Supplementary

Table S1 Demographics and tumor characteristics of patients in screening set and validation set

Characteristics	Screening set (n=30), n (%)			Validation set (n=54), n (%)		
	Noninvasive, Ta–T1 (n=16)	Invasive, T2–T4 (n=14)	P value	Noninvasive, Ta–T1 (n=32)	Invasive, T2–T4 (n=22)	P value
Age, years			0.815			0.561
Mean ± SD	63.27±13.03	64.87±10.89		63.03±10.45	61.18±12.27	
Median [range]	66.0 [34–79]	68.0 [42–78]		64.5 [43–82]	64 [33–84]	
Gender			0.654			0.903
Male	9 (56.3)	9 (64.3)		28 (87.5)	19 (86.3)	
Female	7 (43.7)	5 (35.7)		4 (12.5)	3 (13.7)	
Drink			0.134			0.583
Yes	2 (12.5)	5 (35.7)		8 (25.0)	7 (31.8)	
No	14 (87.5)	9 (64.3)		24 (75.0)	15 (68.2)	
Smoking			0.301			0.421
Yes	4 (25.0)	6 (42.9)		11 (34.4)	10 (45.5)	
No	12 (75.0)	8 (57.1)		21 (65.6)	12 (54.5)	
Tumor grade			0.732			0.071
Low	7 (43.8)	7 (50.0)		15 (46.9)	5 (22.7)	
High	9 (56.3)	7 (50.0)		17 (53.1)	17 (77.3)	
Multifocality			0.654			0.165
>1	9 (56.3)	9 (64.3)		22 (68.8)	11 (50.0)	
1	7 (43.7)	5 (35.7)		10 (31.3)	11 (50.0)	
Recurrence			0.818			0.337
Yes	4 (25.0)	3 (21.4)		14 (43.8)	7 (31.8)	
No	12 (75.0)	11 (78.6)		18 (56.3)	15 (68.2)	

SD, standard deviation.

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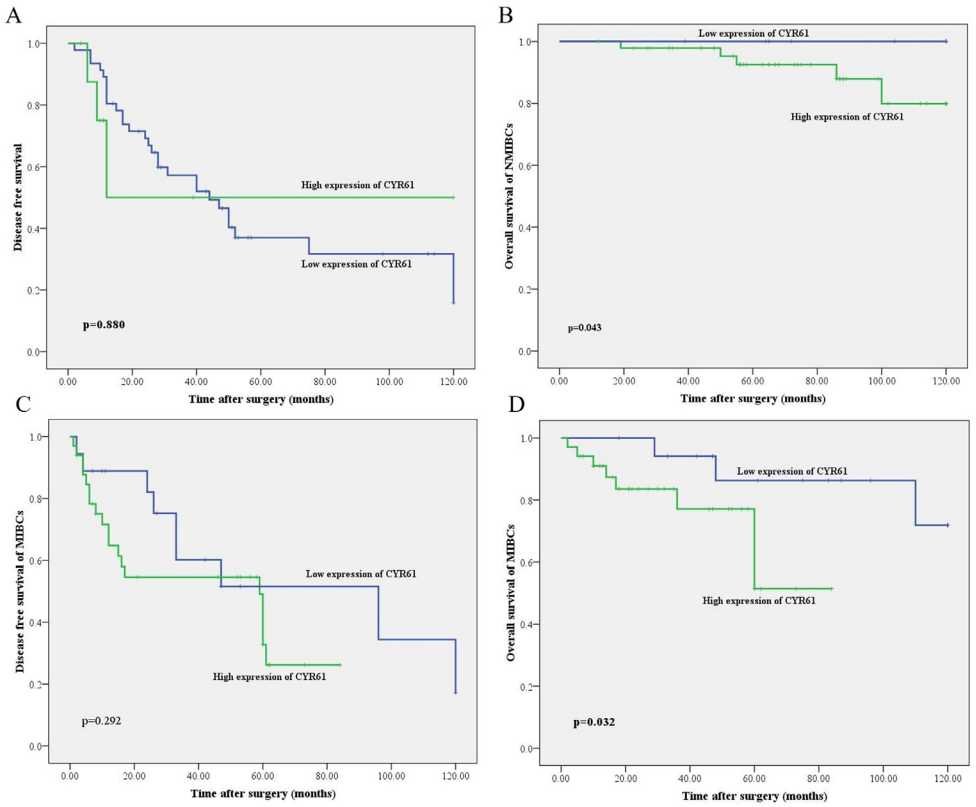

Figure S1 Kaplan-Meier analysis of CYR61 expression in NMIBCs (n=56) and MIBC (n=52). (A) Relationship of CYR61 expression and NMIBCs patients' disease-free survival: low expression, n=46; high expression, n=10 (P=0.880, log-rank =0.023). (B) OS curves of NMIBCs by CYR61 expression (P=0.043, log-rank =5.235). (C) Relationship of CYR61 expression and MIBCs patients' disease-free survival: low expression, n=28; high expression, n=10 (P=0.292, log-rank =1.111). (D) OS curves of NMIBCs by CYR61 expression (P=0.032, log-rank =7.213). CYR61, cysteine-rich angiogenic inducer 61; NMIBC, non-muscle-invasive bladder cancer; MIBC, muscle-invasive bladder cancer; OS, overall survival.

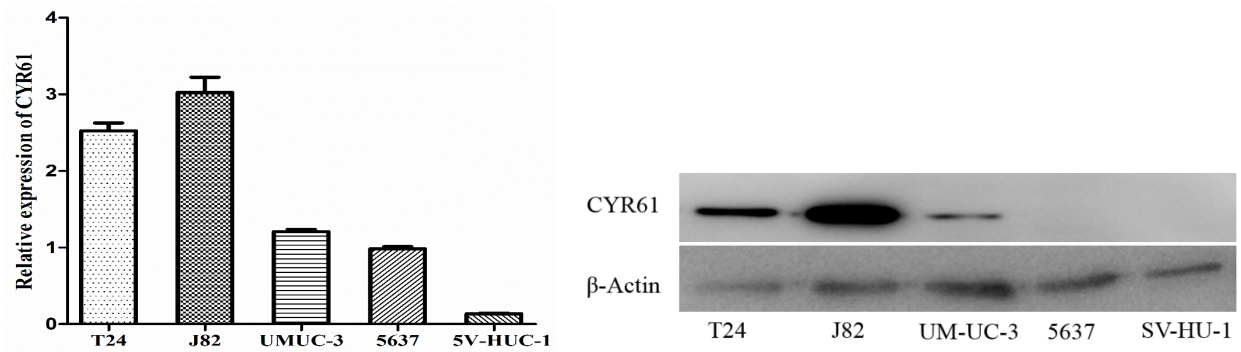

Figure S2 Endogenous levels of CYR61 in different bladder carcinoma cells. CYR61, cysteine-rich angiogenic inducer 61.

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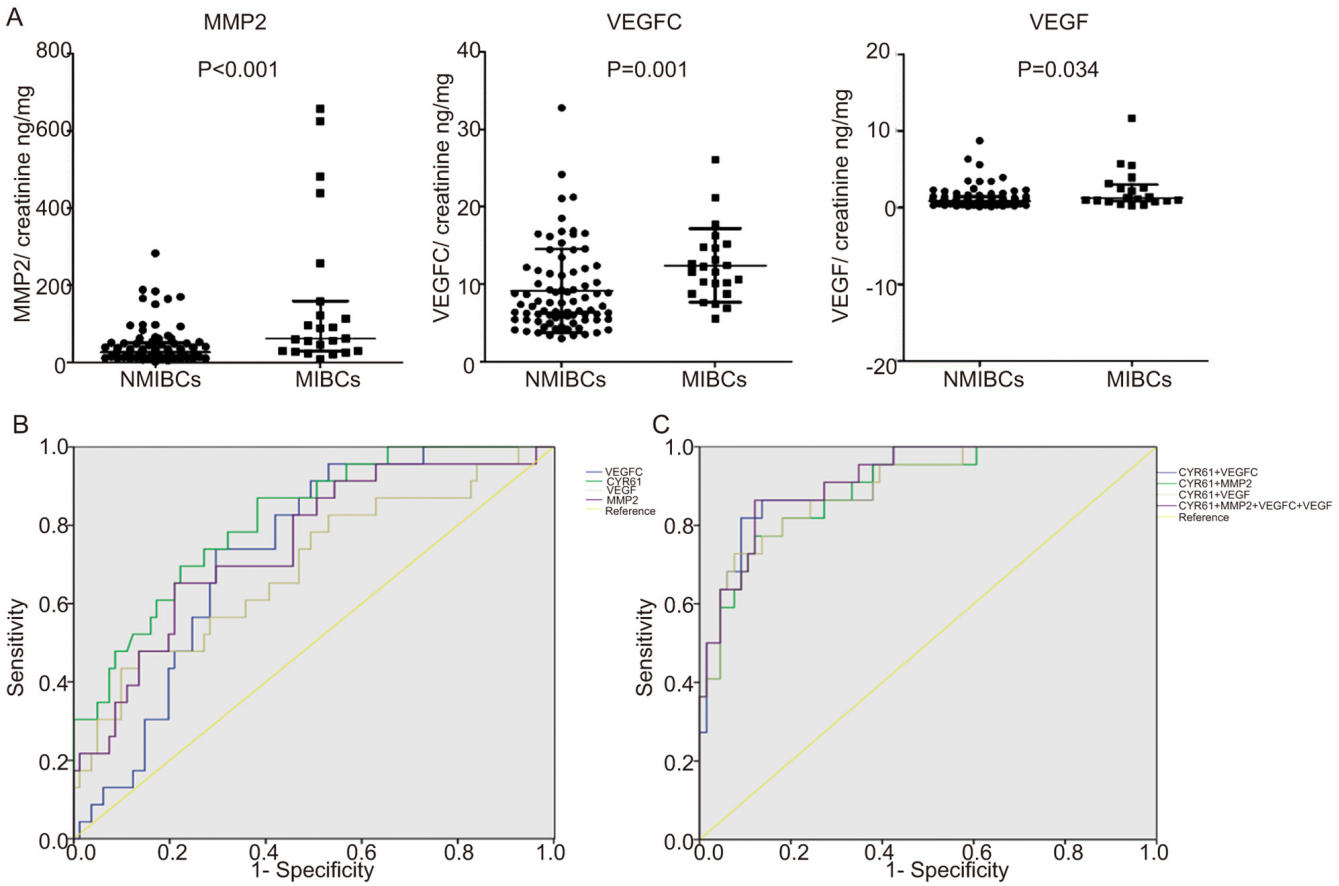

Figure S3 Urine concentration and ROC curves of MMP-2, VEGFC, and VEGF in NMIBCs and MIBCs. (A) Urine concentration of MMP-2, VEGFC, and VEGF in NMIBCs and MIBCs. (B) ROC curves were plotted to compare the diagnostic performance of CYR61, MMP-2, VEGFC, and VEGF individually. (C) ROC curves were plotted to compare the diagnostic performance of CYR61, MMP-2, VEGFC, and VEGF together. ROC, receiver-operating characteristic; MMP-2, matrix metalloproteinase-2; NMIBC, non-muscle-invasive bladder cancer; MIBC, muscle-invasive bladder cancer; CYR61, cysteine-rich angiogenic inducer 61.

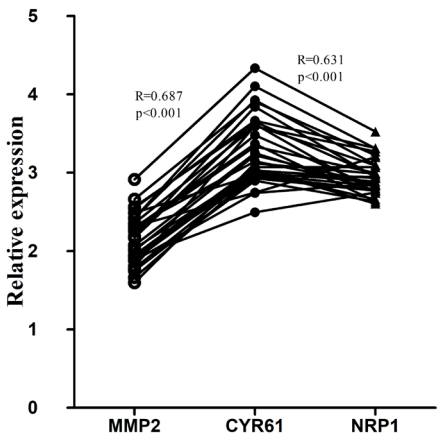

Figure S4 The correlation between expression of CYR61 and MMP-2/NRP-1 in the gene expression profiling of 30 human bladder tumors. CYR61, cysteine-rich angiogenic inducer 61; MMP-2, matrix metalloproteinase-2; NRP-1, neuropilin-1.

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Table S2 Diagnostic performance of CYR61, MMP-2, VEGFC, and VEGF to distinguish MIBC from NMIBC individual

Biomarker	AUC	P value	Cutoff value (ng/mg)	Sensitivity	Specificity
CYR61	0.883	<0.001	4.596	0.727	0.860
MMP-2	0.806	<0.001	54.695	0.682	0.864
VEGFC	0.796	<0.001	9.939	0.727	0.788
VEGF	0.736	0.001	0.790	0.818	0.561

CYR61, cysteine-rich angiogenic inducer 61; MMP-2, matrix metalloproteinase-2; MIBC, muscle-invasive bladder cancer; NMIBC, non-muscle-invasive bladder cancer; AUC, area under the curve.

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