

## **Supplementary Figure Legend:**

**Supplementary Figure 1.** GSEA analysis of differential enrichment metabolic pathways in bladder cancer and adjacent tissues. (A) Pyrimidine metabolism. (B) Purine metabolism. (C) Metabolism of carbohydrates. (D) Metabolism of cofactors. (E) Metabolism of folate and pterines. (F) Tryptophan metabolism. FDR: false discovery rate.

**Supplementary Figure 2.** Inhibitors dose select and reverse validation of pathway molecules. (A) Select the required dose of MPA and MMF for 50% proliferation inhibition in 5637 and UMUC2 cells through western blotting. (B) UCA1 expression in 5637 and UMUC2 cells overexpressing TWIST1 was tested by qRT-PCR. (C) RNA levels of UCA1 and TWIST1 in 5637 and UMUC2 cells overexpressing IMPDH1/2 were tested by qRT-PCR. (D) Western blotting was used to test TWIST1 protein expression in 5637 and UMUC2 cells overexpressing IMPDH1/2. (E) RNA levels of UCA1 and TWIST1 in 5637 and UMUC2 cells that were knocked down with IMPDH1/2 were tested by qRT-PCR. Data are expressed as mean  $\pm$  SEM for qRT-PCR and mean  $\pm$  SD for other analyses. ns, no significance; \*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ ; \*\*\*\*  $p < 0.0001$ .

**Supplementary Figure 3.** Identify the efficiency of UCA1 and IMPDH1/2 in cells. (A) The efficiency of UCA1 in knockdown and overexpression cells was tested by qRT-PCR. (B-C) Western blotting results of IMPDH1 and IMPDH2 proteins expression in 5637 and UMUC2 cells overexpressing IMPDH. (D-E) Western blotting results of the expression of IMPDH1 and IMPDH2 proteins in 5637 and UMUC2 cells knockdown with IMPDH. Data are expressed as mean  $\pm$  SEM for qRT-PCR and mean  $\pm$  SD for other analyses. ns, no significance; \*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ ; \*\*\*\*  $p < 0.0001$ .

## **Supplementary Table Legend:**

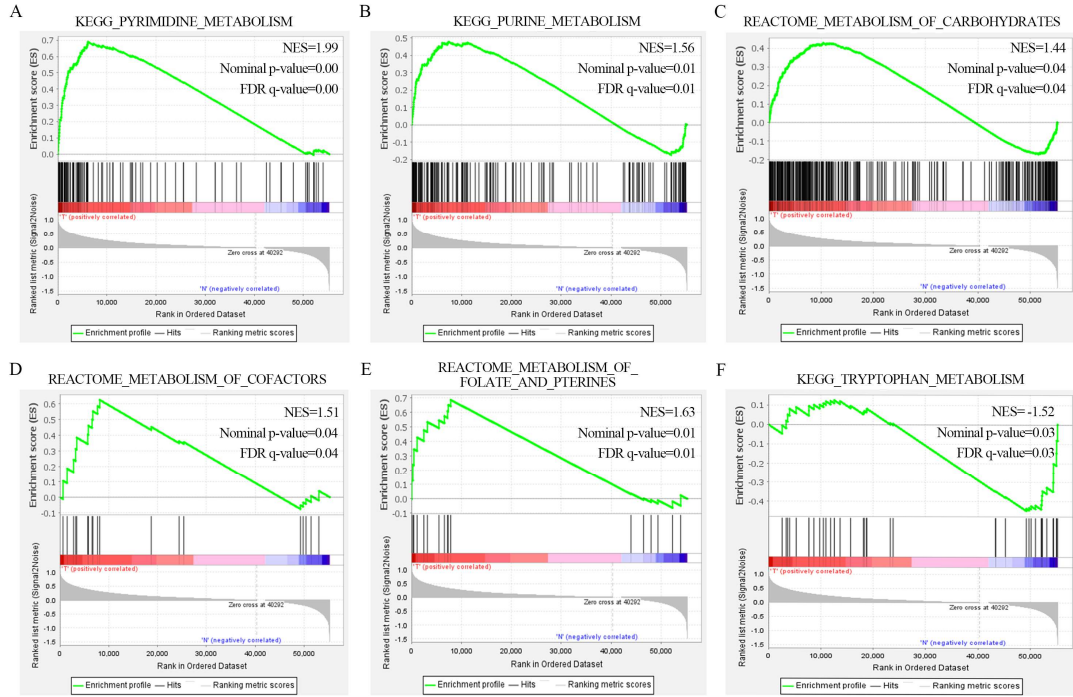
**Supplementary Table 1.** Primers or other sequence information.

**Supplementary Table 2.** Characteristics of bladder cancer patients.

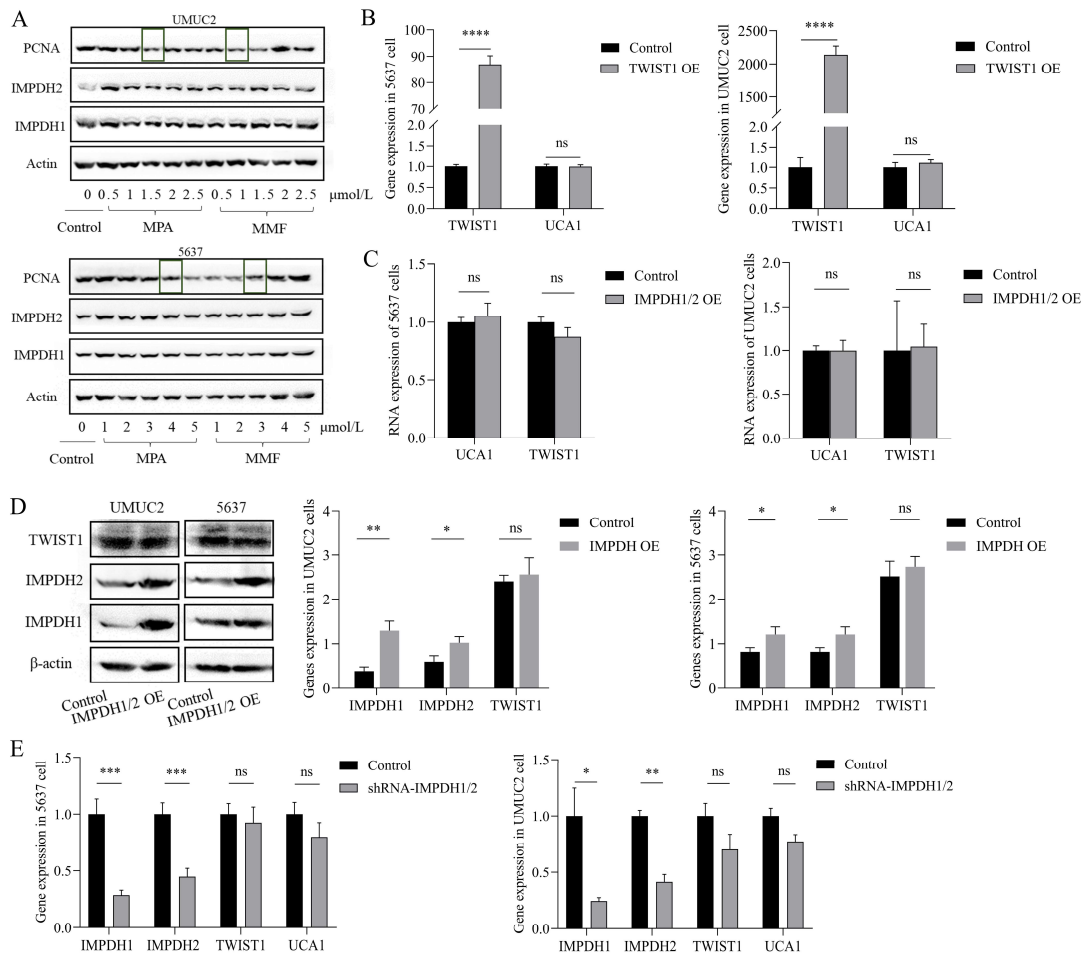
**Supplementary Table 3.** Prediction results of transcription factors.

# Supplementary Figure:

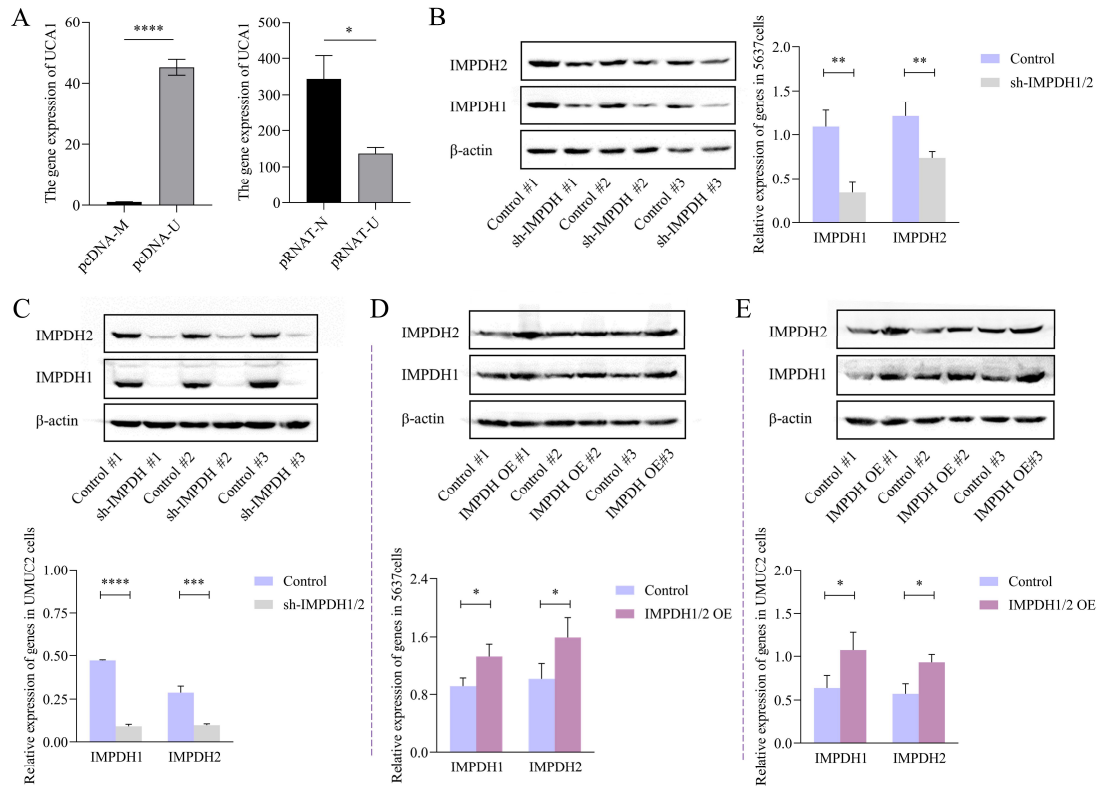
## Supplementary Figure 1.



**Supplementary Figure 2.**



**Supplementary Figure 3.**



## Supplementary Table:

### Supplementary Table 1. Primers or other sequence information.

#### sh-IMPDH1/2 sequence

TGAAGAAGAACCGAGACTA

#### pRNAT-U6.1/Neo-Nc

5'-gatccTTCTCCGAACGTGTCACGTtcaagagaACGTGACACACGTTCGGAGAAttt  
ttgaaa-3'

#### pRNAT-U6.1/Neo- shUCA1.1

5'-gatccGTTAATCCAGGAGACAAAGAttcaagagaTCTTTGTCTCCTGGATTAAttttt  
gga-3'

#### qRCR primers (5'→3')

##### β-actin:

Forward TCCCTGGAGAAGAGCTACGA

Reverse AGCACTGTGTTGGCGTACAG

##### GAPDH:

Forward GTCGGAGTCAACGGATTTG

Reverse TGGGTGGAATCATATTGGAA

##### IMPDH2:

Forward TTCTGCGGTATCCCAATC

Reverse CGAGCAAGTCCAGCCTAT

##### IMPDH1:

Forward CAGGGTCCGTGATGAAGC

Reverse CTCTGATGGGAGGTATTGGTT

##### TWIST1:

Forward TCATGGCCAACGTGCGG

Reverse CTCCATCCTCCAGACCGAGA

##### PRRX1:

Forward GGCTTTGGAGCGTGTCTTTG

Reverse GAGCAGGACGAGGTACGATG

##### ADA:

Forward CCTTCGACAAGCCCAAAGTG

Reverse GATCCCTCTCCTCCTGCCATA

##### ADSL:

Forward GCACAAGATTTGCACCGACA

Reverse GCATCGCACTTGAGCCAATC

##### ADSS:

Forward GCATTCATTGGAAATGGTGTGG

Reverse TTGTTCCCTGGATACCATCAGC

##### ATIC:

Forward GTTGCCTGCAATCTCTATCCCT

Reverse CACTCGAGCGTGGTTTTTGG

##### GMPS:

Forward TCAGAAAGTTGAGAGAGGAGGGA

Reverse GGACCTGGAAATGGATGCCT

##### HPRT1:

Forward CCTGGCGTCGTGATTAGTGAT

Reverse TCGAGCAAGACGTTTCAGTCC

PAICS:  
Forward GCTGAGTATGAAGGGGATGGC  
Reverse GGTTGAACAGCCAAGACCAC

PFAS:  
Forward ACTCACAACCTTTCCCACAGGA  
Reverse TCCCAGGGCAGATTGTAACC

PPAT:  
Forward TGGTGCAAGATATTACCGTGAAG  
Reverse ACTGGGTTTCCTCAGACCT

Pre-rRNA:  
Forward CCGTCCGTCCGTGCTCCTCCTCGC  
Reverse TGTACCGGCCGTGCGTACTTAGAC

5SrRNA:  
Forward GGCGTAGAGGAACACACCAATC  
Reverse GCAGGACCTCCCCTACAGTATCG

SDHB:  
Forward CTCAGGAAGGCAAGCAGCAGTATC  
Reverse ATTTGTCTCCGTTCCACCAGTAGC

E2F4:  
Forward GAGCAAGAACTAGACCAGCACAAGG  
Reverse CCAAGAGGGTATCTCCAGCAAAGC

ATF4:  
Forward TCCTGTCCTCCACTCCAGATCATTC  
Reverse TCATGGCAACGTAAGCAGTGTAGTC

#### **CHIP primer (5'->3')**

IMPDH1-1:  
Forward GTCTCAGTCTCTTGACCTCGTGATC  
Reverse TGGCCAACATGGCGAAACT

IMPDH1 -2:  
Forward TGTTCCCTCAGACTTGTCAGACAAG  
Reverse GGATGGTCTCGATCTTCTGACCTT

IMPDH1-3:  
Forward ACAGAGCGAGACTCCGTCTC  
Reverse GATGGTCTCGACTTACAATGGTTGA

IMPDH1-4:  
Forward GGGCTACCTCAGGGTAAATCCATC  
Reverse TCCTTGCCCTCAGGCAATTTATTTAG

IMPDH1-5:  
Forward ATGTACCCTCGCTGAATCTGGG  
Reverse AATCCGGGAGTCGACTGGG

IMPDH2 -1:  
Forward TATGCCTCTTCTCAACTTAAACACAGC  
Reverse GGAGGGGACACAGGTAGCAAT

IMPDH2 -2:  
Forward TAGCTGGGCTTGGTGGCTC  
Reverse GGCTGGAGTGCAGTGAGG

IMPDH2 -3:  
Forward GACTCACATGAGTCCATGAGAGCC  
Reverse CCACACACTACATCCTGGTCCT

IMPDH2 -4:  
Forward AGTAGCTGTGCCACAATAACTTGG  
Reverse TTCCGGCCTTTCACACTCTGG

IMPDH2 -5:  
Forward ACACCTGAGCCAGTGGTG  
Reverse GCGATGGCCTCCTGAATTTCT

IMPDH2 -6:  
Forward GCGGCAGACTCCTCAGC  
Reverse CTCTTGAAGATGGAAAGGGGCCA

**RNA pull down primer (5'→3')**

T7 UCA1 sense sequences  
Forward CCAGTACCTAATACGACTCACTATAGGGTTGACATTCTTCTGGACAATGA  
Reverse ttttttttttttttttttttttttATCAGGCATATTAGCTTTAATGT

T7 UCA1 antisense sequences  
Forward CCAATCGTAATACGACTCACTATAGGGtttttttttttttttttttttttATCA  
Reverse TTGACATTCTTCTGGACAATGAG

**shRNA-UCA1**  
CCGGGTAAATCCAGGAGACAAAGACTCGAGTCTTTGTCTCCTGGATTAACCTTTTTG

**Supplementary Table 2.** Characteristics of bladder cancer patients.

<b>Characteristic</b>	<b>Patient frequency</b>
<b>Total</b>	48
<b>Issue type</b>	
Suprapubic cystostomy	6
Bladder cancer	35
Paracancerous	17
<b>Gender</b>	
Male	36 (85.7%)
Female	6 (14.3%)
<b>Age</b>	
	63 (48–77)
<60	14 (33.3%)
≥60	28 (66.6%)
<b>TNM stage</b>	
I	12 (28.6%)
II	15 (35.7%)
III	13 (31%)
NA	2 (4.8%)
<b>Tumor stage</b>	
Ta	2 (4.8%)
T1	16 (38.1%)
T2	10 (23.8%)
T3-T4	11 (26.2%)
NA	3 (7.1%)
<b>Histopathological subtype</b>	
Urothelial carcinoma	48 (100%)



**Supplementary Table 3.** Prediction results of transcription factors.

Gene name	IMPDH1					IMPDH2					UCA1
	Binding site	Binding sequences	Binding chain	Combined with score	Correlation coefficient	Binding site	Binding sequences	Binding chain	Combined with score	Correlation coefficient	Correlation coefficient
MYC	960-971	GGCCTCGTGCCG	-	0.89	0.34	719-729	AAGCACGTCTT	+	0.82	0.16	0.33
FLI1	214-223	GCCGGAGATA	+	0.85	0.19	23-32	CCAGGAAAAA	+	0.85	0.17	0.23
MSC	78-87	AGCCCTGTT	+	0.81	0.29	720-729	AAGACGTGCT	-	0.82	0.16	0.25
PRRX1	158-165	CAAATAAC	+	0.83	0.24	94-101	GTAGTTAC	+	0.80	0.21	0.28
TEAD2	305-317	ACCCATTCCTTG	-	0.82	0.23	277-289	TCACAGTCCAAGC	-	0.85	0.26	0.32
IKZF1	272-283	CGGAAAGGAAGG	-	0.83	0.21	9-20	ACAAGAGAAACC	+	0.80	0.23	0.24
MSANTD3	400-409	GGCCACCAA	+	0.82	0.46	45-54	TCACACTAAA	+	0.84	0.20	0.35
GLI2	36-50	GGGCCACCAACTTCT	+	0.87	0.17	830-844	ACCCACACTCCCG	-	0.83	0.15	0.25
NFIL3	361-373	ATTTATGAAAAAT	+	0.86	0.21	680-692	TCATTATGATTCT	+	0.86	0.17	0.27
TWIST1	9-21	GATCCAGATTCT	-	0.88	0.18	217-229	GTGCATATGTCC	+	0.80	0.15	0.26

*\*Note: the p-value of correlation coefficient is less than 0.0001*