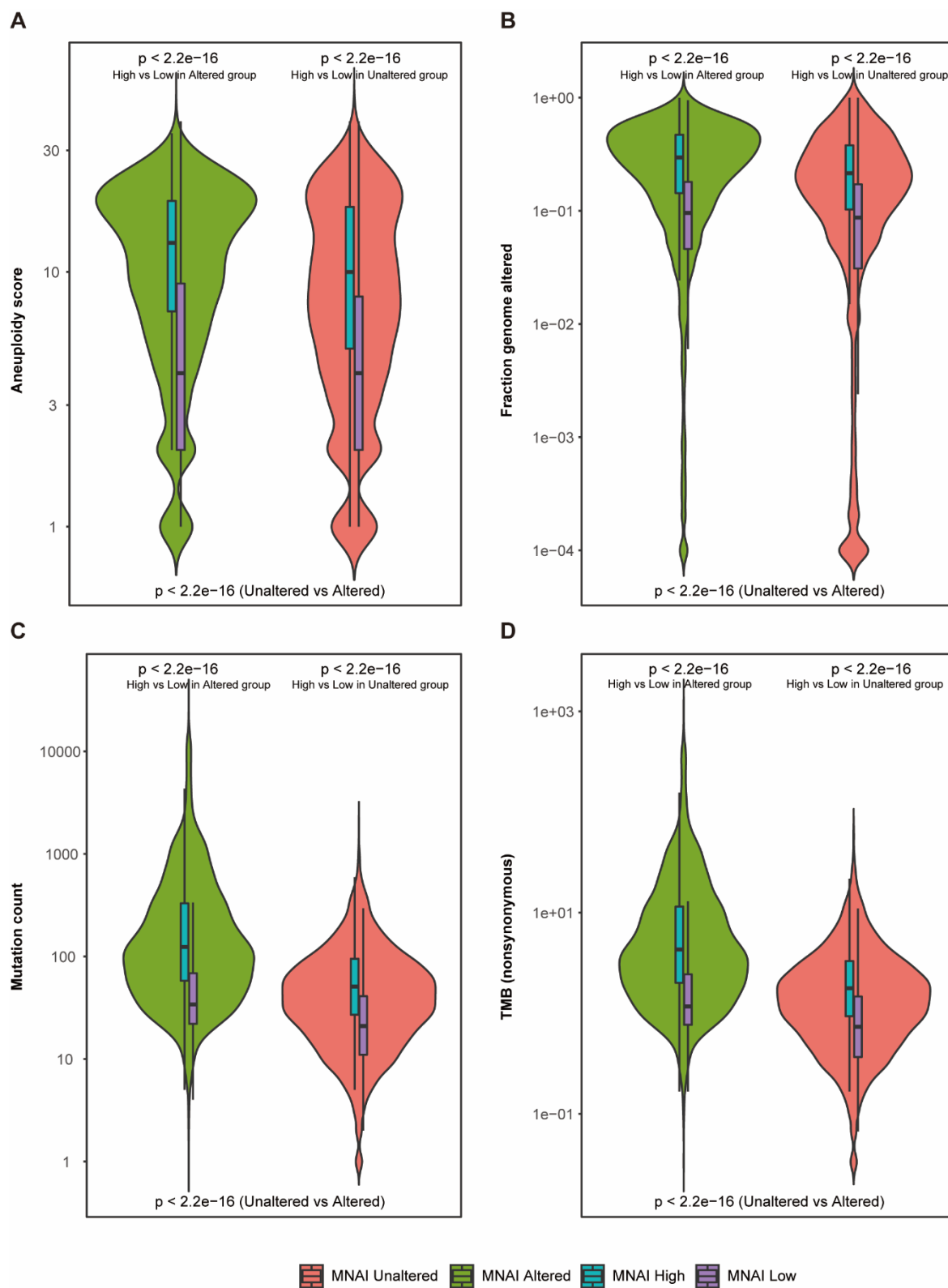
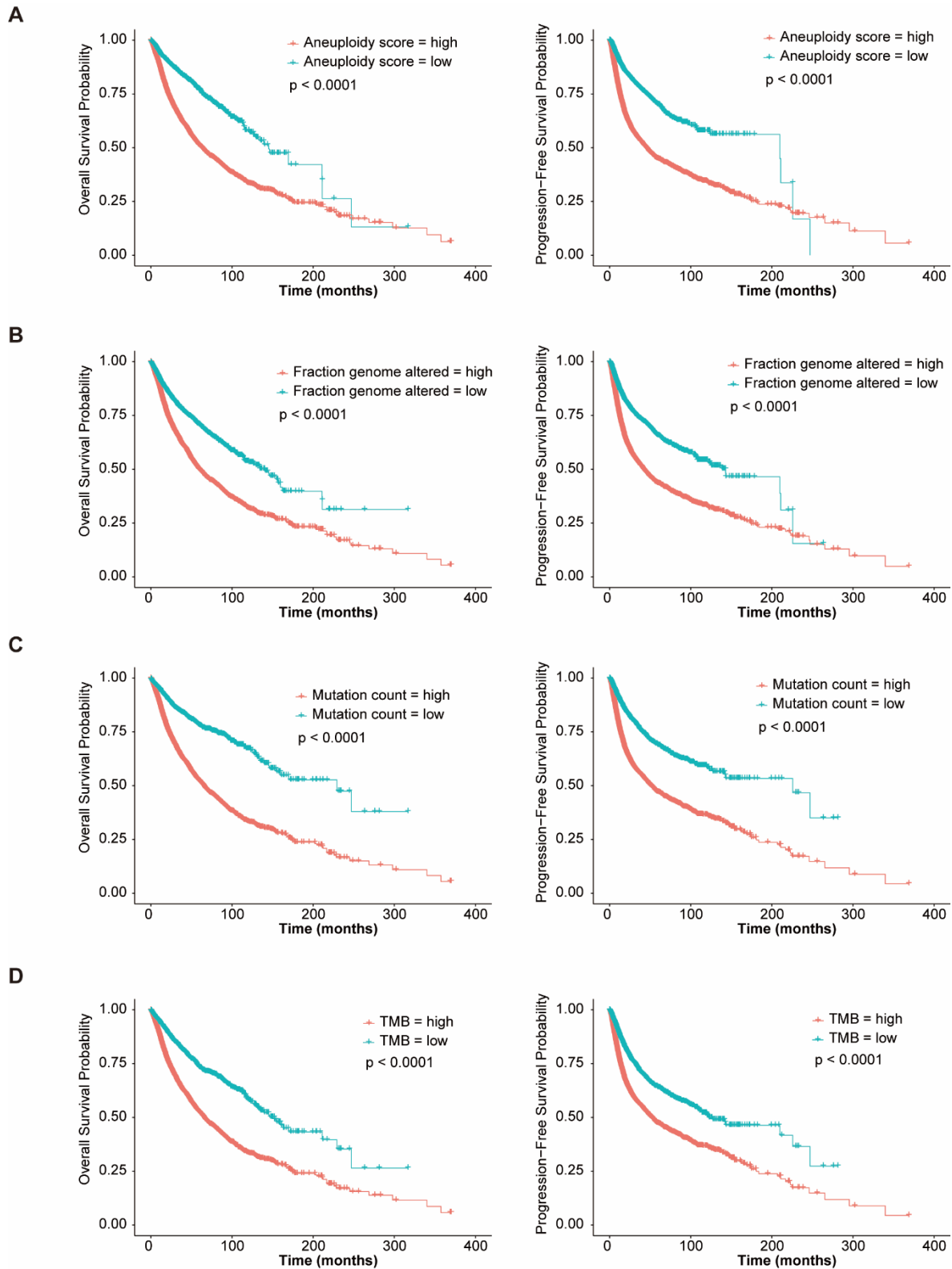
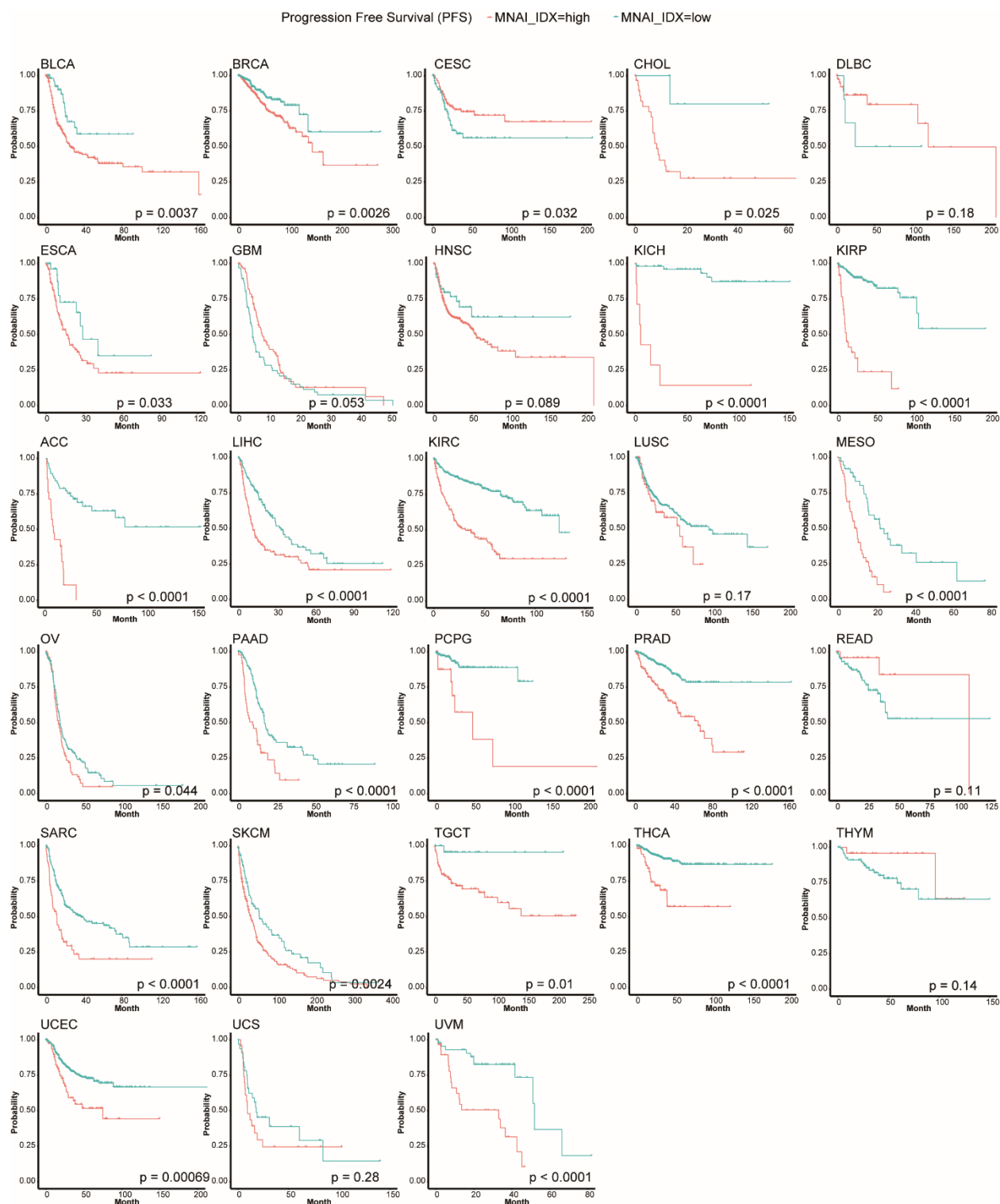




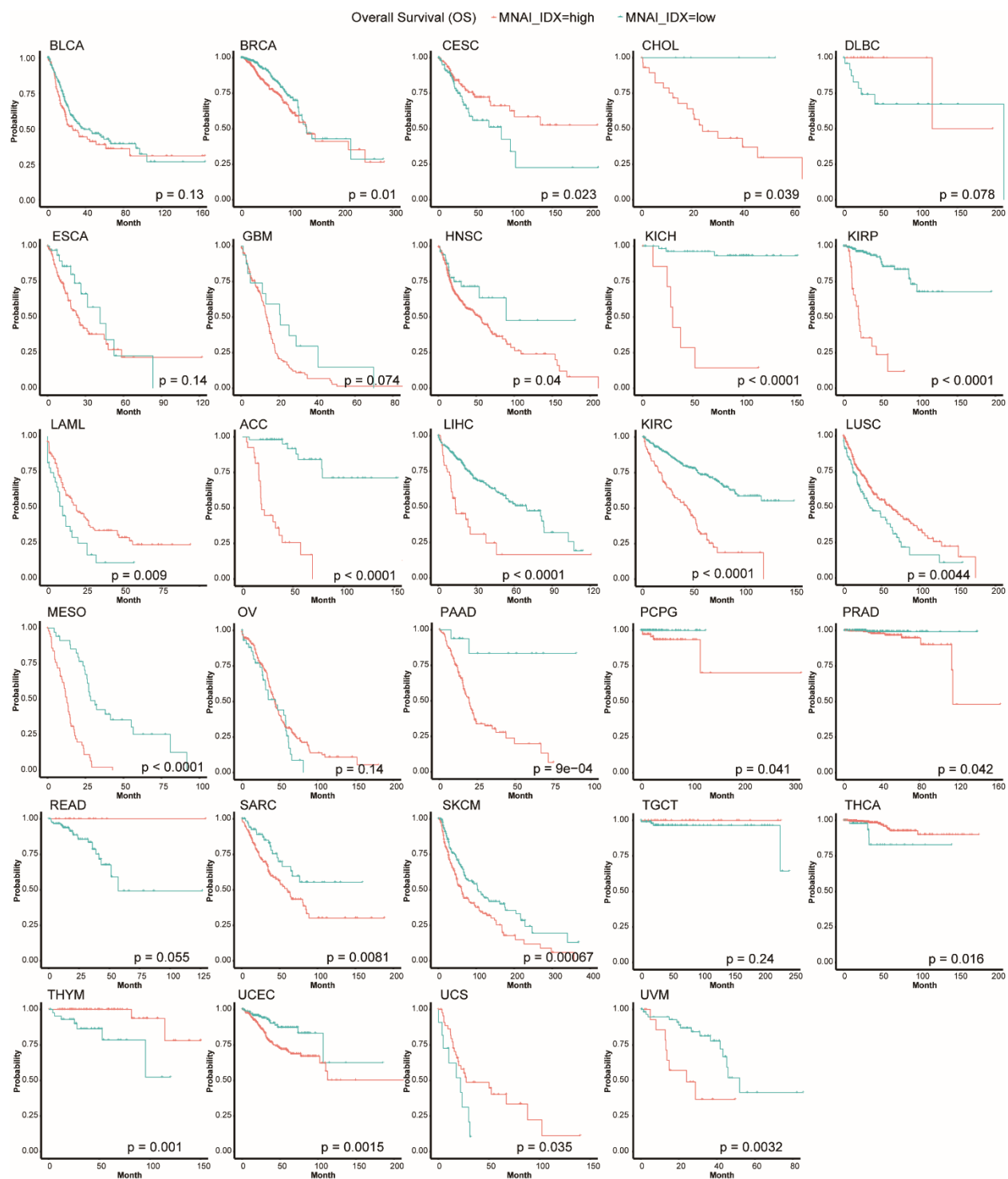
Supplementary Figure 1. Pan-cancer association of MNAI with genomic instability. (A) Aneuploidy score; (B) Fraction genome altered; (C) Mutation count; (D) Tumor mutation burden (TMB, nonsynonymous). The p values were obtained from Wilcoxon test.



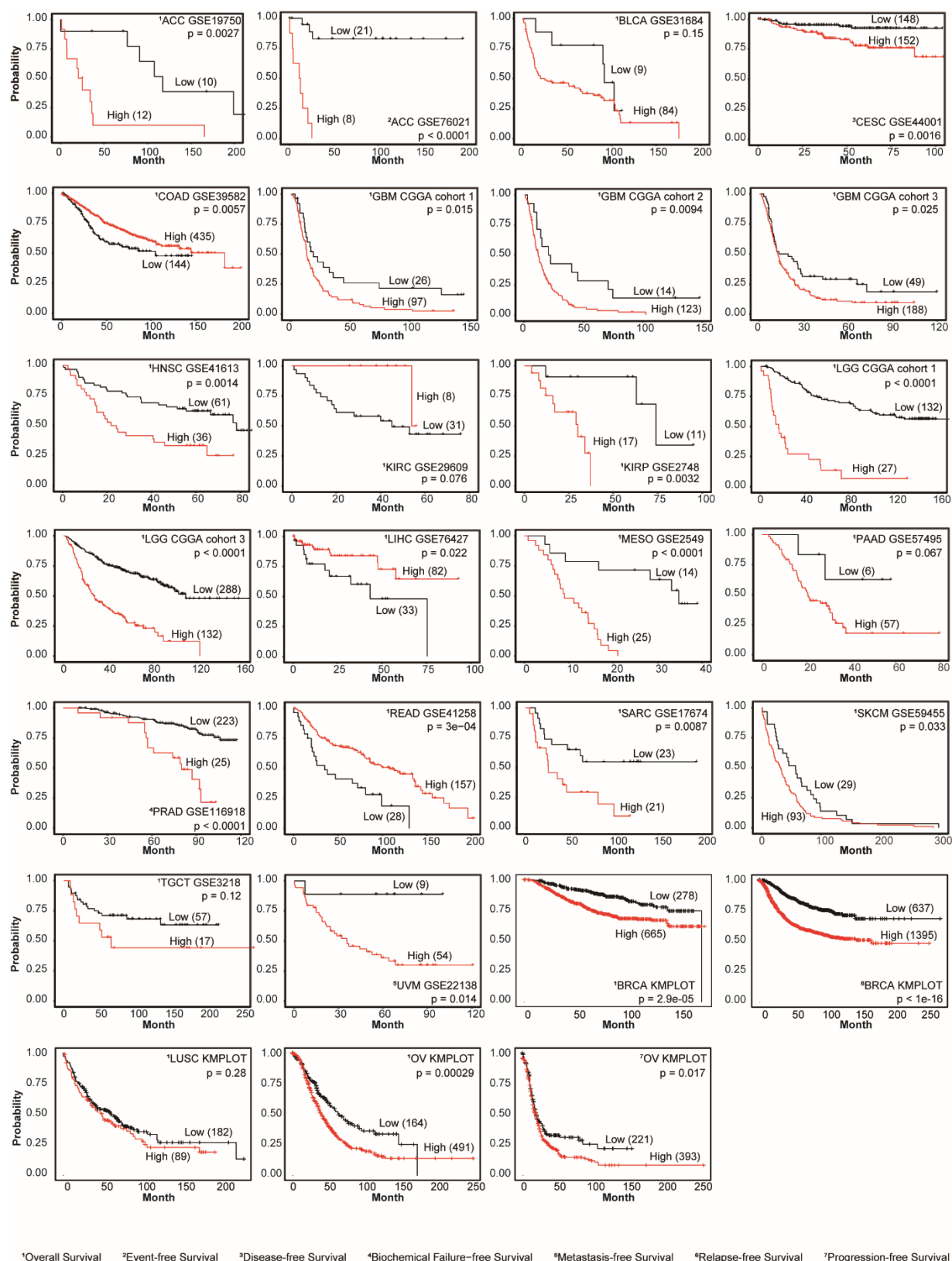
Supplementary Figure 2. Pan-cancer prognostic value of genomic instability on OS and PFS in TCGA. (A) Aneuploidy score; (B) Fraction genome altered; (C) Mutation count; (D) Tumor mutation burden (TMB, nonsynonymous). The p values were obtained from log-rank test.



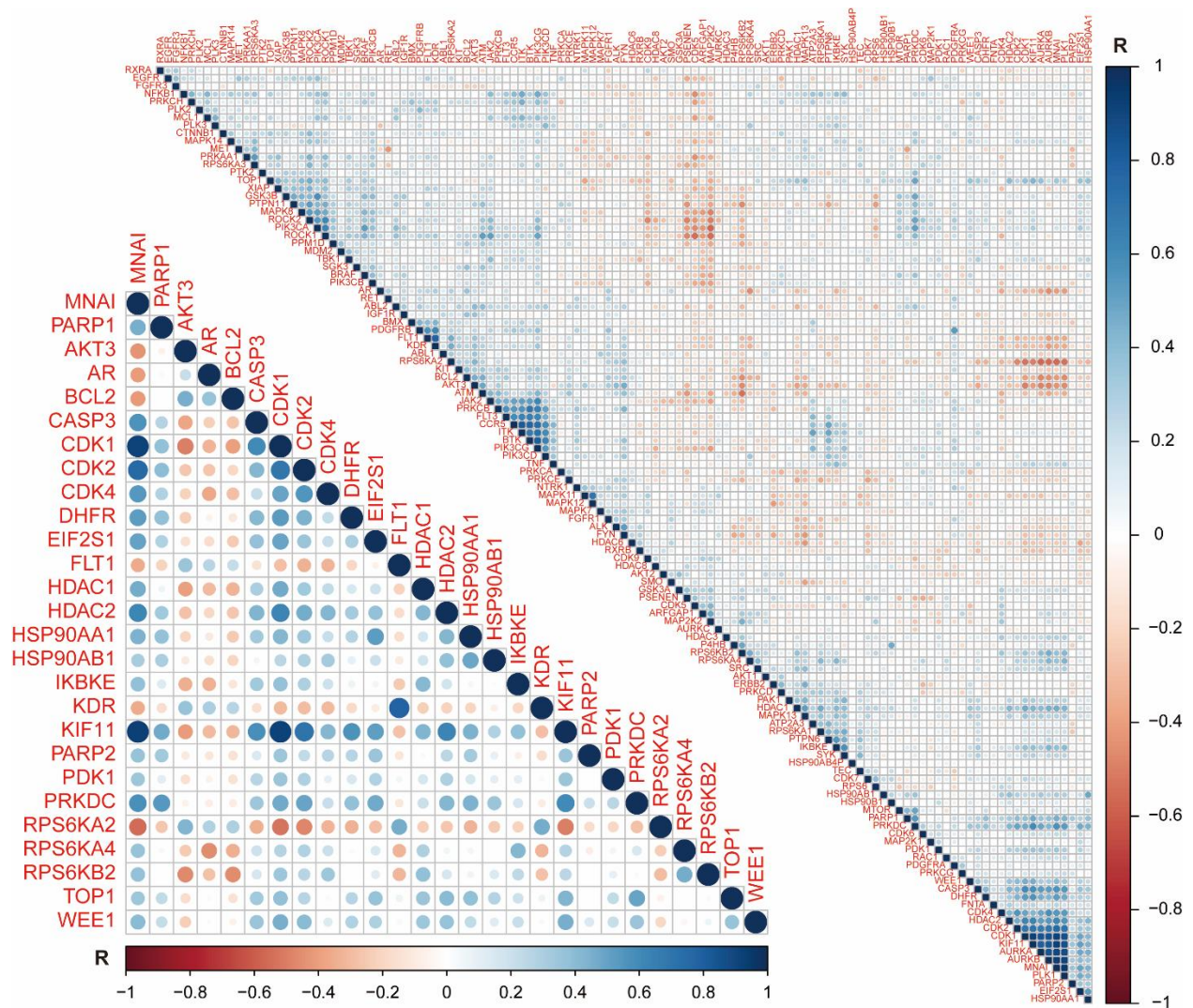
Supplementary Figure 3. Pan-cancer prognostic value of MNAI on PFS in TCGA.



Supplementary Figure 4. Pan-cancer prognostic value of MNAI on OS in TCGA.



Supplementary Figure 5. Pan-cancer prognostic value of MNAI on different prognostic endpoints in validation cohorts.



Supplementary Figure 6. TCGA Pan-cancer association of MNAI with different molecular targets obtained from CancerDR database. Upper pane, correlation plots with all molecular targets available in both CancerDR and TCGA; Lower pane, correlation plots with significant molecular targets (Spearman correlation, $|R| > 0.3$ and $p \text{ value} < 0.05$) available in both CancerDR and TCGA.

Supplementary Table 1. Information on TCGA datasets used in the study.

Study Abbreviation	Study Name	Number of OS events	Number of PFS events	Total number of patients
ACC	Adrenocortical carcinoma	27	40	78
BLCA	Bladder Urothelial Carcinoma	179	174	407
BRCA	Breast invasive carcinoma	151	145	1082
CESC	Cervical squamous cell carcinoma and endocervical adenocarcinoma	68	68	294
CHOL	Cholangiocarcinoma	18	20	36
COAD	Colon adenocarcinoma	98	116	436
DLBC	Lymphoid Neoplasm Diffuse Large B-cell Lymphoma	9	12	48
ESCA	Esophageal carcinoma	76	85	181
GBM	Glioblastoma multiforme	122	121	155
HNSC	Head and Neck squamous cell carcinoma	216	194	515
KICH	Kidney Chromophobe	9	11	65
KIRC	Kidney renal clear cell carcinoma	168	158	510
KIRP	Kidney renal papillary cell carcinoma	41	55	283
LAML	Acute Myeloid Leukemia	114	NA	173
LGG	Brain Lower Grade Glioma	125	192	514
LIHC	Liver hepatocellular carcinoma	129	177	366
LUAD	Lung adenocarcinoma	185	206	510
LUSC	Lung squamous cell carcinoma	207	140	484
MESO	Mesothelioma	74	61	87
OV	Ovarian serous cystadenocarcinoma	180	207	300
PAAD	Pancreatic adenocarcinoma	92	103	177
PCPG	Pheochromocytoma and Paraganglioma	5	20	178
PRAD	Prostate adenocarcinoma	10	93	493
READ	Rectum adenocarcinoma	21	32	154
SARC	Sarcoma	96	137	253
SKCM	Skin Cutaneous Melanoma	212	303	441
STAD	Stomach adenocarcinoma	159	134	412
TGCT	Testicular Germ Cell Tumors	4	34	149
THCA	Thyroid carcinoma	16	51	497
THYM	Thymoma	9	21	119
UCEC	Uterine Corpus Endometrial Carcinoma	87	119	527

UCS	Uterine Carcinosarcoma	35	37	57
UVM	Uveal Melanoma	23	30	80

Supplementary Table 2. Datasets used in validation study

Tumor Type Abbreviation	Tumor Type	Dataset	Clinical Endpoint	Total number of patients
ACC	Adrenocortical carcinoma	GSE19750	overall survival	22
		GSE76021	event-free survival	29
BLCA	Bladder Urothelial Carcinoma	GSE31684	overall survival	93
BRCA	Breast invasive carcinoma	#KMPLLOT	overall survival	943
			relapse-free survival	2032
CESC	Cervical squamous cell carcinoma and endocervical adenocarcinoma	GSE44001	disease-free survival	300
COAD	Colon adenocarcinoma	GSE39582	overall survival	582
GBM	Glioblastoma multiforme	CGGA Cohort 1	overall survival	123
		CGGA Cohort 2	overall survival	137
		CGGA Cohort 3	overall survival	237
HNSC	Head and Neck squamous cell carcinoma	GSE41613	overall survival	97
KIRC	Kidney renal clear cell carcinoma	GSE29609	overall survival	39
KIRP	Kidney renal papillary cell carcinoma	GSE2748	overall survival	28
LGG	Brain Lower Grade Glioma	CGGA Cohort 1	overall survival	159
		CGGA Cohort 2	overall survival	172
		CGGA Cohort 3	overall survival	420
LIHC	Liver hepatocellular carcinoma	GSE76427	overall survival	115
LUAD	Lung adenocarcinoma	KMPLLOT	overall survival	672
LUSC	Lung squamous cell carcinoma	KMPLLOT	overall survival	271
MESO	Mesothelioma	GSE2549	overall survival	39
OV	Ovarian cancer	KMPLLOT	overall survival	655
			progression-free survival	614
PAAD	Pancreatic adenocarcinoma	GSE57495	overall survival	63

PRAD	Prostate adenocarcinoma	GSE116918	Biochemical failure-free survival	248
READ	Rectum adenocarcinoma	GSE41258	overall survival	185
SARC	Sarcoma	GSE17674	overall survival	44
SKCM	Skin Cutaneous Melanoma	GSE59455	overall survival	122
STAD	Gastric cancer	KMPLOT	overall survival	631
TGCT	Testicular Germ Cell Tumors	GSE3218	overall survival	74
UVM	Uveal Melanoma	GSE22138	Metastasis free survival	63

#meta-analysis was carried out using Kaplan-Meier Plotter (<http://kmplot.com/analysis/>)