

1 **Supplementary materials**

2 **Combination of transcriptome and Mendelian Inheritance reveals novel prognostic biomarker**
3 **of CTLA-4-related lncRNAs and protective role of nitrogen metabolism pathway in lung**
4 **adenocarcinoma development**

5 Abbreviations2

6 Supplementary Figure S1.....3

7 Supplementary Figure S2.....5

8 Supplementary Figure S3.....7

9 Supplementary Figure S4.....10

10 Supplementary Figure S5.....11

11 Supplementary Figure S6.....13

12 Supplementary Figure S7.....14

13 Supplementary Table S120

14 Supplementary Table S221

15 Supplementary Table S328

16 Supplementary Table S430

17 Supplementary Table S534

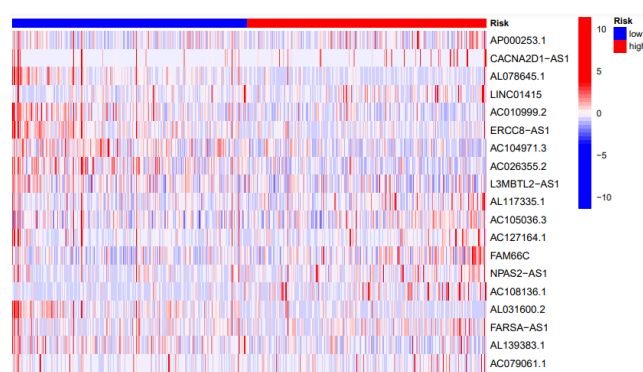
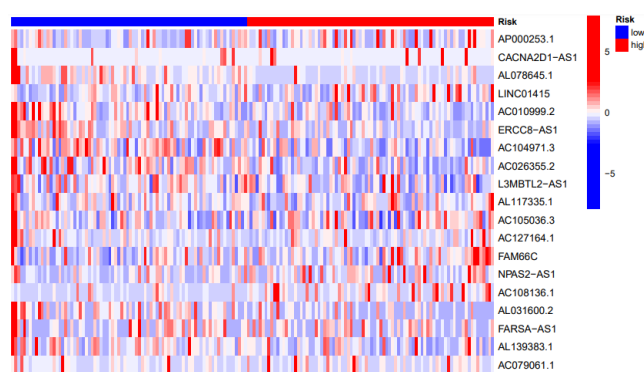
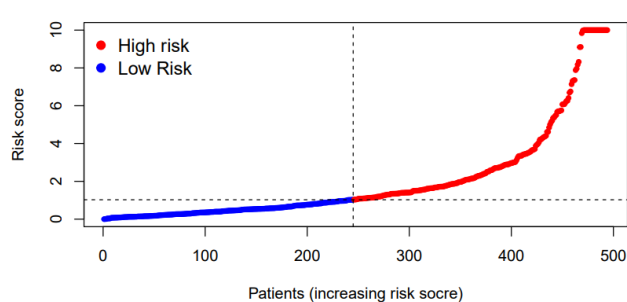
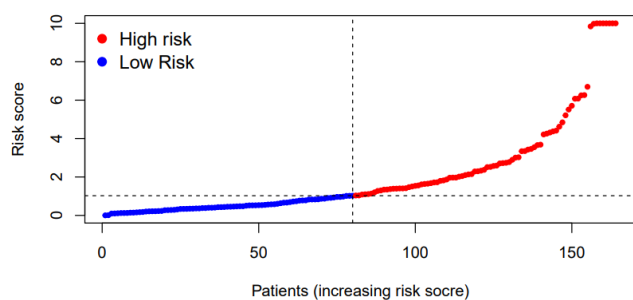
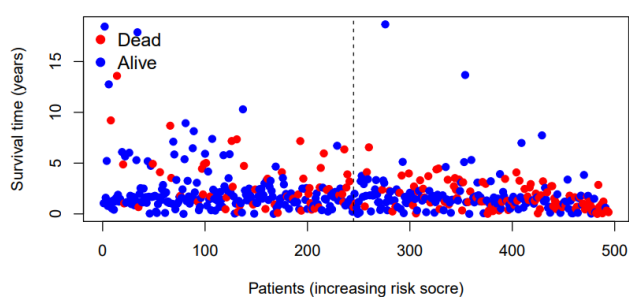
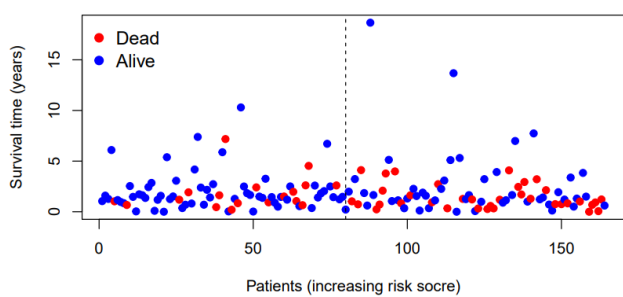
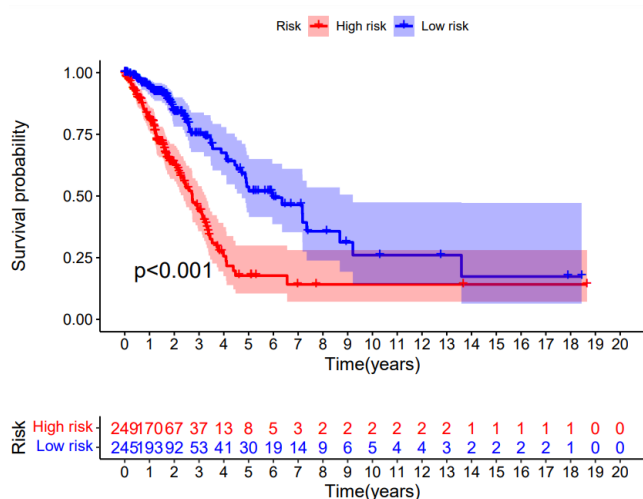
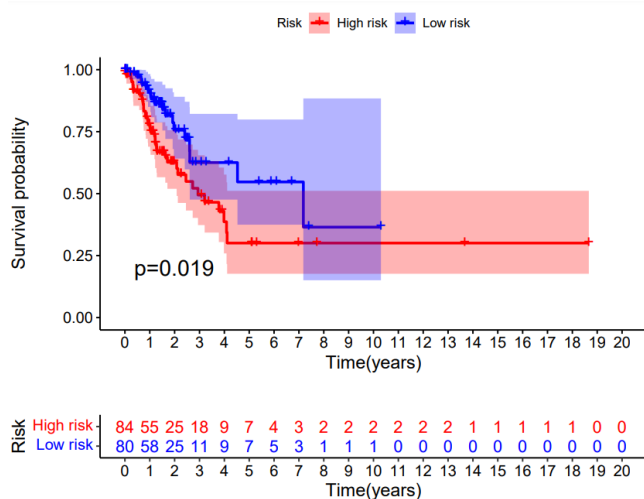
18 Supplementary Table S635

19 Supplementary Table S735

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Abbreviations

AJCC: American Joint Committee on Cancer; AUC: area under curve; BP: biological process; BWMR: Bayesian weighted Mendelian randomization; CAF: cancer-associated fibroblasts; CC: cellular component; CTLA-4: cytotoxic T-lymphocyte-associated protein 4; CTLA4LncSigs: CTLA-4-related lncRNA-based gene signatures; ELBO: Evidence Lower Bound; FDR: false discovery rate; GO: gene ontology; HR: hazard ratio; ICI: immune checkpoint inhibitor; IVW: inverse-variance weighted; KEGG: Kyoto Encyclopedia of Genes and Genomes; LASSO: least absolute shrinkage and selection operator; LncRNA: Long non-coding RNA; LOO MR: Leave-One-Out Mendelian Randomization; LUAD: lung adenocarcinoma; M: distant metastasis; MDSC: Myeloid-derived suppressor cell; MF: molecular function ; N: regional lymph nodes; OS: overall survival; ROC: receiver operating characteristic; T: primary tumor; TCGA: The Cancer Genome Atlas; TMB: Tumor Mutation Burden; TME: tumor microenvironment; 2SMR: 2-sample Mendelian randomization.

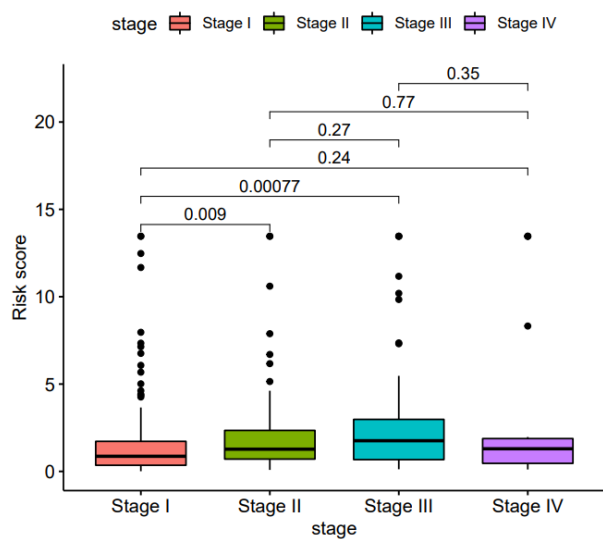


Testing

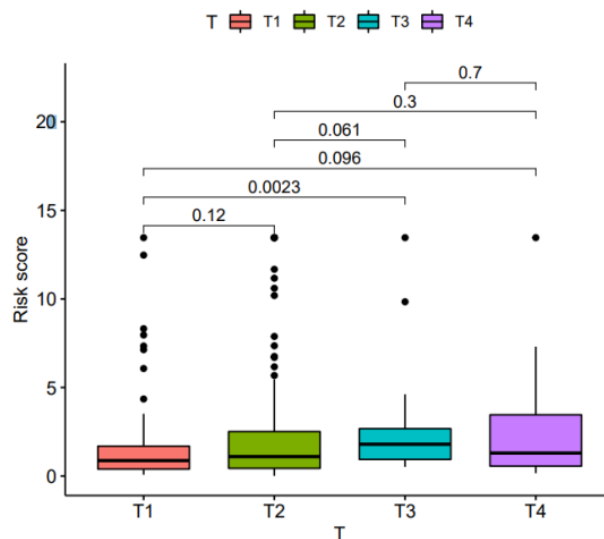
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Supplementary Fig. S1. Results of Kaplan-Meier method in testing and entire datasets.

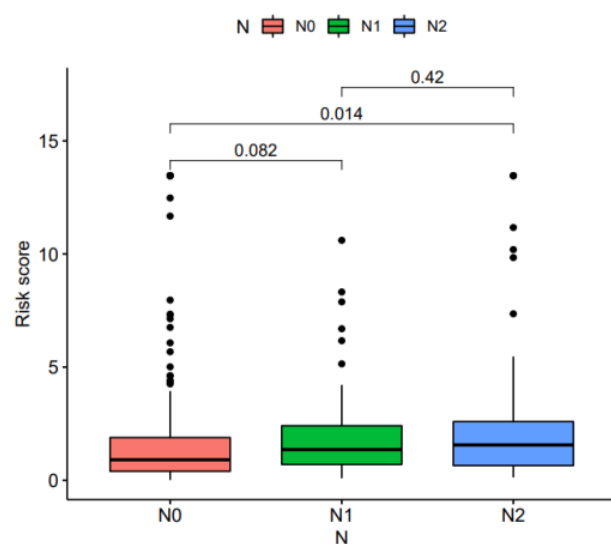
The survival curves of testing (A) and entire datasets (B). (C) and (E) are the distribution of risk scores, and survival status in the testing dataset, respectively. (D), (F) are the distribution of risk scores, and survival status in the entire cohort, respectively. The expression of CTLA4LncSigs in testing (G) and entire datasets (H).



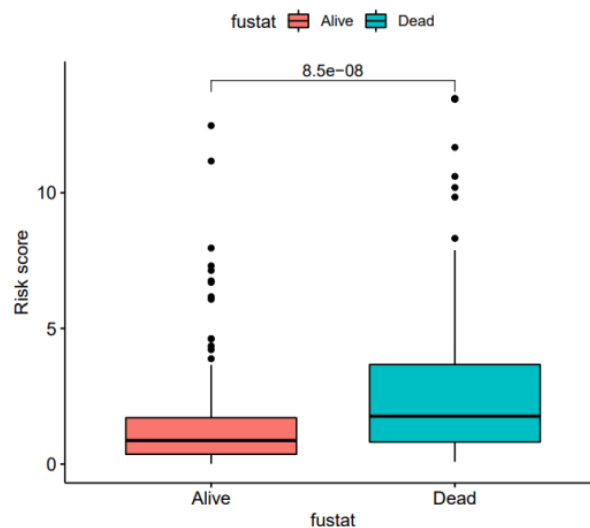
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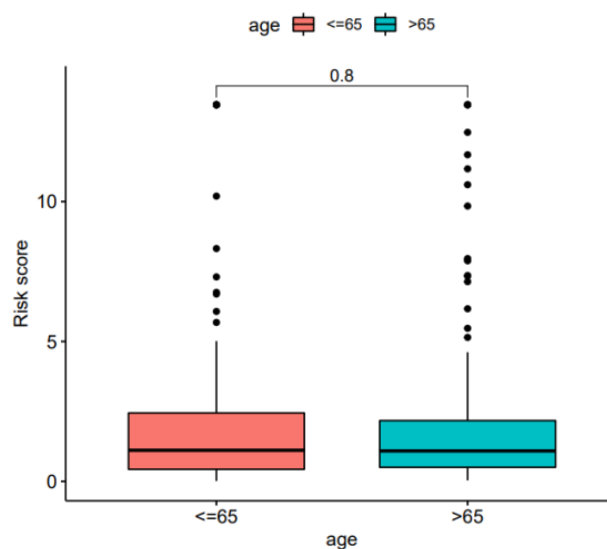
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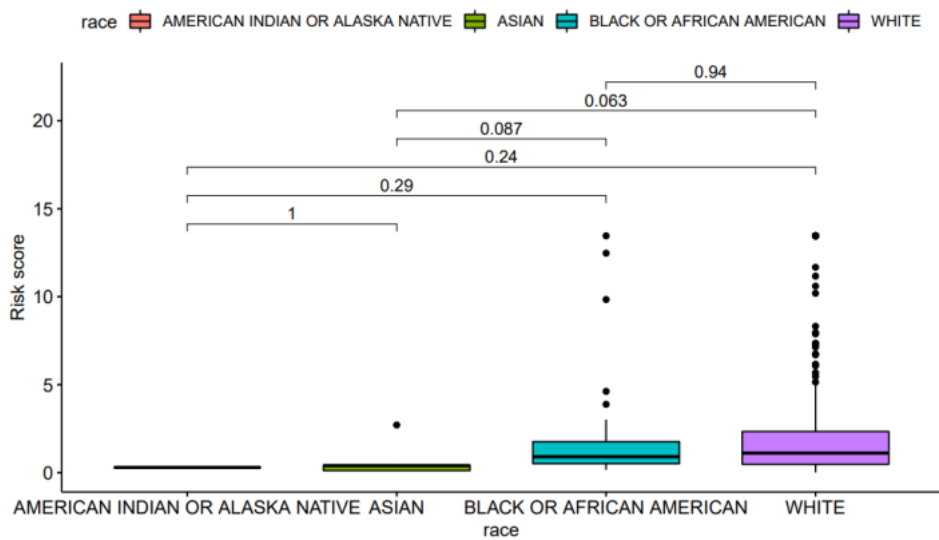
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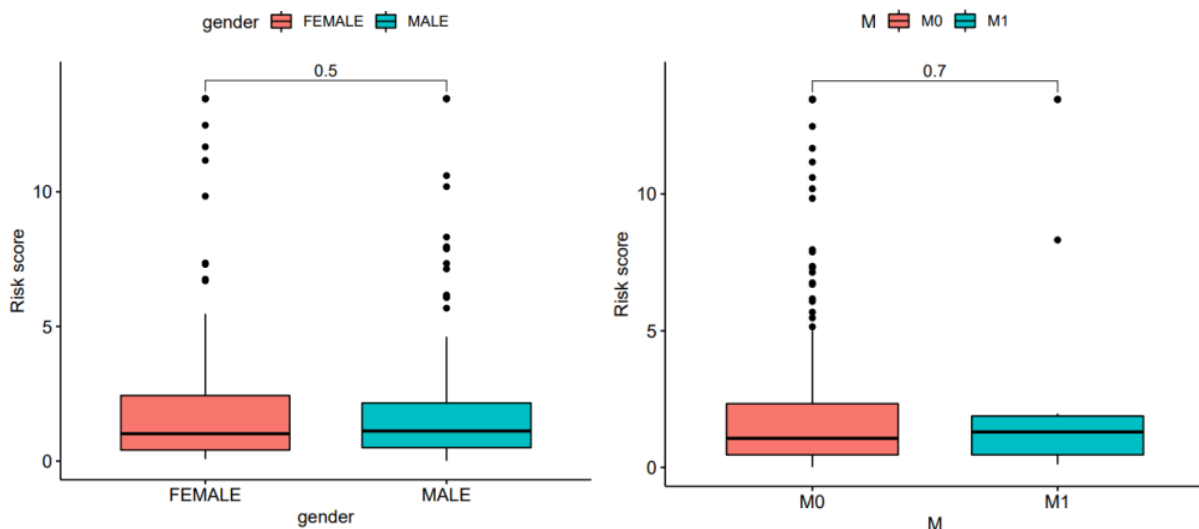
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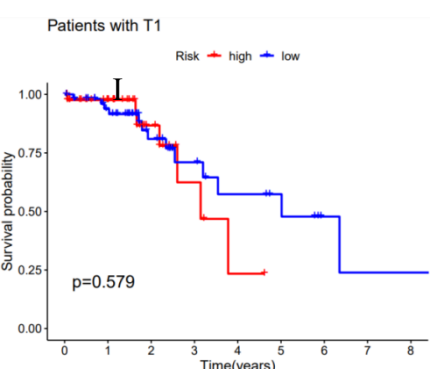
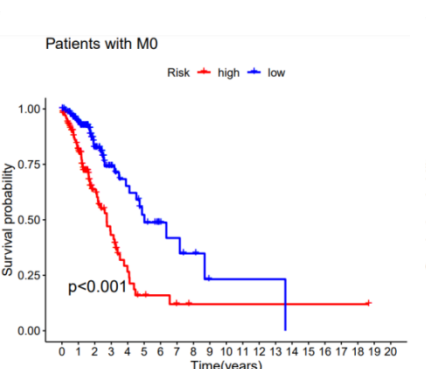
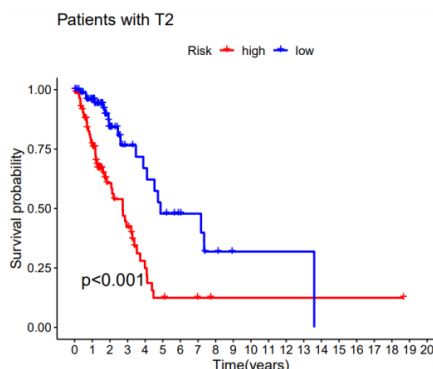
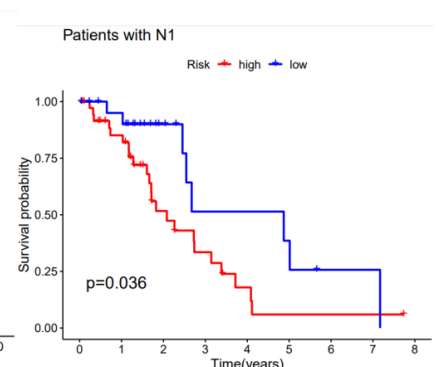
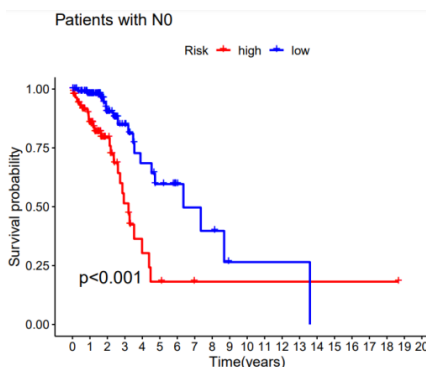
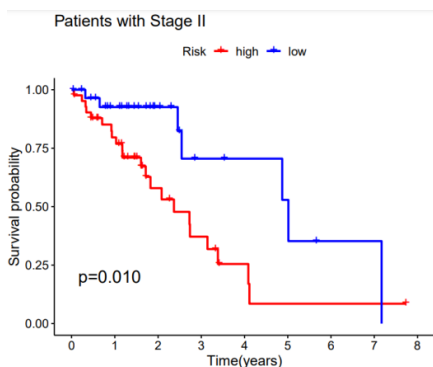
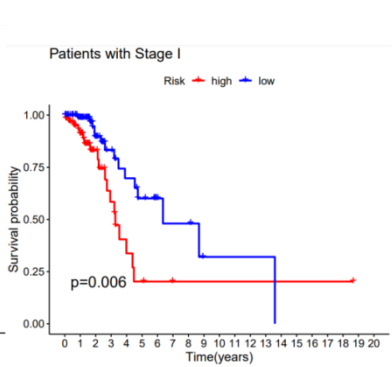
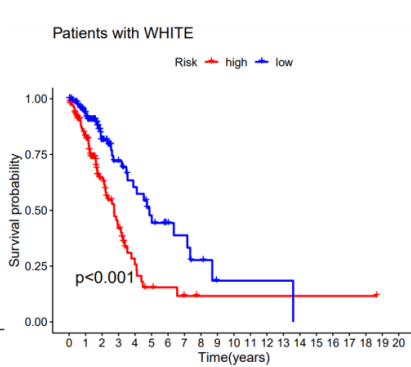
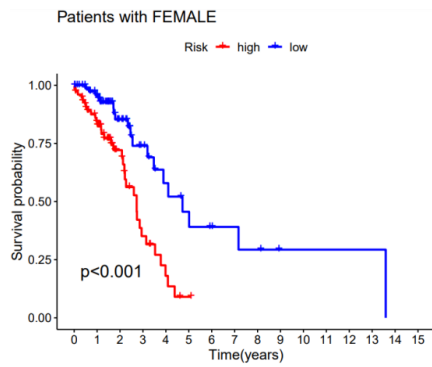
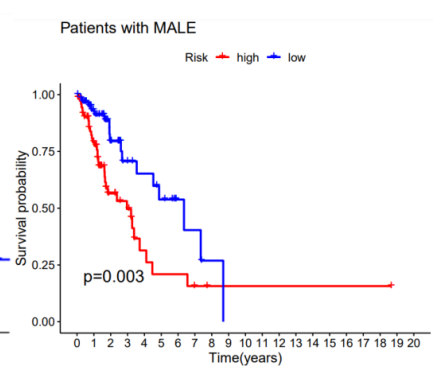
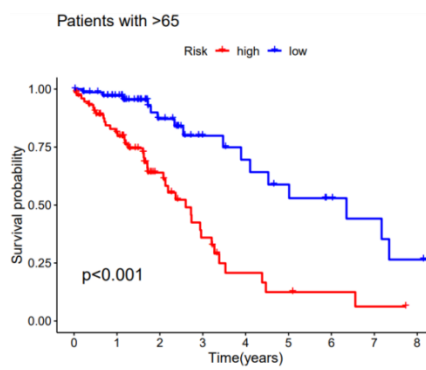
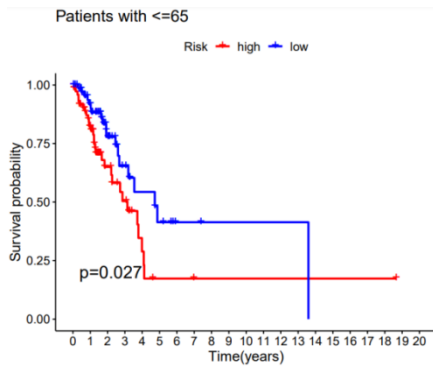


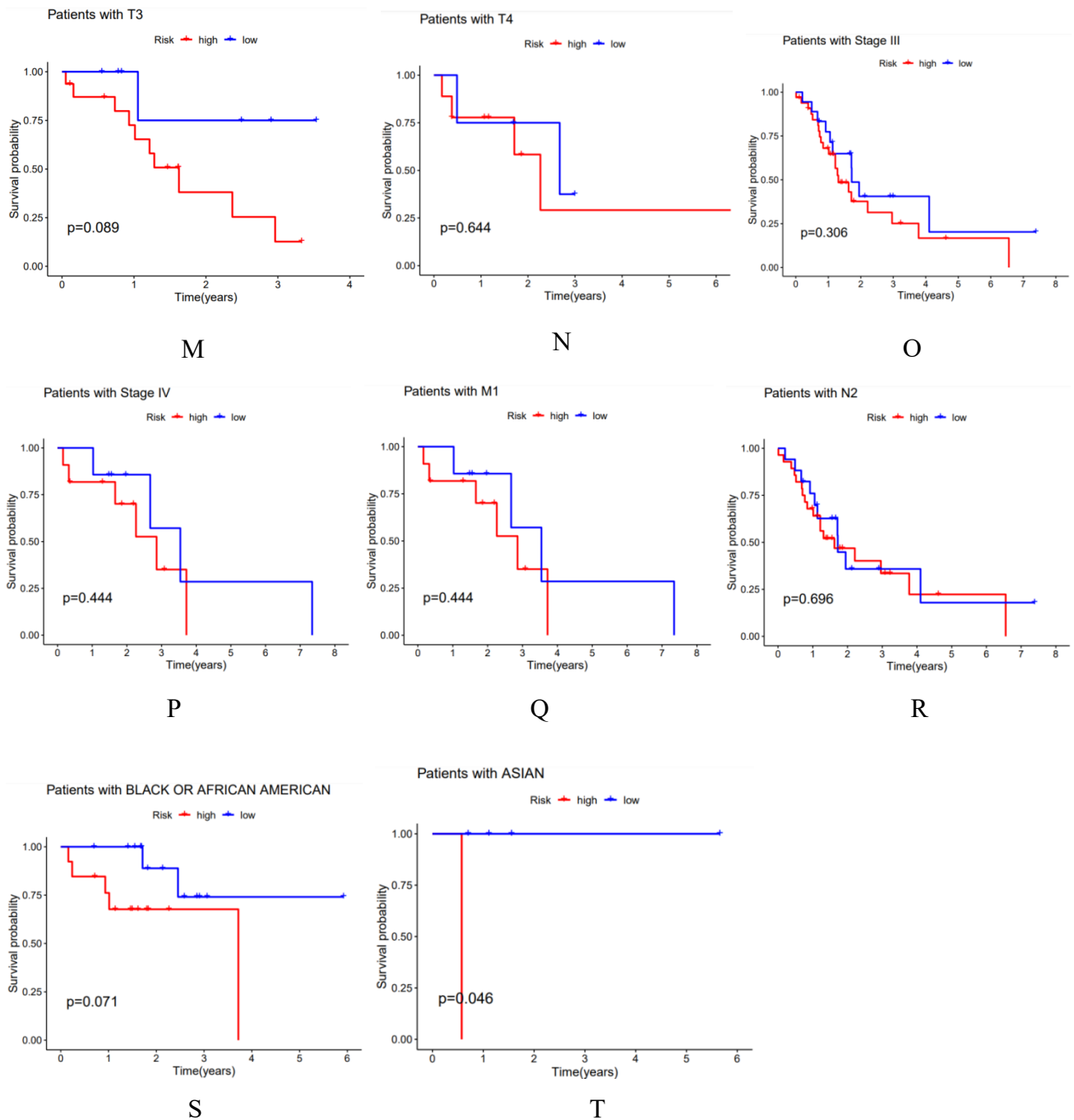
G

H

Supplementary Fig. S2. The Risk Score of Patients Grouping by Different Clinicopathological Factors.

Which include AJCC stage (A), T stage (B), N stage (C), survival state (D), age (E), race (F), gender (G), and M stage (H).





Supplementary Fig. S3. Overall Survival of Patients in High-risk and Low-risk Subgroups with Different Clinicopathological Factors.

The p value less than 0.05 were age ≤ 65 (A) and > 65 (B), male (C) and female (D), race-white (E), AJCC stages I-II (F-G), N0-N1 stage (H-I), T2 stage (J), M0 stage (K) and race-Asian (T). Overall Survival of Patients in High-risk and Low-risk Subgroups with Different Clinicopathological Factors

1 (p $\geq$ 0.05). Which include T1 (L) and T3-T4 stage (M-N), AJCC stages III-IV (O-P), M1 stage (Q),
2 N2 stage (R), race-black or African American (S).

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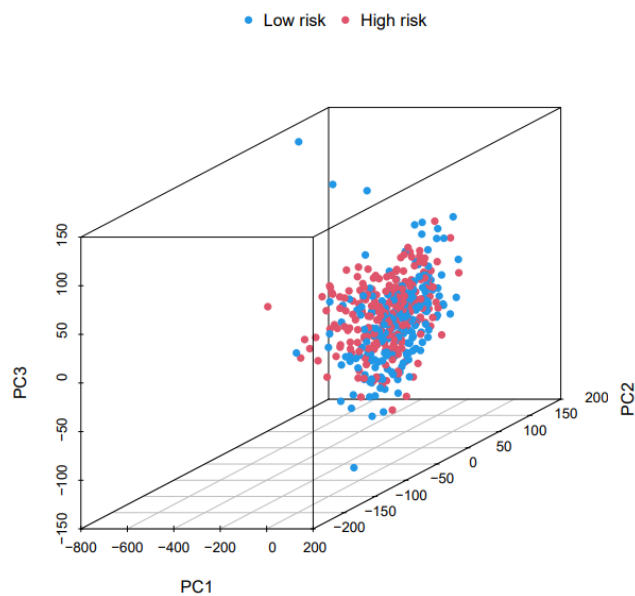
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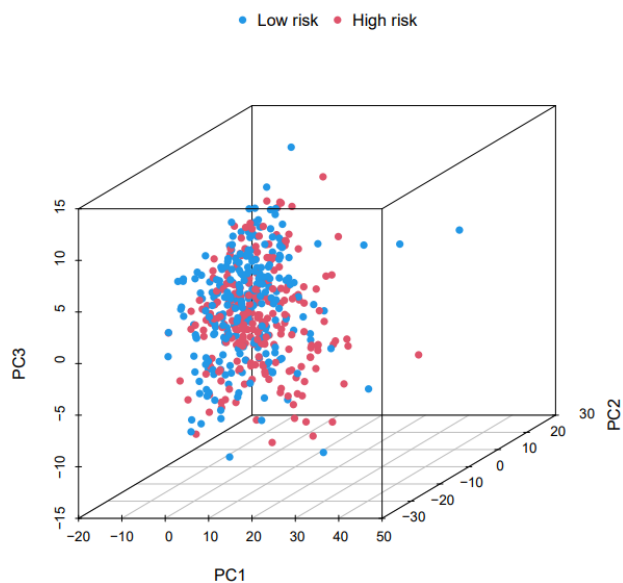
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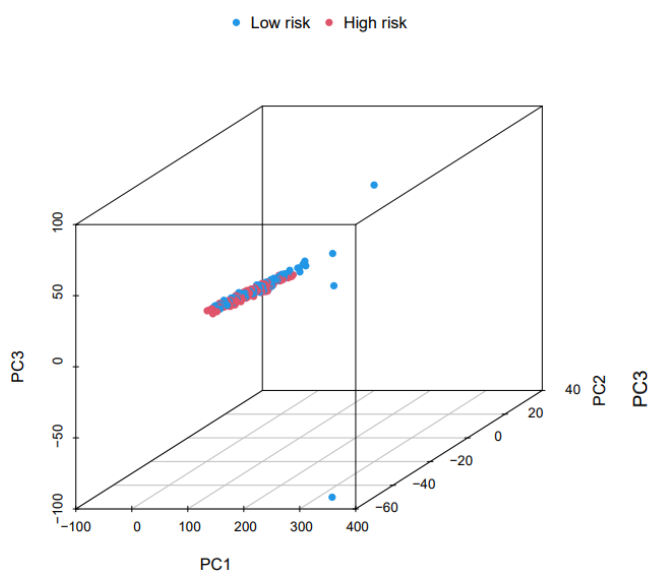
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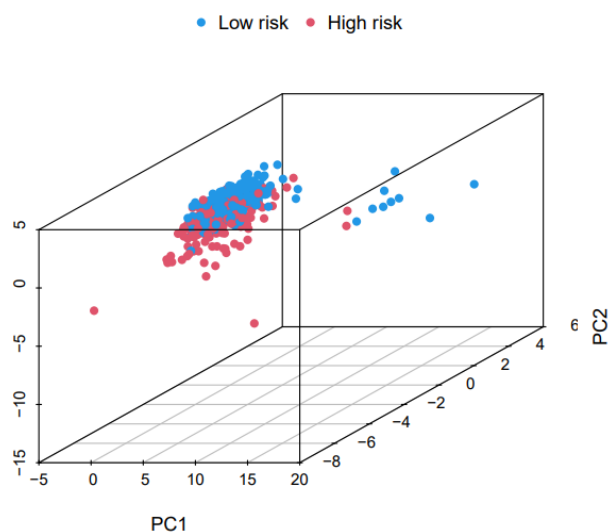
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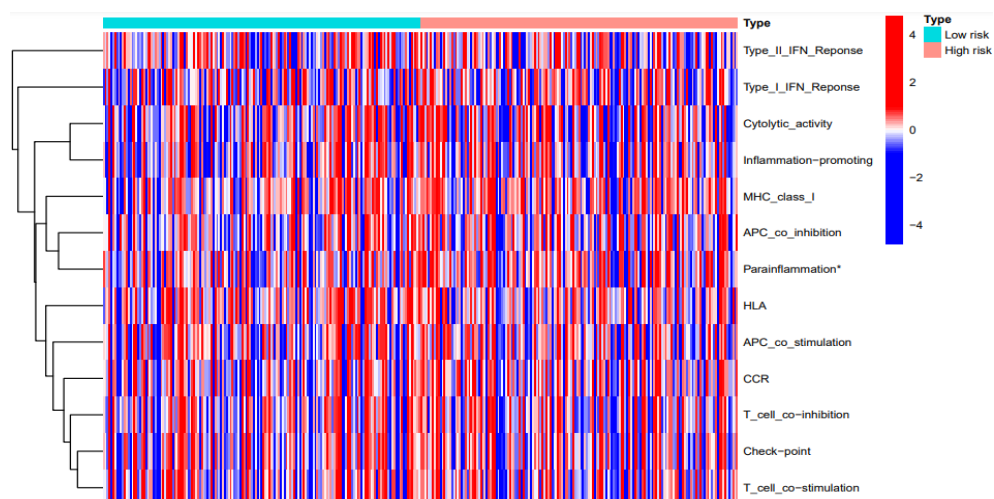
Supplementary Fig. S4. The 3D images of PCA results.

(A) is LUAD's genes. (B) is LUAD's mRNAs. (C) is LUAD's lncRNAs. (D) is 19CTLA4LncSigs.

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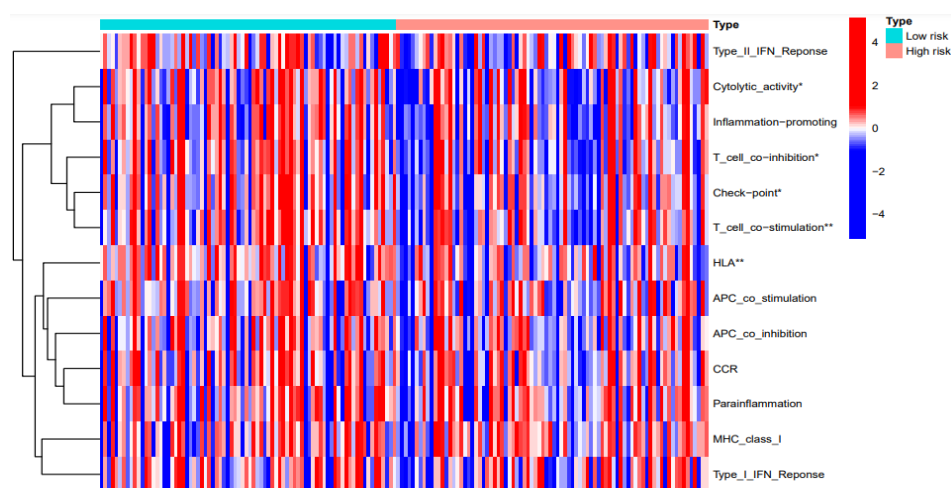
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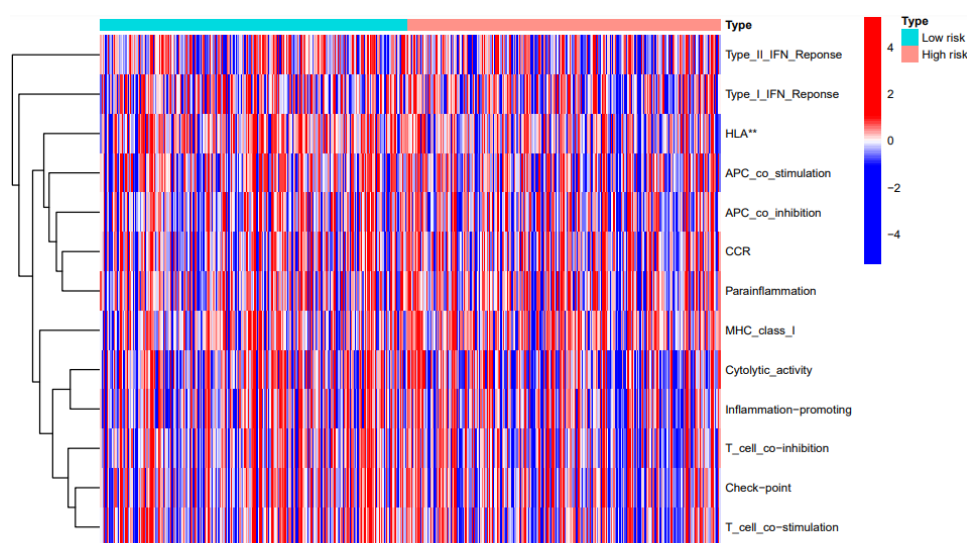
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Supplementary Fig. S5. The heat map of the expression of 13 immune functions between

1 **high-risk and low-risk subgroups.** In the training dataset (A). In the testing dataset (B). In the
2 entire dataset (C).

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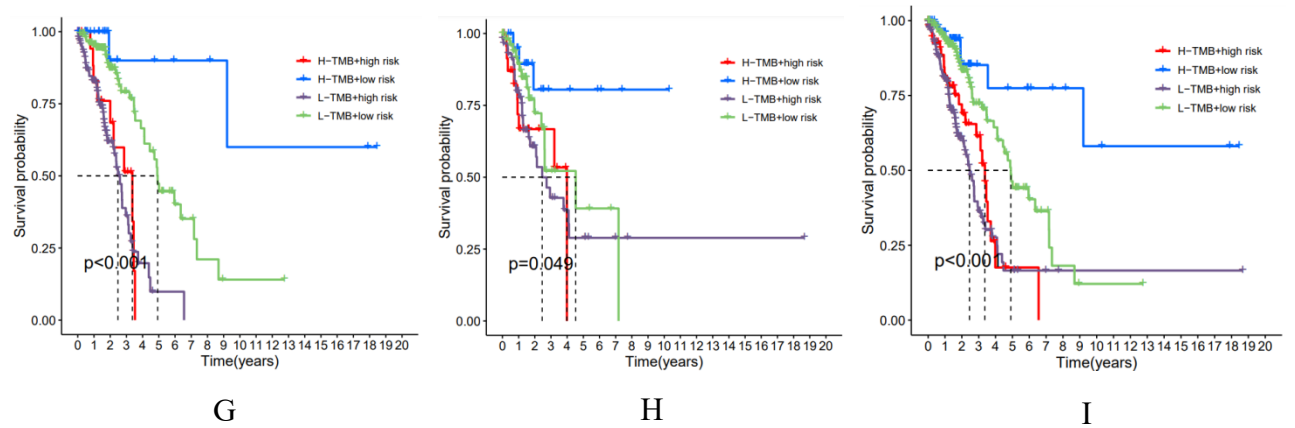
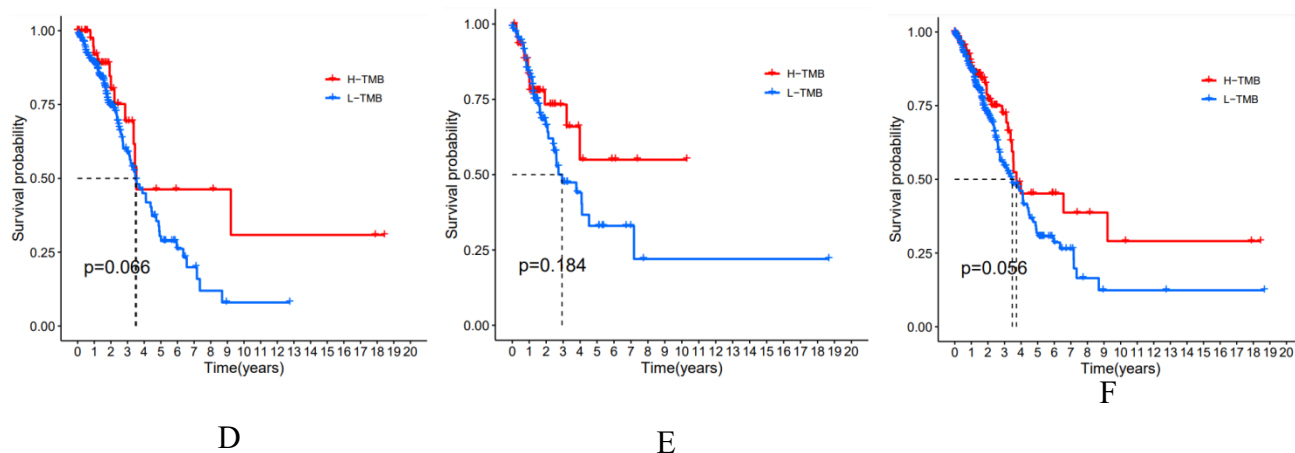
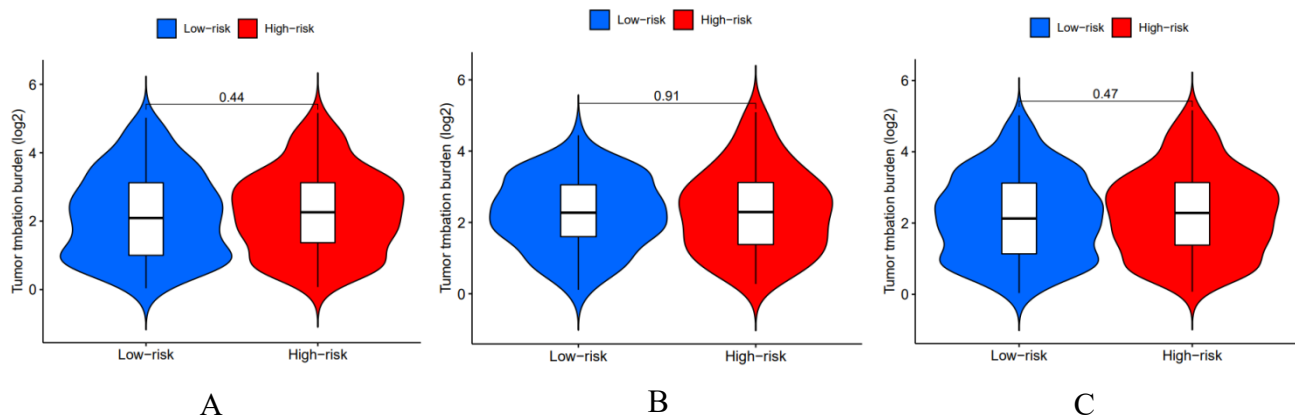
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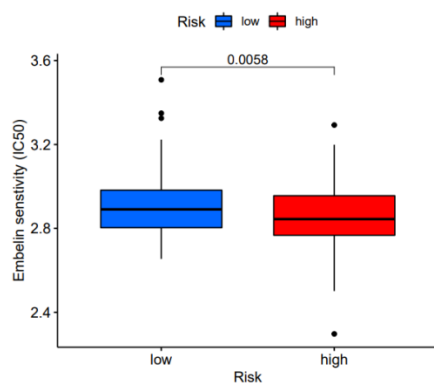
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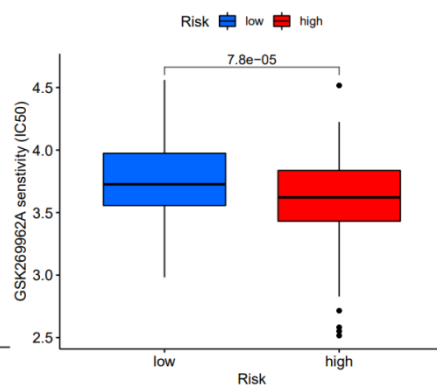
Supplementary Fig. S6. The effect of TMB on OS of LUAD patients.

TMB between high-risk and low-risk subgroups in training (A), testing (B), and entire datasets (C). The relationship between TMB and OS of LUAD patients in training (D), testing (E), and entire dataset (F). The impact of TMB combined with risk score on the OS of LUAD patients in training (G), testing (H), and entire datasets (I).

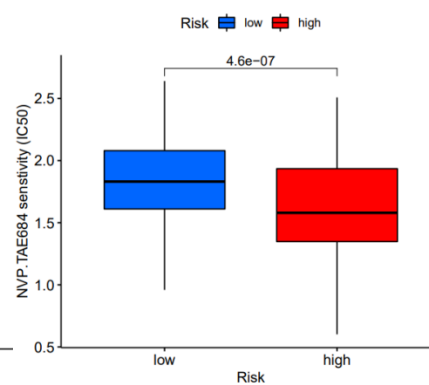
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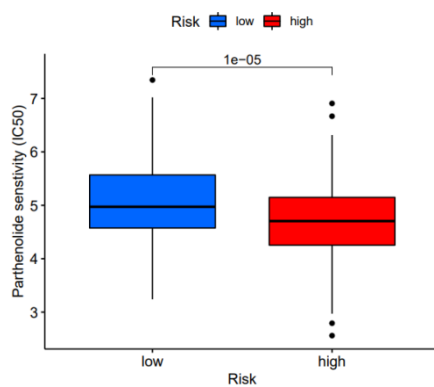
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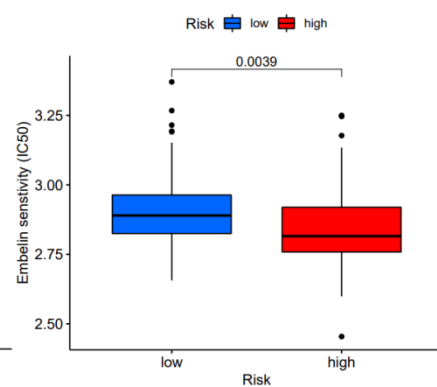
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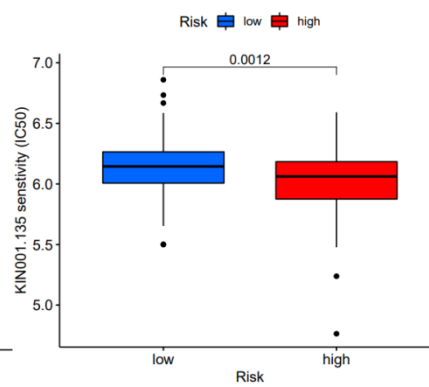
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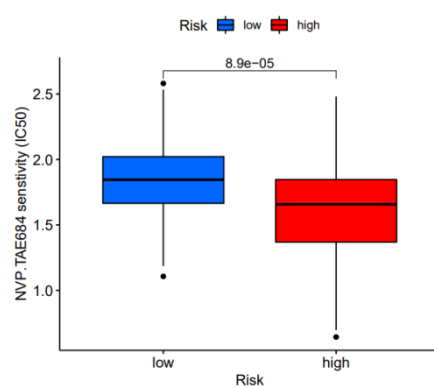
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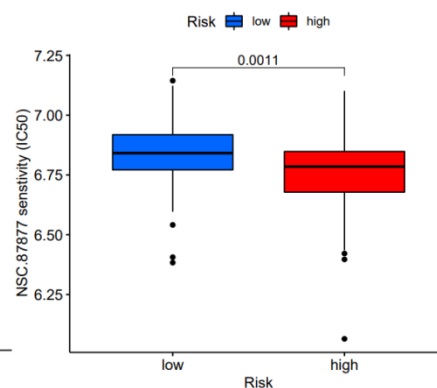
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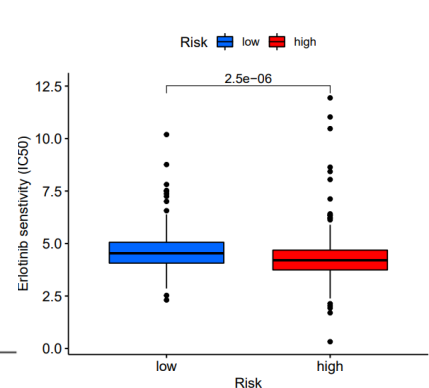
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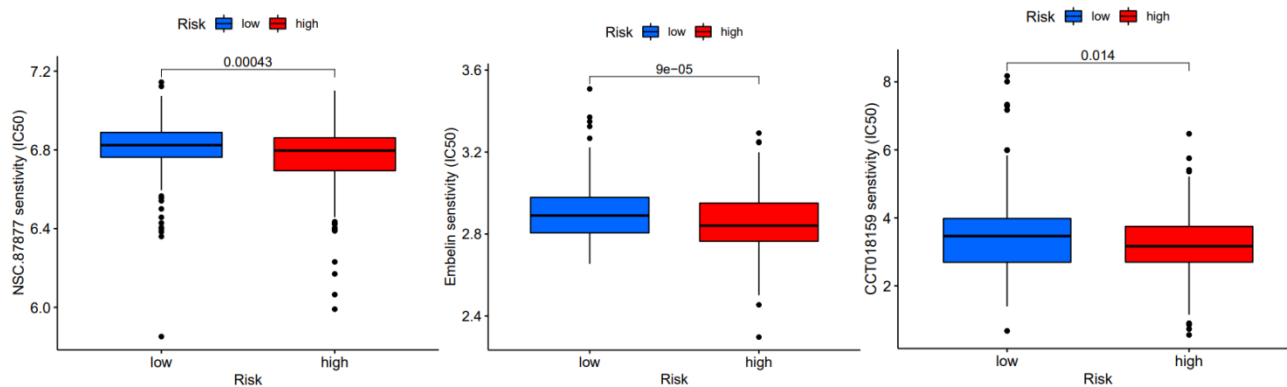
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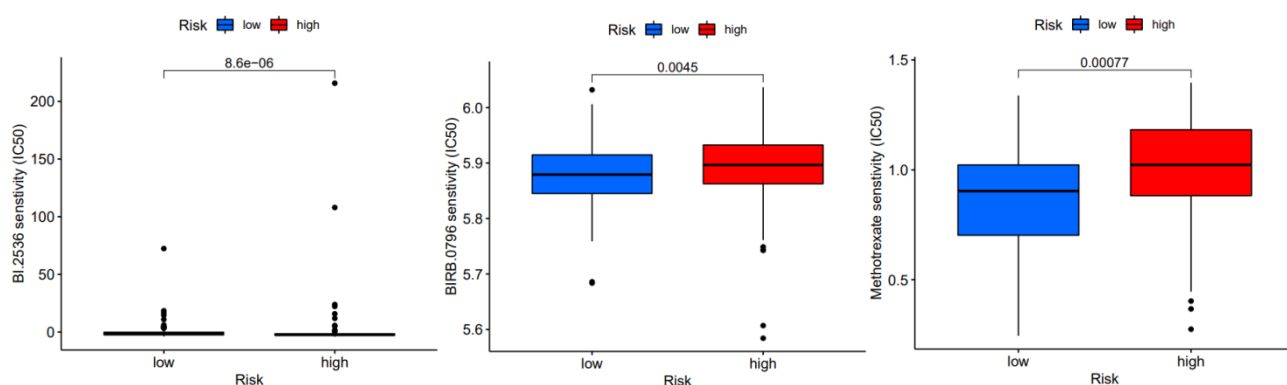
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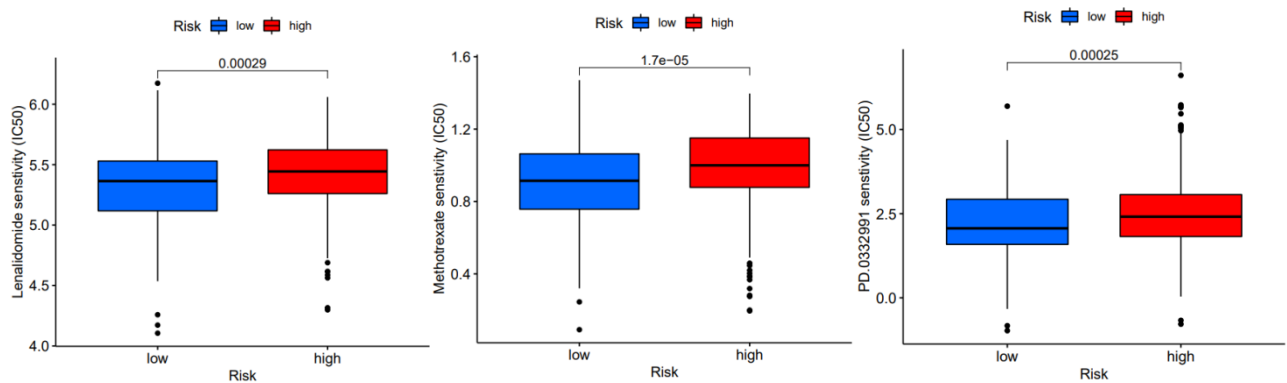
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R

Training

Testing

Entire

Supplementary Fig. S7. The IC50 of the drugs in different subgroups.

(A) to (L) are the drugs that are more sensitive to the high-risk subgroup (partial). (A), (B), (C) and (D) are in the training dataset, (E), (F), (G), and (H) are in the testing dataset, (I), (J), (K) and (L) are in the entire dataset. (M) to (R) are drugs that are more sensitive to the low-risk subgroup. (M) and

1 (N) were in the training dataset, and (O) was in the testing dataset. (P), (Q) and (R) were in the entire
2 dataset.

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1 **Supplementary Table S1. Details of Blood urea nitrogen levels and Lung cancer.**

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Trait	PMID	Year	Population	Sample size	Number of SNPs	Author
Blood urea nitrogen levels	34272381	2021	——	173,149	7,777,636	Stanzick KJ
Lung cancer	28604730	2017	European	85,716	7,857,154	McKay JD

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1 **Supplementary Table S2. Results of the univariate Cox regression analysis of the entire dataset.**

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gene	HR	HR.95L	HR.95H	p-value
AC004080.2	1.082934336	1.032151923	1.13621527	0.00114846
NR2F2-AS1	1.306599356	1.048744571	1.627852885	0.017111935
AC007728.2	0.786468106	0.620938674	0.996124267	0.046352346
AC008073.2	0.407311154	0.169054945	0.981351808	0.045293251
AC064875.1	1.587872928	1.00553295	2.507466748	0.047296609
AC090236.2	0.662104917	0.449126354	0.976079263	0.037321518
AC099788.1	1.34695439	1.027329144	1.766022252	0.03115802
AC011586.2	1.261872188	1.108109735	1.436970877	0.00045086
AF131215.6	0.887368506	0.800090567	0.984167165	0.023692245
LUADT1	1.196861163	1.000992956	1.431055668	0.048741194
AL135960.1	0.233303923	0.06776693	0.803204761	0.021032821
AL021026.1	0.573753614	0.335903377	0.980023521	0.041968097
LINC00996	0.840768241	0.736831905	0.959365671	0.009991709
AL136304.1	0.905141689	0.831744178	0.985016185	0.020895598
SH3BP5-AS1	0.951126208	0.912470271	0.991419767	0.017931681
AC012085.2	1.037142441	1.012903986	1.061960914	0.002505953
AP000302.1	0.380789585	0.159933577	0.906630807	0.029151933
AC018529.1	0.63885936	0.451407665	0.904152308	0.01145316
AL031667.3	1.055275844	1.016132605	1.09592695	0.00527382

AC006017.1	0.851433952	0.740034021	0.979603308	0.024576173
AC015914.1	0.793748458	0.633643571	0.994307594	0.044470351
AC087501.4	0.796909029	0.656399381	0.967496343	0.021799089
AC087854.1	0.691122933	0.485657119	0.983514687	0.040139858
AC025279.1	0.198285619	0.043588409	0.902010141	0.036314309
AL353801.3	0.731647996	0.559237865	0.957211276	0.022671792
ABALON	1.118352717	1.032462494	1.21138812	0.006078346
AC073316.1	1.135614569	1.004062564	1.284402483	0.04291815
LINC01537	1.306531555	1.184129093	1.441586661	9.96E-08
LINC01415	1.373092184	1.125922437	1.674522227	0.001740627
AC083967.1	1.046358692	1.022015394	1.071281822	0.000161214
AP001178.1	1.263705069	1.004861171	1.589225007	0.045345748
AL049775.1	1.190728633	1.032466617	1.373249899	0.016437001
AC012050.1	1.207254856	1.069214997	1.363116202	0.002364009
PAN3-AS1	0.847303211	0.722325745	0.993904393	0.041845007
FAM30A	0.916719953	0.844818444	0.994740916	0.036934112
AL109811.1	0.512169913	0.28061647	0.934791959	0.029285274
AC010999.2	0.562749926	0.367079407	0.862721998	0.008355905
AC021086.1	2.481531523	1.192793485	5.162669627	0.015030732
TMPO-AS1	1.099220753	1.050127106	1.150609539	4.95E-05
LINC02587	1.01053917	1.00416145	1.016957397	0.001172202
PRR34	1.467169103	1.027510304	2.0949524	0.034919188

AC090559.1	0.941808337	0.898195661	0.987538664	0.013200298
ATP13A4-AS1	0.946756479	0.903615246	0.991957401	0.021486819
LINC00519	1.045403901	1.022542401	1.068776527	8.29E-05
IL12A-AS1	1.099924253	1.038743831	1.164708107	0.001107114
AF131215.5	0.911574537	0.840305868	0.9888877	0.025813824
AC009318.2	1.082688727	1.015125777	1.154748412	0.015665776
ADPGK-AS1	0.297316148	0.109276019	0.80893221	0.017540705
AC104971.3	0.86334478	0.750256663	0.993478959	0.040238158
MIR4527HG	1.121364663	1.05771455	1.188845051	0.000122069
LINC00626	1.113982574	1.026782333	1.208588361	0.009445927
AC092171.2	1.017951948	1.002707883	1.033427767	0.020819764
LINC01876	1.055222773	1.007461876	1.105247878	0.022933194
AC009318.3	1.106497465	1.016513364	1.204447165	0.019365336
AC099524.1	0.72835673	0.539526605	0.983275933	0.038441712
AC005291.1	1.039277216	1.011435646	1.067885174	0.005424553
AC026355.2	0.916802154	0.870389078	0.965690184	0.001048816
L3MBTL2-AS1	0.770753714	0.610807399	0.972583646	0.028219451
AC026310.2	0.295973674	0.08774283	0.99837692	0.049694705
AC090948.1	0.865076447	0.762808529	0.98105518	0.023950003
HLA-DQB1-AS1	0.975567788	0.961741079	0.989593281	0.000682884
AL121820.1	1.158074104	1.056123853	1.269865864	0.001800263
SMILR	1.045403997	1.025164542	1.066043031	8.53E-06

AL117335.1	1.302721333	1.063943904	1.595086793	0.010468278
AC105036.3	1.269835586	1.027776973	1.568903038	0.026837373
AC079949.1	1.010203792	1.000286106	1.020219812	0.043717118
AL606834.1	1.057295742	1.004128165	1.113278489	0.034305671
AC108134.4	0.931326444	0.867690202	0.999629758	0.048813283
HAGLR	0.994663907	0.989501019	0.999853734	0.043898925
AL359878.1	0.712798689	0.521658622	0.973974071	0.033542924
FAM66C	1.511295301	1.140214763	2.003143234	0.004069069
LINC01800	0.159773076	0.044083746	0.57906685	0.005245642
AC025419.1	1.022107018	1.012496922	1.031808328	5.71E-06
AL359232.1	1.66091549	1.050364242	2.626365363	0.029996673
AL021368.2	0.761648876	0.580252637	0.999752476	0.049791871
FOCAD-AS1	0.666813592	0.450880406	0.986160324	0.042380174
LINC00598	1.282973887	1.11474256	1.476593838	0.000511547
AP003064.2	0.795293091	0.642010146	0.98517306	0.036019406
LINC02360	1.046899739	1.010074356	1.085067706	0.012120729
AC012676.4	0.661909175	0.455714996	0.961398591	0.030259806
AC108136.1	1.073737122	1.04254361	1.105863961	2.25E-06
AL360270.1	1.136150535	1.007353352	1.281415342	0.037588916
LINC01150	0.863347547	0.766981071	0.97182188	0.014962121
LINC01385	1.081698859	1.029928338	1.136071686	0.001698365
AC034102.8	0.75289254	0.602980774	0.940075043	0.012229738

LINC01600	1.457417177	1.057064035	2.009400337	0.021526096
AL121985.1	0.455818791	0.207952639	0.999125431	0.049745124
AP001528.1	1.097766237	1.018284893	1.183451429	0.014995369
AL356608.1	0.255017943	0.070854663	0.917852802	0.036515016
AC114550.2	0.5377777959	0.290685719	0.994906576	0.048128451
AC103808.6	1.156912255	1.026888805	1.303399121	0.016567364
LINC00892	0.75146881	0.607346068	0.929791766	0.008538081
ABCA9-AS1	1.567709086	1.283962628	1.914161458	1.02E-05
AC107959.1	0.765476361	0.594108125	0.986275115	0.038749139
LINC02410	0.509924384	0.260126444	0.99960186	0.049864612
AC008764.2	0.96430039	0.932004169	0.997715754	0.036479816
AC010998.1	0.762926945	0.584942734	0.995067533	0.045885401
AL031600.2	0.450346933	0.253046479	0.801482642	0.006680274
AL162632.3	3.695901635	1.69840779	8.042643809	0.000983583
GLCCI1-DT	0.661247844	0.447525873	0.977035604	0.037838445
AC087752.3	0.849131091	0.766026139	0.941251966	0.001857739
AC103591.3	0.947287851	0.897790108	0.999514546	0.047962833
AL138789.1	1.038011263	1.013629782	1.062979207	0.002096051
AP000977.1	0.291992556	0.092806311	0.918683784	0.035292162
AC079061.1	1.63700646	1.131837759	2.367645122	0.008852105
AC046143.1	1.1011228	1.042017881	1.163580245	0.000621294
AC026356.1	1.066578976	1.003872934	1.133201895	0.037069134

LINC01747	2.277931742	1.366151381	3.798241611	0.001599421
CYP1B1-AS1	0.750027118	0.563999287	0.997413811	0.047954784
LINC00671	0.322219065	0.106249596	0.977181372	0.045420097
AP001094.3	1.225739043	1.005455273	1.494284471	0.044031609
DIRC3	1.117901687	1.054523193	1.185089329	0.000182015
AC090617.5	0.907419292	0.8395815	0.980738346	0.014263096
AC090023.2	1.123323834	1.063139905	1.186914751	3.48E-05
TSPOAP1-AS1	0.720639205	0.54757979	0.948393043	0.019381398
AC007613.1	0.610590436	0.387570077	0.961943923	0.03339778
LINC02728	0.625632803	0.396747439	0.986563154	0.04357275
AL358115.1	1.299719611	1.058978439	1.595189293	0.01213272
AF121898.1	1.138634374	1.059795219	1.223338448	0.000390672
ZEB2-AS1	0.445124159	0.206371132	0.960093184	0.039036309
AC005291.2	1.021318746	1.00887915	1.033911724	0.000741416
LINC02310	1.197449903	1.079869984	1.327832324	0.000632815
FRMD6-AS1	1.584761118	1.250944422	2.007657379	0.00013606
AL137779.1	0.649380947	0.441341573	0.955485819	0.028447772
AP000695.1	1.064896756	1.027451617	1.103706572	0.00057579
LINC02147	0.100883916	0.021672901	0.469598633	0.003463647
AC007686.2	0.242396846	0.075328008	0.780005111	0.017471814
AC091057.1	1.121974531	1.021803951	1.23196514	0.015864765
AC026368.1	1.039398709	1.013263202	1.066208339	0.002939186

LINC00377	1.322247484	1.106745719	1.57971102	0.002088727
ZFHX4-AS1	1.215366094	1.052344445	1.403641887	0.007947861

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1 **Supplementary Table S3. Clinicopathological factors of lung adenocarcinoma between training**
2 **and testing datasets.**

Covariates	Type	Total	Test	Train	P-value
fustat	Alive	190(64.63%)	59(62.11%)	131(65.83%)	0.6212
fustat	Dead	104(35.37%)	36(37.89%)	68(34.17%)	
age	<=65	147(50%)	48(50.53%)	99(49.75%)	1
age	>65	147(50%)	47(49.47%)	100(50.25%)	
gender	FEMALE	155(52.72%)	45(47.37%)	110(55.28%)	0.2521
gender	MALE	139(47.28%)	50(52.63%)	89(44.72%)	
race	AMERICAN INDIAN OR ALASKA NATIVE	1(0.34%)	0(0%)	1(0.5%)	0.2494
race	ASIAN	5(1.7%)	1(1.05%)	4(2.01%)	
race	BLACK OR AFRICAN AMERICAN	27(9.18%)	13(13.68%)	14(7.04%)	
race	WHITE	261(88.78%)	81(85.26%)	180(90.45%)	
stage	Stage I	153(52.04%)	50(52.63%)	103(51.76%)	0.2399
stage	Stage II	72(24.49%)	26(27.37%)	46(23.12%)	
stage	Stage III	51(17.35%)	17(17.89%)	34(17.09%)	
stage	Stage IV	18(6.12%)	2(2.11%)	16(8.04%)	
T	T1	96(32.65%)	31(32.63%)	65(32.66%)	0.2763
T	T2	162(55.1%)	55(57.89%)	107(53.77%)	
T	T3	23(7.82%)	8(8.42%)	15(7.54%)	

T	T4	13(4.42%)	1(1.05%)	12(6.03%)	
M	M0	276(93.88%)	93(97.89%)	183(91.96%)	0.0845
M	M1	18(6.12%)	2(2.11%)	16(8.04%)	
N	N0	189(64.29%)	57(60%)	132(66.33%)	0.5663
N	N1	60(20.41%)	22(23.16%)	38(19.1%)	
N	N2	45(15.31%)	16(16.84%)	29(14.57%)	

The p value of each clinicopathological factor is over 0.05 which means that there were no statistical differences in each clinicopathological factor between the training and testing datasets. Our grouping is reasonable.

1 **Supplementary Table S4. Selecting the CTLA4LncSigs by univariate Cox regression analysis in**
2 **the risk score model.**

id	HR	HR.95L	HR.95H	p-value
NR2F2-AS1	1.750195139	1.113988336	2.749744253	0.015171044
AP000253.1	4.36550617	1.588968564	11.99372005	0.004262793
AL137782.1	1.399030806	1.042320215	1.877817554	0.025353301
CACNA2D1-AS1	1.905081571	1.228692474	2.953819501	0.003972394
AC092168.2	1.384361407	1.059461203	1.808897297	0.01716253
AL078645.1	0.573863049	0.340010232	0.968555556	0.037562158
AC060809.1	3.1490413	1.40228695	7.071634735	0.005451042
AF131215.6	0.767943581	0.592309903	0.995656735	0.046281614
LUADT1	2.728613187	1.076255477	6.917809092	0.034448028
AC022858.1	2.7076119	1.183600366	6.193950602	0.018314194
AC002546.1	2.070010167	1.128357464	3.797504095	0.018771667
AL603839.3	0.728025283	0.534518723	0.991585121	0.044054683
AC020915.2	1.569803135	1.051434669	2.343732766	0.027437638
AC009135.1	1.911200601	1.216092698	3.003626076	0.004982769
AC087501.4	0.627799753	0.408717769	0.964314643	0.033511328
LINC01537	2.227880162	1.447058632	3.430026887	0.000274345
LINC01415	2.23344205	1.38117306	3.611613586	0.001049506
AC012050.1	1.836074169	1.124883452	2.996904567	0.015068819
PAN3-AS1	0.693013469	0.483274249	0.993778727	0.046163346

AL109811.1	0.458806196	0.223177237	0.943210551	0.03409286
AC025741.1	3.482595043	1.604386997	7.559565279	0.001602421
AC010999.2	0.420407123	0.23534824	0.75098139	0.00341774
TMPO-AS1	1.359042014	1.048004607	1.762392248	0.020691457
AL354696.2	2.070114268	1.095901565	3.910363137	0.024950604
LINC00519	1.285358951	1.015985778	1.626152322	0.036426459
ERCC8-AS1	0.523110471	0.276777049	0.988682286	0.046041928
AC009318.2	1.532040725	1.080328092	2.172625892	0.016690238
AC092111.2	2.537804515	1.07859431	5.9711531	3.29E-02
AC104971.3	0.745066586	0.55821644	0.994460532	0.045752222
LINC00626	1.434825675	1.042162422	1.975435569	0.026890084
AC009318.3	1.392419564	1.02476461	1.891978143	0.034314593
AC026355.2	0.731104658	0.600326267	0.890372537	0.001841238
AC106038.1	6.790080033	1.523621638	30.26025997	0.011996396
L3MBTL2-AS1	0.651257981	0.424633134	0.998831517	0.049376979
AC090948.1	0.701752659	0.516992459	0.952541545	0.023095793
HLA-DQB1-AS1	0.84436719	0.737966419	0.966108936	0.013828434
AL121820.1	1.550837775	1.027660535	2.340362137	0.036625171
SMILR	1.55570094	1.211384808	1.997883248	0.000535393
AL117335.1	2.038473264	1.306130704	3.181437535	1.71E-03
AC105036.3	1.568948836	1.006699135	2.445219596	0.04665094
AC079949.1	1.240771414	1.045542652	1.472454231	0.013517427

AC127164.1	1.770475137	1.193012325	2.627451658	0.004565793
FAM66C	1.896768368	1.093395668	3.29041933	0.022747445
AC025419.1	1.330835024	1.002212311	1.767212237	4.82E-02
DACT3-AS1	4.318243572	1.449506363	12.86453652	0.008627357
LINC00598	2.429689215	1.406785311	4.196368581	0.001451928
AP001363.1	1.469513021	1.089128677	1.982748745	0.011782614
LINC02360	1.500859248	1.126165267	2.000220169	0.005592374
AC012676.4	0.531198862	0.308406077	0.914937327	0.022582554
NPAS2-AS1	2.765663128	1.341092662	5.703478031	0.005874773
AC108136.1	1.938636412	1.492379925	2.518334022	7.07E-07
AC006064.2	1.497510406	1.033879246	2.169051584	0.03266112
AL360270.1	1.556513227	1.131902116	2.140408955	0.006483085
DLEU1	1.482858795	1.035872414	2.122723007	0.031356042
LINC01600	2.17915349	1.150478452	4.12759572	0.016844464
AL122035.1	1.491024239	1.140722502	1.948899297	0.003460534
AP001528.1	1.396040882	1.031756838	1.888943278	0.030571484
AL031666.1	0.757208566	0.582302268	0.984651519	0.037950691
AL031600.2	0.366260709	0.182572894	0.73475807	0.004688917
FARSA-AS1	1.663865996	1.054933353	2.624289056	0.02852511
LINC01776	2.064036501	1.181386907	3.606140081	0.010912669
AC087752.3	0.723638632	0.538731688	0.972010522	0.031671754
AC090971.2	1.443250658	1.029438089	2.02340722	3.33E-02

AC005746.2	1.732662563	1.178072487	2.54833178	0.005229296
AL139383.1	0.443668625	0.202175125	0.973620513	0.042700098
AL138789.1	1.538450932	1.216681697	1.945316738	0.000320468
AC079061.1	2.925950214	1.648568022	5.193103678	0.000244657
AC046143.1	1.607609804	1.116805908	2.314107818	0.010638442
AC026356.1	1.403676218	1.066022249	1.848279364	0.015719391
LINC01747	3.064244478	1.321746896	7.103927574	0.009049199
AC012409.4	1.738352039	1.122705737	2.691593812	0.013181136
AF121898.1	1.756979214	1.279410651	2.412810895	0.000496807
AC007619.1	1.407740954	1.026153667	1.931225954	3.40E-02
LINC02310	2.249583587	1.412947911	3.581608547	0.000633665
LINC02584	1.72119216	1.125525587	2.632105824	0.012224565
AP000695.1	1.32141095	1.056425221	1.652863699	0.014660503
ZFHX4-AS1	1.646934061	1.120857055	2.419926598	0.011051615

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1 **Supplementary Table S5. Selecting the CTLA4LncSigs by multivariate Cox regression analysis**
2 **in the risk score model.**

id	coef	HR	HR.95L	HR.95H	p-value
AP000253.1	1.608746266	4.996542964	1.406925248	17.74468234	0.012848
`CACNA2D1-AS1`	1.125029507	3.080307737	1.631548439	5.815515819	0.000521
AL078645.1	-0.906333235	0.404002895	0.213385517	0.764898863	0.005388
LINC01415	0.662403301	1.939447815	1.131752718	3.323568629	0.015938
AC010999.2	-1.187922481	0.304853947	0.140602297	0.660984429	0.002625
`ERCC8-AS1`	-1.349894184	0.259267694	0.110058933	0.610761301	0.002017
AC104971.3	-0.454416546	0.634818247	0.467873773	0.861331047	0.003514
AC026355.2	-0.203542909	0.815835197	0.653289611	1.018823898	0.07258
`L3MBTL2-AS1`	-0.59542681	0.551327204	0.329648128	0.922079212	0.023261
AL117335.1	0.674354484	1.96276557	1.139696975	3.380239458	0.015039
AC105036.3	0.691925884	1.997558897	1.066091127	3.742870985	0.030794
AC127164.1	0.964229071	2.622764912	1.297796679	5.300441811	0.007229
FAM66C	0.761046206	2.140514469	1.051819052	4.356074538	0.035788
`NPAS2-AS1`	1.266421106	3.548131427	1.19053607	10.57442688	0.023027
AC108136.1	0.41175641	1.5094667	1.121291419	2.032022792	0.006633
AL031600.2	-0.887648317	0.411622621	0.178718774	0.948043561	0.037041
`FARSA-AS1`	0.638161068	1.892996585	1.1238825	3.188443694	0.01644
AL139383.1	-0.735879109	0.479084107	0.186648203	1.229701534	0.126006
AC079061.1	1.126432975	3.084633886	1.546130204	6.154052346	0.001391

1 **Supplementary Table S6. The result of pleiotropic test.**

id.exposure	id.outcome	egger_intercept	se	pval
ebi-a-GCST90103632	ebi-a-GCST004748	-0.00159	0.001975	0.420487

2 “id.exposure” means the exposure ID in IEU Open GWAS platform; “id.outcome” means the
3 outcome ID in IEU Open GWAS platform; “se” means standard error of effect size; “pval” means
4 p-value of statistical significance.

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7 **Supplementary Table S7. Five methods of 2SMR.**

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id.exposure	id.outcome	method	nsnp	b	se	pval	lo_ci	up_ci	or	or_lci95	or_uci95
ebi-a-GCST90103632	ebi-a-GCST004748	Inverse variance weighted	328	-0.416670621	0.208488796	0.045659487	-0.825308662	-0.00803258	0.659238024	0.438099747	0.991999595
ebi-a-GCST90103632	ebi-a-GCST004748	MR Egger	328	-0.103247414	0.441026569	0.815048851	-0.967659489	0.76116466	0.901903802	0.379971325	2.140768037
ebi-a-GCST90103632	ebi-a-GCST004748	Weighted median	328	-0.397367248	0.310367119	0.200434861	-1.005686801	0.210952304	0.672087158	0.365793321	1.234853457
ebi-a-GCST90103632	ebi-a-GCST004748	Simple mode	328	-0.311746208	0.737237566	0.672677394	-1.756731838	1.133239422	0.732167323	0.172608054	3.105700897
9 ebi-a-GCST90103632	ebi-a-GCST004748	Weighted mode	328	-0.229895173	0.373429398	0.538565515	-0.961816793	0.502026447	0.794616895	0.38219788	1.652065704

10 Open GWAS platform; “nsnp” means the number of using SNP; “b” means the estimate of the effect
11 size; “se” means standard error of effect size; “pval” means p-value of statistical significance; “lo_ci”
12 means lower bound confidence interval for the estimate; “up_ci” means upper confidence interval for
13 the estimate; “or” means odds ratio; “or_lci95” means 95% lower bound confidence interval for the
14 odds ratio; “or_uci95” means 95% upper confidence interval for the odds ratio.