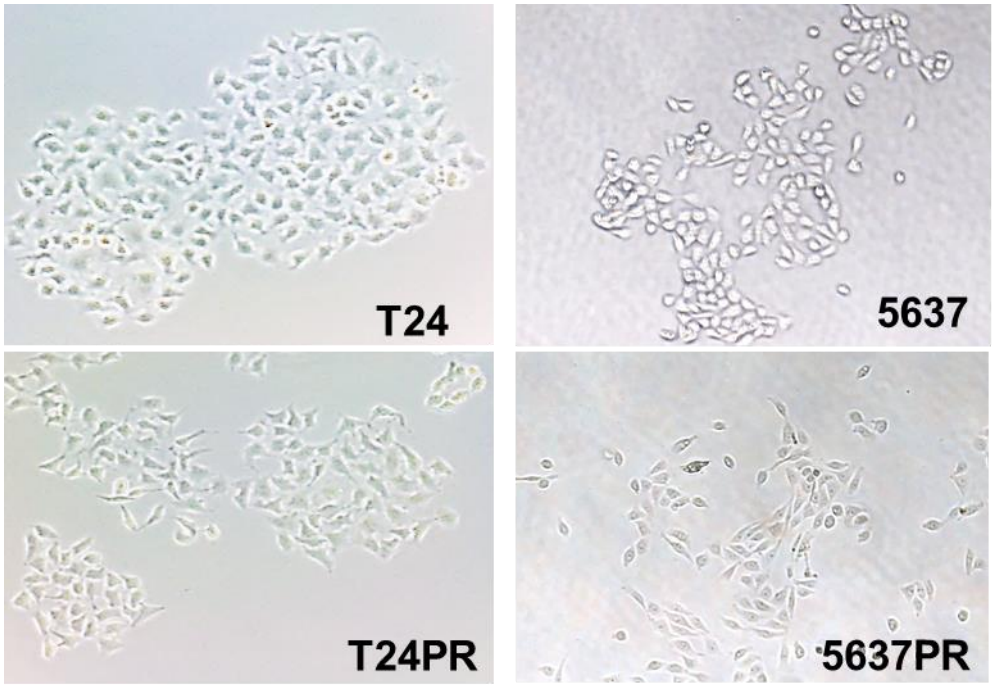
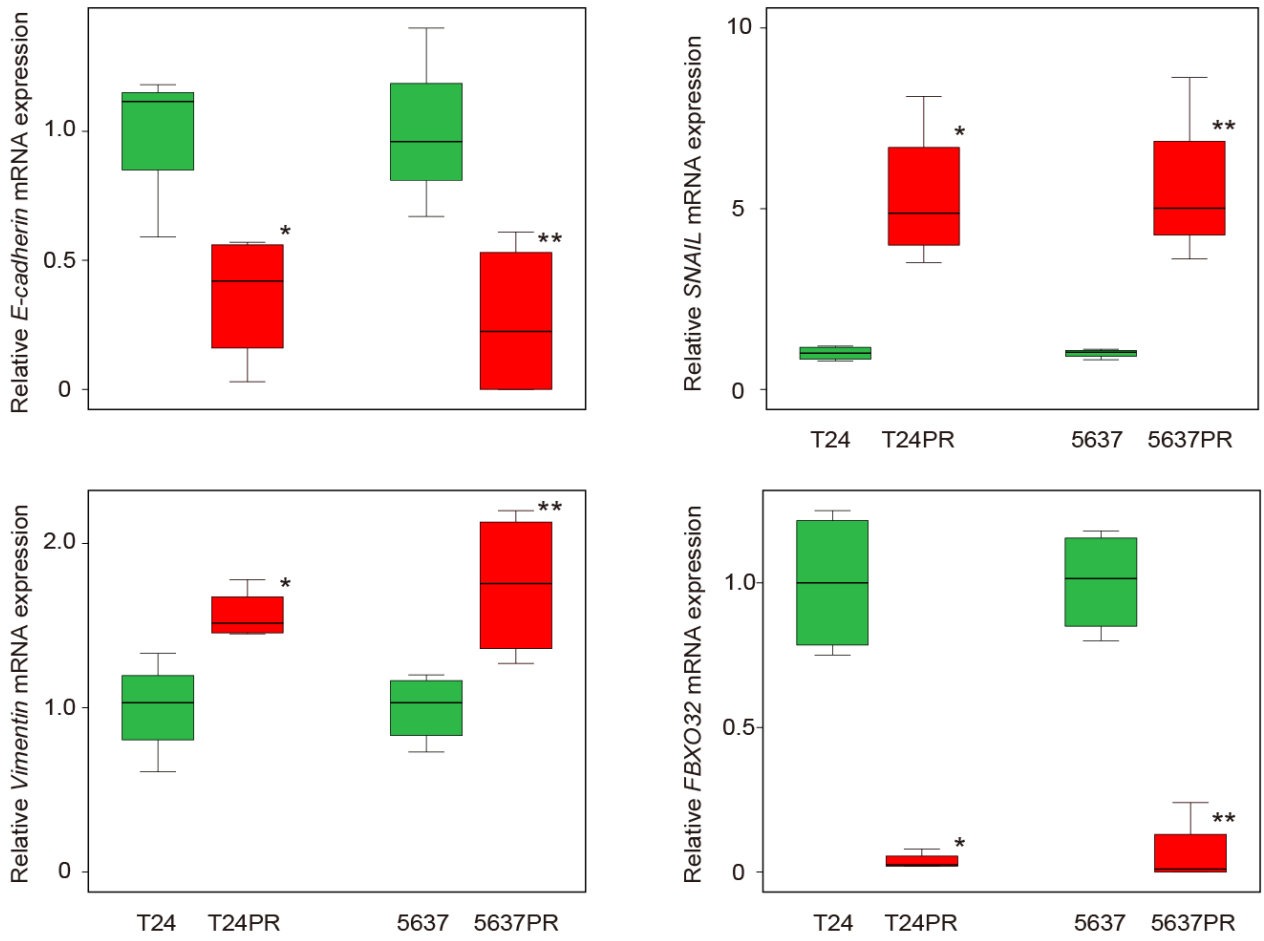
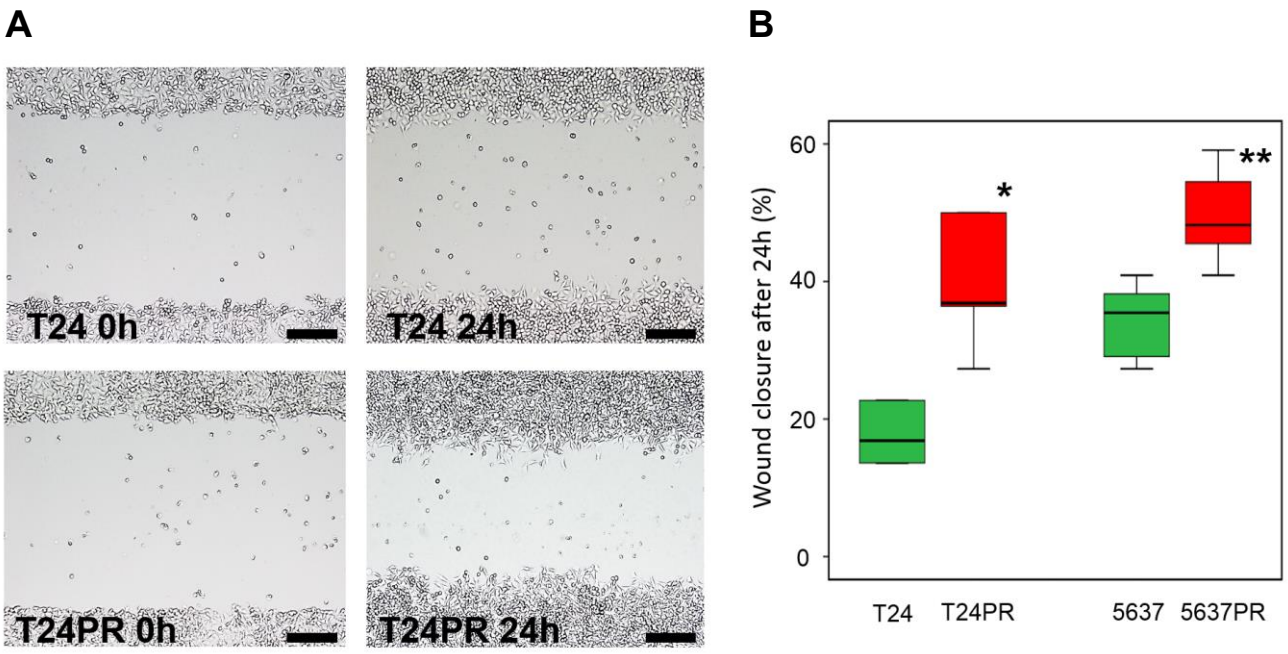


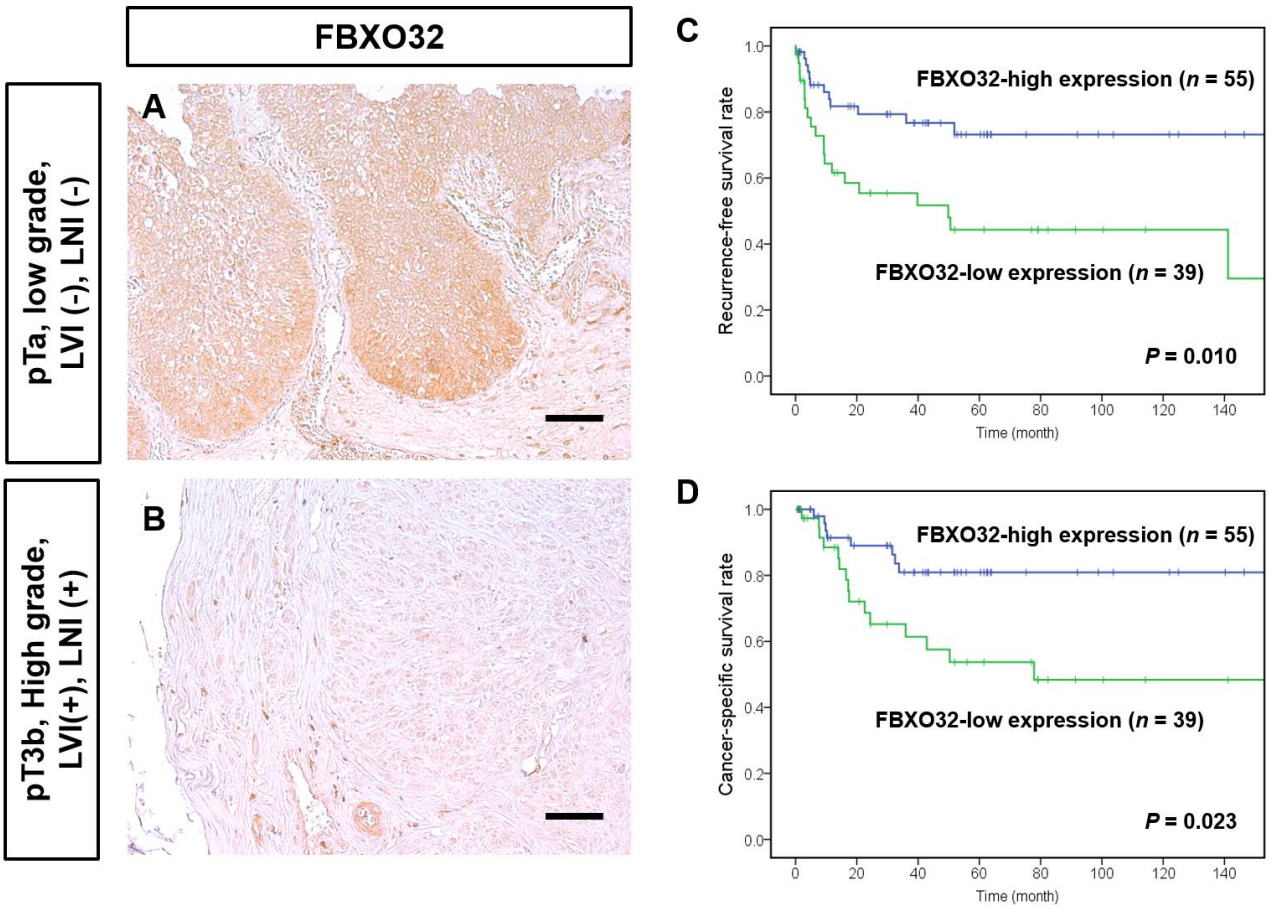
Supplementary Figure S1. Morphological features of T24PR, 5637PR, and their corresponding parent cells (T24 and 5637) in light-microscopic appearance.



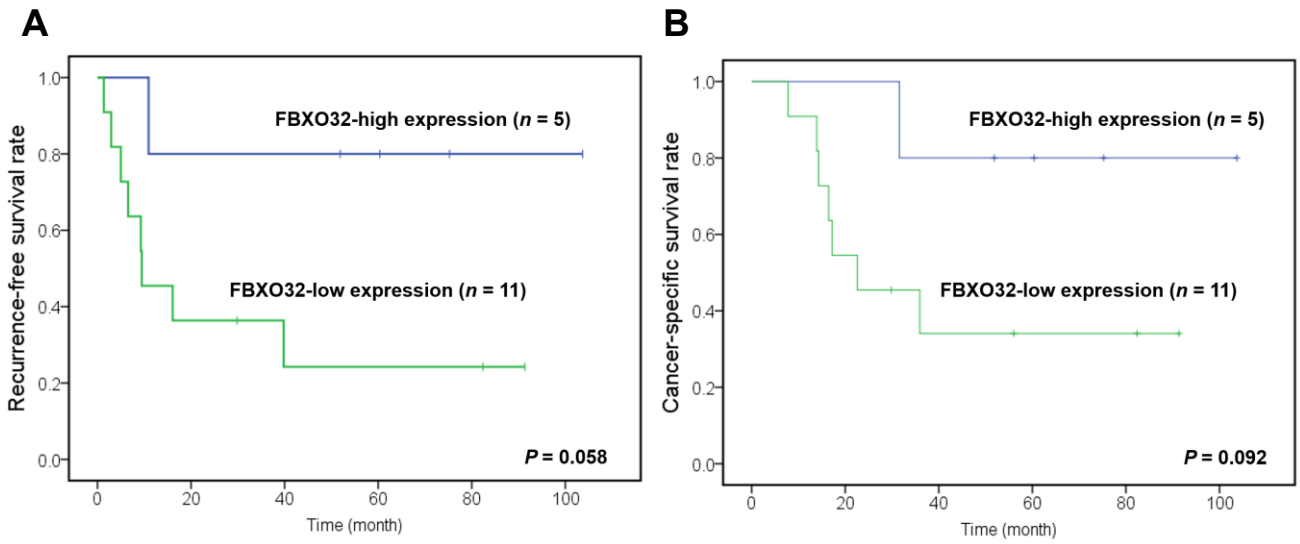
Supplementary Figure S2. mRNA expression of *E-cadherin*, *Vimentin*, *SNAIL*, and *FBXO32* in T24PR, 5637PR, and their corresponding parent cells T24 and 5637. Preparation and the respective primers were described in the “Methods” section. Box-and-whiskers plots show median (line within box), upper and lower quartile (bounds of box), and minimum and maximum values (bars). *, $P < 0.05$, compared with T24 cells; **, $P < 0.05$, compared with 5637 cells.



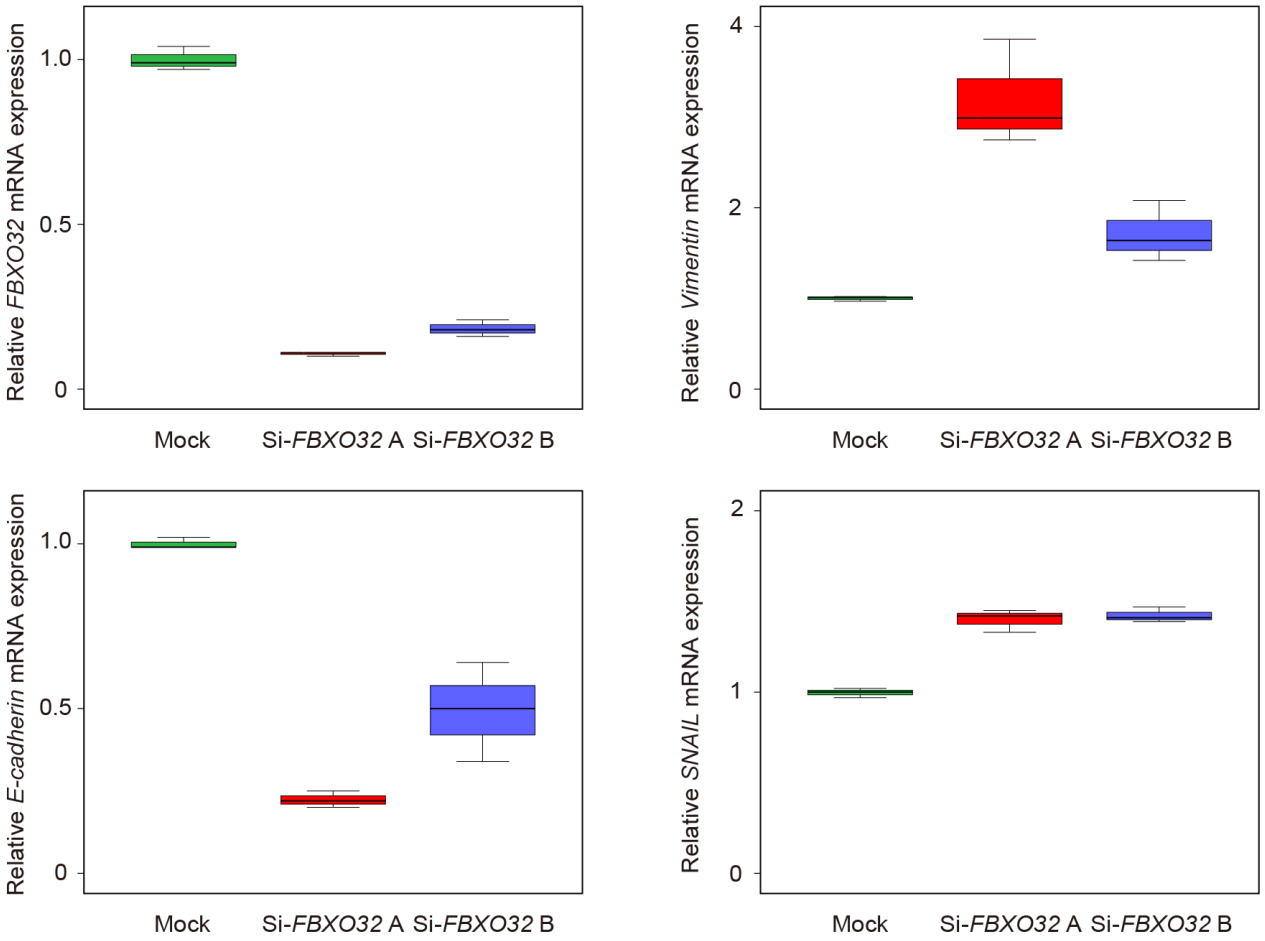
Supplementary Figure S3. (A) Wound-healing assay of T24 and T24PR cells. A scratch was made using a pipet tip after reaching confluence, and visualized with a light microscope with digital photographic capability at 0 and 24h. Scale bar: 200 µm. (B) Wound-healing assay results for T24PR, 5637PR, and their corresponding parent cells T24 and 5637 at 24 hours. The width of the scratches measured at 0 and 24 hours (n = 6). Box-and-whiskers plots show median (line within box), upper and lower quartile (bounds of box), and minimum and maximum values (bars). *, $P < 0.05$, compared with T24 cells, **, $P < 0.05$, compared with 5637 cells.



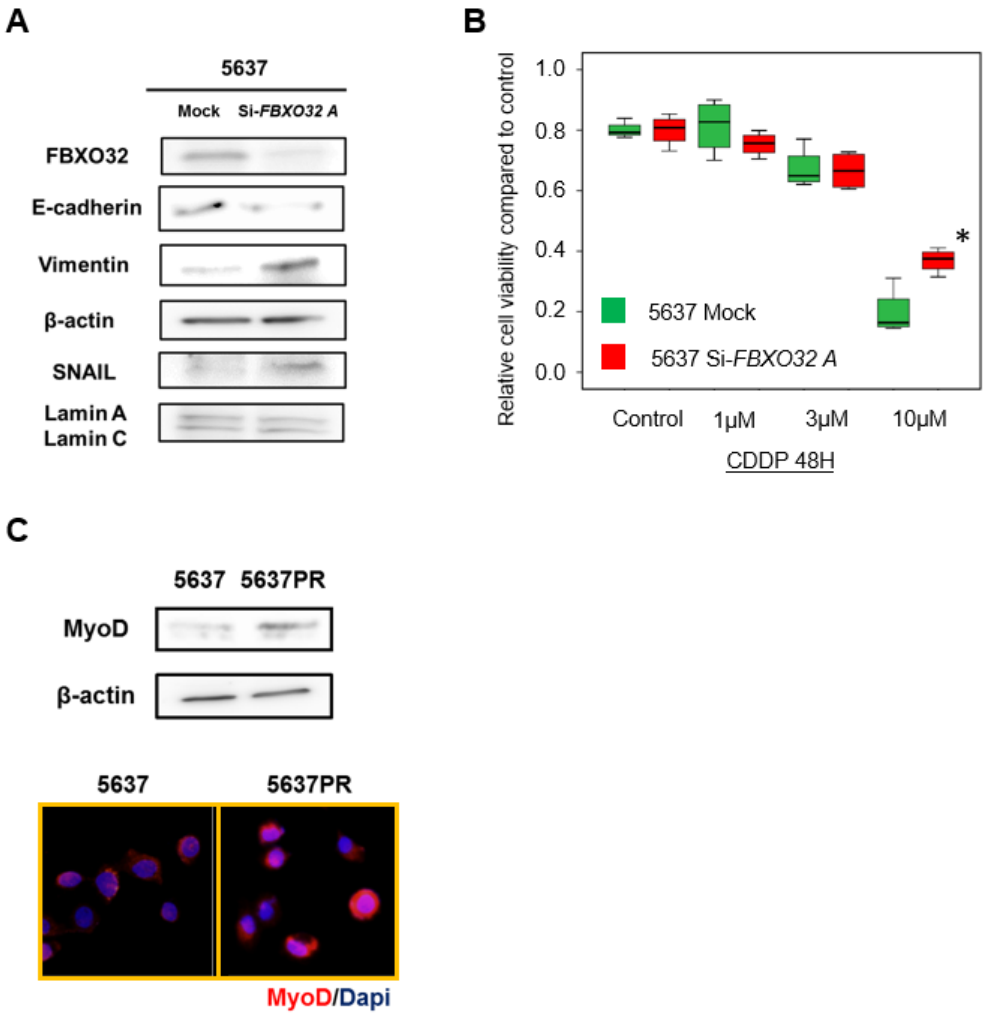
Supplementary Figure S4. Immunostaining for FBXO32 in pTa, low-grade, LVI-negative, and LNI-negative superficial bladder UC (A) and pT3b, high-grade, LVI-positive, and LNI-positive invasive bladder UC (B). Scale bar: 100 μm. Kaplan-Meier curves of the recurrence-free (C) and cancer-specific survivals (D) of patients with bladder UC treated surgically according to the FBXO32 expression. LVI = lymphovascular invasion; LNI = lymph node involvement; UC = urothelial carcinoma.



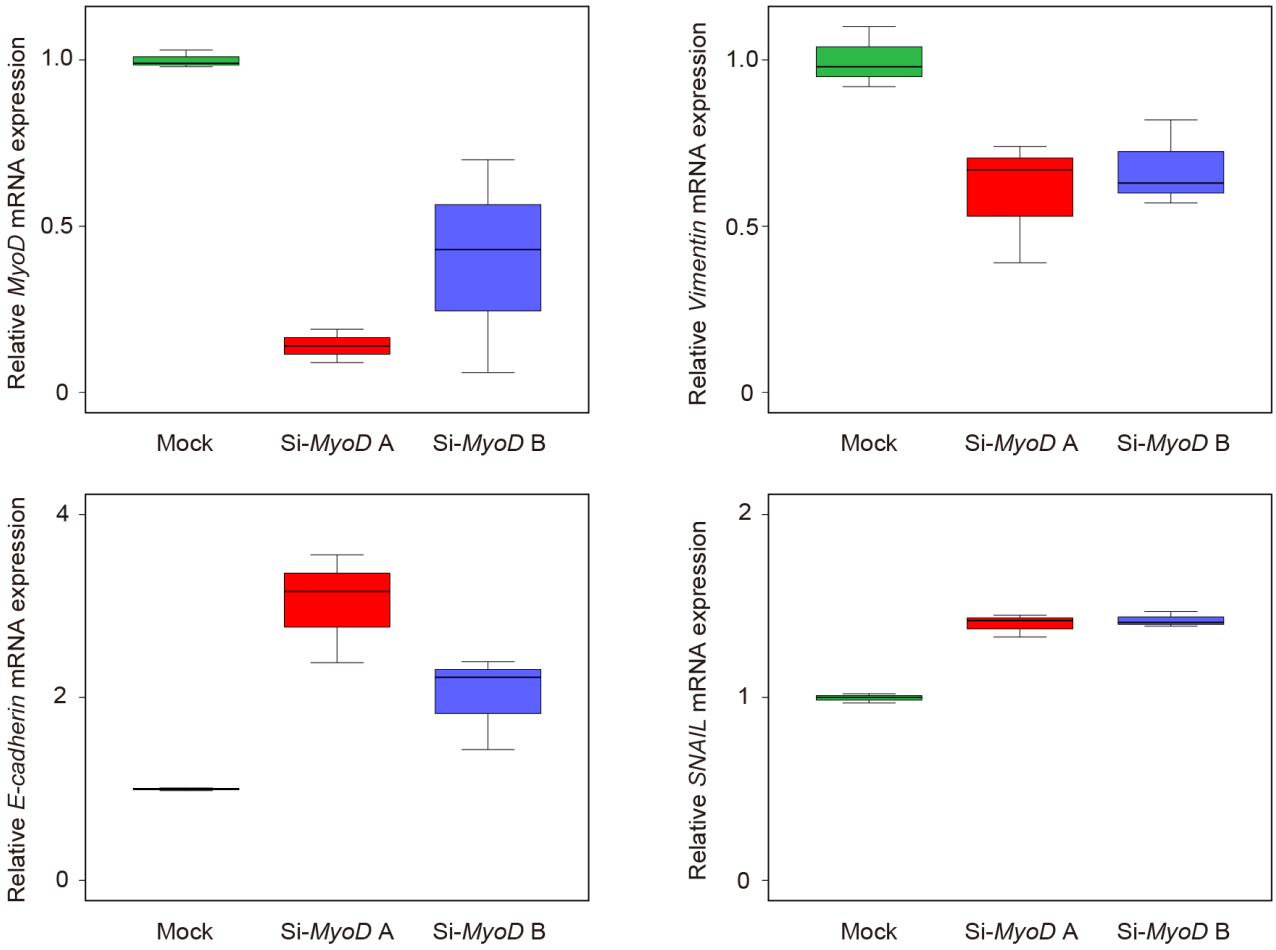
Supplementary Figure S5. Kaplan–Meier recurrence-free (A) and cancer specific survival curves (B) according to FBXO32 expression of 16 patients treated with neoadjuvant CDDP-based chemotherapy before cystectomy



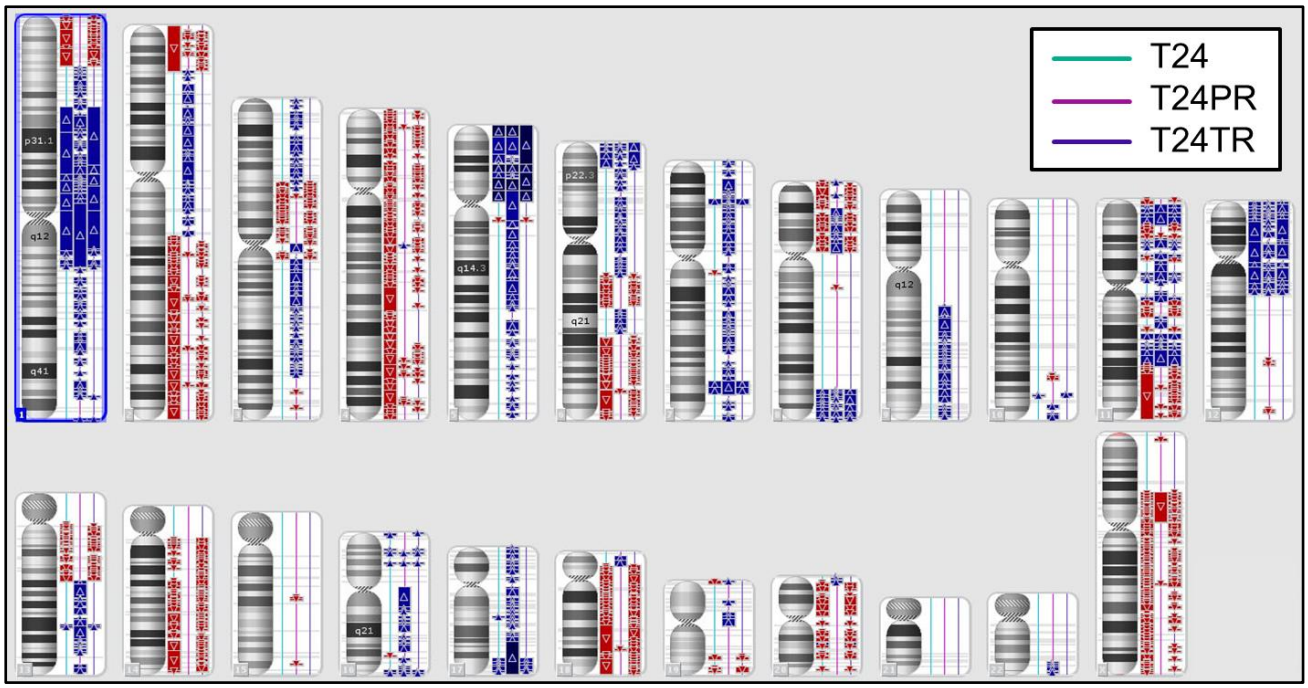
Supplementary Figure S6. mRNA expression of *E-cadherin*, *Vimentin*, and *SNAIL* in T24 cells transfected with si-*FBXO32*. Preparation and the respective primers were described in the “Methods” section. Box-and-whiskers plots show median (line within box), upper and lower quartile (bounds of box), and minimum and maximum values (bars).



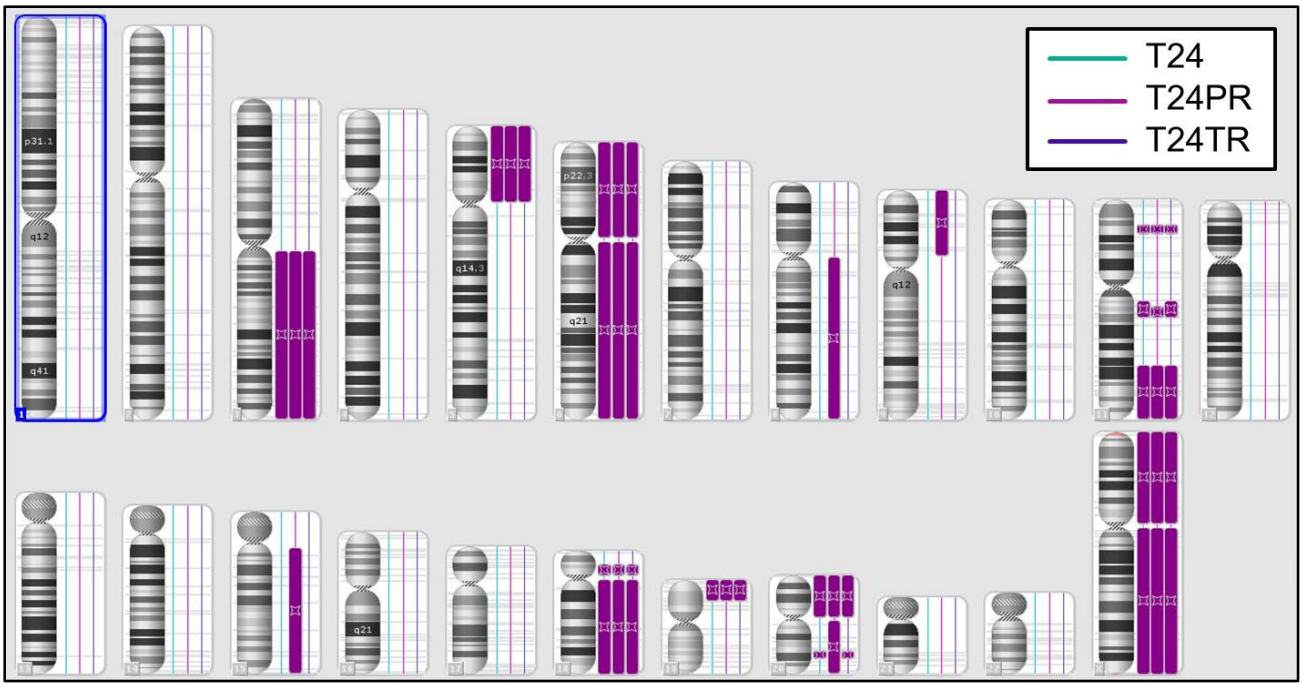
Supplementary Figure S7. (A) Effect of FBXO32 knockdown on the expression of E-cadherin, Vimentin, and SNAIL in 5637 cells. (B) Effect of FBXO32 knockdown on the sensitivity to CDDP in 5637 cells. Box-and-whiskers plots show median (line within box), upper and lower quartile (bounds of box), and minimum and maximum values (bars). *, $P < 0.05$, compared with mock-transfected cells. (C) Western blot analysis and immunofluorescence staining for MyoD in 5637PR and its corresponding parent cells 5637.



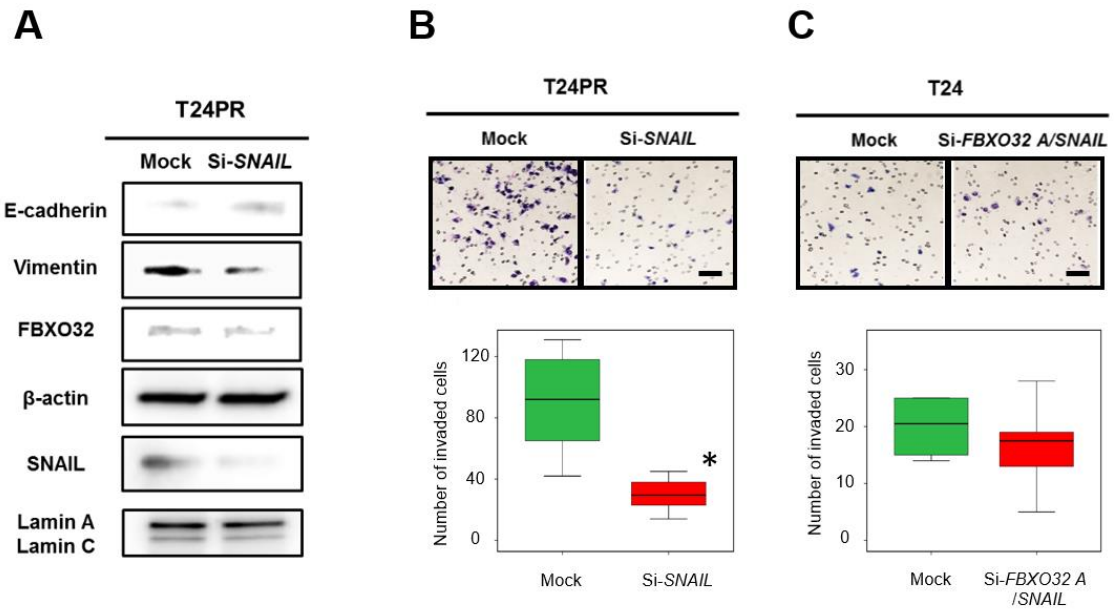
Supplementary Figure S8. mRNA expression of *E-cadherin*, *Vimentin*, and *SNAIL* in T24PR cells transfected with si-*MYOD*. Preparation and the respective primers were described in the “Methods” section. Box-and-whiskers plots show median (line within box), upper and lower quartile (bounds of box), and minimum and maximum values (bars).



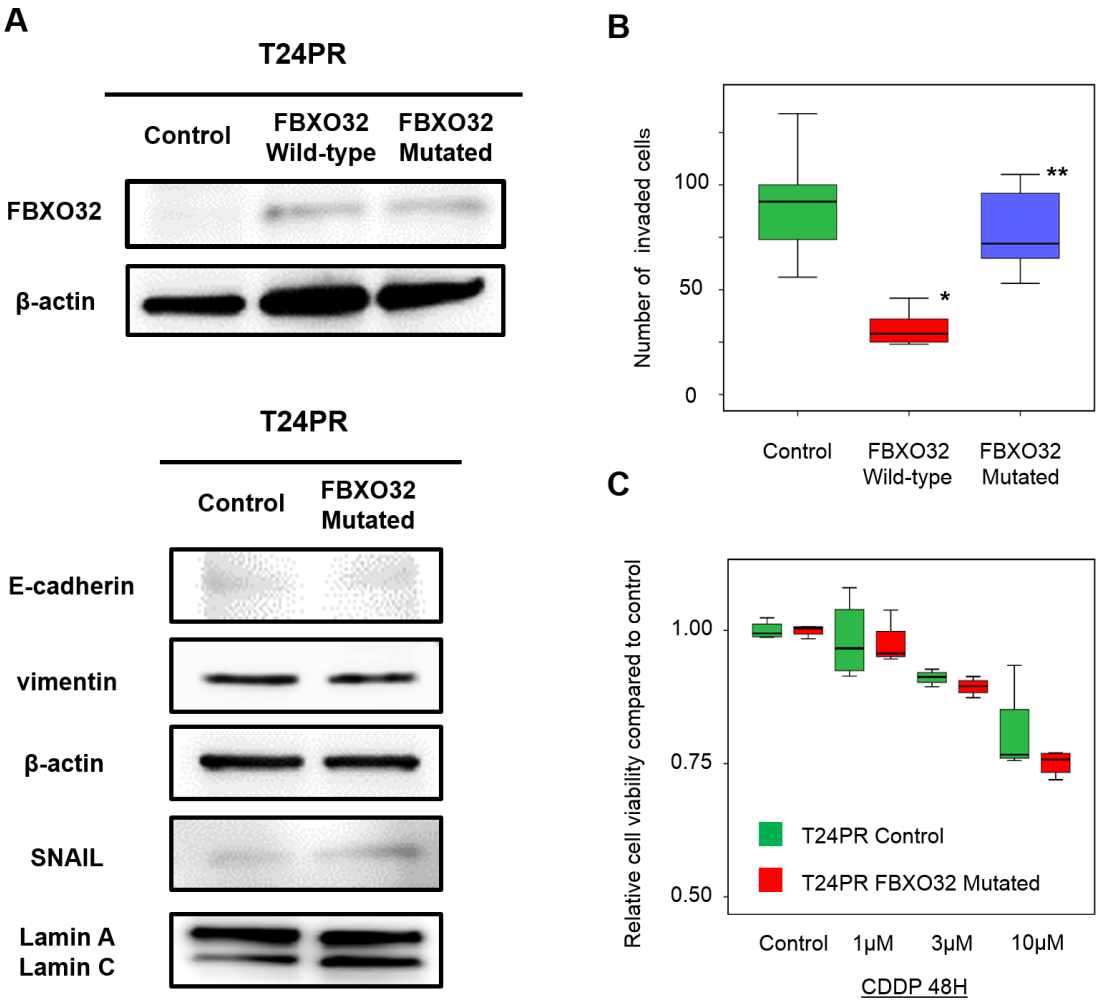
Supplementary Figure S9. Chromosome Analysis Suite representation of DNA copy number events in analyzed T24, T24PR, and T24TR cells. Color annotation indicates copy number loss (red) and gain (blue). Each colored vertical line represents a different cell (T24, green; T24PR, purple; T24TR, blue).



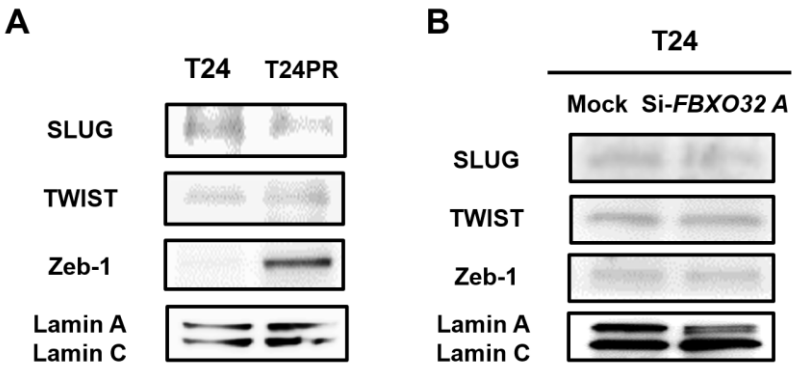
Supplementary Figure S10. Chromosome Analysis Suite representation of loss of heterozygosity (LOH) alterations in analyzed T24, T24PR, and T24TR cells. The purple bar indicated the size of the LOH. Each colored vertical line represents a different cell (T24, green; T24PR, purple; T24TR, blue).



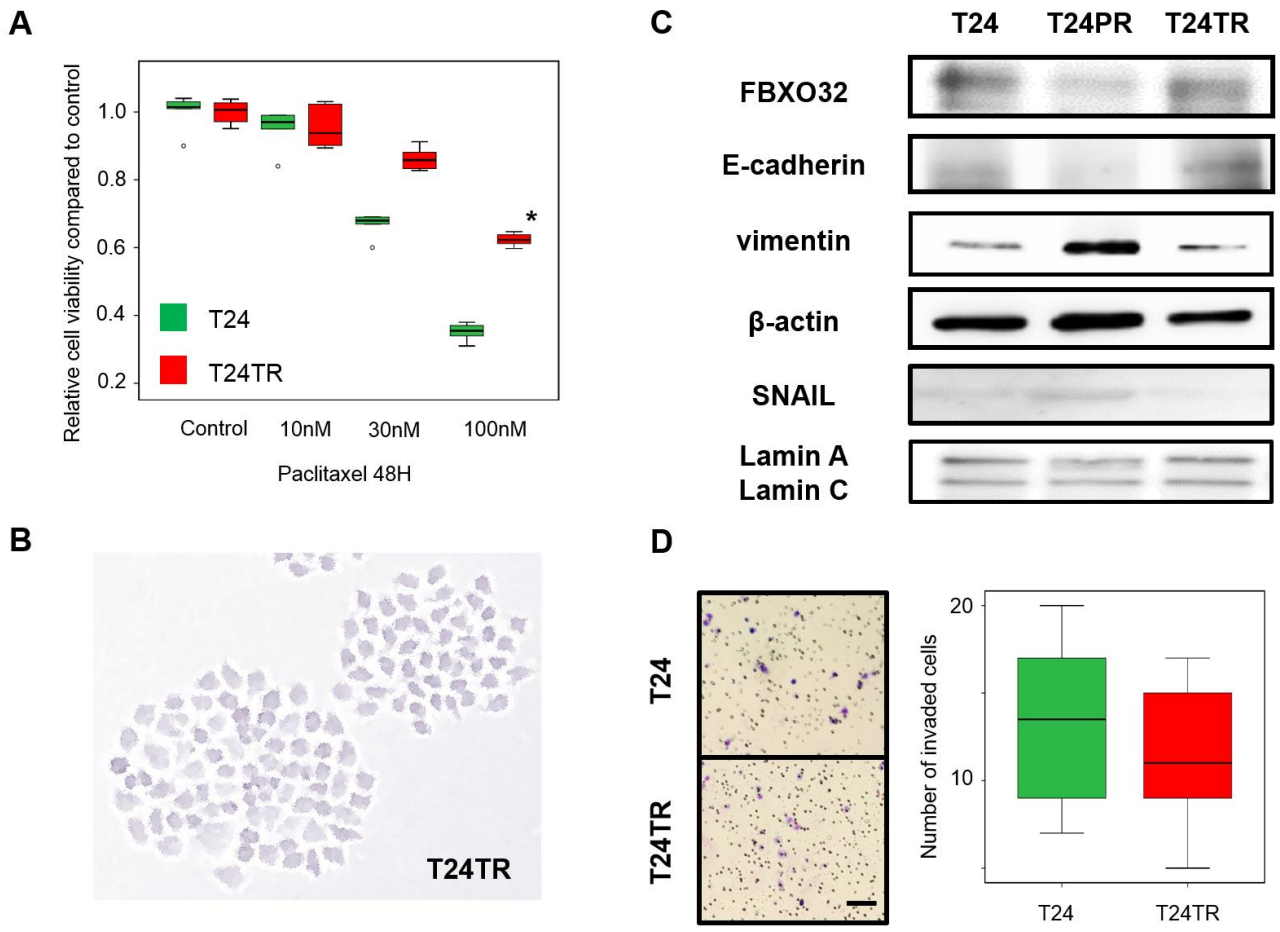
Supplementary Figure S11. (A) Effect of SNAIL knockdown on the expression of E-cadherin, Vimentin, FBXO32, and SNAIL in T24PR cells. (B) Matrigel invasion assay of T24PR cells transfected with si-SNAIL at 24 hours (n = 6). Scale Bar: 100 μm. The invading cells were stained with Diff-Quik. *, $P < 0.05$, compared with mock-transfected cells. (C) Matrigel invasion assay of T24 cells transfected with si-FBXO32/SNAIL at 24 hours (n = 6). Scale Bar: 100 μm. The invading cells were stained with Diff-Quik. Box-and-whiskers plots show median (line within box), upper and lower quartile (bounds of box), and minimum and maximum values (bars).



Supplementary Figure S12. (A) Effect of FBXO32 overexpression on the expression of FBXO32, E-cadherin, vimentin, and SNAIL in T24PR cells. (B) Matrigel invasion assay of T24PR cells transfected with FBXO32 at 24 hours (n = 6). *, $P < 0.05$, compared with control cells. **, $P < 0.05$, compared with FBXO32 wild-type transfected cells. (C) Effect of mutated FBXO32 overexpression on the sensitivity to CDDP in T24PR cells. Box-and-whiskers plots show median (line within box), upper and lower quartile (bounds of box), and minimum and maximum values (bars).



Supplementary Figure S13. (A) Western blot analysis of T24 and T24PR nuclear extracts for SLUG, TWIST, and Zeb-1. (B) Effect of FBXO32 knockdown on the expression of SLUG, TWIST, and Zeb-1 in T24 cells.



Supplementary Figure S14. (A) In vitro paclitaxel-induced changes in cell viability at 48 hours before and after the development of acquired taxane resistance. *, $P < 0.05$, compared with T24 cells. (B) Morphological features of T24TR cells under light microscopy. (C) Western blot analysis of E-cadherin and Vimentin in cell lysates and SNAIL in nuclear extracts in T24PR, T24TR, and their corresponding parent cells T24. (D) Matrigel invasion assay of T24TR and their corresponding parent cells T24 at 24 hours (n = 6). Scale bar: 100 μm. The invading cells were stained with Diff-Quik. Box-and-whiskers plots show median (line within box), upper and lower quartile (bounds of box), and minimum and maximum values (bars).

Supplementary Table S1. Common up-regulated/down-regulated genes upon platinum resistance acquisition in T24PR and 5637PR cells

Gene symbol
Up-regulated (25)
ABCA2, ANGEL1, BDKRB1, CRAT, EFNA3, GAMT, H1F0, ICAM1, IFI6, IFITM1, LOC554202, MAPRE3, MFSD3, PLCXD1, PRDX5, RAB3A, REEP6, SCARNA10, SNORD24|RPL7A, SNORD45A|RABGGTB, SNORD68|RPL13, STARD10, TNFIP2, TPP1, TSPAN1.
Down-regulated (24)
AP1S3, C20orf111, FBXO32, GOSR1, GTF3C6, H3F3B, HERPUD1, KLF4, LANCL2, LYPD3, NCOA5, ODC1, PLAGL1|HYMAI, PLIN2, POP4, RBM3, RBX1|XPNPEP3, RPS3A, RPS7, SERPINB8, SLC38A, SNORD28, TXNL1, ZNF552|ZNF814|ZNF587|LOC100288322.

Supplementary Table S2. Predictive risk factors for disease recurrence and cancer-specific mortality following radical nephroureterectomy in 201 patients

Characteristic	Recurrence-free survival			Cancer-specific mortality		
	Univariate	Multivariate		Univariate	Multivariate	
	P value	HR (95%CI)	*P* value	*P* value	HR (95%CI)	*P* value
Age (> 70yr vs. ≤ 70yr)	0.774			0.500		
Gender (male vs. female)	0.239			0.236		
Tumor grade (high vs. low)	< 0.001			< 0.001		
Pathological T stage (≥ pT2 vs. < pT2)	< 0.001	5.46 (1.79-16.6)	0.003	< 0.001	15.7 (3.80-65.0)	< 0.001
Lymphovascular invasion (positive vs. negative)	< 0.001	2.07 (1.09-3.93)	0.027	< 0.001		
Lymph node involvement (pN+ vs. pNx or pN0)	< 0.001			0.002		
Adjuvant chemotherapy (yes vs. no)	0.001			0.006		
FBXO32 score (low vs. high)	0.003	2.11 (1.12-3.84)	0.015	0.018	1.93 (1.02-3.66)	0.044

Supplementary Table S3. Baseline characteristics of 94 patients treated with cystectomy and FBXO32 expression

Characteristic	No of patients (%)	FBX032 score (mean ± SE)	*P* value
Age			0.764
< 70 years	48 (51.1)	51.3 ± 7.4	
≥ 70 years	46 (48.9)	49.4 ± 7.3	
Gender			0.763
Male	70 (74.5)	51.7 ± 6.2	
Female	24 (25.5)	46.1 ± 9.4	
Tumor grade			0.198
Low	14 (14.9)	43.4 ± 11.6	
High	80 (85.1)	51.4 ± 5.7	
Pathological T stage			0.076
< pT2	19 (20.2)	60.9 ± 14.0	
≥ pT2	75 (79.8)	46.4 ± 5.4	
Lymphovascular invasion			0.342
Negative	32 (34.0)	51.5 ± 9.1	
Positive	62 (66.0)	49.7 ± 6.3	
Lymph node involvement			0.366
pNx or pN0	73 (77.7)	50.2 ± 5.9	
pN+	21 (22.3)	50.4 ± 11.0	
Adjuvant chemotherapy			0.782
No	68 (72.3)	50.5 ± 6.1	
Yes	26 (27.7)	49.9 ± 9.8	
E-cadherin expression			0.010
Low	48 (51.1)	45.5 ± 6.7	
High	46 (48.9)	51.7 ± 7.5	
SNAIL expression			0.013
Low	46 (48.9)	54.7 ± 8.1	
High	48 (51.1)	42.7 ± 6.2	

Supplementary Table S4. Baseline characteristics of 16 patients treated with neoadjuvant CDDP-based chemotherapy before cystectomy

Characteristic	Number of patients (%)
Age	
< 70 years	9 (56.3)
≥ 70 years	7 (43.8)
Gender	
Male	12 (75.0)
Female	4 (25.0)
Tumor grade	
Low	1 (6.3)
High	15 (93.8)
Pathological T stage	
< pT2	2 (12.5)
≥ pT2	14 (63.6)
Lymphovascular invasion	
Negative	5 (31.3)
Positive	11 (61.1)
Lymph node involvement	
pNx or pN0	9 (56.3)
pN+	7 (43.8)
Adjuvant chemotherapy	
No	10 (62.5)
Yes	6 (37.5)
E-cadherin expression at cystectomy specimens	
Low	13 (81.3)
High	3 (18.8)
SNAIL expression at cystectomy specimens	
Low	7 (43.8)
High	9 (56.3)