

**Supplementary**

**Table S1** Survival analysis on the correlation of *NPRL2* expression and prognosis of STAD patients with different pathological features accessed from KM plotter

Factor	Subgroup	Sample size	OS		FP		PPS	
			HR	P	HR	P	HR	P
Stage	Stage 1	69	0.61	0.33	0.49	0.21	6.50E+10	3.40E-05
	Stage 2	145	0.4	0.0059	0.4	0.0063	0.51	0.068
	Stage 3	319	1.63	0.0016	0.79	0.23	1.25	0.3
	Stage 4	152	0.59	0.01	0.57	0.0048	0.78	0.27
Stage T	T2	253	0.42	0.0014	0.45	0.0016	0.66	0.16
	T3	208	0.83	0.3	0.78	0.16	1.24	0.28
	T4	39	2.2	0.15	1.89	0.2	1.51	0.42
Stage N	N0	76	0.14	0.027	0.12	0.013	2.32	0.19
	N1	232	0.6	0.019	0.64	0.031	0.65	0.073
	N2	129	0.73	0.18	0.81	0.36	1.43	0.17
	N3	76	0.52	0.021	0.48	0.0086	0.63	0.11
Stage M	M0	459	0.61	0.00084	0.59	0.00018	0.82	0.22
	M1	58	0.5	0.026	0.45	0.01	1.34	0.44
Lauren classification	Intestinal	336	1.33	0.094	0.71	0.066	1.31	0.21
	Diffuse	248	0.67	0.028	0.53	0.00094	0.66	0.032
	Mixed	33	0.47	0.14	1.85	0.25	NA	NA
Differentiation	Poorly	166	0.83	0.45	1.39	0.2	0.55	0.11
	Moderately	67	0.7	0.28	0.59	0.1	3.06	0.025
	Well	32	0.54	0.16	NA	NA	NA	NA
Gender	Female	244	0.66	0.021	0.52	0.00086	0.76	0.2
	Male	566	0.78	0.023	0.71	0.0051	0.8	0.086
Perforation	No	169	0.62	0.03	0.58	0.011	1.6	0.086
Treatment	Surgery alone	393	0.58	5.00E-04	0.554	2.00E-04	0.77	0.16
	5-Fu based adjuvant	157	1.4	0.09	1.34	0.13	1.61	0.013
	Other adjuvant	80	0.34	0.012	0.46	0.051	0.25	0.0021
HER2	Negative	641	0.7	0.0022	0.52	1.30E-05	0.65	0.003
	Positive	425	0.85	0.24	0.77	0.17	1.48	0.032

**Table S2** The top 100 gene co-expressed with *NPRL2* acquired from GEPIA 2

Gene symbol	Gene ID	PCC
<i>APEH</i>	ENSG00000164062.12	0.63
<i>NME6</i>	ENSG00000172113.8	0.63
<i>NCKIPSD</i>	ENSG00000213672.7	0.6
<i>RHOA</i>	ENSG00000067560.10	0.59
<i>ATRIP</i>	ENSG00000164053.17	0.58
<i>QARS</i>	ENSG00000172053.14	0.58
<i>OXSM</i>	ENSG00000151093.7	0.58
<i>EAF1</i>	ENSG00000144597.13	0.57
<i>UQCRC1</i>	ENSG00000010256.10	0.57
<i>CYB561D2</i>	ENSG00000114395.10	0.57
<i>IMPDH2</i>	ENSG00000178035.11	0.56
<i>CCDC51</i>	ENSG00000164051.13	0.56
<i>DALRD3</i>	ENSG00000178149.16	0.56
<i>LZTFL1</i>	ENSG00000163818.16	0.55
<i>RASSF1</i>	ENSG00000068028.17	0.55
<i>IFRD2</i>	ENSG00000214706.10	0.55
<i>CHCHD4</i>	ENSG00000163528.12	0.55
<i>TEX264</i>	ENSG00000164081.12	0.55
<i>RFT1</i>	ENSG00000163933.9	0.55
<i>POC1A</i>	ENSG00000164087.7	0.55
<i>ELP6</i>	ENSG00000163832.15	0.54
<i>GNL3</i>	ENSG00000163938.16	0.53
<i>TRAIIP</i>	ENSG00000183763.8	0.53
<i>HEMK1</i>	ENSG00000114735.9	0.52
<i>RPP14</i>	ENSG00000255154.7	0.52
<i>POMGNT2</i>	ENSG00000144647.5	0.52
<i>TADA1</i>	ENSG00000152382.5	0.51
<i>P4HTM</i>	ENSG00000178467.17	0.51
<i>NARF</i>	ENSG00000141562.17	0.51
<i>XRCC6</i>	ENSG00000196419.12	0.51
<i>TUSC2</i>	ENSG00000114383.9	0.51
<i>QRICH1</i>	ENSG00000198218.10	0.51
<i>WDR82</i>	ENSG00000164091.11	0.5
<i>TIPRL</i>	ENSG00000143155.12	0.5

**Table S2** (continued)

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Gene symbol	Gene ID	PCC
<i>TMEM115</i>	ENSG00000126062.3	0.5
<i>EIF3I</i>	ENSG00000084623.11	0.5
<i>SHQ1</i>	ENSG00000144736.13	0.5
<i>PDHB</i>	ENSG00000168291.12	0.5
<i>MKRN2</i>	ENSG00000075975.15	0.5
<i>PRMT5</i>	ENSG00000100462.15	0.5
<i>XYLB</i>	ENSG00000093217.9	0.49
<i>CCT3</i>	ENSG00000163468.14	0.49
<i>SEC13</i>	ENSG00000157020.17	0.49
<i>KIAA1143</i>	ENSG00000163807.5	0.49
<i>C1orf109</i>	ENSG00000116922.14	0.49
<i>TOMM22</i>	ENSG00000100216.5	0.49
<i>DHX30</i>	ENSG00000132153.14	0.49
<i>ORC4</i>	ENSG00000115947.13	0.49
<i>ZNF35</i>	ENSG00000169981.10	0.49
<i>AZI2</i>	ENSG00000163512.13	0.49
<i>MAPKAPK3</i>	ENSG00000114738.10	0.49
<i>PDE12</i>	ENSG00000174840.8	0.49
<i>RAD51</i>	ENSG00000051180.16	0.49
<i>METTL6</i>	ENSG00000206562.11	0.48
<i>VPRBP</i>	ENSG00000145041.15	0.48
<i>RTN3</i>	ENSG00000133318.13	0.48
<i>HSPA8</i>	ENSG00000109971.13	0.48
<i>TCAIM</i>	ENSG00000179152.18	0.48
<i>EIF3D</i>	ENSG00000100353.17	0.48
<i>TMEM183A</i>	ENSG00000163444.11	0.48
<i>BUB3</i>	ENSG00000154473.17	0.48
<i>CACYBP</i>	ENSG00000116161.17	0.48
<i>NIF3L1</i>	ENSG00000196290.14	0.48
<i>NEK4</i>	ENSG00000114904.12	0.48
<i>NOLC1</i>	ENSG00000166197.16	0.48
<i>TMED10</i>	ENSG00000170348.8	0.48
<i>SRP72</i>	ENSG00000174780.15	0.48
<i>DEPDC1</i>	ENSG00000024526.16	0.47

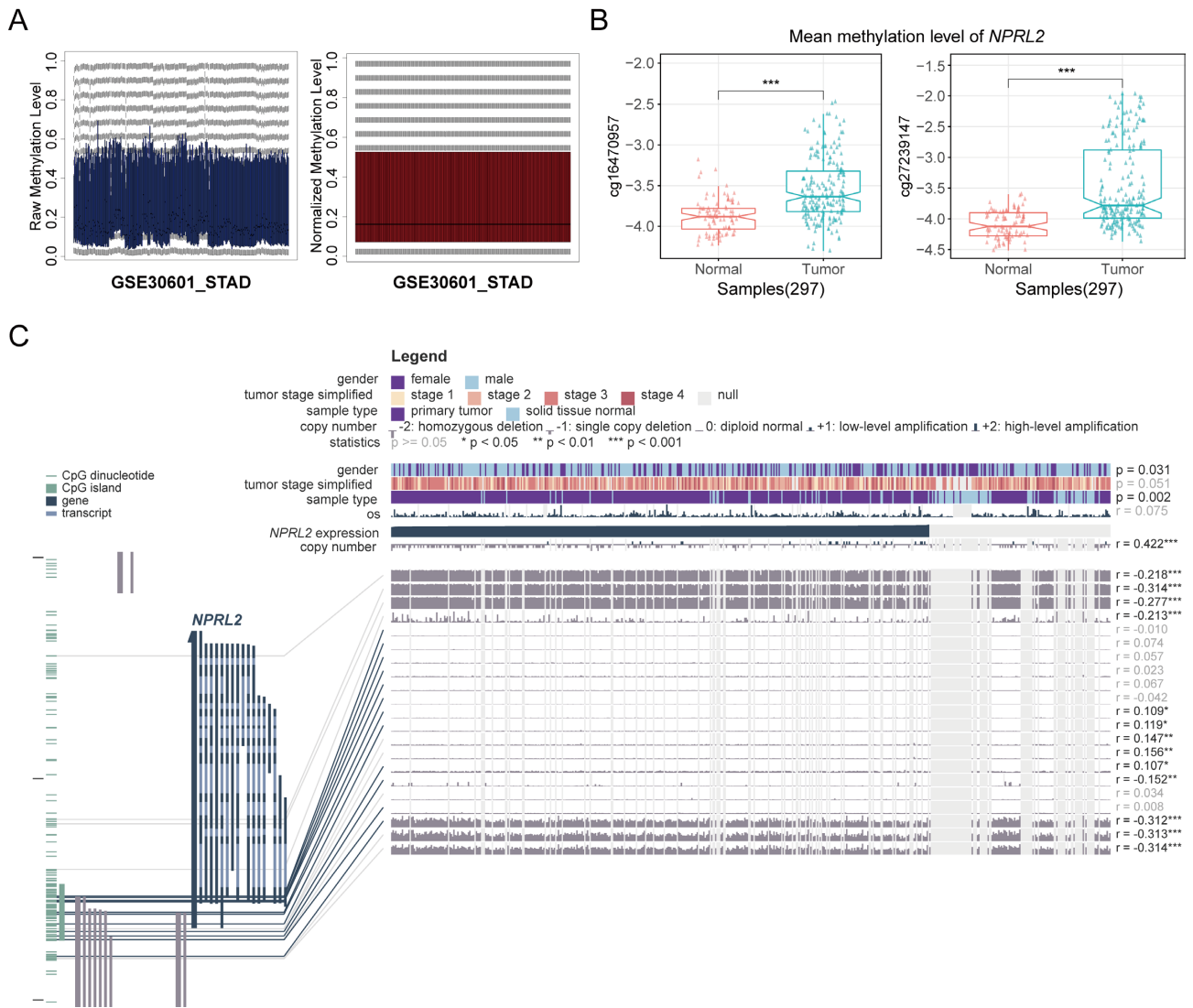
**Table S2** (continued)

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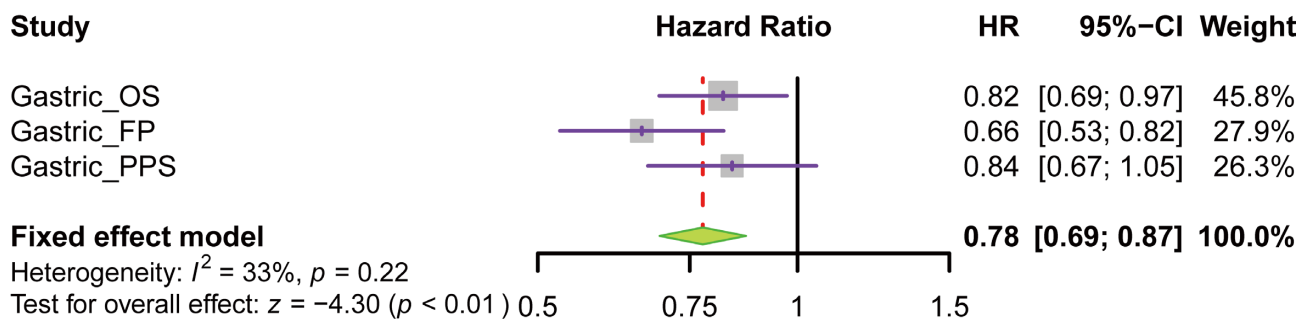
Gene symbol	Gene ID	PCC
<i>PHF7</i>	ENSG00000010318.19	0.47
<i>C1orf174</i>	ENSG00000198912.10	0.47
<i>ARIH2</i>	ENSG00000177479.19	0.47
<i>RRP9</i>	ENSG00000114767.6	0.47
<i>PGM3</i>	ENSG00000013375.15	0.47
<i>LARP4</i>	ENSG00000161813.20	0.47
<i>NUP43</i>	ENSG00000120253.13	0.47
<i>THUMPD3</i>	ENSG00000134077.15	0.47
<i>WDR3</i>	ENSG00000065183.15	0.47
<i>ACTR8</i>	ENSG00000113812.13	0.47
<i>L2HGDH</i>	ENSG00000087299.11	0.47
<i>ACAT2</i>	ENSG00000120437.8	0.47
<i>NGLY1</i>	ENSG00000151092.16	0.47
<i>CCDC47</i>	ENSG00000108588.13	0.47
<i>NDC1</i>	ENSG00000058804.11	0.47
<i>GLB1</i>	ENSG00000170266.15	0.47
<i>STIP1</i>	ENSG00000168439.16	0.47
<i>SACM1L</i>	ENSG00000211456.10	0.47
<i>UBQLN4</i>	ENSG00000160803.7	0.47
<i>LARS2</i>	ENSG00000011376.9	0.47
<i>RP11-651P23.4</i>	ENSG00000224831.3	0.47
<i>NSUN4</i>	ENSG00000117481.10	0.46
<i>TCTA</i>	ENSG00000145022.4	0.46
<i>TCP1</i>	ENSG00000120438.11	0.46
<i>PRPSAP1</i>	ENSG00000161542.16	0.46
<i>SSRP1</i>	ENSG00000149136.7	0.46
<i>BAP1</i>	ENSG00000163930.9	0.46
<i>TKT</i>	ENSG00000163931.15	0.46
<i>USP19</i>	ENSG00000172046.18	0.46
<i>PRDX3</i>	ENSG00000165672.6	0.46
<i>C1orf43</i>	ENSG00000143612.18	0.46
<i>NMD3</i>	ENSG00000169251.12	0.46

**Table S3** Correlation of *NPRL2* with different TICS in STAD analyzed with TISIDB

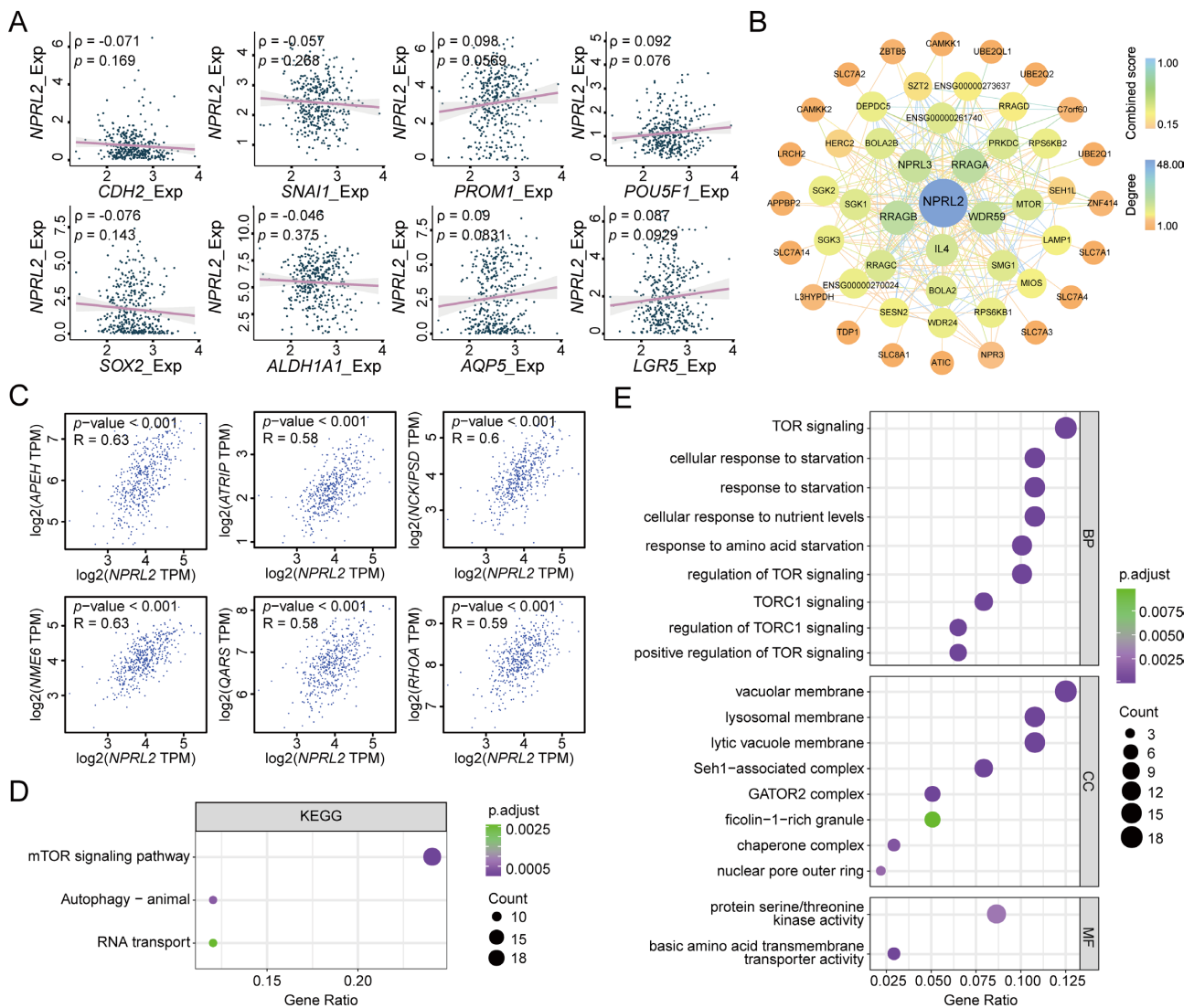
TICS	STAD	
	R	P
Activated CD8 T cell (Act_CD8)	0.055	2.65E-01
Central memory CD8 T cell (Tcm_CD8)	0.015	7.67E-01
Effector memory CD8 T cell (Tem_CD8)	-0.239	9.04E-07
Activated CD4 T cell (Act_CD4)	0.054	2.76E-01
Central memory CD4 T cell (Tcm_CD4)	-0.072	1.40E-01
Effector memory CD4 T cell (Tem_CD4)	-0.316	5.97E-11
T follicular helper cell (Tfh)	-0.244	5.54E-07
Gamma delta T cell (Tgd)	0.01	8.42E-01
Type 1 T helper cell (Th1)	-0.259	1.01E-07
Type 17 T helper cell (Th17)	0.001	9.87E-01
Type 2 T helper cell (Th2)	-0.27	2.47E-08
Regulatory T cell (Treg)	-0.236	1.27E-06
Activated B cell (Act_B)	-0.261	7.48E-08
Immature B cell (Imm_B)	-0.256	1.33E-07
Memory B cell (Mem_B)	-0.275	1.41E-08
Natural killer cell (NK)	-0.252	2.17E-07
CD56bright natural killer cell (CD56bright)	0.07	1.55E-01
CD56dim natural killer cell (CD56dim)	0.206	2.40E-05
Myeloid derived suppressor cell (MDSC)	-0.157	1.31E-03
Natural killer T cell (NKT)	-0.288	2.84E-09
Activated dendritic cell (Act_DC)	0.126	1.03E-02
Plasmacytoid dendritic cell (pDC)	-0.102	3.84E-02
Immature dendritic cell (iDC)	0.1	4.14E-02
Macrophage (macrophage)	-0.21	1.65E-05
Eosinophil (eosinophil)	-0.273	1.89E-08
Mast cell (Mast)	-0.31	1.33E-10
Monocyte (monocyte)	0.227	3.29E-06
Neutrophil (neutrophil)	-0.102	3.80E-02



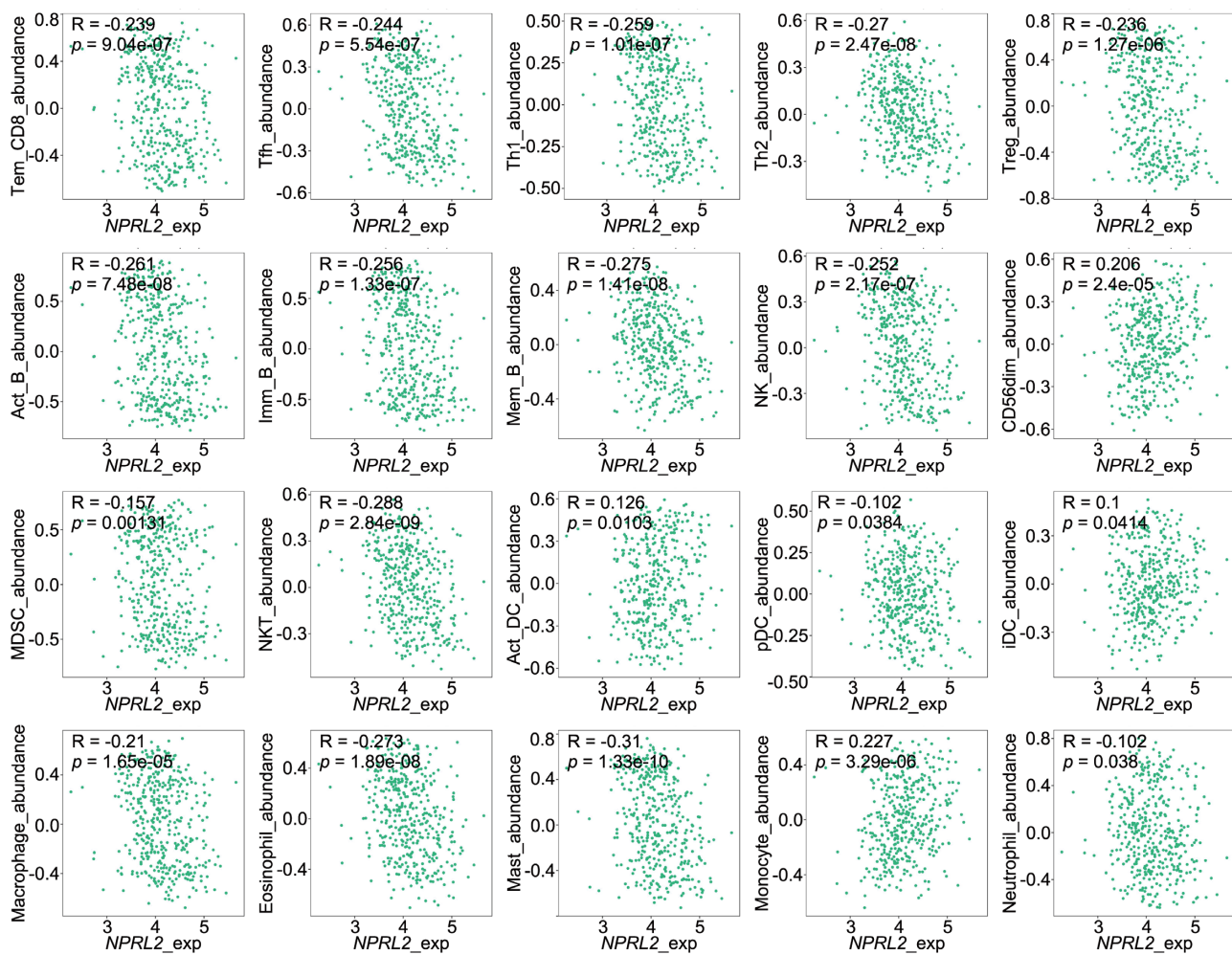
**Figure S1** Methylation of *NPRL2* in STAD. (A) It presented the raw and normalized methylation data in STAD from the GSE30601 dataset. (B) It shows the methylation data of cg16470957 and cg27239147 probes of *NPRL2* in STAD and normal tissues analyzed by *t*-test (\*\* $P < 0.001$ ). (C) MEXPRESS assessed the relationship between *NPRL2* expression, methylation probes and clinical data in STAD. STAD, stomach adenocarcinoma.



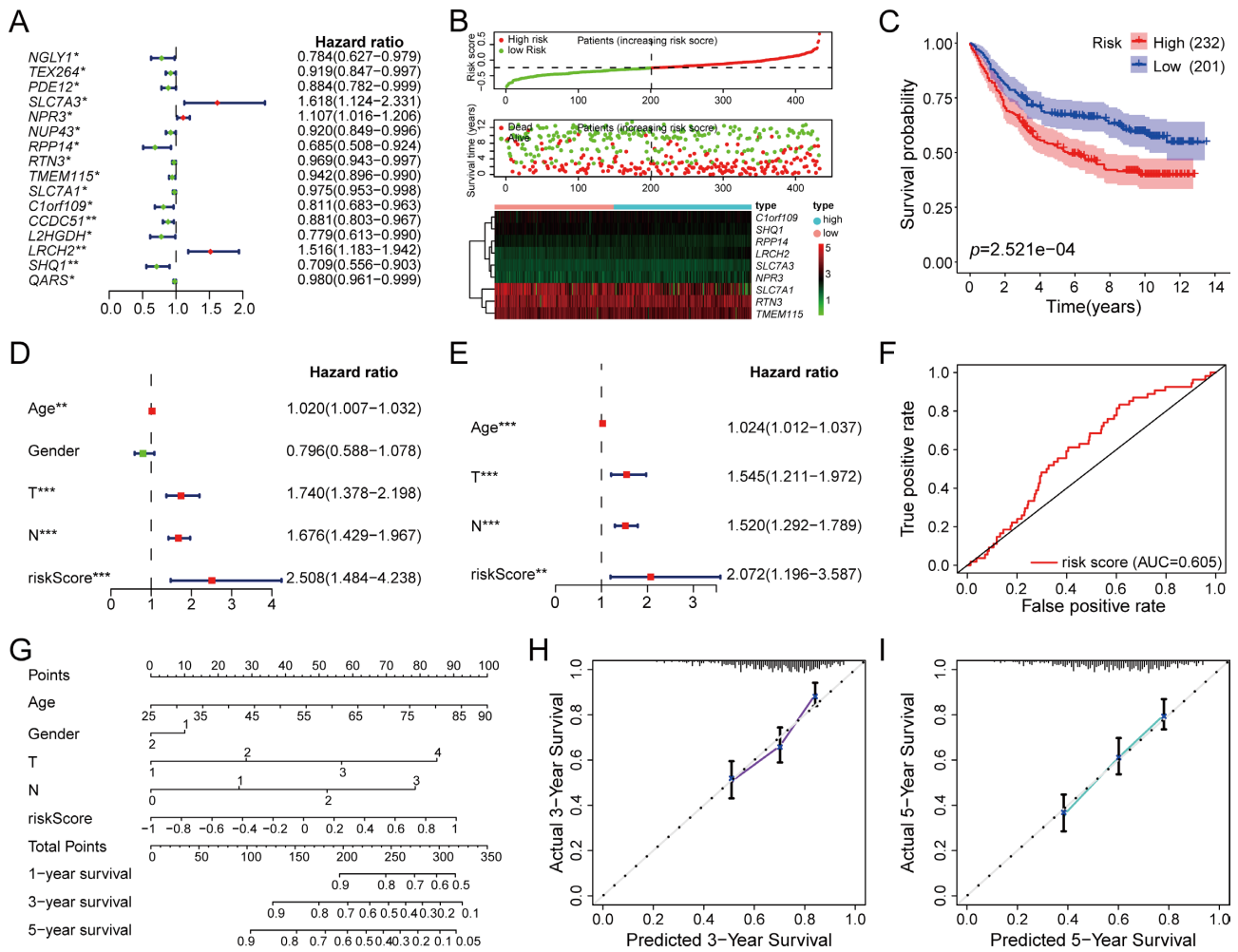
**Figure S2** Meta-analysis of survival data based on the expression of the *NPRL2* (HR =0.78, 95% CI: 0.69–0.87, P<0.01).



**Figure S3** Functional analysis of *NPRL2*-related genes. (A) Scatter plot shows the correlation between *NPRL2* and biomarkers of EMT and stem cells in STAD tested by Spearman's rank correlation. (B) It presents the PPI network constructed by *NPRL2*-interacting proteins. The color and size of each node varies according to degree score. (C) It shows the correlation of *NPRL2* with the co-expressed genes of *NPRL2* screened by GEPIA 2 (Spearman's rank correlation,  $P < 0.001$ ). (D,E) They show the enrichment analysis of *NPRL2*-related genes. STAD, stomach adenocarcinoma; KEGG, Kyoto Encyclopedia of Genes and Genomes pathways; BP, biological process; CC, cellular component; MF, molecular function.



**Figure S4** Comparison of the infiltration levels of different TICS in STAD and normal tissues. TICS, tumour-infiltrating immune cells; STAD, stomach adenocarcinoma.



**Figure S5** Validation of a prognostic risk model based on NPRL2-related genes in the GEO cohort. (A) It shows prognosis-related genes screened out by univariate cox regression analysis of the 148 NPRL2-related genes obtained from the PPI network and GEPIA 2 (\* $P < 0.05$ , \*\* $P < 0.01$ ). (B) It shows the distribution of the risk scores, survival status, and gene expression profiles of samples from GSE84437 dataset in high- and low-risk groups. (C) It shows the survival analysis of overall survival for STAD patients with different risk score. (D,E) They show univariate and multivariate cox regression analysis of risk scores and other clinical characters for STAD patients in the GEO cohort (\*\* $P < 0.01$ , \*\*\* $P < 0.001$ ). (F) It shows the ROC curves for the clinicopathological features and risk score. (G) It shows the Nomogram constructed based on STAD clinicopathological features and risk score. (H,I) the Calibration curves show the risk model could effectively predict the probability of patient survival at 3 and 5 years.