



Figure S1 Western blotting to verify the expression of GPRC5A in lung cancer cell lines. (A) Western blot for GAPDH (37 kDa). (B) Western blot for GPRC5A (about 37–43 kDa). GPRC5A, G-protein-coupled receptor family C group 5 type A.

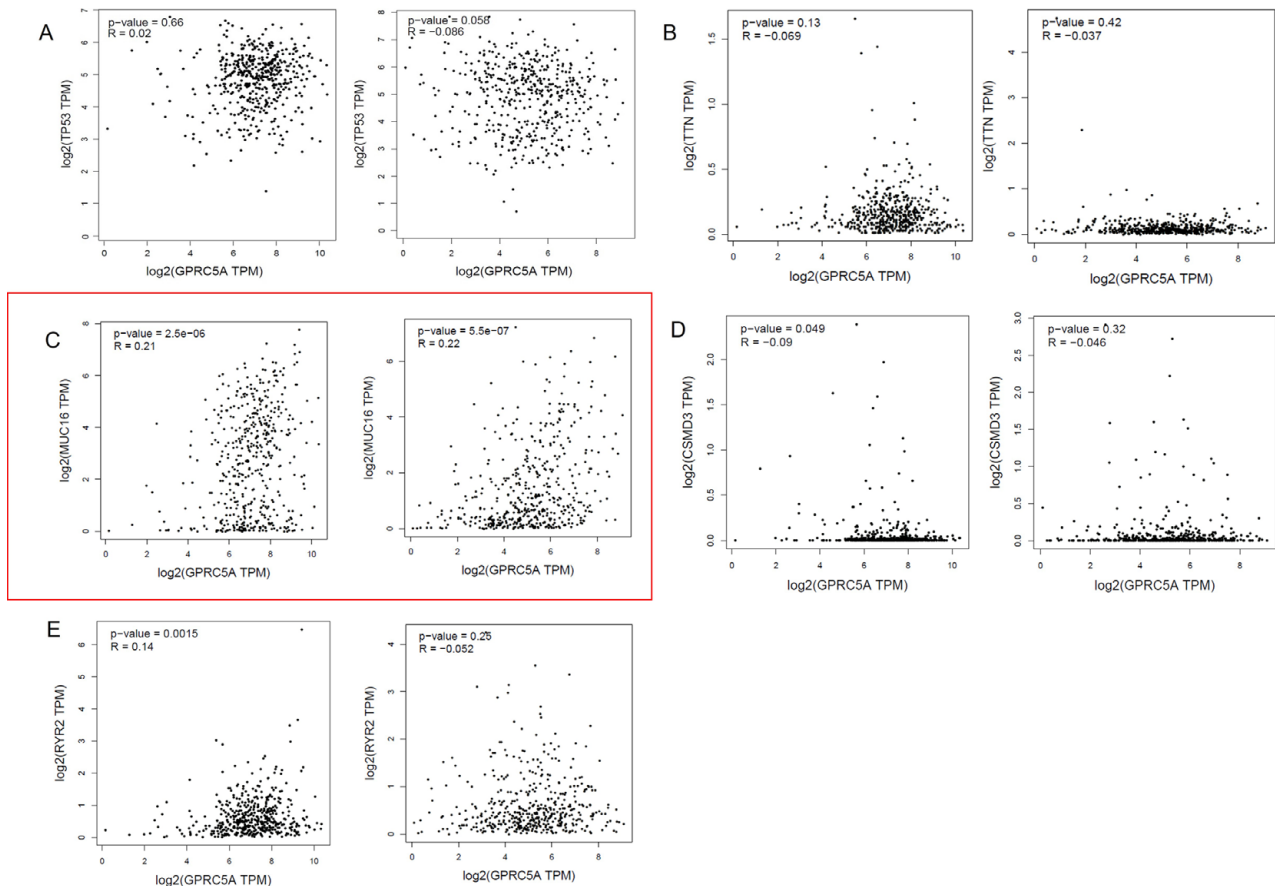
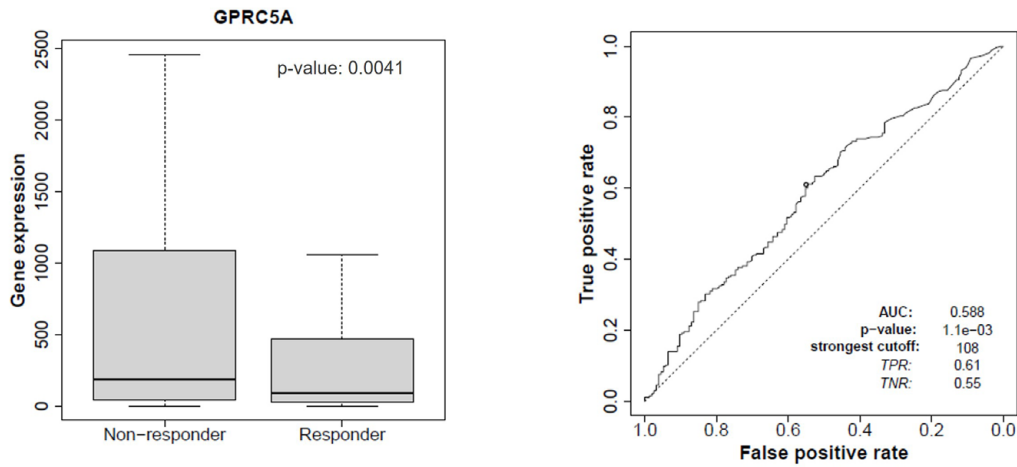


Figure S2 Correlation analysis of genes in the top 5 mutated genes with *GPRC5A* [this figure was automatically exported by GEPIA (<http://gepia.cancer-pku.cn/>)]. (A) The correlation between *GPRC5A* and *TP53* in LUAD and LUSC was verified by GEPIA. (B) The correlation between *GPRC5A* and *TTN* in LUAD and LUSC was verified by GEPIA. (C) The correlation between *GPRC5A* and *MUC16* in LUAD and LUSC was verified by GEPIA. (D) The correlation between *GPRC5A* and *CSMD3* in LUAD and LUSC was verified by GEPIA. (E) The correlation between *GPRC5A* and *RYR2* in LUAD and LUSC was verified by GEPIA. The red square represented the association between *GPRC5A* and *MUC16* in LUAD and LUSC, and the correlation coefficients were 0.21 and 0.22, respectively. *GPRC5A*, G-protein-coupled receptor family C group 5 type A; *TTN*, titin; *MUC16*, mucin16; *CSMD3*, CUB and Sushi multiple domains 3; *RYR2*, ryanodine receptor 2; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; GEPIA, Gene Expression Profiling Interactive Analysis; TPM, transcripts per million.

A. The relationship between GPRC5A expression and anti-PD-1 efficacy in pan-cancer.



B. The relationship between GPRC5A expression and anti-CTLA-4 efficacy in pan-cancer.

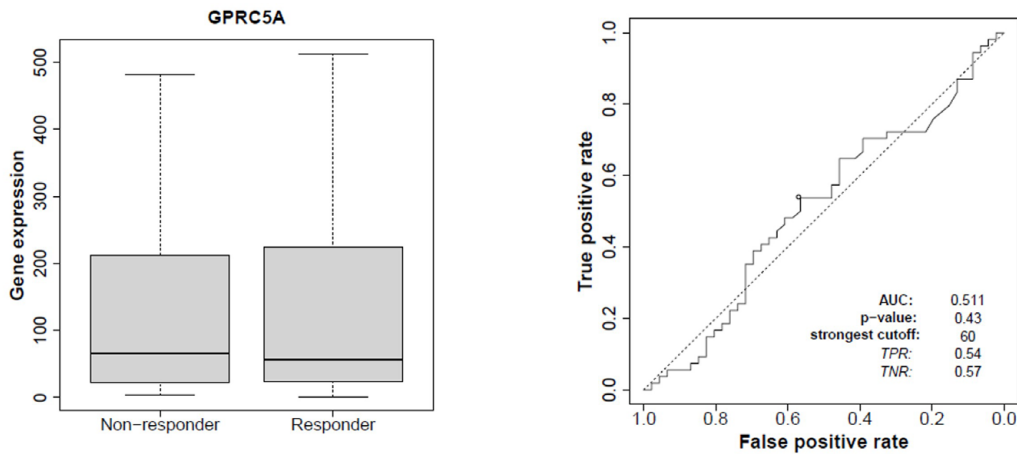


Figure S3 The association of GPRC5A expression and immunotherapy efficacy in pan-cancer. (A) The relationship between GPRC5A expression and anti-PD-1 efficacy in pan-cancer. (B) The relationship between GPRC5A expression and anti-CTLA-4 efficacy in pan-cancer. GPRC5A, G-protein-coupled receptor family C group 5 type A; anti-PD-1, anti-programmed cell death protein 1; anti-CTLA4, anti-cytotoxic T-lymphocyte-associated protein 4; AUC, area under the curve; TPR, true positive rate; TNR, true negative rate.

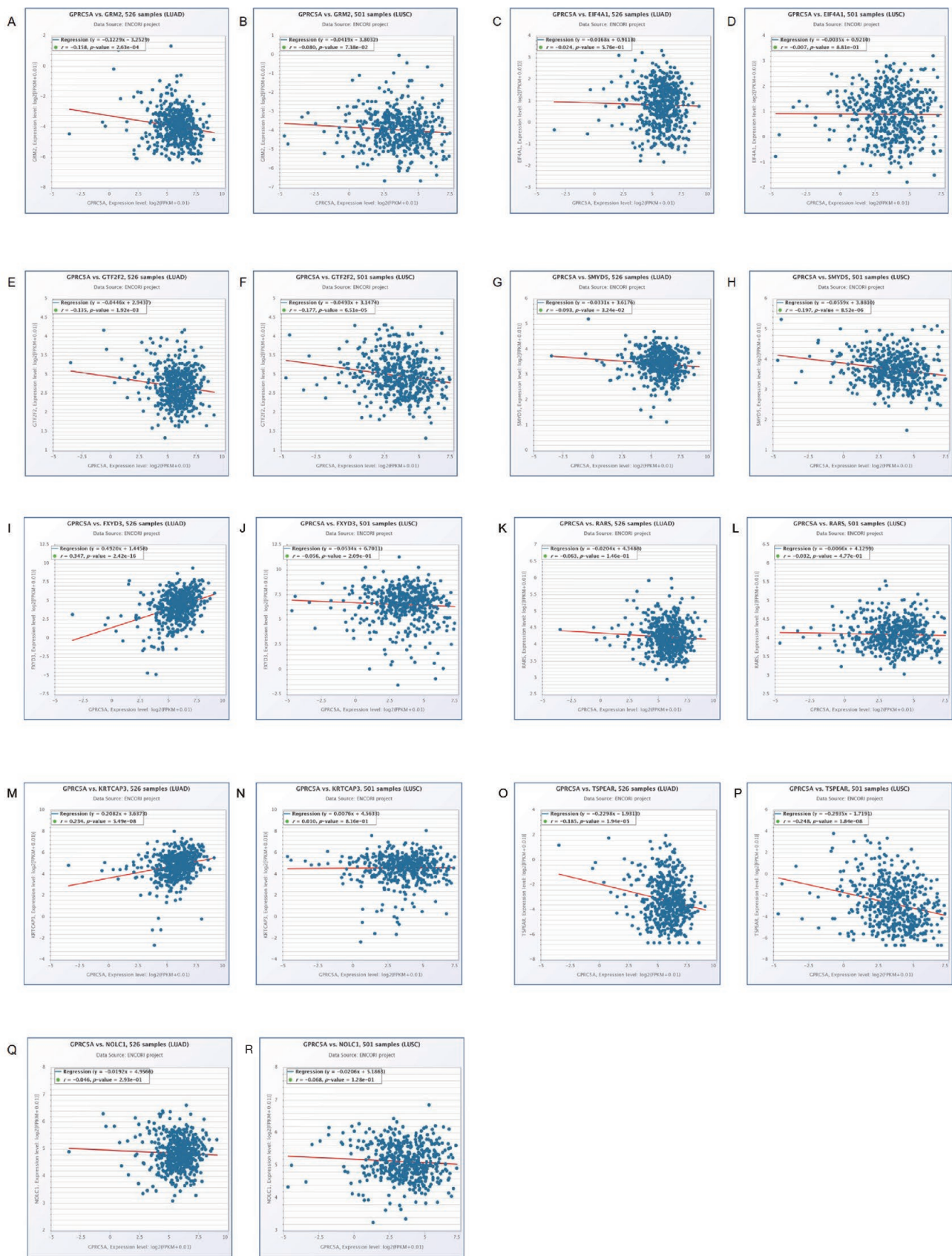


Figure S4 Correlation analysis of genes in the PPI network with *GPRC5A*. (A,B) The correlation between *GPRC5A* and *GRM2* was verified by ENCORI. (C,D) The correlation between *GPRC5A* and *EIF4A1* was verified by ENCORI. (E,F) The correlation between *GPRC5A* and *GTF2F2* was verified by ENCORI. (G,H) The correlation between *GPRC5A* and *SMYD5* was verified by ENCORI. (I,J) The correlation between *GPRC5A* and *FXYD3* was verified by ENCORI. (K,L) The correlation between *GPRC5A* and *RARS* was verified by ENCORI. (M,N) The correlation between *GPRC5A* and *KRTCAP3* was verified by ENCORI. (O,P) The correlation between *GPRC5A* and *TSPEAR* was verified by ENCORI. (Q,R) The correlation between *GPRC5A* and *NOLC1* was verified by ENCORI. PPI, protein-protein interaction; LUAD, lung adenocarcinoma; LUSC, lung squamous cell carcinoma; *GPRC5A*, G-protein-coupled receptor family C group 5 type A; *GRM2*, glutamate metabotropic receptor 2; *EIF4A1*, eukaryotic translation initiation factor 4A1; *GTF2F2*, general transcription factor III F subunit 2; *SMYD5*, SMYD family member 5; *FXYD3*, FXYD domain containing ion transport regulator 3; *RARS*, arginine-tRNA ligase; *KRTCAP3*, keratinocyte associated protein 3; *TSPEAR*, thrombospondin-type laminin G domain and EAR repeat-containing protein; *NOLC1*, nucleolar and coiled-body phosphoprotein 1.

Table S1 Correlations between GPRC5A expression and clinicopathological characteristics of patients with NSCLC in TCGA cohort

Characteristics	Total (N=1011)	Low expression (N=512)	High expression (N=499)	P value
Sex				0.88
Male	600 (59%)	305 (60%)	295 (59%)	
Female	411 (41%)	207 (40%)	204 (41%)	
Age (years)				0.11
<62	303 (30%)	165 (32%)	138 (28%)	
≥62	708 (70%)	347 (68%)	361 (72%)	
Smoking status				0.71
Never	238 (24%)	123 (24%)	115 (23%)	
Ever	773 (76%)	389 (76%)	384 (77%)	
Histological type				0.96
ADC	528 (52%)	267 (52%)	261 (52%)	
SCC	483 (48%)	245 (48%)	238 (48%)	
pStage				0.04*
I	527 (52%)	254 (50%)	273 (54%)	
II	287 (28%)	164 (32%)	123 (25%)	
III	165 (17%)	82 (16%)	83 (17%)	
IV	32 (3%)	12 (2%)	20 (4%)	
T stage				0.18
T1	282 (28%)	134 (26%)	148 (30%)	
T2	570 (56%)	296 (58%)	274 (55%)	
T3	116 (12%)	65 (13%)	51 (10%)	
T4	43 (4%)	17 (3%)	26 (5%)	
N stage				0.27
N0	672 (66%)	331 (65%)	341 (68%)	
N1	222 (22%)	123 (24%)	99 (20%)	
N2-3	117 (12%)	58 (11%)	59 (12%)	
M stage				0.13
M0	979 (97%)	500 (98%)	479 (96%)	
M1	32 (3%)	12 (2%)	20 (4%)	

*, P value <0.05. GPRC5A, G-protein-coupled receptor family C group 5 type A; NSCLC, non-small cell lung cancer; TCGA, The Cancer Genome Atlas; ADC, adenocarcinoma; SCC, squamous cell carcinoma; pStage, pathological stage; T stage, tumor stage; N stage, node stage; M stage, metastasis stage.

Table S2 Predictors of DFS in NSCLC assessed by univariate and multivariate Cox regression

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Sex	0.374 (0.146–0.954)	0.04	0.414 (0.095–1.806)	0.24
Smoking	1.663 (0.813–3.400)	0.16	0.894 (0.309–2.590)	0.84
pStage	1.850 (1.372–2.495)	<0.001	3.397 (1.419–8.131)	0.006
Size	1.755 (1.440–2.138)	<0.001	0.609 (0.293–1.265)	0.18
T stage	3.411 (2.261–5.147)	<0.001	4.814 (1.280–18.10)	0.02
N stage	1.608 (1.153–2.243)	0.005	0.573 (0.255–1.284)	0.18
M stage	1.986 (0.701–5.625)	0.20	0.244 (0.047–1.268)	0.09
PI	1.279 (0.689–2.373)	0.43	0.743 (0.345–1.597)	0.45
VI	2.256 (1.217–4.182)	0.01	1.277 (0.486–3.353)	0.62
PNI	1.844 (0.647–5.255)	0.25	1.108 (0.261–4.703)	0.89
Low GPRC5A	0.623 (0.330–1.179)	0.15	0.165 (0.034–0.796)	0.02

DFS, disease-free survival; NSCLC, non-small cell lung cancer; HR, hazard ratio; CI, confidence interval; pStage, pathological stage; T stage, tumor stage; N stage, node stage; M stage, metastasis stage; PI, pleural invasion; VI, vascular invasion; PNI, perineural invasion; GPRC5A, G-protein-coupled receptor family C group 5 type A.