

Fig S1

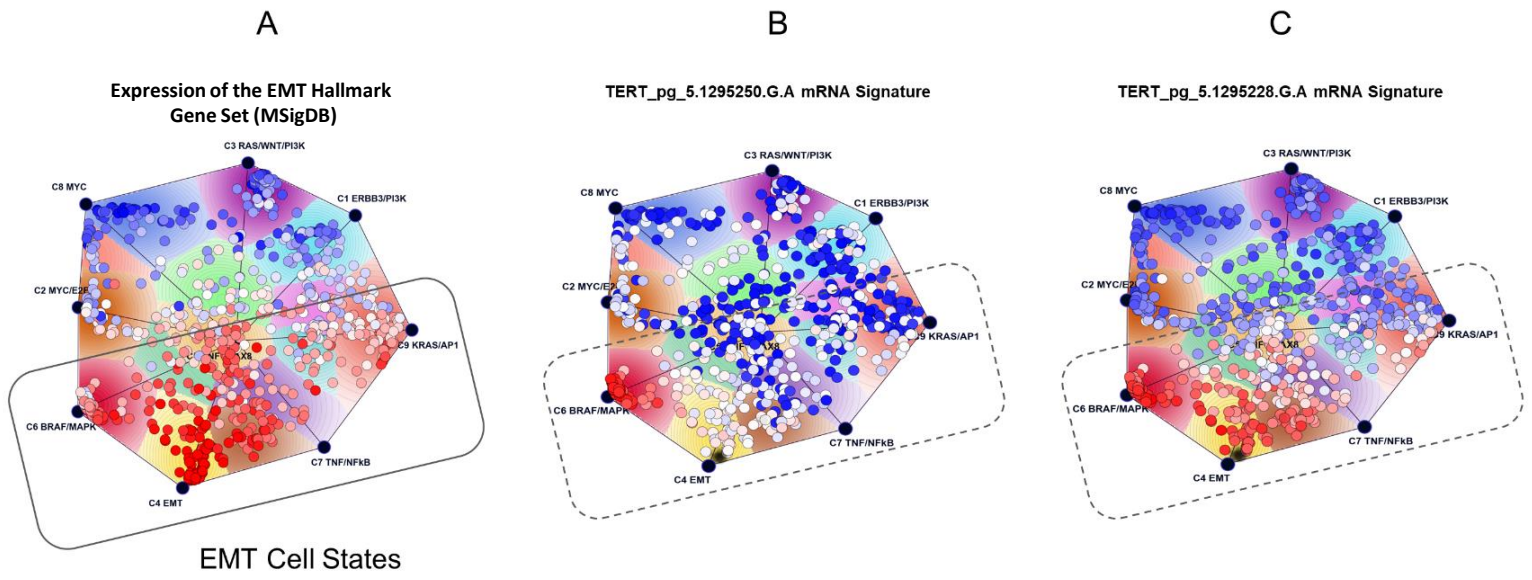


Figure S1. Projecting the individual TERTp mutations transcriptional signatures on top of the Onco-GPS map of cellular states (Kim et al. 2017).

Fig S2

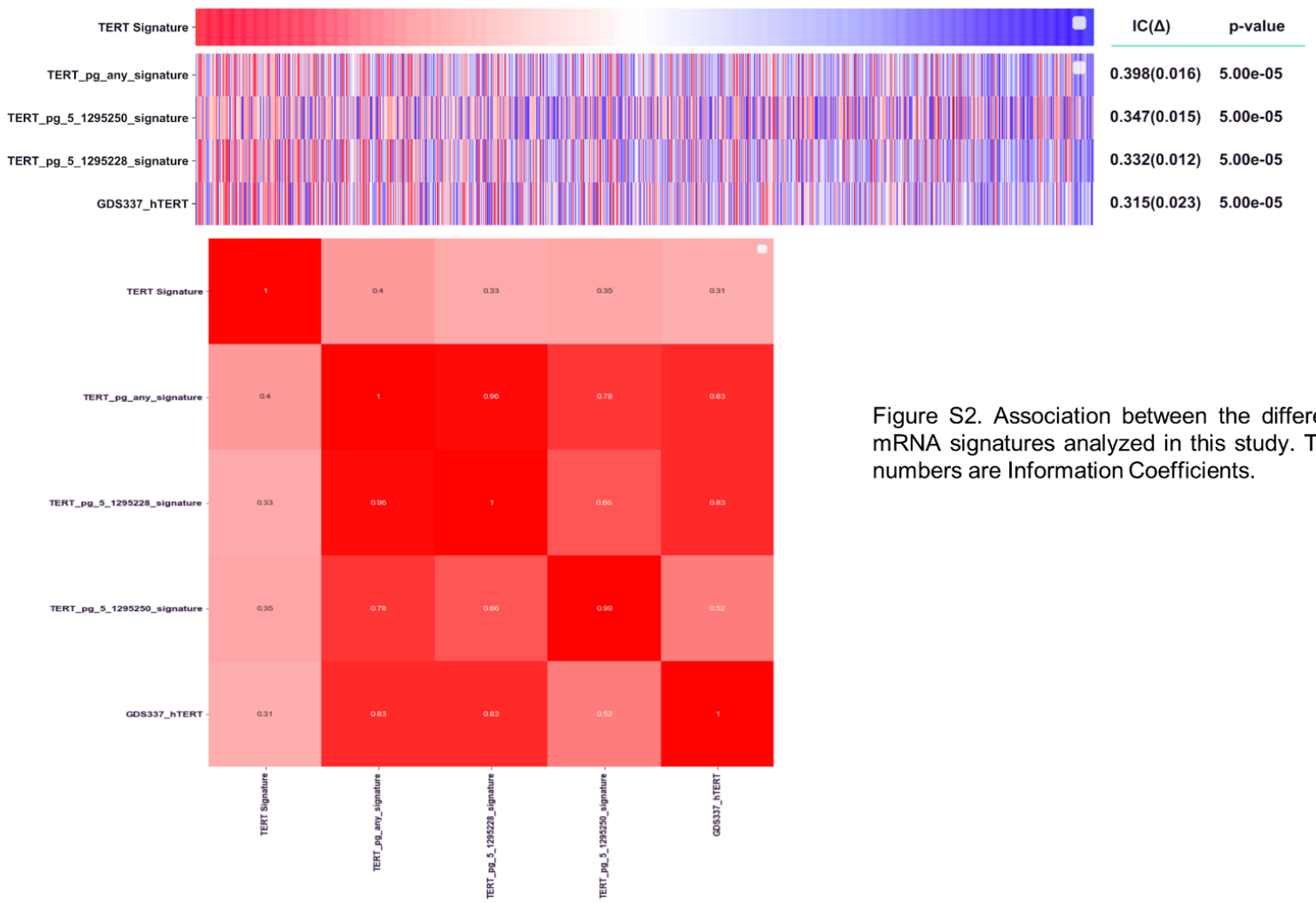


Figure S2. Association between the different mRNA signatures analyzed in this study. The numbers are Information Coefficients.

Fig S3A

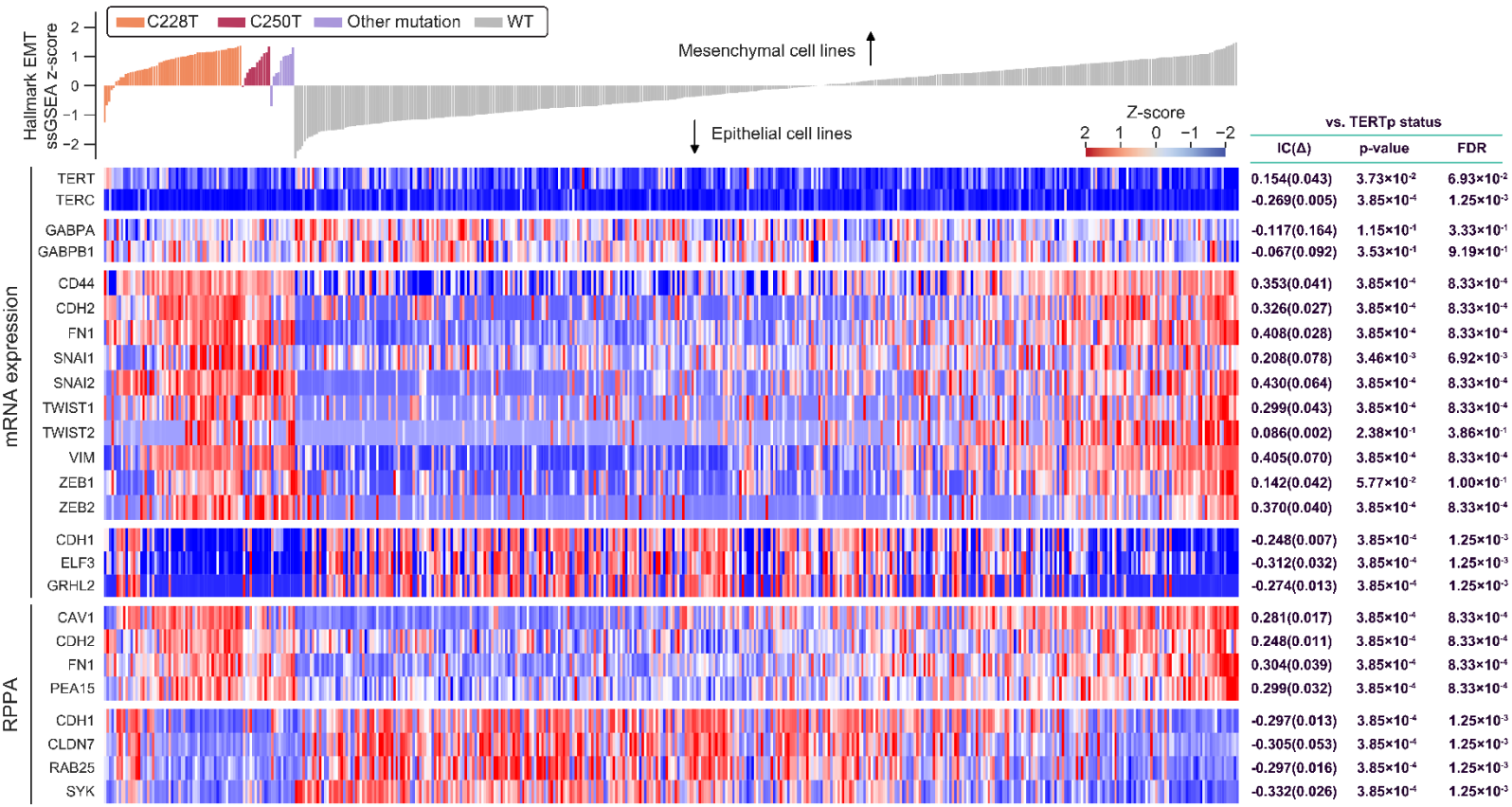


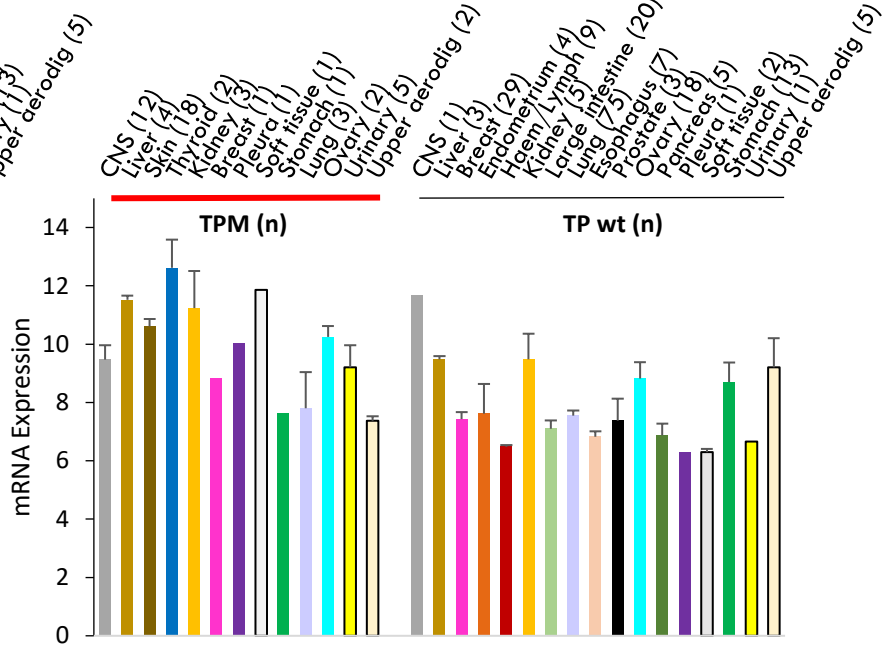
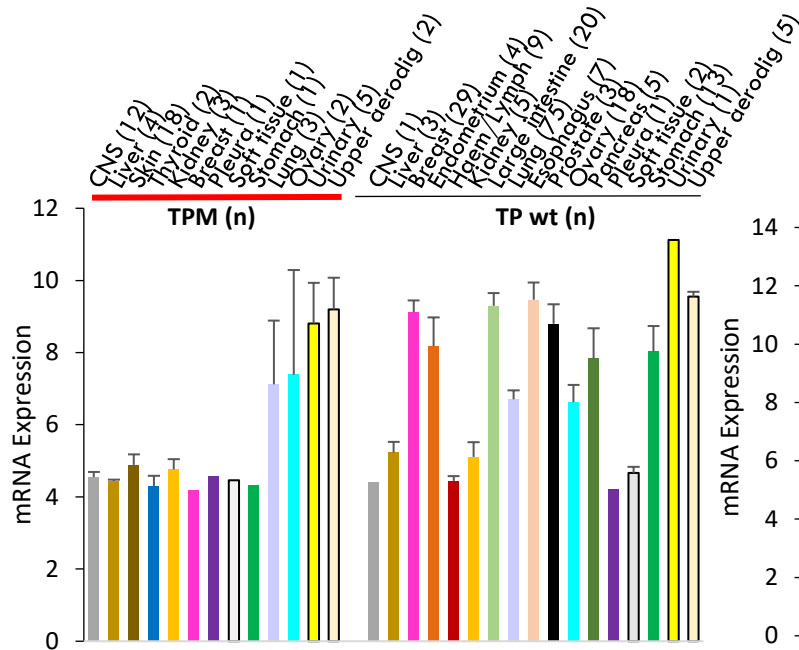
Fig S3B

Epithelial marker genes

Mesenchymal marker genes

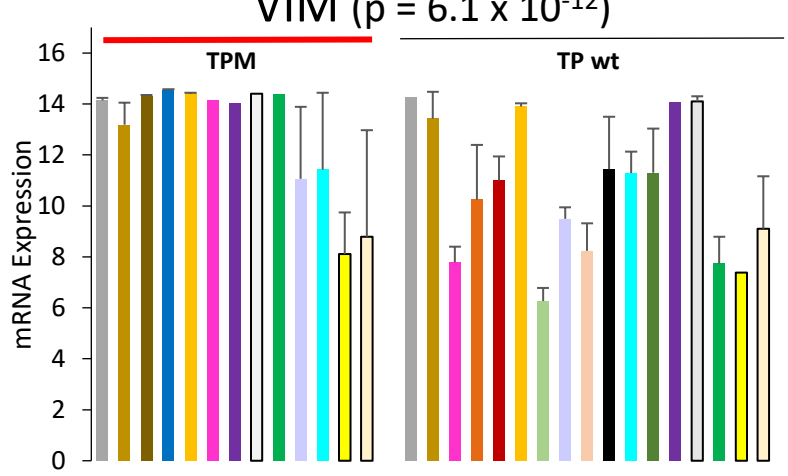
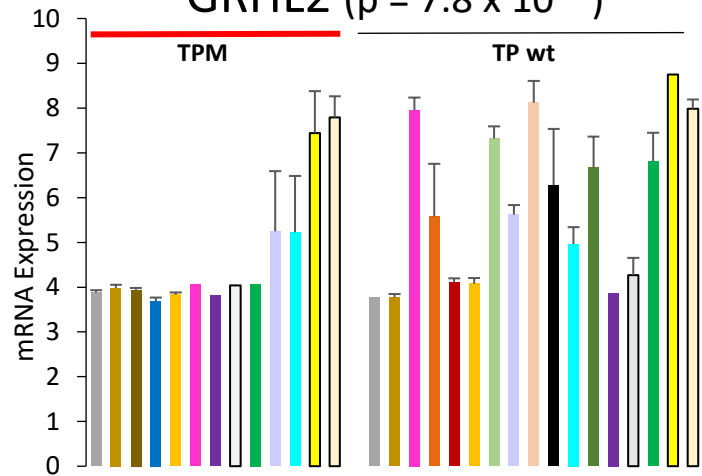
CDH1 ($p = 2.9 \times 10^{-8}$)

FN1 ($p = 5.8 \times 10^{-8}$)



GRHL2 ($p = 7.8 \times 10^{-10}$)

VIM ($p = 6.1 \times 10^{-12}$)



ELF3 ($p = 4.7 \times 10^{-15}$)

CDH2 ($p = 4.8 \times 10^{-8}$)

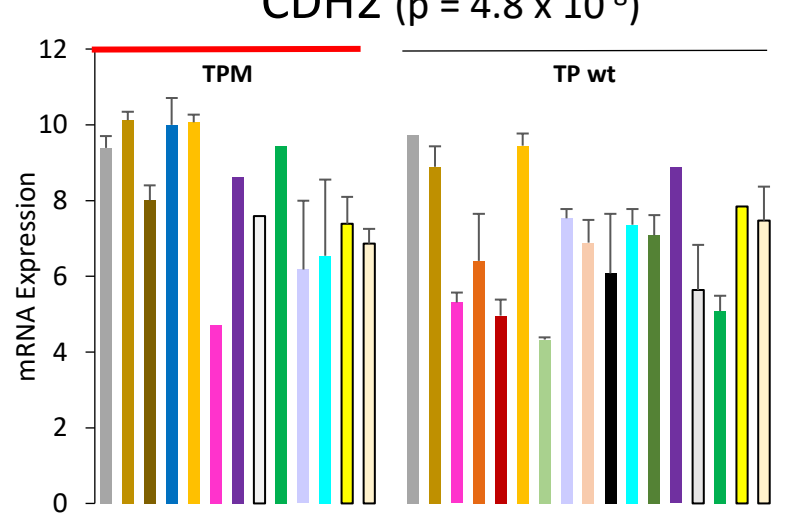
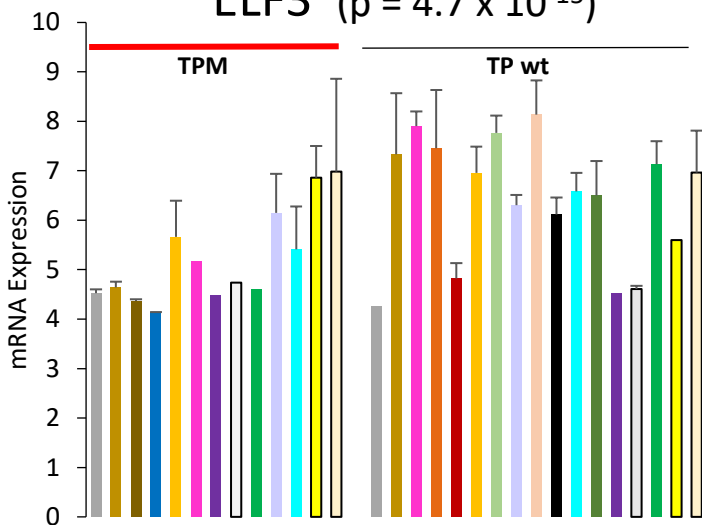
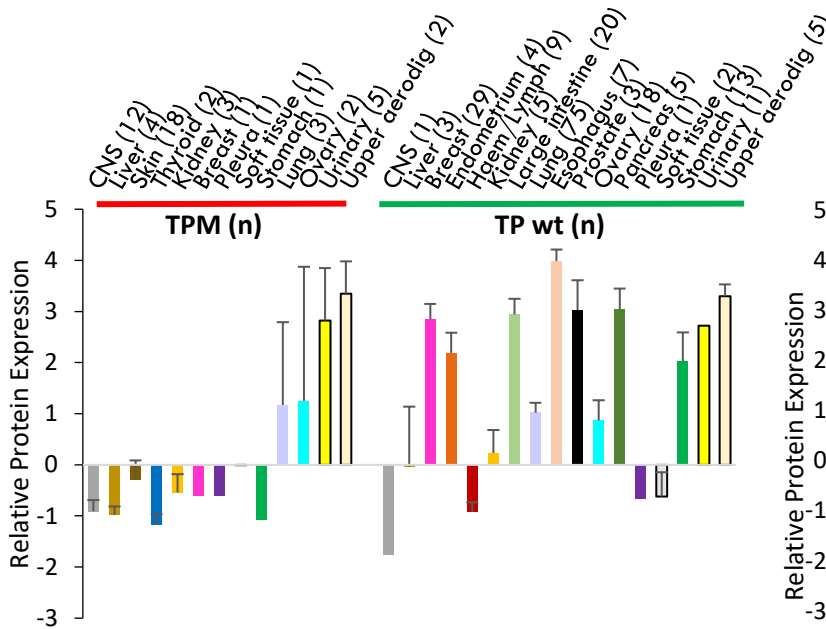


Fig S3C

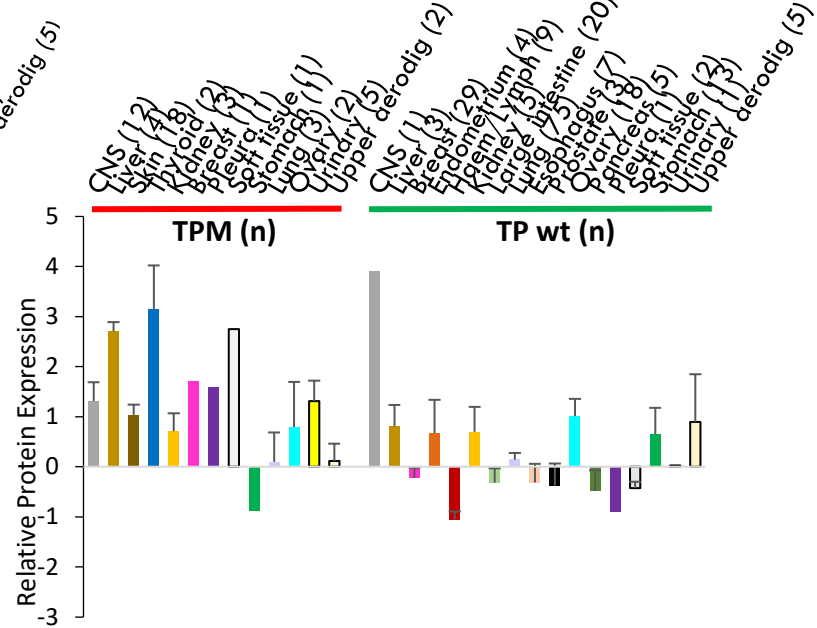
Epithelial marker proteins

CDH1 ($p = 9 \times 10^{-7}$)

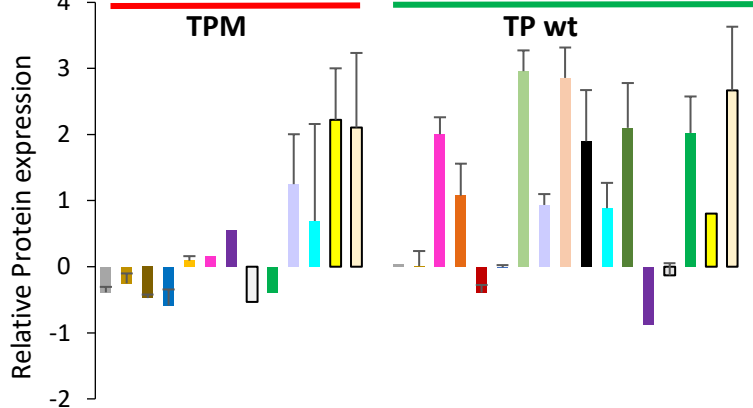


Mesenchymal marker proteins

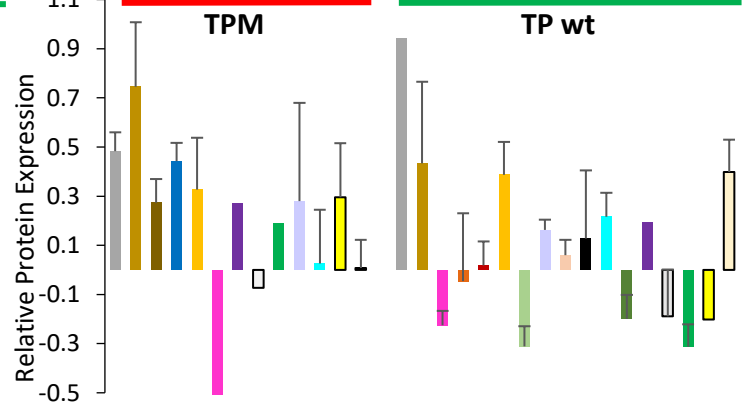
FN1 ($p = 1.7 \times 10^{-8}$)



CLDN7 ($p = 1.5 \times 10^{-9}$)



CDH2 ($p = 6.1 \times 10^{-6}$)



D.

Patient HCC

Patient skin melanomas

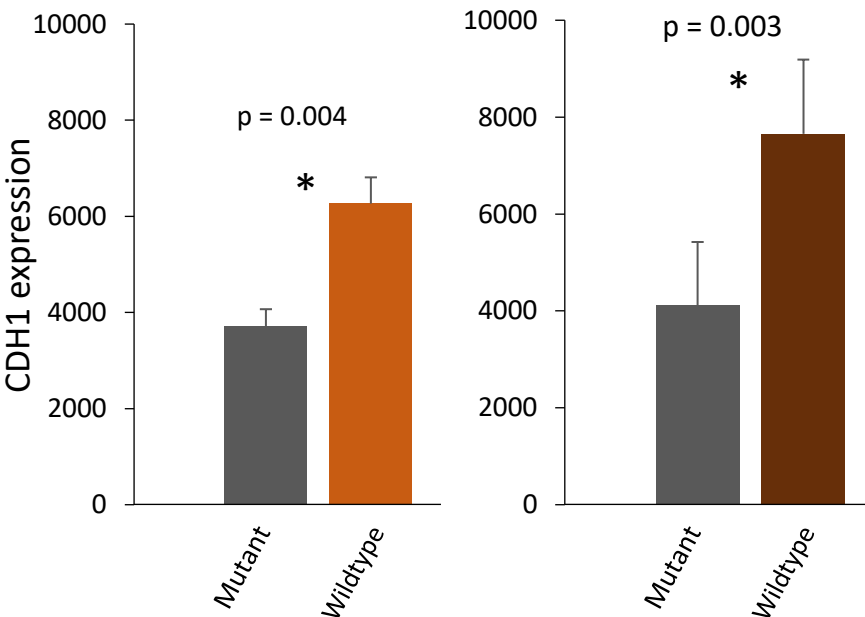


Fig S3. Expression of epithelial and mesenchymal markers in TERTp mutants (TPM) and wild-type (wt) cancer cell lines. (A) EMT markers arranged by TERTp mutation. See Fig 3 for full description. (B) Differences in expression of genes according to tissue type of origin for CCLE cell lines. (C) Differences in expression of proteins according to tissue type of origin for CCLE cell lines. (D) E-cadherin gene (*CDH1*) mRNA expression in TERTp mutant vs TERTp wild-type clinical tumor samples of liver cancer and melanoma. TPM, TERTp mutant; TP wt, wild-type lines. Skin = melanoma.

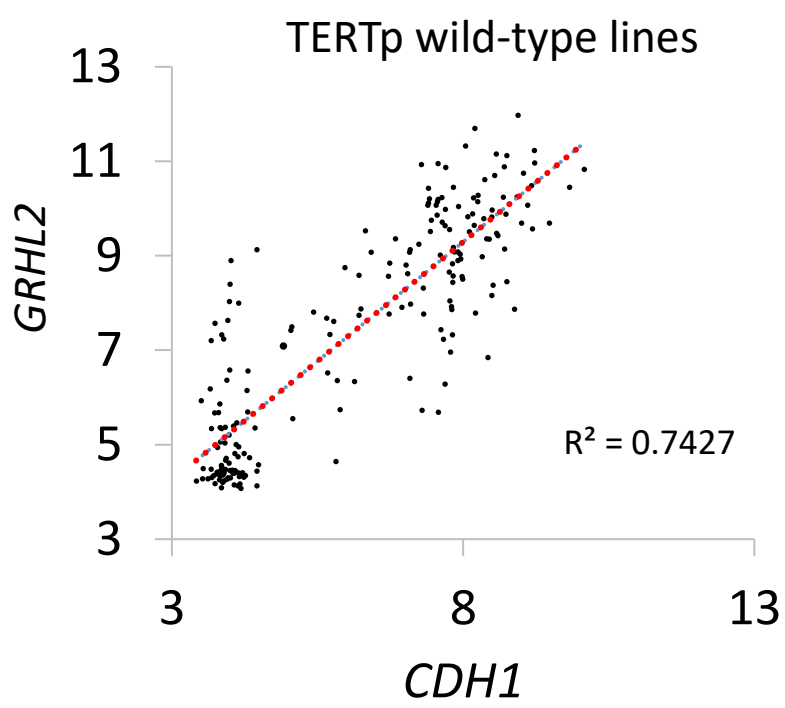
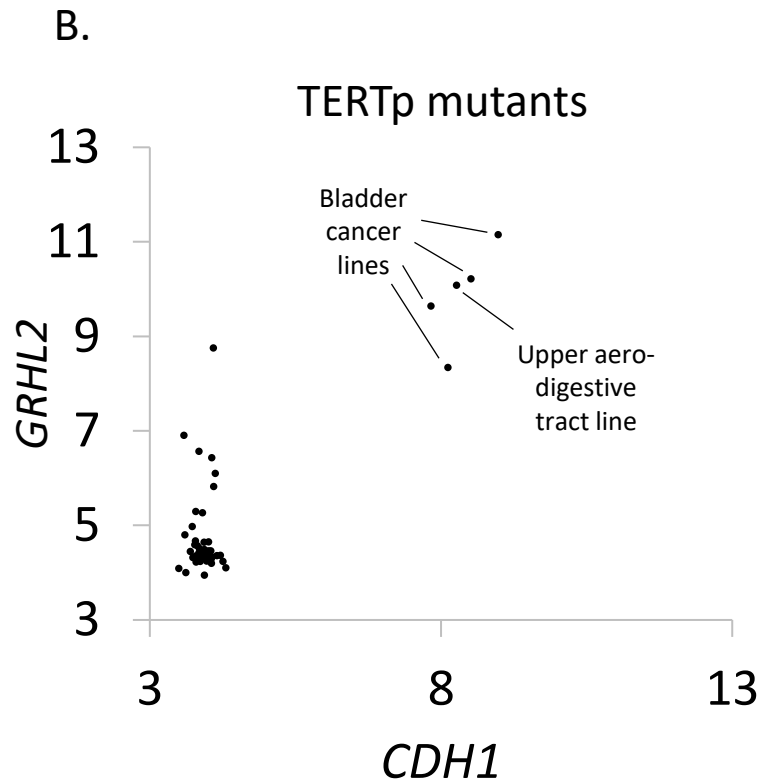
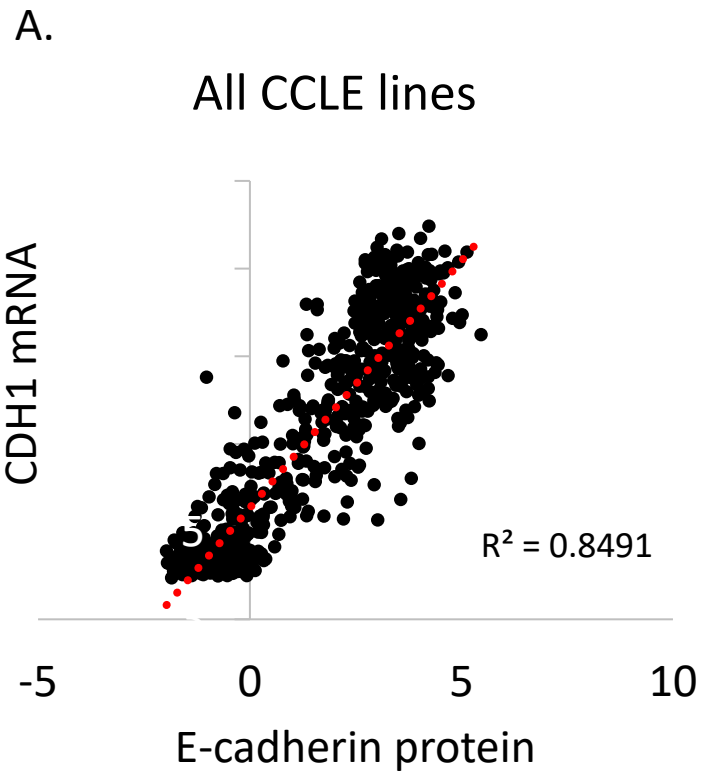


Fig S4. CDH1 expression levels in CCLE lines. (A) Correlation between CDH1 gene expression and E-cadherin protein for all CCLE lines. (B) Relationship between CDH1 and GRHL2 gene expression in CCLE lines separated by TERTp status.

Fig S5

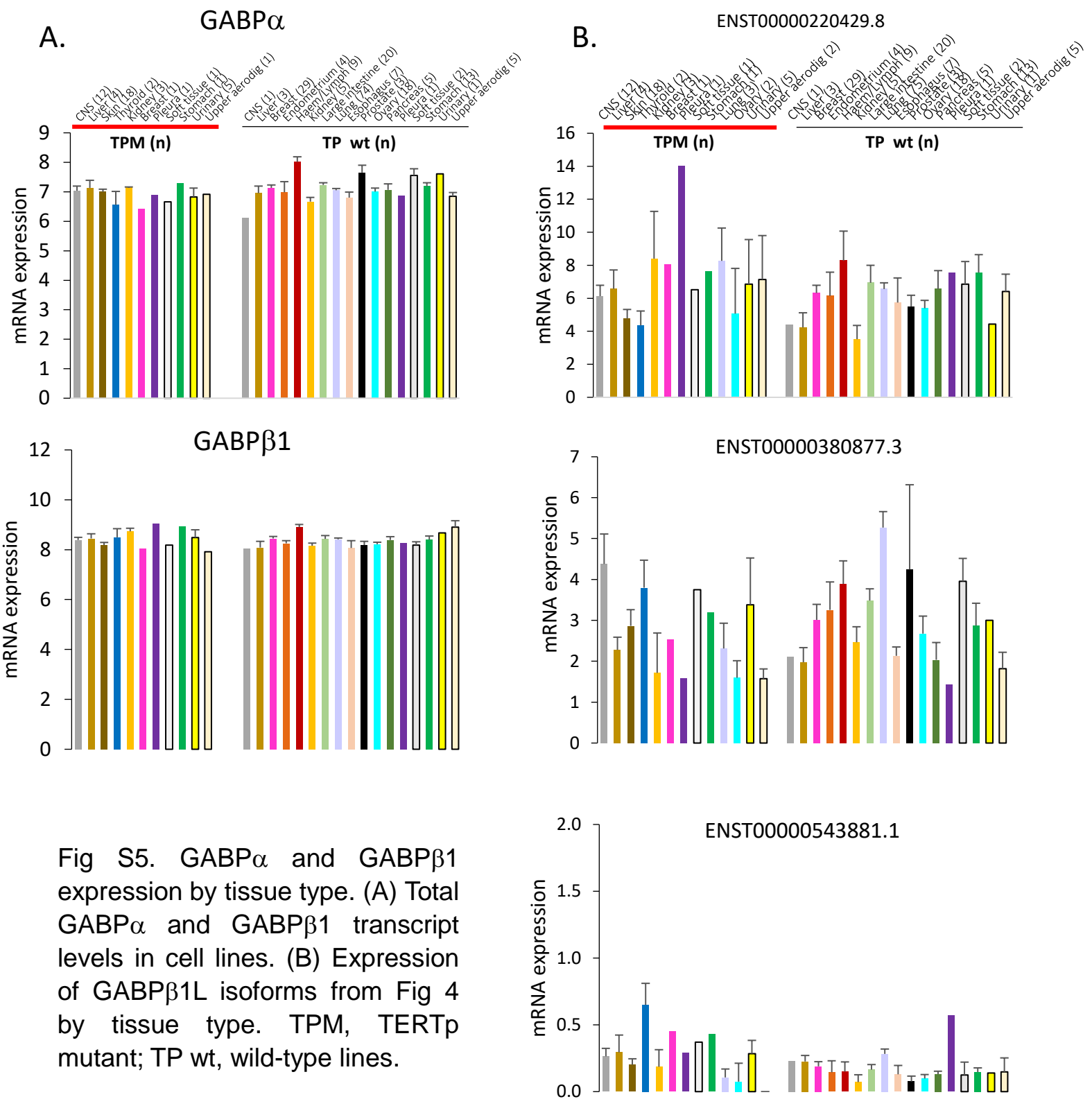


Fig S5. GABP α and GABP β 1 expression by tissue type. (A) Total GABP α and GABP β 1 transcript levels in cell lines. (B) Expression of GABP β 1L isoforms from Fig 4 by tissue type. TPM, TERTp mutant; TP wt, wild-type lines.

ccl_class	ccl	lineage	apparent_ec50_umol	log2_ec50	cpd_name	BRAF_status	log2_ec50
SKIN	IGR39	melanoma	1.23E-09	1.77E-09	dabrafenib	missense_mutation	1.77E-09
SKIN	UACC257	melanoma	0.0006078	0.000876604	dabrafenib	missense_mutation	0.000876604
SKIN	SKMEL24	melanoma	0.0007939	0.001144901	dabrafenib	missense_mutation	0.001144901
SKIN	HT144	melanoma	0.0009089	0.00131067	dabrafenib	missense_mutation	0.00131067
SKIN	WM2664	melanoma	0.0009455	0.001363424	dabrafenib	missense_mutation	0.001363424
SKIN	WM2664	melanoma	0.0009455	0.001363424	dabrafenib	missense_mutation	0.001363424
SKIN	HS294T	melanoma	0.001155	0.001665351	dabrafenib	missense_mutation	0.001665351
SKIN	COLO829	melanoma	0.001309	0.001887253	dabrafenib	missense_mutation	0.001887253
SKIN	A101D	melanoma	0.003024	0.004356127	dabrafenib	missense_mutation	0.004356127
SKIN	LOXIMVI	melanoma	2.102	1.633198686	dabrafenib	missense_mutation	1.633198686
SKIN	A2058	melanoma	2.159	1.659467937	dabrafenib	missense_mutation	1.659467937
CENTRAL_NERVOUS_SYSTEM	GI1	glioma	0.003343	0.004814886	dabrafenib	wildtype	0.004814886
CENTRAL_NERVOUS_SYSTEM	U251MG	glioma	0.01942	0.027748563	dabrafenib	wildtype	0.027748563
LIVER	SNU475	liver	0.02138	0.030519715	dabrafenib	wildtype	0.030519715
SKIN	SKMEL2	melanoma	0.08481	0.117442383	dabrafenib	wildtype	0.117442383
LIVER	SNU423	liver	0.1393	0.188147687	dabrafenib	wildtype	0.188147687
URINARY_TRACT	T24	urinary_tract	0.1794	0.238053099	dabrafenib	wildtype	0.238053099
KIDNEY	786O	kidney	0.2125	0.277984747	dabrafenib	wildtype	0.277984747
URINARY_TRACT	SCABER	urinary_tract	0.2541	0.326652391	dabrafenib	wildtype	0.326652391
LIVER	SNU387	liver	0.5177	0.601886645	dabrafenib	wildtype	0.601886645
STOMACH	SH10TC	stomach	0.5833	0.66293464	dabrafenib	wildtype	0.66293464
THYROID	SW579	thyroid	1.182	1.125651102	dabrafenib	wildtype	1.125651102
CENTRAL_NERVOUS_SYSTEM	SW1783	glioma	3.983	2.317014574	dabrafenib	wildtype	2.317014574
UPPER_AERODIGESTIVE_TRACT	CAL27	upper_aerodigestive	42.93	5.457134594	dabrafenib	wildtype	5.457134594
LUNG	CALU1	lung_NSC	313	8.294620749	dabrafenib	wildtype	8.294620749

Response to dabrafenib in TERTp mutant lines with wild-type vs mutant BRAF

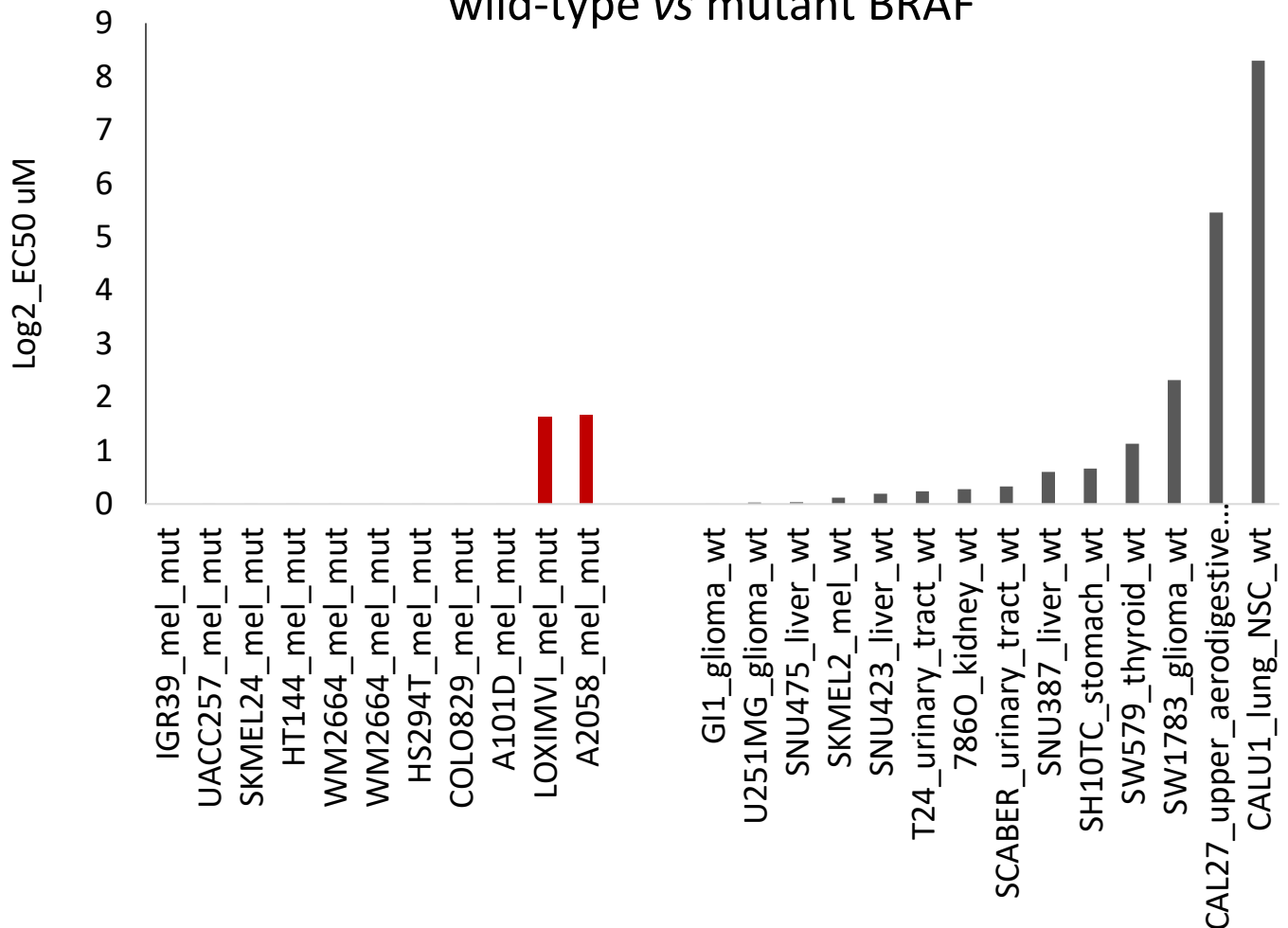


Fig S6. Stratification of TERTp mutant cell lines in The Cancer Therapeutics Response Portal (CTRP) by BRAF status reveals inhibition of growth in the absence of BRAF mutation. (A) Cell lines with growth data following dabrafenib treatment and their BRAF status. (B) Graphical representation of data from (A). Skin, mel = melanoma.

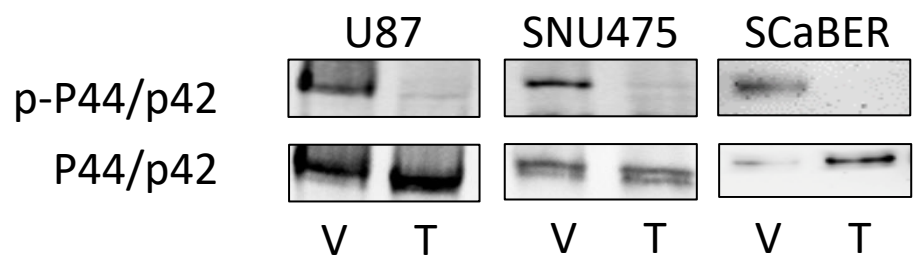


Fig. S7. Representative immunoblots of *TERT* promoter cell lines treated with trametinib for 24 hours. ERK1/2 (P42/p44). p-, phosphorylated form. V = vehicle, T = 250 nM trametinib 24 h

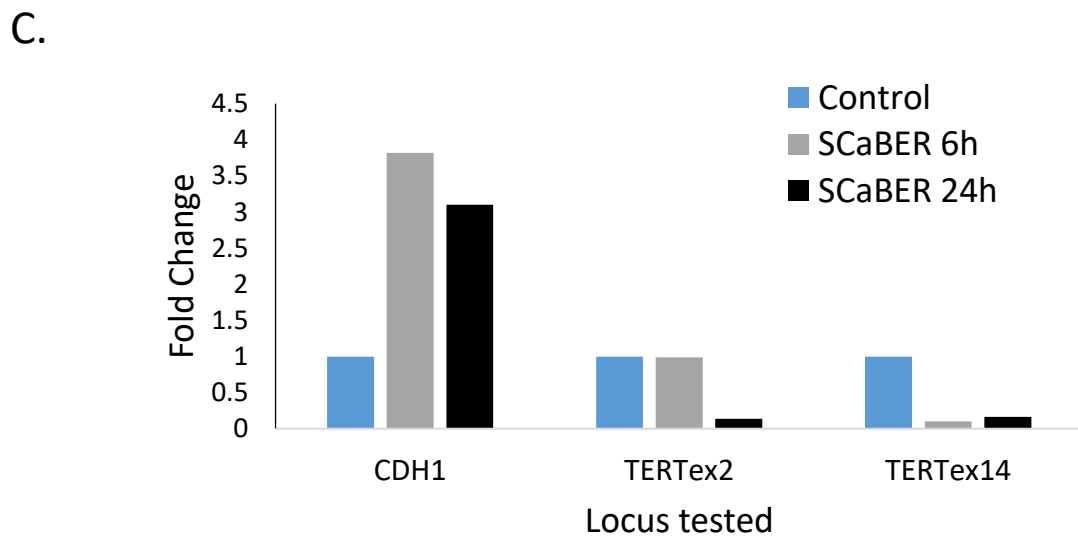
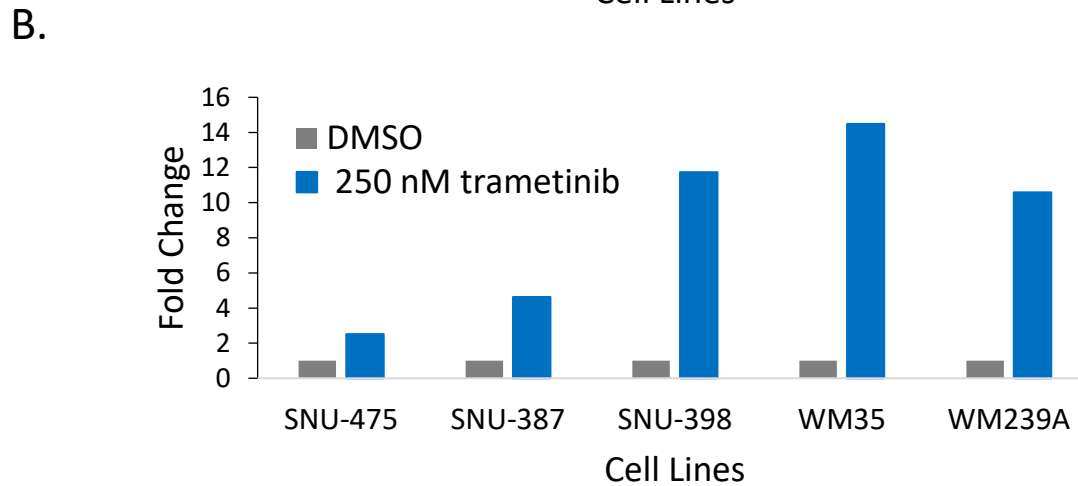
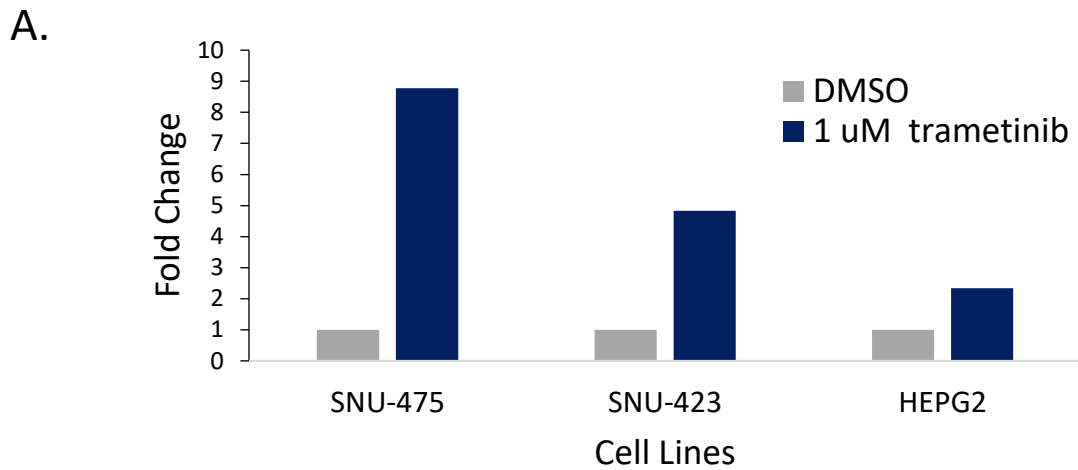


Fig. S8. Trametinib increases CDH1 expression in TERTp mutants. (A) CDH1 mRNA expression after 1 uM trametinib in TERTp mutant liver cancer cells. (B) CDH1 mRNA expression after 250 nM trametinib in TERTp mutant liver cancer cells SNU-475, SNU-387, SNU-398, and melanoma lines WM35 and WM239A. (C) CDH1 and TERT mRNA expression following 6h and 24h trametinib treatment. TERTex2, TERT exon 2 mRNA levels; TERTex14, TERT exon 14 mRNA levels.