A

1
0.5
0
-0.5

Normal

PCRC

Normal   PCRC

B

1
0.8
0.6
0.4
0.2
0

Normal

PCRC

Normal   PCRC

C

PCA

7.5

5.0

2.5

0.0

-2.5

PC2(12.6%)

group
● Normal
▲ PCRC

-12   -8   -4   0
PC1(61.9%)

D

PCA

2

0

-2

PC2(8%)

-5.0   -2.5   0.0   2.5
PC1(83.7%)

E

The Differentially Expressed Genes On Chromosomes

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y

— Over-expressed Genes
— Under-expressed Genes

The gene positions are based on GRCh38.p2(NCBI). 5362 Genes.

Figure S1: Verification for repeatability of intra-group data and the differentially expressed genes on chromosomes.

(A) Heat map indicating the strong correlations among samples in the PCRC group, and also strong correlations among samples in the control group in the GSE41258 via the Pearson's correlation test. The 0<correlation<1 showed that there is a positive correlation. The -1<correlation<0 showed that there is a negative correlation. The larger the absolute value is, the stronger the correlation is. (B) Heat map indicating the strong correlations among samples in the PCRC group, and also strong correlations among samples in the control group in the GSE81558 via the Pearson's correlation test. The 0<correlation<1 showed that there is a positive correlation. The -1<correlation<0 showed that there is a negative correlation. The larger the absolute value is, the stronger the correlation is. (C) The PCA manifested that the repeatability of the data in GSE41258 was fine. The distances between per samples in the PCRC group were close, and the distances between per samples in the control group were also close in the dimension of PC1. (D) The PCA manifested that the repeatability of the data in GSE81558 was fine. The distances between per samples in the PCRC group were close, and the distances between per samples in the control group were also close in the dimension of PC1. (E) The differentially expressed genes on chromosomes between PCRC and normal colorectal tissue.
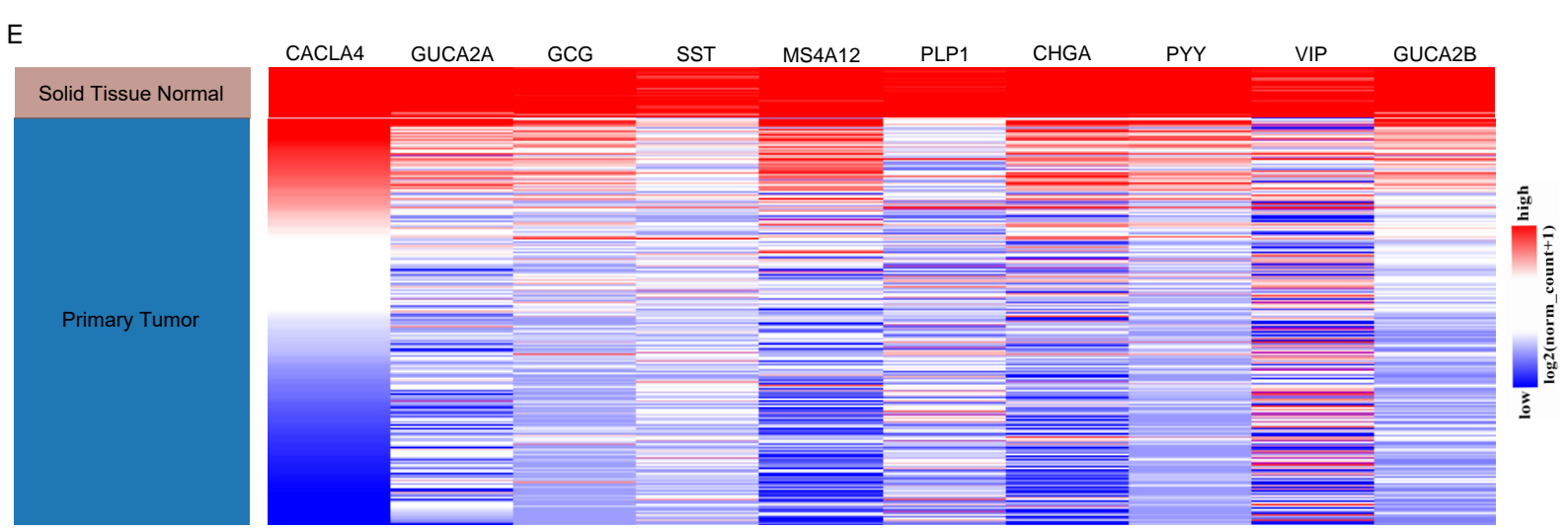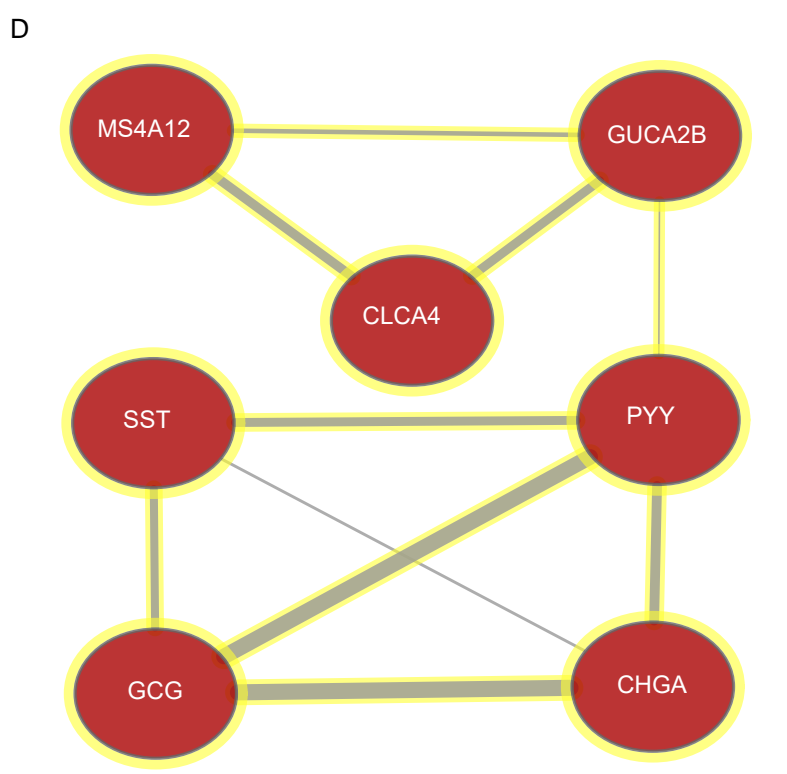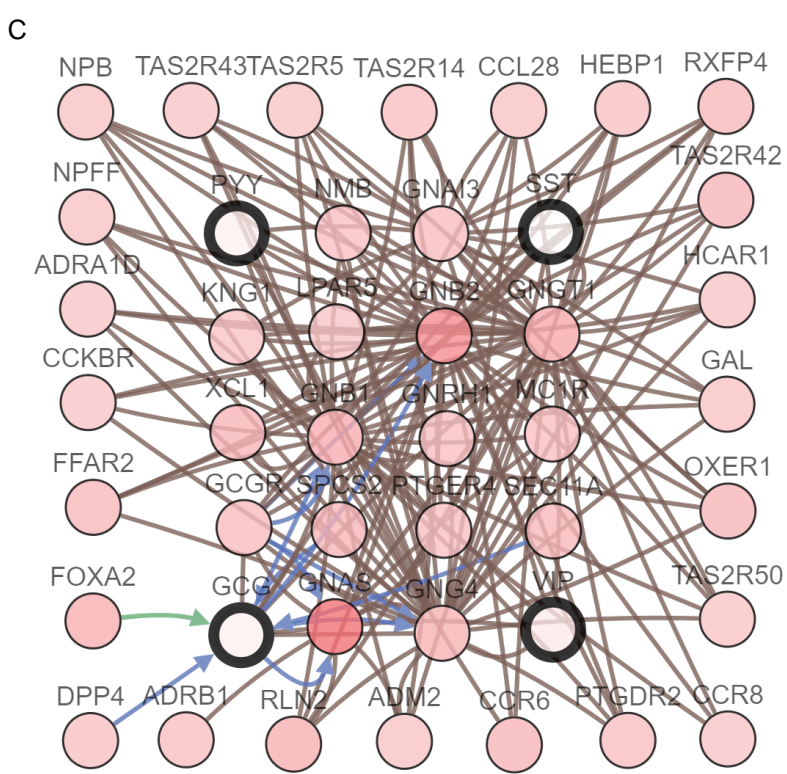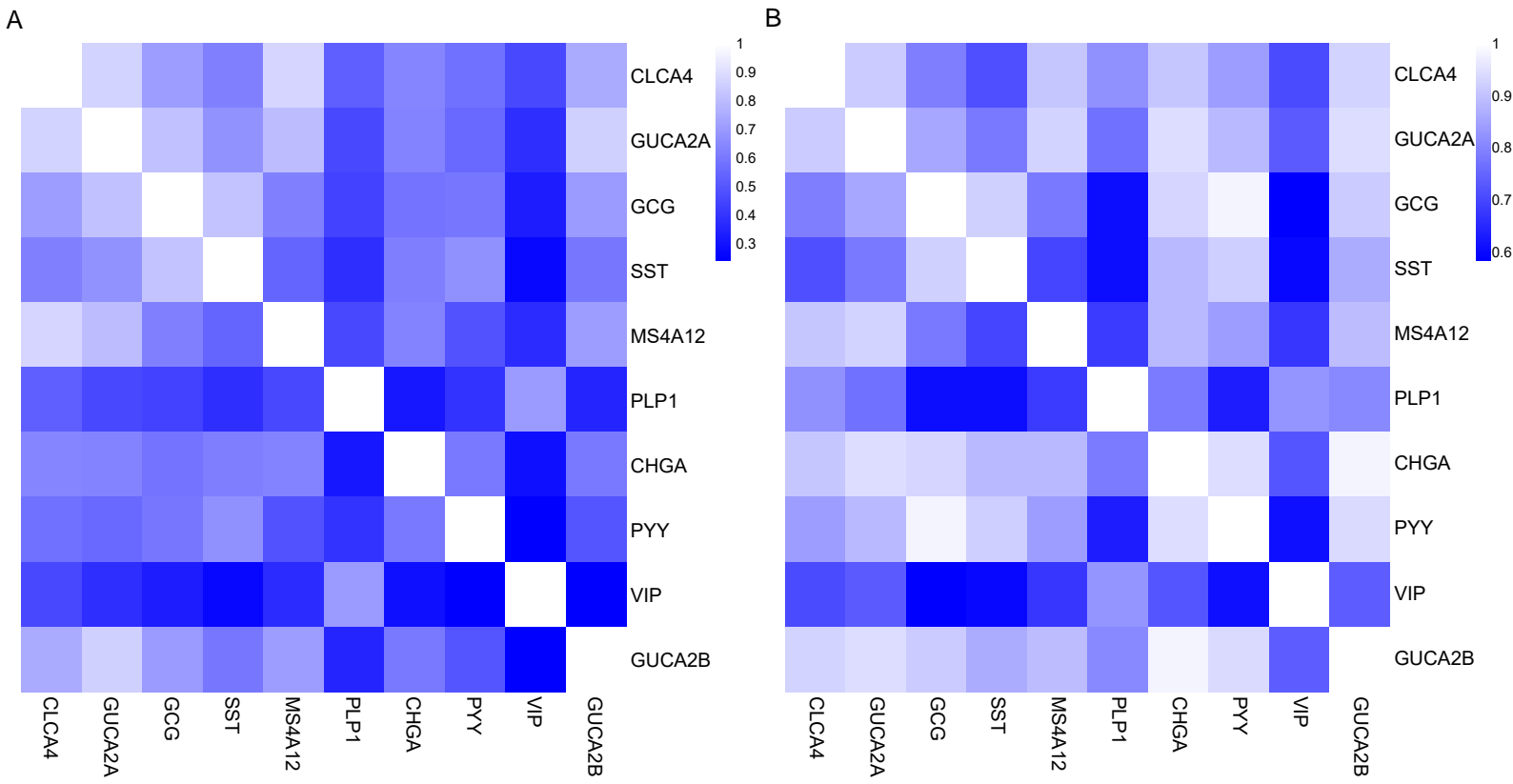
Figure S2: The correlation analysis among the hub genes and the UCSC analysis.

(A) Heat maps showing the correlations between hub genes in the GSE41258datasets.

(B) Heat maps showing the correlations between hub genes in the GSE81558datasets.

The color reflects the intensity of the correlation. The 0<correlation<1 showed that

there is a positive correlation. The -1<correlation<0 showed that there is a negative

correlation. The larger the absolute value is, the stronger the correlation is. (C) PYY,

SST, GCG, and VIP existed simultaneously in the co-expression network via

cBioPortal. (D) Through the analysis of Coexpedia, there were strong interactions

among PYY, SST, GCG, CHGA, CLCA4, GUCA2B, and MS4A12. (E) Heat map

showed that the expressions of all the hub genes were lower in the PCRC samples
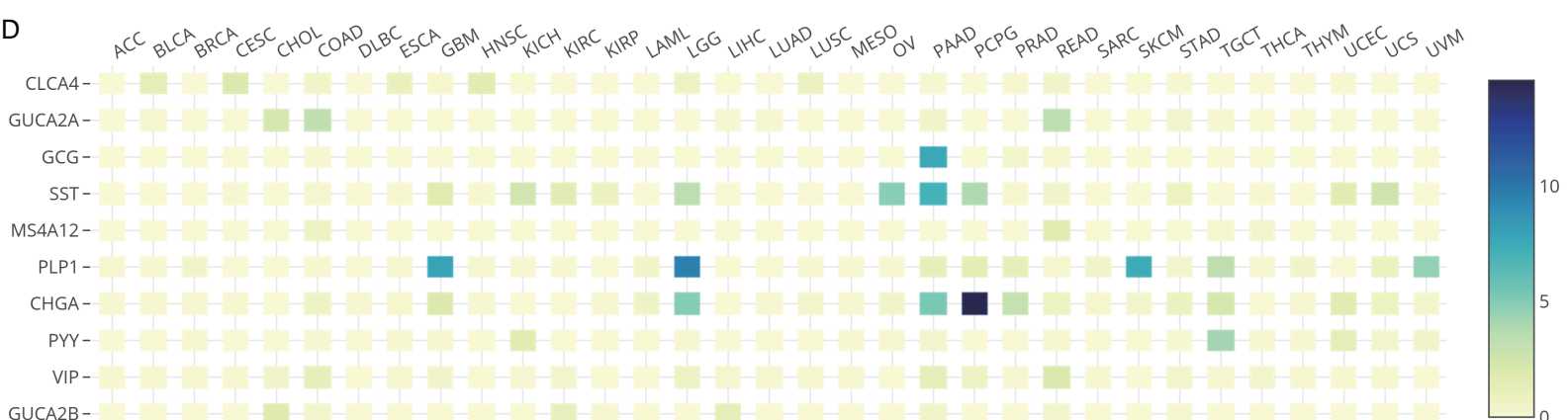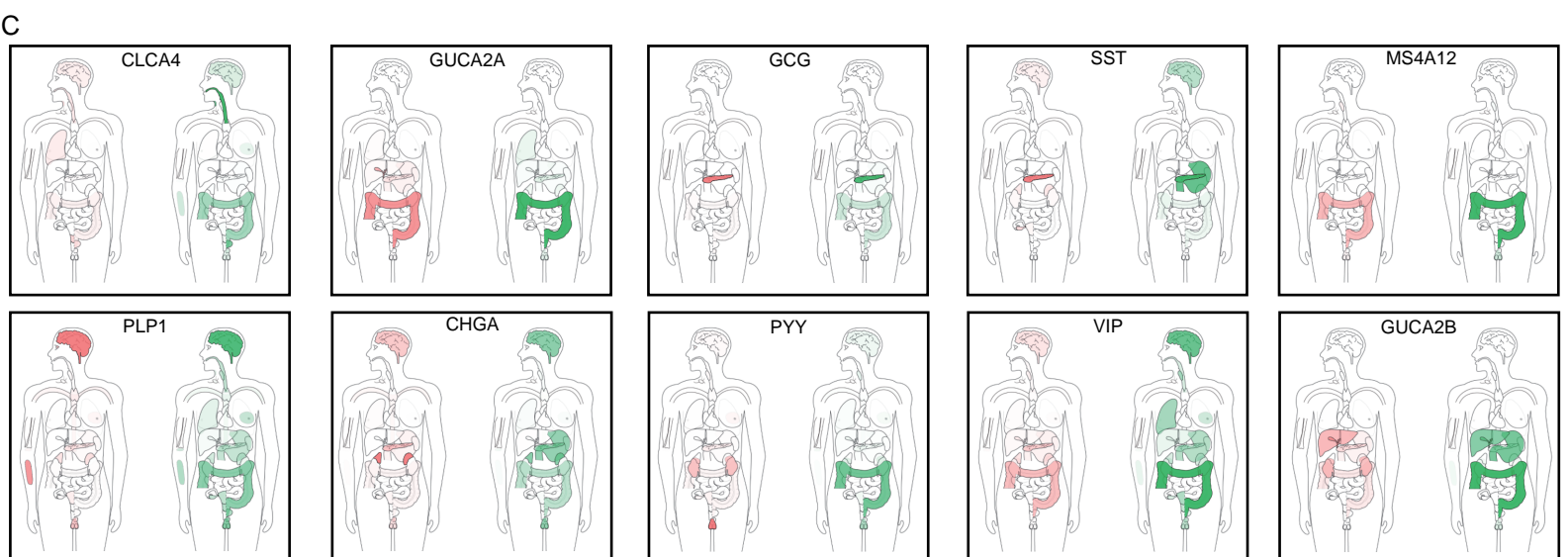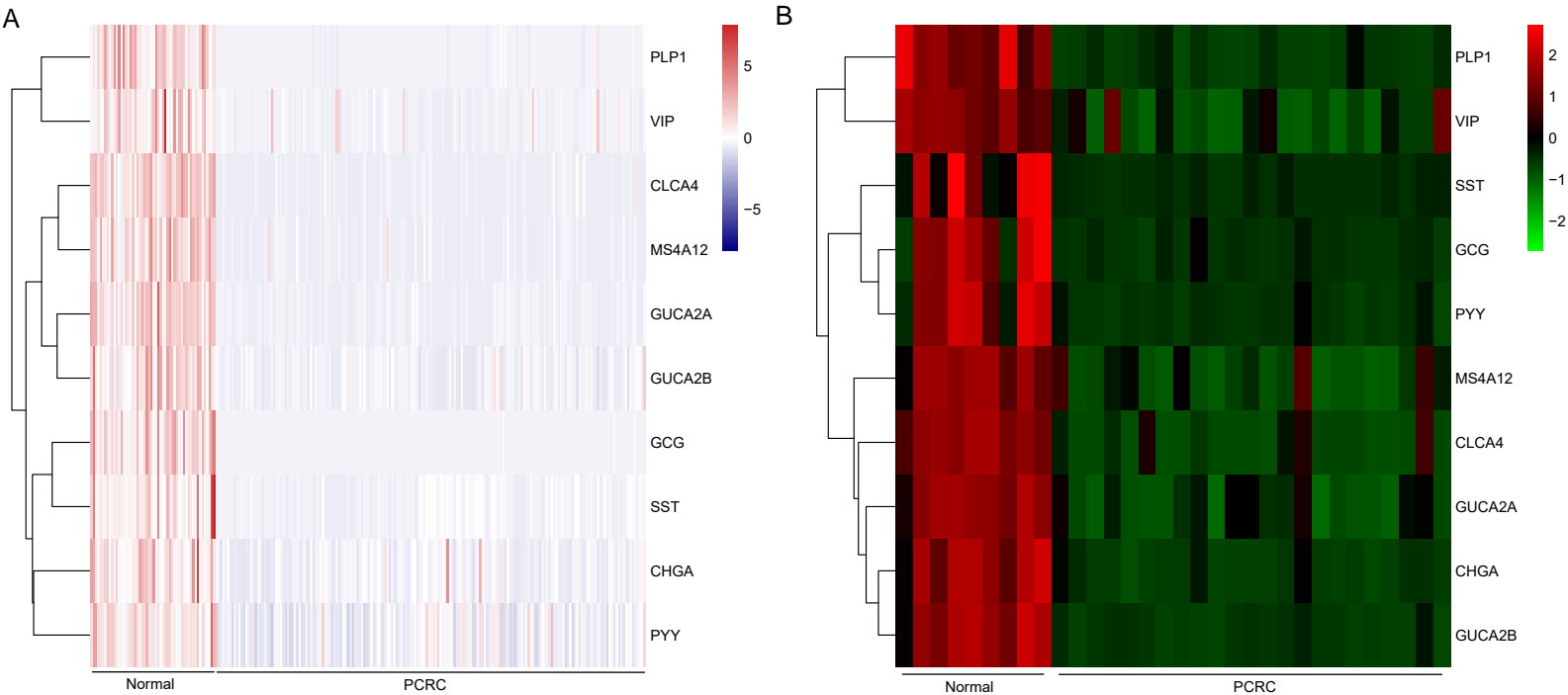
than the control samples.

Figure S3: The expression analysis of the hub genes.

(A) A hierarchical clustering heat-map of the hub genes from PCRC and normal colorectal tissue from the GSE41258 dataset. The X-axis represents sample symbols (from left to right: samples of normal colorectal tissue and samples of PCRC tissue); the Y-axis represents hub genes. Blue, low expression; white, medium expression; and pink, high expression. (B) A hierarchical clustering heat-map of the hub genes from PCRC and normal colorectal tissue from the GSE81558 dataset. The X-axis represents sample symbols (from left to right: samples of normal colorectal tissue and samples of PCRC tissue); the Y-axis represents hub genes. Green, low expression; black, medium expression; and red, high expression. (C) The expression of hub genes (CLCA4, GUCA2A, GCG, SST, MS4A12, PLP1, CHGA, PYY, VIP, and GUCA2B) in the colorectum was higher in the normal individuals compared with the tumor samples. (D) The comparison of expressions of all hub genes in the various tumors. ACC: Adrenocortical carcinoma; BLCA: Bladder Urothelial Carcinoma; BRCA: Breast invasive carcinoma; CESC: Cervical squamous cell carcinoma and endocervical adenocarcinoma; CHOL: Cholangio carcinoma; COAD: Colon adenocarcinoma; DLBC: Lymphoid Neoplasm Diffuse Large B-cell Lymphoma; ESCA: Esophageal carcinoma; GBM: Glioblastoma multiforme; HNSC: Head and Neck squamous cell carcinoma; KICH: Kidney Chromophobe; KIRC: Kidney renal clear cell carcinoma; KIRP: Kidney renal papillary cell carcinoma; LAML: Acute Myeloid Leukemia; LGG: Brain Lower Grade Glioma; LIHC: Liver hepatocellular carcinoma; LUAD: Lung adenocarcinoma; LUSC: Lung squamous cell carcinoma; OA: Ovarian serous cystadenocarcinoma; PAAD: Pancreatic adenocarcinoma; PCPG: Pheochromocytoma and Paraganglioma; PRAD: Prostate adenocarcinoma; READ: Rectum adenocarcinoma; SARC: Sarcoma; SKCM: Skin Cutaneous Melanoma;

STAD: Stomach adenocarcinoma; TGCT: Testicular Germ Cell Tumors; THCA: Thyroid carcinoma; THYM: Thymoma; UCEC: Uterine Corpus Endometrial Carcinoma; UCS: Uterine Carcinosarcoma.
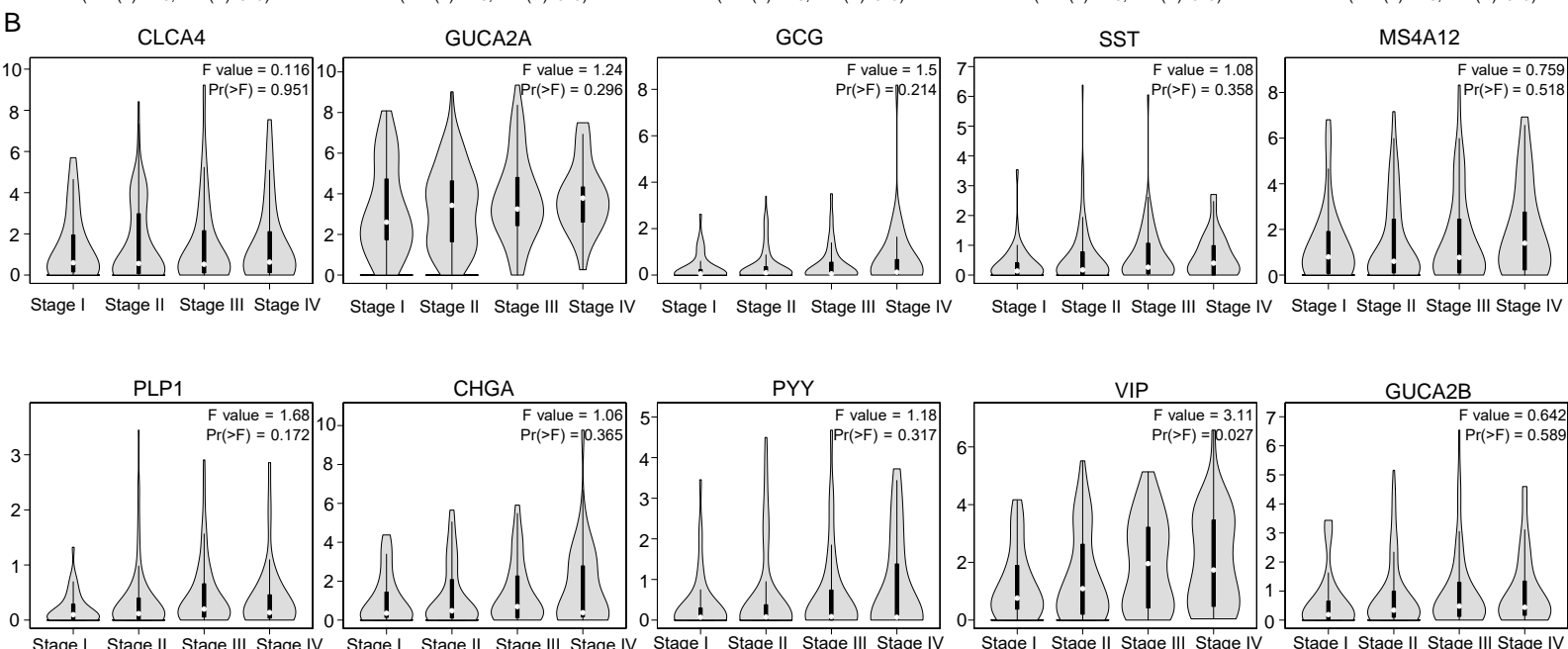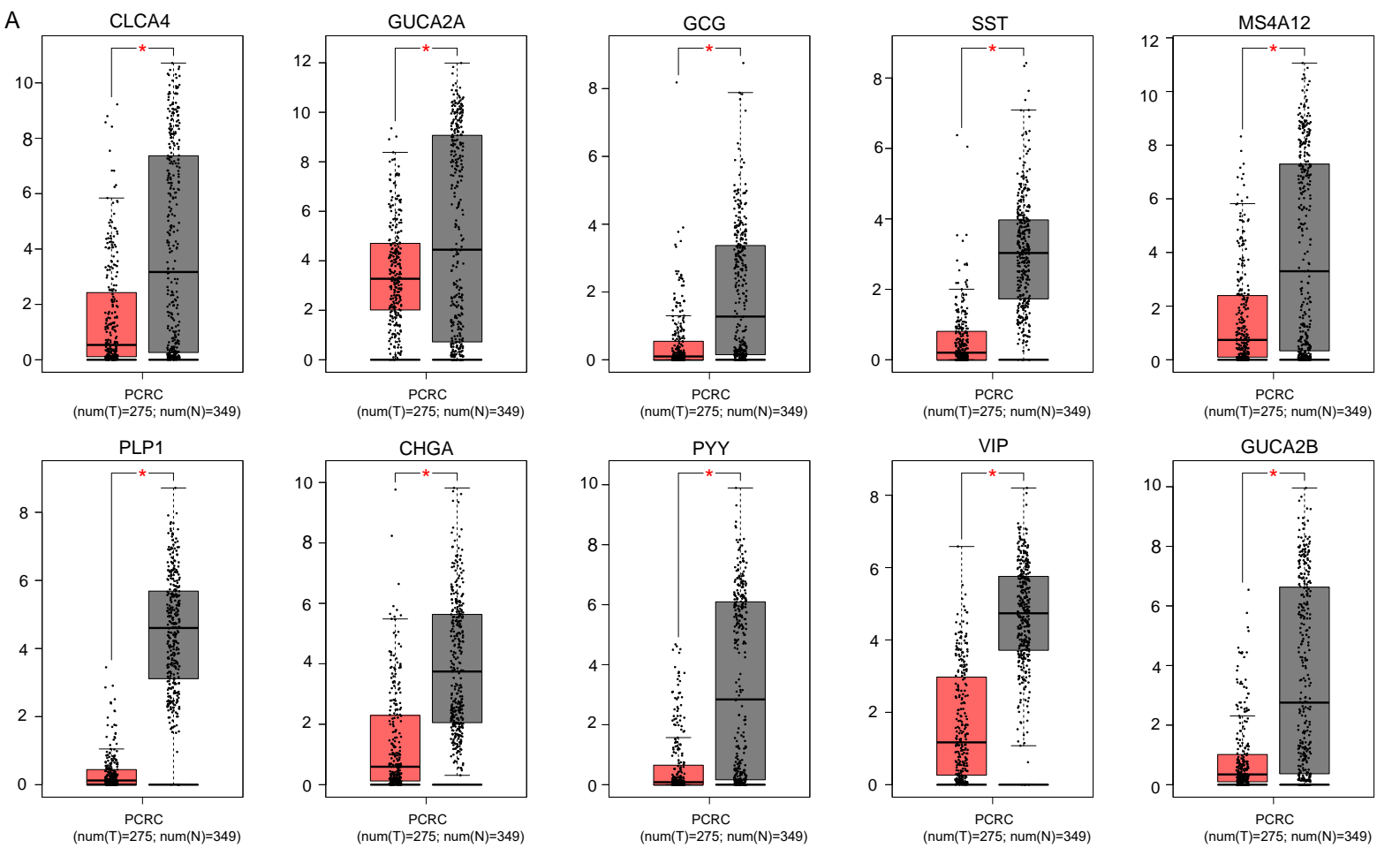
A

| CLCA4 | GUCA2A | GCG | SST | MS4A12 |

PLP1 | CHGA | PYY | VIP | GUCA2B

PCRC
(num(T)=275; num(N)=349)

B

CLCA4 — F value = 0.116, Pr(>F) = 0.951
GUCA2A — F value = 1.24, Pr(>F) = 0.296
GCG — F value = 1.5, Pr(>F) = 0.214
SST — F value = 1.08, Pr(>F) = 0.358
MS4A12 — F value = 0.759, Pr(>F) = 0.518

PLP1 — F value = 1.68, Pr(>F) = 0.172
CHGA — F value = 1.06, Pr(>F) = 0.365
PYY — F value = 1.18, Pr(>F) = 0.317
VIP — F value = 3.11, Pr(>F) = 0.027
GUCA2B — F value = 0.642, Pr(>F) = 0.589

Stage I   Stage II   Stage III   Stage IV

Figure S4: The box plots of expression level of hub genes and the violin plots of pathological stage.

(A) The comparison of expressions of all hub genes between PCRC and normal colorectal samples. (B) The relationship between expression of hub genes (CLCA4, GUCA2A, GCG, SST, MS4A12, PLP1, CHGA, PYY, VIP, and GUCA2B) and pathological stage.

A CHGA

HR = 1.69 (1.12 − 2.56)
logrank P = 0.011

Expression
— low
— high

B PYY

HR = 1.33 (0.93 − 1.9)
logrank P = 0.12

Expression
— low
— high

C VIP

HR = 1.19 (0.84 − 1.67)
logrank P = 0.33

Expression
— low
— high

D GUCA2B

HR = 1.25 (0.89 − 1.76)
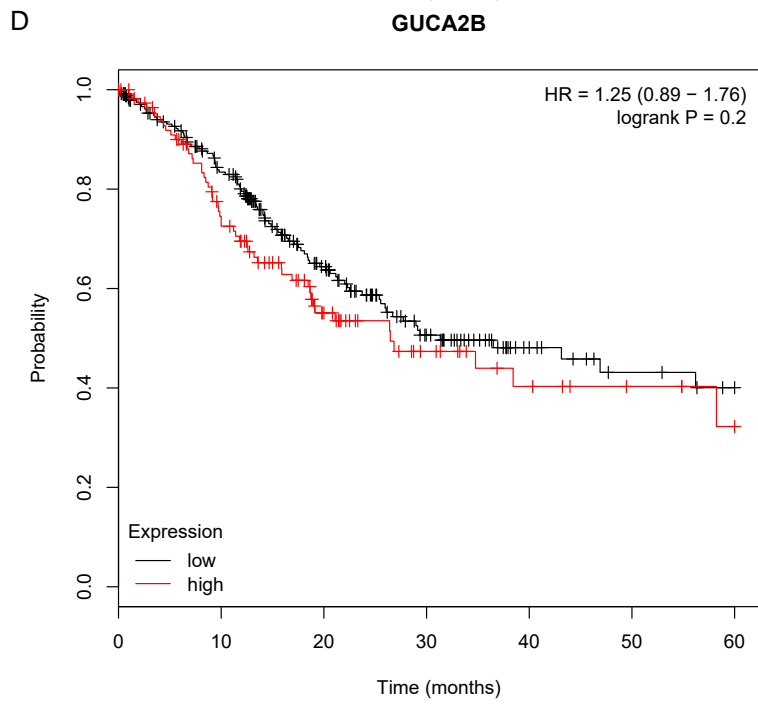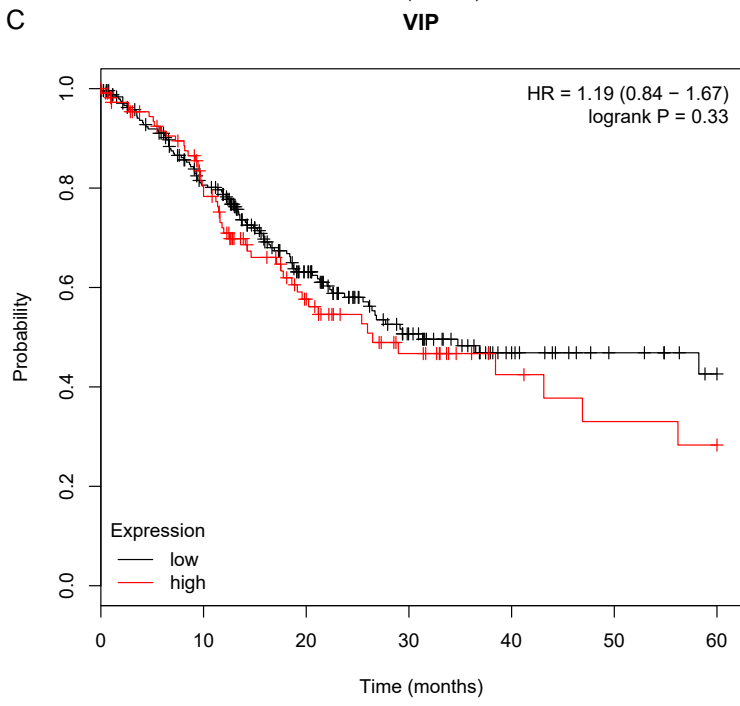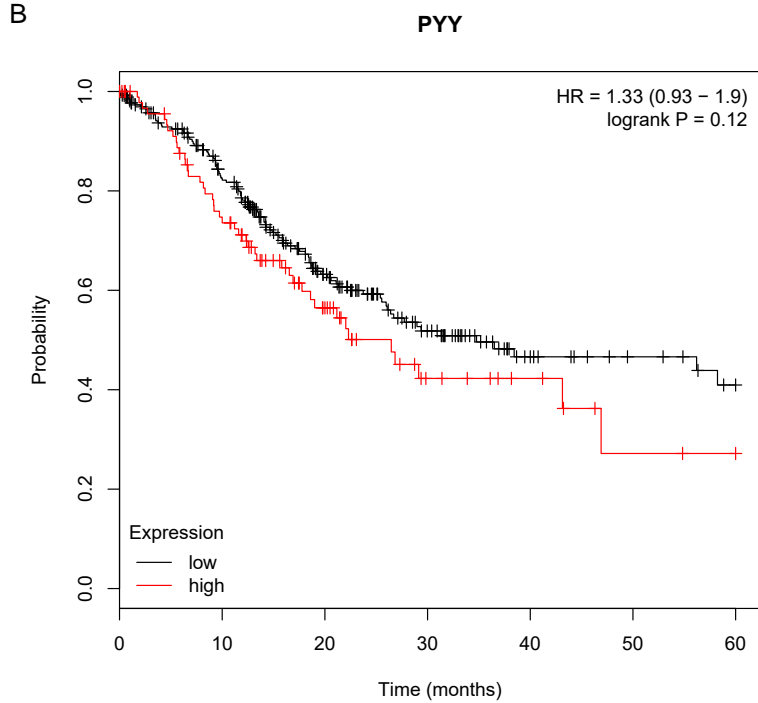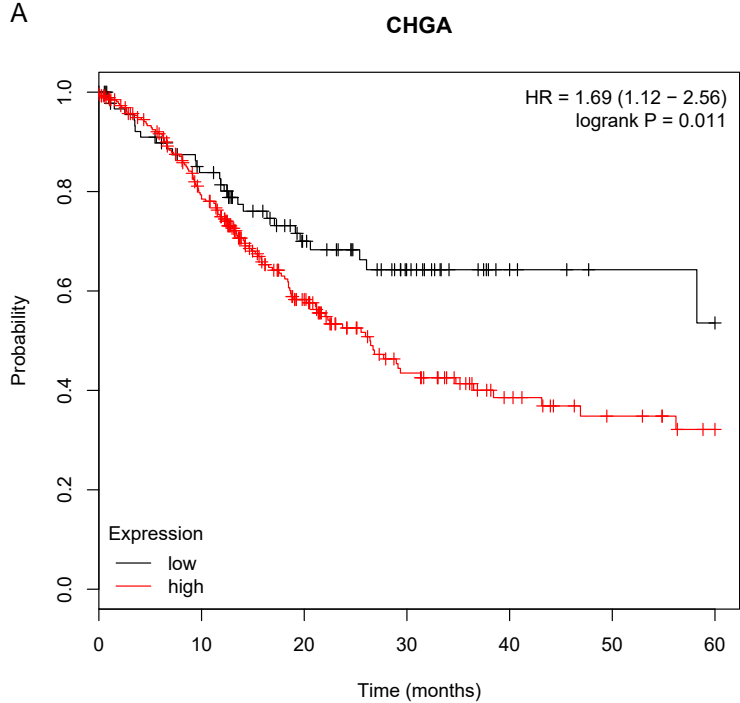logrank P = 0.2

Expression
— low
— high

Figure S5: The overall survival Kaplan-Meier of another four hub genes.

(A) CHGA, (B) PYY, (C) VIP, (D) GUCA2B