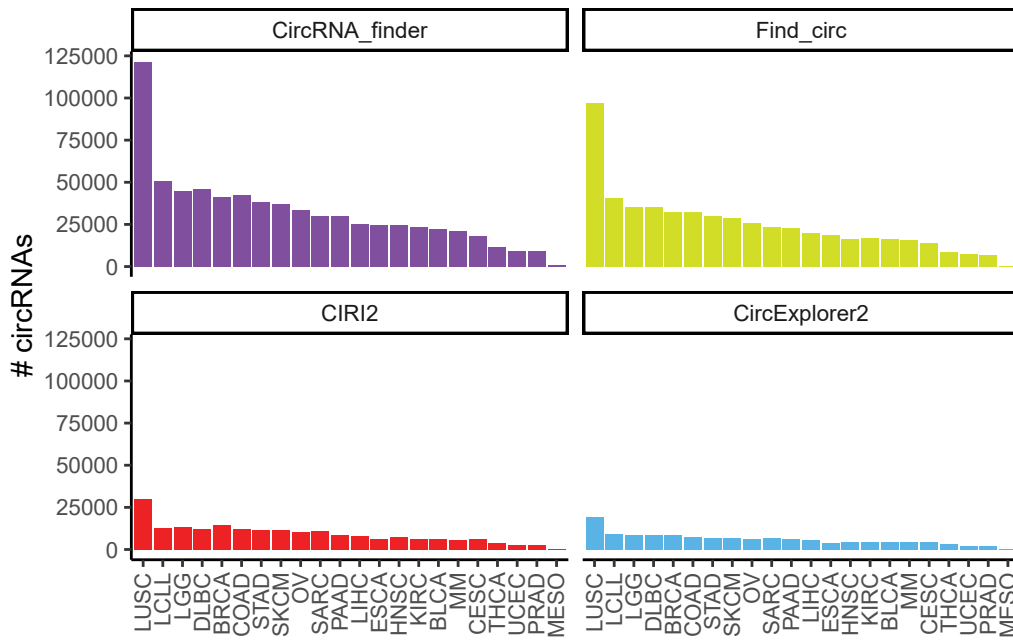
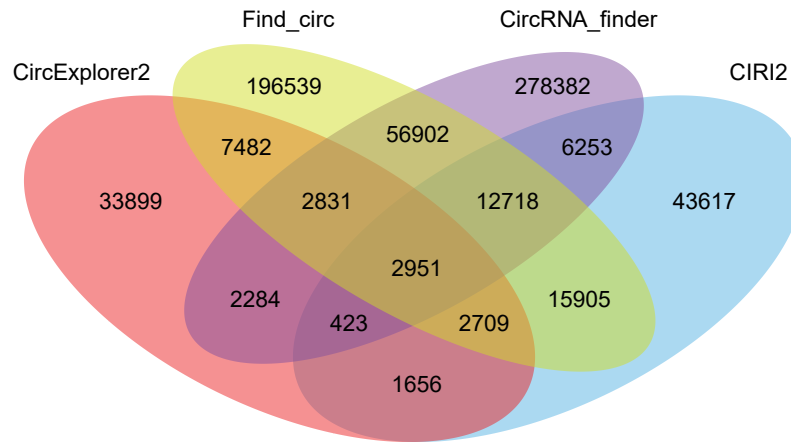


Figure S1

A



B



C

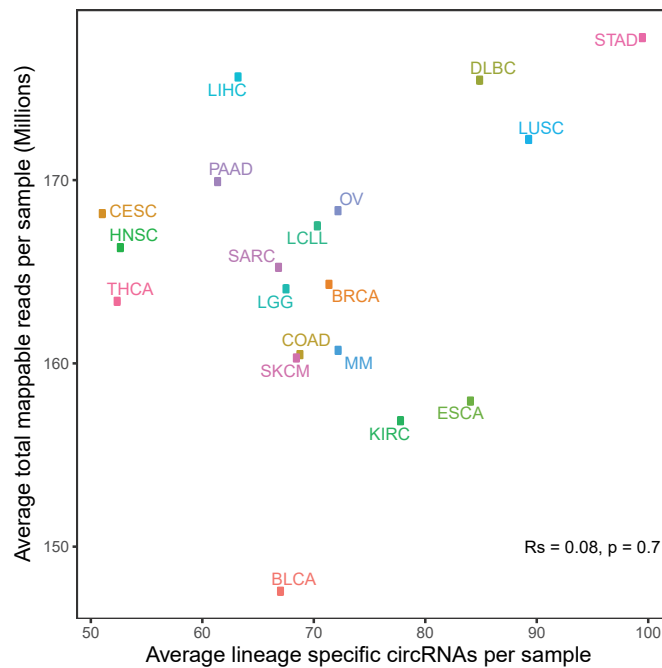


Figure S1. Expression landscape of circRNAs across cancer cell lines.

(A) Numbers of circRNAs detected by four circRNA identification algorithms across cancer cell lines (CircRNA_finder, Find_circ, CIRI2, CircExplorer2). (B) Venn diagram depicting the overlap among the four algorithms. (C) No significant correlation ($R_s = 0.08$, $p = 0.7$) between average cancer lineage specific circRNA and average mappable reads across cancer lineages.

Figure S2

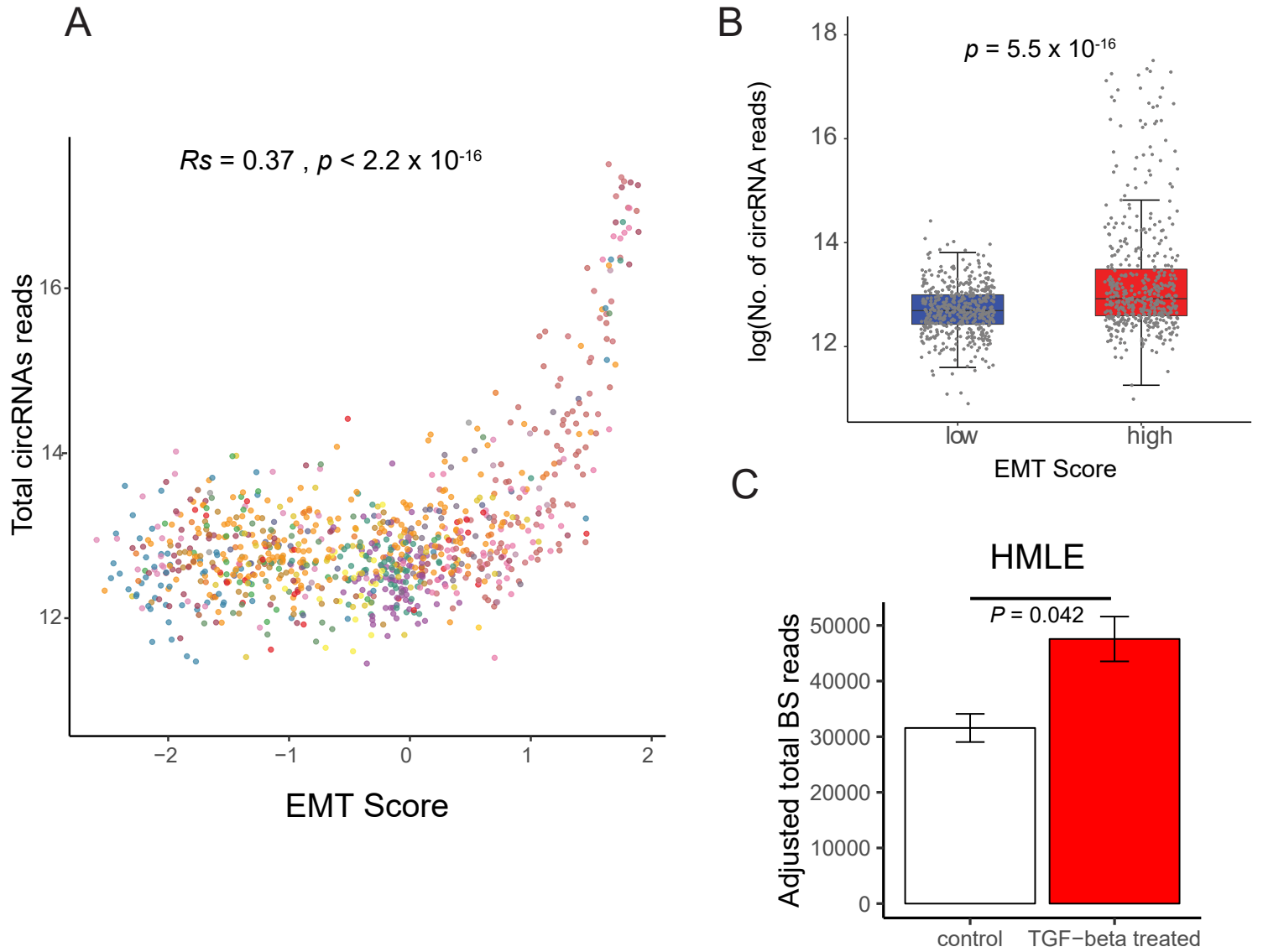
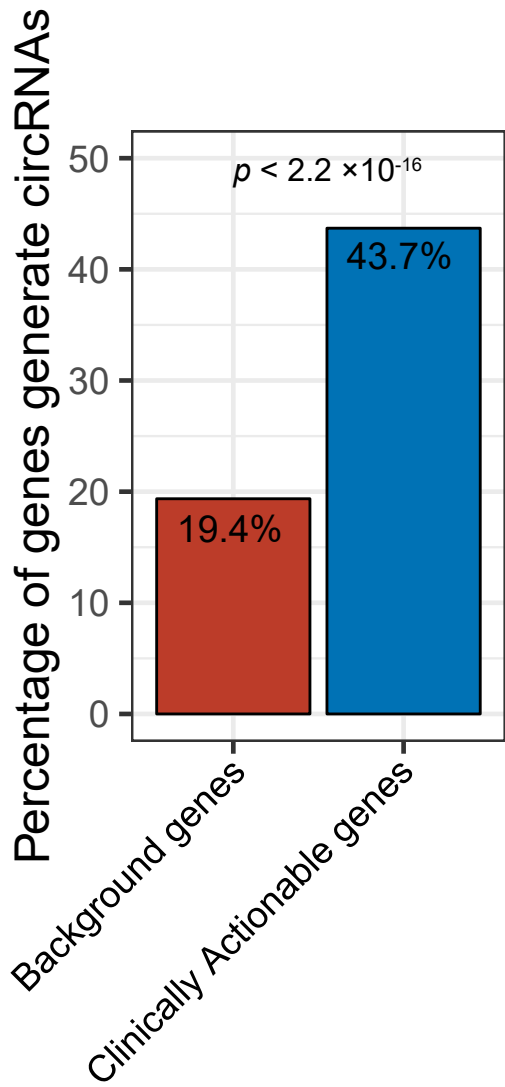


Figure S2. Potential regulation of EMT on biogenesis of circRNAs. (A) Significant correlation between EMT score and total circRNA backsplicing reads across cancer cell lines. (B) Increased number of circRNA backsplicing reads detected from high EMT Score cell lines compared to low EMT Score cell lines. (C) Increased backsplicing reads upon TGF- β treatment in human HMLE cells.

Figure S3

A



B

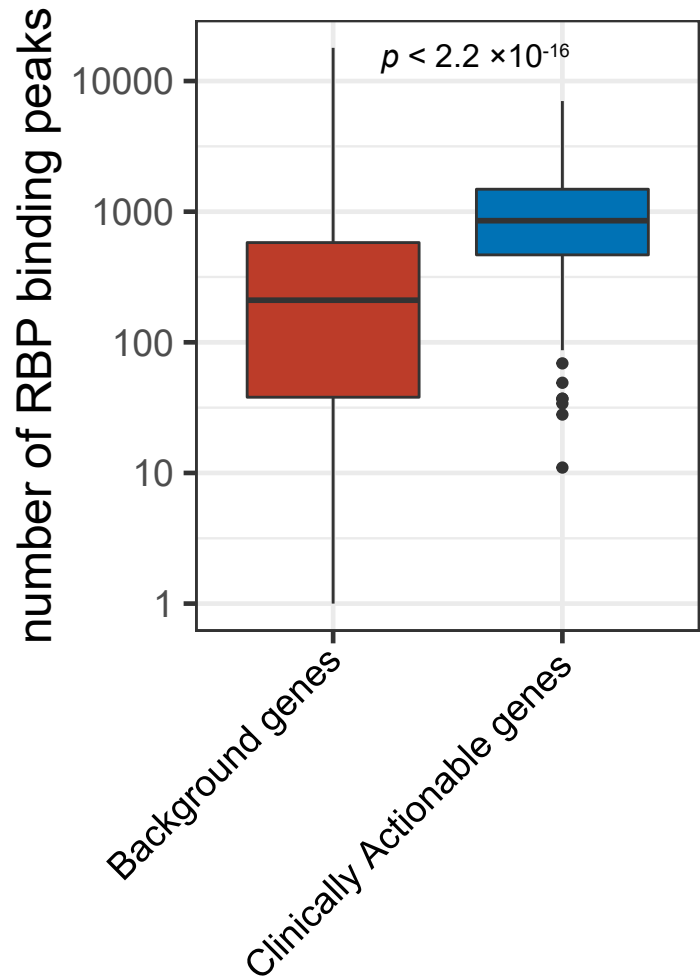


Figure S3. Enrichment of circRNAs in clinically actionable genes.

(A) Enrichment of circRNAs from clinically actionable genes compared with that of background genes (Pearson's Chi-squared test, $p < 2.2 \times 10^{-16}$). (B) Significantly higher number of RBP binding peaks of clinically actionable genes compared to that of background genes (Wilcoxon rank-sum test, $p < 2.2 \times 10^{-16}$).

Figure S4

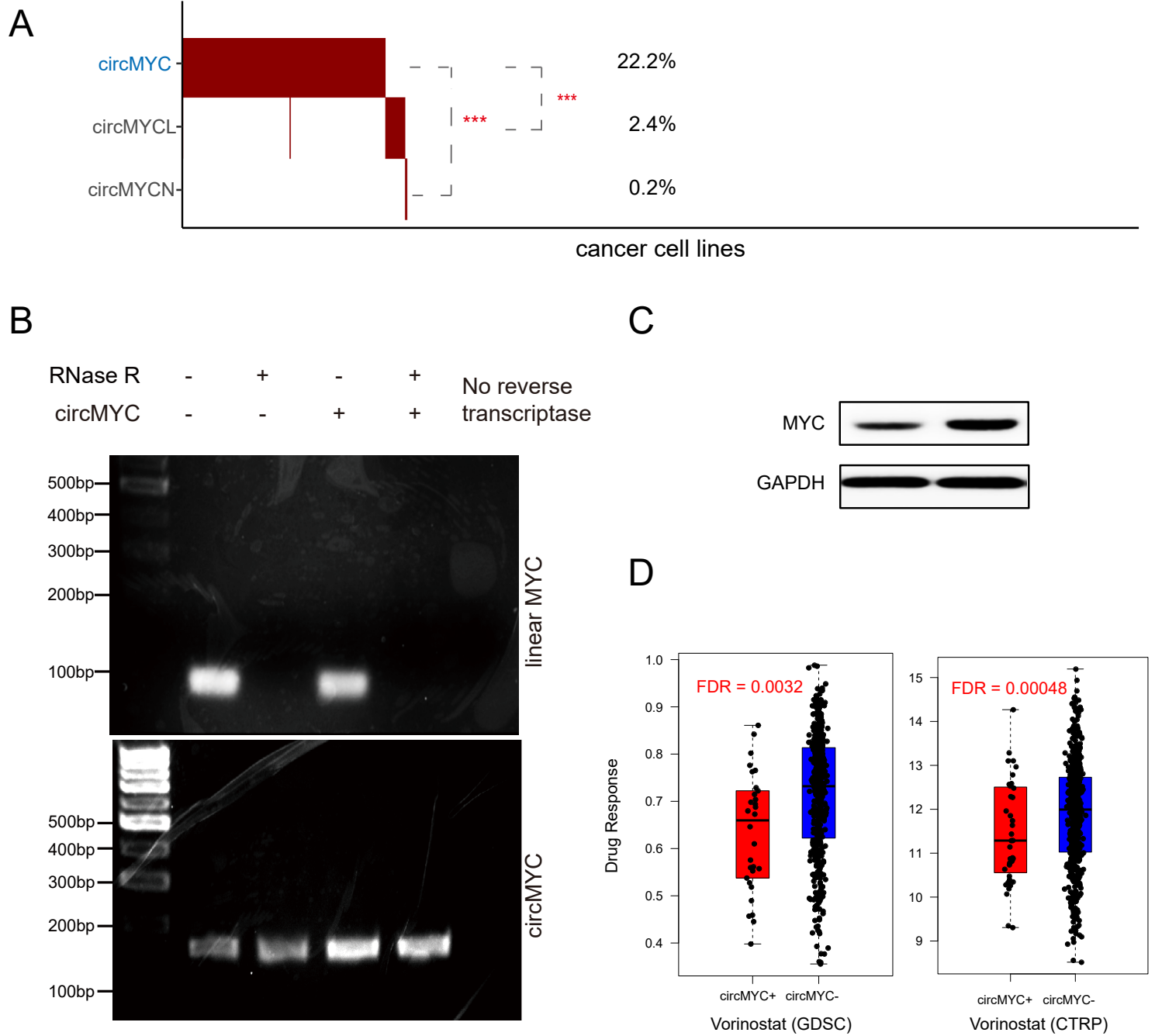


Figure S4. Characterization of functional effects and drug response of circMYC in cancer. (A) CircRNA expression of MYC, MYC human paralogous genes (MYCN and MYCL) across cancer cell lines. (B) PCR of linear MYC and circMYC with or without treatment of RNase R. (C) Overexpression of MYC protein level in MDA-MB-231 cells transfected with circMYC. (D) Comparison of Vorinostat response between circMYC positive and negative cells from GDSC and CTRP dataset (FDR calculated from Wilcoxon rank-sum test with multiple adjustment).

*** : $p < 0.001$

Figure S5

HDAC inhibitors in CTRP

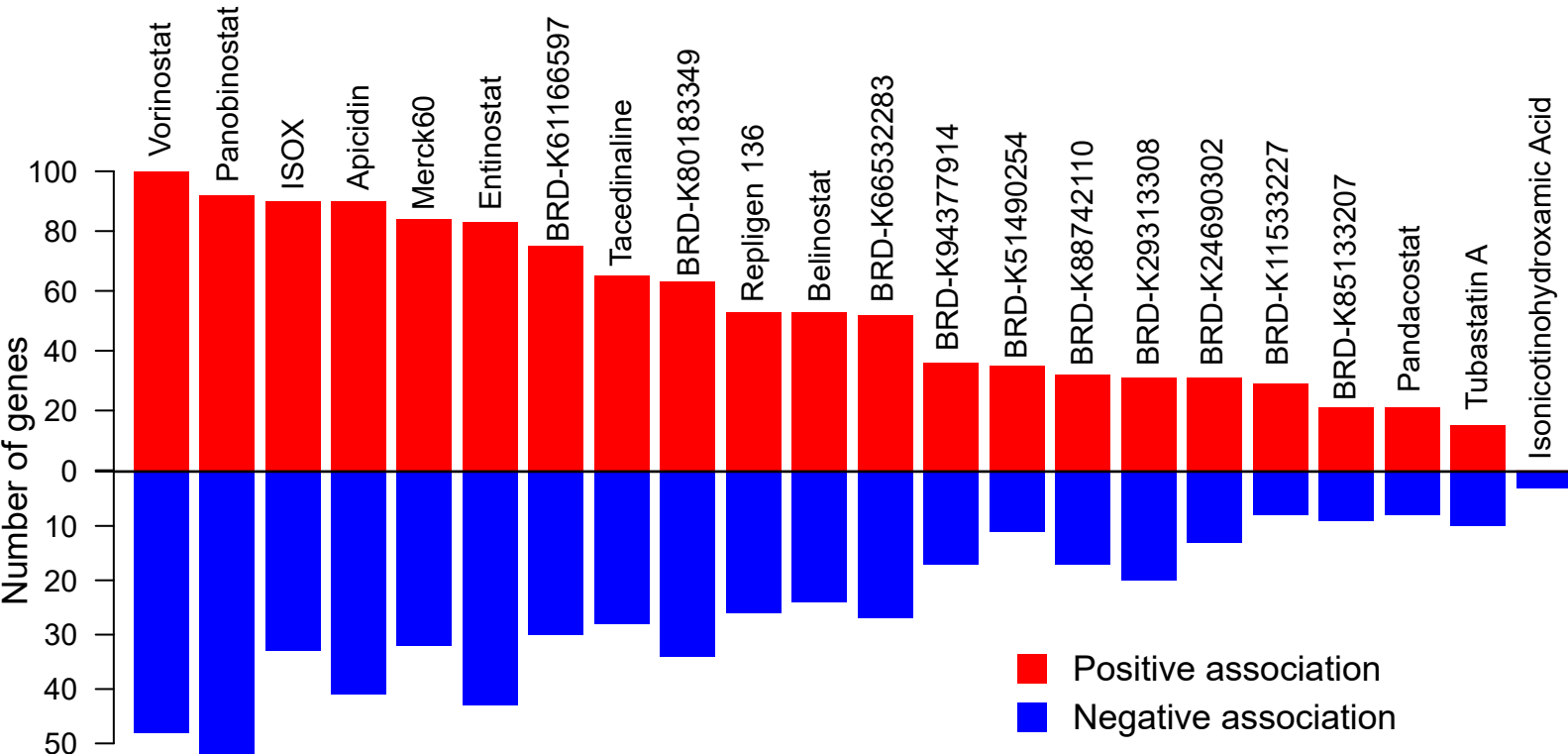


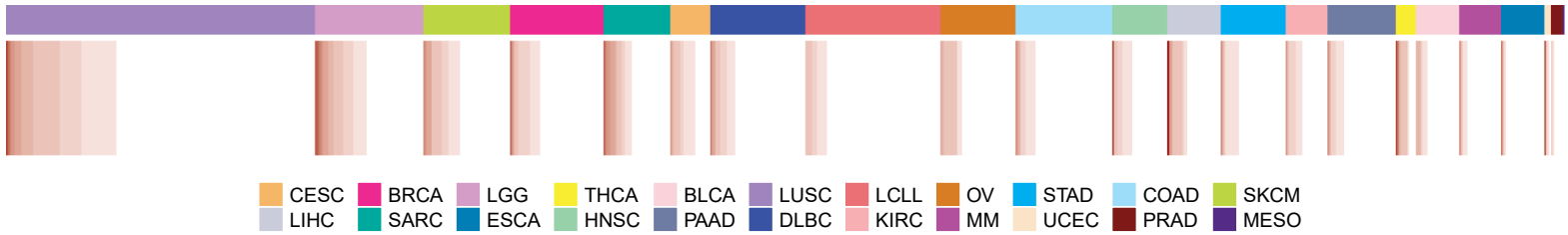
Figure S5. Therapeutic liability of circRNAs in CTRP.

The numbers of HDAC inhibitor drugs significantly associated with circRNAs in Cancer Therapeutic Response Portal (CTRP) dataset. Blue bar denotes negative association and red bar denotes positive association.

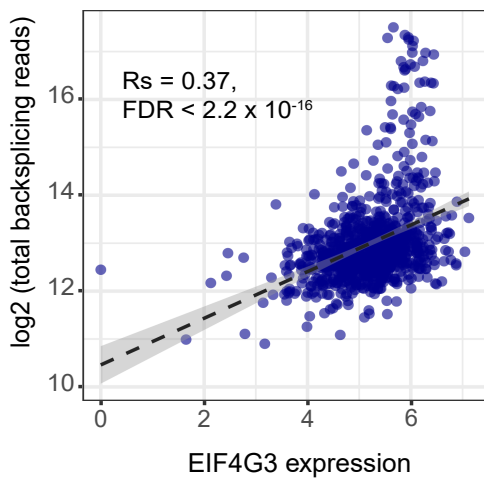
Figure S6

A

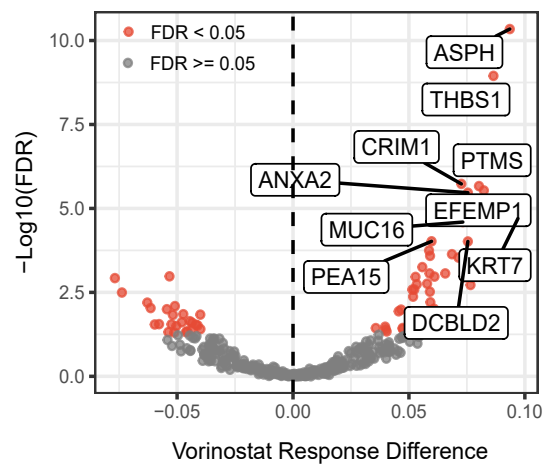
circNotch2:chr1_120508075_120508189



B



C



D

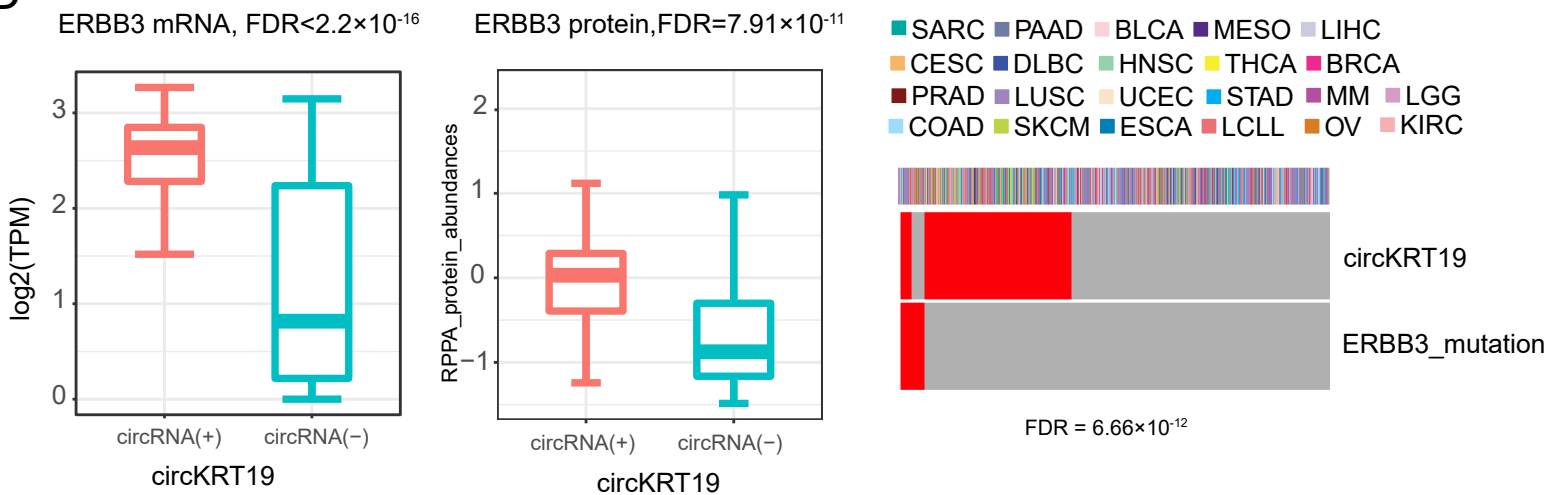


Figure S6. Examples of modules in CircRiC.

(A) Expression landscape of circMYC across different cancer cell lines. (B) Correlation of EIF4G3 gene expression with total backsplicing reads. (C) Association between circRNAs and sensitivity to vorinostat using GDSC drug-response dataset. (D) Associations between circKRT19 and ERBB3 mRNA, protein and mutation profile.

Table S1. Summary of circRNAs identified across different cancer cell lines

Cancer Lineages	No. of cell lines	No. of circRNA
Lung squamous cell carcinoma [LUSC]	186	77284
Chronic lymphocytic leukemia [LCLL]	81	26172
Brain lower grade glioma [LGG]	65	26038
Colon adenocarcinoma [COAD]	58	21450
Diffuse large B-cell lymphoma [DLBC]	57	20654
Breast invasive carcinoma [BRCA]	56	20525
Skin cutaneous melanoma [SKCM]	52	19366
Ovarian serous cystadenocarcinoma [OV]	45	18296
Pancreatic adenocarcinoma [PAAD]	41	17639
Sarcoma [SARC]	40	15715
Stomach adenocarcinoma [STAD]	39	13381
Head and neck squamous cell carcinoma [HNSC]	33	11476
Liver hepatocellular carcinoma [LIHC]	32	10157
Bladder urothelial carcinoma [BLCA]	26	9132
Esophageal carcinoma [ESCA]	26	8899
Kidney renal clear cell carcinoma [KIRC]	25	8177
Multiple myeloma plasma cell leukemia [MM]	25	7786
Cervical squamous cell carcinoma and endocervical adenocarcinoma [CESC]	24	7427
Thyroid carcinoma [THCA]	12	4186
Prostate adenocarcinoma [PRAD]	7	2704
Uterine corpus endometrial carcinoma [UCEC]	4	2684
Mesothelioma [MESO]	1	181