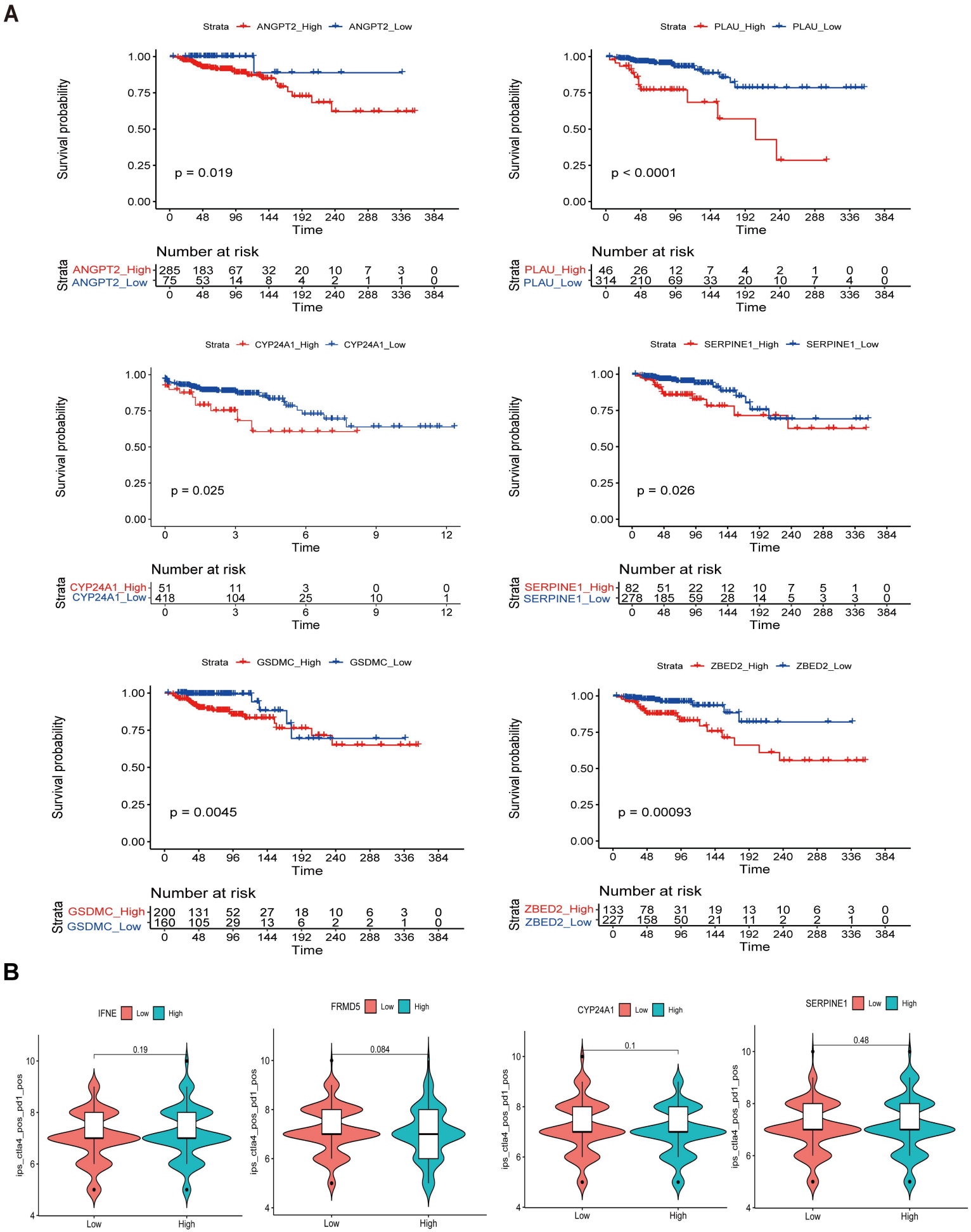


Fig. S1. A. K-M curves showing the prognostic value of genes in the TCGA database. B. Relationship between gene expression and IPS scores.

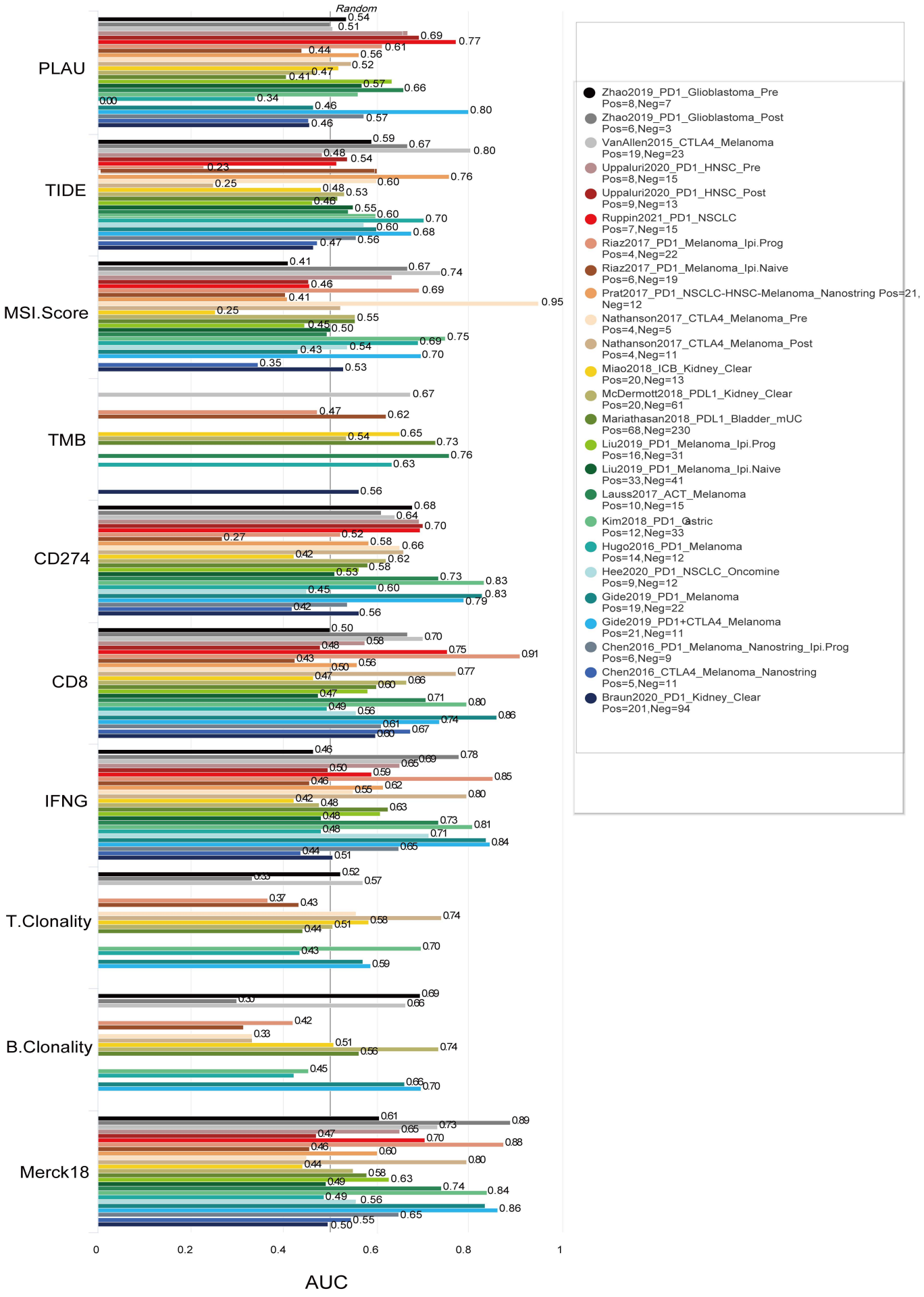


Fig. S2. The predictive capability of PLAU for immunotherapy efficacy in multiple human immunotherapy cohorts. AUC values >0.5 means that the algorithm outperformed random.

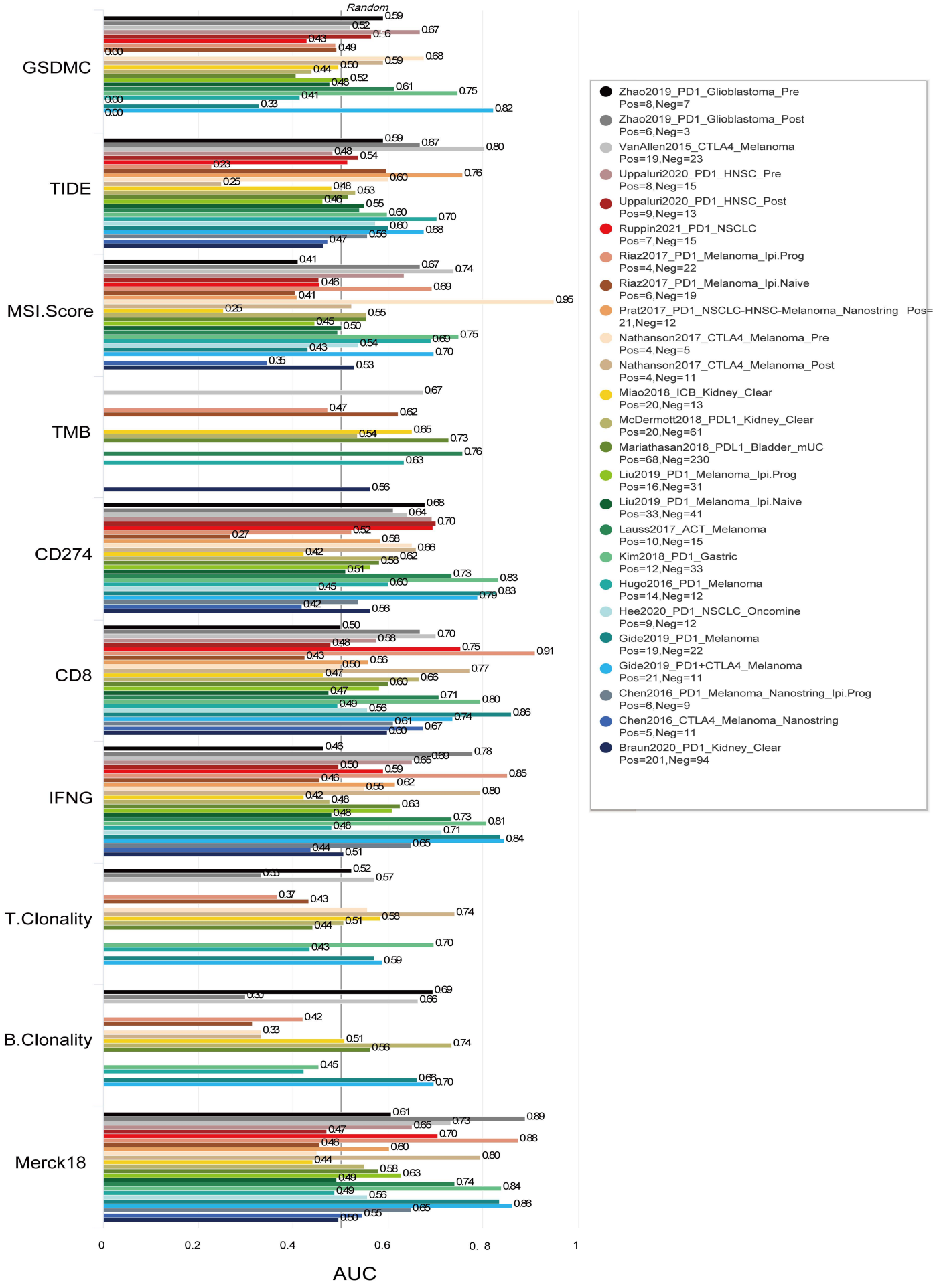


Fig. S3. The predictive capability of GSDMC for immunotherapy efficacy in multiple human immunotherapy cohorts. AUC values >0.5 means that the algorithm outperformed random.

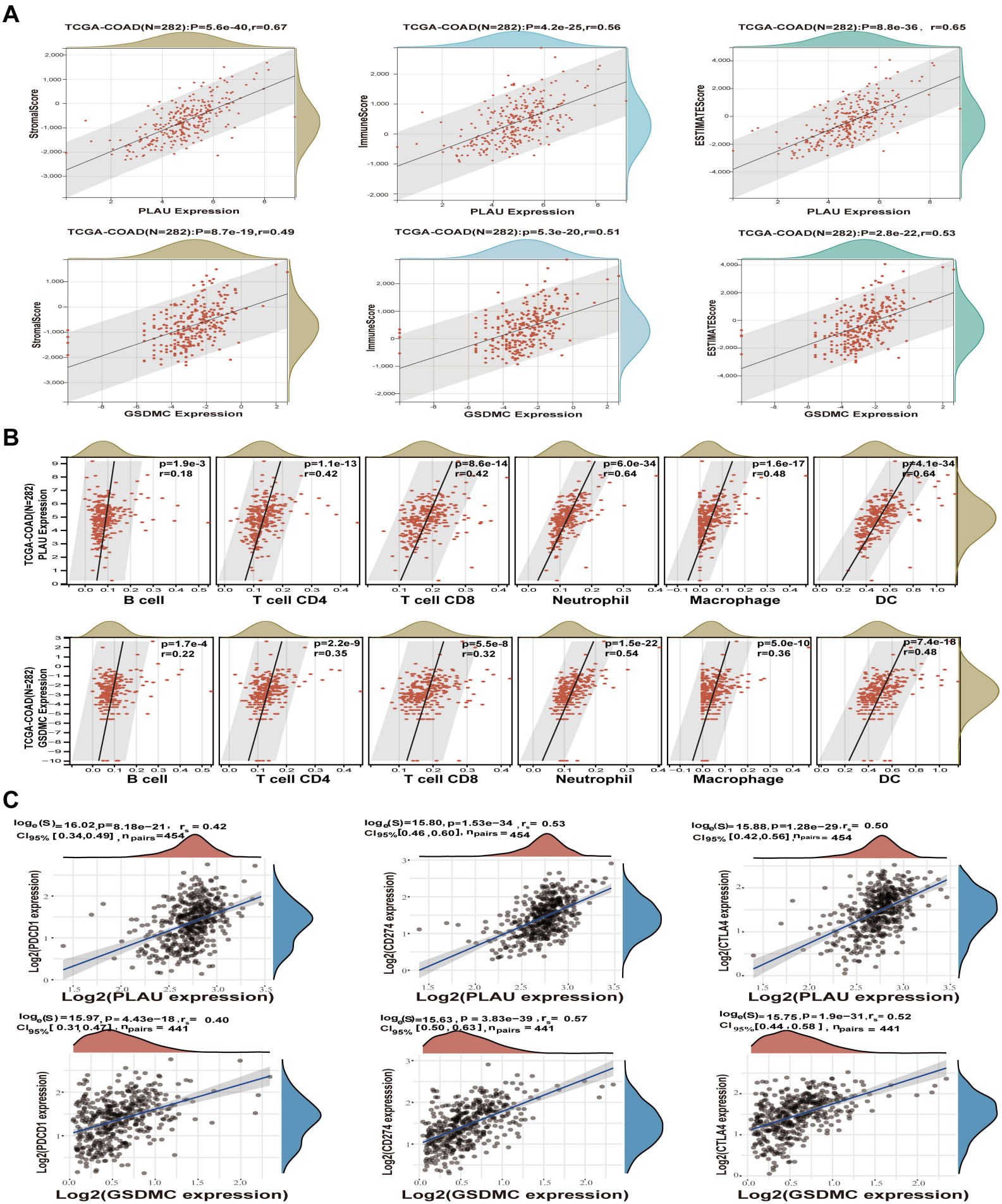
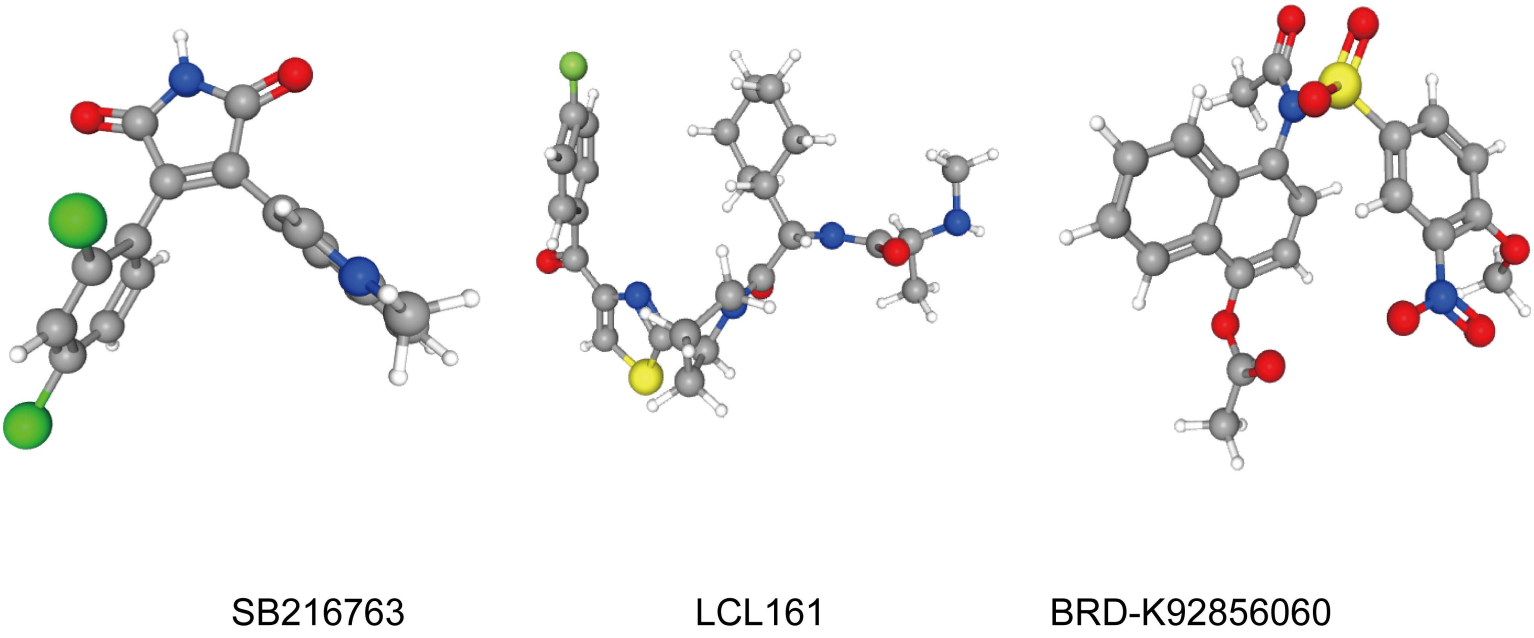


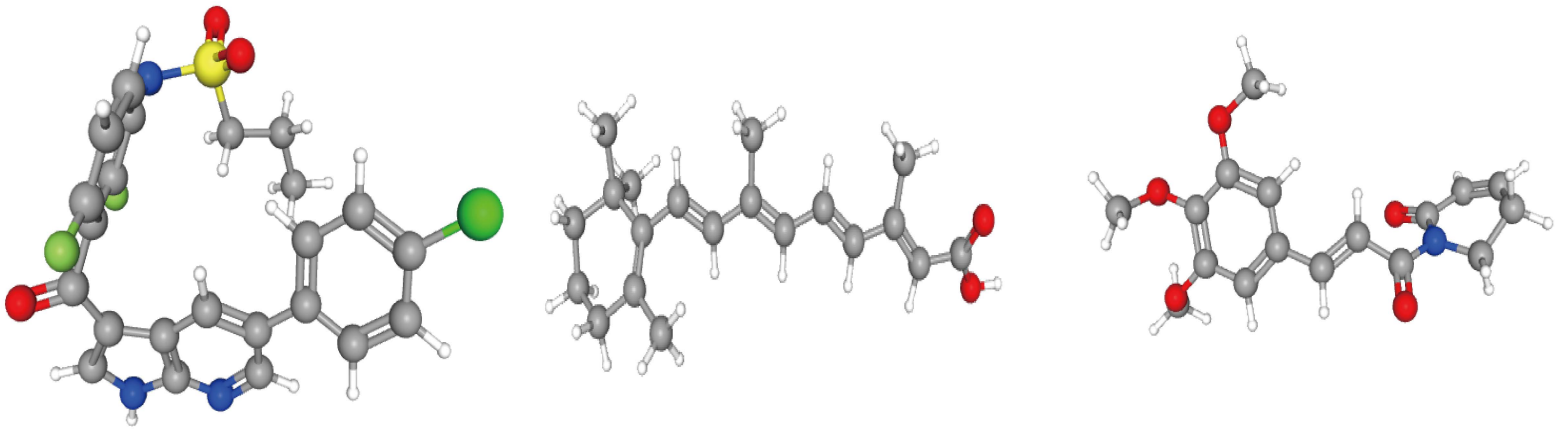
Fig. S4. The correlation between PLAU and GSDMC and tumor microenvironment. A. Spearman correlation between PLAU and GSDMC and immune infiltration scores in COAD. B. Spearman correlation of PLAU and GSDMC expression with immune cell infiltration in COAD. C. Spearman correlation of PLAU and GSDMC expression with immune checkpoint genes in COAD.

A



SB216763 LCL161 BRD-K92856060

B



PLX-4032 Tretinoin Piperlongumine

Fig. S5. Three-dimensional structure of small molecule drugs. A. Three drug structures with revelance to PLAU protein. B. Three drug structures with relevance to GSDMC protein.

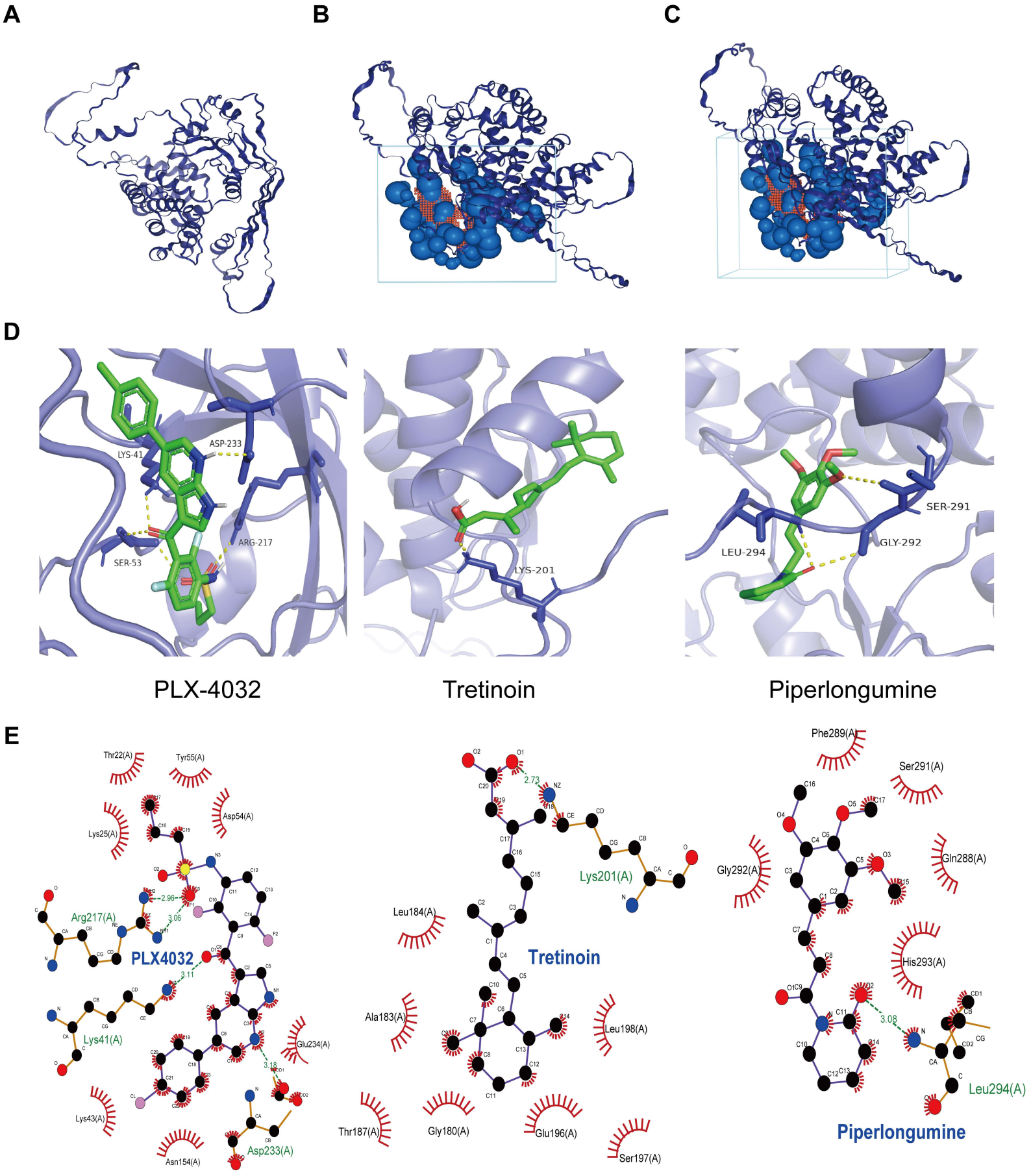


Fig. S6. Screening sensitive drugs for GSDMC protein. A. Three-dimensional structure of the GSDMC protein. B-C. Predicting the potential binding sites and box on GSDMC protein. D. Analysis of the binding conformation of sensitive drugs to GSDMC protein. E. Visualization of the two-dimensional structure of drugs bound to GSDMC protein.

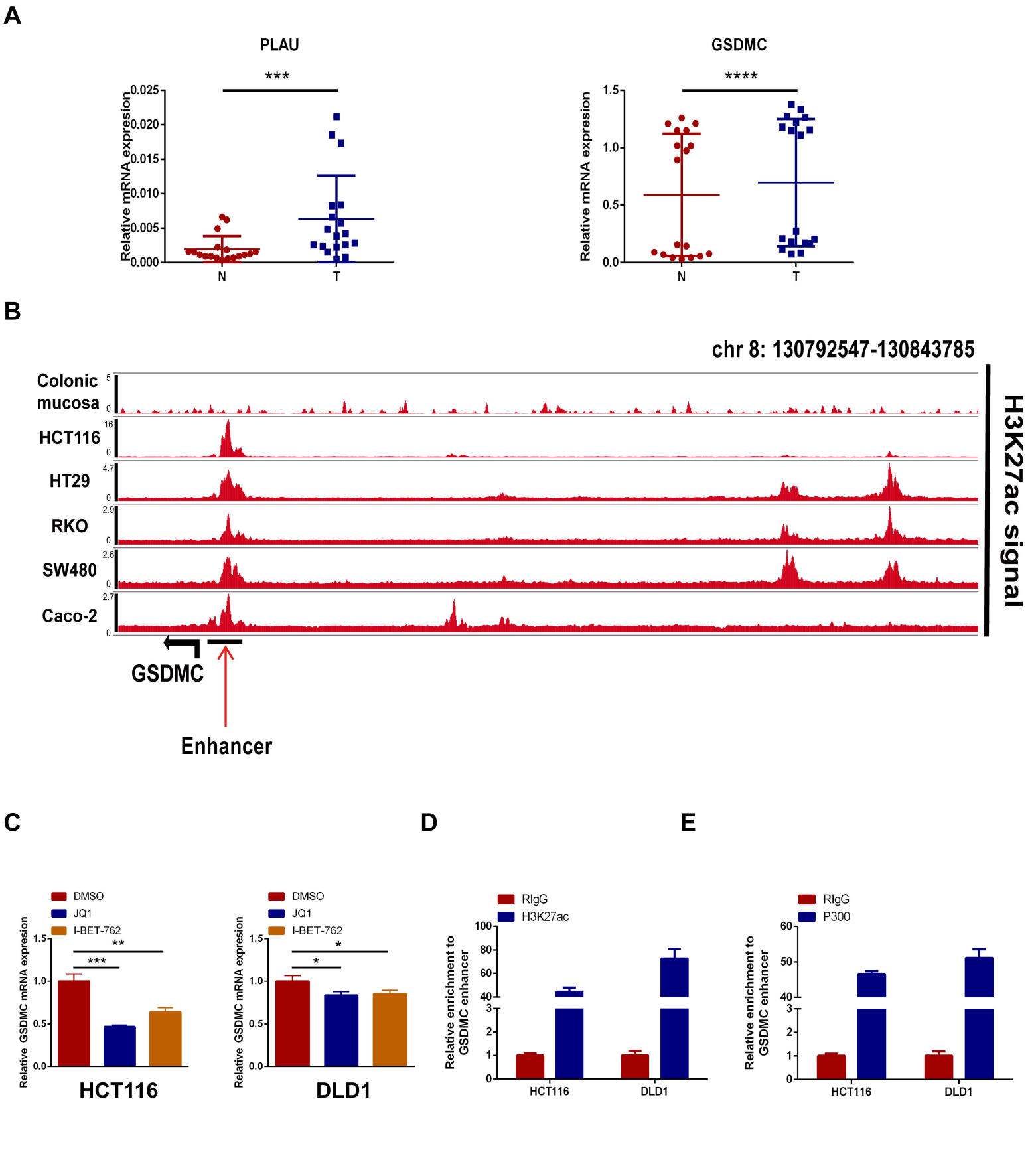


Fig. S7. A. The PLAU and GSDMC mRNA levels are upregulated in colorectal cancer tissues. B. ChIP-seq profiles of H3K27ac signal in the GSDMC gene locus in different colorectal cancer cells. C. The expression levels of GSDMC in HCT116 and DLD1 cells treated with JQ1 and I-BET-762 were detected by qPCR. D. The relative enrichment of H3K27ac in the GSDMC gene locus by ChIP-qPCR. E. The relative enrichment of P300 in the GSDMC gene locus by ChIP-qPCR.

Table S1. Optimal cutpoint values for survival analysis in TCGA data

Gene	Cutpoint	Statistic
ANGPT2	4.9976	1.920288
PLAU	22.6167	4.614342
ZBED2	0.4577	3.527775
GSDMC	0.3892	2.780785
SERPINE1	13.1105	2.318292
CYP24A1	0.0122	2.193734

Table S2. Risk genes through LASSO-COX regression analysis

Gene	Coef
FRMD5	0.216124258026923
SERPINE1	0.380973652346092
IFNE	0.0324982140801412
GSDMC	-0.100682905697296
PLAU	-0.426532126648938
CYP24A1	-0.0722131730892283

Table S3. Predicted sensitive drugs for PLAU and GSDMC protein

Gene	Drug	correlation	P value
PLAU	LCL161	-0.384101575864601	0.0100508963427865
PLAU	BRD-K92856060	-0.354598006593615	0.0181894618432729
PLAU	SB216763	-0.345849056176333	0.0214749590774912
PLAU	pifithrin-alpha	-0.345438430151654	0.0216406558417136
PLAU	OSI-027	-0.322293723193538	0.0328749889192166
PLAU	BRD4132	-0.303956960192454	0.0448650047546461
PLAU	CZC24832	-0.314594126928421	0.0375401854291833
PLAU	KH-CB19	-0.298226223304054	0.0492687879305438
GSDMC	PLX-4032	-0.604406556849717	1.39463661374655e-05
GSDMC	compound 1B	-0.44997122838213	0.00217956637794985
GSDMC	tretinoin	-0.392861597977969	0.0083414534268593
GSDMC	ciclosporin	-0.390148362319898	0.00884187985649159
GSDMC	navitoclax:piperlongumine (1:1 mol/mol)	-0.348109390957182	0.02058180123836
GSDMC	tretinoin:navitoclax (4:1 mol/mol)	-0.329892280309851	0.0287506472488793
GSDMC	navitoclax:pluripotin (1:1 mol/mol)	-0.324118006689932	0.0318427945125299
GSDMC	navitoclax:MST-312 (1:1 mol/mol)	-0.313115279046431	0.0384955684563447
GSDMC	tretinoin:carboplatin (2:1 mol/mol)	-0.302258813280389	0.0461352281859266

Table S4. Energy values docking simulation of PLAU and GSDMC with drugs

Gene	Drug	Estimated Free Energy of Binding
PLAU	SB216763	-4.15 kcal/mol
PLAU	LCL161	-5.59 kcal/mol
PLAU	BRD-K92856060	- 6.17kcal/mol
GSDMC	PLX-4032	-3.57 kcal/mol
GSDMC	Tretinoin	-4.08 kcal/mol
GSDMC	Piperlongumine	-2.99 kcal/mol