Figure S1A

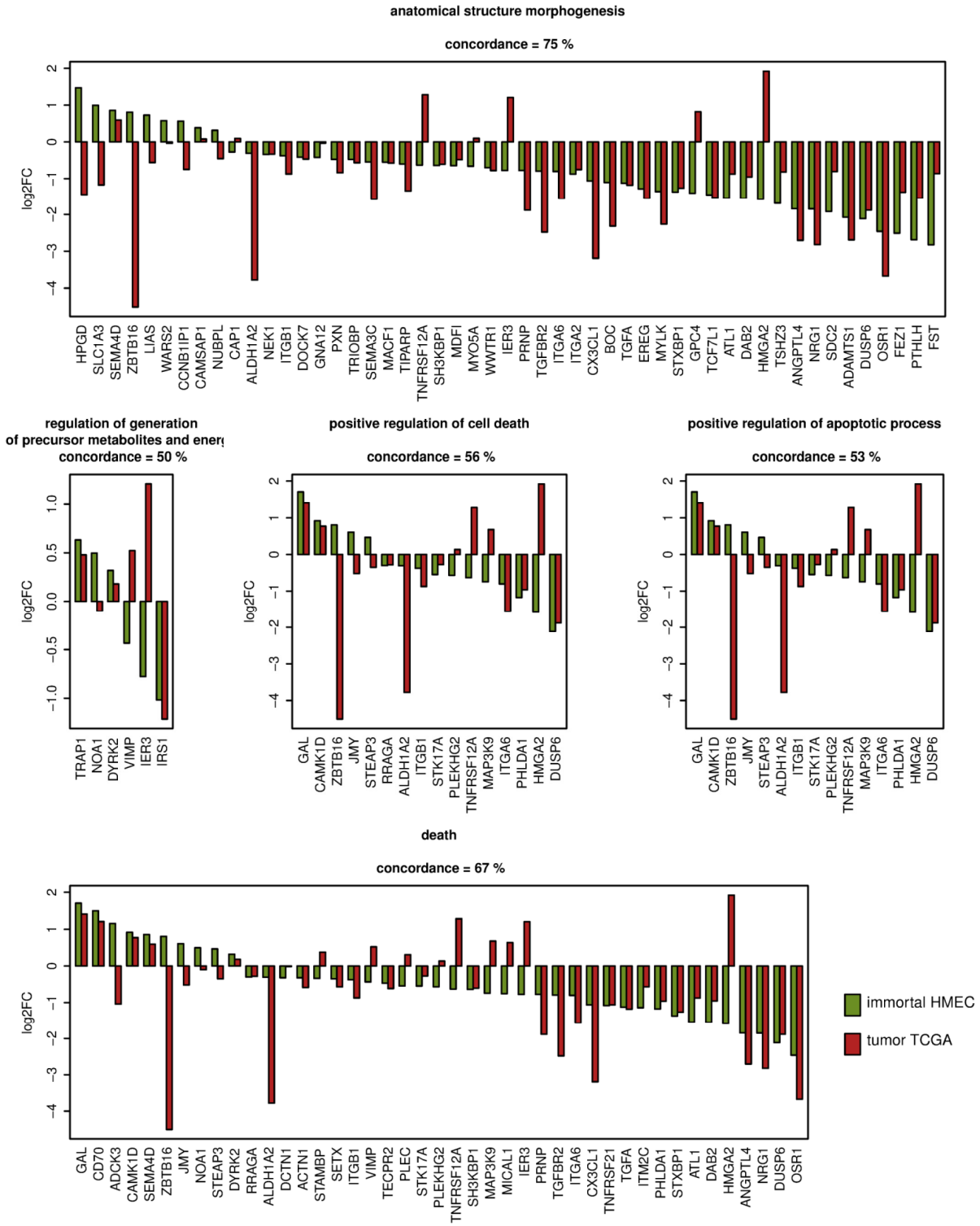
anatomical structure morphogenesis
concordance = 75 %
log2FC
HPGD SLC1A3 SEMA4D ZBTB16 LIAS WARS2 CCNB1IP1 CAMSAP1 NUBPL CAP1 ALDH1A2 NEK1 ITGB1 DOCK7 GNA12 PXN TRIOBP SEMA3C MACF1 TIPARP TNFRSF12A SH3KBP1 MDFI MYO5A WWTR1 IER3 PRNP TGFBR2 ITGA6 ITGA2 CX3CL1 BOC TGFA EREG MYLK STXBP1 GPC4 TCF7L1 ATL1 DAB2 HMGA2 TSHZ3 ANGPTL4 NRG1 SDC2 ADAMTS1 DUSP6 OSR1 FEZ1 PTHLH FST
regulation of generation of precursor metabolites and ener
concordance = 50 %
log2FC
TRAP1 NOA1 DYRK2 VIMP IER3 IRS1
positive regulation of cell death
concordance = 56 %
log2FC
GAL CAMK1D ZBTB16 JMY STEAP3 RRAGA ALDH1A2 ITGB1 STK17A PLEKHG2 TNFRSF12A MAP3K9 ITGA6 PHLDA1 HMGA2 DUSP6
positive regulation of apoptotic process
concordance = 53 %
log2FC
GAL CAMK1D ZBTB16 JMY STEAP3 ALDH1A2 ITGB1 STK17A PLEKHG2 TNFRSF12A MAP3K9 ITGA6 PHLDA1 HMGA2 DUSP6
death
concordance = 67 %
log2FC
GAL CD70 ADCK3 CAMK1D SEMA4D ZBTB16 JMY NOA1 STEAP3 DYRK2 RRAGA ALDH1A2 DCTN1 ACTN1 STAMBP SETX ITGB1 VIMP TECPR2 PLEC STK17A PLEKHG2 TNFRSF12A SH3KBP1 MAP3K9 MICAL1 IER3 PRNP TGFBR2 ITGA6 CX3CL1 TNFRSF21 TGFA ITM2C PHLDA1 STXBP1 ATL1 DAB2 HMGA2 ANGPTL4 NRG1 DUSP6 OSR1
immortal HMEC
tumor TCGA

Figure S1B

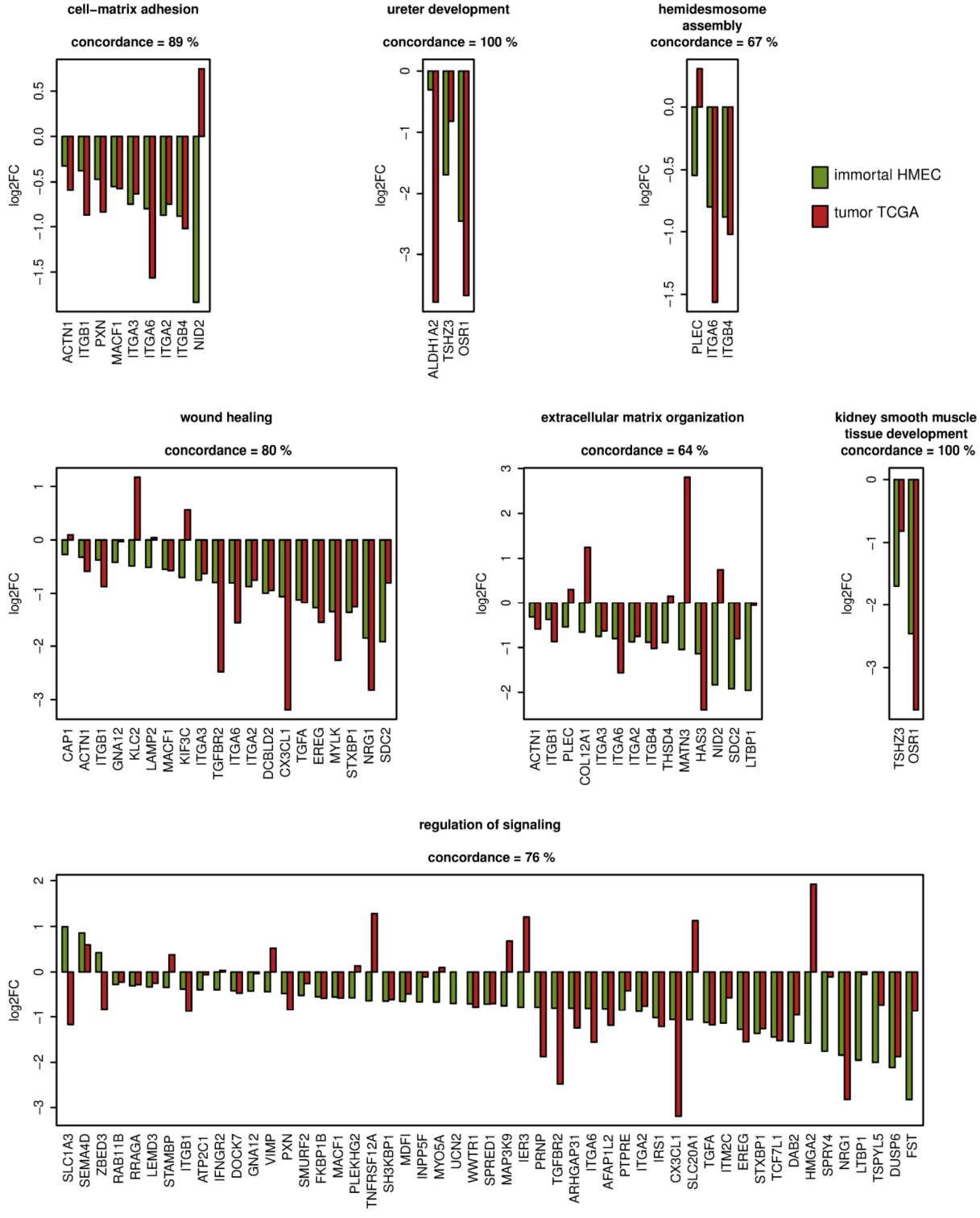
cell−matrix adhesion
concordance = 89 %
log2FC
ACTN1
ITGB1
PXN
MACF1
ITGA3
ITGA6
ITGA2
ITGB4
NID2
ureter development
concordance = 100 %
log2FC
ALDH1A2
TSHZ3
OSR1
hemidesmosome assembly
concordance = 67 %
log2FC
PLEC
ITGA6
ITGB4
immortal HMEC
tumor TCGA
wound healing
concordance = 80 %
log2FC
CAP1
ACTN1
ITGB1
GNA12
KLC2
LAMP2
MACF1
KIF3C
ITGA3
TGFBR2
ITGA6
ITGA2
DCBLD2
CX3CL1
TGFA
EREG
MYLK
STXBP1
NRG1
SDC2
extracellular matrix organization
concordance = 64 %
log2FC
ACTN1
ITGB1
PLEC
COL12A1
ITGA3
ITGA6
ITGA2
ITGB4
THSD4
MATN3
HAS3
NID2
SDC2
LTBP1
kidney smooth muscle tissue development
concordance = 100 %
log2FC
TSHZ3
OSR1
regulation of signaling
concordance = 76 %
log2FC
SLC1A3
SEMA4D
ZBED3
RAB11B
RRAGA
LEMD3
STAMBP
ITGB1
ATP2C1
IFNGR2
DOCK7
GNA12
VIMP
PXN
SMURF2
FKBP1B
MACF1
PLEKHG2
TNFRSF12A
SH3KBP1
MDFI
INPP5F
MYO5A
UCN2
WWTR1
SPRED1
MAP3K9
IER3
PRNP
TGFBR2
ARHGAP31
ITGA6
AFAP1L2
PTPRE
ITGA2
IRS1
CX3CL1
SLC20A1
TGFA
ITM2C
EREG
STXBP1
TCF7L1
DAB2
HMGA2
SPRY4
NRG1
LTBP1
TSPYL5
DUSP6
FST

Figure S1C

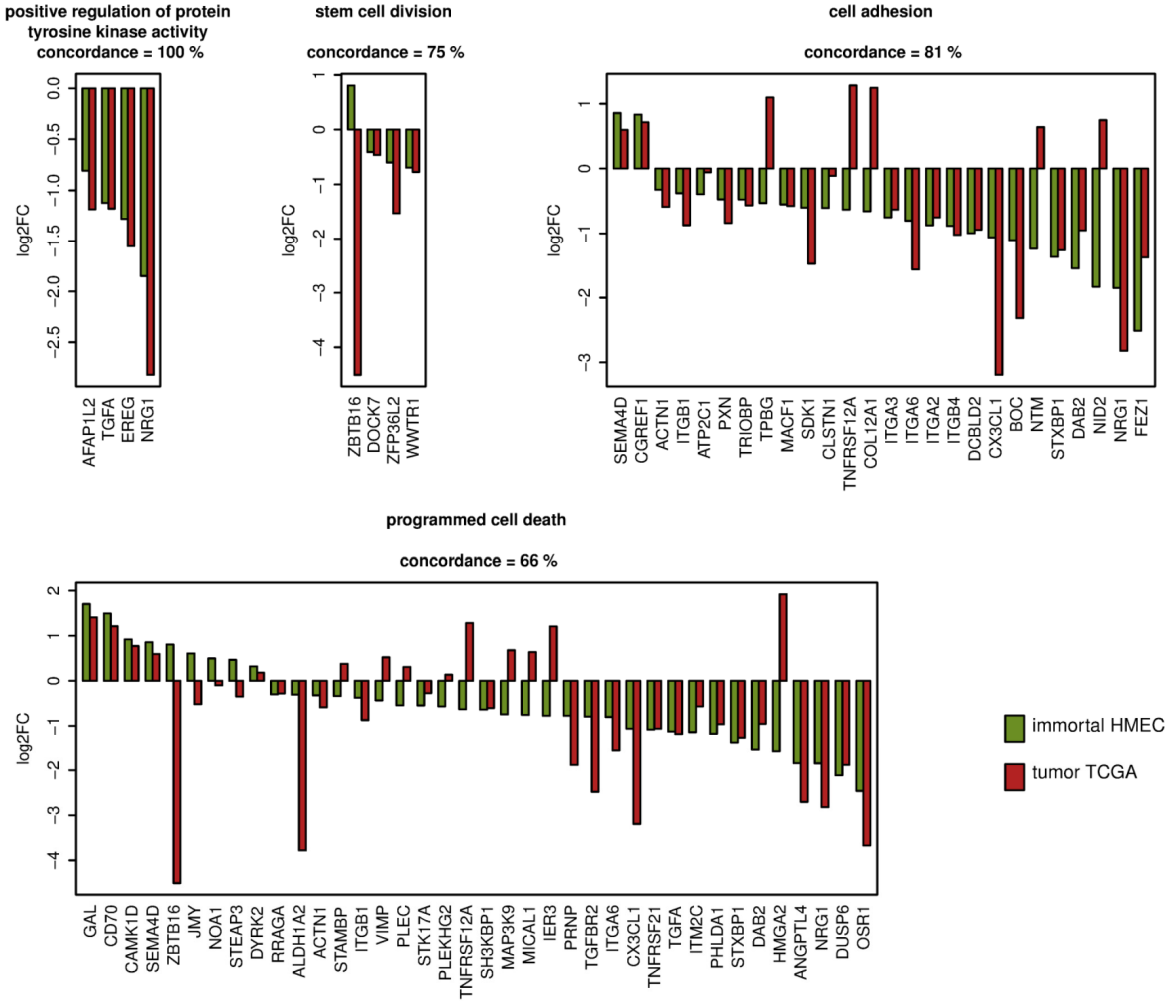

Figure S1. Comparison of gene expression changes in individual enriched GO categories in the in vitro immortalization model with those in the TCGA breast invasive carcinoma samples relative to non-tumor samples.

Figure S2

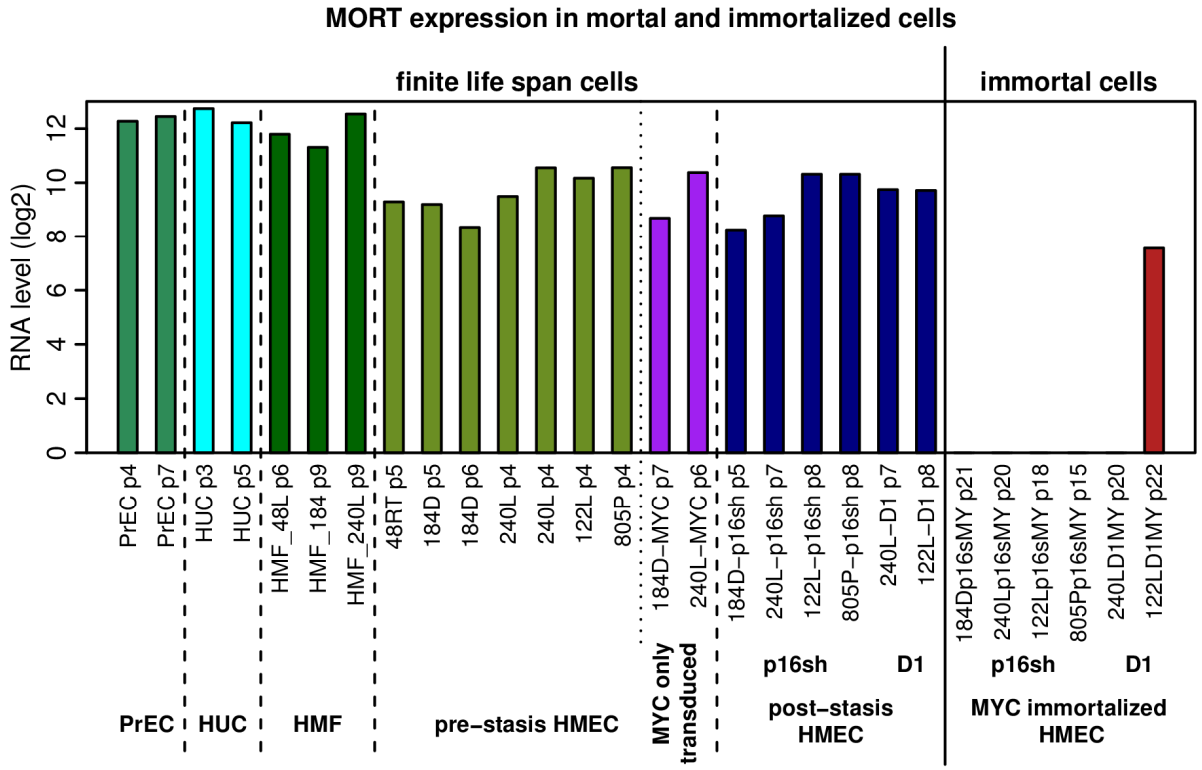

Figure S2. MORT expression in HMEC immortalization model cultures, additional primary cell types, and additional controls. Primary cell types - prostate epithelial cells (PrEC), human urothelial cells (HUC), human mammary fibroblasts (HMF) and human mammary epithelial cells (HMEC), as well as MYC only transduced HMEC and post-stasis HMEC do express MORT. MYC alone likely has a little to no effect on MORT expression. MYC immortalized p16 or D1 cells have MORT either completely silenced or substantialy reduced (122LD1MY).

Figure S3

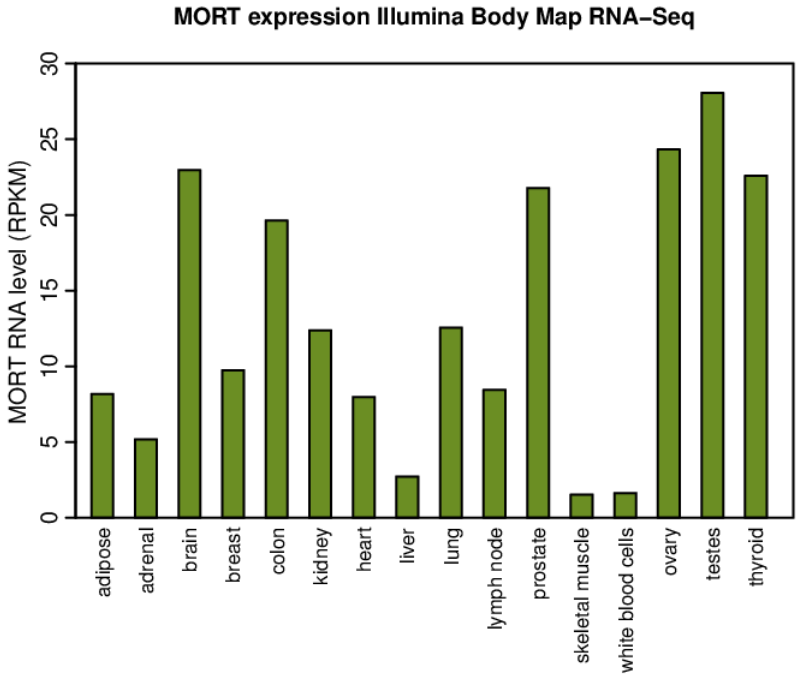

Figure S3. MORT expression across 16 tissues of Illumina Body Map.

Figure S4

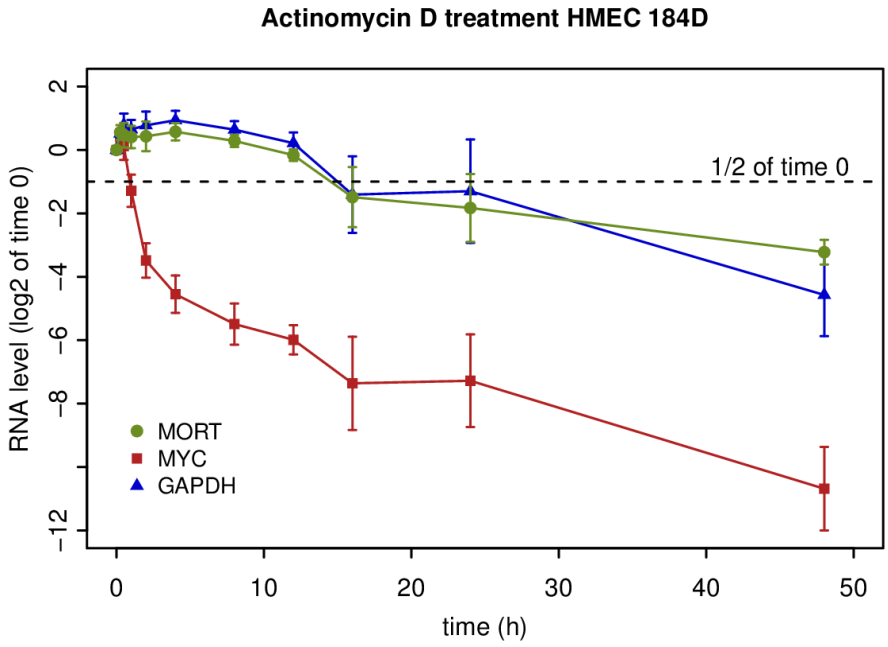

Figure S4. Determination of MORT transcript half-life using actinomycin D (1 µg/ml) treatment. MYC was used as a short half-life reference gene and GAPDH was used as a long half-life reference gene (Yang et al. 2003). The results indicate that MORT has a long half-life of ~15 hrs comparable to GAPDH. The error bars show the SEM of 3 independent experiments.

Figure S5

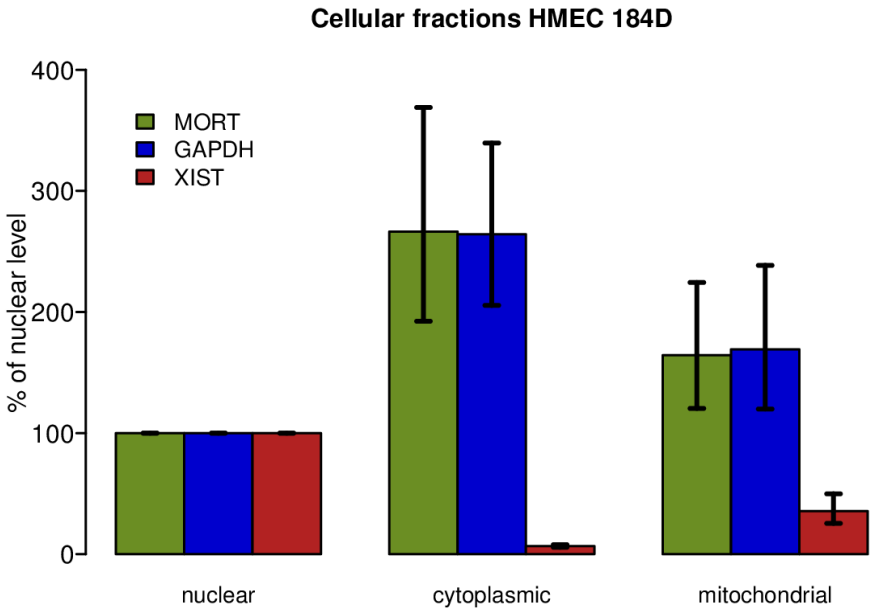

Figure S5. Cellular localization of MORT. HMEC cells were lysed in hypotonic conditions using a Dounce homogenizer and the lysate was separated by differential centrifugation to nuclear, mitochondrial and cytoplasmic fractions. Relative representation of MORT, GAPDH (cytoplasmic) and XIST (nuclear) transcripts was determined by real-time PCR. All data are displayed relative to the nuclear fraction, which is set to 100 %. The error bars show the SEM of 3 independent experiments. MORT is localized predominantly in the cytoplasmic fraction, similar to GAPDH.

Figure S6

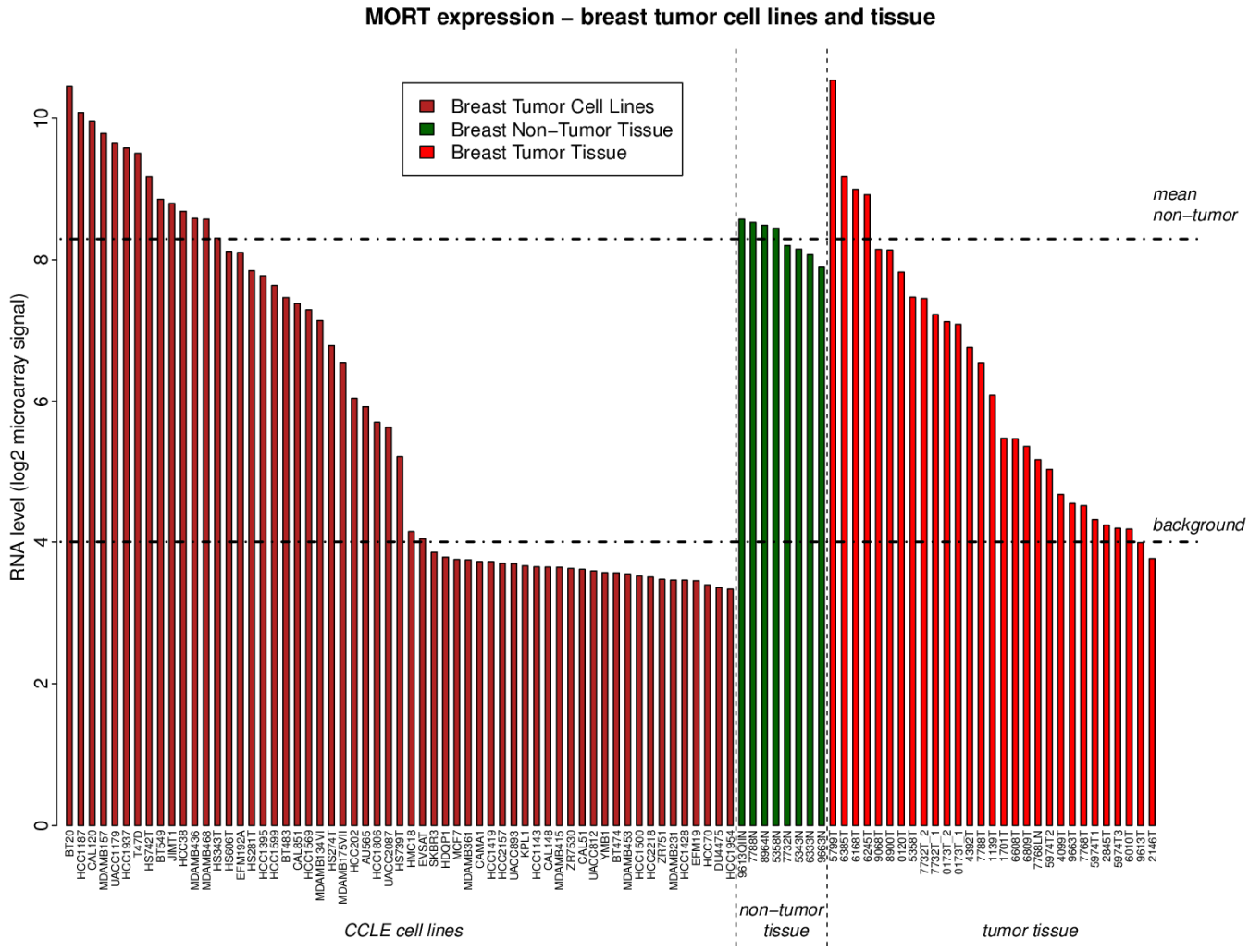

Figure S6. MORT expression level across breast cancer cell lines from cancer cell line encyclopedia (CCLE) and a set of 8 breast non-tumor samples and 27 breast carcinomas.

Figure S7

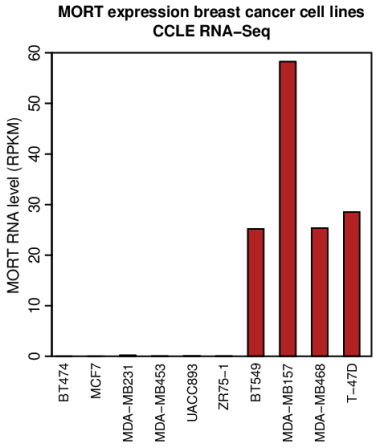

Figure S7. MORT expression level across 10 breast cancer cell lines from cancer cell line encyclopedia (CCLE) as determined by RNA-seq

Figure S8A

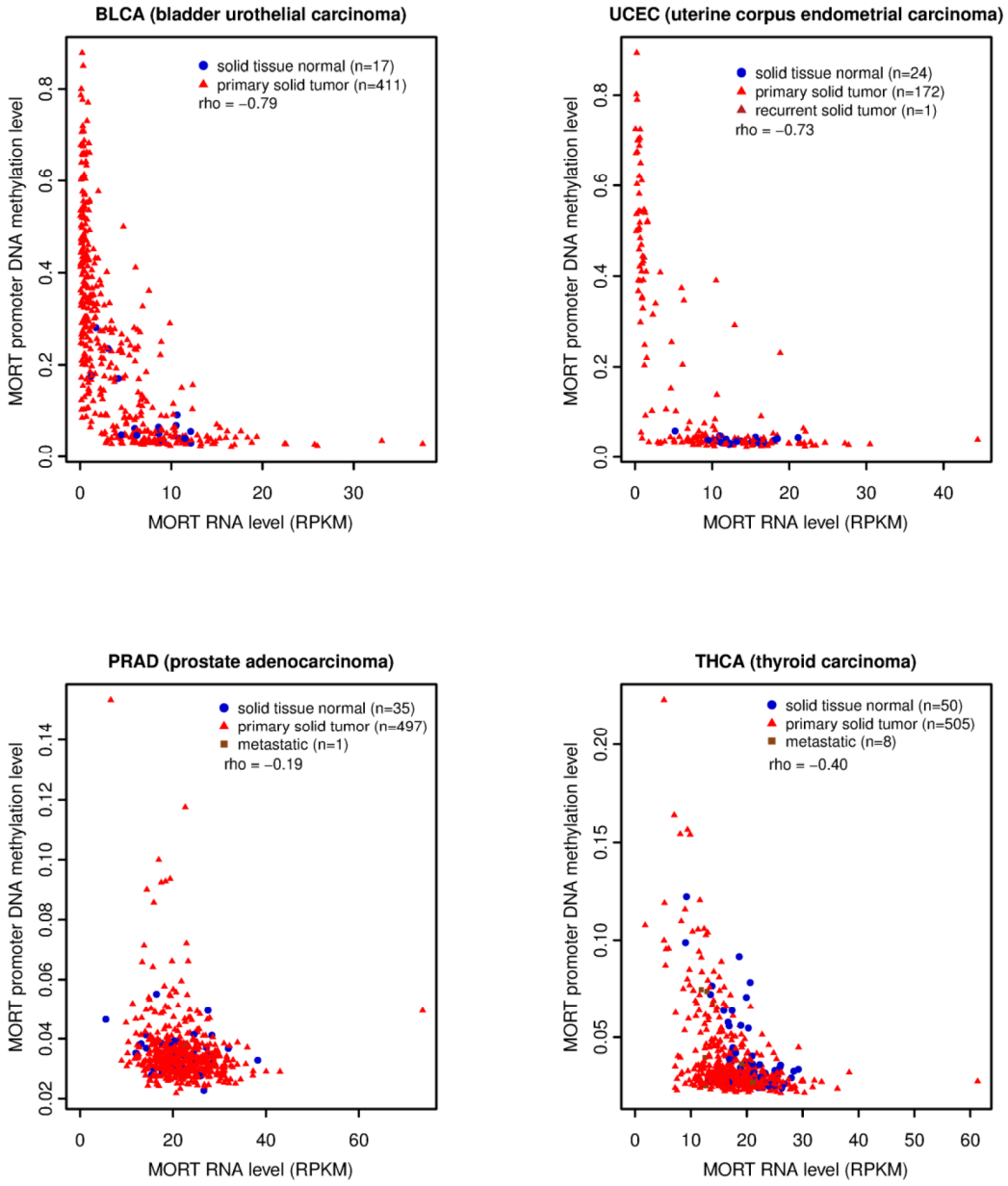
BLCA (bladder urothelial carcinoma)
solid tissue normal (n=17)
primary solid tumor (n=411)
rho = −0.79
MORT promoter DNA methylation level
MORT RNA level (RPKM)
UCEC (uterine corpus endometrial carcinoma)
solid tissue normal (n=24)
primary solid tumor (n=172)
recurrent solid tumor (n=1)
rho = −0.73
MORT promoter DNA methylation level
MORT RNA level (RPKM)
PRAD (prostate adenocarcinoma)
solid tissue normal (n=35)
primary solid tumor (n=497)
metastatic (n=1)
rho = −0.19
MORT promoter DNA methylation level
MORT RNA level (RPKM)
THCA (thyroid carcinoma)
solid tissue normal (n=50)
primary solid tumor (n=505)
metastatic (n=8)
rho = −0.40
MORT promoter DNA methylation level
MORT RNA level (RPKM)

Figure S8B

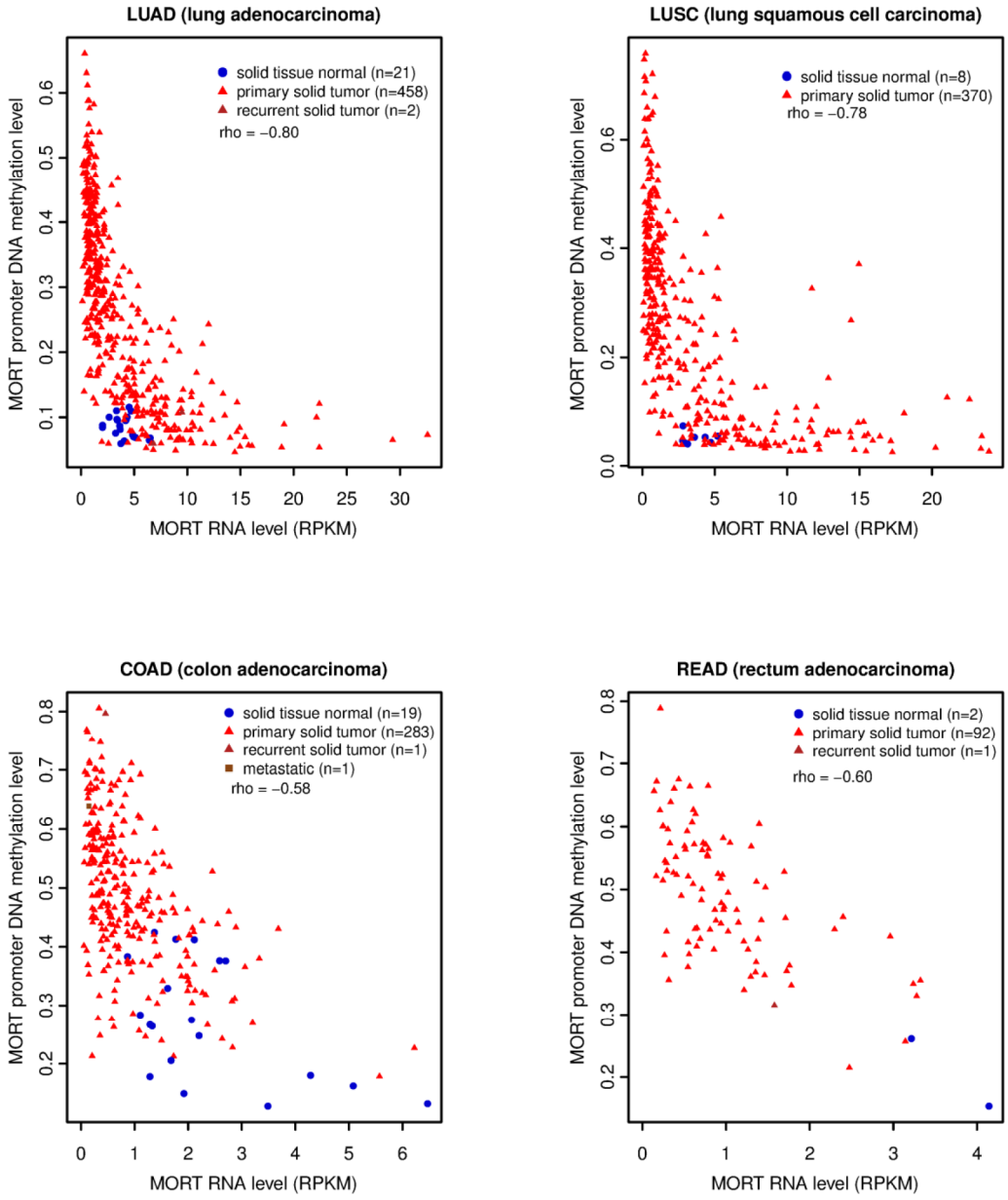
LUAD (lung adenocarcinoma)
solid tissue normal (n=21)
primary solid tumor (n=458)
recurrent solid tumor (n=2)
rho = −0.80
MORT promoter DNA methylation level
MORT RNA level (RPKM)
LUSC (lung squamous cell carcinoma)
solid tissue normal (n=8)
primary solid tumor (n=370)
rho = −0.78
MORT promoter DNA methylation level
MORT RNA level (RPKM)
COAD (colon adenocarcinoma)
solid tissue normal (n=19)
primary solid tumor (n=283)
recurrent solid tumor (n=1)
metastatic (n=1)
rho = −0.58
MORT promoter DNA methylation level
MORT RNA level (RPKM)
READ (rectum adenocarcinoma)
solid tissue normal (n=2)
primary solid tumor (n=92)
recurrent solid tumor (n=1)
rho = −0.60
MORT promoter DNA methylation level
MORT RNA level (RPKM)

Figure S8C

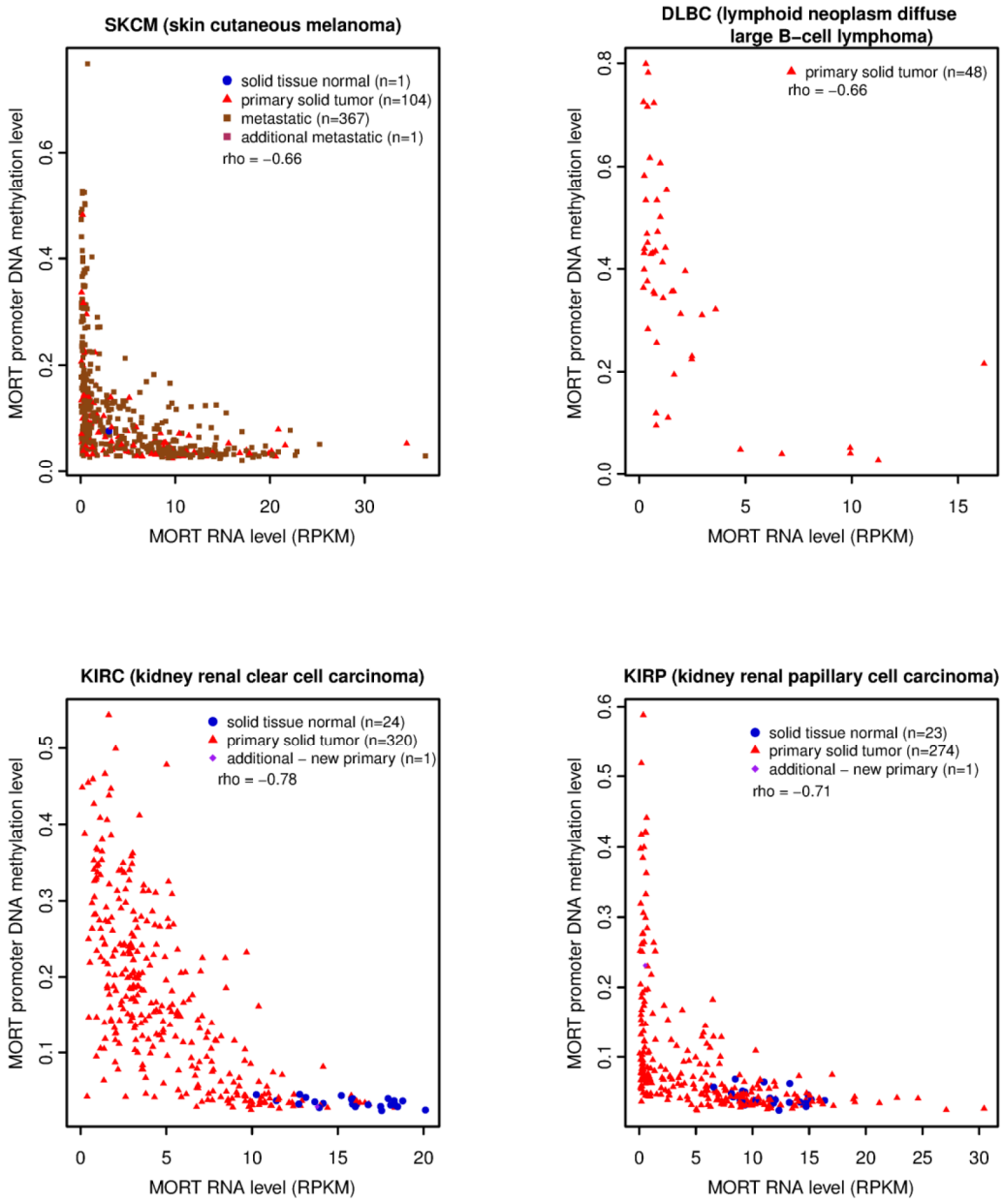
SKCM (skin cutaneous melanoma)
solid tissue normal (n=1)
primary solid tumor (n=104)
metastatic (n=367)
additional metastatic (n=1)
rho = −0.66
MORT promoter DNA methylation level
MORT RNA level (RPKM)
DLBC (lymphoid neoplasm diffuse large B−cell lymphoma)
primary solid tumor (n=48)
rho = −0.66
MORT promoter DNA methylation level
MORT RNA level (RPKM)
KIRC (kidney renal clear cell carcinoma)
solid tissue normal (n=24)
primary solid tumor (n=320)
additional − new primary (n=1)
rho = −0.78
MORT promoter DNA methylation level
MORT RNA level (RPKM)
KIRP (kidney renal papillary cell carcinoma)
solid tissue normal (n=23)
primary solid tumor (n=274)
additional − new primary (n=1)
rho = −0.71
MORT promoter DNA methylation level
MORT RNA level (RPKM)

Figure S8D

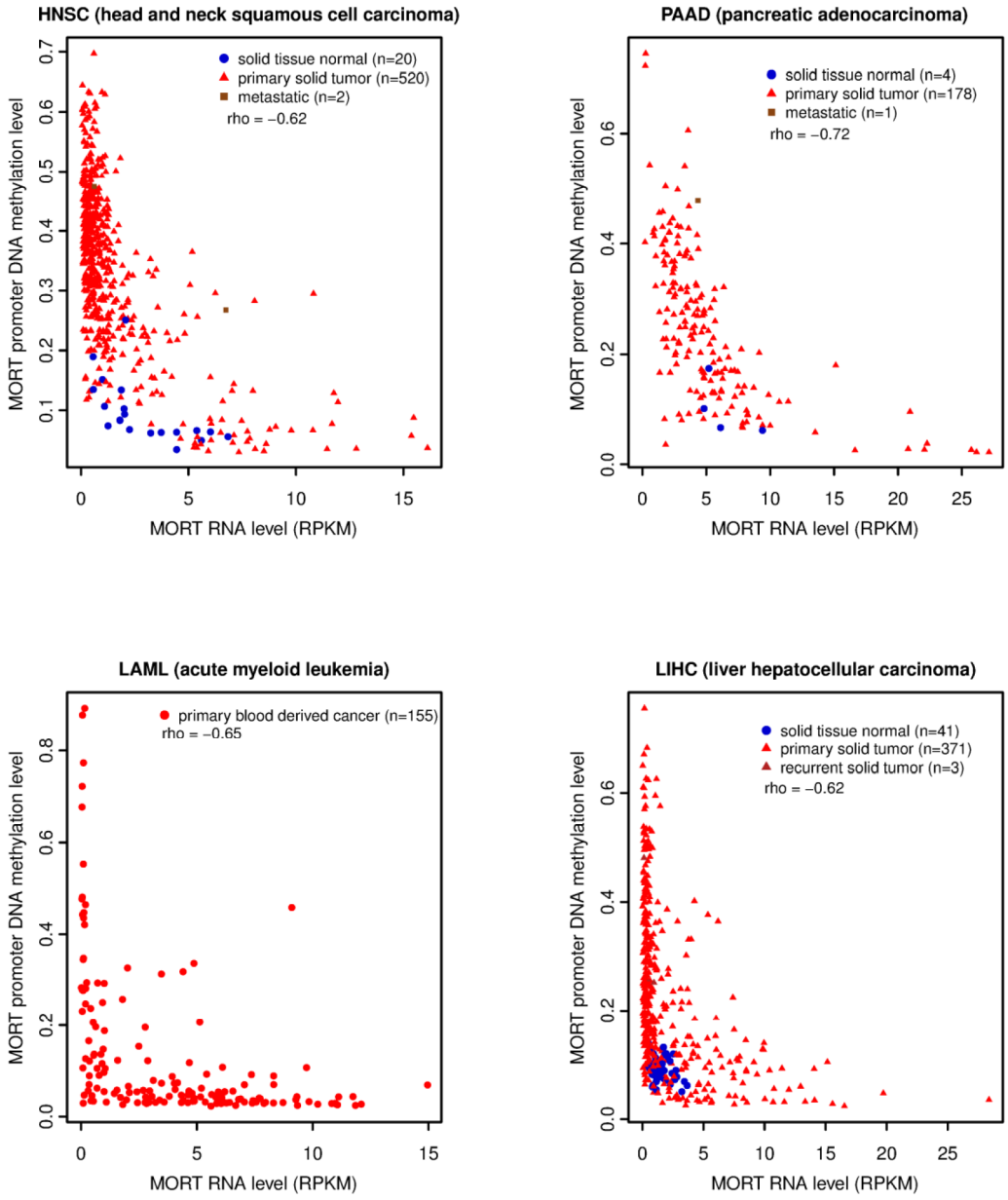

Figure S8. Integration of MORT expression and DNA methylation TCGA data for 16 additional TCGA tumor types. The x-axis shows MORT expression level according to RNA-seq and y-axis shows the level of MORT promoter methylation according to Illumina HumanMethylation450 microarray. The correlation coefficient rho between MORT expression and promoter methylation for each tumor type is displayed.

Figure S9

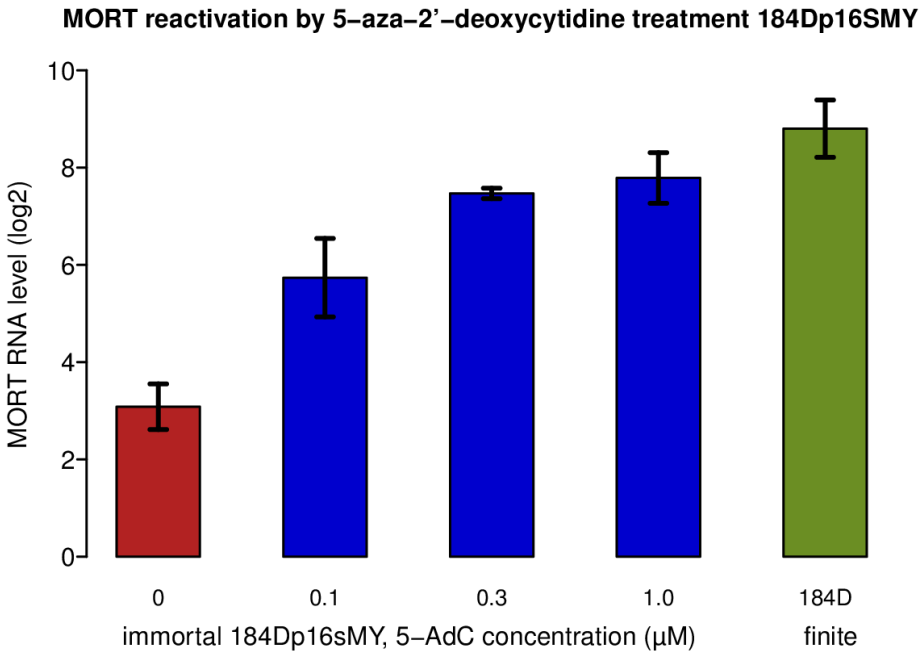

Figure S9. MORT is reactivated by 5-AdC treatment of immortalized HMEC 184Dp16SMY.
The figure shows MORT transcript level in untreated 184Dp16SMY (red), an increased MORT level after 96 h treatment with three concentrations of 5-AdC (blue) and the MORT level in untreated finite parental 184D HMEC (green). The error bars show the SEM of 3 independent experiments.

Supplemental References

Yang E, van Nimwegen E, Zavolan M, Rajewsky N, Schroeder M, Magnasco M, Darnell JE, Jr. 2003. Decay rates of human mRNAs: correlation with functional characteristics and sequence attributes. *Genome Res* **13**(8): 1863-1872.