Gene symbol	Types of gynecology cancer vs. Norma	Fold change	t-test	p-value	Ref	PMID
	Cervical squamous cell carcinoma vs. Normal	1.801	5.612	4.24E-7	Scotto Cervix 2	18506748
CIRBP	Cervical squamous cell carcinoma vs. Normal	1.362	6.305	1.61E-4	Biewenga Cervix	18191186
	Cervical Squamous Cell Carcinoma Epithelia vs. Normal	1.658	4.310	1.01E-4	Zhai Cervix	17974957
CIRBP	Ovarian Serous Adenocarcinoma vs. Normal	5.365	9.222	1.63E-5	Adib Ovarian	14760385
	Ovarian Carcinoma vs. Normal	4.637	15.090	1.79E-10	Bonome Ovarian	18593951
	Ovarian Serous Surface Papillary Carcinoma vs. Normal	4.238	13.077	3.16E-9	Welsh Ovarian	11158614
	Ovarian Serous Adenocarcinoma vs. Normal	3.801	9.944	1.61E-11	Yoshihara Ovarian	19486012
	Ovarian Serous Cystadenocarcinoma vs. Normal	3.177	13.192	7.24E-7	TCGA Ovarian	
	Ovarian Endometrioid Adenocarcinoma vs. Normal	2.900	4.272	0.001	Lu Ovarian	15161682
	Ovarian Mucinous Adenocarcinoma vs. Normal	2.327	3.294	0.004	Lu Ovarian	15161682
	Ovarian Serous Adenocarcinoma vs. Normal	1.880	5.334	2.07E-5	Lu Ovarian	15161682
	Ovarian Clear Cell Adenocarcinoma vs. Normal	1.615	3.335	0.004	Lu Ovarian	15161682
	Ovarian Serous Adenocarcinoma vs. Normal	1.538	12.974	1.21E-7	Hendrix Ovarian	16452189
	Cervical Squamous Cell Carcinoma vs. Normal	1.23	2.880	0.003	Scotto Cervix 2	18506748
INPP5K	Cervical Non-Keratinizing Squamous Cell Carcinoma vs. Normal	1.207	3.067	0.005	TCGA Cervix (DNA)	
	Cervical Squamous Cell Carcinoma vs. Normal	1.103	5.522	1.86E-7	TCGA Cervix (DNA)	
	Ovarian Serous Adenocarcinoma vs. Normal	1.950	6.543	1.43E-7	Yoshihara Ovarian	19486012
	Ovarian Serous Surface Papillary Carcinoma vs. Normal	4.267	2.093	0.041	Welsh Ovarian	11158614
INPP5K	Ovarian Serous Adenocarcinoma vs. Normal	1.143	2.498	0.021	Adib Ovarian	14760385
	Ovarian Endometrioid Adenocarcinoma vs. Normal	1.052	2.916	0.003	Hendrix Ovarian	16452189
	Ovarian Serous Adenocarcinoma vs. Normal	1.029	1.989	0.030	Hendrix Ovarian	16452189

**Table S1:** The transcriptional levels of CIRBP and INPP5K in different types of gynecological cancer and normal tissues (ONCOMINE).

### **Supplementary figure legends**

**Figure.S1**: Functional enrichment of prognostic genes in CESC (Metascape). (A) Heatmap of enriched terms across the included prognostic genes colored by P-values. (B) GO terms identified in the GO analysis of the prognostic genes in the categories biological processes, cellular components, and molecular functions with 20 minimum P-values. (C) Networks of enriched terms and MCODE components identified in the gene lists.

**Figure.S2:** Functional enrichment of prognostic genes in UCEC (Metascape). (A) Heatmap of enriched terms across the included prognostic genes colored by P-values. (B) GO terms identified in the GO analysis of the prognostic genes in the categories biological processes, cellular components, and molecular functions with 20 minimum P-values. (C-D) Networks of enriched terms and MCODE components identified in the gene lists.

**Figure.S3:** Functional enrichment of prognostic genes in OV (Metascape). (A) Heatmap of enriched terms across the included prognostic genes colored by P-values. (B) GO terms identified in the GO analysis of the prognostic genes in the categories biological processes, cellular components, and molecular functions with 20 minimum P-values. (C) Networks of enriched terms and MCODE components identified in the gene lists.

**Figure.S4**: Functional enrichment of 70 overlapping and intersecting prognostic genes in gynecological cancers (Metascape). (A) Number of overlapping and intersecting prognostic genes. (B) Heatmap of enriched terms across the 70 included prognostic genes colored by P-values. (C) PPI network. (D) Networks of enriched terms and MCODE components identified in the gene lists.

**Figure.S5:** Correlation between the expression level of CIRBP/INPP5K and the clinicopathologic features (including TP53 mutation) of gynecologic cancers (UALCAN), P<0.05.

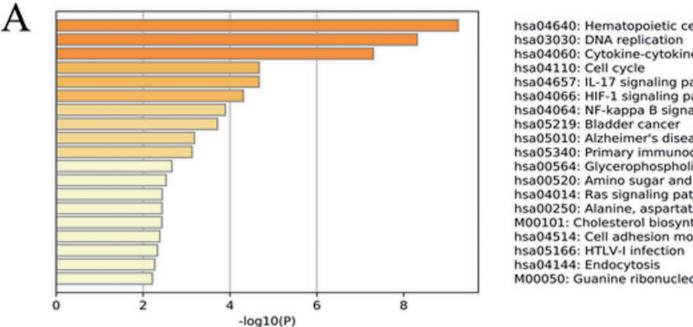
**Figure.S6:** CIRBP expression in gynecologic cancers tissues. (A) CIRBP expression in tumor cells. (B) CIRBP Localized to the nucleoplasm. (C) CIRBP expression in

immune cells. ( The data from Cell Atlas: <u>https://www.proteinatlas.org</u> )

**Figure.S7:** Correlation between the DNA methylation level of CIRBP and the clinicopathologic features (including TP53 mutation) of gynecologic cancers (UALCAN), P<0.05.

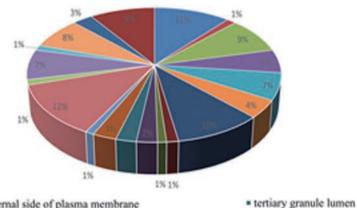
**Figure.S8:** Correlation between the DNA methylation level of INPP5K and the clinicopathologic features (including TP53 mutation) of gynecologic cancers (UALCAN), P<0.05.

**Figure.S9:** Prognostic value of APA events of CIRBP and INPP5K in gynecological cancer patients (Kaplan–Meier plotter). Patients were divided into high (red) and low (blue) PDUI value groups based on the best cut-off values using the R package.



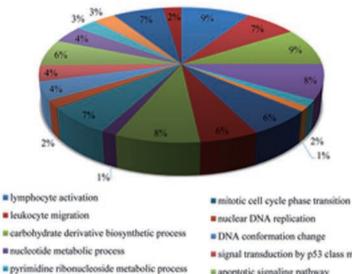
hsa04640: Hematopoietic cell lineage hsa04060: Cytokine-cytokine receptor interaction hsa04657: IL-17 signaling pathway hsa04066: HIF-1 signaling pathway hsa04064: NF-kappa B signaling pathway hsa05010: Alzheimer's disease hsa05340: Primary immunodeficiency hsa00564: Glycerophospholipid metabolism hsa00520: Amino sugar and nucleotide sugar metabolism hsa04014: Ras signaling pathway hsa00250: Alanine, aspartate and glutamate metabolism M00101: Cholesterol biosynthesis, squalene 2,3-epoxide => cholesterol hsa04514: Cell adhesion molecules (CAMs) M00050: Guanine ribonucleotide biosynthesis IMP => GDP,GTP

### Β Cellular Components



- · external side of plasma membrane
- · alpha-beta T cell receptor complex
- chromosomal region
- · coated vesicle membrane
- · mitochondrial membrane part
- nuclear chromosome, telomeric region
- · mitochondrial matrix
- nuclear lamina
- DNA replication factor C complex
- · intrinsic component of mitochondrial inner membrane

## **Biological Processes**



4-hydroxyproline metabolic process

small molecule catabolic process

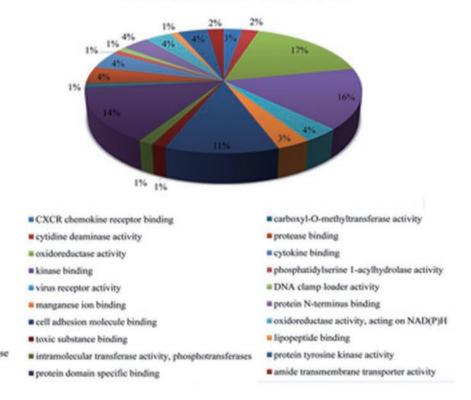
positive T cell selection

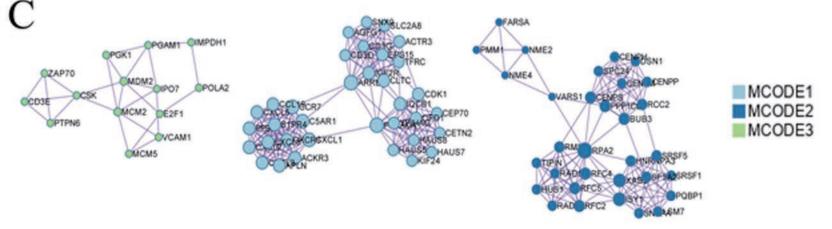
cytokine-mediated signaling pathway

generation of precursor metabolites and energy

- signal transduction by p53 class mediator
  - apoptotic signaling pathway viral life cycle
  - negative regulation of leukocyte activation
  - regulation of leukocyte mediated immunity
  - leukocyte activation involved in immune response
  - antibiotic metabolic process

### Molecular Functions





replication fork

HAUS complex

· Golgi membrane

· early endosome

BLOC complex

focal adhesion

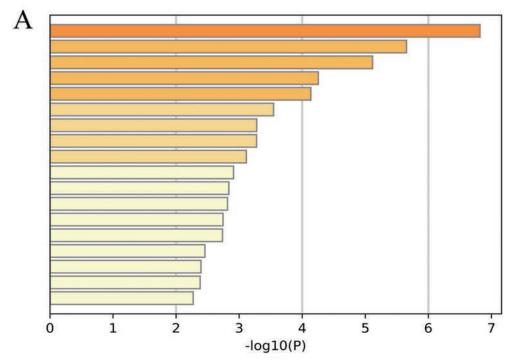
melanosome

centrosome

· filopodium membrane

MCODE 1 ciliary basal body-plasma membrane docking (Log10(P)=-18.1) MCODE 1 chemokine-mediated signaling pathway (Log10(P)=-16.4) MCODE 1 cellular response to chemokine (Log10(P)=-15.9) MCODE 2 Spliceosome (Log10(P)=-13.0) MCODE 2 condensed chromosome (Log10(P)=-12.7) MCODE 2 chromosomal region (Log10(P)=-12.3) MCODE 3 G1/S transition of mitotic cell cycle (Log10(P)=-8.2) MCODE 3 cell cycle G1/S phase transition (Log10(P)=-8.0) MCODE\_3 positive regulation of T cell activation (Log10(P)=-7.1)

Fig.S1



hsa04110: Cell cycle hsa04658: Th1 and Th2 cell differentiation hsa05166: HTLV-I infection hsa05219: Bladder cancer hsa05169: Epstein-Barr virus infection hsa04141: Protein processing in endoplasmic reticulum hsa04064: NF-kappa B signaling pathway hsa05164: Influenza A hsa04211: Longevity regulating pathway hsa05418: Fluid shear stress and atherosclerosis hsa04514: Cell adhesion molecules (CAMs) hsa00564: Glycerophospholipid metabolism hsa00250: Alanine, aspartate and glutamate metabolism hsa04940: Type I diabetes mellitus hsa00600: Sphingolipid metabolism hsa01212: Fatty acid metabolism M00089: Triacylglycerol biosynthesis

protein kinase binding

· transcription factor binding

protein domain specific binding

nucleoside binding

kinase activity

p53 binding

ATPase binding

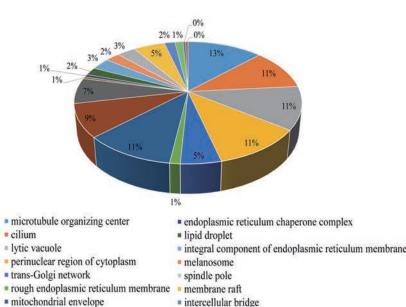
lipid binding

transcription corepressor activity

nucleoside-triphosphatase regulator activity

hsa00051: Fructose and mannose metabolism

### B **Cellular** Components



myelin sheath

dendritic filopodium

insulin-like growth factor ternary complex

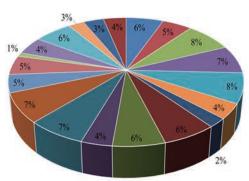
MED MED16

cell body

= cell-substrate junction

alpha-beta T cell receptor complex

## **Biological Processes**

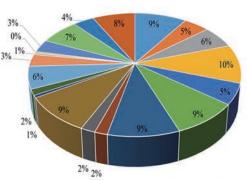


T cell activation

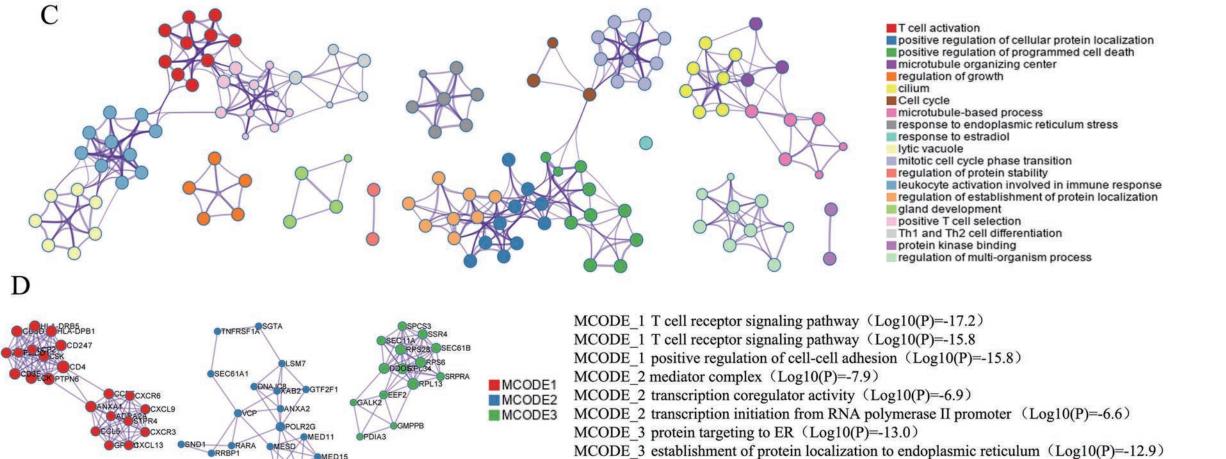
- positive regulation of cellular protein localization positive regulation of programmed cell death
- regulation of growth
- microtubule-based process
- response to endoplasmic reticulum stress
- · response to estradiol
- protein localization to membrane
- mitotic cell cycle phase transition regulation of protein stability

 leukocyte activation involved in immune response · regulation of establishment of protein localization cilium organization gland development positive T cell selection regulation of multi-organism process chordate embryonic development Iymphocyte activation involved in immune resp microtubule-based movement urogenital system development

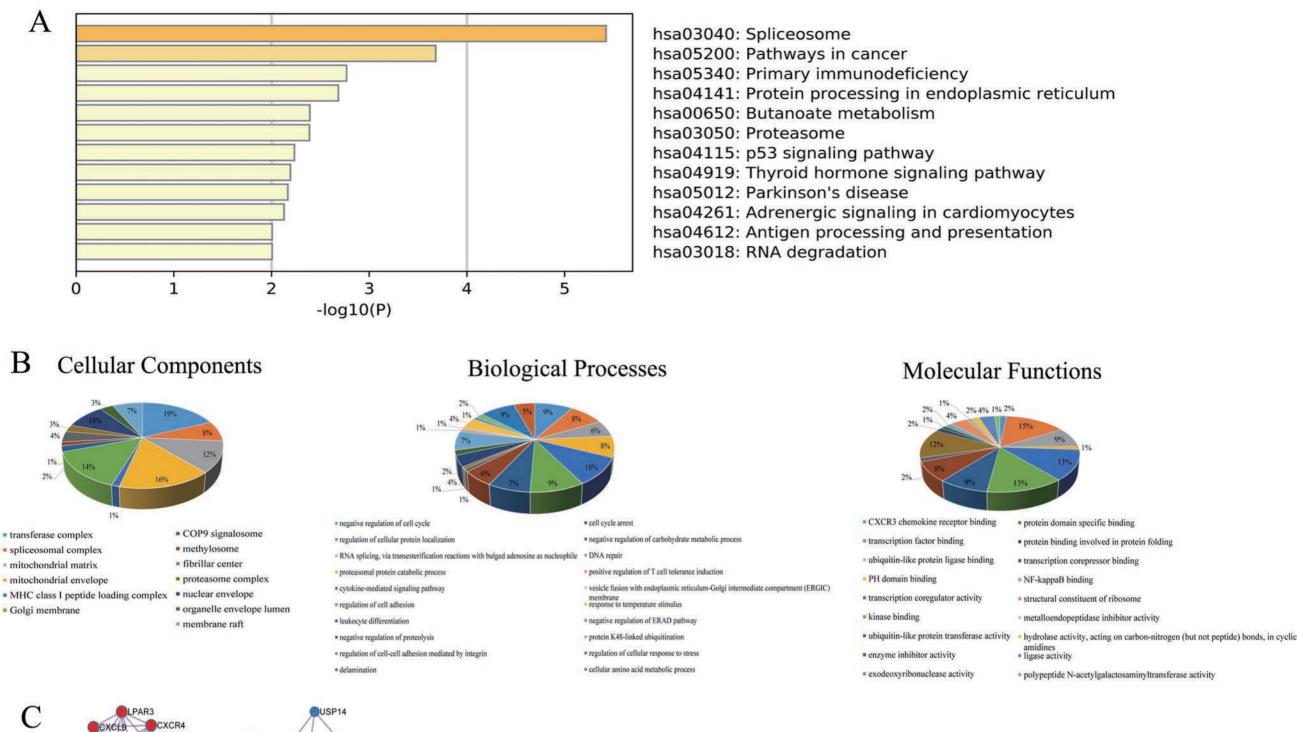
## Molecular Functions

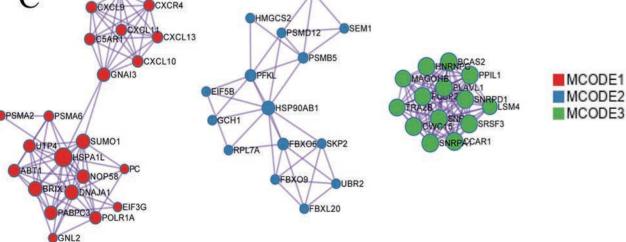


· cyclin-dependent protein serine/threonine kinase inhibitor activity calcium-dependent protein binding DNA-binding transcription activator activity, RNA polymerase II-specific protein C-terminus binding · CD4 receptor binding · very-low-density lipoprotein particle receptor activity transferase activity, transferring hexosyl groups · GTPase binding microtubule binding peptidase activity



- MCODE 3 establishment of protein localization to endoplasmic reticulum (Log10(P)=-12.9)
- MCODE 3 protein localization to endoplasmic reticu (Log10(P)=-12.2)
- Fig.S2





$MCODE_1 CXCR3$ chemokine receptor binding (Log10(P)=-11.6)
MCODE_1 CXCR chemokine receptor binding (Log10(P)=-8.8)
MCODE_1 Chemokine signaling pathway $(Log10(P)=-7.9)$
MCODE_2 proteasome-mediated ubiquitin-dependent protein catabolic process (Log10(P)=-12.2)
MCODE_2 proteasomal protein catabolic process (Log10(P)=-11.7)
MCODE_2 SCF-dependent proteasomal ubiquitin-dependent protein catabolic process (Log10(P)=-10.8)
MCODE 2 BNA spliging via transactorification reactions with huland adapaging as muchambile. (Las10/D)

- MCODE\_3 RNA splicing, via transesterification reactions with bulged adenosine as nucleophile (Log10(P)=-25.9)
- MCODE\_3 mRNA splicing, via spliceosome (Log10(P)=-25.9)
- MCODE\_3 RNA splicing, via transesterification reactions (Log10(P)=-25.9)

Fig.S3

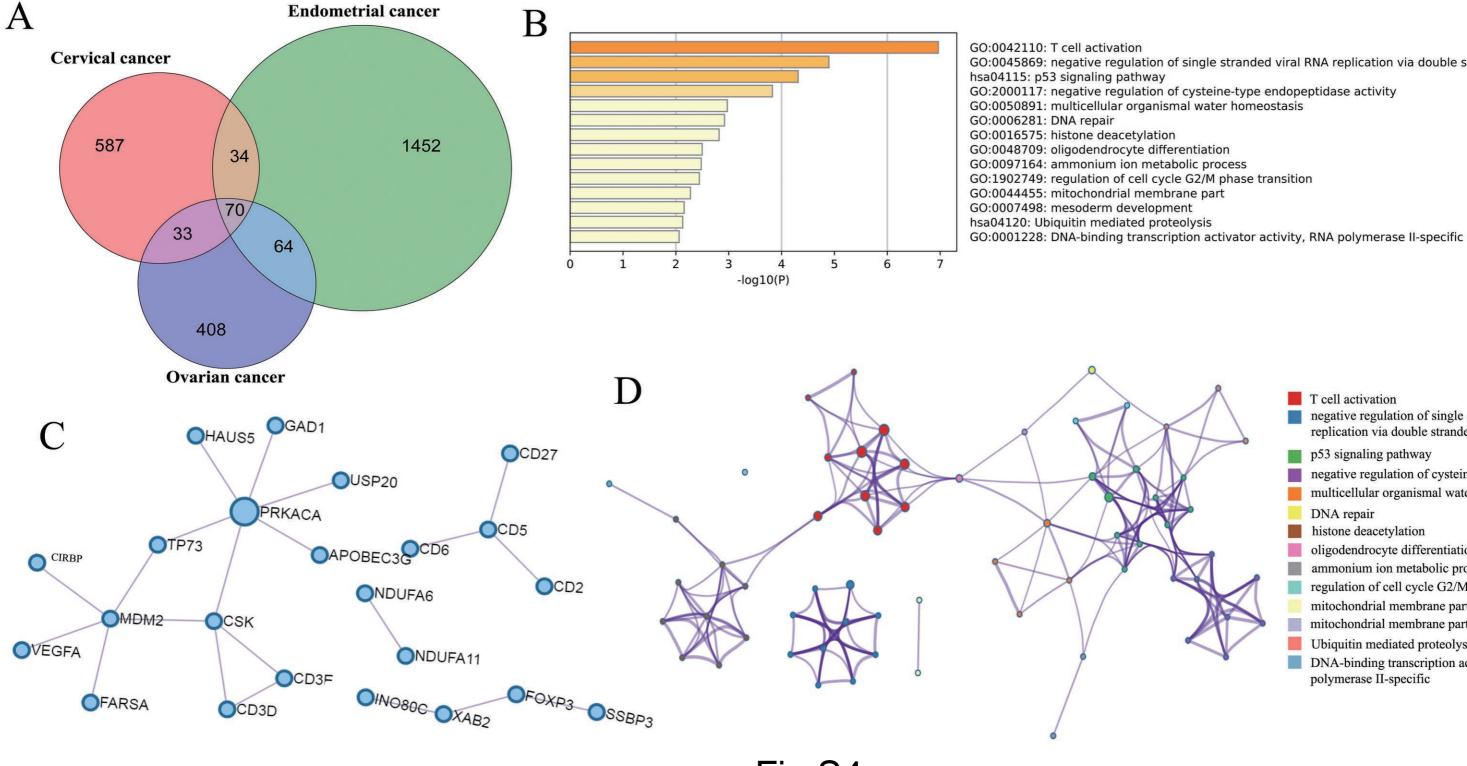
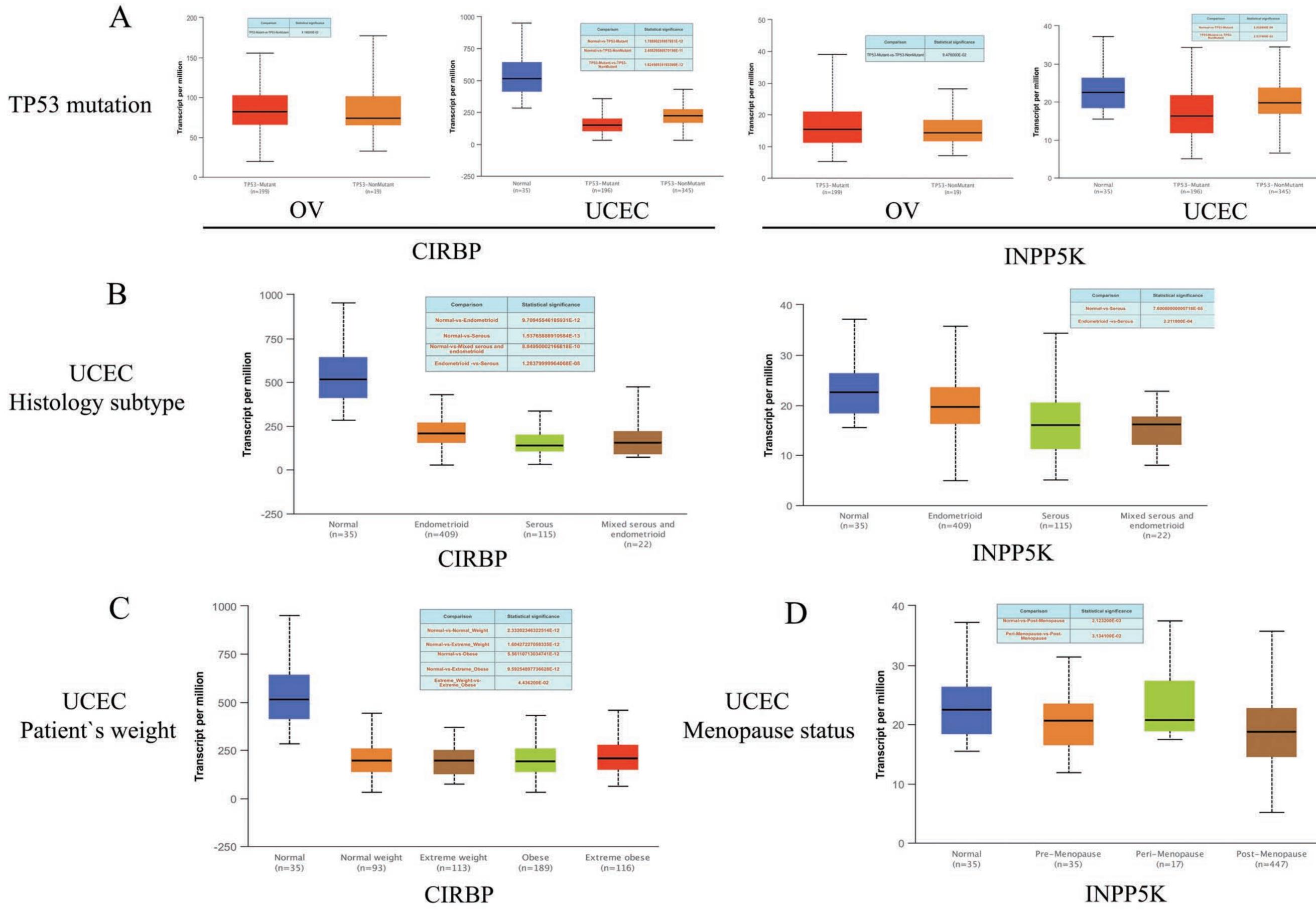
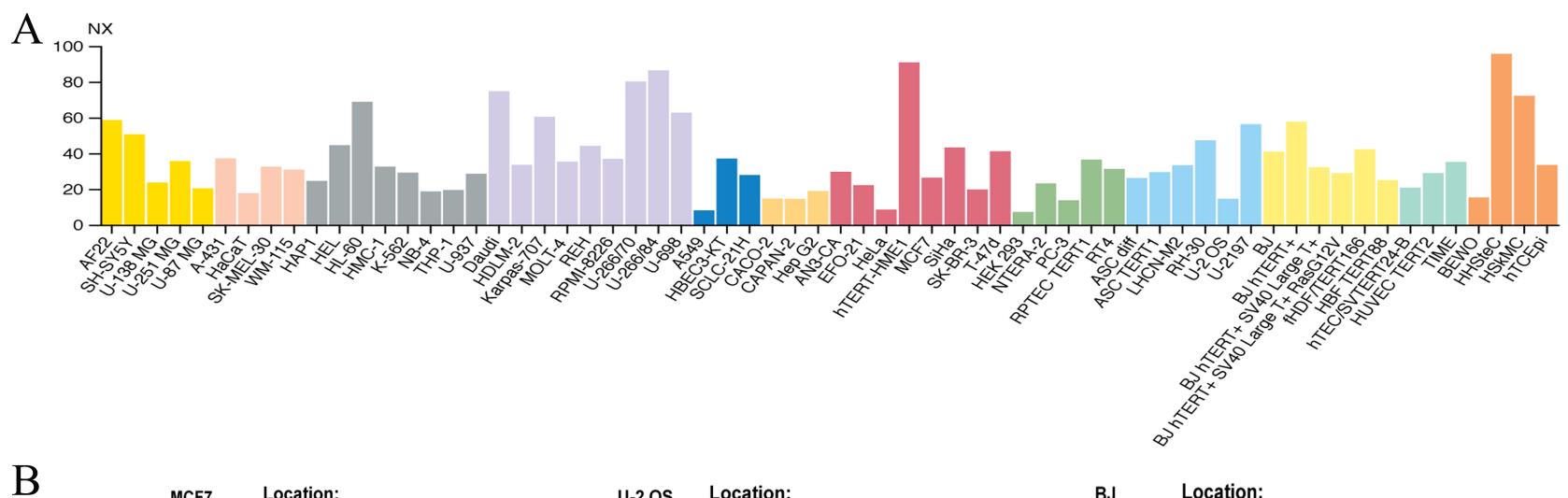


Fig.S4

GO:0045869: negative regulation of single stranded viral RNA replication via double stranded DNA intermediate

- T cell activation
- negative regulation of single stranded viral RNA replication via double stranded DNA intermediate
- p53 signaling pathway
- negative regulation of cysteine-type endopeptidase activity multicellular organismal water homeostasis
- DNA repair
- histone deacetylation
- oligodendrocyte differentiation
- ammonium ion metabolic process
- regulation of cell cycle G2/M phase transition
- mitochondrial membrane part
- mitochondrial membrane part
- Ubiquitin mediated proteolysis
- DNA-binding transcription activator activity, RNA polymerase II-specific



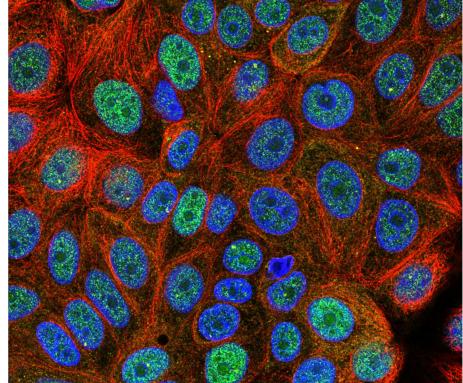


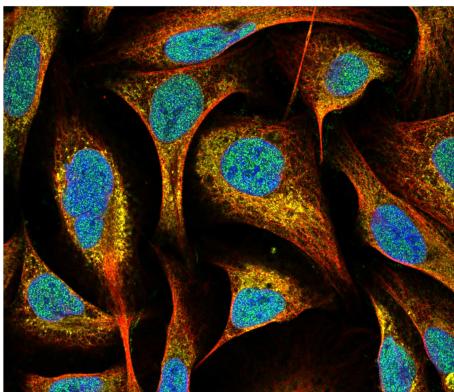


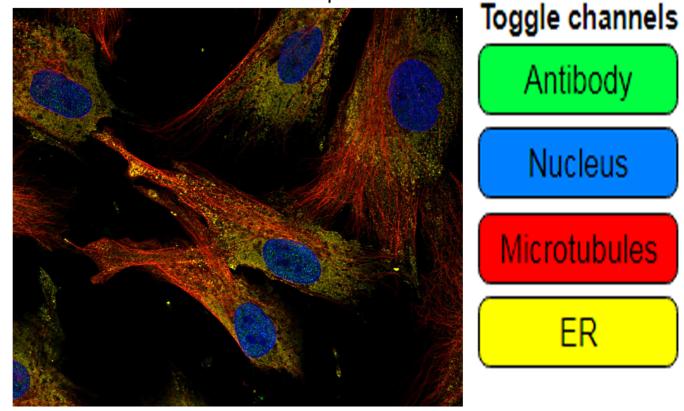
Location: Nucleoplasm

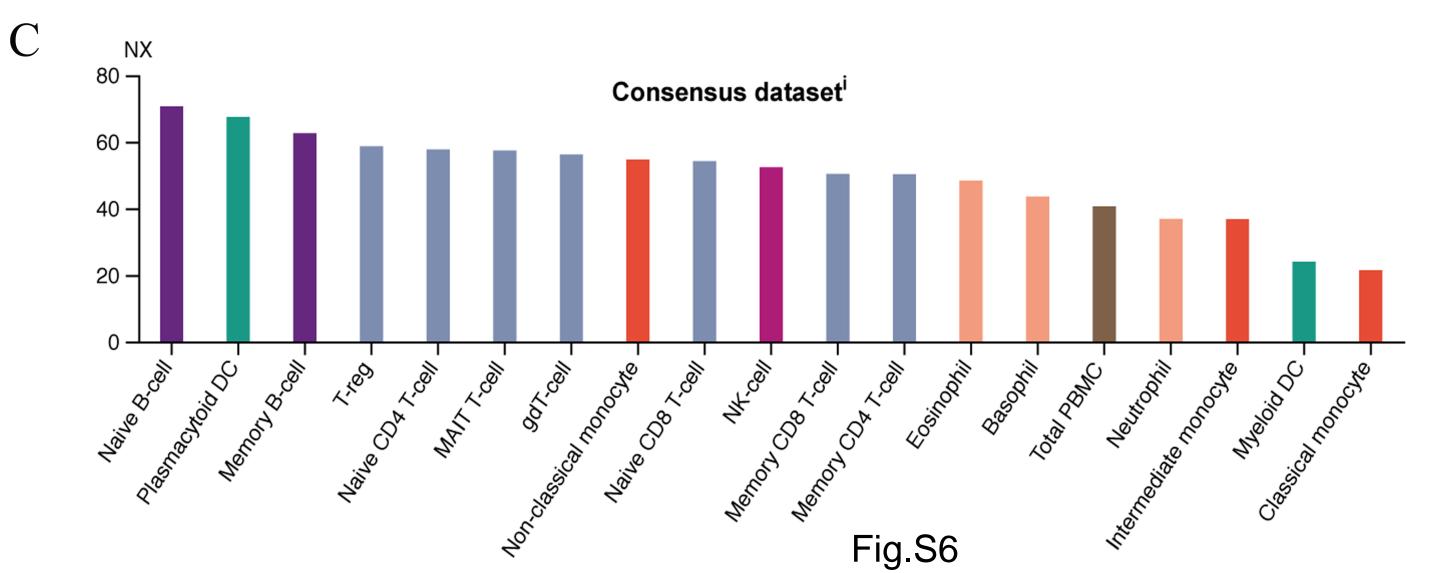
Location: U-2 OS HPA060537 Nucleoplasm

BJ HPA060537

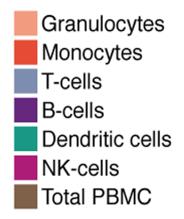


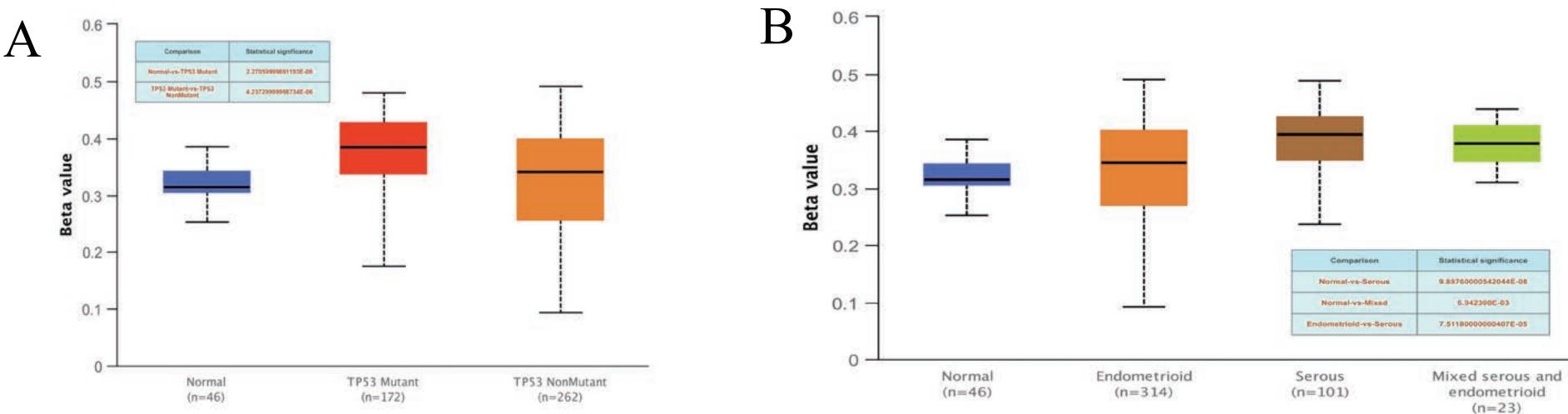






Location: Nucleoplasm





## **UCEC TP53 mutation**

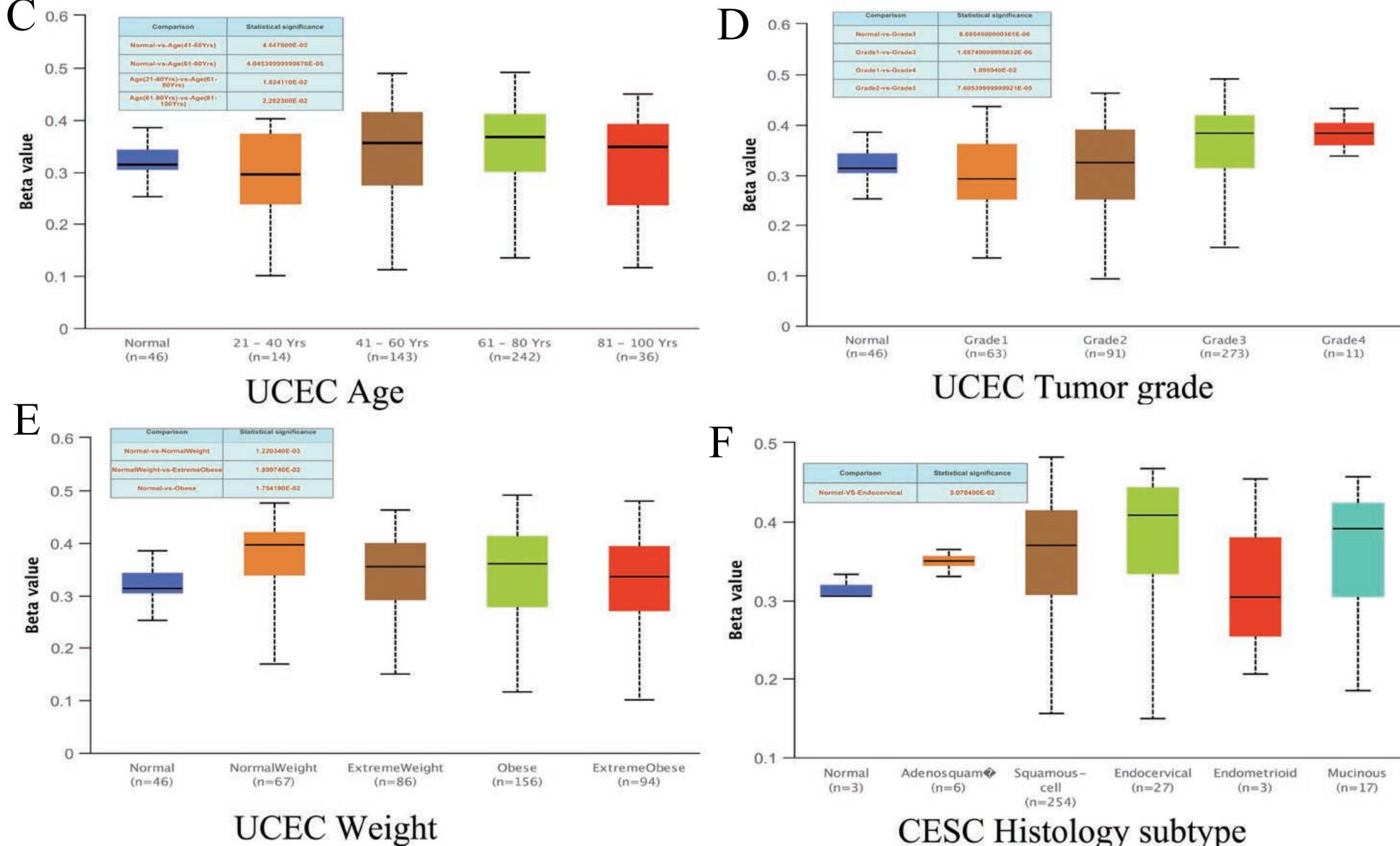
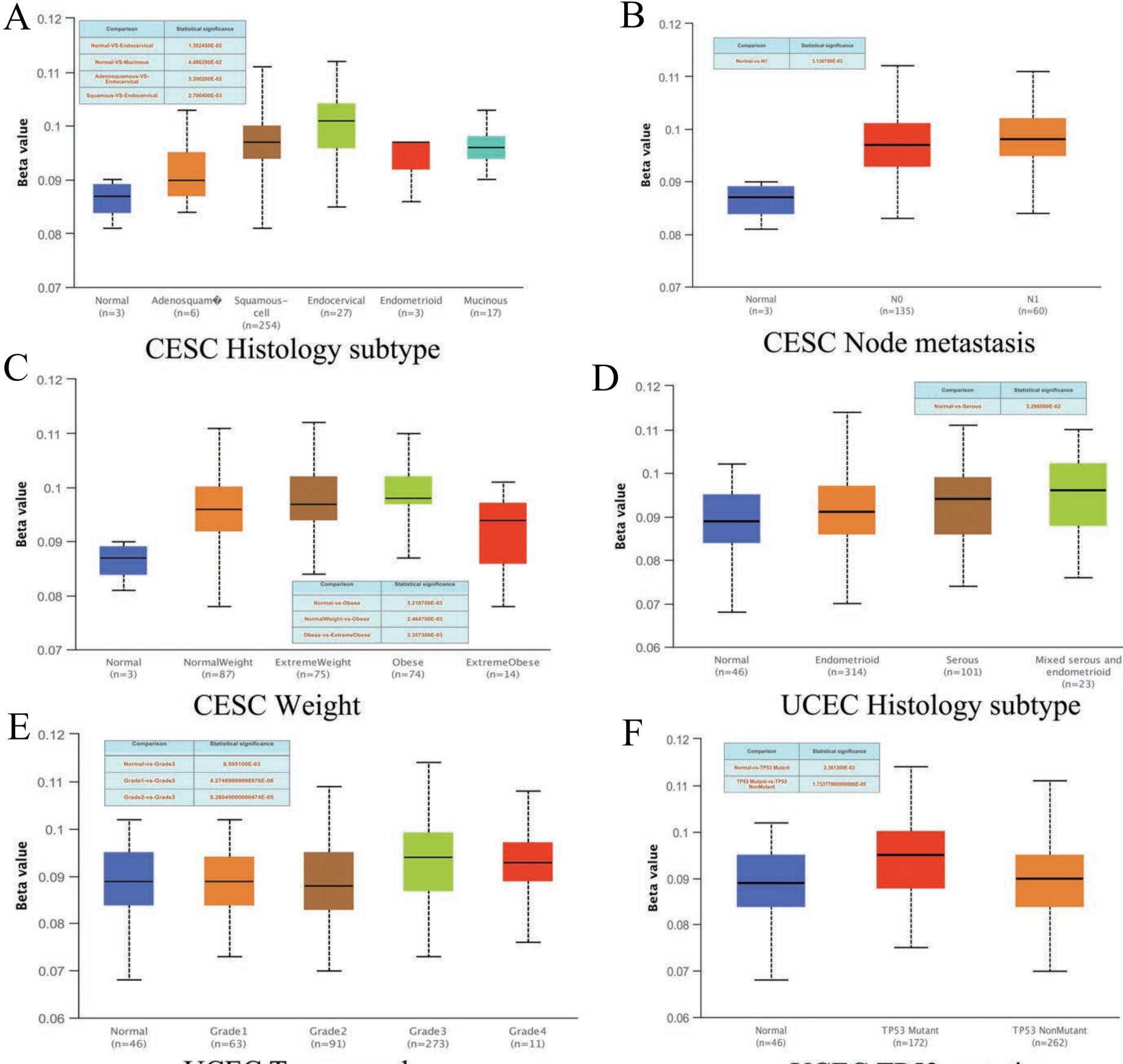


Fig. S7

(n=23)

# UCEC Histology subtype

# **CESC** Histology subtype



UCEC Tumor grade

Fig.S8

## **UCEC TP53 mutation**

CIRBP

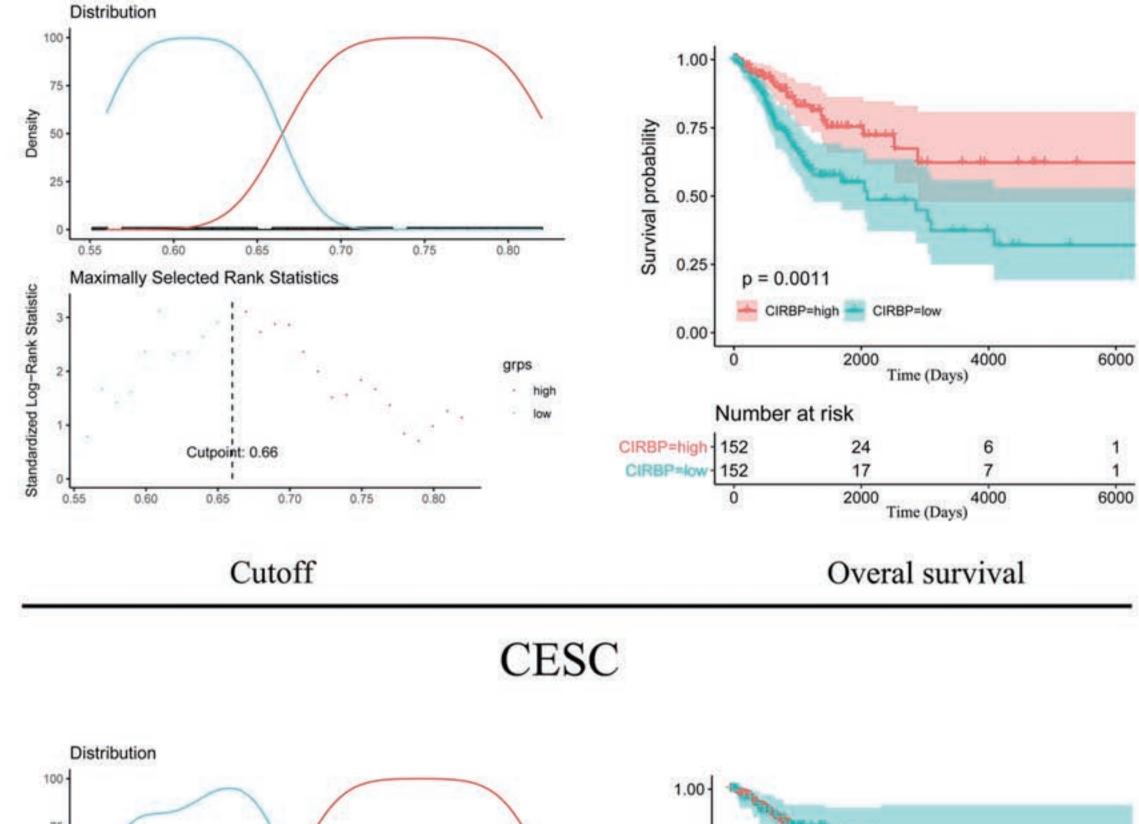
A

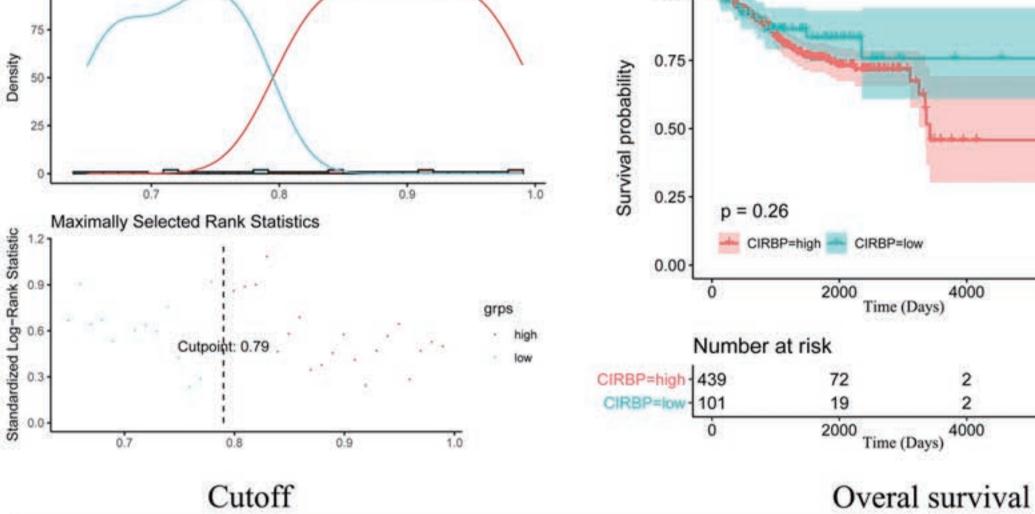
₹

å

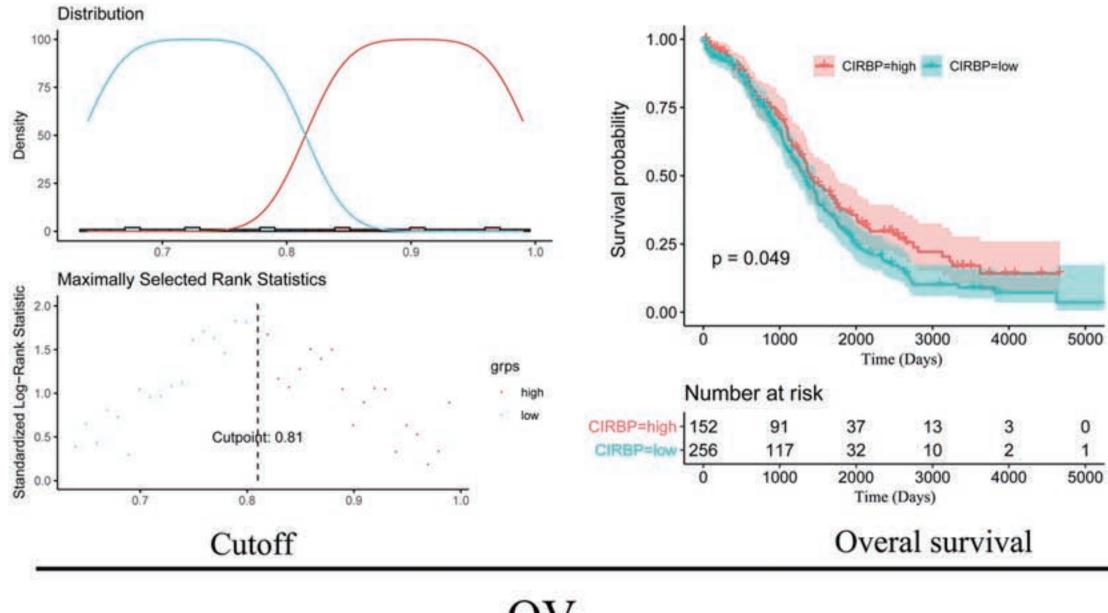
S

S



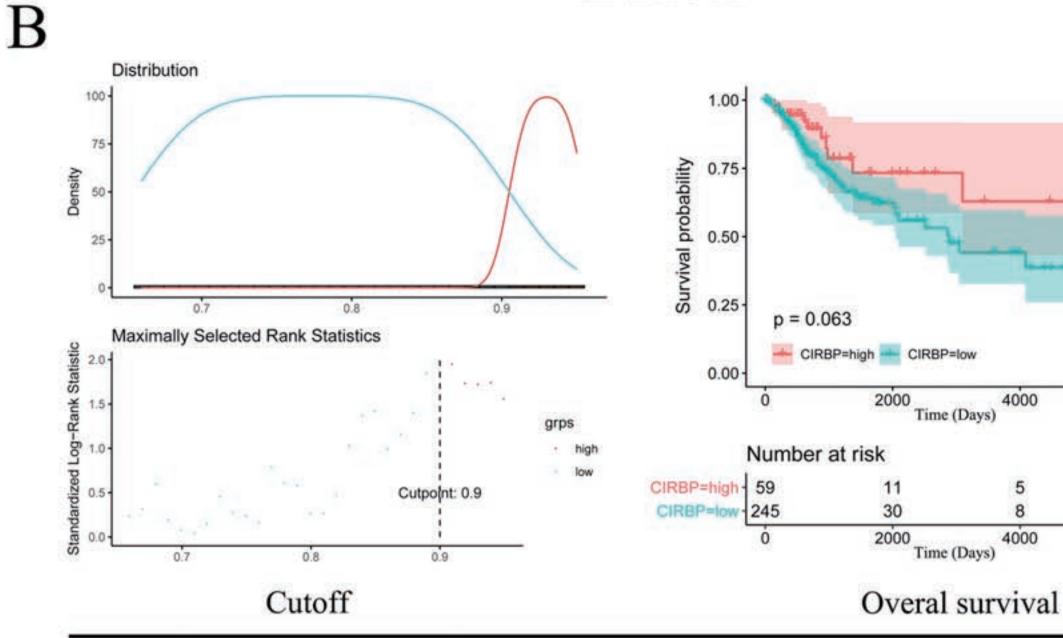


UCEC

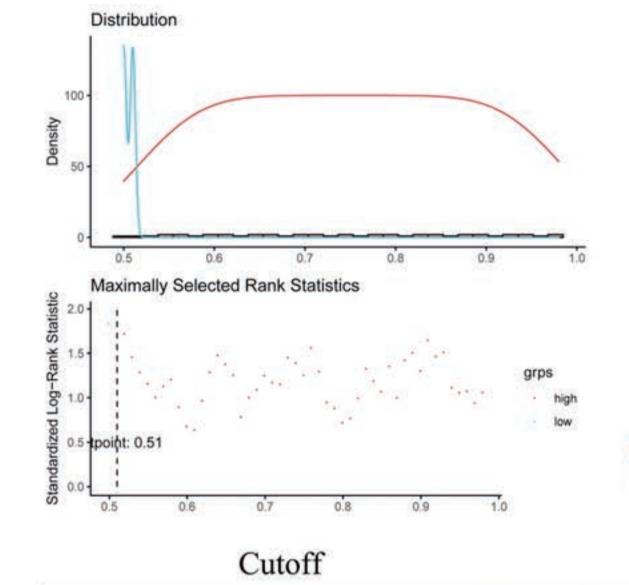


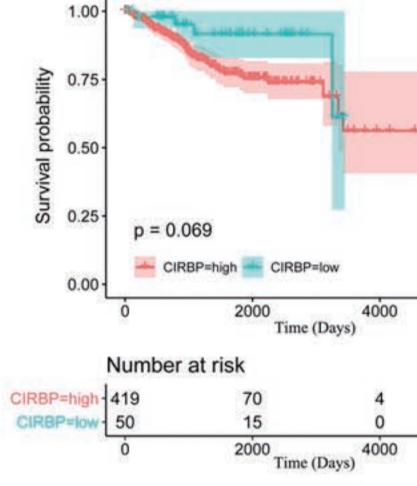
OV

INPP5K



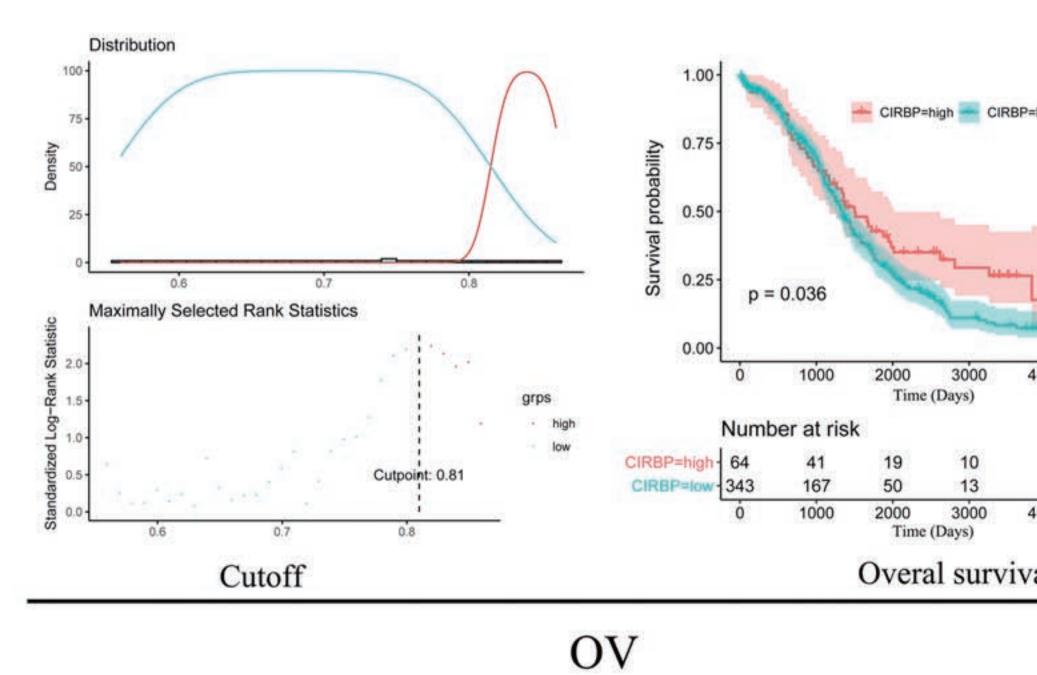








0



6000

0

1

6000

4000

2

2

344		****	
CIRBP=lo	w		
			6000
000 Time (D	ays)		0000
11	5		4
30	8		1
000 Time (D	4000 ays)		6000
veral s	urviva	al	
	_		
	Leve		
	4		
	1 Carlos		
CIRBP=	ow		
2000	4000	6	6000
Time (I	Days)		0000
(			
70			4
15	4		1
2000	4000	17	6000
Time (I	Days)		12010
woral		101	
Overal	surviv	al	
- CIRBP=h	igh 📥 CIR	BP=low	
CIRBP=h	igh <mark>—</mark> CIR	BP=low	
CIRBP=h	igh <mark>–</mark> CIR	BP=low	
CIRBP=h	igh <mark>–</mark> CIR	BP=low	
CIRBP=h	igh 📥 CIR	BP=low	
CIRBP=h	igh 📥 CIR	BP=low	
CIRBP=h	igh 📻 CIR	BP=low	
CIRBP=h	igh 📻 CIR	BP=low	
CIRBP=h	igh CIR	BP=low	
The same			
2000	3000	BP=low	5000
2000 Time (	3000		5000
2000 Time (	3000		5000
2000 Time ( K 19	3000 Days)	4000	5000
2000 Time ( 19 50	3000 Days)	4000	0 1
2000 Time ( 19	3000 Days) 10 13 3000	4000	0