

Figure S1 Immunohistochemistry staining of 4 markers in TMAs. (A) Overview of training cohort TMAs. (B) Overview of validation cohort TMAs. (C) Representative immunohistochemical images of tumors expressing both luminal and basal markers based on the higher score. TMA, tissue microarray.

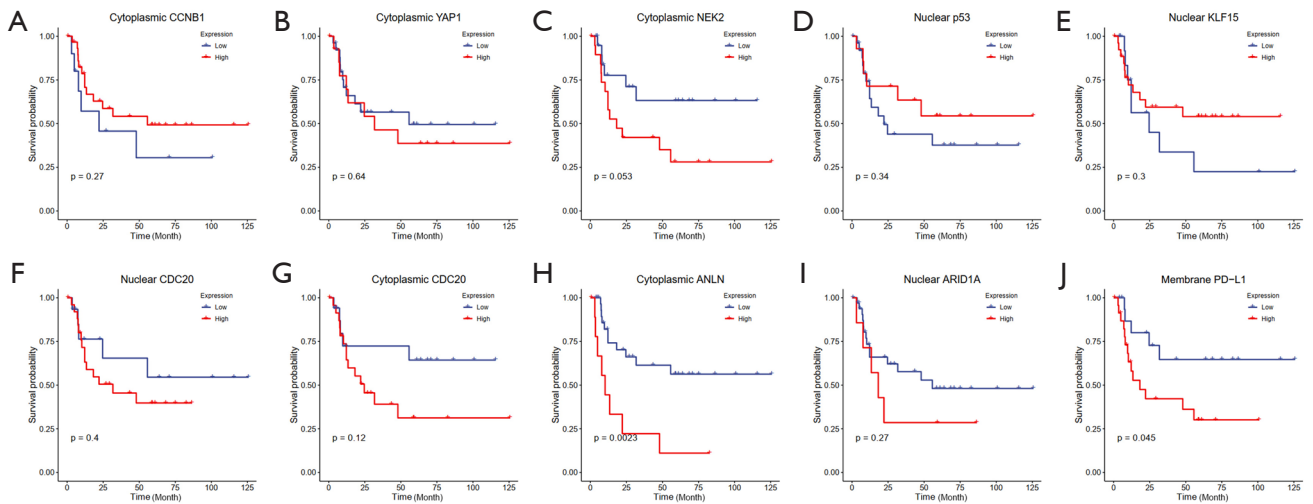


Figure S2 Kaplan-Meier curves of different markers in predicting prognosis of basal MIBC patient in training cohort. MIBC, muscle-invasive bladder cancer.

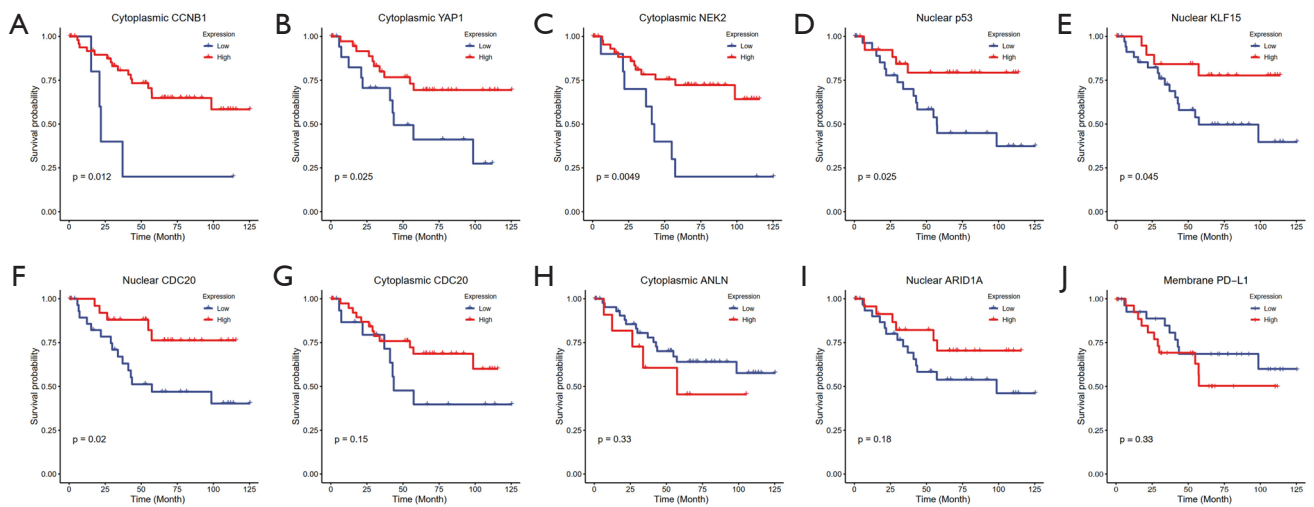


Figure S3 Kaplan-Meier curve of different markers in predicting prognosis of luminal MIBC patient in training cohort. MIBC, muscle-invasive bladder cancer.

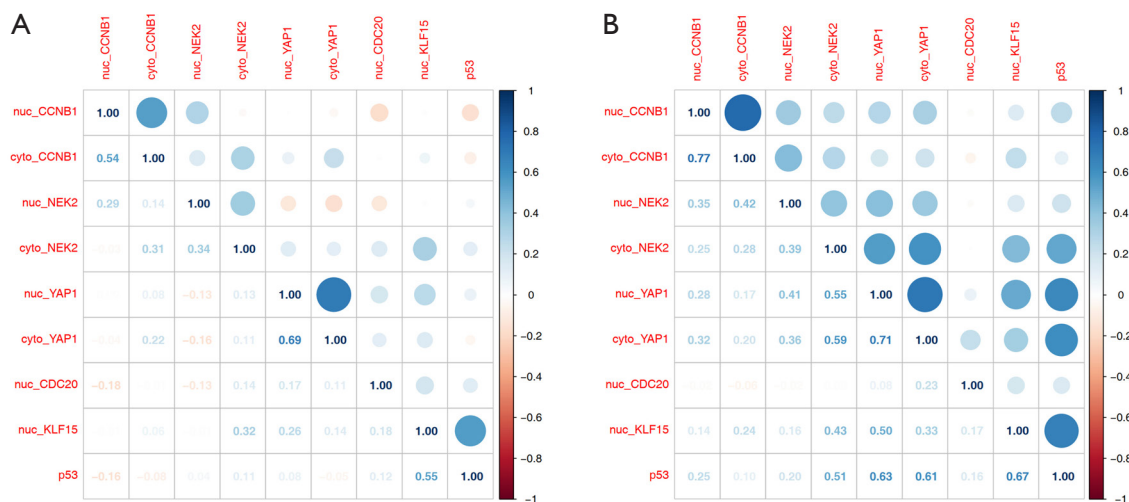


Figure S4 Correlation heatmaps of immunohistochemical scores of all markers used in training group (A) and validation group (B), the area of each circle is proportional to the absolute value of corresponding correlation coefficient.

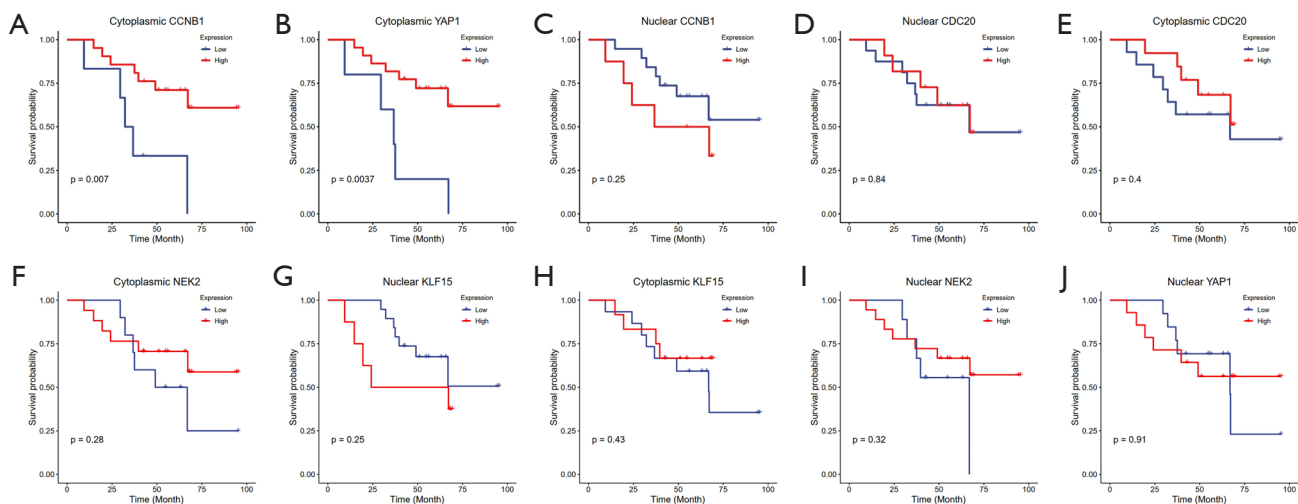


Figure S5 Kaplan-Meier curves of different markers in predicting prognosis of luminal MIBC patients in the validation cohort. MIBC, muscle-invasive bladder cancer.

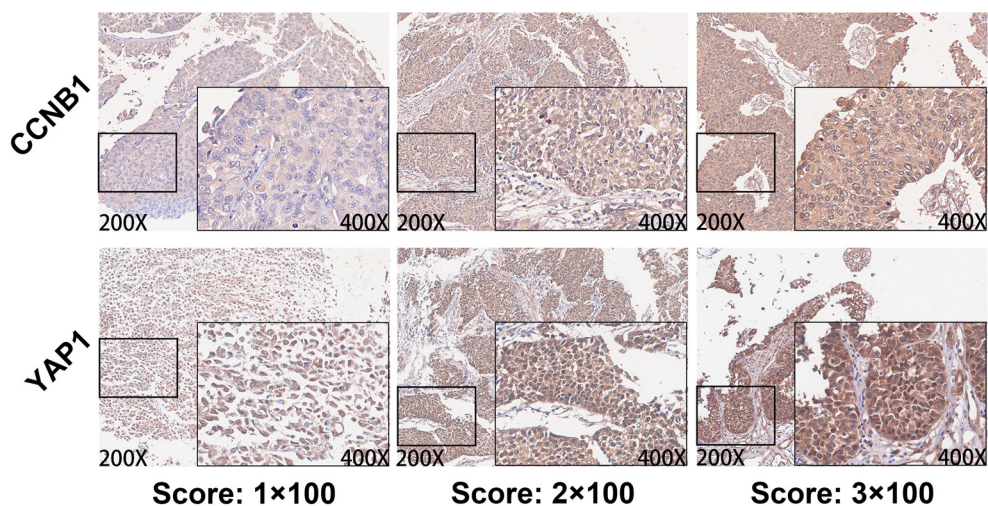


Figure S6 Examples of different immunohistochemistry staining intensity of cytoplasmic CCNB1 and YAP1. YAP1, yes 1 associated transcriptional regulator; CCNB1, cyclin B1.

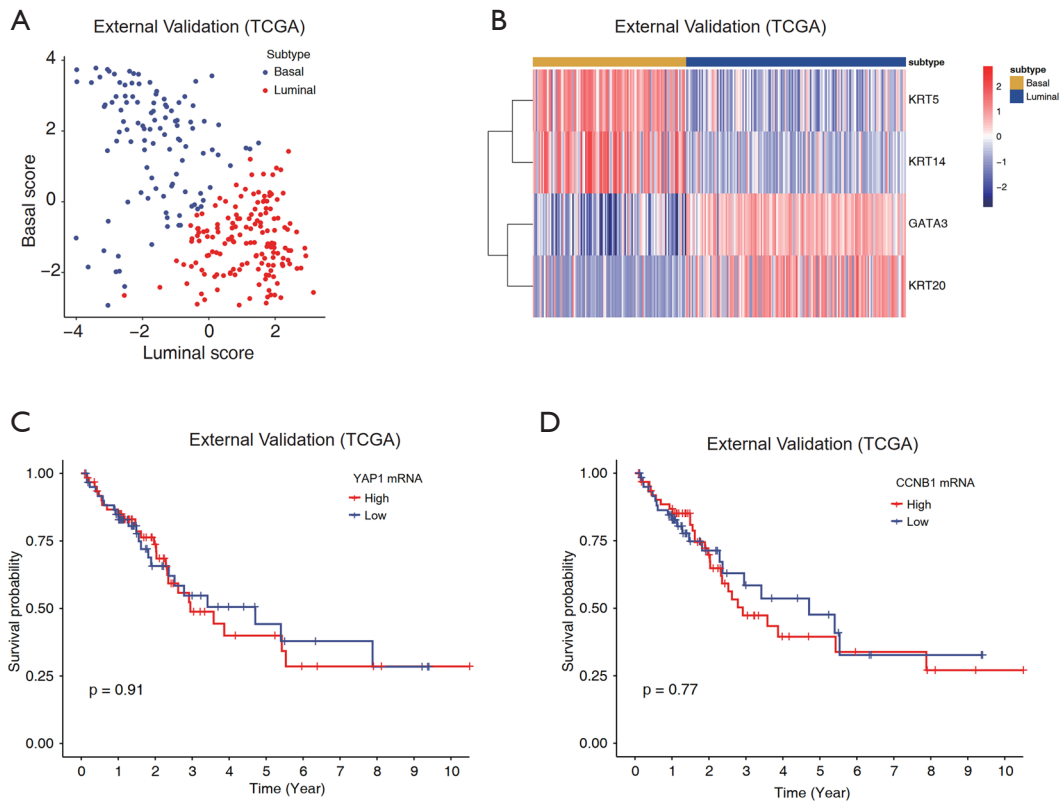


Figure S7 External validation of prognostic model. (A,B) Patients were grouped into luminal- and basal-types by luminal- and basal-score. Kaplan-Meier curves of YAP1 (C) and CCNB1 (D) mRNA expression among luminal patients using TCGA database. YAP1, yes 1 associated transcriptional regulator; CCNB1, cyclin B1; TCGA, The Cancer Genome Atlas.

Table S1 Patient characteristics of different subtypes in two cohorts

Risk factors	Training Cohort			Validation Cohort		
	Basal (n=57)	Luminal (n=104)	P value	Basal (n=28)	Luminal (n=44)	P value
Age (years, mean ± SD)	65.35±8.17	66.52±10.81	0.44	65.46±11.58	66.39±9.44	0.73
Gender						
Male	48	98	0.07	26	39	0.44
Female	9	6		2	5	
Size group						
≤3 cm	23	59	0.13	15	16	0.23
>3 cm	31	45		13	28	
Tumor grade						
Low	13	23	1	5	7	1
High	44	81		23	37	
Tumor number						
Single	22	18	0.01	13	14	0.32
Multiple	35	86		15	30	
T stage						
Ta & T1	16	47	0.003	4	17	0.14
T2	10	31		11	13	
T3	21	18		9	11	
T4	10	8		4	3	
N stage						
Negative	45	92	0.16	21	36	0.69
Positive	12	12		7	8	
Recurrent tumor						
Primary	34	75	0.15	19	34	0.54
Recurrent	23	29		9	10	

SD, standard deviation.

Table S2 Univariable and multivariable Cox regression model for predicting cancer specific survival in training cohort

Risk factors	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Age group (≤ 65 years as referent)						
>65 years	1.63	1.02-2.59	0.04*	1.64	1.02-2.63	0.04*
Tumor Grade (low as referent)						
High	3.2	1.47-6.97	<0.01**	1.76	0.78-3.98	0.18
Subtype (Luminal as referent)						
Basal	2.18	1.39-3.43	<0.01**	1.91	1.19-3.05	<0.01**
Gender (female as referent)						
Male	0.77	0.38-1.55	0.46	NA		
Recurrent tumor (primary as referent)						
Recurrent	1.16	0.71-1.88	0.55	NA		
T stage (NMIBC as referent)						
MIBC	7.83	3.59-17.07	<0.01**	5.28	2.32-12.02	<0.01**
N stage (negative as referent)						
Positive	2.46	1.477-4.12	<0.01**	1.32	0.77-2.26	0.31
Tumor size (≤ 3 cm as referent)						
>3 cm	1.69	1.06-2.68	0.03*	1.42	0.87-2.30	0.16
Tumor number (single as referent)						
Multiple	1.736	1.08-2.79	0.02*	1.07	0.65-1.77	0.80

* $P < 0.05$; ** $P < 0.01$. CI, confidence interval; HR, hazard ratio; NA, not available; MIBC, muscle invasive bladder cancer; NMIBC, non-muscle invasive bladder cancer.

Table S3 Immunohistochemical markers and cancer specific survival in luminal MIBC patients

Expression	Median survival	95%CI	P value
Cytoplasmic CCNB1			
Low	22.0	21.0-NR	0.012
High	NR	98.6-NR	
Cytoplasmic YAP1			
Low	43.6	41-NR	0.025
High	NR	NR	
Cytoplasmic NEK2			
Low	NR	41.0-NR	0.0049
High	NR	98.6-NR	
Nuclear p53			
Low	57.2	42.8-NR	0.025
High	NR	NR	
Nuclear KLF15			
Low	57.4	42.8-NR	0.045
High	NR	NR	
Nuclear CDC20			
Low	57.4	37-NR	0.02
High	NR	NR	
Cytoplasmic CDC20			
Low	43.6	41.0-NR	0.15
High	NR	NR	
Cytoplasmic ANLN			
Low	NR	98.6-NR	0.33
High	57.4	33.8-NR	
Cytoplasmic ARID1A			
Low	98.6	42.8-NR	0.18
High	NR	NR	
Membrane PD-L1			
Low	NR	98.6-NR	0.33
High	NR	54.8-NR	

CI, confidence interval; NR, not reached; MIBC, muscle invasive bladder cancer.

Table S4 Univariable and multivariable Cox regression model for predicting cancer specific survival in luminal MIBC patients

Risk factors	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Age group (≤ 65 years as referent)						
>65 years	1.22	0.75-3.24	0.23			
Tumor Grade (low as referent)						
High	2.80	0.67-11.73	0.16			
Gender (female as referent)						
Male	0.41	0.10-1.73	0.22			
Recurrent tumor (primary as referent)						
Recurrent	0.58	0.24-1.40	0.22			
T stage (T2 as referent)						
T3-4	2.73	1.32-5.67	<0.01**	2.31	1.06-5.01	0.03*
N stage (Negative as referent)						
Positive	1.42	0.66-3.07	0.37			
M stage (M0 as referent)						
M1	2.74	1.05-7.13	0.04*	2.82	1.07-7.48	0.04*
Tumor size (≤ 3 cm as referent)						
>3 cm	1.84	0.87-3.89	0.11			
Tumor number (single as referent)						
Multiple	1.74	0.84-3.62	0.14			
Risk (low as referent)						
High	2.93	1.46-5.89	<0.01**	2.19	1.04-4.62	0.04*

* $P < 0.05$; ** $P < 0.01$. CI, confidence interval; HR, hazard ratio; MIBC, muscle invasive bladder cancer.