
Protein	**Fold change (Log)**	**adj. *P*-value**
EGFRPY1173	3.54	0.00E+00
EGFRPY1068	4.24	0.00E+00
EGFR	1.55	3.53E-236
HER2PY1248	1.07	4.27E-81
SRCPY416	0.57	4.99E-22
PEA15PS116	-0.60	7.60E-14
HER2	-0.44	4.21E-11
P70S6KPT389	-0.24	2.59E-08
SHCPY317	0.19	3.63E-06
NOTCH1	0.16	7.16E-06
SMAD1	0.15	1.10E-05
ETS1	-0.26	3.40E-05
MEK1PS217S221	-0.19	6.34E-04
CDK1	0.10	8.93E-03
NDRG1PT346	-0.31	1.27E-02
PKCDELTAPS664	0.08	1.27E-02
PCADHERIN	0.08	1.30E-02
SYK	-0.21	1.47E-02
BETACATENIN	0.24	1.69E-02
AKT	0.14	1.89E-02
IRS1	-0.10	2.39E-02
MTORPS2448	-0.07	2.56E-02
RAD51	-0.08	2.56E-02
S6PS240S244	-0.20	2.90E-02
PTEN	-0.15	3.17E-02

Discriminators for cluster_III		
Protein	**Fold change (Log)**	**adj. *P*-value**
HER2PY1248	-0.61	9.67E-125
EGFRPY1173	-0.60	4.14E-112
EGFRPY1068	-0.98	1.88E-99
PEA15PS116	-0.64	1.00E-72
BRAF	0.45	4.72E-62
ETS1	-0.39	1.18E-51
BAP1C4	0.25	1.01E-47
EGFR	-0.29	7.38E-46
MTOR	0.20	2.65E-43
ERALPHAPS118	0.26	1.10E-38
ERALPHA	0.60	7.74E-36
FIBRONECTIN	-0.38	1.85E-33
MYH11	-0.78	9.78E-32
ECADHERIN	0.52	9.56E-31
RBM15	0.32	1.03E-30
PAI1	-0.45	1.91E-30
CAVEOLIN1	-0.54	1.06E-29
COLLAGENVI	-0.30	3.00E-29
HSP70	-0.43	3.28E-29
SRCPY416	-0.29	3.70E-29
X53BP1	0.28	1.80E-27
TAZ	-0.15	6.80E-27
YB1	-0.20	3.05E-26
LCK	-0.20	1.08E-25
CHK2	0.20	1.46E-25

Discriminators for cluster_IV		
Protein	**Fold change (Log)**	**adj. *P*-value**
EGFRPY1173	-0.58	2.98E-145
PEA15PS116	-0.60	8.22E-89
HER2PY1248	-0.40	8.28E-80
GSK3PS9	0.43	8.24E-64
GSK3ALPHABETAPS21S9	0.44	2.41E-63
AKTPS473	0.54	1.96E-58
EGFRPY1068	-0.59	4.17E-52
TUBERINPT1462	0.21	1.59E-51
HER2	-0.37	3.12E-51
NDRG1PT346	0.54	2.73E-46
PKCPANBETAIIPS660	0.28	9.67E-45
EGFR	-0.22	4.99E-37
AKTPT308	0.39	1.38E-34
MAPKPT202Y204	0.40	1.44E-33
ETS1	-0.25	8.64E-32
YB1	-0.18	8.09E-30
P90RSKPT359S363	0.15	8.73E-30
VHL	0.57	2.42E-27
PDCD4	0.29	4.59E-25
TAZ	-0.12	2.03E-24
MTORPS2448	0.09	4.20E-24
MEK1PS217S221	0.18	2.38E-23
BADPS112	0.12	5.86E-23
S6PS235S236	0.26	1.25E-22
P38PT180Y182	0.23	1.33E-22

Discriminators for cluster_V		
Protein	**Fold change (Log)**	**adj. *P*-value**
MYH11	1.97	2.84E-211
RICTOR	0.94	1.27E-139
CAVEOLIN1	1.02	8.18E-122
HER2	-0.62	4.63E-117
HER2PY1248	-0.52	3.29E-112
COLLAGENVI	0.55	2.41E-108
EGFRPY1068	-0.88	2.62E-98
RBM15	-0.49	1.41E-86
EEF2	-0.46	4.47E-67
CYCLINB1	-0.60	2.74E-64
S6	-0.37	6.82E-56
EGFRPY1173	-0.36	9.39E-54
GAPDH	-0.78	1.79E-48
STAT3PY705	0.25	2.77E-46
CHK2	-0.24	5.41E-41
FOXM1	-0.25	6.08E-41
PEA15PS116	-0.42	7.89E-40
PKCALPHAPS657	0.27	9.00E-38
ECADHERIN	-0.51	1.77E-36
P70S6K	-0.22	1.16E-35
RAB11	0.20	1.35E-35
EGFR	-0.22	4.20E-34
MAPKPT202Y204	0.42	2.68E-32
HSP70	0.41	9.01E-32
ASNS	-0.31	1.40E-31

Discriminators for cluster_VI		
Protein	**Fold change (Log)**	**adj. *P*-value**
CHK1	0.38	9.64E-154
EIF4G	-0.60	1.65E-142
HER2	-0.78	3.54E-129
AKT	-0.53	5.12E-120
BETACATENIN	-0.89	3.99E-112
EGFRPY1068	-1.05	1.82E-97
TUBERIN	-0.45	4.80E-97
X53BP1	-0.55	7.17E-86
TSC1	-0.40	9.64E-83
RBM15	-0.56	1.08E-77
BRAF	-0.55	1.08E-77
STAT5ALPHA	-0.61	1.51E-77
MTOR	-0.29	7.63E-74
HER2PY1248	-0.49	3.42E-71
KU80	-0.38	3.77E-71
STATHMIN	0.24	3.78E-71
BAP1C4	-0.33	3.99E-71
MRE11	0.18	8.37E-67
CMETPY1235	0.17	1.21E-66
X1433EPSILON	0.17	1.27E-63
PAI1	0.71	6.86E-63
P70S6K	-0.34	1.82E-60
TAZ	0.25	2.93E-60
AMPKPT172	-0.52	3.29E-60
ERK2	-0.43	5.54E-59

Discriminators for cluster_VII		
Protein	**Fold change (Log)**	**adj. *P*-value**
HER2PY1248	-0.69	2.12E-182
EGFRPY1068	-1.23	1.23E-175
EGFRPY1173	-0.52	4.69E-101
HER2	-0.54	1.41E-86
SRCPY527	-0.55	9.35E-76
P38PT180Y182	-0.43	1.74E-62
GSK3PS9	-0.46	2.12E-61
GSK3ALPHABETAPS21S9	-0.45	2.86E-57
SRCPY416	-0.38	9.66E-56
MAPKPT202Y204	-0.56	4.20E-54
RBPS807S811	-0.35	2.14E-40
PEA15PS116	-0.41	3.66E-37
EGFR	-0.23	3.74E-36
NDRG1PT346	-0.49	4.85E-33
AKTPS473	-0.43	1.75E-32
BADPS112	-0.16	3.88E-32
X4EBP1PT37T46	-0.32	3.98E-31
NFKBP65PS536	-0.37	3.30E-29
BIM	0.24	3.17E-28
PRAS40PT246	-0.17	3.95E-28
SHCPY317	-0.17	8.23E-26
MEK1PS217S221	-0.21	8.23E-26
PI3KP85	0.15	2.80E-24
GATA3	0.24	7.58E-22
RAPTOR	0.15	7.67E-22

Top 25 protein discriminators (according to adjusted *P*-value (Benjamini Hochberg)) of each MC clusters are listed. Positive values (highlighted in red) in Fold change (Log) column indicate a fold change increase, in log scale, of the protein level of particular protein comparing to that in all other clusters by LIMMA analysis, while negative values indicate fold change decrease. Full list is available at http://bioinformatics.mdanderson.org/main/TCGA/Pancan11/RPPA.

Supplementary Table 10: Top 25 RNA discriminators for MC clusters

MC clusters							
I	IIa	IIb	III	IV	V	VI	VII
CLCA1	ERBB2	SEC61G	STARD3	STARD3	MYH11	PGAP3	PGAP3
REG4	STARD3	LANCL2	C13orf18	C17orf37	SYNPO2	SOCS3	ZG16
ZG16	PGAP3	PMP2	VOPP1	PSMD3	C17orf37	SERPINB4	ERBB2
GPA33	C17orf37	KRT18	FEZ1	GBAS	SLIT3	IMPA2	CLCA1
NOX1	ORMDL3	KRT8	SLC38A5	CHCHD2	CNN1	CYP24A1	REG4
CDX1	PSMD3	ARHGEF5	GAP43	PGAP3	COL14A1	RAB38	STARD3
PHGR1	MED1	OLIG2	SEC61G	PPP2R3A	LMOD1	SERPINB3	KRT20
MEP1A	CDK12	GRB7	NT5E	C1orf186	AOC3	ORMDL3	FABP1
FABP1	MSL1	HEPACAM	PSMD3	ERBB2	PSMD3	FOSL2	NOS2
CDX2	GRB7	DSG2	TNC	RIPK4	ACTA2	AHNAK2	ESR1
CDH17	PNMT	C1orf61	DSE	ORMDL3	MYLK	GNA15	LANCL2
SPINK4	CASC3	GFAP	F3	WDR91	IGF1	RIPK4	PSMD3
REG3A	MED24	NCAN	GNA12	STAT6	TAGLN	DUSP7	MEP1A
SLC26A3	ABCC11	HOOK1	HEPH	SLC26A9	PPP1R12B	LTBR	SLC26A3
KRT20	MUCL1	PRSS8	S100B	MPZL2	HSPG2	CTSC	FAM3D
MUC17	SEC16A	SPINT1	PLA2G2A	LANCL2	SEC61G	SPRR2D	CEACAM7
LGALS4	ZNF652	SPINT2	ACTB	FAIM2	CPXM2	RHBDF2	NOX1
ITLN1	CYB561	AP1M2	HGSNAT	KIAA1217	ADH1B	A4GALT	C17orf37
DEFA6	WIPF2	GBAS	EMILIN1	HOOK1	PGR	TYMP	SPINK4
RIMKLB	SCGB2A2	FEZ1	PMEPA1	IL1R1	GPR124	CXCL5	REG3A
MUC2	SERHL2	KIAA1217	CD99	CCT6A	TNXB	CXCL1	C12orf35
EPS8L3	CLTC	GAP43	PDGFRA	CASC3	IL1R1	GBAS	PHGR1
C2orf89	CREB3L4	TMEM184A	PARD6B	DCTPP1	GJA5	S100A8	LGALS4
MUC12	MIA3	CLDN4	CALM1	LFNG	COL15A1	SPRR1B	IGF1
RPS3A	NUFIP2	ELF3	ZBTB44	ALPL	HMCN1	EHBP1L1	CCL5

Top 25 RNA discriminators (according to adjusted *P*-value (Benjamini Hochberg)) of each MC clusters are listed. Discriminators with positive fold change are highlighted in red, while discriminators with negative fold change are highlighted in green. Full list is available at http://bioinformatics.mdanderson.org/main/TCGA/Pancan11/RPPA.

Supplementary Table 11: Top 25 miRNA discriminators for MC clusters

MC clusters							
I	IIa	IIb	III	IV	V	VI	VII
hsa.mir.552	hsa.mir.3150b	hsa.mir.944	hsa.mir.379	hsa.mir.369	hsa.mir.145	hsa.mir.223	hsa.mir.584
hsa.mir.192	hsa.mir.184	hsa.mir.3917	hsa.mir.369	hsa.mir.889	hsa.mir.130b	hsa.mir.190b	hsa.mir.342
hsa.mir.215	hsa.mir.3677	hsa.mir.2355	hsa.mir.381	hsa.mir.552	hsa.mir.133a	hsa.mir.486	hsa.mir.552
hsa.mir.194	hsa.mir.4326	hsa.mir.3648	hsa.mir.223	hsa.mir.885	hsa.mir.17	hsa.mir.144	hsa.mir.192
hsa.mir.2355	hsa.mir.3127	hsa.mir.3199	hsa.mir.134	hsa.mir.411	hsa.mir.99a	hsa.mir.31	hsa.mir.1301
hsa.mir.3613	hsa.mir.190b	hsa.mir.205	hsa.mir.889	hsa.mir.379	hsa.mir.33b	hsa.mir.29a	hsa.mir.203
hsa.mir.577	hsa.mir.577	hsa.mir.2115	hsa.mir.337	hsa.mir.382	hsa.mir.210	hsa.mir.212	hsa.mir.215
hsa.mir.3065	hsa.mir.135b	hsa.mir.421	hsa.mir.199a	hsa.mir.134	hsa.mir.148b	hsa.mir.140	hsa.mir.194
hsa.mir.3607	hsa.mir.223	hsa.mir.451	hsa.mir.382	hsa.mir.381	hsa.mir.33a	hsa.mir.184	hsa.mir.320a
hsa.mir.3647	hsa.mir.486	hsa.mir.185	hsa.mir.199b	hsa.mir.500b	hsa.mir.629	hsa.mir.451	hsa.mir.429
hsa.mir.95	hsa.mir.193a	hsa.mir.3613	hsa.mir.758	hsa.mir.500a	hsa.let.7c	hsa.mir.24	hsa.mir.125b
hsa.let.7e	hsa.mir.191	hsa.mir.3615	hsa.mir.654	hsa.mir.3150b	hsa.mir.140	hsa.mir.221	hsa.mir.760
hsa.mir.3127	hsa.mir.27b	hsa.mir.3687	hsa.mir.411	hsa.mir.539	hsa.mir.139	hsa.mir.99a	hsa.mir.200a
hsa.mir.147b	hsa.mir.2115	hsa.mir.144	hsa.mir.495	hsa.mir.494	hsa.mir.7	hsa.mir.504	hsa.mir.125a
hsa.mir.3677	hsa.mir.615	hsa.mir.223	hsa.mir.409	hsa.mir.34b	hsa.mir.3934	hsa.mir.3127	hsa.mir.361
hsa.mir.365	hsa.mir.642a	hsa.mir.541	hsa.mir.30c	hsa.mir.655	hsa.mir.125b	hsa.mir.27a	hsa.mir.99b
hsa.mir.205	hsa.mir.323b	hsa.mir.3676	hsa.mir.493	hsa.mir.378c	hsa.mir.1	hsa.mir.376b	hsa.mir.452
hsa.mir.181b	hsa.mir.144	hsa.mir.340	hsa.mir.664	hsa.mir.320a	hsa.mir.93	hsa.mir.182	hsa.mir.484
hsa.mir.3653	hsa.mir.199a	hsa.mir.3065	hsa.mir.143	hsa.mir.135a	hsa.mir.18a	hsa.mir.132	hsa.mir.19a
hsa.mir.1301	hsa.mir.1287	hsa.mir.130b	hsa.mir.496	hsa.mir.493	hsa.mir.3150b	hsa.mir.375	hsa.mir.193a
hsa.let.7c	hsa.mir.425	hsa.mir.24	hsa.mir.127	hsa.mir.664	hsa.mir.942	hsa.mir.1246	hsa.let.7a
hsa.mir.584	hsa.mir.149	hsa.mir.18b	hsa.mir.136	hsa.mir.376c	hsa.mir.100	hsa.mir.196a	hsa.mir.92b
hsa.mir.3130	hsa.mir.199b	hsa.mir.550a	hsa.mir.30d	hsa.mir.758	hsa.mir.3648	hsa.mir.1287	hsa.mir.223
hsa.mir.99a	hsa.mir.20b	hsa.mir.145	hsa.mir.299	hsa.mir.125a	hsa.mir.345	hsa.mir.584	hsa.let.7e
hsa.mir.378c	hsa.mir.365	hsa.mir.3158	hsa.mir.152	hsa.mir.215	hsa.mir.497	hsa.mir.191	hsa.mir.33a

Top 25 miRNA discriminators (according to adjusted *P*-value (Benjamini Hochberg)) of each RBN clusters are listed. Discriminators with positive fold change are highlighted in red, while discriminators with negative fold change are highlighted in green. Full list is available at http://bioinformatics.mdanderson.org/main/TCGA/Pancan11/RPPA.

Supplementary Table 12: Top 25 Mutation discriminators for MC clusters

MC clusters							
I	IIa	IIb	III	IV	V	VI	VII
APC	PTEN	EGFR	PTEN	PTEN	NALCN	DNMT3A	GATA3
KRAS	VHL	VHL	OR56A1	TRIM23	ERBB4	HACE1	SLC9A2
TCF7L2	TP53	ARID1A	DOCK5	ARID1A	PCDH11X	LRP1B	DCAF8L1
EDNRB	APC	PBRM1	PRF1	ZNF429	ROBO4	EP300	MAGEB6
HYDIN	ZNF384	HMCN1	MAP2	FAM135B	PREX2	CDH8	MET
KIRREL3	KRAS	KRAS	ZNF835	CDH4	FAT3	KIAA1429	KRAS
EVC	DST	PIK3CA	EGFR	TRPM6	BRCA2	IQGAP1	DNAJC6
RUVBL1	NAV3	WNT2	NLRP4	DOPEY2	SEMA5B	TPO	HNRNPU
REV3L	DNAH9	OR9G1	ATXN2	TTC3	USP6	ADAMTSL3	EML4
MARCH10	ANK2	PCSK6	OR1C1	CHST9	CHRM3	MST1P9	APC
FBXW7	RYR1	CDKN2A	KHDRBS2	DOCK5	VCAN	MAP3K1	SLC4A3
IQCB1	MAP3K10	OBSCN	GALNT14	PVRL4	TRPA1	TRHR	ZNF425
TBC1D22A	CUBN	SLCO6A1	TGFBR2	TNRC6A	FAM171B	ATP10A	ARMC5
GPC6	LRP1B	SERPINI1	TRIM71	ZFAT	LPPR4	APPBP2	ZNF282
TGFBR2	EPB41	CUBN	FASN	MAN2C1	PCDHGA6	CNST	POLK
ROBO1	CSMD2	MYSM1	PPP1R13B	EIF2C3	ZDBF2	AHI1	THSD1
KRIT1	ARHGEF25	RBBP8	NLRP13	COL27A1	C10orf90	ANKIB1	SLC6A14
BCR	RUNX1	HCK	TOP3A	ZFYVE1	PRDM14	IL1RAPL1	BRD8
THBS1	NF1	LGSN	WDR78	SCN8A	KCND3	ZCCHC6	C3orf30
EVC2	ZC3H7A	SCNN1G	ZNF546	CMYA5	ASPM	PCDH11X	SLITRK4
ISL1	FRAS1	MDN1	PPARGC1B	SIPA1L2	FPGT.TNNI3K	OR4A5	RGPD3
AIM2	DNAH10	SETD2	SLC6A4	UGT2A1	SLC17A8	CSMD3	ZNF257
CAP2	HERC2	DNAH10	ZNF235	TTC16	TPO	ALMS1	WDR70
FAM22F	TRRAP	KIAA1109	PITPNM1	ARMC9	SGIP1	HINFP	TMC7
VHL	RIMS2	CACNA1E	CWH43	ZNF749	ZIM3	NOTCH1	ITGA7

Top 25 mutation discriminators (according to information gain) of each RBN clusters are listed. Mutations enriched in cluster are highlighted in red, while mutations depleted in cluster are highlighted in green. Full list is available at http://bioinformatics.mdanderson.org/main/TCGA/Pancan11/RPPA.

Supplementary Table 13: Pathway score members

Apoptosis score[4]	**Direction**	**EMT score**[5, 6]	**Direction**	**Ras/MAPK score**[7, 8, 9, 10, 11]	**Direction**
BAK	+	FIBRONECTIN	+	ARAFPS299	+
BAX	+	NCADHERIN	+	CJUNPS73	+
BID	+	COLLAGENVI	+	CRAFPS338	+
BIM	+	CLAUDIN7	-	JNKPT183Y185	+
CASPASE7CLEAVEDD198	+	ECADHERIN	-	MAPKPT202Y204	+
BADPS112	-			MEK1PS217S221	+
BCL2	-	**Hormone_a score**[12]	**Direction**	P38PT180Y182	+
BCLXL	-	ERALPHA	+	P90RSKPT359S363	+
CIAP	-	ERALPHAPS118	+	SHCPY317	+
		PR	+	YB1PS102	+
Cell cycle score[13]	**Direction**				
CDK1	+	**Hormone_b score**[14, 15, 16]	**Direction**	**RTK score**[17, 18]	**Direction**
CYCLINB1	+	AR	+	EGFRPY1068	+
CYCLIND1	+	INPP4B	+	EGFRPY1173	+
CYCLINE1	+	GATA3	+	HER2PY1248	+
CYCLINE2	+	BCL2	+	HER3PY1298	+
P27PT157	+			SHCPY317	+
P27PT198	+	**PI3K/Akt score**[19, 20, 21, 22]	**Direction**	SRCPY416	+
PCNA	+	AKTPS473	+	SRCPY527	+
		AKTPT308	+		
DNA damage response score[23]	**Direction**	GSK3ALPHABETAPS21S9	+	**TSC/mTOR score**[19, 22, 24]	**Direction**
53BP1	+	GSK3PS9	+	4EBP1PS65	+
ATM	+	P27PT157	+	4EBP1PT37T46	+
BRCA2	+	P27PT198	+	4EBP1PT70	+
CHK1PS345	+	PRAS40PT246	+	P70S6KPT389	+
CHK2PT68	+	TUBERINPT1462	+	MTORPS2448	+
KU80	+	INPP4B	-	S6PS235S236	+
MRE11	+	PTEN	-	S6PS240S244	+
P53	+			RICTORPT1135	+
RAD50	+				
RAD51	+				
XRCC1	+				

Supplementary Table 14: Outcome prediction by pathways and actionable proteins

		Training set			Test set					
					Optimized percentage as cut-off			Optimized value as cut-off		
Tumor	**Predictor**	**n High/Low**	**Hazard ratio**	***P*-value**	**n High/Low**	**Hazard ratio**	***P*-value**	**n High/Low**	**Hazard ratio**	***P*-value**
BRCA	BCL2	338/139	0.38	0.0005				162/75	0.40	0.0250
BRCA	BRAF	350/127	2.31	0.0250	174/63	3.60	0.0390			
BRCA	SRCPY416	130/347	2.22	0.0070	65/172	2.54	0.0230	71/166	2.86	0.0100
COAD	FASN	58/163	0.37	0.0420	29/81	0.19	0.0160	40/70	0.11	0.0070
HNSC	PTEN	62/80	0.60	0.0400	31/39	0.43	0.0270			
HNSC	SRCPY416	101/41	0.54	0.0180	50/20	0.25	0.0001	55/15	0.32	0.0021
KIRC	ACC1	64/239	3.27	0.0000	32/119	2.29	0.0140	29/122	2.46	0.0100
KIRC	AR	203/100	0.39	0.0000	102/49	0.33	0.0001	97/54	0.32	0.0001
KIRC	HER2	242/61	0.51	0.0016	121/30	0.38	0.0016	123/28	0.40	0.0033
KIRC	HER3	216/87	0.32	0.0000	108/43	0.52	0.0330	108/43	0.52	0.0330
KIRC	HER3PY1298	150/153	0.43	0.0001	75/75	0.56	0.0470	81/70	0.44	0.0049
KIRC	Hormone_b	236/67	0.51	0.0019	118/33	0.41	0.0045	116/35	0.44	0.0079
KIRC	PI3K/Akt	185/118	0.67	0.0430	93/58	0.53	0.0260	95/56	0.52	0.0220
KIRC	RTK	242/61	0.29	0.0000	121/30	0.53	0.0470	133/18	0.32	0.0019
KIRC	SRCPY416	237/66	0.36	0.0000				136/15	0.38	0.0072
KIRC	TFRC	117/186	2.62	0.0000	59/92	1.85	0.0310	58/93	1.87	0.0280
LUAD	TFRC	96/44	2.75	0.0110	49/22	3.60	0.0440	50/21	3.60	0.0440
LUSC	TFRC	75/47	0.44	0.0066	37/23	0.37	0.0150	30/30	0.44	0.0490
OVCA	AR	212/57	0.64	0.0230				114/19	0.49	0.0260
OVCA	DNA Damage Response	167/102	0.69	0.0300	83/50	0.57	0.0250			
OVCA	EGFRPY1173	108/161	0.59	0.0029	54/79	0.58	0.0340	66/67	0.56	0.0150

		Test set								
		Median as cut-off			Top vs. bottom tertile			Top vs. bottom quartile		
Tumor	**Predictor**	**n High/Low**	**Hazard ratio**	***P*-value**	**n High/Low**	**Hazard ratio**	***P*-value**	**n High/Low**	**Hazard ratio**	***P*-value**
BRCA	BCL2	118/119	0.47	0.0780	79/79	0.45	0.1000	59/60	0.47	0.1700
BRCA	BRAF	118/119	1.01	0.9800	79/79	1.46	0.4900	59/60	2.87	0.1200
BRCA	SRCPY416	118/119	1.68	0.2100	79/79	2.00	0.1200	59/60	1.56	0.4400
COAD	FASN	55/55	0.14	0.0050	37/37	0.17	0.0510	28/28	0.11	0.0550
HNSC	PTEN	35/35	0.60	0.1500	23/23	0.61	0.2600	18/18	0.75	0.5500
HNSC	SRCPY416	35/35	0.51	0.0660	23/23	0.29	0.0096	18/18	0.25	0.0140
KIRC	ACC1	75/76	1.87	0.0340	50/50	1.92	0.0990	38/38	4.08	0.0130
KIRC	AR	75/76	0.34	0.0005	50/50	0.29	0.0011	38/38	0.20	0.0003
KIRC	HER2	75/76	0.62	0.1000	50/50	0.30	0.0042	38/38	0.27	0.0025
KIRC	HER3	75/76	0.50	0.0200	50/50	0.37	0.0054	38/38	0.45	0.0540
KIRC	HER3PY1298	75/76	0.56	0.0470	50/50	0.47	0.0300	38/38	0.57	0.1500
KIRC	Hormone_b	75/76	0.53	0.0390	50/50	0.41	0.0310	38/38	0.34	0.0160
KIRC	PI3K/Akt	75/76	0.65	0.1300	50/50	0.44	0.0260	38/38	0.50	0.1100
KIRC	RTK	75/76	0.35	0.0007	50/50	0.25	0.0012	38/38	0.29	0.0096
KIRC	SRCPY416	75/76	0.68	0.1900	50/50	0.75	0.4000	38/38	0.61	0.2000
KIRC	TFRC	75/76	1.78	0.0490	50/50	1.46	0.2500	38/38	1.41	0.3300
LUAD	TFRC	35/36	2.28	0.0840	24/24	2.35	0.1400	18/18	2.28	0.2400
LUSC	TFRC	30/30	0.44	0.0490	20/20	0.32	0.0240	15/15	0.54	0.2800
OVCA	AR	66/67	0.70	0.1500	44/44	0.68	0.2100	33/34	0.55	0.0940
OVCA	DNA Damage Response	66/67	0.77	0.2800	44/44	0.76	0.3600	33/34	0.91	0.8000
OVCA	EGFRPY1173	66/67	0.56	0.0150	44/44	0.53	0.0320	33/34	0.58	0.1100

Upper table shows the outcome prediction results in 11 individual diseases by pathways (listed in Supplementary Table 13) and actionable proteins (shown in Fig. 5) using a training-and-test-set approach finding the optimized cutoff. Only the pathways and actionable proteins confirmed in test set are shown. Bottom table shows the results using median as cutoff, top vs. bottom tertile and top vs. bottom quartile in the same test sets. Hazard ratios >1.00 (highlighted in red) indicate higher pathway score or protein expression predicting poor overall survival, while hazard ratios <1.00 (highlighted in green) indicate higher score or expression predicting better survival. Significant *P*-values (<0.05) are in red. The smallest *P*-value for each pathway or actionable protein is highlighted in yellow.

Supplementary Table 15: Literature reference and independent validation of top 25 links shown in Supplementary Figure 13

Rank	Protein-protein link	Literature	Validated in Independent BRCA, OVCA and UCEC sets (0.25 as cutoff)
1	GAB2–MIG6		N/A
2	HER2–HER2PY1248		BRCA, UCEC
3	BETACATENIN–ECADHERIN	[25]	BRCA
4	PTEN–PI3KP85	[26]	N/A
5	EGFRPY1068–HER2PY1248	[27]	OVCA-1
6	MAPKPT202Y204–MEK1PS217S221	[28]	OVCA-1, UCEC
7	MYH11–RICTOR		BRCA
8	CIAP–YAPPS127	[29, 30]	N/A
9	EGFRPY1068–EGFRPY1173		N/A
10	AKTPT308–CDK1	[31]	N/A
11	EGFRPY1068–EGFR		N/A
12	CDK1–CYCLINB1	[32]	OVCA-1
13	PKCDELTAPS664–PKCPANBETAIIPS660	[32, 33, 34]	
14	EGFRPY1173–HER2PY1248		N/A
15	PEA15PS116–ETS1		N/A
16	RAD50–MYH11		N/A
17	P90RSKPT359S363–YB1PS102	[10]	
18	CYCLINB1–FOXM1	[35]	BRCA, UCEC
19	EIF4E–MEK1	[36]	UCEC
20	HER3–XBP1		
21	EGFRPY1068–SHCPY317	[37]	
22	PKCALPHAPS657–PKCDELTAPS664	[38]	
23	CHK2PT68–PI3KP110ALPHA	[39]	N/A
24	BECLIN–XBP1	[40]	OVCA-2
25	BECLIN–TAZ		N/A

Four independent datasets were used for the validation of the protein links; 2 ovarian cancer sets (OVCA-1; Japanese set and OVCA-2; Philadelphia set[41]), a breast cancer set[42] and an endometrial cancer set[43]. Additionally a Pubmed search was performed to confirm links. In cases where strong correlation for a link was only found in tumor lineages for which no external dataset could be retrieved, this has been indicated with N/A (not available). 10 of the 25 links were validated using literature search, and 9 out of 14 links (without NA's) were validated in the independent datasets. Overall, 17 out of 25 links were validated using either approach.

Supplementary Table 16: Key clinical variables in pan-cancer dataset

Clinical variable	Number of cases (n (%))										
Tumor lineage	**BLCA[1]**	**BRCA[2]**	**COAD[3]**	**GBM[4]**	**HNSC[5]**	**KIRC[6]**	**LUAD[7]**	**LUSC[8]**	**OVCA[9]**	**READ[10]**	**UCEC[11]**
Age (median)	68[12]	58	69	60	62	61	66	69	58	66	64
Stage											
1	1 (1)[15]	112 (15)[19]	50 (16)	NA	9 (5)[20]	219 (48)	125 (53)	98 (51)[14]	14 (3)[15]	21 (17)[16]	230 (62)
2	35 (29)	423 (59)	135 (44)		39 (20)	44 (10)	50 (21)	57 (30)	20 (5)	40 (32)	32 (9)
3	40 (34)	173 (24)	79 (26)		31 (16)	115 (25)	49 (21)	37(19)	320 (79)	43 (35)	88 (24)
4	43 (36)	15 (2)	42 (14)		121 (61)	76 (17)	13 (5)	0 (0)	51 (13)	20 (15)	21 (6)
Adjuvant treatment											
Chemo- /Hormonal	2 (2)	272 (37)	48 (15)	122 (58)	35 (17)	4 (1)	30 (13)	22 (11)	238 (58)	16 (12)	82 (22)
Radio-	0(0)	183 (25)	3 (1)	144 (68)	55 (26)	0 (0)	12 (5)	9 (5)	2 (0)	5 (4)	119 (32)
Smoking status											
Current	23 (20)[16]	NA	NA	NA	67 (33)[17]	NA	52 (23)[18]	39 (21)[16]	NA	NA	NA
Reformed	66 (56)				100 (49)		144 (63)	142 (75)			
Never	28 (24)				37 (18)		32 (14)	8 (4)			
Death events	34 (28)[13]	81 (11)	45 (14)[14]	137 (65)	107 (51)	151 (33)	72 (30)[21]	75 (39)[17]	213 (52)1[6]	11 (9)	32 (9)[12]
Median survival (months)	7	15	5	8	13	35	12	16	29	1	14
Range of survival (months)	0-120	0-191	137	0-1	0-214	0-113	0-227	0-176	0-183	0-123	0-176

[1]BLCA: data available for 123 patients; [2]BRCA: data available for 733 patients; [3]COAD: data available for 331 patients; [4]GBM: data available for 211 patients; [5]HNSC: data available for 212 patients; [6]KIRC: data available for 454 patients; [7]LUAD: data available for 237 patients; [8]LUSC: data available for 195 patients; [9]OVCA: data available for 410 patients; [10]READ: data available for 130 patients; [11]UCEC: data available for 371 patients; [12]data missing for 1 patient; [13]data missing for 2 patients; [14]data missing for 3 patients; [15]data missing for 4 patients; [16]data missing for 6 patients; [17]data missing for 8 patients; [18]data missing for 9 patients; [19]data missing for 10 patients; [20]data missing for 12 patients; [21]data missing for 16 patients

Supplementary Table 17: Histological subtypes of BRCA, COAD, READ and UCEC

Clinical variable	Number of cases (n (%))			
Tumor lineage	**BRCA**	**COAD**	**READ**	**UCEC**
Histological subtype	Ductal 578 (79) Lobular 89 (12) Medullary 4 (1) Mixed 22 (3) Mucinous 9 (1) Other 31 (4)	Adenocarcinoma 292 (88) Mucinous adenocarcinoma 39 (12)	Adenocarcinoma 117 (92)[a] Mucinous adenocarcinoma 10 (8)	Endometrioid 289 (78) Serous 69 (19) Mixed 13 (4)

[a] Data missing for 3 patients

Supplementary Method 1: Literature and clinical trials targeting actionable proteins

Potentially actionable proteins (n = 25, Fig. 5) were selected based on a literature review[44, 45, 46, 47, 48] for associations with proteomic and genomic events as well as for potential ability of proteomics to identify patients likely to benefit from targeted therapies (Fig. 5a,b). There are registered phase 1 and 2 trials (clinicaltrials.gov) targeting many of the actionable proteins or their related pathways (examples in parentheses), such as pTEN[49, 50] (NCT01458067), HER3[51] (NCT01918254, NCT01482377, NCT00730470); Notch1[52, 53, 54] (NCT01208441, NCT01158274), TFRC67 (NCT00003082), HER2[55, 56, 57, 58, 59] (NCT00679341, NCT00943670, NCT00875979, NCT00005831, NCT00006089); BCL2[60, 61] (NCT00005032, NCT00039481, NCT00059813, NCT00063934); pSTAT3[62] (NCT00955812: NCT01563302, NCT01839604); cMET[63] (NCT01324479, NCT01523340, NCT01121575, NCT01610336; AR (NCT01889238, NCT01918306, NCT01616758); AMPK[50] (NCT01477060, NCT01210911, NCT01266486); BRAF (NCT00095459, NCT01266967). Some proteins have been suggested as targets in only preclinical studies so far: MYC[46], FASN[64, 65, 66] and XRCC1[67, 68, 69]. ARID1A has been linked to the PI3K pathway, suggesting tumors with loss of ARID1A could potentially be sensitive to drugs targeting this pathway[43]. Yap[70], lastly has been suggested as an interesting potential target due to its links with the WNT pathway and the EMT process.

Supplementary Method 2: RPPA methodology

All TCGA samples were evaluated by a board-certified pathologist (H&E stained slide) for confirmation of histological diagnosis and included only if tumor purity passed a predefined threshold (that varied by tissue type) but in general greater than 70%. For TCGA inclusion, no further specific requirements were specified regarding tumor heterogeneity. To prepare the lysate, protein was extracted using RPPA lysis buffer (1% Triton X-100, 50 mmol/L Hepes (pH 7.4), 150 mmol/L NaCl, 1.5 mmol/L MgCl2, 1 mmol/L EGTA, 100 mmol/L NaF, 10 mmol/L NaPPi, 10% glycerol, 1 mmol/L phenylmethylsulfonyl fluoride, 1 mmol/L Na3VO4, and aprotinin 10 ug/mL) and Precellys homogenization from fresh frozen tumor tissue and RPPA was performed as described previously[45, 71, 72, 73, 74]. Concentration of the lysates was adjusted to 1 µg/µL (assessed by bicinchoninic acid assay) and boiled with 1% SDS. Tumor lysates were then serially diluted in two-fold of 5 dilutions with lysis buffer and printed on nitrocellulose-coated slides fitting 1056 samples (Grace Bio-Labs) using an Aushon Biosystems 2470 arrayer (Burlington, MA) (Supplementary Fig. S6.3). The RPPA antibody validation process, including assessment for specificity, quantification and dynamic range, was previously described[75] and includes the presence and density of a single and appropriately sized band on immunoblots. We use labels 'validated' and 'use with caution', based on the degree of validation by the above-mentioned criteria[45]. Signal was captured using a DakoCytomation-catalyzed system and DAB colorimetric reaction. Slides were scanned in CanoScan 9000F and spot intensities analyzed and quantified using Microvigene software (VigeneTech Inc., Carlisle, MA) (Level 1 data). The software SuperCurveGUI[45, 71, 72], available at http://bioinformatics.mdanderson.org/Software/supercurve/, was used to estimate the protein EC50 values in each dilution series (log2 scale). Briefly, a fitted curve ("supercurve") was plotted with the signal intensities on the Y-axis and the relative log2 concentration of each protein on the X-axis using the non-parametric, monotone increasing B-spline model[74]. During the process, the raw spot intensity data were adjusted to correct spatial bias before model fitting. A quality control metric[71] was generated for each slide and the slide was discarded when the score was <0.8 (scale 0-1), followed in most cases by a new staining procedure to obtain a high quality score. The slide with the highest QC score was used for analysis (Level 2 data), if multiple slides were stained for an antibody. Protein measurements were corrected for loading as described[71, 72, 76] using median centering across antibodies (level 3 data). Finally, median centering across all the antibodies for each sample was used to correct for sample loading differences, which arise because protein concentrations are not uniformly distributed per unit volume, due to differences in protein concentrations of large and small cells, differences in the amount of proteins per cell, or heterogeneity of the cells comprising the samples f.e.. Differences in the total amount of protein in that sample vs. other samples can be estimated observing the expression levels across a large number or proteins from a sample. Subtracting the median protein expression level forces the median value to become zero, allowing protein expression comparison across samples[77]. More extensive information can be found in various articles[78].

Supplementary References

1. Cardnell RJ*, et al.* Proteomic markers of DNA repair and PI3K pathway activation predict response to the PARP inhibitor BMN 673 in small cell lung cancer. *Clinical cancer research : an official journal of the American Association for Cancer Research* **19**, 6322-6328 (2013).

2. Komurov K, White MA, Ram PT. Use of data-biased random walks on graphs for the retrieval of context-specific networks from genomic data. *PLoS computational biology* **6**, (2010).

3. Shannon P*, et al.* Cytoscape: a software environment for integrated models of biomolecular interaction networks. *Genome research* **13**, 2498-2504 (2003).

4. Igney FH, Krammer PH. Death and anti-death: tumour resistance to apoptosis. *Nature reviews Cancer* **2**, 277-288 (2002).

5. De Craene B, Berx G. Regulatory networks defining EMT during cancer initiation and progression. *Nature reviews Cancer* **13**, 97-110 (2013).

6. Katsuno Y, Lamouille S, Derynck R. TGF-beta signaling and epithelial-mesenchymal transition in cancer progression. *Current opinion in oncology* **25**, 76-84 (2013).

7. Dhillon AS, Hagan S, Rath O, Kolch W. MAP kinase signalling pathways in cancer. *Oncogene* **26**, 3279-3290 (2007).

8. Hauge C, Frodin M. RSK and MSK in MAP kinase signalling. *Journal of cell science* **119**, 3021-3023 (2006).

9. Ravichandran KS. Signaling via Shc family adapter proteins. *Oncogene* **20**, 6322-6330 (2001).

10. Stratford AL*, et al.* Y-box binding protein-1 serine 102 is a downstream target of p90 ribosomal S6 kinase in basal-like breast cancer cells. *Breast cancer research : BCR* **10**, R99 (2008).

11. Wagner EF, Nebreda AR. Signal integration by JNK and p38 MAPK pathways in cancer development. *Nature reviews Cancer* **9**, 537-549 (2009).

12. Sommer S, Fuqua SA. Estrogen receptor and breast cancer. *Seminars in cancer biology* **11**, 339-352 (2001).

13. Vermeulen K, Van Bockstaele DR, Berneman ZN. The cell cycle: a review of regulation, deregulation and therapeutic targets in cancer. *Cell proliferation* **36**, 131-149 (2003).

14. Hodgson MC*, et al.* Decreased expression and androgen regulation of the tumor suppressor gene INPP4B in prostate cancer. *Cancer research* **71**, 572-582 (2011).

15. Liu S*, et al.* Expression of autotaxin and lysophosphatidic acid receptors increases mammary tumorigenesis, invasion, and metastases. *Cancer cell* **15**, 539-550 (2009).

16. Prat A, Adamo B, Cheang MC, Anders CK, Carey LA, Perou CM. Molecular characterization of basal-like and non-basal-like triple-negative breast cancer. *The oncologist* **18**, 123-133 (2013).

17. Hynes NE, Lane HA. ERBB receptors and cancer: the complexity of targeted inhibitors. *Nature reviews Cancer* **5**, 341-354 (2005).

18. Sibilia M, Kroismayr R, Lichtenberger BM, Natarajan A, Hecking M, Holcmann M. The epidermal growth factor receptor: from development to tumorigenesis. *Differentiation; research in biological diversity* **75**, 770-787 (2007).

19. Altomare DA, Testa JR. Perturbations of the AKT signaling pathway in human cancer. *Oncogene* **24**, 7455-7464 (2005).

20. Fedele CG*, et al.* Inositol polyphosphate 4-phosphatase II regulates PI3K/Akt signaling and is lost in human basal-like breast cancers. *Proceedings of the National Academy of Sciences of the United States of America* **107**, 22231-22236 (2010).

21. Vander Haar E, Lee SI, Bandhakavi S, Griffin TJ, Kim DH. Insulin signalling to mTOR mediated by the Akt/PKB substrate PRAS40. *Nature cell biology* **9**, 316-323 (2007).

22. Vivanco I, Sawyers CL. The phosphatidylinositol 3-Kinase AKT pathway in human cancer. *Nature reviews Cancer* **2**, 489-501 (2002).

23. Sancar A, Lindsey-Boltz LA, Unsal-Kacmaz K, Linn S. Molecular mechanisms of mammalian DNA repair and the DNA damage checkpoints. *Annual review of biochemistry* **73**, 39-85 (2004).

24. Treins C, Warne PH, Magnuson MA, Pende M, Downward J. Rictor is a novel target of p70 S6 kinase-1. *Oncogene* **29**, 1003-1016 (2010).

25. Valenta T, Hausmann G, Basler K. The many faces and functions of beta-catenin. *The EMBO journal* **31**, 2714-2736 (2012).

26. Liang K*, et al.* Recombinant human erythropoietin antagonizes trastuzumab treatment of breast cancer cells via Jak2-mediated Src activation and PTEN inactivation. *Cancer cell* **18**, 423-435 (2010).

27. Xia W, Liu LH, Ho P, Spector NL. Truncated ErbB2 receptor (p95ErbB2) is regulated by heregulin through heterodimer formation with ErbB3 yet remains sensitive to the dual EGFR/ErbB2 kinase inhibitor GW572016. *Oncogene* **23**, 646-653 (2004).

28. Owens DM, Keyse SM. Differential regulation of MAP kinase signalling by dual-specificity protein phosphatases. *Oncogene* **26**, 3203-3213 (2007).

29. Jie L*, et al.* The hippo-yes association protein pathway in liver cancer. *Gastroenterology research and practice* **2013**, 187070 (2013).

30. Mauviel A, Nallet-Staub F, Varelas X. Integrating developmental signals: a Hippo in the (path)way. *Oncogene* **31**, 1743-1756 (2012).

31. Kalous J, Solc P, Baran V, Kubelka M, Schultz RM, Motlik J. PKB/AKT is involved in resumption of meiosis in mouse oocytes. *Biology of the cell / under the auspices of the European Cell Biology Organization* **98**, 111-123 (2006).

32. Porter LA, Donoghue DJ. Cyclin B1 and CDK1: nuclear localization and upstream regulators. *Progress in cell cycle research* **5**, 335-347 (2003).

33. Schwegmann A*, et al.* Protein kinase C delta is essential for optimal macrophage-mediated phagosomal containment of Listeria monocytogenes. *Proceedings of the National Academy of Sciences of the United States of America* **104**, 16251-16256 (2007).

34. Wadsworth SJ, Goldfine H. Mobilization of protein kinase C in macrophages induced by Listeria monocytogenes affects its internalization and escape from the phagosome. *Infection and immunity* **70**, 4650-4660 (2002).

35. Leung TW*, et al.* Over-expression of FoxM1 stimulates cyclin B1 expression. *FEBS letters* **507**, 59-66 (2001).

36. Cammarota M, Bevilaqua LR, Medina JH, Izquierdo I. ERK1/2 and CaMKII-mediated events in memory formation: is 5HT regulation involved? *Behavioural brain research* **195**, 120-128 (2008).

37. Shiraishi K, Ascoli M. Activation of the lutropin/choriogonadotropin receptor in MA-10 cells stimulates tyrosine kinase cascades that activate ras and the extracellular signal regulated kinases (ERK1/2). *Endocrinology* **147**, 3419-3427 (2006).

38. Nawaratne R, Gray A, Jorgensen CH, Downes CP, Siddle K, Sethi JK. Regulation of insulin receptor substrate 1 pleckstrin homology domain by protein kinase C: role of serine 24 phosphorylation. *Molecular endocrinology* **20**, 1838-1852 (2006).

39. Li J, Stern DF. Regulation of CHK2 by DNA-dependent protein kinase. *The Journal of biological chemistry* **280**, 12041-12050 (2005).

40. Margariti A*, et al.* XBP1 mRNA splicing triggers an autophagic response in endothelial cells through BECLIN-1 transcriptional activation. *The Journal of biological chemistry* **288**, 859-872 (2013).

41. Yang JY*, et al.* Predicting time to ovarian carcinoma recurrence using protein markers. *The Journal of clinical investigation* **123**, 5410 (2013).

42. Aure MR*, et al.* From DNA to RNA to protein: Integrated analyses of high-throughput molecular data from primary breast carcinomas. In: *Department of genetics, institute for cancer research, the Norwegian radiumhospitalet* (ed^(eds). Thesis, Oslo university hospital and University of Oslo (2013).

43. Liang H*, et al.* Whole-exome sequencing combined with functional genomics reveals novel candidate driver cancer genes in endometrial cancer. *Genome research* **22**, 2120-2129 (2012).

44. Heiser LM*, et al.* Subtype and pathway specific responses to anticancer compounds in breast cancer. *Proceedings of the National Academy of Sciences of the United States of America* **109**, 2724-2729 (2012).

45. Hennessy BT*, et al.* Pharmacodynamic markers of perifosine efficacy. *Clinical cancer research : an official journal of the American Association for Cancer Research* **13**, 7421-7431 (2007).

46. Horiuchi D*, et al.* MYC pathway activation in triple-negative breast cancer is synthetic lethal with CDK inhibition. *The Journal of experimental medicine* **209**, 679-696 (2012).

47. Kim N*, et al.* Systematic analysis of genotype-specific drug responses in cancer. *International journal of cancer Journal international du cancer* **131**, 2456-2464 (2012).

48. Park ES*, et al.* Integrative analysis of proteomic signatures, mutations, and drug responsiveness in the NCI 60 cancer cell line set. *Molecular cancer therapeutics* **9**, 257-267 (2010).

49. Gonzalez-Angulo AM, Blumenschein GR, Jr. Defining biomarkers to predict sensitivity to PI3K/Akt/mTOR pathway inhibitors in breast cancer. *Cancer treatment reviews* **39**, 313-320 (2013).

50. Slomovitz BM, Coleman RL. The PI3K/AKT/mTOR pathway as a therapeutic target in endometrial cancer. *Clinical cancer research : an official journal of the American Association for Cancer Research* **18**, 5856-5864 (2012).

51. Desai MD, Saroya BS, Lockhart AC. Investigational therapies targeting the ErbB (EGFR, HER2, HER3, HER4) family in GI cancers. *Expert opinion on investigational drugs* **22**, 341-356 (2013).

52. McAuliffe SM*, et al.* Targeting Notch, a key pathway for ovarian cancer stem cells, sensitizes tumors to platinum therapy. *Proceedings of the National Academy of Sciences of the United States of America* **109**, E2939-2948 (2012).

53. Strosberg JR*, et al.* A phase II study of RO4929097 in metastatic colorectal cancer. *European journal of cancer* **48**, 997-1003 (2012).

54. Tolcher AW*, et al.* Phase I study of RO4929097, a gamma secretase inhibitor of Notch signaling, in patients with refractory metastatic or locally advanced solid tumors. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* **30**, 2348-2353 (2012).

55. Ballantyne A, Dhillon S. Trastuzumab emtansine: first global approval. *Drugs* **73**, 755-765 (2013).

56. Barginear MF, John V, Budman DR. Trastuzumab-DM1: a clinical update of the novel antibody-drug conjugate for HER2-overexpressing breast cancer. *Molecular medicine* **18**, 1473-1479 (2012).

57. Fleming GF*, et al.* Phase II trial of trastuzumab in women with advanced or recurrent, HER2-positive endometrial carcinoma: a Gynecologic Oncology Group study. *Gynecologic oncology* **116**, 15-20 (2010).

58. Verma S*, et al.* Trastuzumab emtansine for HER2-positive advanced breast cancer. *The New England journal of medicine* **367**, 1783-1791 (2012).

59. Wulfing C*, et al.* A single-arm, multicenter, open-label phase 2 study of lapatinib as the second-line treatment of patients with locally advanced or metastatic transitional cell carcinoma. *Cancer* **115**, 2881-2890 (2009).

60. Hall C, Troutman SM, Price DK, Figg WD, Kang MH. Bcl-2 family of proteins as therapeutic targets in genitourinary neoplasms. *Clinical genitourinary cancer* **11**, 10-19 (2013).

61. Ott PA*, et al.* Oblimersen in combination with temozolomide and albumin-bound paclitaxel in patients with advanced melanoma: a phase I trial. *Cancer chemotherapy and pharmacology* **71**, 183-191 (2013).

62. Zhao M, Jiang B, Gao FH. Small molecule inhibitors of STAT3 for cancer therapy. *Current medicinal chemistry* **18**, 4012-4018 (2011).

63. Robinson KW, Sandler AB. The role of MET receptor tyrosine kinase in non-small cell lung cancer and clinical development of targeted anti-MET agents. *The oncologist* **18**, 115-122 (2013).

64. Jin Q*, et al.* Fatty acid synthase phosphorylation: a novel therapeutic target in HER2-overexpressing breast cancer cells. *Breast cancer research : BCR* **12**, R96 (2010).

65. Luo DX*, et al.* Targeting acetyl-CoA carboxylases: small molecular inhibitors and their therapeutic potential. *Recent patents on anti-cancer drug discovery* **7**, 168-184 (2012).

66. Pandey PR, Liu W, Xing F, Fukuda K, Watabe K. Anti-cancer drugs targeting fatty acid synthase (FAS). *Recent patents on anti-cancer drug discovery* **7**, 185-197 (2012).

67. Abdel-Fatah T*, et al.* Clinicopathological and functional significance of XRCC1 expression in ovarian cancer. *International journal of cancer Journal international du cancer* **132**, 2778-2786 (2013).

68. Ang MK*, et al.* High XRCC1 protein expression is associated with poorer survival in patients with head and neck squamous cell carcinoma. *Clinical cancer research : an official journal of the American Association for Cancer Research* **17**, 6542-6552 (2011).

69. Sultana R*, et al.* Targeting XRCC1 deficiency in breast cancer for personalized therapy. *Cancer research* **73**, 1621-1634 (2013).

70. Piccolo S, Cordenonsi M, Dupont S. Molecular Pathways: YAP and TAZ Take Center Stage in Organ Growth and Tumorigenesis. *Clinical cancer research : an official journal of the American Association for Cancer Research*, (2013).

71. Coombes KR. ClassDiscovery: Classes and methods for "class discovery" with microarrays or proteomics. R package version 2.13.4. (ed^(eds) (2012).

72. Hu J, He X, Baggerly KA, Coombes KR, Hennessy BT, Mills GB. Non-parametric quantification of protein lysate arrays. *Bioinformatics* **23**, 1986-1994 (2007).

73. Liang J*, et al.* The energy sensing LKB1-AMPK pathway regulates p27(kip1) phosphorylation mediating the decision to enter autophagy or apoptosis. *Nature cell biology* **9**, 218-224 (2007).

74. Tibes R*, et al.* Reverse phase protein array: validation of a novel proteomic technology and utility for analysis of primary leukemia specimens and hematopoietic stem cells. *Molecular cancer therapeutics* **5**, 2512-2521 (2006).

75. Hennessy BT*, et al.* A Technical Assessment of the Utility of Reverse Phase Protein Arrays for the Study of the Functional Proteome in Non-microdissected Human Breast Cancers. *Clinical proteomics* **6**, 129-151 (2010).

76. Gonzalez-Angulo AM*, et al.* Functional proteomics can define prognosis and predict pathologic complete response in patients with breast cancer. *Clinical proteomics* **8**, 11 (2011).

77. Neeley ES, Kornblau SM, Coombes KR, Baggerly KA. Variable slope normalization of reverse phase protein arrays. *Bioinformatics* **25**, 1384-1389 (2009).

78. Cancer Genome Atlas Research N. Comprehensive molecular characterization of clear cell renal cell carcinoma. *Nature* **499**, 43-49 (2013).