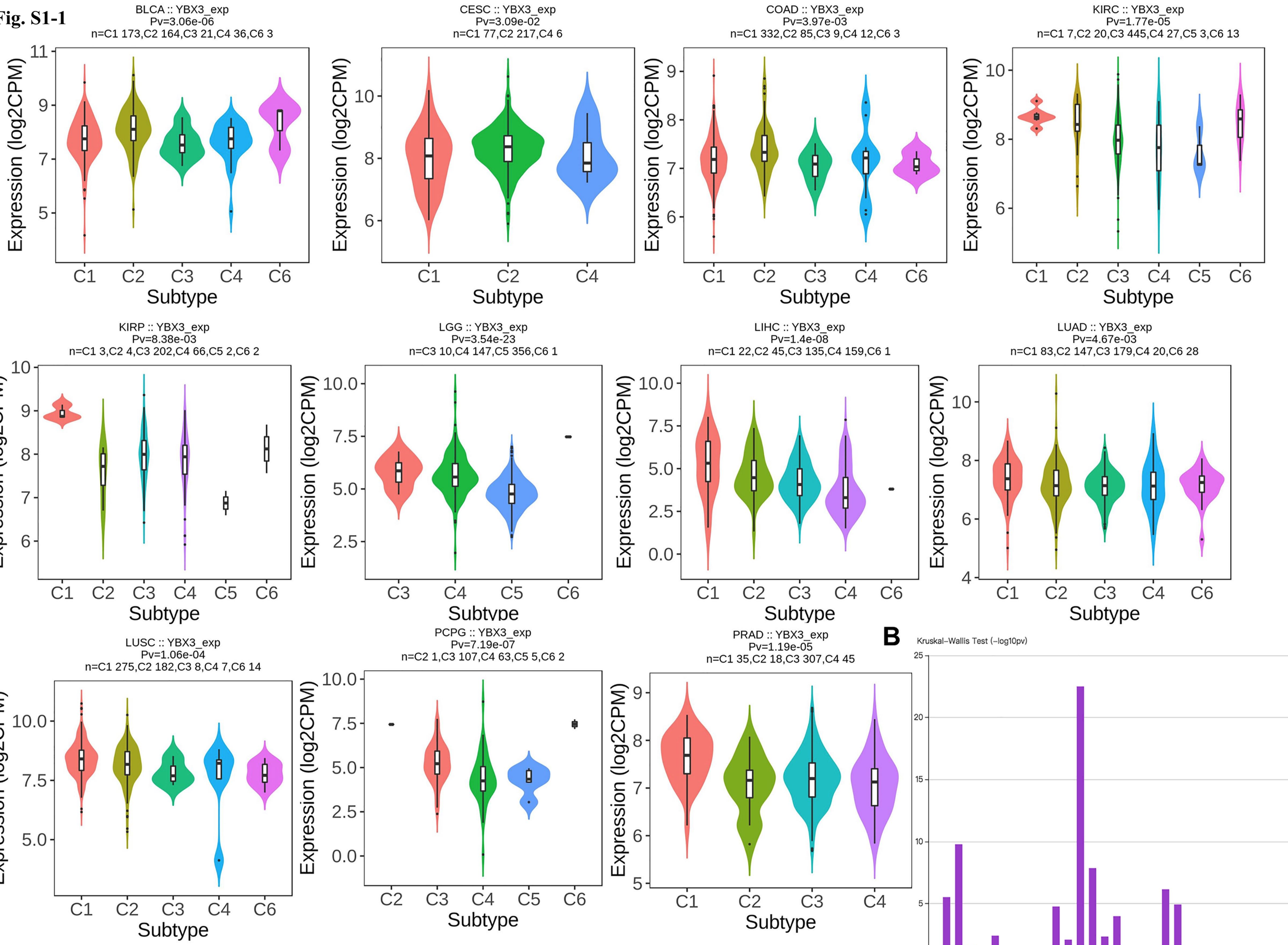
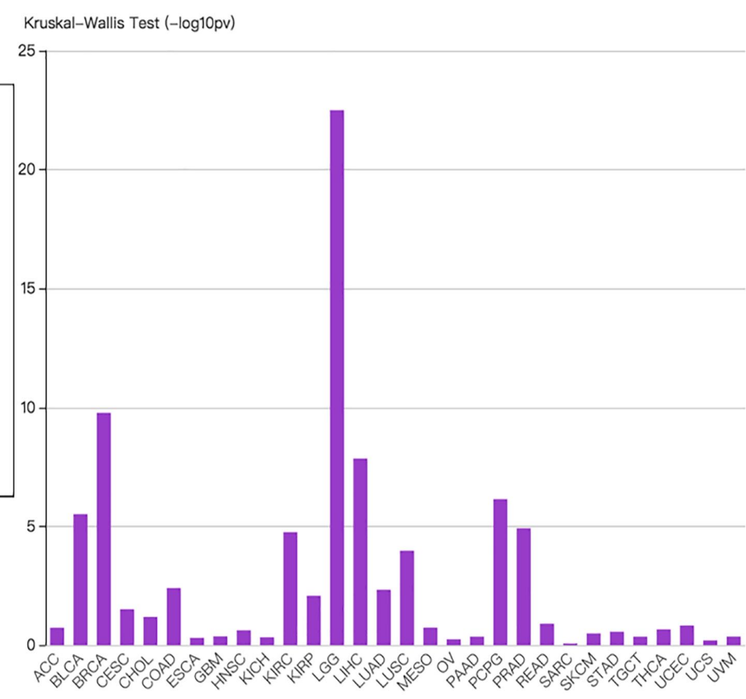
Fig. S1-1

A

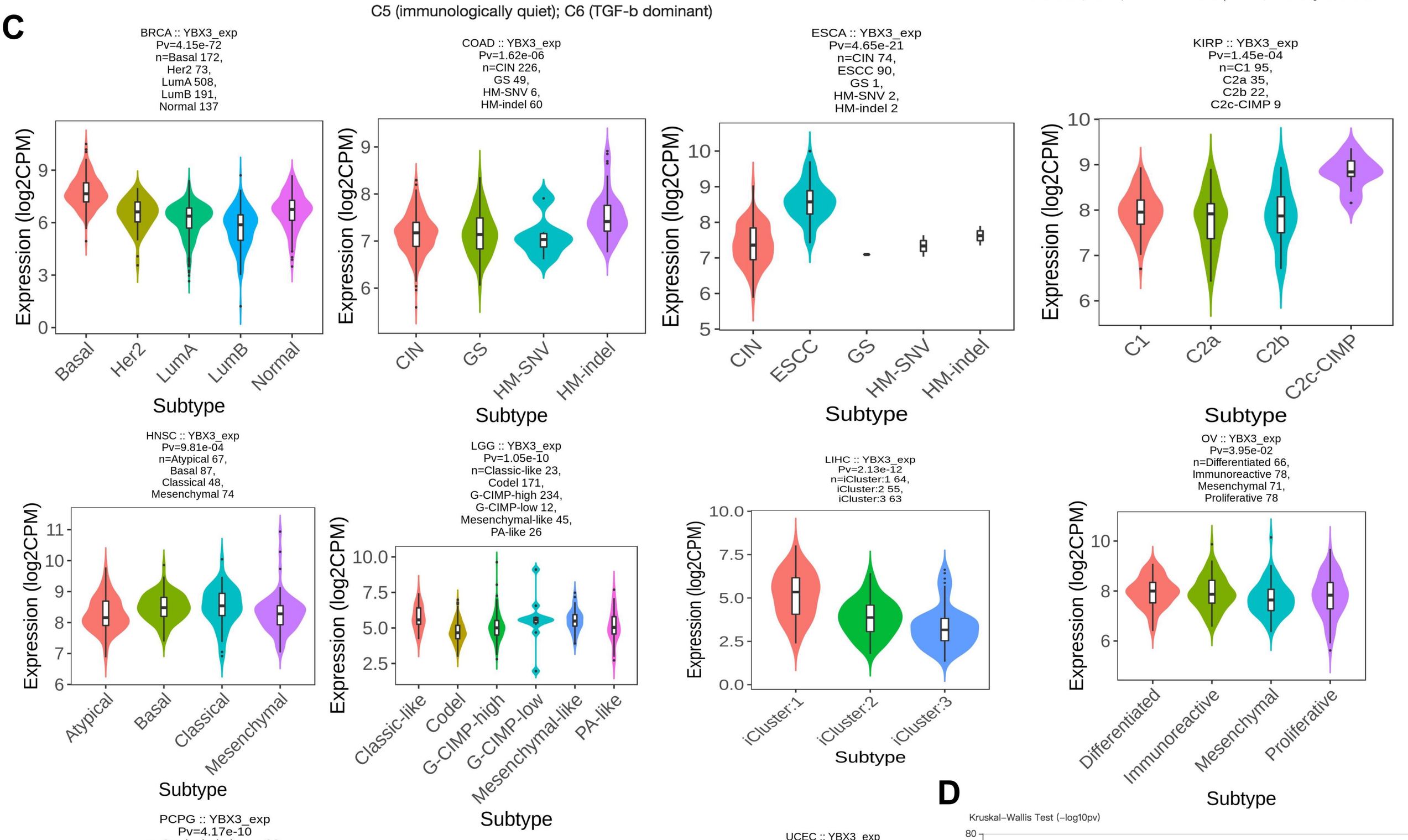


B



Legend: C1 (wound healing); C2 (IFN-gamma dominant);
C3 (inflammatory); C4 (lymphocyte depleted);
C5 (immunologically quiet); C6 (TGF-b dominant)

C



D

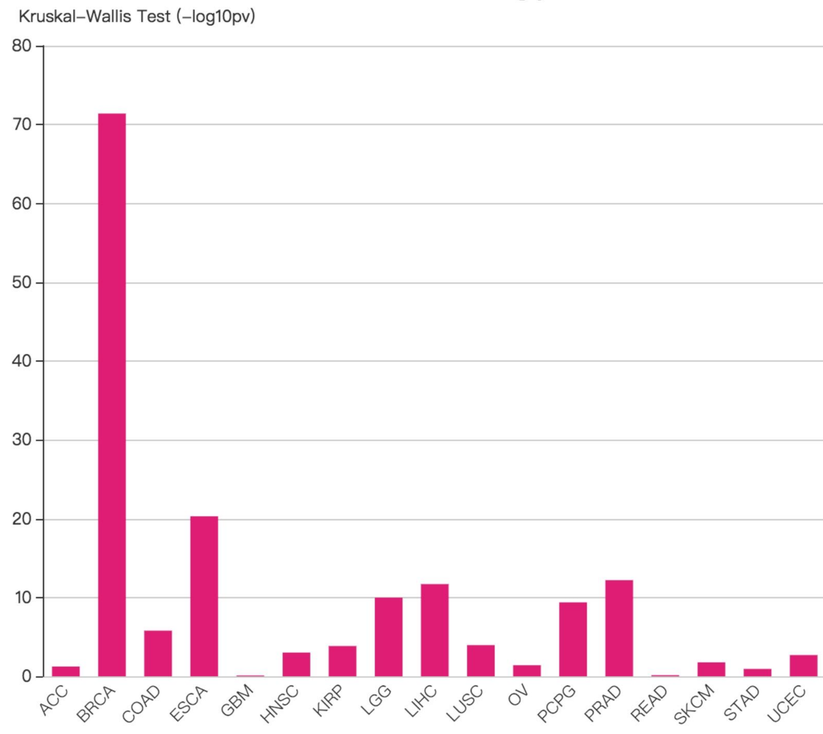


Fig. S1-2

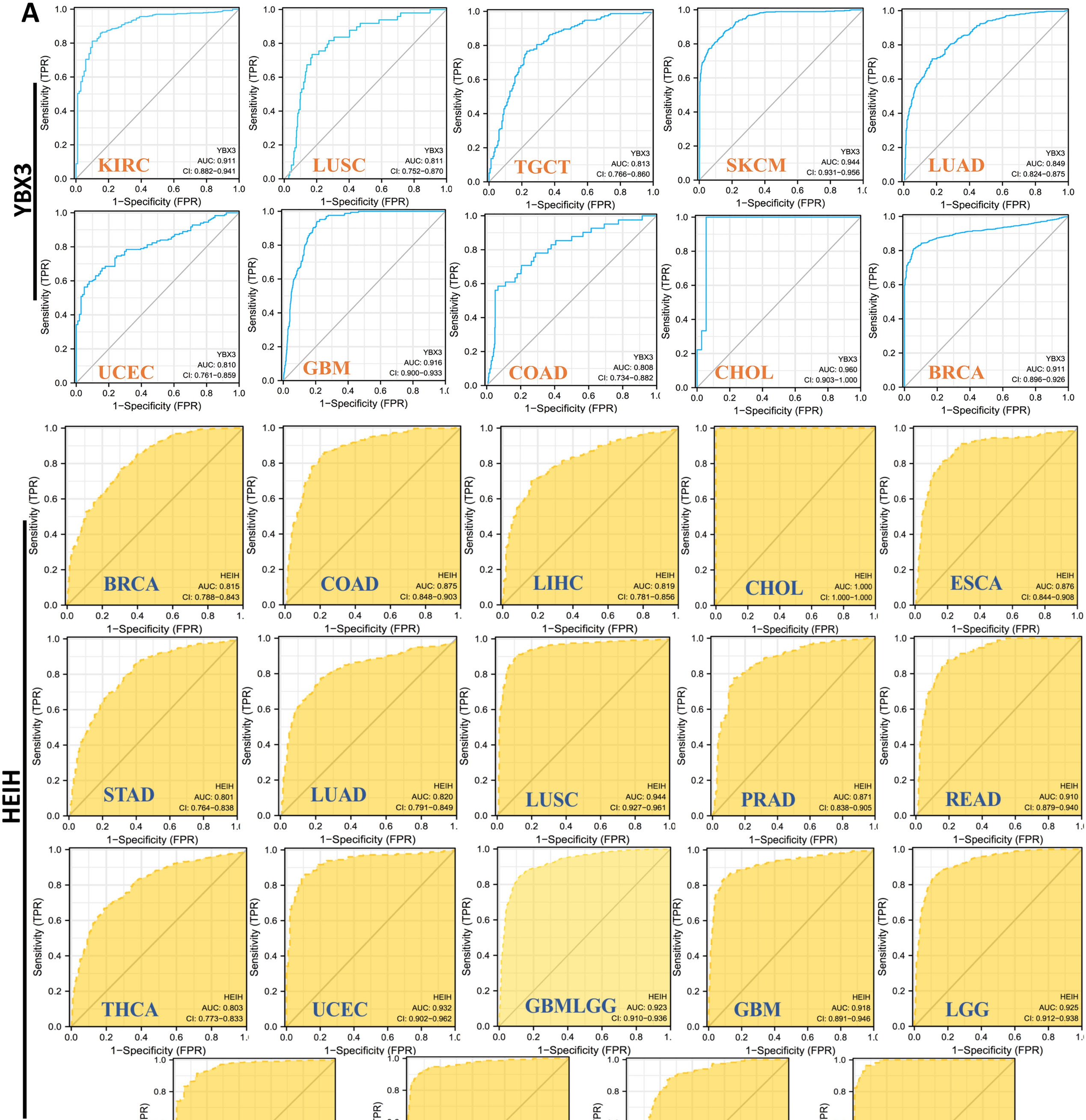
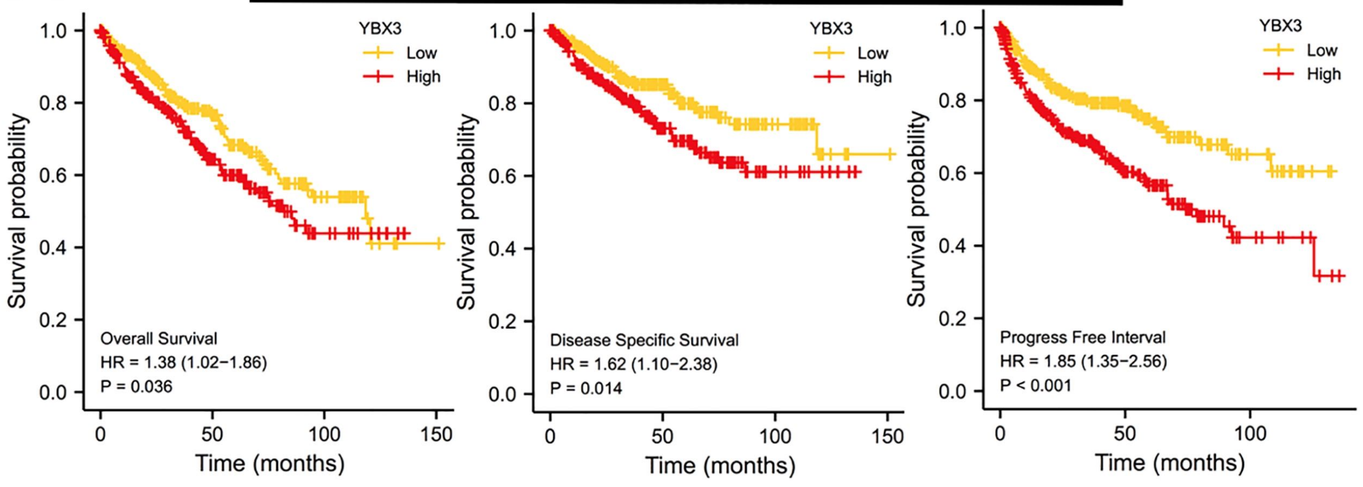

A
YBX3
KIRC
YBX3
AUC: 0.911
CI: 0.882−0.941
LUSC
YBX3
AUC: 0.811
CI: 0.752−0.870
TGCT
YBX3
AUC: 0.813
CI: 0.766−0.860
SKCM
YBX3
AUC: 0.944
CI: 0.931−0.956
LUAD
YBX3
AUC: 0.849
CI: 0.824−0.875
UCEC
YBX3
AUC: 0.810
CI: 0.761−0.859
GBM
YBX3
AUC: 0.916
CI: 0.900−0.933
COAD
YBX3
AUC: 0.808
CI: 0.734−0.882
CHOL
YBX3
AUC: 0.960
CI: 0.903−1.000
BRCA
YBX3
AUC: 0.911
CI: 0.896−0.926
HEIH
BRCA
HEIH
AUC: 0.815
CI: 0.788−0.843
COAD
HEIH
AUC: 0.875
CI: 0.848−0.903
LIHC
HEIH
AUC: 0.819
CI: 0.781−0.856
CHOL
HEIH
AUC: 1.000
CI: 1.000−1.000
ESCA
HEIH
AUC: 0.876
CI: 0.844−0.908
STAD
HEIH
AUC: 0.801
CI: 0.764−0.838
LUAD
HEIH
AUC: 0.820
CI: 0.791−0.849
LUSC
HEIH
AUC: 0.944
CI: 0.927−0.961
PRAD
HEIH
AUC: 0.871
CI: 0.838−0.905
READ
HEIH
AUC: 0.910
CI: 0.879−0.940
THCA
HEIH
AUC: 0.803
CI: 0.773−0.833
UCEC
HEIH
AUC: 0.932
CI: 0.902−0.962
GBMLGG
HEIH
AUC: 0.923
CI: 0.910−0.936
GBM
HEIH
AUC: 0.918
CI: 0.891−0.946
LGG
HEIH
AUC: 0.925
CI: 0.912−0.938
OV
HEIH
AUC: 0.953
CI: 0.930−0.975
TGCT
HEIH
AUC: 0.968
CI: 0.950−0.986
THYM
HEIH
AUC: 0.843
CI: 0.809−0.878
UCS
HEIH
AUC: 0.990
CI: 0.979−1.000
Sensitivity (TPR)
1−Specificity (FPR)
0.0
0.2
0.4
0.6
0.8
1.0

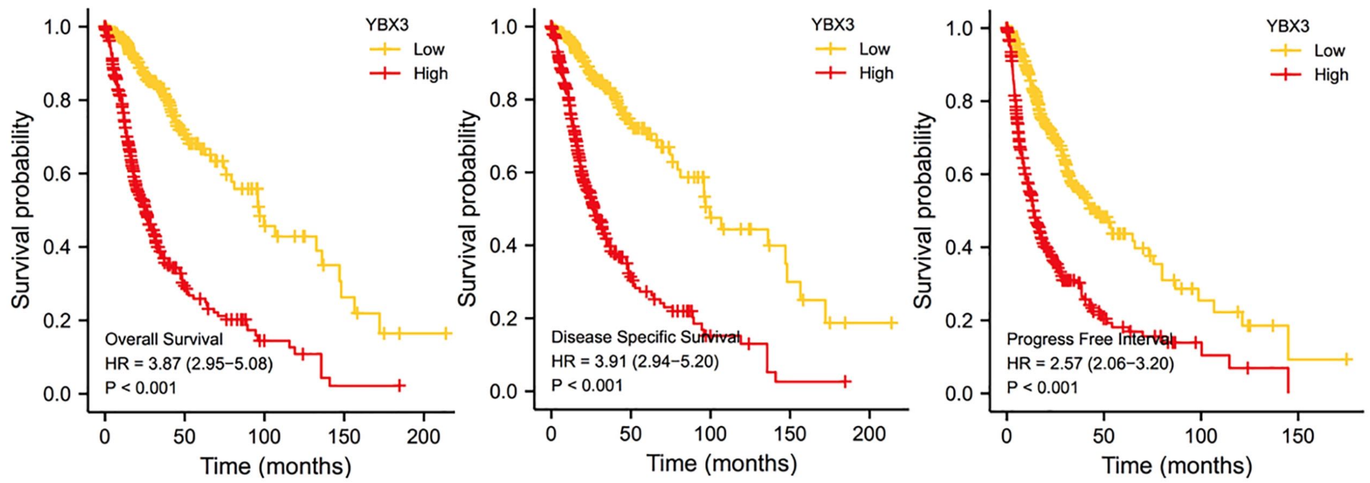
Fig. S1-3

A

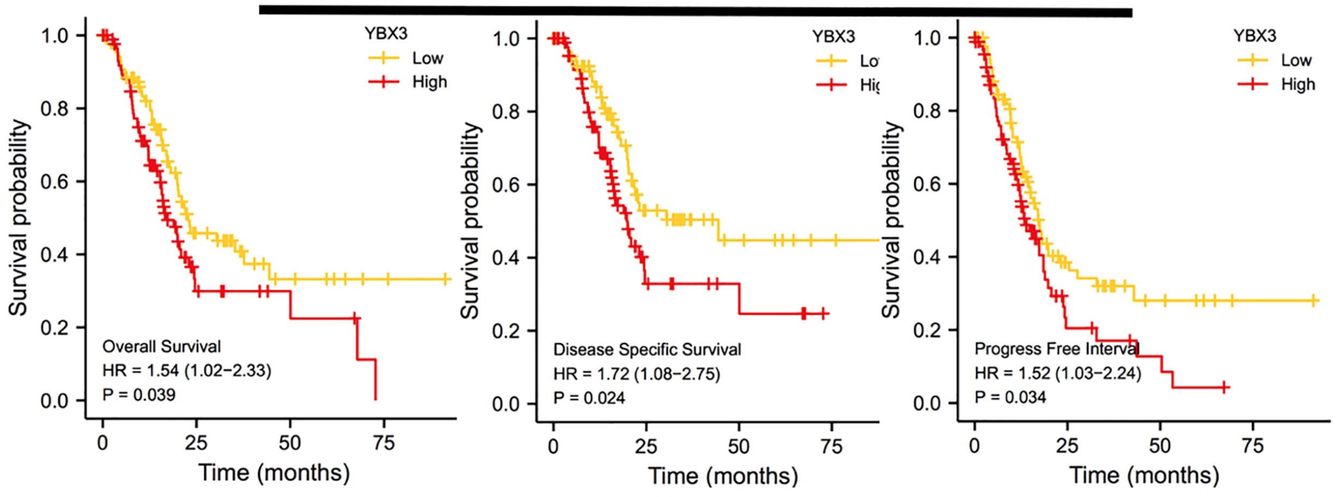
KIRC



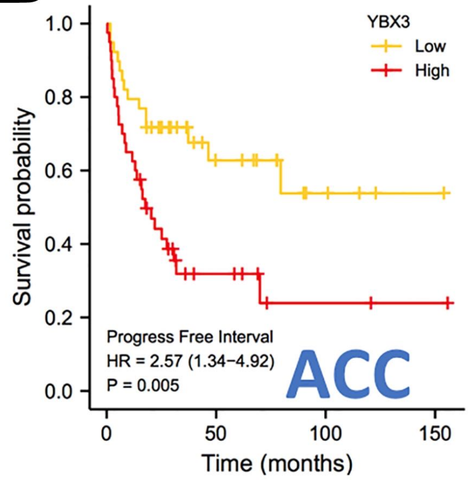
LGG+GBM

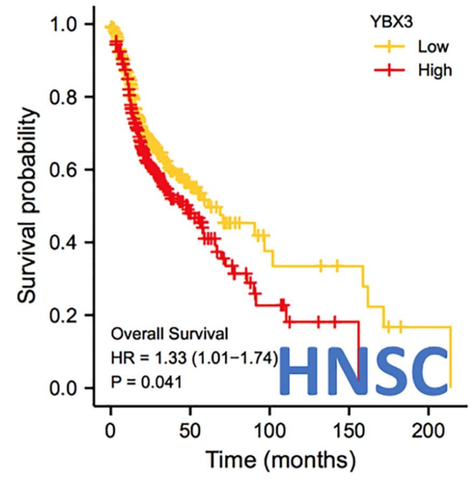


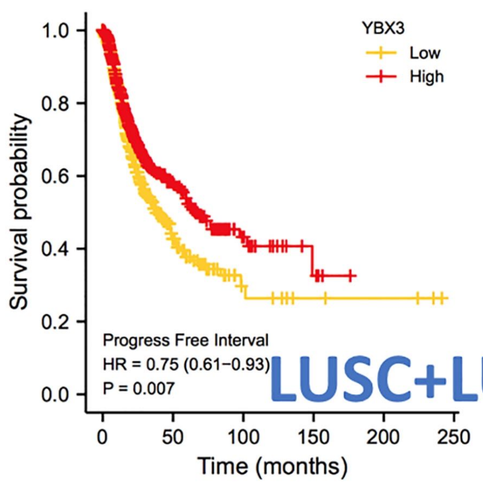
PAAD



B

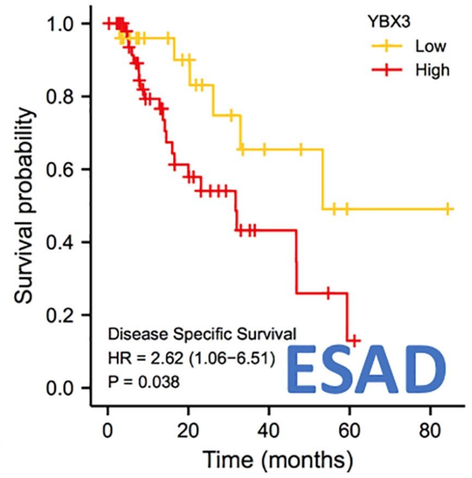


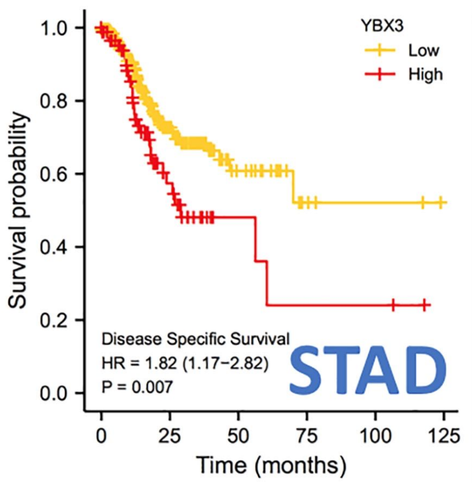


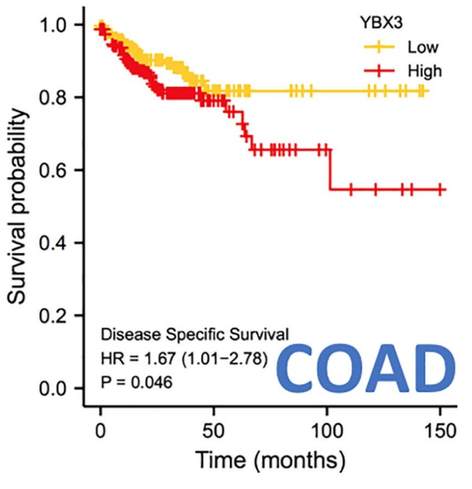


C

YBX3 in Head, Neck & Thoracic Tumor







*YBX3 in Digestive Tract Tumor

D

*HEIH in Digestive Tract Tumor

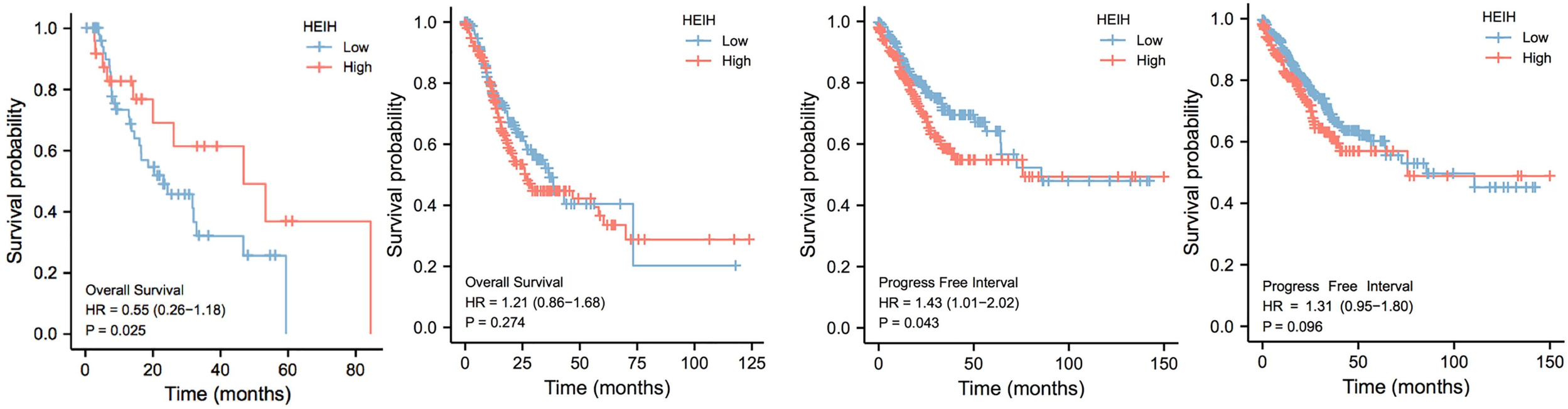
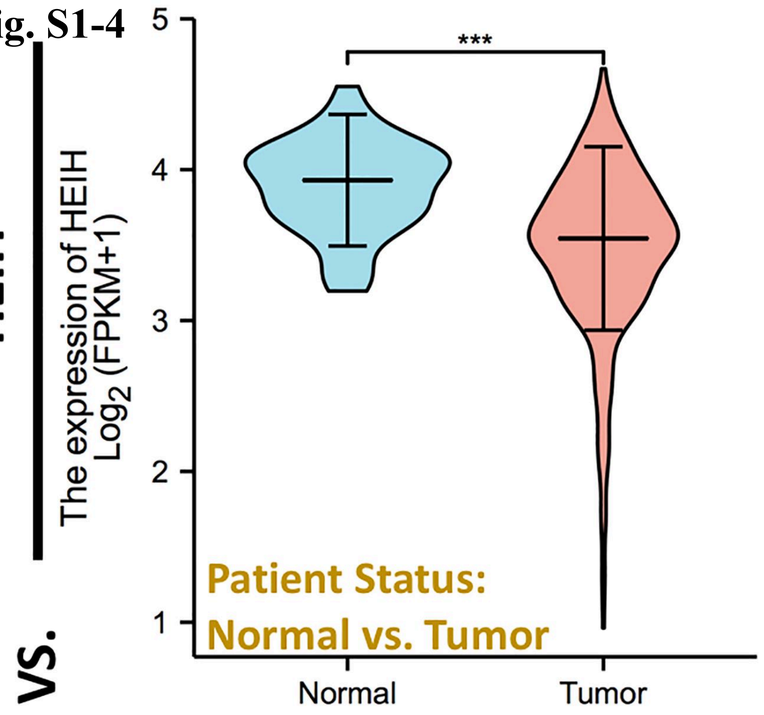
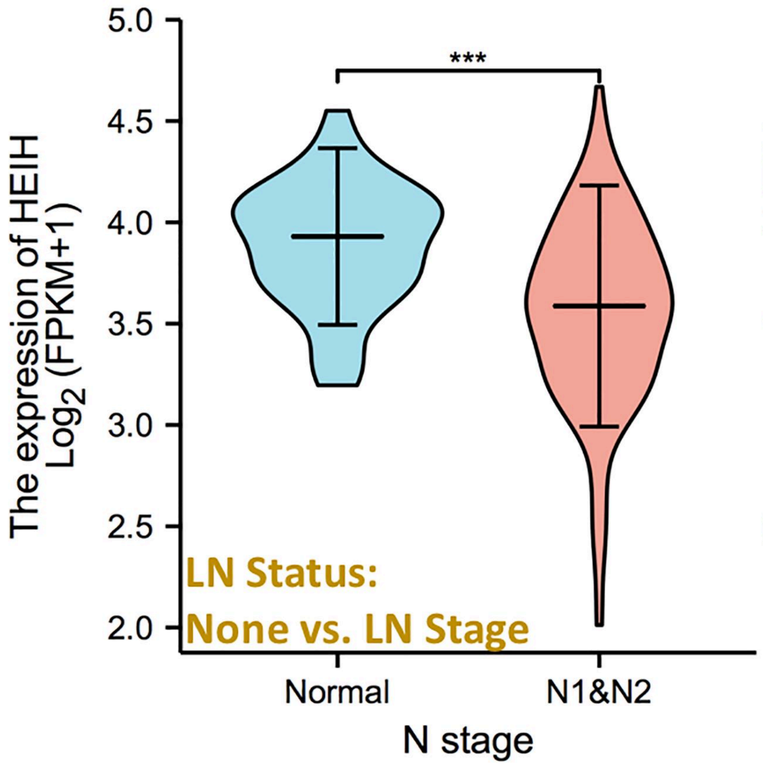
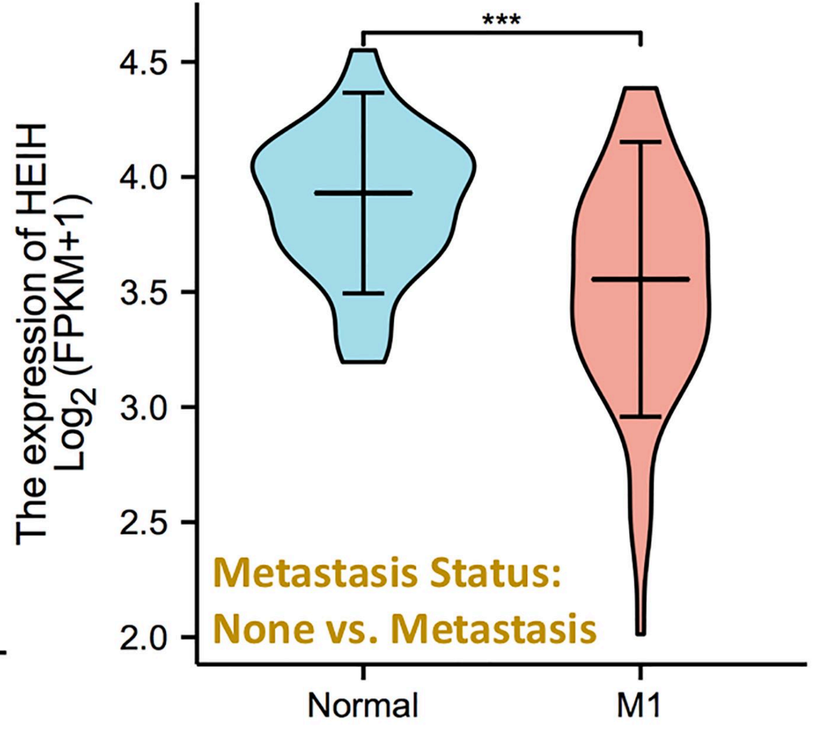


Fig. S1-4

HEIH

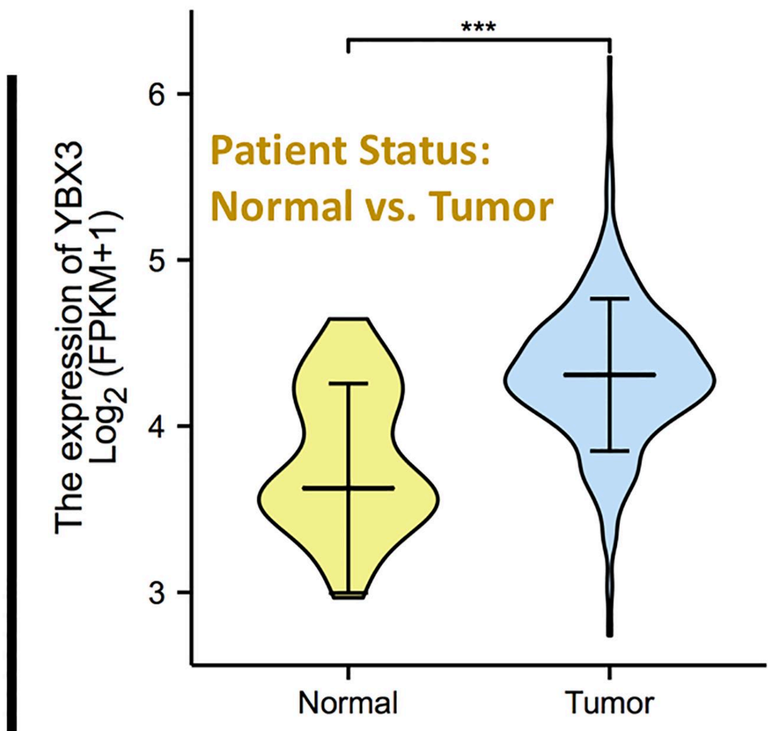


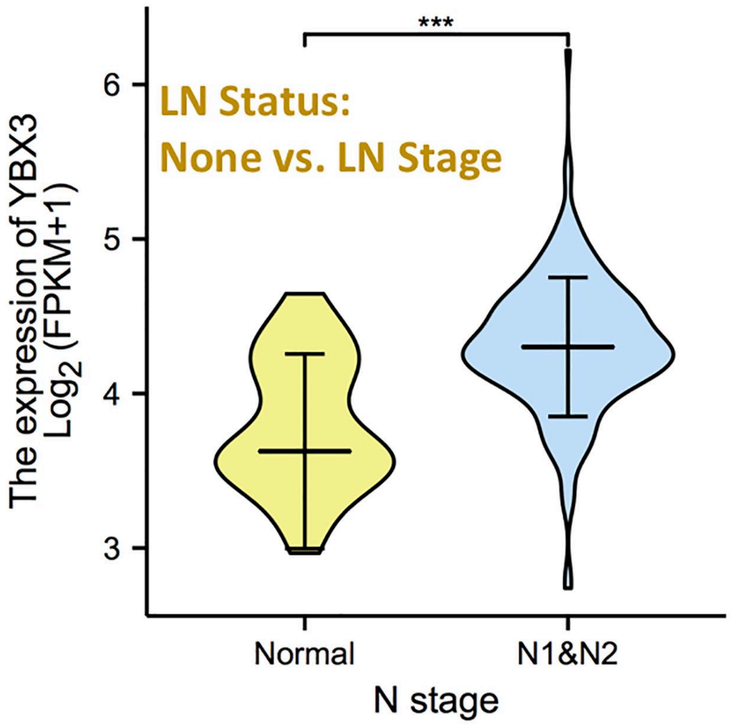


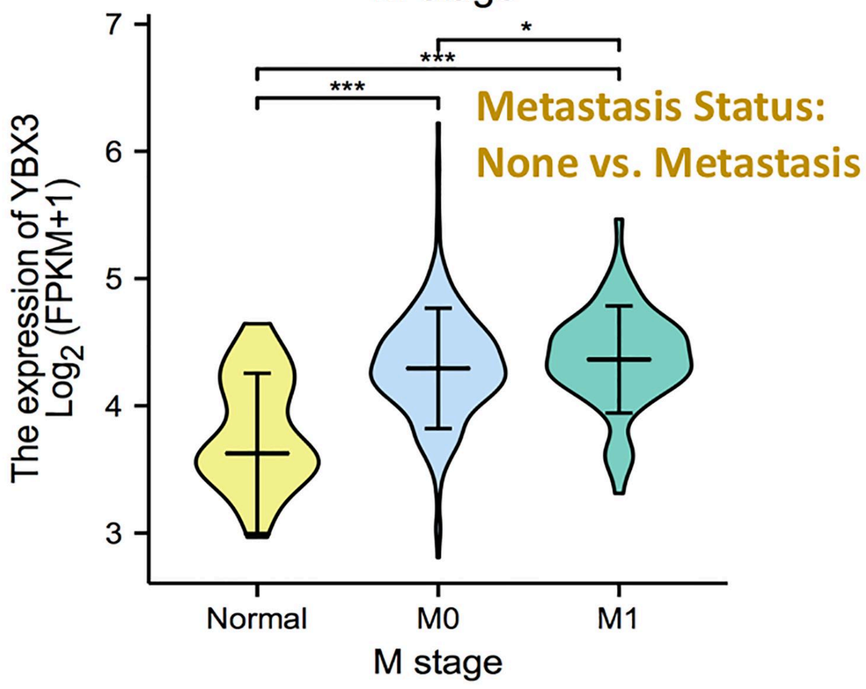


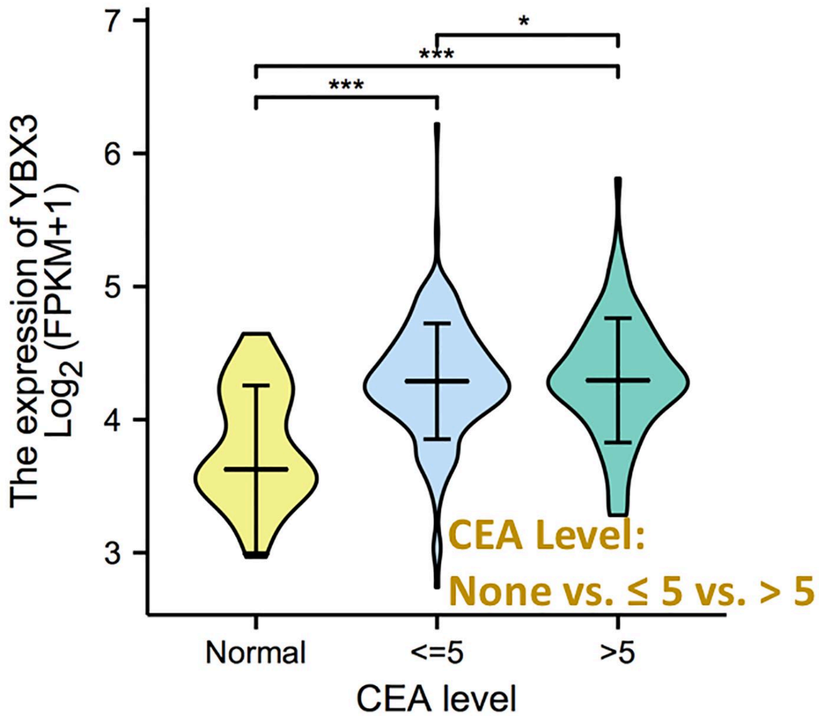
VS.

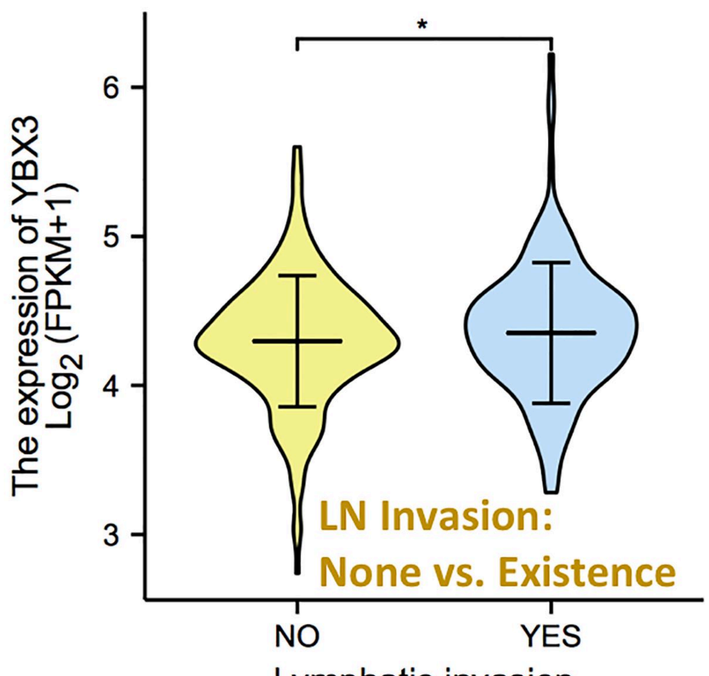
YBX3











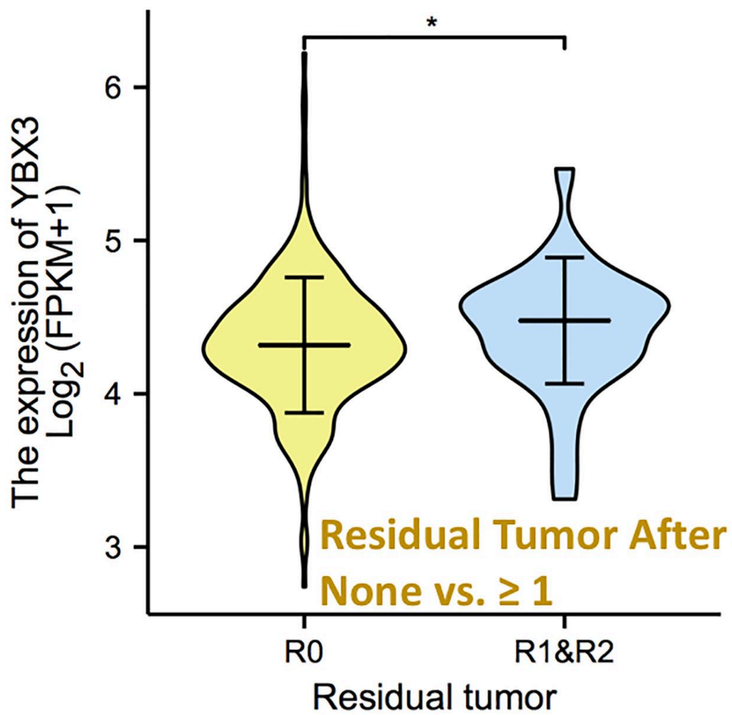
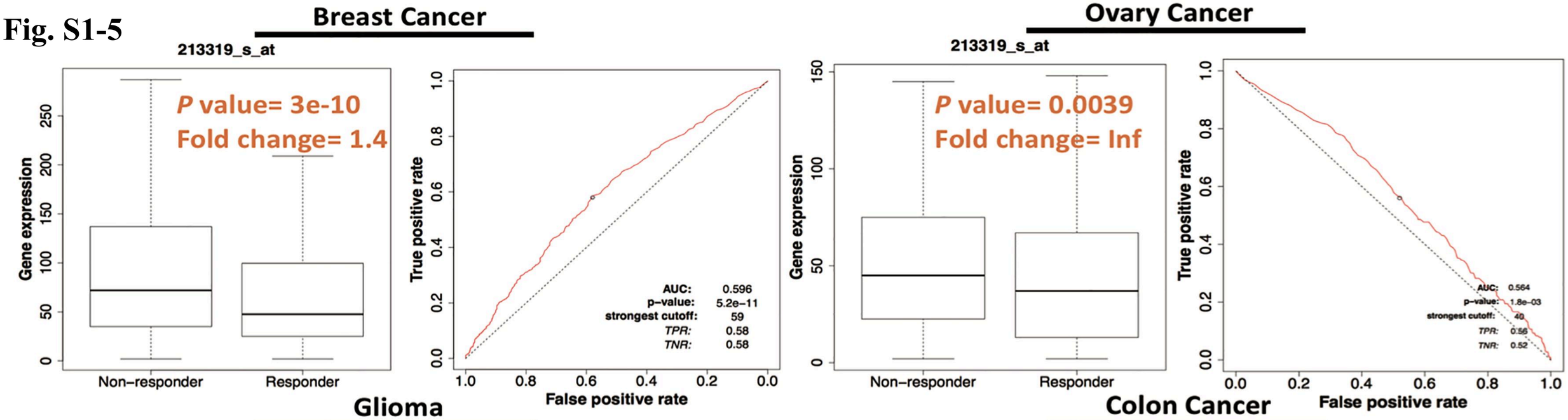


Fig. S1-5

A


Breast Cancer
213319_s_at
P value= 3e-10
Fold change= 1.4
Gene expression
Non−responder
Responder
True positive rate
False positive rate
AUC: 0.596
p−value: 5.2e−11
strongest cutoff: 59
TPR: 0.58
TNR: 0.58
Ovary Cancer
213319_s_at
P value= 0.0039
Fold change= Inf
Gene expression
Non−responder
Responder
True positive rate
False positive rate
AUC: 0.564
p−value: 1.8e−03
strongest cutoff: 40
TPR: 0.56
TNR: 0.52
Glioma
213319_s_at
P value= 0.0065
Fold change= 1.2
Gene expression
Non−responder
Responder
True positive rate
False positive rate
AUC: 0.574
p−value: 3e−03
strongest cutoff: 20
TPR: 0.61
TNR: 0.53
Colon Cancer
213319_s_at
P value= 0.011
Fold change= 1.1
Gene expression
Non−responder
Responder
True positive rate
False positive rate
AUC: 0.573
p−value: 5e−03
strongest cutoff: 2331
TPR: 0.59
TNR: 0.54

B

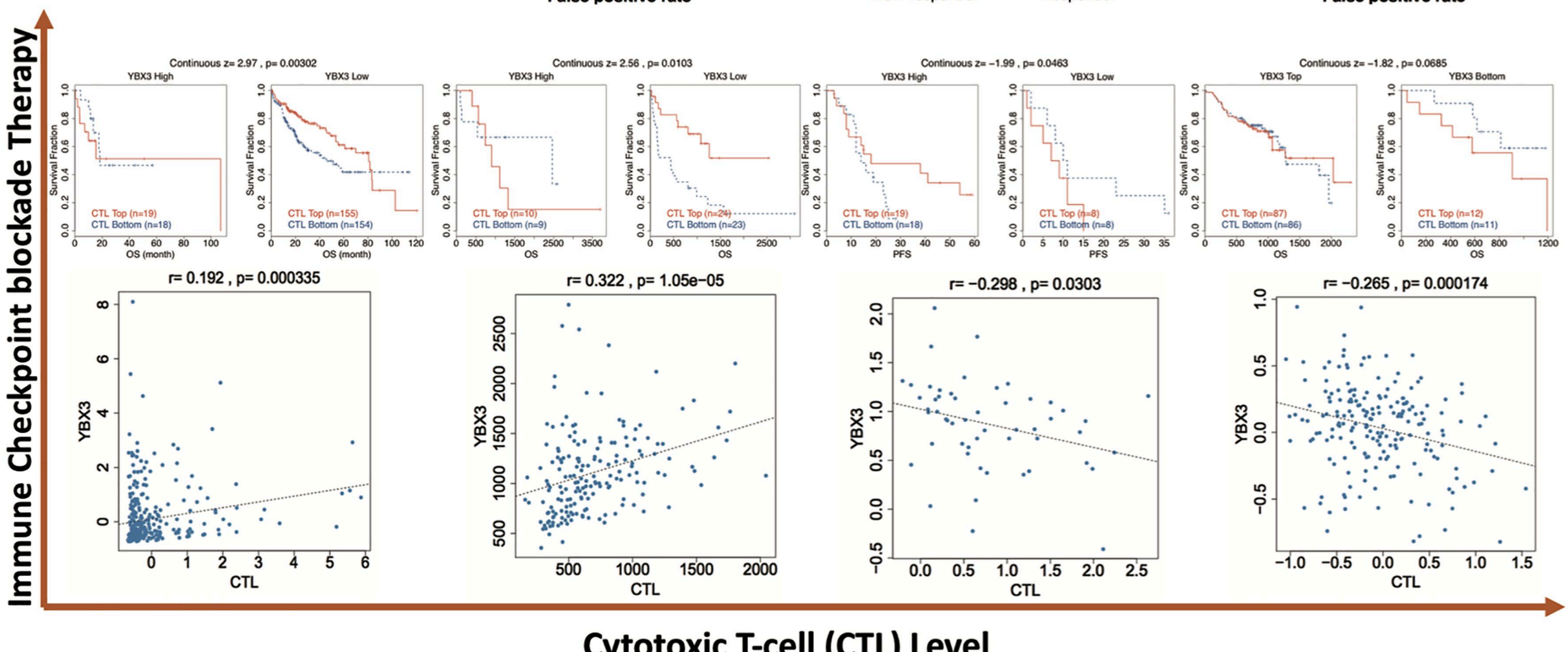

Immune Checkpoint blockade Therapy
Continuous z= 2.97 , p= 0.00302
YBX3 High
YBX3 Low
CTL Top (n=19)
CTL Bottom (n=18)
CTL Top (n=155)
CTL Bottom (n=154)
OS (month)
Continuous z= 2.56 , p= 0.0103
CTL Top (n=10)
CTL Bottom (n=9)
CTL Top (n=24)
CTL Bottom (n=23)
OS
Continuous z= −1.99 , p= 0.0463
CTL Top (n=19)
CTL Bottom (n=18)
CTL Top (n=8)
CTL Bottom (n=8)
PFS
Continuous z= −1.82 , p= 0.0685
YBX3 Top
YBX3 Bottom
CTL Top (n=87)
CTL Bottom (n=86)
CTL Top (n=12)
CTL Bottom (n=11)
Survival Fraction
r= 0.192 , p= 0.000335
r= 0.322 , p= 1.05e−05
r= −0.298 , p= 0.0303
r= −0.265 , p= 0.000174
YBX3
CTL
Cytotoxic T-cell (CTL) Level

Fig. S1-6

Flow Chart of Manuscript

① [Fig. 1] LncRNA-HEIH and YBX3 expression in various cancers (which finds that the trends of the expression of the 2 genes are quite opposite in the same cancer type, and here is the first evidence suggesting that the potential interaction between HEIH and YBX3)

② [Fig. S1-1] The YBX3 expression in different molecular and immune subtypes of various TCGA cancer types (which illustrates that there is relatively obvious difference of YBX3 expression among diverse subtypes of different TCGA cancer types, suggesting YBX3 is a potential immune biomarker)

③ [Fig. S1-2]The role of LncRNA-HEIH/YBX3 in the field of clinical diagnosis of different cancers (which proved the 2 points below: 1. Both LncRNA-HEIH and YBX3 have huge diagnostic potential in cancers. 2. Similar diagnostic ability indicating the two factors can form an integral oncogenic predicting system)

④ [Fig. S1-3 and 4]The role of HEIH and YBX3 in prognosis of digestive tract tumors (the results indicate that the two play just quite opposite roles in prognosis of digestive system cancers and their effects on prognosis are significant, which, from a clinical view, reconfirms that the HEIH and YBX3 can constitute an integral oncogenic system, especially in gastrointestinal cancers)

Transition: from pancaner to specific caner, namely, from commonality to individuality

⑤ [Fig. 2]The role of LncRNA-HEIH/YBX3 in crucial clinical characteristics of colon cancer (which further identified the oncogenic system composed by the two, and meanwhile, setting a stage for their potential effect on immunotherapy)

⑥ [Fig. 3-6]The DEGs of LncRNA-HEIH and YBX3 in colon cancer → constructions of hub genes networks → the distribution of their expression in immune cells via scRNA-seq and their inducing the immune infiltration as well as T-cell exclusion in colon cancer (which provides further evidence for immunotherapeutic target)

⑦ [Fig. S1-5] the effect of the oncogenic system on immune checkpoint blockade therapy in colon cancer (identifying its potential in ICB of cancer)

⑧[Fig. 7] Taking colon cancer as an example: proving that the interaction between LncRNA-HEIH and YBX3 can form a carcinogenic system in colon cancer from the aspect of experiment

Experimental Validation

Annotation of Border Color

* Green: The interaction of LncRNA-HEIH and YBX3 in pan-cancer (from plane-commonality).
* Red: The interaction of LncRNA-HEIH and YBX3 in digestive tract tumors (line-transition).
* Black: The interaction of LncRNA-HEIH and YBX3 in colon cancer (to point-individuality).