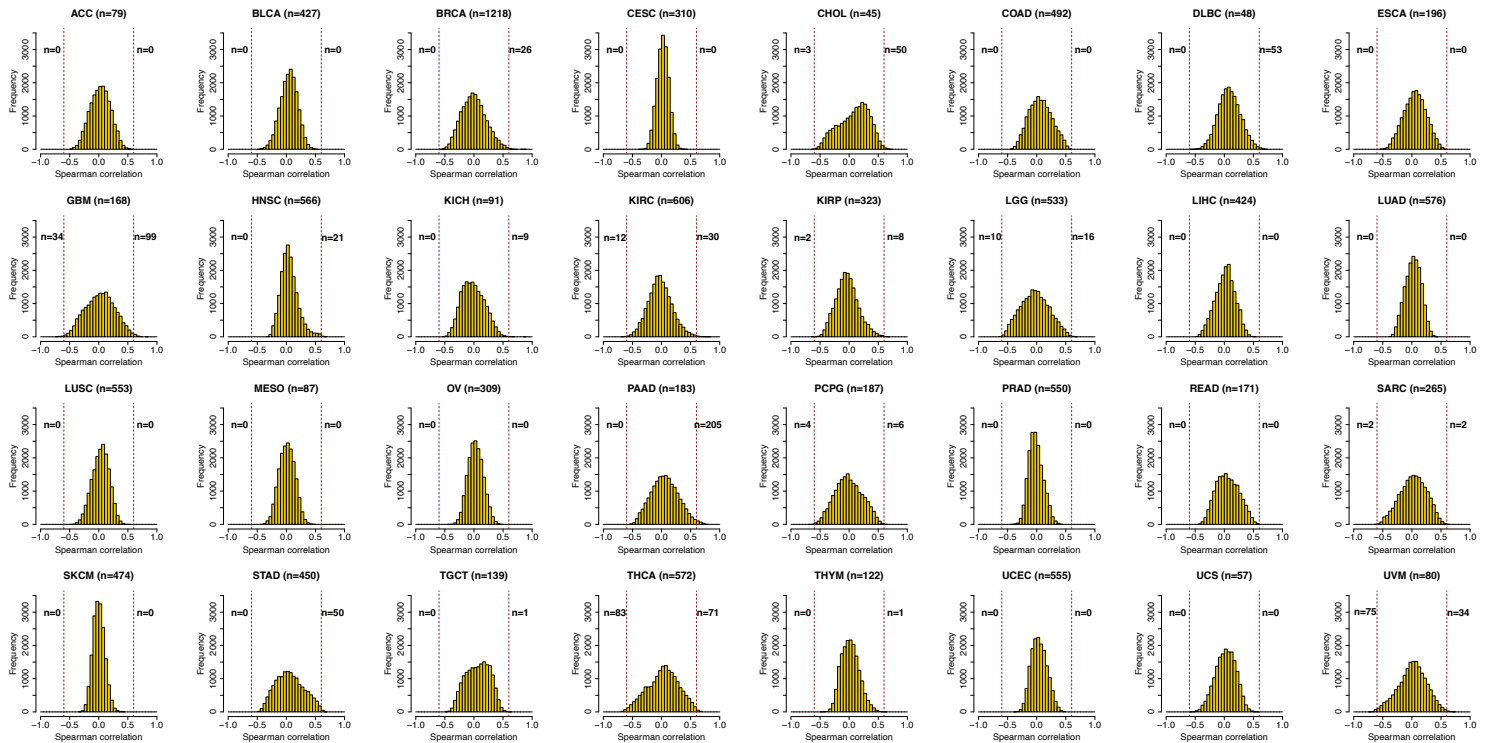
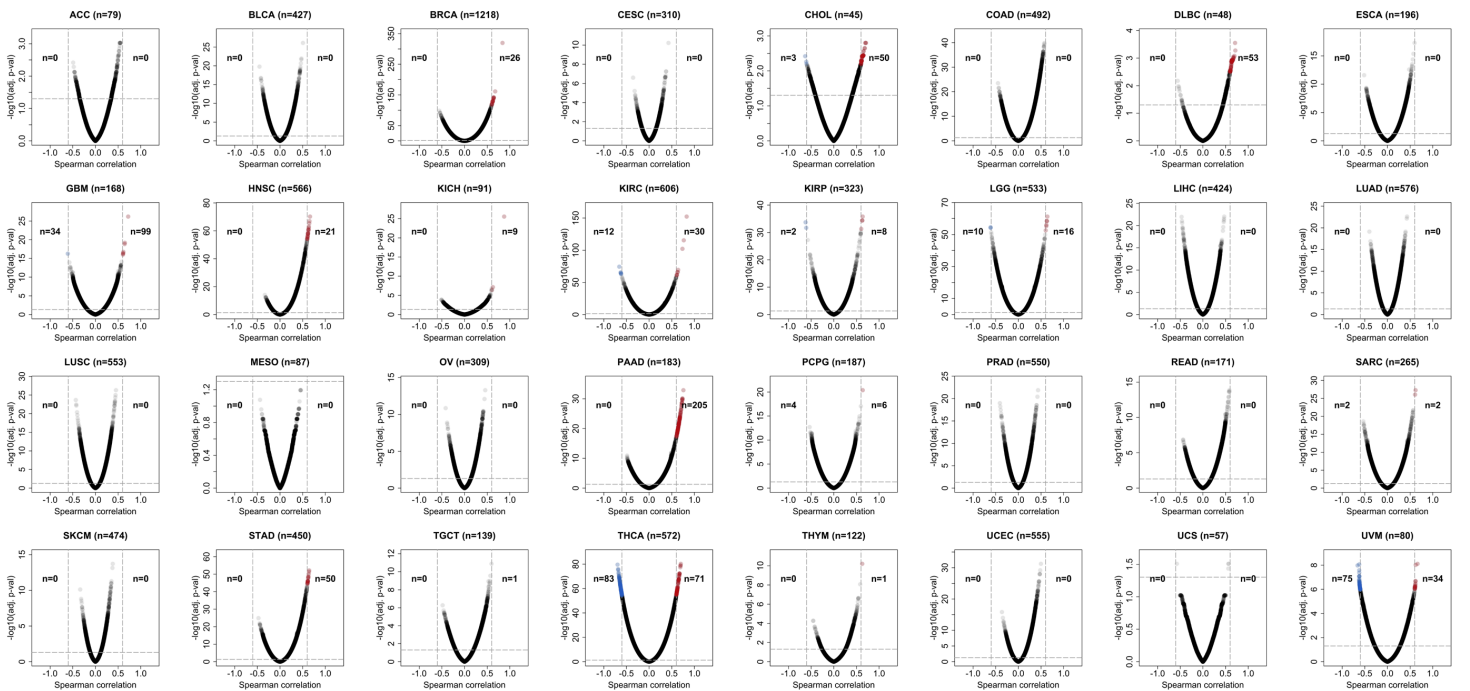


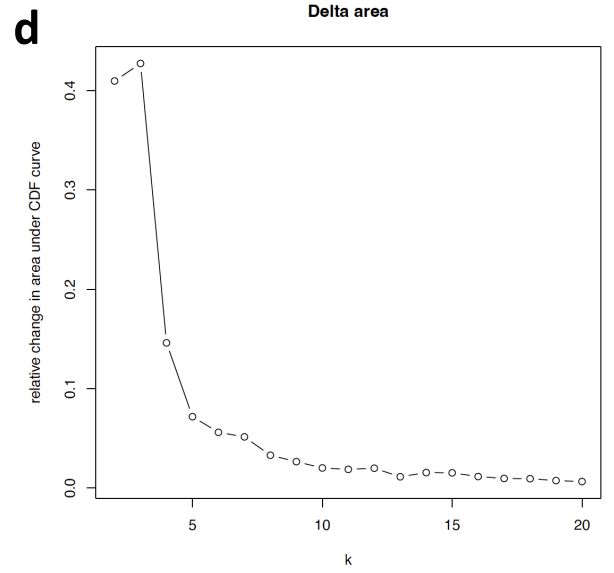
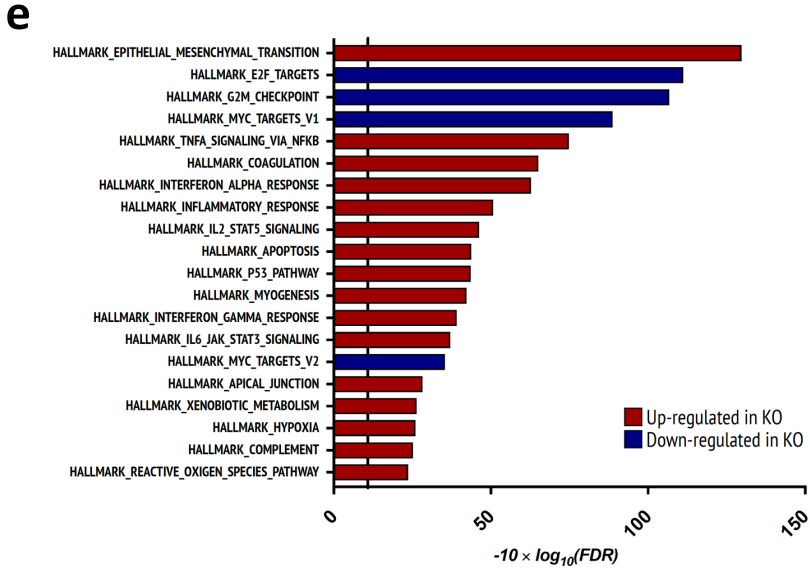
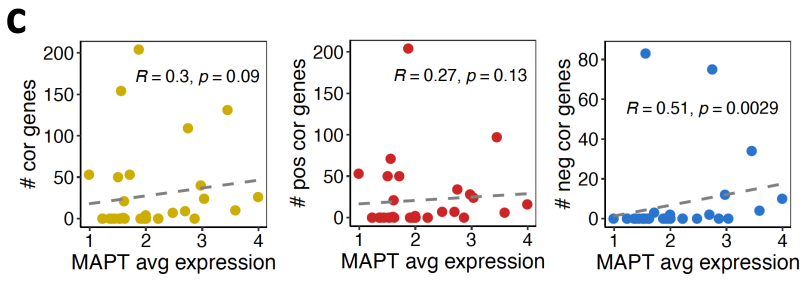
# Supplementary Figure 1

**a**

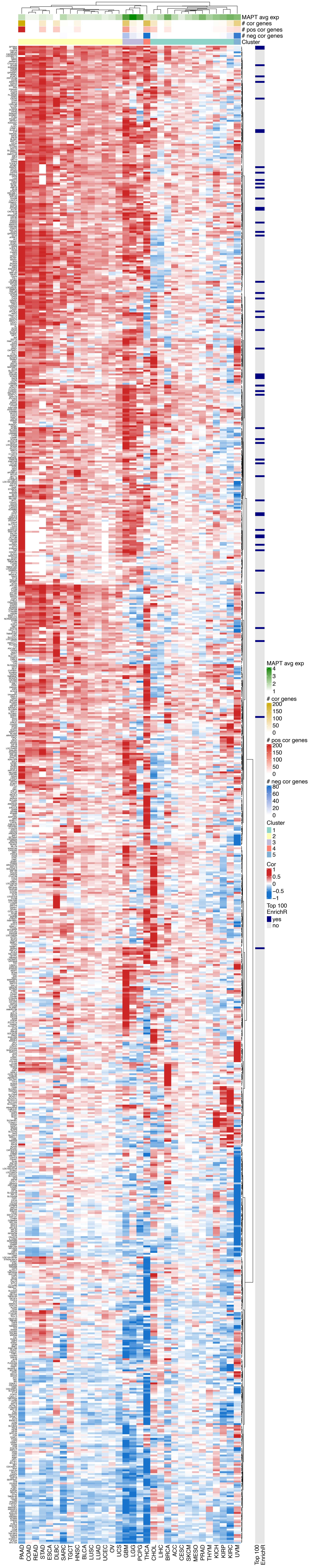


**b**



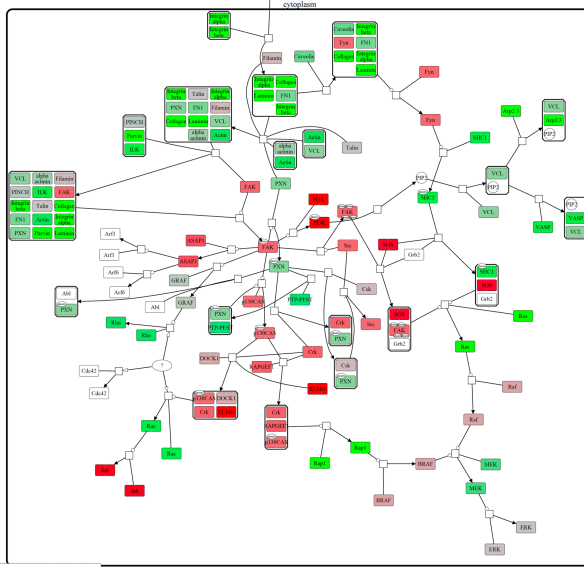


Supplementary figure 2



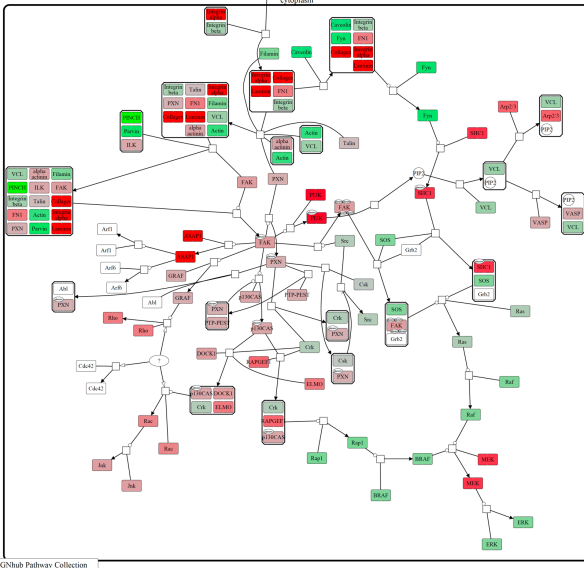
**a** *Integrin signalling pathway*

GBM



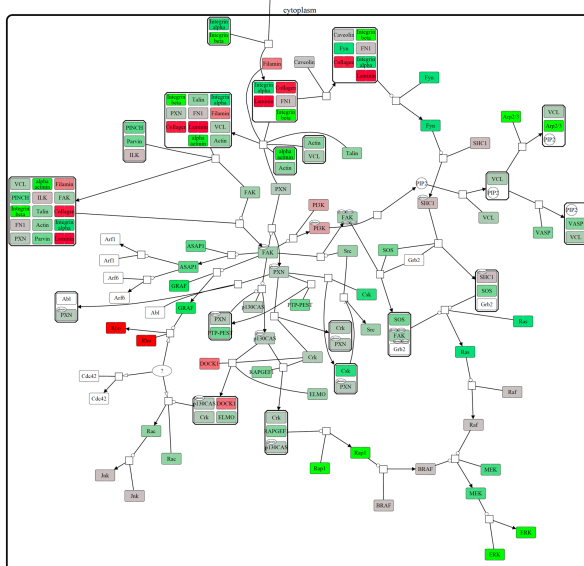
SBGH Pathway Collection

UVM



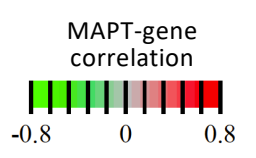
SBGH Pathway Collection

BRCA



SBGH Pathway Collection

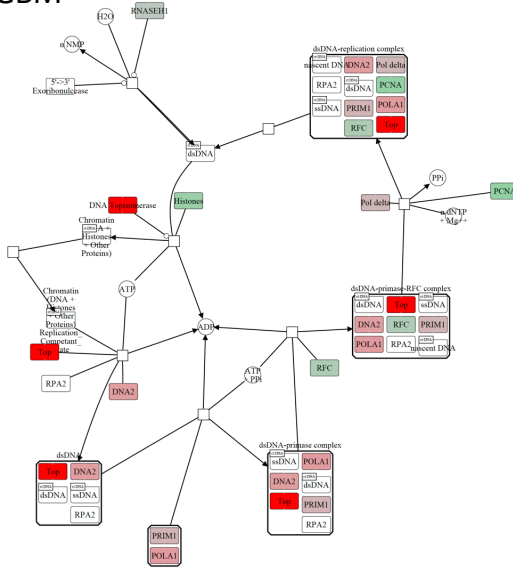
Rendered by SBGN



b

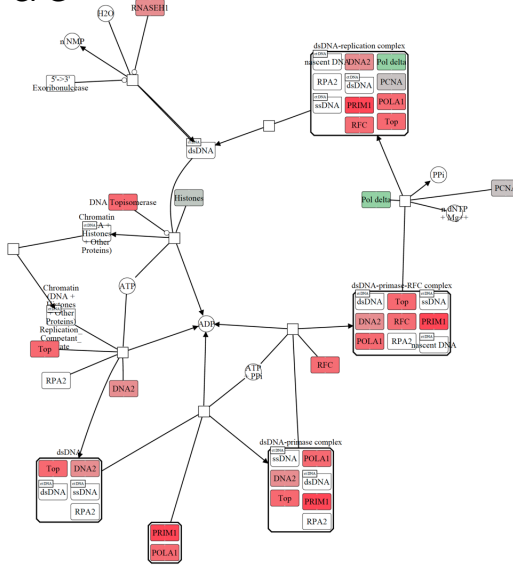
# DNA replication

GBM



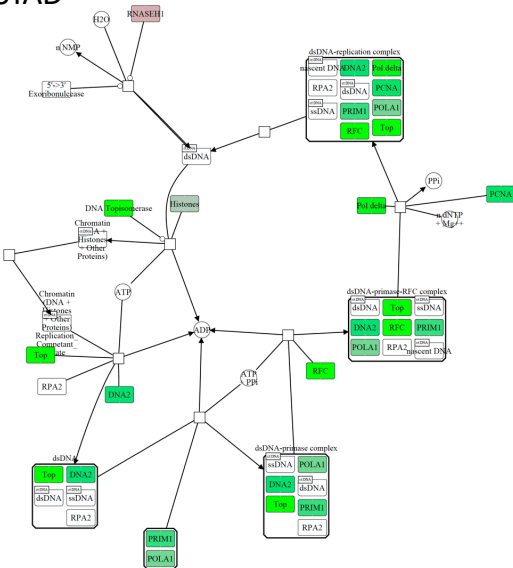
SBGN Pathway Collection  
Rendered by SBGNView

PCPG

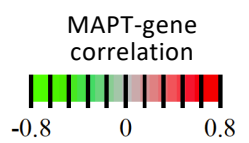


SBGN Pathway Collection  
Rendered by SBGNView

STAD

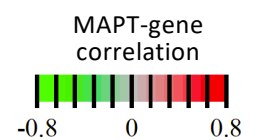
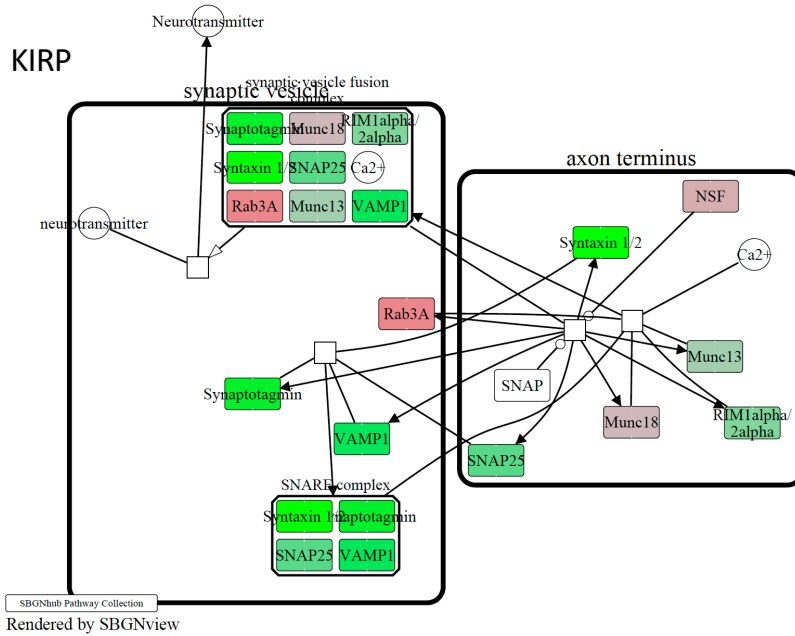
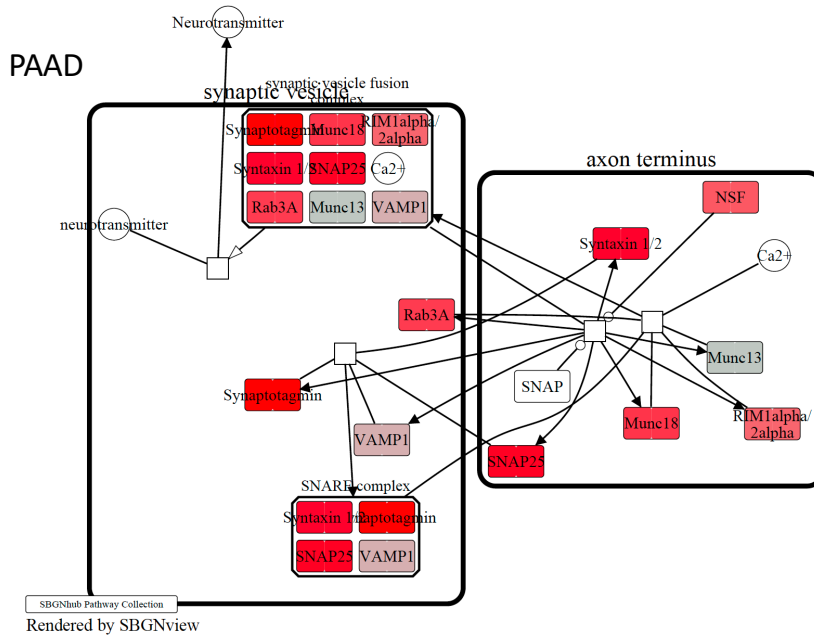
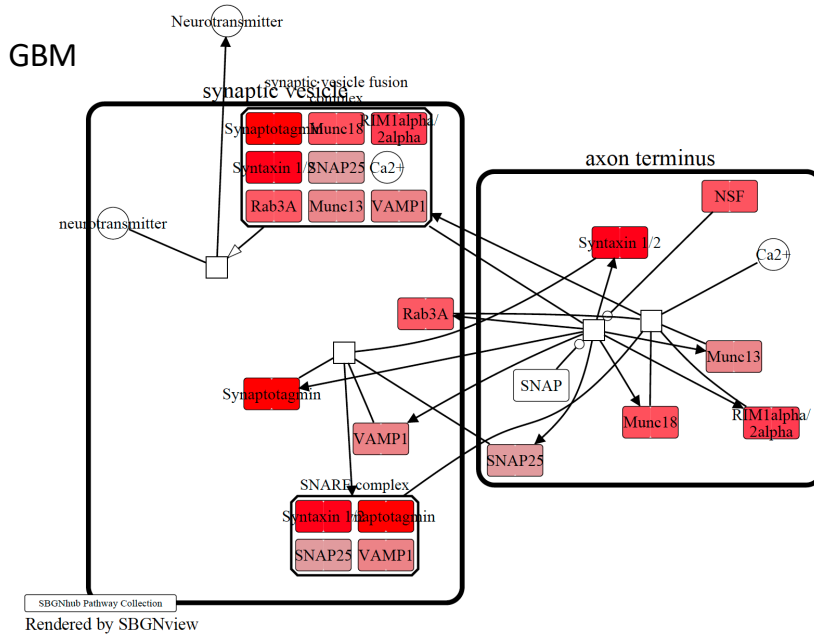


SBGN Pathway Collection  
Rendered by SBGNView



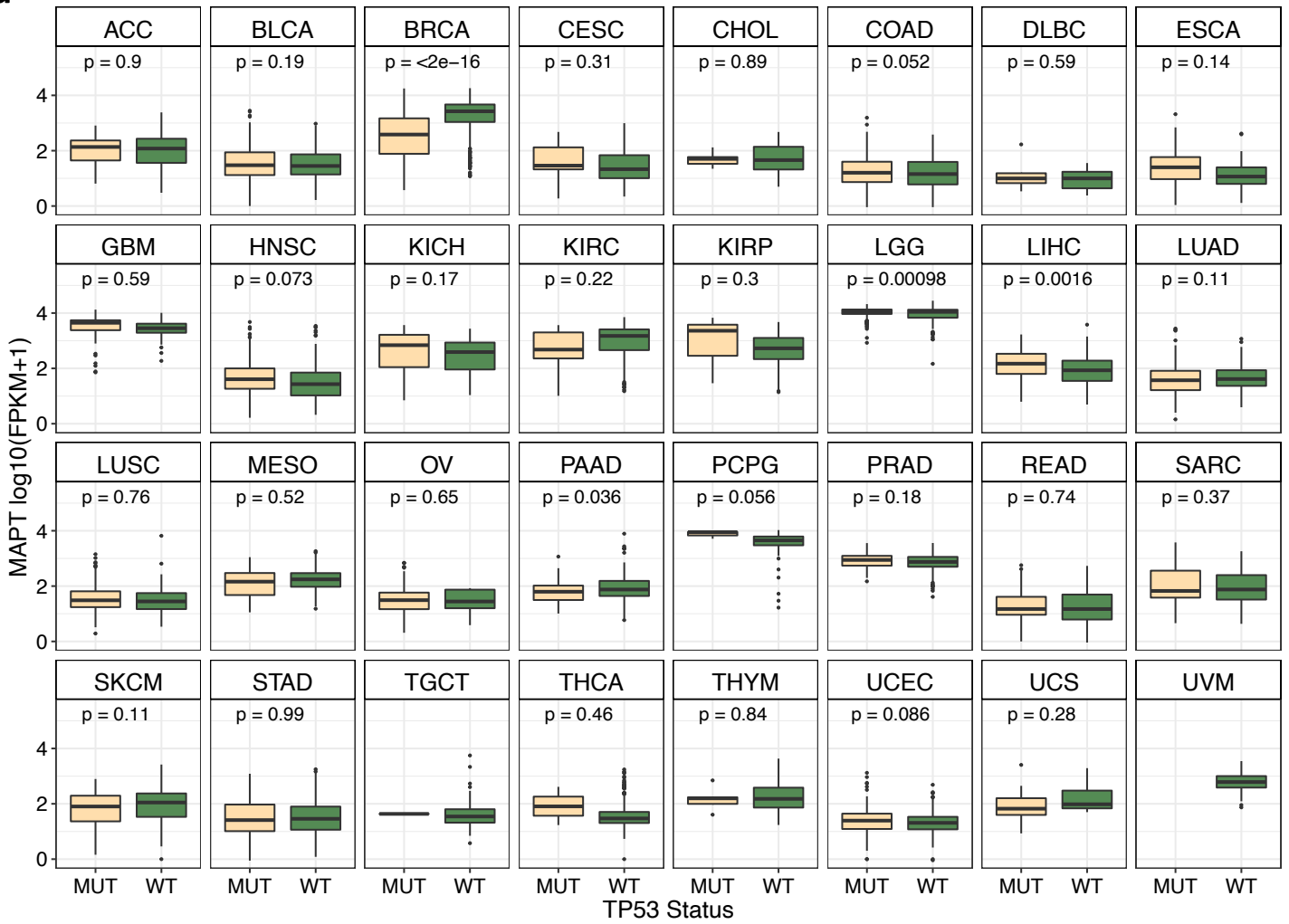
C

### Synaptic vesicle trafficking

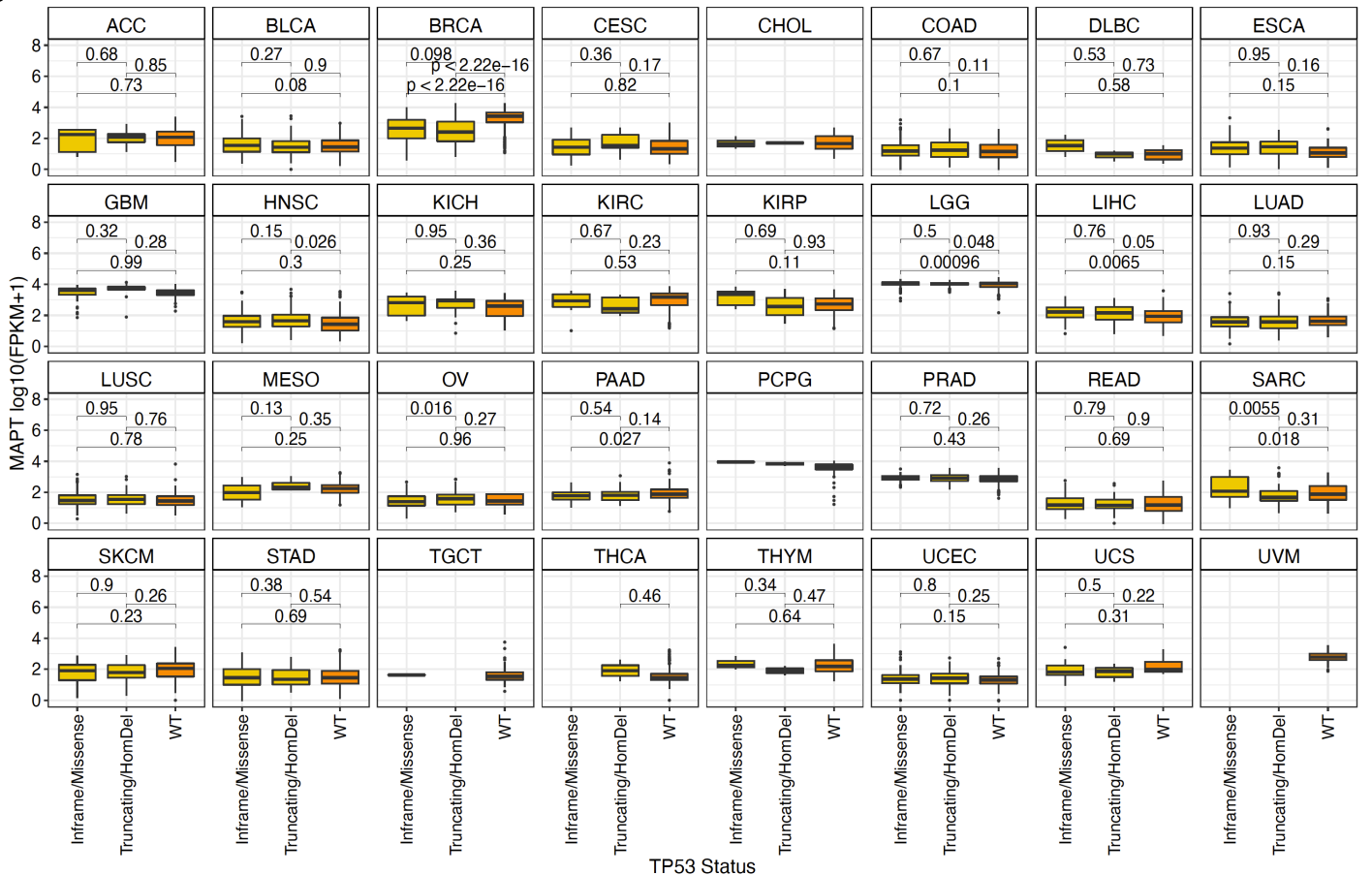


Supplementary Figure 4

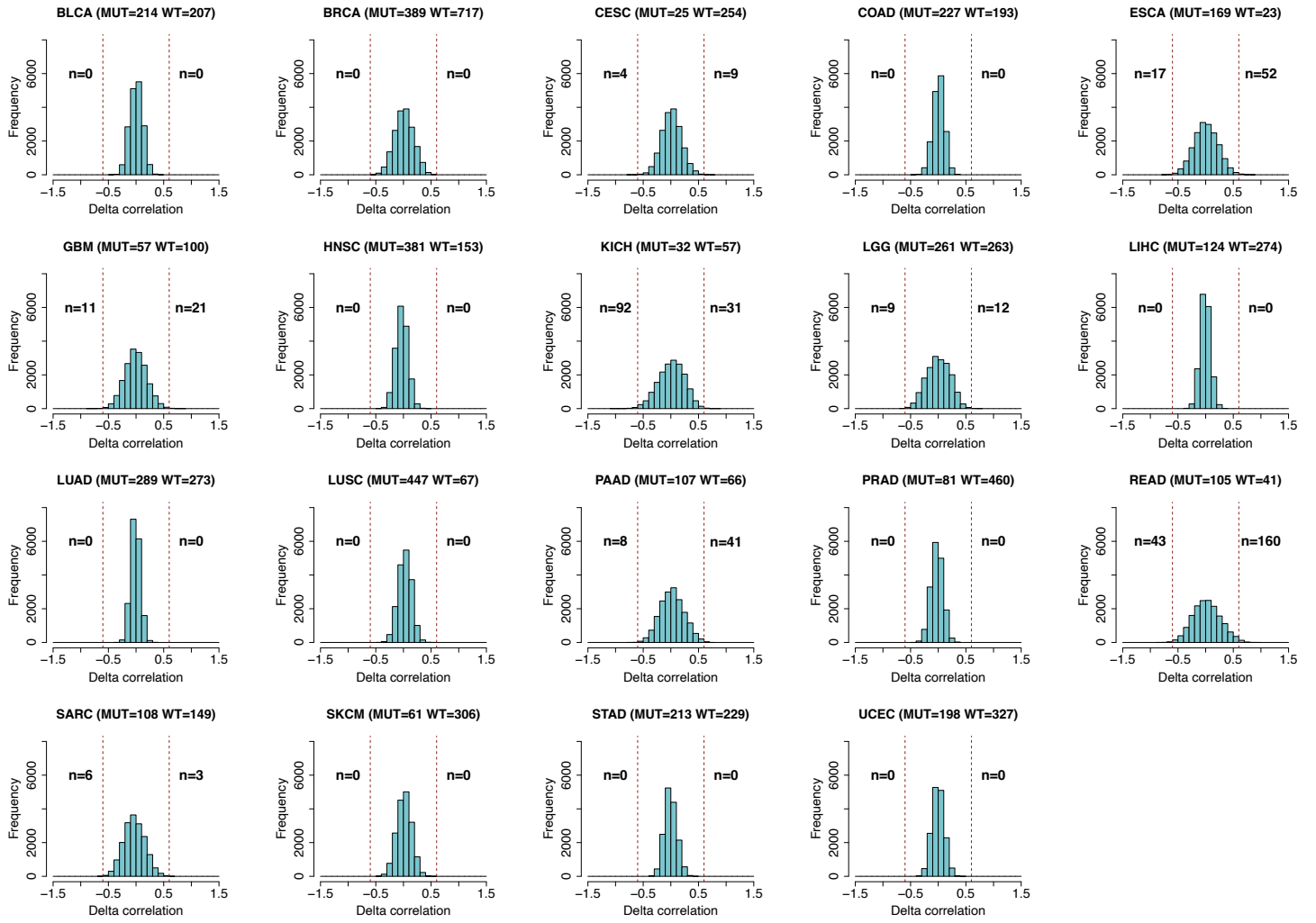
**a**



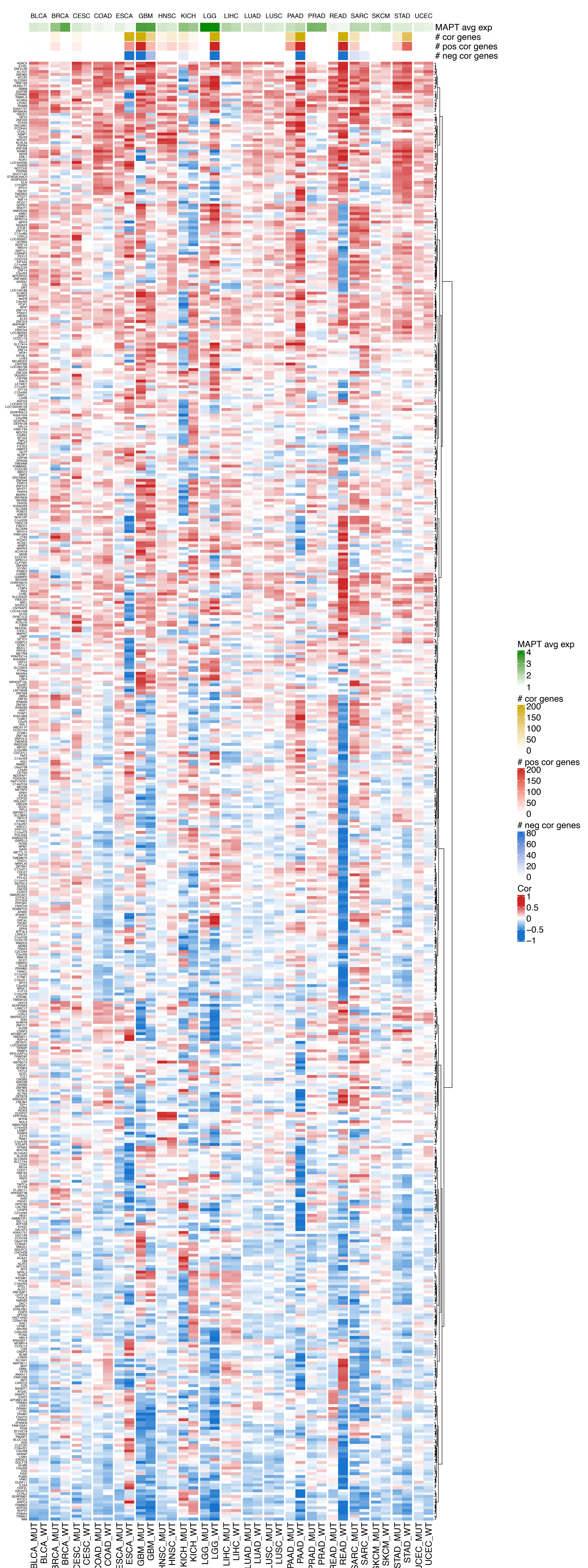
**b**



# Supplementary Figure 5

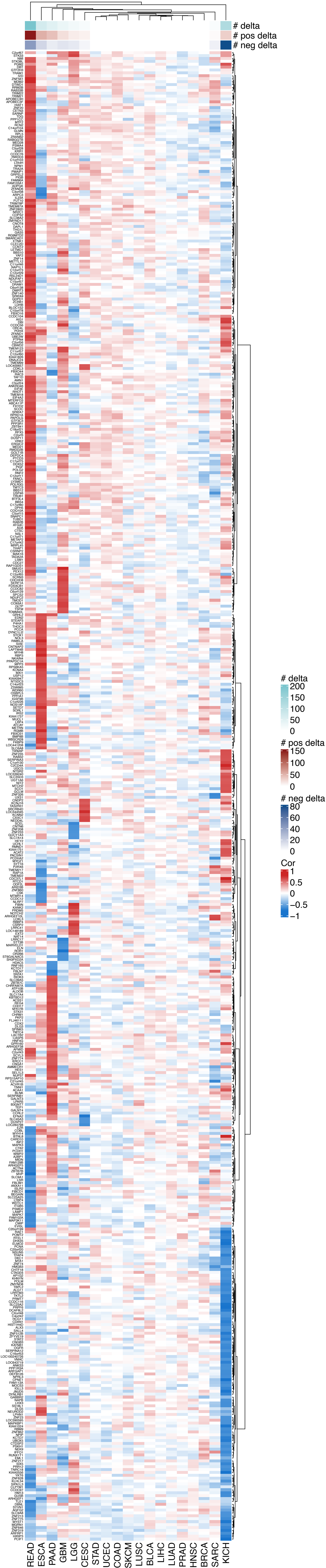


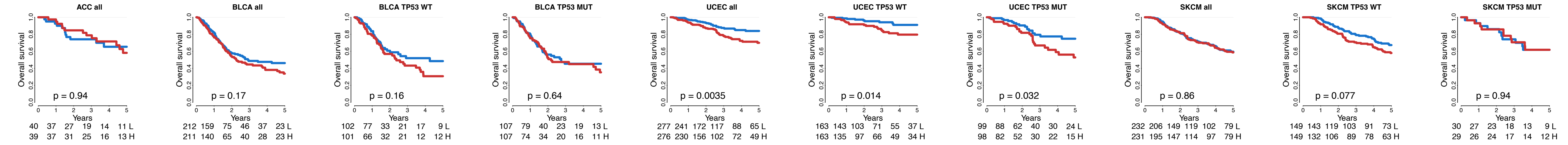
Supplementary figure 6



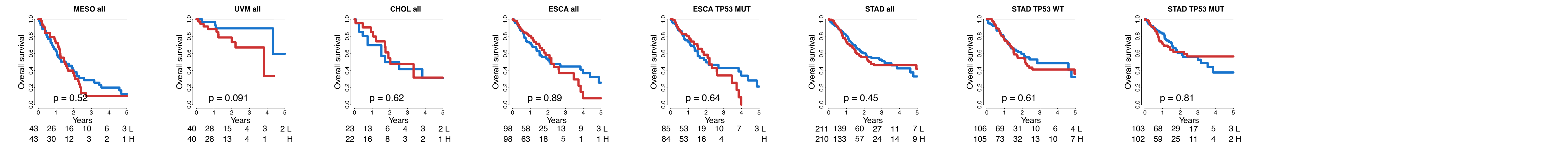
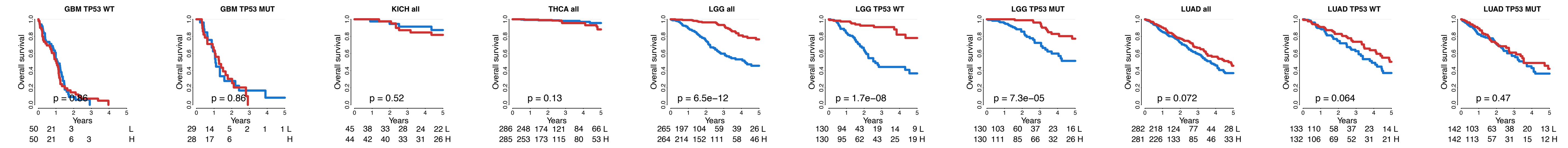
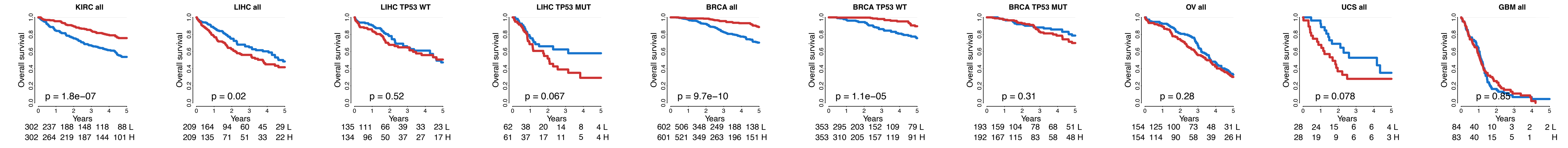
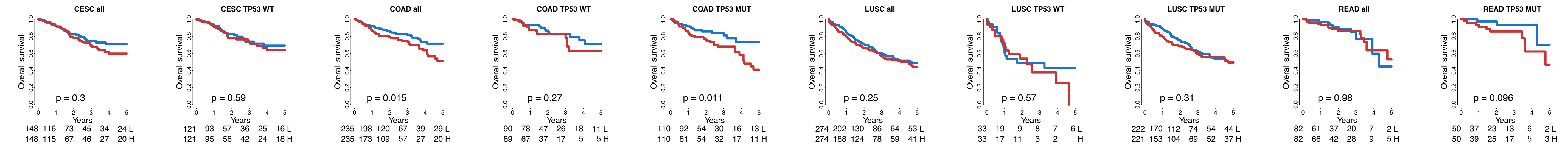
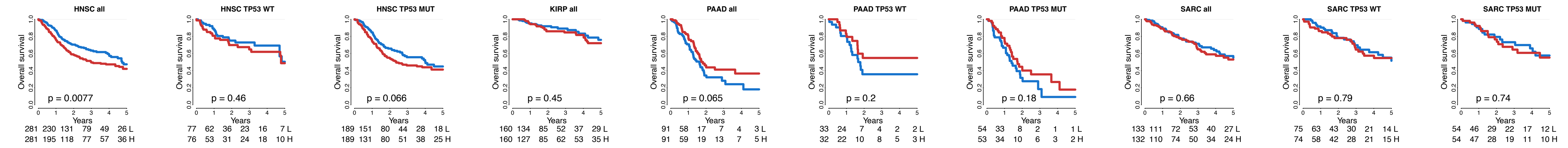
Text  
 Text

Supplementary figure 7

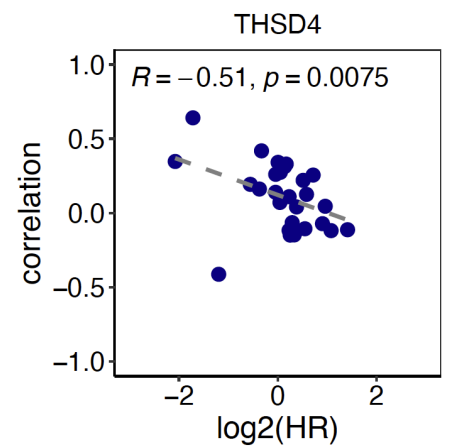
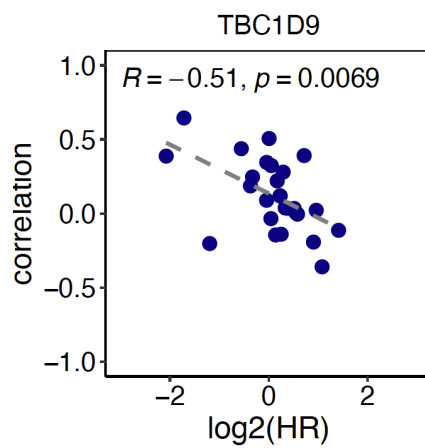
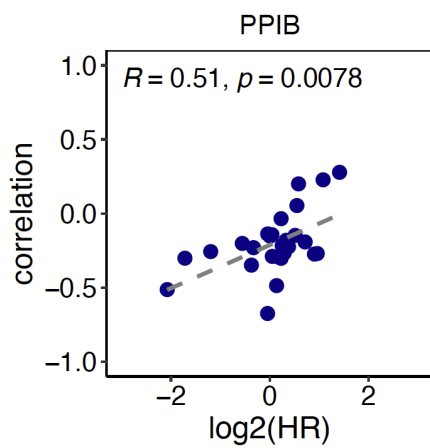
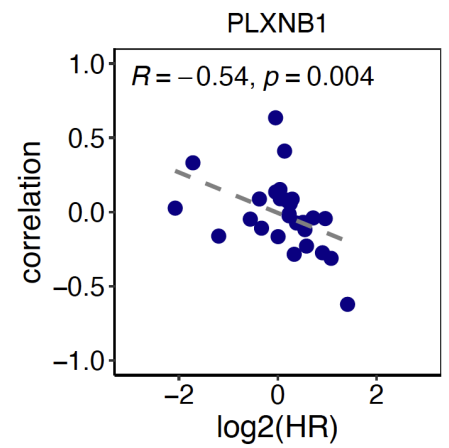
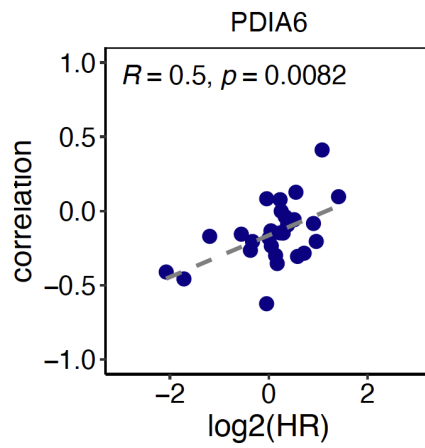
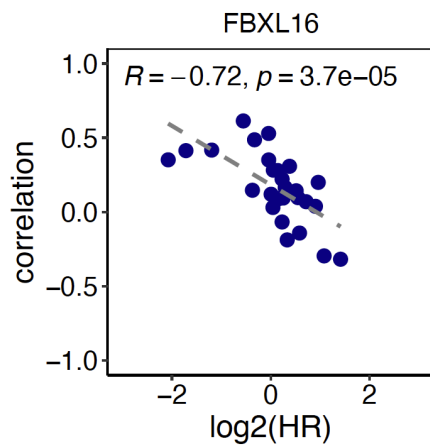
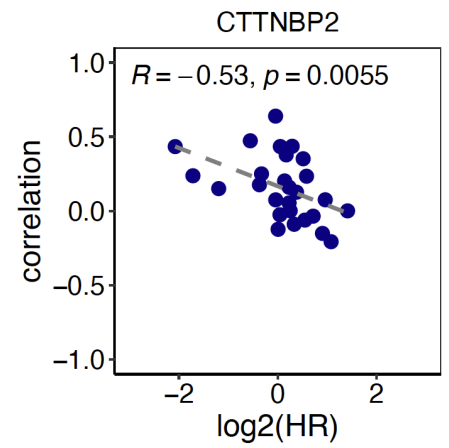
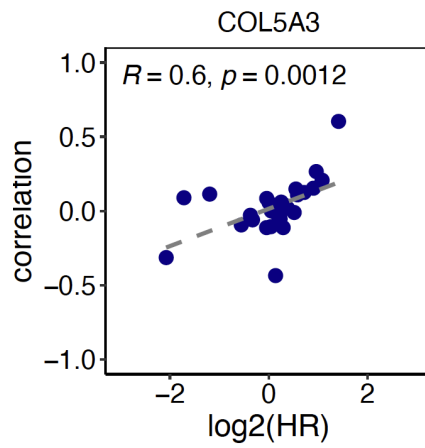
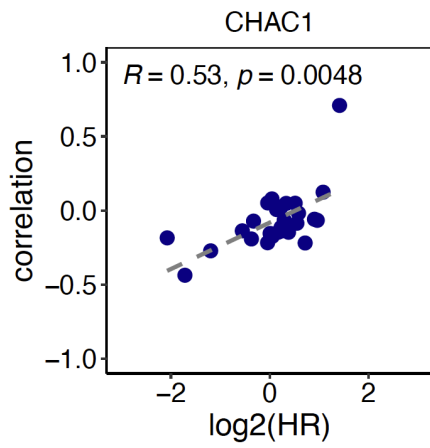
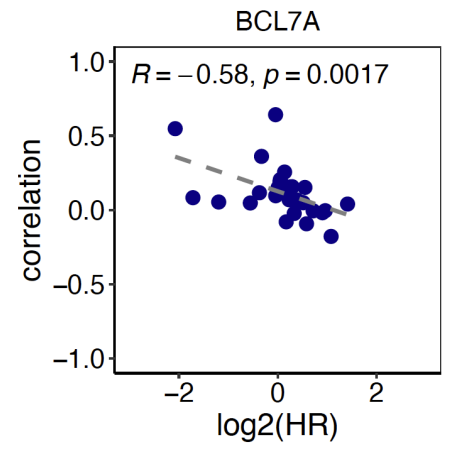
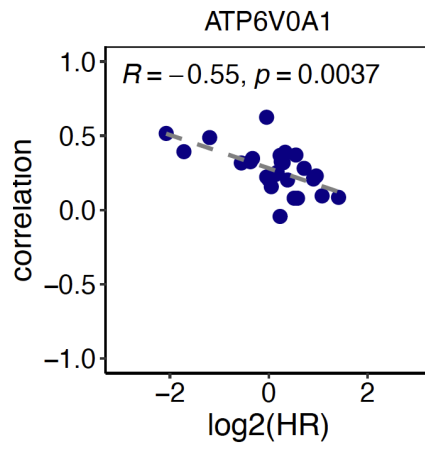
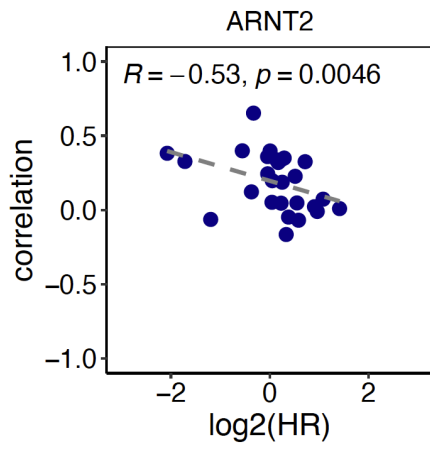




Supplementary figure 8



Supplementary Figure 9



1 **Figure S1 - (a)** Correlation of *MAPT* gene expression with all expressed genes. Each histogram shows the  
2 correlation value distribution obtained for each cancer type. The number of genes with high  
3 positive/negative correlation (i.e. above 0.6 or below -0.6) is reported. (b) For the same analysis in (a),  
4 Benjamini-Hochberg adjusted p-values were computed and shown alongside correlation values in  
5 volcanoplots. An adjusted p-value threshold of 0.05 is indicated. (c) Association between *MAPT* average  
6 expression and the number of correlated genes per cancer type. The total number (left), the number of  
7 positively correlated genes (centre), and the number of negatively correlated genes (right) were evaluated.  
8 (d) All cancer types were clustered based on gene correlation with *MAPT*. The ConsensusClusterPlus  
9 algorithm was used. The plot shows changes in the 'area under the CDF curve' when increasing the number  
10 of clusters 'k', used as a parameter to select the optimal number of clusters, in this case 5. (e) Top 20 enriched  
11 Hallmark genesets in the comparison between *MAPT* KO and WT neuroblastoma cells.

12 **Figure S2** - Heatmap of 809 genes correlated with *MAPT* expression in at least one cancer type. Both genes  
13 and cancer types are ordered based on the hierarchical clustering of the correlation values. Fifty-two of the  
14 top 100 genes co-expressed with *MAPT* according to EnrichR (ARCHS<sup>4</sup> dataset) are overlapping with the 809  
15 genes and are annotated in the heatmap. For each cancer type, the average *MAPT* expression and the  
16 number of genes correlated with *MAPT* are shown. Cancer types were grouped in 5 distinct clusters based  
17 on the correlation profiles using ConsensusClusterPlus and labels are indicated.

18 **Figure S3** – Selected PANTHER pathways in selected cancer types overlaid with the *MAPT*-gene correlation  
19 values for all evaluated genes.

20 **Figure S4 - (a)** Expression of *MAPT* in *TP53* WT and *TP53* MUT tumors. The analysis is stratified by cancer  
21 type. Differences are evaluated by a two-sided Student's t-test. (b) Expression of *MAPT* in tumors with WT  
22 P53 or with either a Truncating/HomDel mutation or an Inframe/Missense mutation in PT53. Differences  
23 were evaluated by a two-sided Student's t-test.

24 **Figure S5** - Correlation with *MAPT* for all genes was computed separately for *TP53* MUT and *TP53* WT tumors.  
25 The delta correlation distribution (correlation in *TP53* MUT – correlation in *TP53* WT) is reported in the figure  
26 for each cancer type. The number of genes with an absolute delta above 0.6 is indicated.

27 **Figure S6** - Heatmap of 514 genes with an absolute delta correlation above 0.6 in P53 WT vs P53 MUT tumors  
28 for at least one cancer type. The correlation analysis was performed only for 19 cancer types with at least 20  
29 patients with P53 WT and 20 P53 MUT. *MAPT* correlation values are shown. For each group identified by the  
30 combination of cancer type and P53 status, the average *MAPT* expression and the number of genes  
31 correlated with *MAPT* are shown.

32 **Figure S7** - Heatmap of 514 genes with an absolute delta correlation above 0.6 in P53 WT vs P53 MUT tumors  
33 for at least one cancer type. The correlation analysis was performed for 19 cancer types with at least 20  
34 patients with P53 WT and 20 P53 MUT.

35 **Figure S8 - *MAPT* cancer-specific association with survival.** Kaplan-Meier curves showing the association  
36 between *MAPT* (High/Low using the median as threshold) and survival in the overall population and  
37 stratifying according to P53 status. P-value obtained by log-rank test

38 **Figure S9** - Scatterplots for genes showing an absolute correlation >0.5 between the *MAPT*-gene correlation  
39 and *MAPT* hazard ratio across different cancer types. The 12 genes achieving an absolute *MAPT*-gene  
40 correlation >0.6 (as in **Figure 1b**) are shown.

41

1 **Table S1** Percentage of *TP53* mutations per cancer type. Mutation frequency is separated according to the  
 2 different mutation types (inframe/missense or truncating/homdel).  
 3

Cancer	Inframe/Missense	Truncating/HomDel	WT
ACC	5 (6.58%)	11 (14.47%)	60 (78.95%)
BLCA	136 (32.3%)	78 (18.53%)	207 (49.17%)
BRCA	237 (21.43%)	152 (13.74%)	717 (64.83%)
CESC	15 (5.38%)	10 (3.58%)	254 (91.04%)
CHOL	4 (8.89%)	1 (2.22%)	40 (88.89%)
COAD	160 (38.1%)	67 (15.95%)	193 (45.95%)
DLBC	2 (5.41%)	3 (8.11%)	32 (86.49%)
ESCA	102 (53.12%)	67 (34.9%)	23 (11.98%)
GBM	44 (28.03%)	13 (8.28%)	100 (63.69%)
HNSC	197 (36.89%)	184 (34.46%)	153 (28.65%)
KICH	19 (21.35%)	13 (14.61%)	57 (64.04%)
KIRC	8 (1.91%)	5 (1.19%)	406 (96.9%)
KIRP	6 (1.95%)	2 (0.65%)	299 (97.39%)
LGG	199 (37.98%)	62 (11.83%)	263 (50.19%)
LIHC	72 (18.09%)	52 (13.07%)	274 (68.84%)
LUAD	169 (30.07%)	120 (21.35%)	273 (48.58%)
LUSC	284 (55.25%)	163 (31.71%)	67 (13.04%)
MESO	10 (12.2%)	4 (4.88%)	68 (82.93%)
OV	113 (55.39%)	80 (39.22%)	11 (5.39%)
PAAD	67 (38.73%)	40 (23.12%)	66 (38.15%)
PCPG	1 (0.59%)	2 (1.18%)	166 (98.22%)
PRAD	41 (7.58%)	40 (7.39%)	460 (85.03%)
READ	70 (47.95%)	35 (23.97%)	41 (28.08%)
SARC	51 (19.84%)	57 (22.18%)	149 (57.98%)
SKCM	31 (8.45%)	30 (8.17%)	306 (83.38%)
STAD	130 (29.41%)	83 (18.78%)	229 (51.81%)
TGCT	1 (0.75%)	0 (0%)	132 (99.25%)
THCA	0 (0%)	3 (0.55%)	540 (99.45%)
THYM	3 (2.48%)	2 (1.65%)	116 (95.87%)
UCEC	145 (27.62%)	53 (10.1%)	327 (62.29%)
UCS	39 (69.64%)	12 (21.43%)	5 (8.93%)
UVM	0 (0%)	0 (0%)	80 (100%)

4

5 **Table S2** Breakdown of pan-cancer TP53 mutational status describing the number of cases for each available classification (based on mutational and copy number  
6 status). The table also describe our grouping into WT, inframe/missense or truncating/homdel categories.

7

Status (mutation;CNA)	count	WT/MUT classification	MUT group
wt;wt	6097	WT	WT
wt;homdel_rec	79	MUT	Truncating/HomDel
Inframe Mutation (putative driver);wt	80	MUT	Inframe/Missense
Inframe Mutation (putative driver);homdel_rec	1	MUT	Truncating/HomDel
Inframe Mutation (putative passenger);wt	1	WT	WT
Missense Mutation (putative driver);wt	2274	MUT	Inframe/Missense
Missense Mutation (putative driver);Amplification	7	MUT	Inframe/Missense
Missense Mutation (putative driver);homdel_rec	31	MUT	Truncating/HomDel
Missense Mutation (putative passenger);wt	16	WT	WT
Truncating mutation (putative driver);wt	1320	MUT	Truncating/HomDel
Truncating mutation (putative driver);Amplification	5	MUT	Truncating/HomDel
Truncating mutation (putative driver);homdel_rec	8	MUT	Truncating/HomDel

8