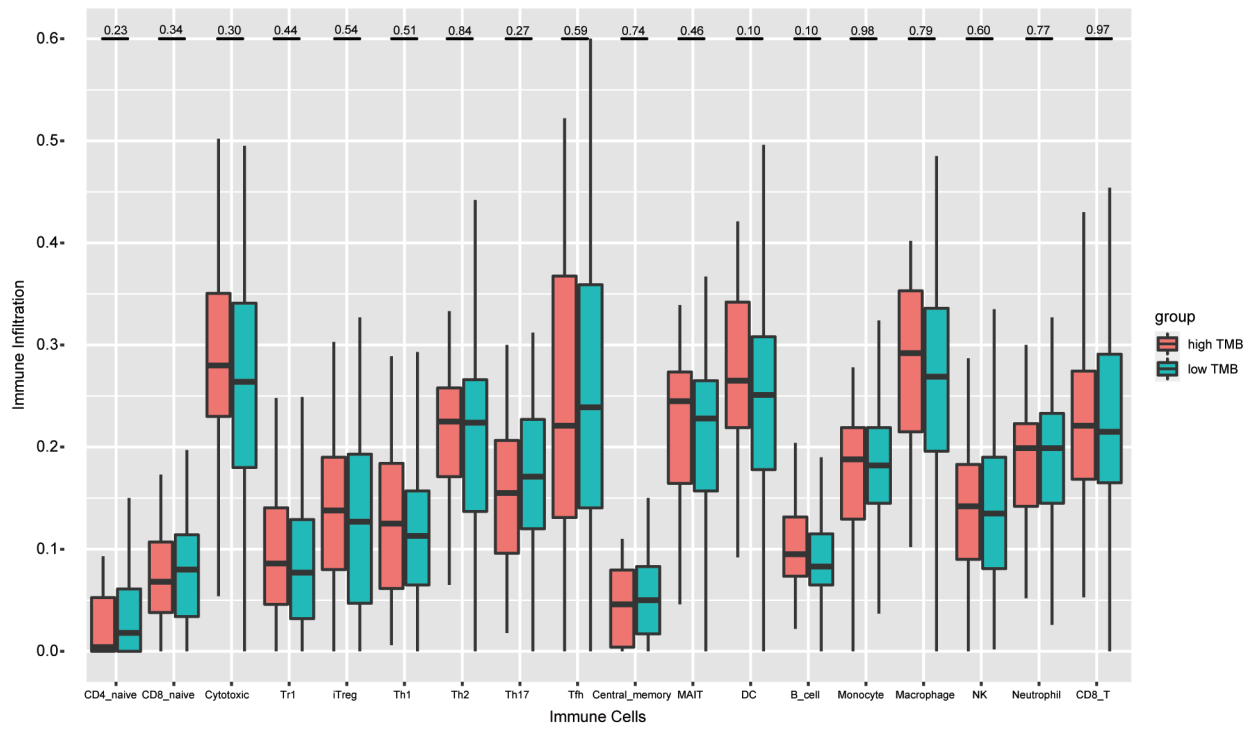


**Figure S1** No significant difference was observed with AJCC-TNM and pathological stages. The relationship of TMB to T (A), N (B), M (C) and stages (D). TMB, tumor mutation burden.



**Figure S2** No significant differences were observed in the infiltration levels of other immune cells between the two TMB groups. TMB, tumor mutation burden.

Table S1 DEGs between high- and low-TMB groups

Genes	logFC	P value	FDR
SMR3B	10.25878	8.00E-38	1.01E-33
INS	5.359809	7.96E-23	3.34E-19
PAGE1	5.34612	2.93E-22	9.19E-19
KRT12	5.223938	6.64E-32	4.18E-28
TBX10	3.625035	6.47E-13	1.16E-09
MAGEA4	2.95182	4.61E-06	0.000673
DCD	2.874008	1.15E-05	0.001305
ACHE	2.601691	7.20E-18	1.81E-14
TRPA1	2.340315	2.84E-07	8.93E-05
FABP7	2.30691	0.000368	0.014285
PRR4	2.302624	3.27E-07	9.56E-05
B4GALNT2	2.27809	1.39E-08	7.97E-06
FAM3D	2.116634	3.80E-07	9.95E-05
SOSTDC1	2.062557	2.07E-07	7.14E-05
ZFP57	2.044209	4.43E-06	0.000655
CLCA2	1.915096	6.37E-06	0.000837
C2CD4A	1.912346	3.54E-07	9.74E-05
MUC20	1.883634	1.16E-11	1.82E-08
CEL	1.878968	4.31E-06	0.000655
PADI3	1.789345	7.78E-06	0.000978
HOXB9	1.715189	3.03E-09	2.93E-06
ACE2	1.709743	0.000459	0.016447
NUDT8	1.699212	1.69E-11	2.36E-08
MFSD2A	1.662663	3.38E-13	7.07E-10
CYP4F22	1.643059	4.10E-06	0.000644
ABCC2	1.62889	2.54E-06	0.000432
PCP4L1	1.619974	1.33E-06	0.000279
SUSD2	1.618094	3.28E-11	4.12E-08
MUC5B	1.570947	8.56E-05	0.005541
FFAR2	1.560783	8.56E-10	8.97E-07
FIBCD1	1.551579	4.04E-07	0.000104
GSDMB	1.506932	8.89E-08	3.49E-05
CEACAM5	1.472854	0.000273	0.011875
SNPH	1.460376	1.37E-07	5.24E-05
GAL3ST2	1.457622	1.21E-05	0.001345
NUDT10	1.445567	2.10E-07	7.14E-05
HEPACAM2	1.41274	2.59E-05	0.002305
CRTAC1	1.405487	2.32E-05	0.002186
ASCL2	1.398084	3.72E-08	1.61E-05
VNN2	1.382991	5.74E-09	4.51E-06
KRT4	1.35923	0.00224	0.0455
AC131097.2	1.35631	0.000328	0.013225
NXPH4	1.332861	9.62E-06	0.001162
SLPI	1.326106	0.000425	0.015714
CALML3	1.319611	0.000968	0.027063
SOX11	1.305224	8.60E-05	0.005541
C2CD4B	1.298414	1.17E-05	0.001315
PRAC2	1.285974	0.000145	0.007868
ABCC3	1.284305	1.68E-06	0.000321
FGFR4	1.248674	1.51E-05	0.001592
ATP6V0A4	1.232072	5.11E-05	0.003711
C1QTNF2	1.220568	1.62E-08	8.86E-06
MELTF	1.197576	0.000106	0.006433
SLC13A3	1.187259	4.94E-08	2.07E-05
FUT3	1.161173	0.000309	0.012644
KRT86	1.147976	0.001942	0.041732
ITGB6	1.128633	4.11E-05	0.00329
ORMDL3	1.117312	5.20E-06	0.000727
ABCA12	1.111848	5.06E-05	0.003711
SDCBP2	1.103393	4.62E-07	0.000114
NME2	1.095368	3.86E-09	3.47E-06
AKR1C1	1.079418	0.001151	0.030834
TMEM40	1.076595	7.48E-05	0.005002
NME1-NME2	1.063632	3.36E-05	0.002777
MYCN	1.06004	0.000469	0.016528
CLEC7A	1.055267	8.95E-07	0.000194
ATP13A5	1.050073	0.000984	0.027363
MIEN1	1.039653	3.96E-05	0.003213
POF1B	1.02342	0.000285	0.012195
AIF1L	1.015252	2.75E-06	0.00046
GRB7	1.007611	0.0002	0.009455
DLX5	1.005459	0.001299	0.032426
SLC16A6	-1.00435	0.002539	0.049495
BCL2	-1.00957	0.000119	0.00704
THSD4	-1.01274	9.28E-05	0.005859
LPL	-1.02257	0.000139	0.007811
PHYHD1	-1.02559	0.000741	0.022125
IL6ST	-1.03921	2.27E-06	0.000413
CMYA5	-1.04512	3.15E-05	0.002655
IGFBP5	-1.05864	0.000247	0.01108
MS4A14	-1.06188	0.001649	0.037894
MPP2	-1.06684	0.000125	0.00725
FAM107A	-1.07561	0.002321	0.046752
REPS2	-1.07944	0.000125	0.00725
TIMP4	-1.08507	0.001292	0.032426
TRIM17	-1.09937	0.001699	0.038528
ELP2	-1.10439	1.85E-06	0.000341
KCNF1	-1.11507	0.002195	0.045179
FAM189A2	-1.1232	0.000149	0.00796
CALB2	-1.14576	0.000876	0.025069
NTRK2	-1.15761	0.000186	0.009212
MAPT	-1.17744	0.000131	0.007469
KCNE4	-1.19758	0.000698	0.021138
TUBA3D	-1.20616	0.001394	0.033691
ARTN	-1.21416	0.000236	0.010755
GREB1	-1.21593	0.000261	0.011472
AOX1	-1.24501	0.00063	0.019878
ESR1	-1.25336	0.001315	0.032497
CCDC170	-1.27815	1.24E-05	0.001364
DCDC2	-1.28487	0.000126	0.007251
SUSD3	-1.30191	0.000159	0.008397
KRT15	-1.32542	0.001482	0.035139
KCNK15	-1.3452	1.60E-05	0.001637
PARD6B	-1.3477	7.25E-07	0.000163
MMP7	-1.34811	0.00017	0.008677
AFF3	-1.36781	2.35E-05	0.002186
PRRT2	-1.39042	2.06E-05	0.002012
FABP5	-1.39257	1.42E-06	0.000287
CIDEA	-1.39277	0.001379	0.033386
SLC39A6	-1.4068	6.39E-06	0.000837
RLN2	-1.41498	0.000647	0.020078
SLC7A2	-1.42259	0.000304	0.012512
TFPI2	-1.42269	0.000329	0.013225
GFRA1	-1.44406	0.000529	0.01802
SERPINA3	-1.48629	1.47E-05	0.001561
FGF10	-1.50813	0.000231	0.010577
TFF3	-1.517	0.000343	0.013678
S100A2	-1.54293	0.00253	0.049462
EGR3	-1.55636	6.48E-07	0.000148
PXDNL	-1.57631	0.000625	0.01986
WNK4	-1.5802	0.000146	0.007868
SNORC	-1.58104	0.000725	0.021844
EN1	-1.61877	0.000102	0.006245
INSYN2	-1.64617	0.001631	0.037636
CORO6	-1.67716	0.000379	0.014514
TPRG1	-1.68165	7.23E-05	0.00488
CLIC6	-1.69964	0.000242	0.010976
PTX3	-1.70825	0.000216	0.010042
CST2	-1.72492	6.85E-06	0.000887
GABRP	-1.72599	0.001759	0.03921
KCNK2	-1.74063	0.000164	0.00861
CXCL14	-1.75219	7.21E-05	0.00488
RIMS4	-1.8241	3.61E-05	0.002966
CRISPLD1	-1.83803	2.34E-05	0.002186
CAPN6	-1.8442	0.000198	0.009435
FMO3	-1.89431	3.08E-05	0.002625
PDZK1	-1.8974	5.17E-05	0.003733
VGLL1	-1.89776	0.002086	0.043851
RGS22	-1.92686	2.34E-05	0.002186
STC2	-2.01357	3.56E-07	9.74E-05
FCRLB	-2.0321	9.38E-06	0.001156
CRABP1	-2.08692	0.000576	0.019166
IGF1R	-2.15058	1.26E-08	7.52E-06
BMPRI1B	-2.15899	4.44E-05	0.003444
TFF1	-2.16091	7.69E-05	0.005059
SCUBE2	-2.1872	8.69E-08	3.49E-05
PGR	-2.22122	2.35E-06	0.000414
SLITRK6	-2.26521	1.84E-05	0.001849
KCNJ3	-2.27728	0.000645	0.020076
CDC20B	-2.3208	0.000257	0.011451
LGALS7B	-2.39592	0.000168	0.008658
PLP1	-2.39796	0.000166	0.008627
GRPR	-2.40321	1.36E-06	0.000281
KRTDAP	-2.42576	0.000316	0.012753
ATP1A2	-2.43927	9.76E-06	0.001168
AGTR1	-2.46258	4.43E-06	0.000655
STAC2	-2.51485	4.53E-05	0.003449
SCGB3A1	-2.52054	0.000506	0.017437
HPD	-2.61451	4.04E-05	0.003257
GSTM1	-2.63201	4.50E-05	0.003449
FGL1	-2.66648	0.000645	0.020076
C20orf85	-2.71947	0.001226	0.031707
ART3	-2.72052	6.58E-05	0.004572
KRT1	-2.88843	0.000171	0.008677
PCDH10	-2.98383	0.000258	0.011472
PI15	-3.20526	2.77E-08	1.29E-05
SCGB1A1	-3.22629	0.000246	0.01108
CSN3	-3.23506	0.000507	0.017437
PZP	-3.30545	0.000111	0.00669
KRT79	-3.49986	4.67E-05	0.003539
DSG1	-3.59386	2.94E-05	0.002549
TRH	-3.93223	4.15E-05	0.003304
MUC5AC	-3.94699	5.10E-05	0.003711
RPS4Y1	-4.14079	0.000662	0.020454
CGA	-4.37307	5.59E-07	0.000135
CST5	-4.59896	7.15E-06	0.000907
S100G	-4.61529	9.54E-06	0.001162
CARTPT	-4.67963	0.000441	0.016083
FDCSP	-4.97844	2.65E-08	1.28E-05
CYP2A7	-5.16347	7.66E-07	0.000169
SERPINA6	-5.78324	6.54E-09	4.83E-06
CYP2A6	-6.43218	1.58E-10	1.80E-07

DEGs, differentially expressed genes; TMB, tumor mutation burden.

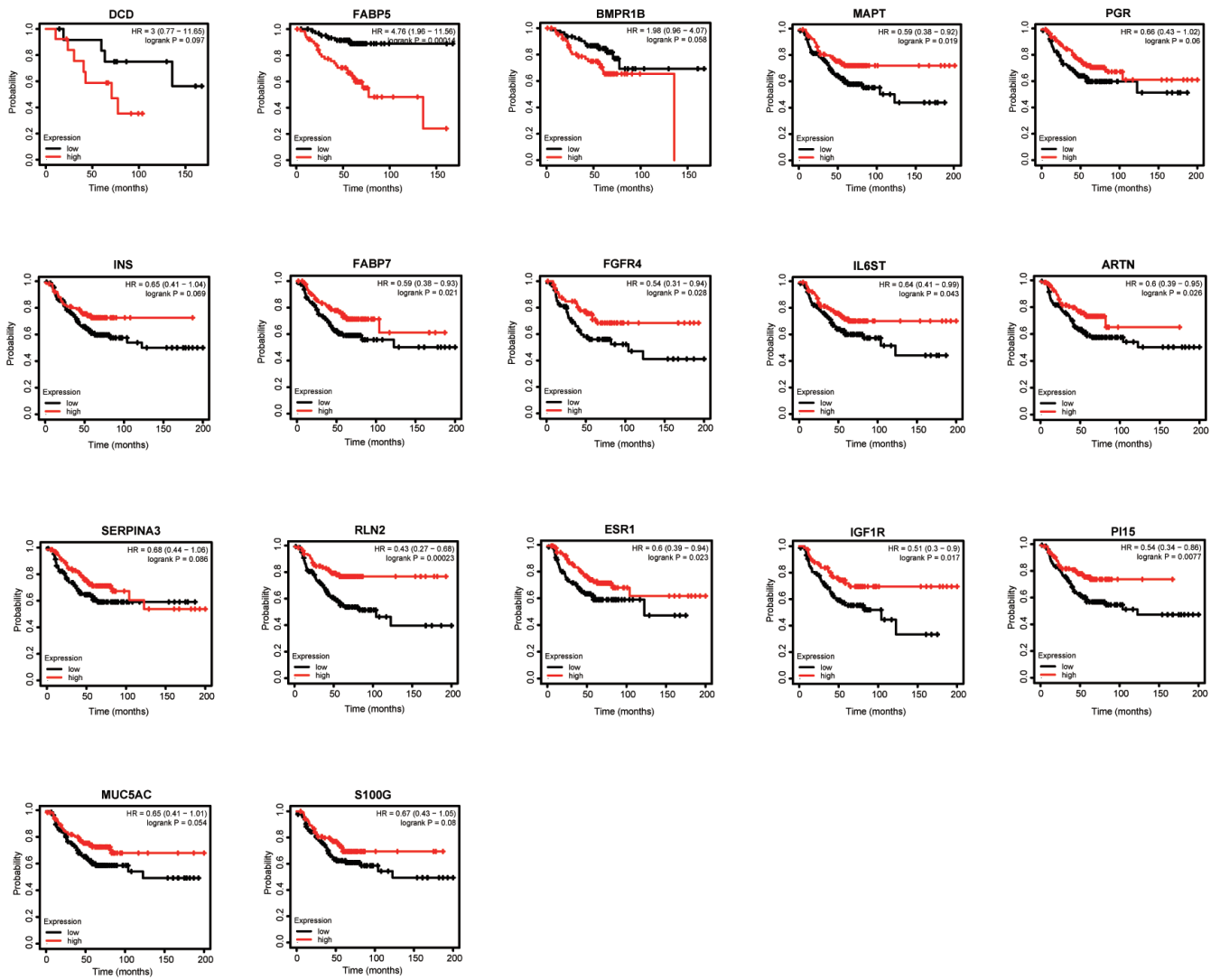
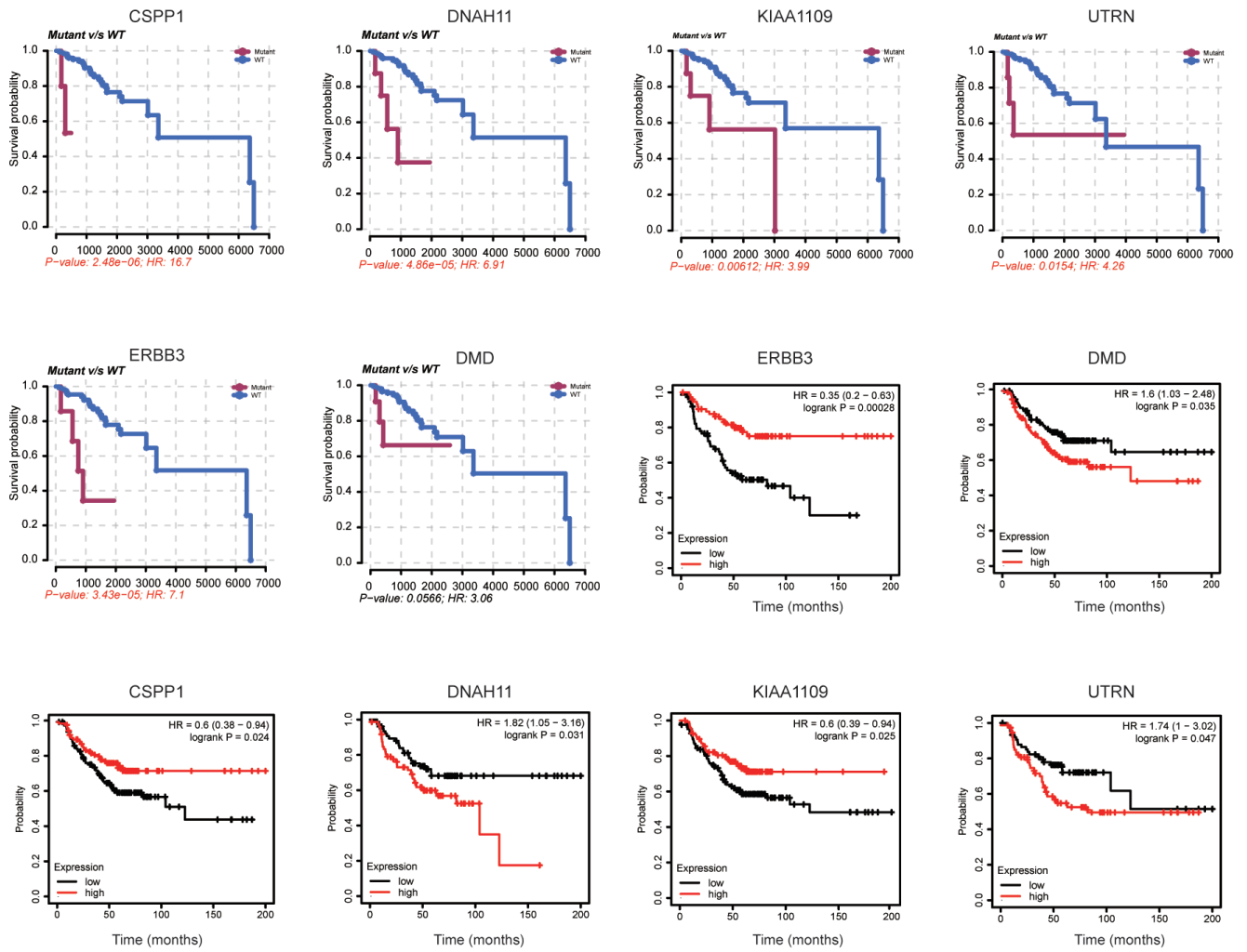


Figure S3 Survival analysis of 17 TMB-related immune genes. TMB, tumor mutation burden.

**Table S2** Differentially mutated genes between high- and low-TMB groups (top 30)

Genes	Mutation rate		P value	OR	CI. up	CI. low
	High TMB	Low TMB				
<i>TTN</i>	0.44186	0.115607	5.09E-06	5.986984	13.83298	2.620877
<i>CSPP1</i>	0.162791	0	8.17E-06	Inf	Inf	6.483162
<i>SYNE1</i>	0.209302	0.011561	9.45E-06	22.14357	218.8382	4.321598
<i>DNAH11</i>	0.186047	0.00578	1.08E-05	38.41108	1,736.446	4.894684
<i>MUC17</i>	0.255814	0.028902	1.25E-05	11.35118	44.61093	3.365185
<i>ITSN2</i>	0.139535	0	4.64E-05	Inf	Inf	5.172873
<i>PIWIL1</i>	0.139535	0	4.64E-05	Inf	Inf	5.172873
<i>ASPM</i>	0.162791	0.00578	5.55E-05	32.72031	1,502.429	4.007348
<i>CMYA5</i>	0.162791	0.00578	5.55E-05	32.72031	1,502.429	4.007348
<i>KIAA1109</i>	0.162791	0.00578	5.55E-05	32.72031	1,502.429	4.007348
<i>OTOGL</i>	0.162791	0.00578	5.55E-05	32.72031	1,502.429	4.007348
<i>HUWE1</i>	0.186047	0.017341	0.000143	12.72391	78.13288	2.876491
<i>USH2A</i>	0.186047	0.017341	0.000143	12.72391	78.13288	2.876491
<i>NCOA6</i>	0.162791	0.011561	0.000212	16.31668	167.0088	2.947262
<i>PEG3</i>	0.162791	0.011561	0.000212	16.31668	167.0088	2.947262
<i>UTRN</i>	0.162791	0.011561	0.000212	16.31668	167.0088	2.947262
<i>SYNE2</i>	0.209302	0.028902	0.000212	8.759255	35.46074	2.459223
<i>DEPDC4</i>	0.116279	0	0.000257	Inf	Inf	3.937605
<i>KAT6A</i>	0.116279	0	0.000257	Inf	Inf	3.937605
<i>KIF1B</i>	0.116279	0	0.000257	Inf	Inf	3.937605
<i>LRCH1</i>	0.116279	0	0.000257	Inf	Inf	3.937605
<i>MAST2</i>	0.116279	0	0.000257	Inf	Inf	3.937605
<i>MYLK</i>	0.116279	0	0.000257	Inf	Inf	3.937605
<i>PAPPA2</i>	0.116279	0	0.000257	Inf	Inf	3.937605
<i>RALGAPB</i>	0.116279	0	0.000257	Inf	Inf	3.937605
<i>SHANK1</i>	0.116279	0	0.000257	Inf	Inf	3.937605
<i>SZT2</i>	0.116279	0	0.000257	Inf	Inf	3.937605
<i>TG</i>	0.116279	0	0.000257	Inf	Inf	3.937605
<i>THSD7B</i>	0.116279	0	0.000257	Inf	Inf	3.937605
<i>QSER1</i>	0.139535	0.00578	0.000275	27.28709	1,280.418	3.171417

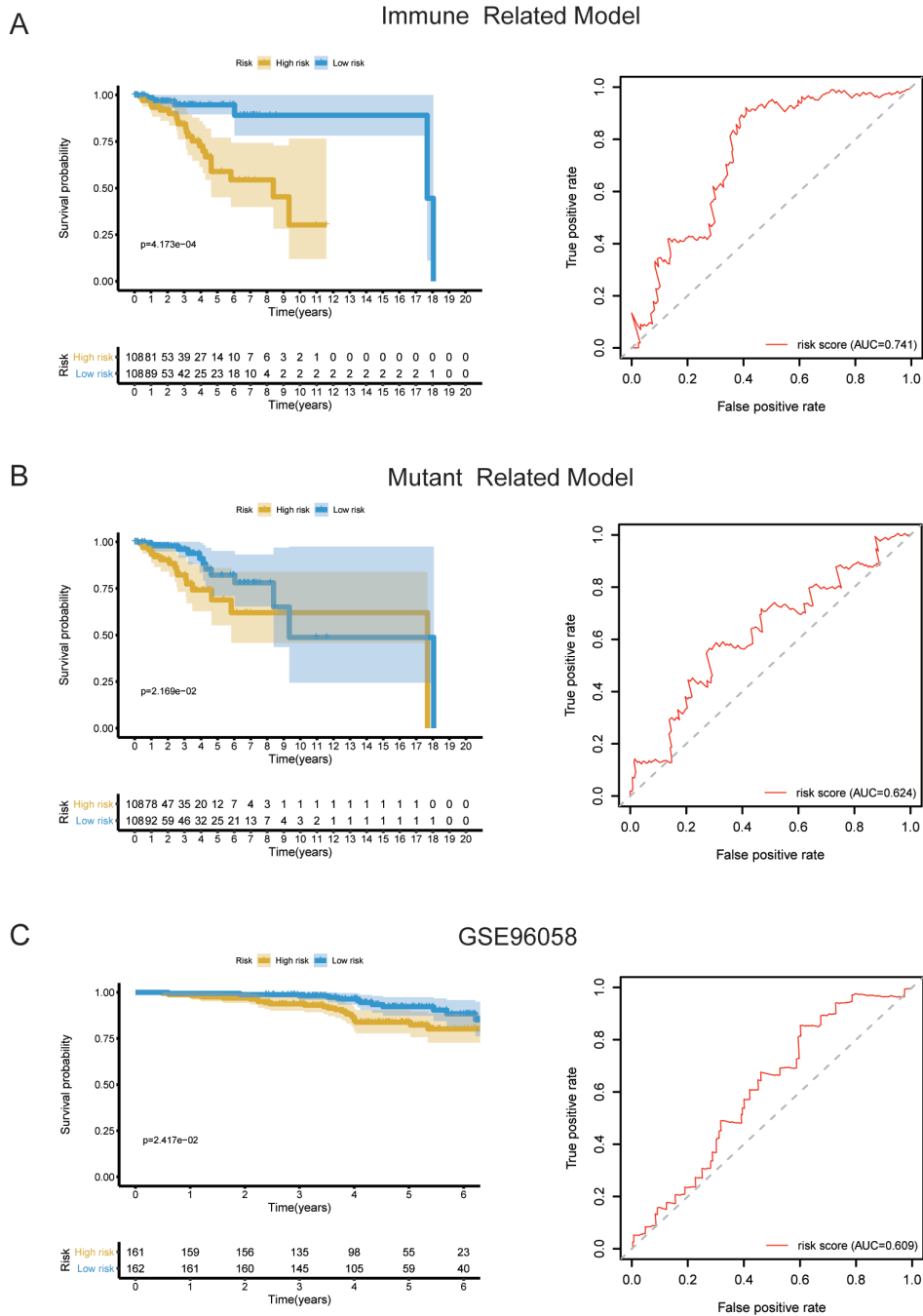
TMB, tumor mutation burden; CI, confidence interval; Inf, infinity.



**Figure S4** SMutation- and expression-related prognosis of 6 TMB-related mutant genes. TMB, tumor mutation burden.

**Table S3** The univariate Cox regression analysis of 23 genes

Genes	HR	HR.95L	HR.95H	P value
<i>ARTN</i>	0.698959	0.389483	1.254338	0.229966
<i>BMPR1B</i>	1.03753	0.869087	1.23862	0.683557
<i>CSPP1</i>	0.689729	0.365589	1.301261	0.251423
<i>DCD</i>	1.068362	0.950345	1.201035	0.268205
<i>DMD</i>	0.90872	0.417437	1.978196	0.809426
<i>DNAH11</i>	2.021264	1.029951	3.966699	0.04078
<i>ERBB3</i>	1.545548	0.933522	2.558823	0.090543
<i>ESR1</i>	0.986851	0.834388	1.167173	0.877152
<i>FABP5</i>	0.57418	0.339193	0.971963	0.038842
<i>FABP7</i>	0.982491	0.833521	1.158086	0.833241
<i>FGFR4</i>	1.191269	0.952273	1.490248	0.125543
<i>IGF1R</i>	0.846196	0.643828	1.112173	0.231082
<i>IL6ST</i>	0.916109	0.682802	1.229135	0.559046
<i>INS</i>	0.350101	0.000503	243.566	0.753296
<i>KIAA1109</i>	1.312052	0.738614	2.33069	0.354214
<i>MAPT</i>	0.693917	0.498978	0.965015	0.029886
<i>MUC5AC</i>	1.119383	0.869683	1.440778	0.381172
<i>PGR</i>	0.463558	0.229164	0.937694	0.032441
<i>PI15</i>	0.92759	0.652778	1.318095	0.674998
<i>RLN2</i>	0.878205	0.529463	1.456651	0.614929
<i>S100G</i>	1.013108	0.757935	1.354191	0.929909
<i>SERPINA3</i>	0.745016	0.413917	1.340967	0.326307
<i>UTRN</i>	0.929572	0.548193	1.576275	0.786355



**Figure S5** Identification and validation of the combined risk scoring system. (A,B) Independent immune- and mutant-related models were established, respectively. (C) Survival analysis and ROC curve of the combined model in the validation cohort (GSE96058). AUC, area under curve; ROC, receiver operating characteristic.

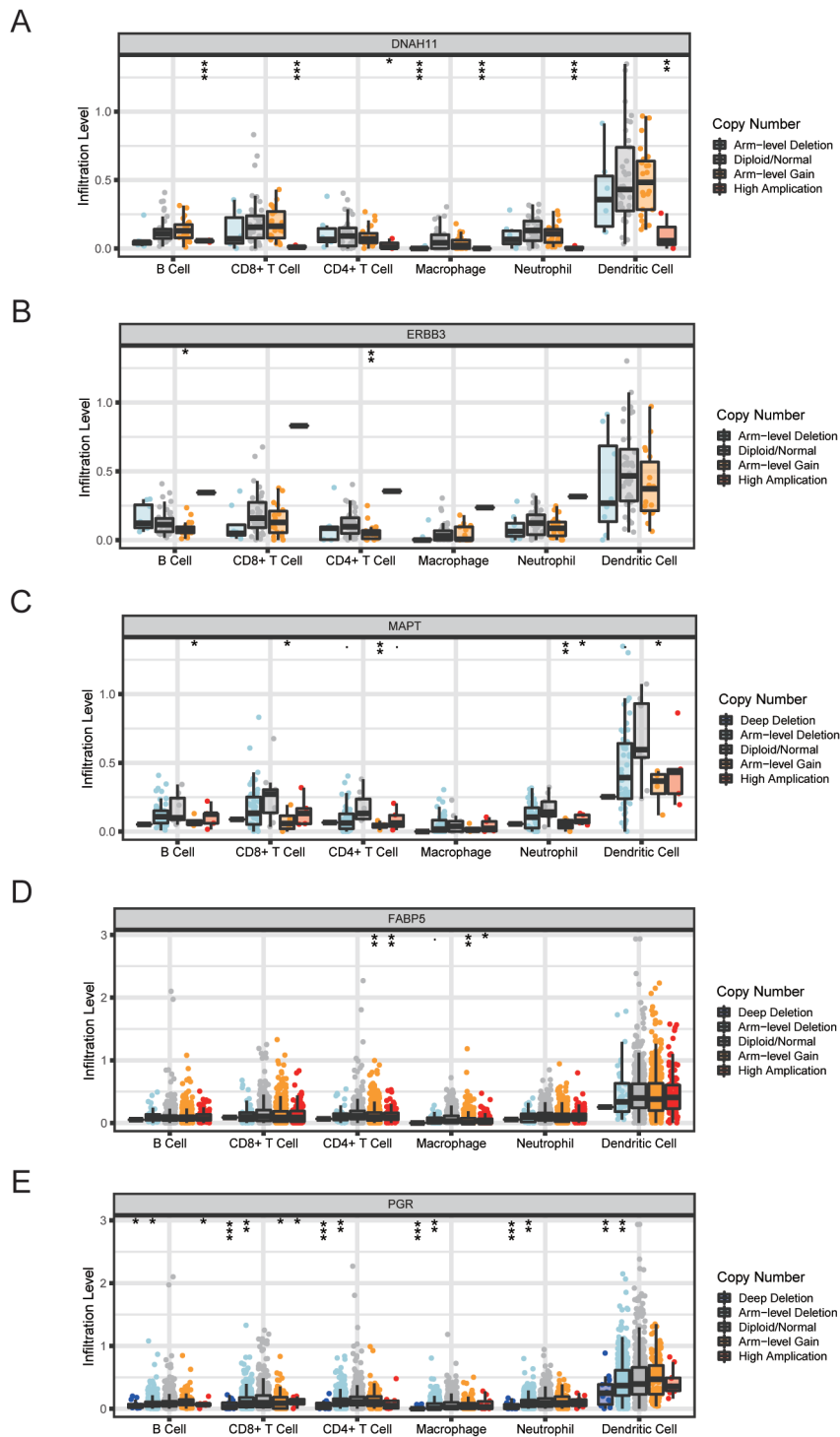
**Table S4** The immune related risk scoring system

Genes	Coef	HR	HR.95L	HR.95H	P value
<i>FABP5</i>	-0.48906	0.613205	0.365736	1.02812	0.063626
<i>FGR</i>	-0.71156	0.49088	0.238077	1.012122	0.053939
<i>MAPT</i>	-0.42131	0.656186	0.470435	0.915282	0.01309

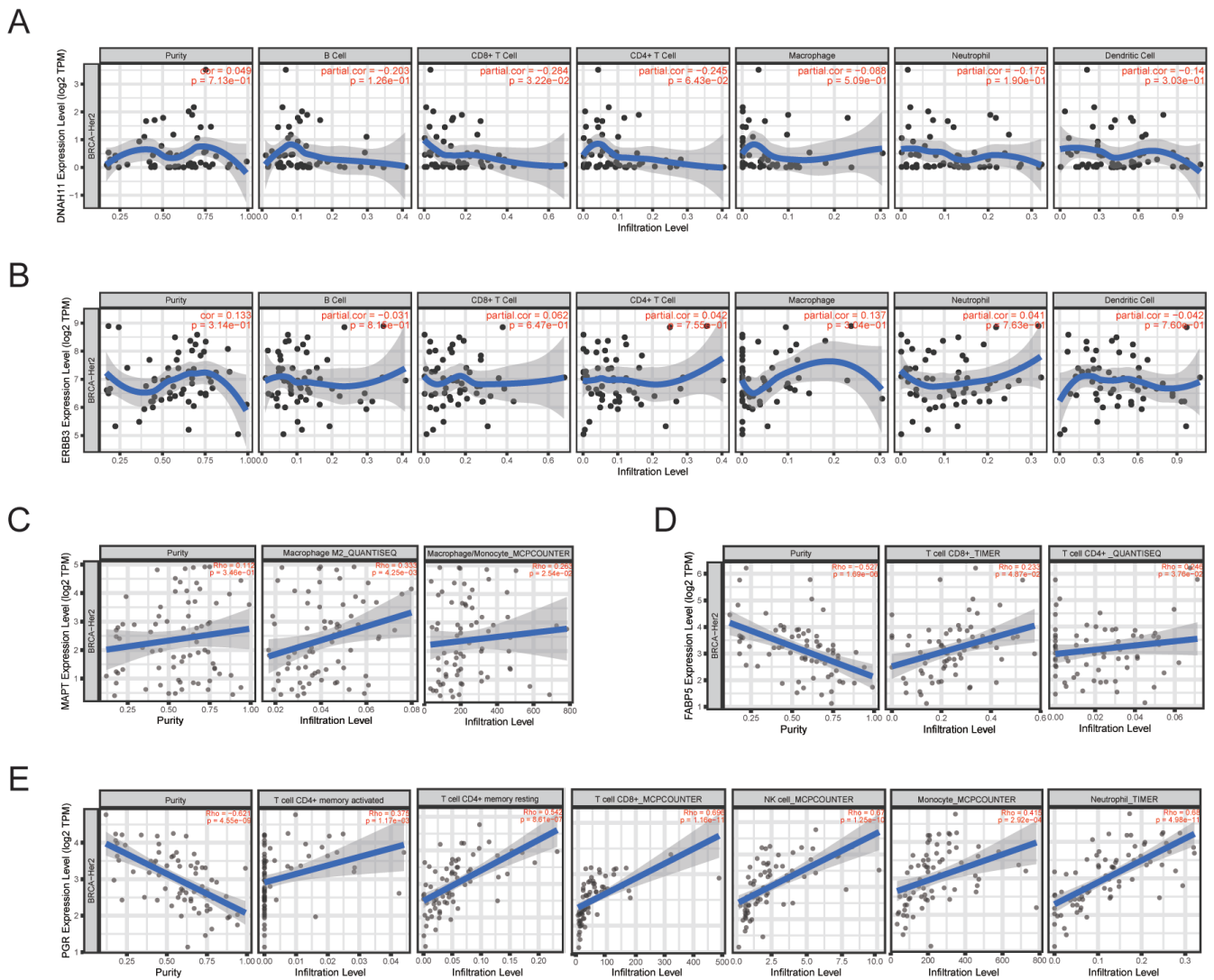
**Table S5** The mutant related risk scoring system

Genes	Coef	HR	HR.95L	HR.95H	P value
<i>CSPP1</i>	-0.21612	0.805641	0.618523	1.049365	0.109015
<i>DNAH11</i>	0.499844	1.648465	1.17012	2.322357	0.004258
<i>ERBB3</i>	0.01506	1.015174	1.001624	1.028908	0.028045





**Figure S6** Associations of 5 hub TMB-related signature mutants with immune cell infiltration. (A-E) Mutants of 5 TMB-related genes conferred the low infiltration levels of immune cells. \*,  $P < 0.05$ ; \*\*,  $P < 0.01$ ; \*\*\*,  $P < 0.001$ . TMB, tumor mutation burden.



**Figure S7** Correlation of the expression of 5 hub TMB-related signatures with immune infiltration levels in HER2+ BC. (A) The expression of DNAH11 was negatively correlated with the levels of CD8<sup>+</sup> T cells and CD4<sup>+</sup> T cells. (B) There was no significant correlation between the expression of ERBB3 and the levels of 6 immune cells. (C) The expression of MAPT was associated with the levels of macrophage M2 and monocytes. (D) The expression of FABP5 was associated with the levels of CD8<sup>+</sup> T cells and CD4<sup>+</sup> T cells. (E) The expression of PGR was associated with the levels of 6 immune cells. TMB, tumor mutation burden; BC, breast cancer.