

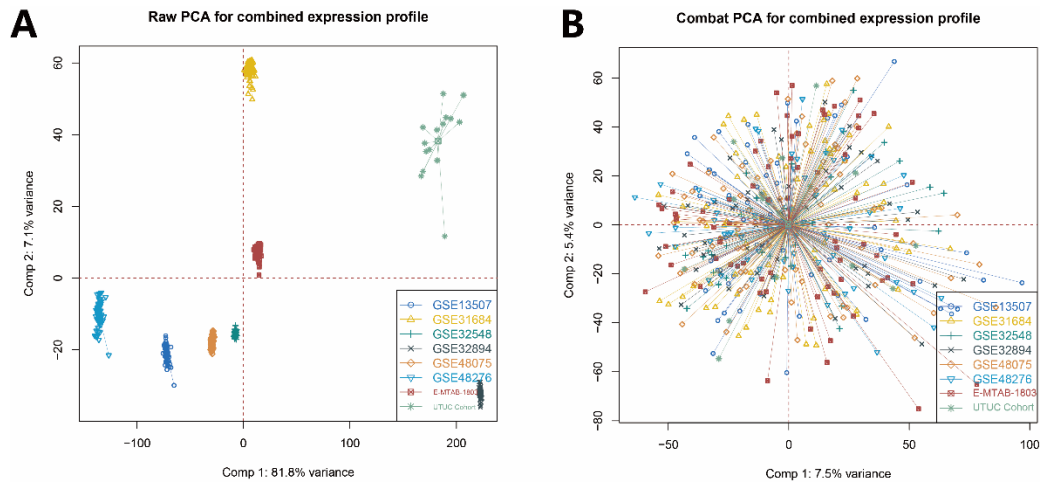
**OMTN, Volume 33**

**Supplemental information**

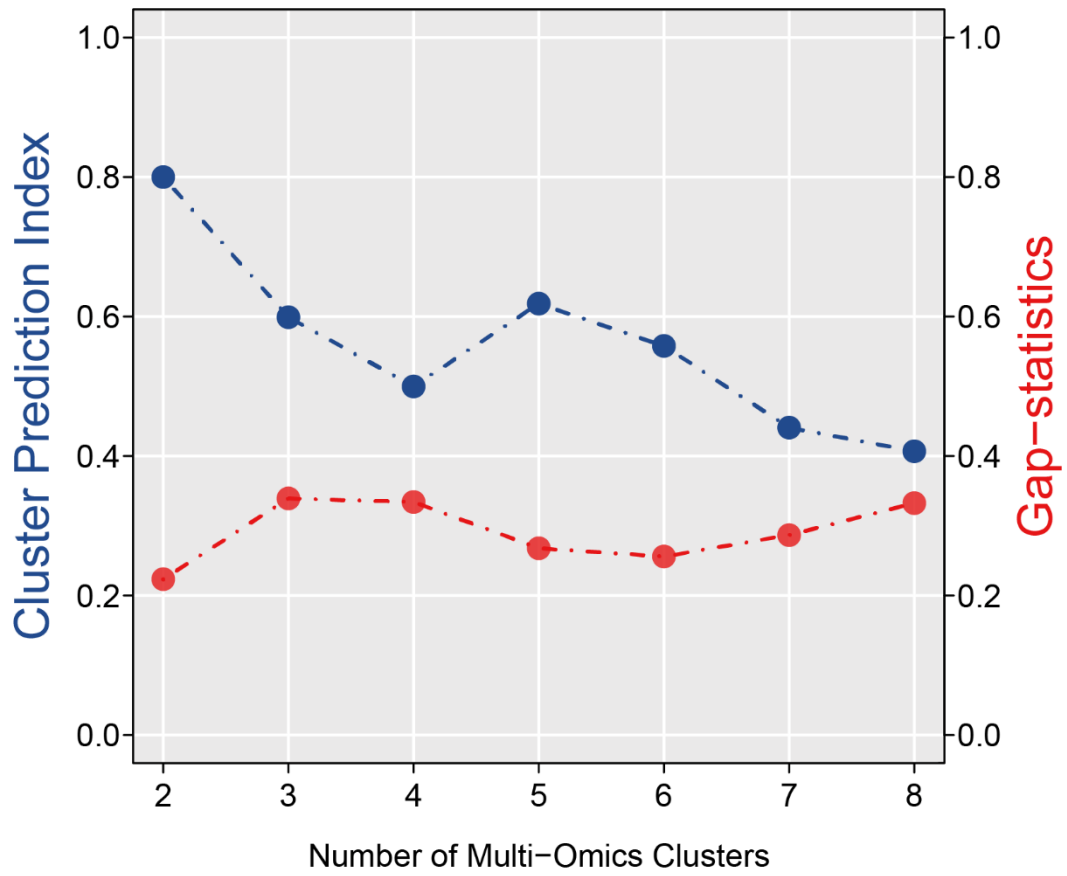
**Integrated multiomics analysis and  
machine learning refine molecular subtypes and  
prognosis for muscle-invasive urothelial cancer**

**Guangdi Chu, Xiaoyu Ji, Yonghua Wang, and Haitao Niu**

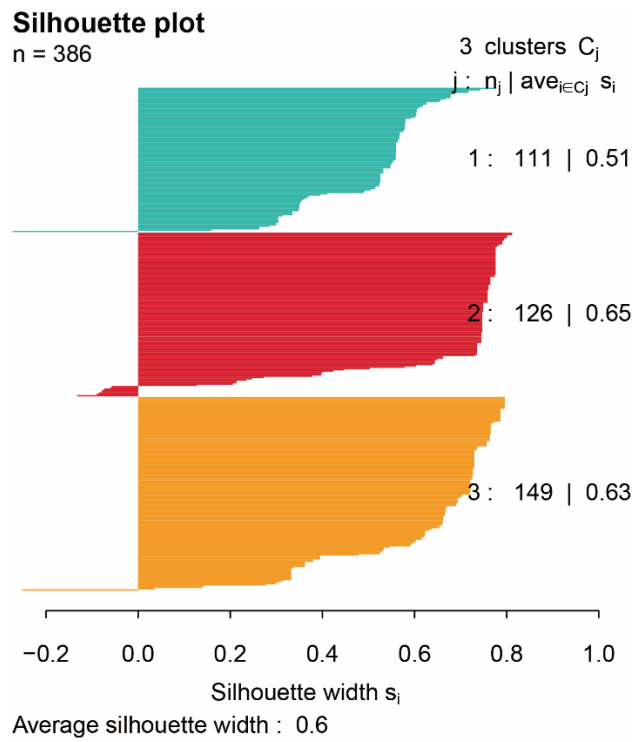
## Supplemental Figures :



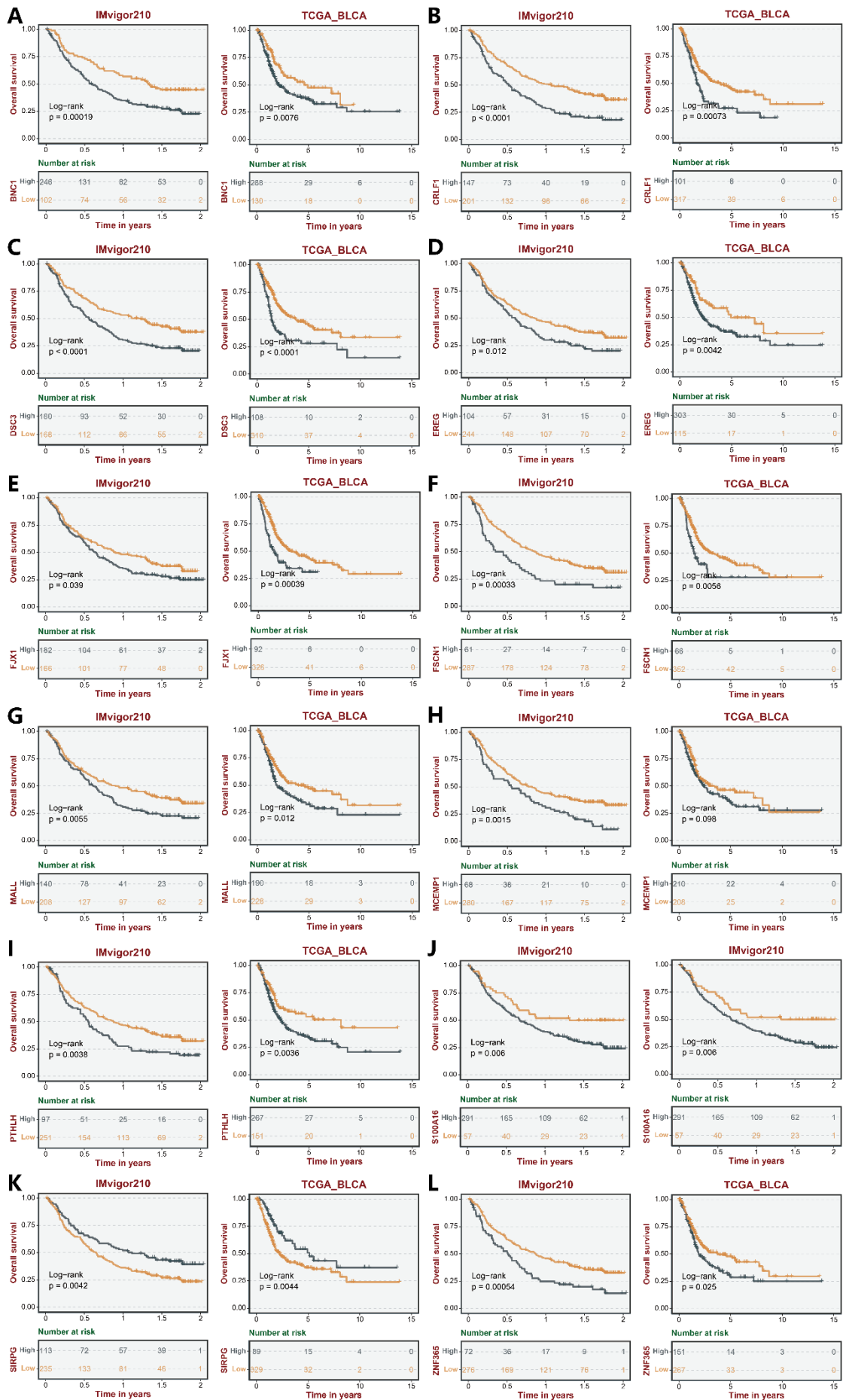
**Figure S1: The distribution of each data set before and after batch correction through the PCA algorithm. (A) Before batch correction, (B) After batch correction.**



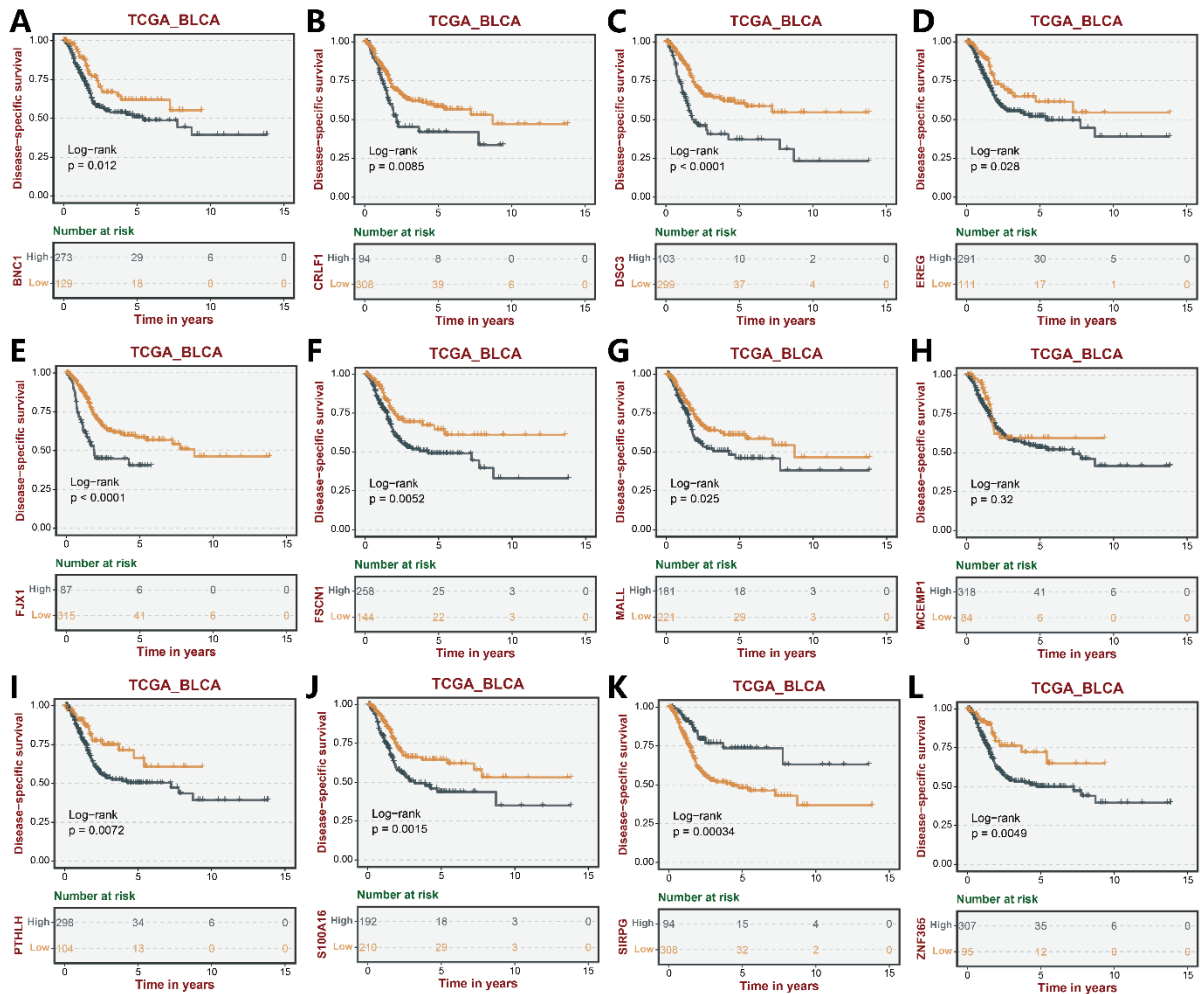
**Figure S2: The Cluster Prediction Index and Gap Statistical Analysis of the multiomics clusters.**



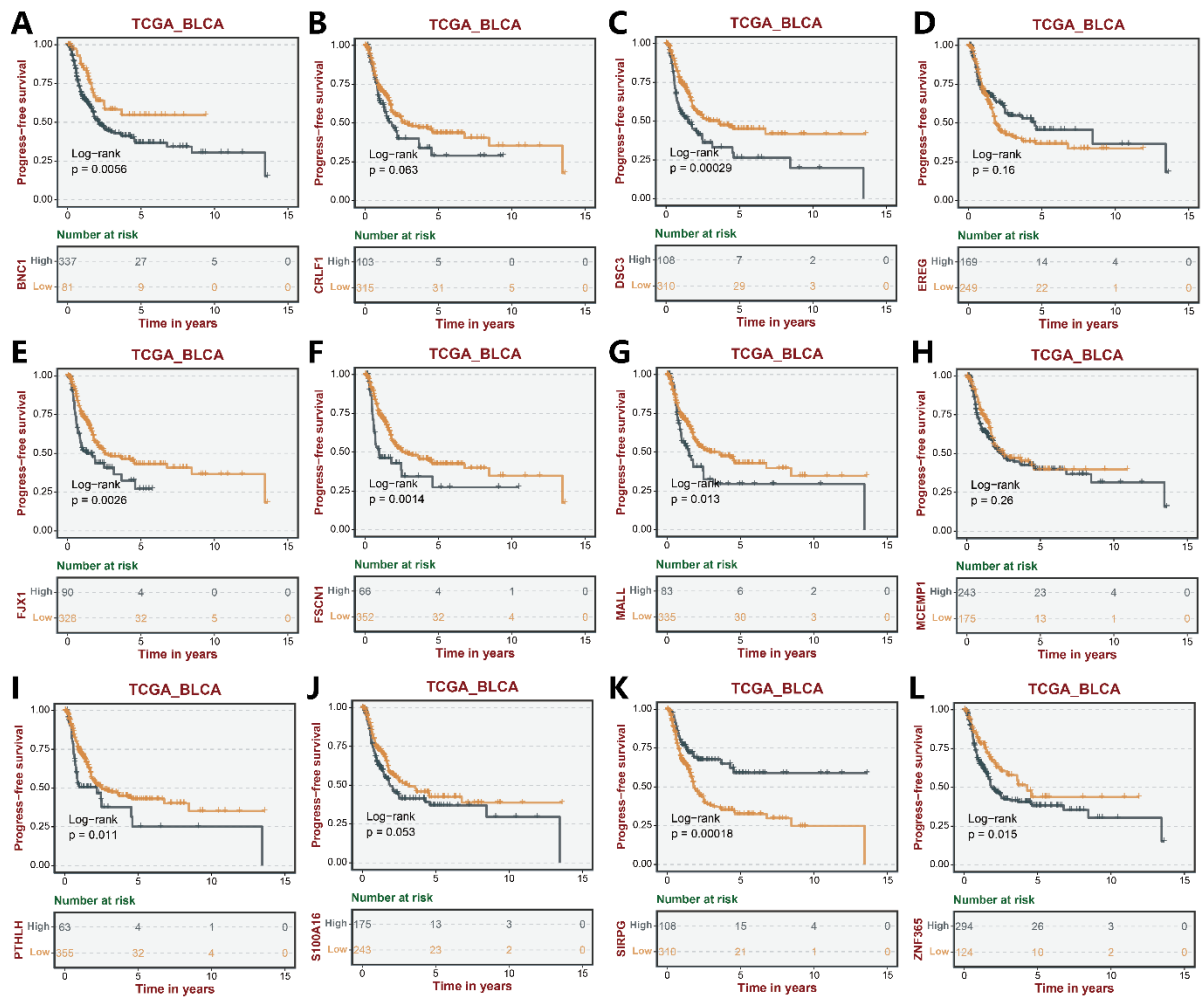
**Figure S3: The sample similarity of each subgroup was assessed by calculating the Silhouette score.**



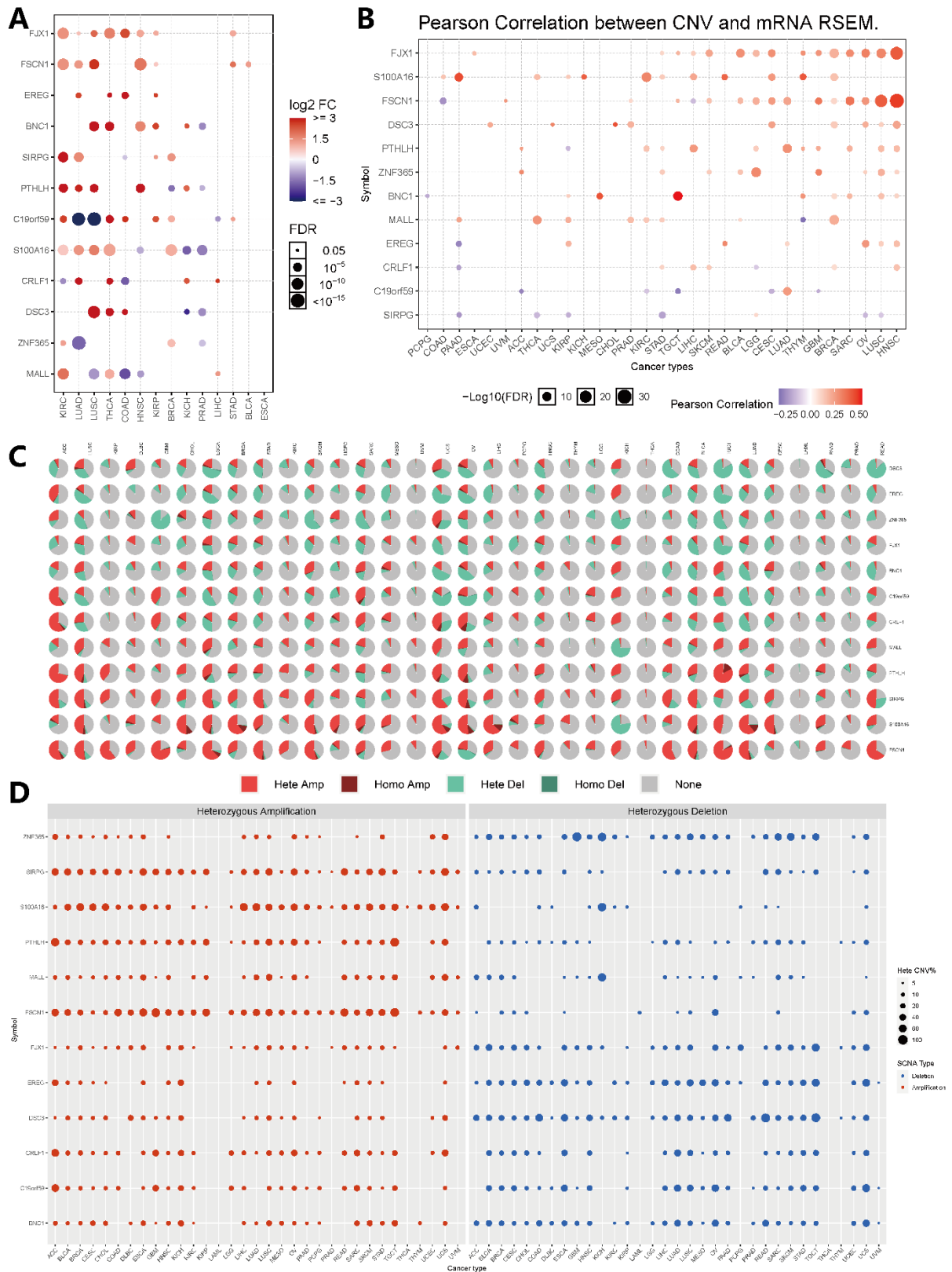
**Figure S4: Survival analysis of hub genes in CMLS (OS) in IMvigor cohort and TCGA-BLCA cohort. (A) BNC1, (B) CRLF1, (C) DSC3, (D) EREG, (E) FJX1, (F) FSCN1, (G) MALL, (H) MCEMP1, (I) PTHLH, (J) S100A16, (K) SIRPG, (L) ZNF365.**



**Figure S5: Survival analysis of hub genes in CMLS (DSS) in TCGA-BLCA cohort. (A) BNC1, (B) CRLF1, (C) DSC3, (D) EREG, (E) FJX1, (F) FSCN1, (G) MALL, (H) MCEMP1, (I) PTHLH, (J) S100A16, (K) SIRPG, (L) ZNF365.**



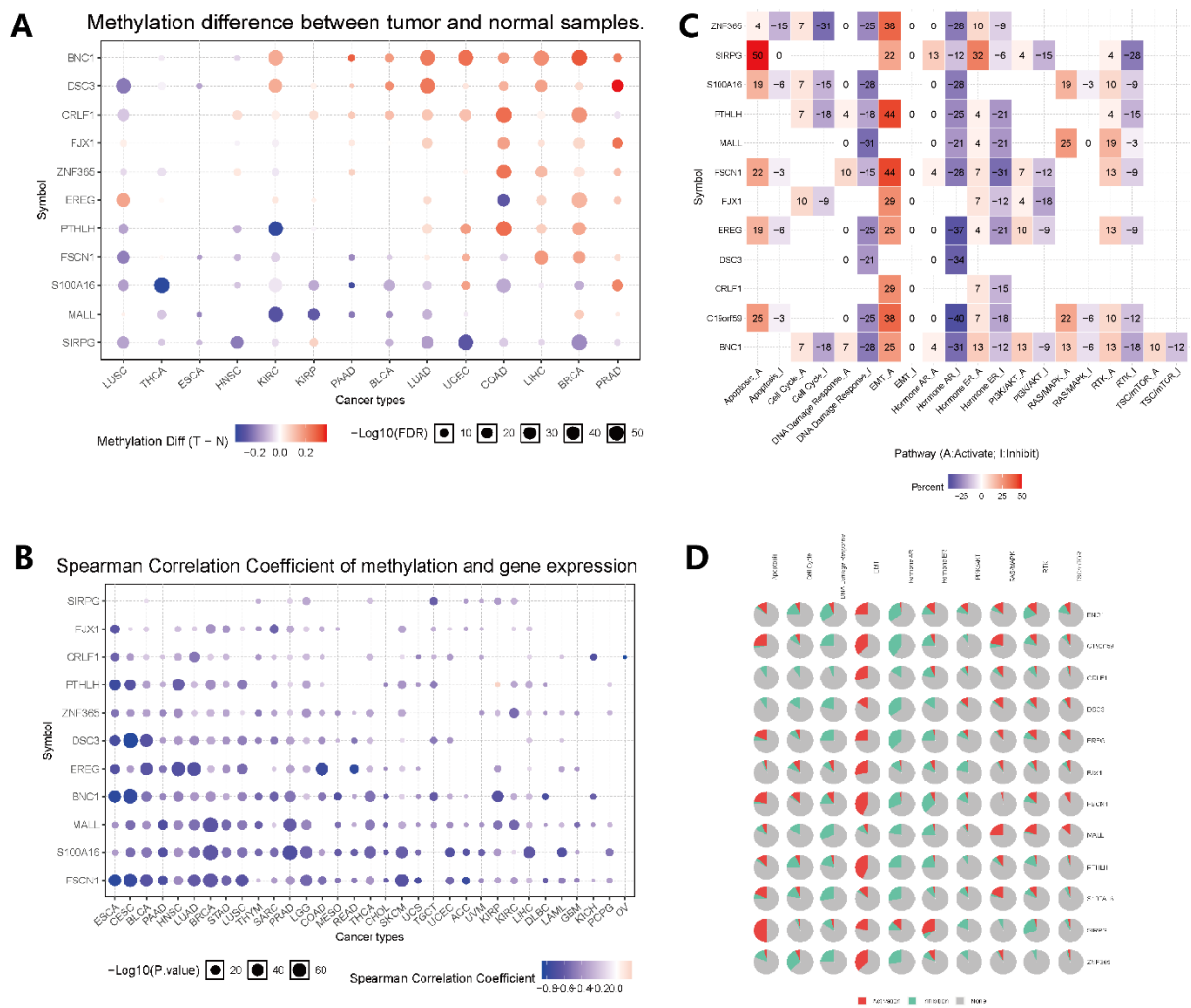
**Figure S6: Survival analysis of hub genes in CMLS (PFS) in TCGA-BLCA cohort.** (A) BNC1, (B) CRLF1, (C) DSC3, (D) EREG, (E) FJX1, (F) FSCN1, (G) MALL, (H) MCEMP1, (I) PTHLH, (J) S100A16, (K) SIRPG, (L) ZNF365.



**Figure S7: Differential expression analysis and CNV-related analysis of hub genes in CMLS. (A) Differential expression analysis of hub genes in CMLS. (B) Correlation analysis between CNV and mRNA expression level of hub genes in**

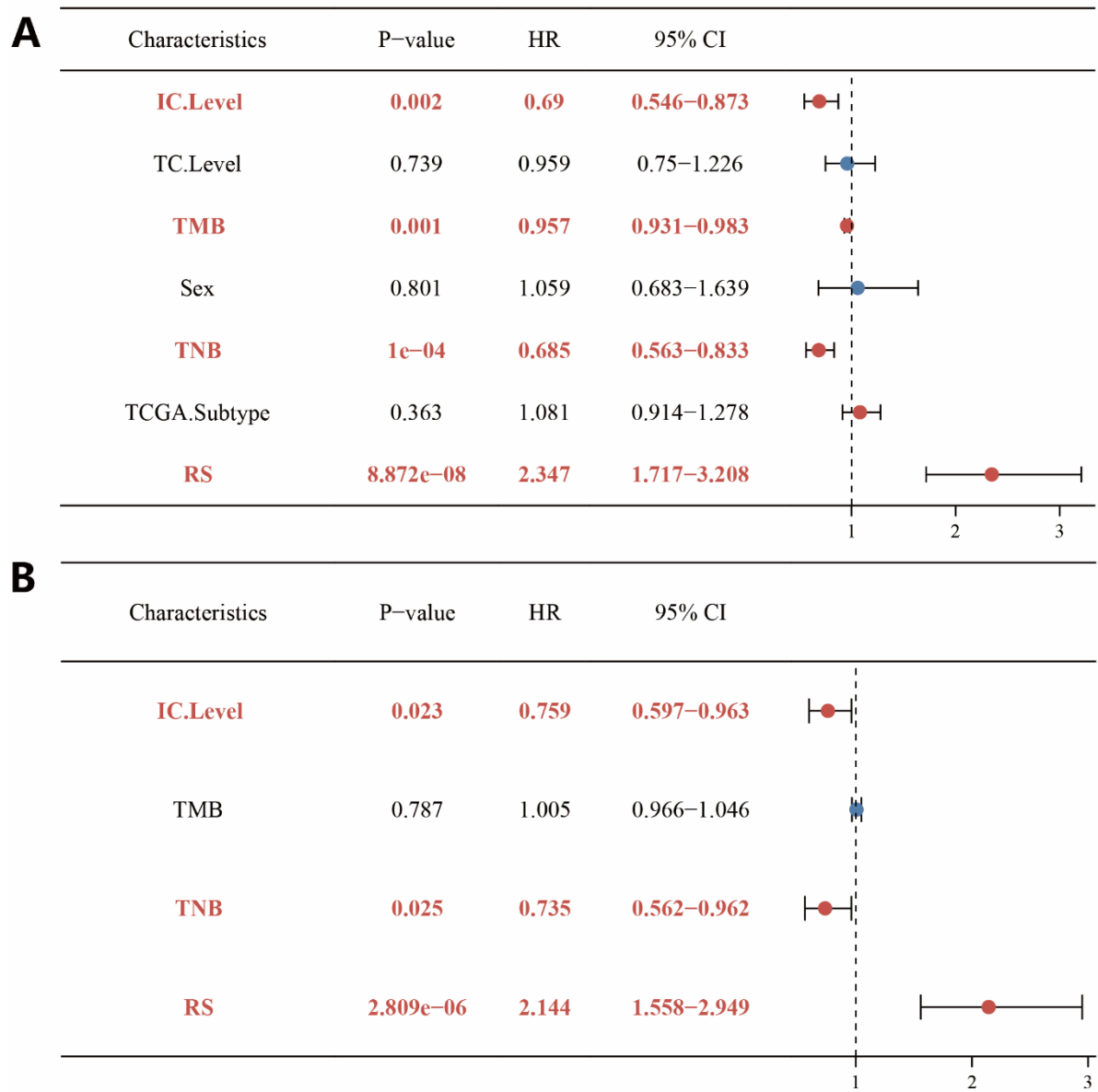


CMLS. (C) The CNV pie distribution indicates the constitution of Heterozygous/Homozygous CNV of each hub genes in CMLS in each cancer. (D) The distribution of heterozygous and homozygous CNV of hub genes in CMLS in each cancer.



**Figure S8: Methylation-related analysis and pathway analysis of hub genes in CMLS.** (A) Differential methylation expression analysis of hub genes in CMLS. (B) Correlation analysis between methylation and mRNA expression level of hub genes in CMLS. (C)-(D) The Heatmap and the pie chart shows the

activation and repression status of hub genes in CMLS on related pathways.



**Figure S9: The independent prognostic analysis of hub genes in CMLS. (A)** The univariate Cox analysis of hub genes in CMLS. **(B)** The multivariate Cox analysis of hub genes in CMLS.

## Supplemental Table Legends:

**Table S1: The result of differential expression analysis for three molecular subgroups.**

**Table S2: Annotation information of 12 hub genes of CMLS.**

SYMBOL	ENSEMBL	Description
BNC1	ENSG00000169594	Basonuclin 1
CRLF1	ENSG00000006016	Cytokine Receptor Like Factor 1
DSC3	ENSG00000134762	Desmocollin 3
EREG	ENSG00000124882	Epiregulin
FJX1	ENSG00000179431	Four-Jointed Box Kinase 1
FSCN1	ENSG00000075618	Fascin Actin-Bundling Protein 1
MALL	ENSG00000144063	Mal, T Cell Differentiation Protein Like
MCEMP1	ENSG00000183019	Mast Cell Expressed Membrane Protein 1
PTH1H	ENSG00000087494	Parathyroid Hormone Like Hormone
S100A16	ENSG00000188643	S100 Calcium Binding Protein A16
SIRPG	ENSG00000089012	Signal Regulatory Protein Gamma

**Table S3: The 22 collected signatures.**

ID	PMID	Author	Gene	Coef
1	33204364	Cao-DSM	ACTA2	-0.000950773
1	33204364	Cao-DSM	ANPEP	0.000485521
1	33204364	Cao-DSM	COMP	-0.000333665
1	33204364	Cao-DSM	DAB2	0.008354169
1	33204364	Cao-DSM	ELN	0.007837673
1	33204364	Cao-DSM	FOXC2	-0.02707915
1	33204364	Cao-DSM	IGFBP2	-0.003429749
1	33204364	Cao-DSM	MGP	1.66E-06
1	33204364	Cao-DSM	MMP1	-5.03E-05
1	33204364	Cao-DSM	MYL9	-0.000124407
1	33204364	Cao-DSM	OXTR	0.003535212
1	33204364	Cao-DSM	PRSS2	-0.000130369
1	33204364	Cao-DSM	PTX3	0.00323547
1	33204364	Cao-DSM	RGS4	0.03024129
1	33204364	Cao-DSM	SPP1	4.99E-05
1	33204364	Cao-DSM	TAGLN	0.001122562

1	33204364	Cao-DSM	WNT5A	-0.001098872
2	31657881	Cao-JCMM	LAMA2	0.0382
2	31657881	Cao-JCMM	GPC1	0.0726
2	31657881	Cao-JCMM	ECM1	0.0717
2	31657881	Cao-JCMM	FBN2	0.0386
2	31657881	Cao-JCMM	LRP1	0.0685
2	31657881	Cao-JCMM	PVR	0.00903
2	31657881	Cao-JCMM	FUCA1	-0.0475
3	31737111	Chen-JC	TMPRSS11E	1.414
3	31737111	Chen-JC	SCEL	2.471
3	31737111	Chen-JC	KRT78	5.305
3	31737111	Chen-JC	TMEM185A	-2.988
4	32884943	Jiang-BRI	MMP9	0.0003617
4	32884943	Jiang-BRI	RBP7	0.0096326
4	32884943	Jiang-BRI	PDGFRA	0.0399101
4	32884943	Jiang-BRI	AHNAK	0.014035
4	32884943	Jiang-BRI	OAS1	-0.008116
4	32884943	Jiang-BRI	OLR1	0.0072663
4	32884943	Jiang-BRI	RAC3	0.0297334
4	32884943	Jiang-BRI	SLIT2	-0.209438
4	32884943	Jiang-BRI	IGF1	0.2684786
4	32884943	Jiang-BRI	AGTR1	0.1416244
5	34026819	Jiang-FMB	ANXA2	0.7752
5	34026819	Jiang-FMB	GALK1	0.764
5	34026819	Jiang-FMB	COL5A1	0.1973
5	34026819	Jiang-FMB	HS3ST1	-0.3086
6	34150627	Luo-FIO	ALDH1L2	0.096626563
6	34150627	Luo-FIO	ANXA1	0.035594173
6	34150627	Luo-FIO	CERCAM	0.016800805
6	34150627	Luo-FIO	GNA12	0.006655467
6	34150627	Luo-FIO	PLOD1	0.003607814
6	34150627	Luo-FIO	GSDMB	-0.175524875
7	32733809	Na-FIO	MMP9	0.000325672
7	32733809	Na-FIO	PDGFRA	0.029410199
7	32733809	Na-FIO	AHNAK	0.013037691
7	32733809	Na-FIO	OAS1	-0.007175947
7	32733809	Na-FIO	OLR1	0.00516244
7	32733809	Na-FIO	RAC3	0.023591819
7	32733809	Na-FIO	IGF1	0.282607117
7	32733809	Na-FIO	PGF	0.017645622
7	32733809	Na-FIO	SH3BP2	-0.083043743

8	32117435	Qiu-FIG	RBP7	0.0044
8	32117435	Qiu-FIG	PDGFRA	0.0021
8	32117435	Qiu-FIG	AHNAK	0.0054
8	32117435	Qiu-FIG	OAS1	-0.0021
8	32117435	Qiu-FIG	RAC3	0.0043
8	32117435	Qiu-FIG	EDNRA	0.0142
8	32117435	Qiu-FIG	SH3BP2	-0.0019
9	32749145	Quan-BM	MMP9	0.00036
9	32749145	Quan-BM	RBP7	0.00963
9	32749145	Quan-BM	PDGFRA	0.03991
9	32749145	Quan-BM	AHNAK	0.01403
9	32749145	Quan-BM	OAS1	-0.008112
9	32749145	Quan-BM	OLR1	0.00727
9	32749145	Quan-BM	RAC3	0.02973
9	32749145	Quan-BM	SLIT2	-0.20944
9	32749145	Quan-BM	IGF1	0.26848
9	32749145	Quan-BM	AGTR1	0.14162
10	33459039	Shen-ACNB	ANXA6	0.0082
10	33459039	Shen-ACNB	AHNAK	0.0161
10	33459039	Shen-ACNB	CACYBP	0.0252
10	33459039	Shen-ACNB	STAT1	-0.0079
10	33459039	Shen-ACNB	CALR	0.0011
11	33292266	Shen-CCI	PLOD1	0.0049
11	33292266	Shen-CCI	CKB	0.0018
11	33292266	Shen-CCI	PYGB	0.0033
11	33292266	Shen-CCI	AKR1B1	0.0031
11	33292266	Shen-CCI	PDE5A	0.0486
12	33456631	Shen-DM	AHNAK	0.0009
12	33456631	Shen-DM	NR2F6	-0.006
13	34112144	Wang-BMC	ACAP1	-0.0589
13	34112144	Wang-BMC	ADAMTS9	0.0515
13	34112144	Wang-BMC	TAP1	-0.0022
13	34112144	Wang-BMC	IFIT3	-0.001
13	34112144	Wang-BMC	FBN1	0.0184
13	34112144	Wang-BMC	FSTL1	0.0029
13	34112144	Wang-BMC	COL6A2	2.46E-06
14	32841548	Wang-CM	SULT1C2	-0.285729313
14	32841548	Wang-CM	EGFL6	-0.132834959
14	32841548	Wang-CM	DUSP2	-0.047080965
14	32841548	Wang-CM	BLNK	-0.036593582
14	32841548	Wang-CM	BATF	-0.027054952

14	32841548	Wang-CM	PPFIBP2	-0.015812131
14	32841548	Wang-CM	HES1	-0.00830084
14	32841548	Wang-CM	THBS4	0.011476589
14	32841548	Wang-CM	CPA3	0.061002869
14	32841548	Wang-CM	NEFL	0.069959198
14	32841548	Wang-CM	VWF	0.0806877
14	32841548	Wang-CM	LRP8	0.09542848
14	32841548	Wang-CM	PDGFD	0.110454703
15	33391264	Wu-FIM	ORM1	-0.42
15	33391264	Wu-FIM	PTHLH	0.17
15	33391264	Wu-FIM	CTSE	-0.39
16	33545950	Wu-Med	CHPF	0.156689
16	33545950	Wu-Med	AK3	-0.40384
16	33545950	Wu-Med	GALK1	0.350739
16	33545950	Wu-Med	NUP188	0.444476
17	33209669	Xing-TAU	TAP1	-0.000824
17	33209669	Xing-TAU	RBP7	0.00397
17	33209669	Xing-TAU	STAT1	-0.000031
17	33209669	Xing-TAU	PDGFRA	0.005626
17	33209669	Xing-TAU	AHNAK	0.004692
17	33209669	Xing-TAU	OLR1	0.00029
17	33209669	Xing-TAU	RAC3	0.009473
17	33209669	Xing-TAU	EDNRA	0.001882
17	33209669	Xing-TAU	IGF1	0.078175
17	33209669	Xing-TAU	SH3BP2	-0.009884
18	33408272	Yan-Aging	AHNAK	0.2427
18	33408272	Yan-Aging	CALR	0.3584
18	33408272	Yan-Aging	PLA2G2A	-0.0863
18	33408272	Yan-Aging	OAS1	-0.188
18	33408272	Yan-Aging	CDH1	-0.0401
18	33408272	Yan-Aging	PDGFRA	0.2079
18	33408272	Yan-Aging	SEMA3F	-0.0014
18	33408272	Yan-Aging	RAC3	0.2281
18	33408272	Yan-Aging	IRF5	-0.0702
18	33408272	Yan-Aging	CARD11	-0.1192
19	31134129	Yan-FIG	BUB1B	0.347
19	31134129	Yan-FIG	CCNB1	0.324
19	31134129	Yan-FIG	CDK1	0.218
19	31134129	Yan-FIG	ISG15	0.264
19	31134129	Yan-FIG	KIF15	0.268
19	31134129	Yan-FIG	RAD54L	0.386

20	34221960	Yan-FIO	BOC	0.009
20	34221960	Yan-FIO	FGF7	0.064
20	34221960	Yan-FIO	MAP1A	0.178
21	32194788	Yan-JC	ASPM	-0.135
21	32194788	Yan-JC	C4orf46	-0.142
21	32194788	Yan-JC	CCNB1	0.632
21	32194788	Yan-JC	DIAPH3	0.105
21	32194788	Yan-JC	MLF1	0.803
21	32194788	Yan-JC	MTFR2	-0.456
21	32194788	Yan-JC	NSUN6	-0.287
21	32194788	Yan-JC	OIP5	0.05
22	31894276	Yin-OR	S100A8	0.17027
22	31894276	Yin-OR	CTHRC1	0.06678
22	31894276	Yin-OR	C15orf48	0.10548
22	31894276	Yin-OR	MPPED2	-0.16639
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