

Table S1 Patient characteristics of the GSE13507 BCa cohort

Variable	Number	CYP19A1 (high)	CYP19A1 (low)	P value
Total	165	147	18	
Age				0.4559
≥65	96	87	9	
<65	69	60	9	
Gender				0.1412
Male	135	118	17	
Female	30	29	1	
Grade				0.7771
Low	105	93	12	
High	60	54	6	
Stage				0.6632
Ta	24	20	4	
T1	80	72	8	
T2	31	28	3	
T3	19	18	1	
T4	11	9	2	

BCa, bladder cancer.

Table S2 Patient characteristics of the TCGA-BLCA BCa cohort

Variable	Number	CYP19A1 (high)	CYP19A1 (low)	P value
Total	404	45	359	
Age				0.1871
≥68	214	28	186	
<68	190	17	173	
Gender				0.1317
Male	298	29	269	
Female	106	16	90	
Stage				0.1402
T2	120	12	108	
T3	193	24	169	
T4	58	2	56	
Lymph node				0.7329
N0	234	27	207	
N1	46	6	40	
N2	75	6	69	
N3	8	1	7	
Metastasis				0.0684
M0	194	19	175	
M1	11	3	8	
Histologic subtype				0.3885
Non-papillary	270	33	237	
Papillary	129	12	117	

BCa, bladder cancer.

Table S3 Patient characteristics of the E-MTAB-4321 BCa cohort

Variable	Number	CYP19A1 (high)	CYP19A1 (low)	P value
Total	460	61	399	
Age				0.6623
≥65	298	38	260	
<65	162	23	139	
Gender				0.6582
Male	357	46	311	
Female	103	15	88	
Grade				0.5160
Low	277	35	242	
High	176	26	150	
Stage				0.0283
Cis	3	0	3	
Ta	345	38	307	
T1	112	23	89	

BCa, bladder cancer.

Table S4 Patient characteristics of the E-MTAB-1803 BCa cohort

Variable	Number	CYP19A1 (high)	CYP19A1 (low)	P value
Total	73	10	63	
Age				0.5379
≥65	43	5	38	
<65	30	5	25	
Gender				0.5022
Male	62	8	54	
Female	11	2	9	
Grade				0.4124
G2	4	0	4	
G3	69	10	59	
Stage				0.1029
T2	25	1	24	
T3	29	4	25	
T4	19	5	14	
Lymph node				0.0280
N0	36	2	34	
N1	26	7	19	
Metastasis				0.9433
M0	59	8	51	
M1	14	2	12	
Molecular subtype				0.9261
Basal-like	21	3	18	
Non-basal-like	52	7	45	

BCa, bladder cancer.

Table S5 Female patient characteristics of the TCGA-BLCA BCa cohort

Factor	CYP19A1 (high)	CYP19A1 (low)	P value
Age			0.6082
≥68	7	55	
<68	4	44	
Stage			0.05587
T2	1	28	
T3	10	44	
T4	0	14	
Lymph node			0.4992
N0	6	57	
N1-3	5	27	
Metastasis			0.4048
M0	3	41	
M1	1	5	
MX	7	51	
Histologic subtype			0.2853
Non-papillary	10	69	
Papillary	1	25	

BCa, bladder cancer.

Table S6 Female patient characteristics of the E-MTAB-4321 BCa cohort

Factor	CYP19A1 (high)	CYP19A1 (low)	P value
Age			0.978
≥65	33	31	
<65	20	19	
Grade			0.2526
Low	34	26	
High	18	22	
Stage			0.564
cis	0	1	
Ta	41	39	
T1	12	10	

BCa, bladder cancer.

Table S7 Female patient characteristics of the E-MTAB-1803 BCa cohort

Factor	CYP19A1 (high)	CYP19A1 (low)	P value
Age			1
≥67	4	3	
<67	2	2	
Stage			0.1775
T2	0	2	
T3	2	2	
T4	4	1	
Grade			0.4545
G2	0	1	
G3	6	4	
Lymph node			1
Negative	3	3	
Positive	3	2	
Distant metastasis			1
Negative	4	4	
Positive	2	1	

BCa, bladder cancer.

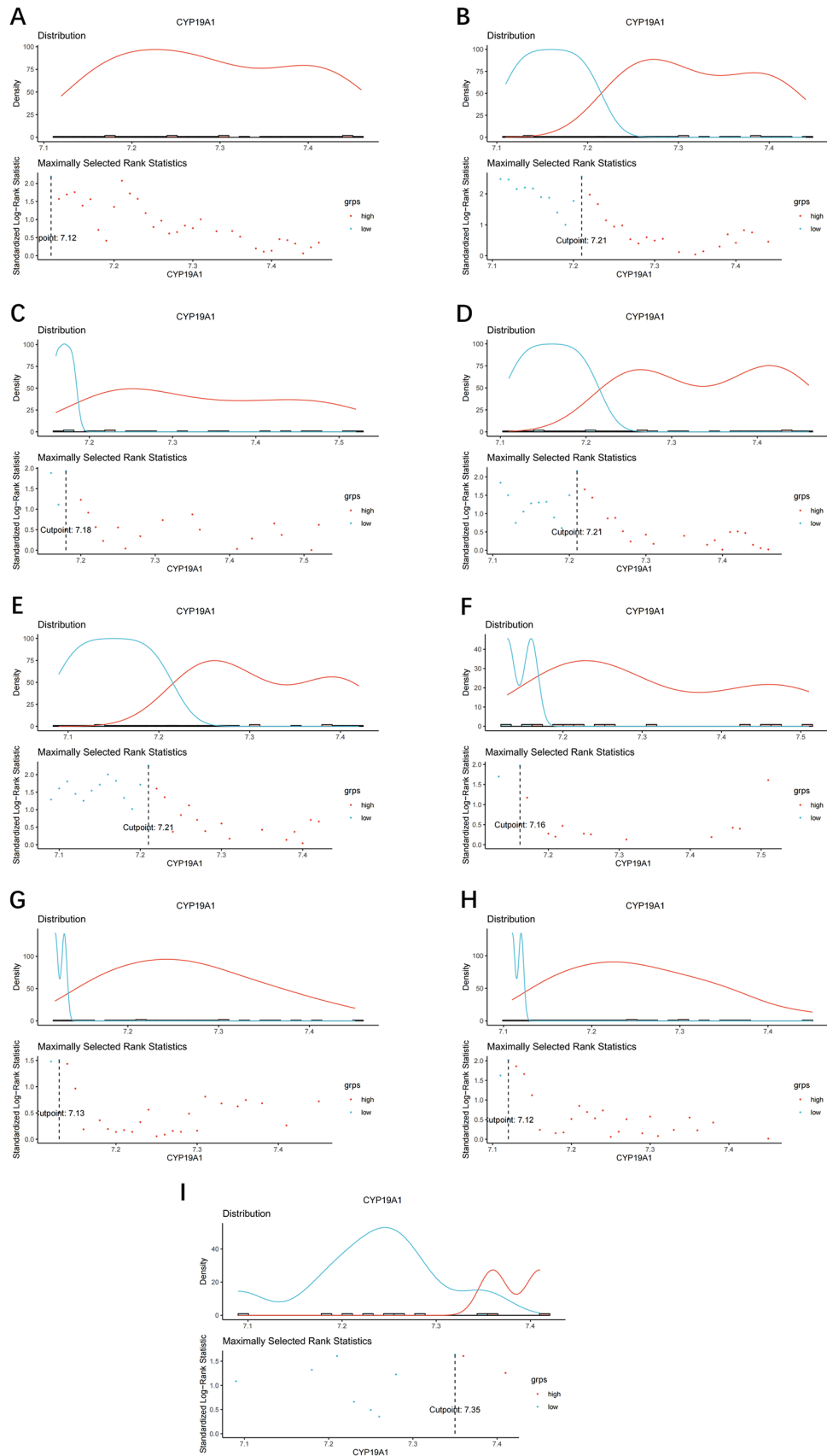


Figure S1 The cut-off value of CYP19A1 in the GSE13507 BCa cohort. (A) The cut-off value of CYP19A1 of entire patients in the GSE13507. (B) The cut-off value of CYP19A1 of all of the male patients in the GSE13507. (C) The cut-off value of CYP19A1 of all of the female patients in the GSE13507. (D) The cut-off value of CYP19A1 of NMIBC patients in the GSE13507. (E) The cut-off value of CYP19A1 of NMIBC male patients in the GSE13507. (F) The cut-off value of CYP19A1 of NMIBC female patients in the GSE13507. (G) The cut-off value of CYP19A1 of MIBC patients in the GSE13507. (H) The cut-off value of CYP19A1 of MIBC male patients in the GSE13507. (I) The cut-off value of CYP19A1 of MIBC female patients in the GSE13507. BCa, bladder cancer; NMIBC, non-muscle-invasive bladder cancer; MIBC, muscle-invasive bladder cancer.

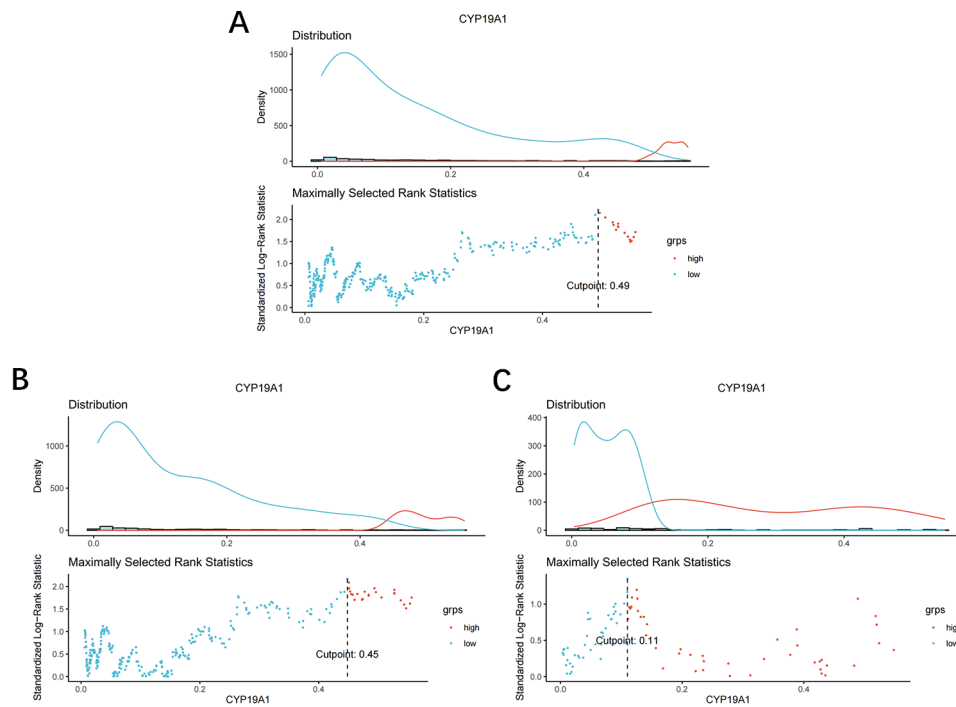


Figure S2 The cut-off value of CYP19A1 in the E-MTAB-4321 BCa cohort. (A) The cut-off value of CYP19A1 of NMIBC patients in the E-MTAB-4321. (B) The cut-off value of CYP19A1 of NMIBC male patients in the E-MTAB-4321. (C) The cut-off value of CYP19A1 of NMIBC female patients in the E-MTAB-4321. BCa, bladder cancer; NMIBC, non-muscle-invasive bladder cancer.

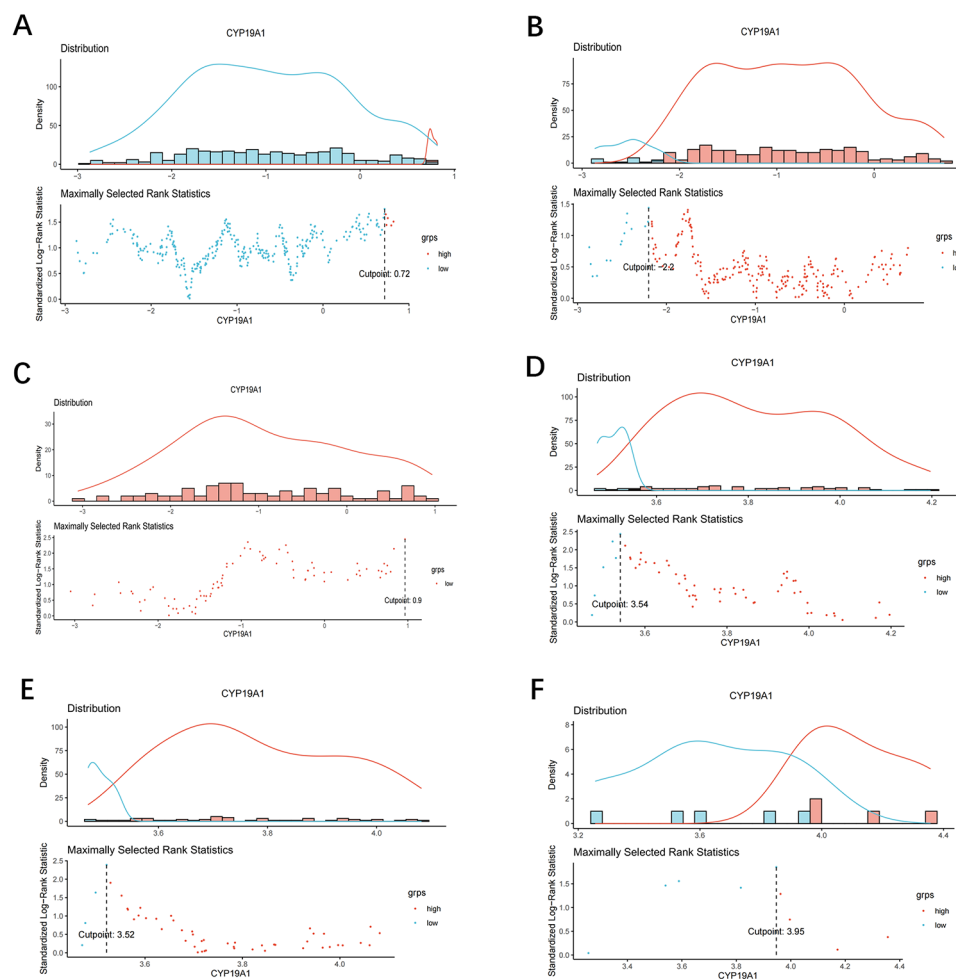


Figure S3 The cut-off value of CYP19A1 in the TCGA and E-MTAB-1803 BCa cohort. (A) The cut-off value of CYP19A1 of MIBC patients in the TCGA. (B) The cut-off value of CYP19A1 of MIBC male patients in the TCGA. (C) The cut-off value of CYP19A1 of MIBC female patients in the TCGA. (D) The cut-off value of CYP19A1 of MIBC patients in the E-MTAB-1803. (E) The cut-off value of CYP19A1 of MIBC male patients in the E-MTAB-1803. (F) The cut-off value of CYP19A1 of MIBC female patients in the E-MTAB-1803. BCa, bladder cancer; MIBC, muscle-invasive bladder cancer.

Table S8 Gene set enrichment analysis of NMIBC-male group in GSE13507

ID	Set size	Enrichment score	NES	P value	Padjust	Qvalues	Rank	Leading edge
HALLMARK_OXIDATIVE_PHOSPHORYLATION	177	-0.559967187	-1.961959774	5.91E-09	2.95E-07	1.37E-07	3434	tags=52%, list=14%, signal=45%
HALLMARK_FATTY_ACID_METABOLISM	146	-0.547701502	-1.885365225	4.26E-07	1.07E-05	4.94E-06	4096	tags=51%, list=17%, signal=42%
HALLMARK_G2M_CHECKPOINT	172	0.485096805	1.856657182	1.33E-06	2.02E-05	9.34E-06	2345	tags=33%, list=10%, signal=30%
HALLMARK_ADIPOGENESIS	178	-0.507484437	-1.777359344	1.61E-06	2.02E-05	9.34E-06	4122	tags=42%, list=17%, signal=35%
HALLMARK_PROTEIN_SECRETION	91	-0.584347118	-1.898191198	7.59E-06	7.59E-05	3.52E-05	3612	tags=48%, list=15%, signal=41%
HALLMARK_COMPLEMENT	191	-0.473142627	-1.67101166	4.00E-05	0.000333035	0.000154248	5020	tags=41%, list=21%, signal=33%
HALLMARK_COAGULATION	136	-0.502209567	-1.7131716	5.49E-05	0.000392143	0.000181624	4118	tags=31%, list=17%, signal=26%
HALLMARK_MYC_TARGETS_V1	165	-0.483133051	-1.68229054	7.12E-05	0.00044514	0.00020617	4371	tags=43%, list=18%, signal=36%
HALLMARK_XENOBIOTIC_METABOLISM	189	-0.458627496	-1.616879141	0.000126426	0.000599783	0.000277794	4168	tags=35%, list=17%, signal=29%
HALLMARK_BILE_ACID_METABOLISM	111	-0.51633476	-1.717279723	0.000126476	0.000599783	0.000277794	4894	tags=44%, list=20%, signal=35%
HALLMARK_HEME_METABOLISM	178	-0.461348091	-1.615776326	0.000131952	0.000599783	0.000277794	2853	tags=26%, list=12%, signal=23%
HALLMARK_MYC_TARGETS_V2	51	0.584960812	1.894207379	0.000165795	0.000690814	0.000319956	3581	tags=51%, list=15%, signal=44%
HALLMARK_ESTROGEN_RESPONSE_LATE	191	-0.441418566	-1.558970865	0.000532383	0.002047628	0.000948375	3770	tags=39%, list=15%, signal=33%
HALLMARK_TNFA_SIGNALING_VIA_NFKB	185	0.369851266	1.435026511	0.002667351	0.009526254	0.00441216	2388	tags=25%, list=10%, signal=23%
HALLMARK_PEROXISOME	100	-0.474382794	-1.559911738	0.003178412	0.010594707	0.004907022	4978	tags=50%, list=20%, signal=40%
HALLMARK_GLYCOLYSIS	187	-0.397701058	-1.399293535	0.005473292	0.017104039	0.007921871	3263	tags=33%, list=13%, signal=28%
HALLMARK_INTERFERON_GAMMA_RESPONSE	188	-0.399600864	-1.407577725	0.006384718	0.018778583	0.008697449	4619	tags=39%, list=19%, signal=32%
HALLMARK_ESTROGEN_RESPONSE_EARLY	179	-0.40732484	-1.428327744	0.00728637	0.020071189	0.00929613	4616	tags=42%, list=19%, signal=35%
HALLMARK_KRAS_SIGNALING_UP	186	-0.392343387	-1.380691013	0.007838121	0.020071189	0.00929613	1803	tags=21%, list=7%, signal=20%
HALLMARK_DNA_REPAIR	134	-0.425042603	-1.445729777	0.008028476	0.020071189	0.00929613	5410	tags=44%, list=22%, signal=34%
HALLMARK_APOPTOSIS	157	-0.407543588	-1.412490092	0.008841272	0.021050647	0.009749774	4663	tags=45%, list=19%, signal=37%
HALLMARK_P53_PATHWAY	177	-0.38845323	-1.361025485	0.010492025	0.023845512	0.011044237	4361	tags=38%, list=18%, signal=32%
HALLMARK_INTERFERON_ALPHA_RESPONSE	85	-0.467358559	-1.514063802	0.011266286	0.024491926	0.011343629	4619	tags=45%, list=19%, signal=36%
HALLMARK_ANDROGEN_RESPONSE	91	-0.448259421	-1.456124383	0.014145996	0.028326867	0.013119812	3878	tags=42%, list=16%, signal=35%
HALLMARK_IL2_STAT5_SIGNALING	180	-0.39331732	-1.379268346	0.014163433	0.028326867	0.013119812	4689	tags=36%, list=19%, signal=29%

NMIBC, non-muscle-invasive bladder cancer.

Table S9 Gene set enrichment analysis of NMIBC-female group in GSE13507

ID	Set size	Enrichment score	NES	P value	P.adjust	Qvalues	Rank	Leading edge
HALLMARK_E2F_TARGETS	171	-0.776088779	-2.614570306	1.00E-10	8.33E-10	3.16E-10	2960	tags=71%, list=12%, signal=63%
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION	191	0.565614922	2.330145827	1.00E-10	8.33E-10	3.16E-10	2805	tags=45%, list=12%, signal=40%
HALLMARK_G2M_CHECKPOINT	172	-0.723904873	-2.441124828	1.00E-10	8.33E-10	3.16E-10	3381	tags=59%, list=14%, signal=51%
HALLMARK_MTORC1_SIGNALING	187	-0.609516014	-2.067773306	1.00E-10	8.33E-10	3.16E-10	4567	tags=54%, list=19%, signal=44%
HALLMARK_MYC_TARGETS_V1	165	-0.765531016	-2.565767189	1.00E-10	8.33E-10	3.16E-10	4208	tags=76%, list=17%, signal=63%
HALLMARK_OXIDATIVE_PHOSPHORYLATION	177	-0.608743158	-2.057054864	1.00E-10	8.33E-10	3.16E-10	4022	tags=49%, list=17%, signal=41%
HALLMARK_INTERFERON_GAMMA_RESPONSE	188	-0.578995427	-1.967531255	3.61E-10	2.58E-09	9.78E-10	4765	tags=49%, list=20%, signal=40%
HALLMARK_DNA_REPAIR	134	-0.610795203	-2.007550375	7.95E-10	4.97E-09	1.88E-09	4221	tags=50%, list=17%, signal=42%
HALLMARK_INTERFERON_ALPHA_RESPONSE	85	-0.67044919	-2.09354555	1.77E-09	9.82E-09	3.72E-09	3479	tags=53%, list=14%, signal=46%
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	97	-0.646215803	-2.057706399	6.92E-09	3.46E-08	1.31E-08	4577	tags=51%, list=19%, signal=41%
HALLMARK_KRAS_SIGNALING_UP	186	0.479822645	1.977011152	1.48E-08	6.75E-08	2.56E-08	2989	tags=37%, list=12%, signal=32%
HALLMARK_FATTY_ACID_METABOLISM	146	-0.573788024	-1.901995754	2.77E-08	1.15E-07	4.38E-08	4756	tags=52%, list=20%, signal=42%
HALLMARK_COAGULATION	136	0.497030428	1.953699039	2.30E-07	8.85E-07	3.35E-07	3412	tags=32%, list=14%, signal=27%
HALLMARK_APICAL_JUNCTION	187	0.44626909	1.836345257	4.63E-07	1.65E-06	6.27E-07	2869	tags=30%, list=12%, signal=27%
HALLMARK_MYOGENESIS	191	0.434338633	1.789331068	8.73E-07	2.91E-06	1.10E-06	3806	tags=35%, list=16%, signal=29%
HALLMARK_MITOTIC_SPINDLE	183	-0.513752713	-1.741476401	2.43E-06	7.61E-06	2.88E-06	5544	tags=44%, list=23%, signal=34%
HALLMARK_ANGIOGENESIS	36	0.679887097	2.155090084	1.17E-05	3.45E-05	1.31E-05	2150	tags=42%, list=9%, signal=38%
HALLMARK_TNFA_SIGNALING_VIA_NFKB	185	0.410930681	1.686868897	1.81E-05	5.02E-05	1.90E-05	3362	tags=33%, list=14%, signal=29%
HALLMARK_ADIPOGENESIS	178	-0.488690704	-1.649471403	6.18E-05	0.000162683	6.16E-05	5199	tags=51%, list=21%, signal=41%
HALLMARK_PEROXISOME	100	-0.550591448	-1.756063668	7.88E-05	0.000196993	7.47E-05	3909	tags=43%, list=16%, signal=36%
HALLMARK_P53_PATHWAY	177	0.393978342	1.609003638	0.00013862	0.000330048	0.000125071	3056	tags=30%, list=13%, signal=26%
HALLMARK_MYC_TARGETS_V2	51	-0.61939341	-1.803546659	0.000195342	0.000443959	0.000168237	4452	tags=53%, list=18%, signal=43%
HALLMARK_PROTEIN_SECRETION	91	-0.523409907	-1.651679526	0.000811579	0.001764301	0.000668577	5044	tags=51%, list=21%, signal=40%
HALLMARK_SPERMATOGENESIS	122	-0.474038378	-1.534629411	0.001137864	0.002287275	0.000866757	4823	tags=27%, list=20%, signal=22%
HALLMARK_KRAS_SIGNALING_DN	179	0.35405565	1.454771637	0.001143638	0.002287275	0.000866757	3235	tags=23%, list=13%, signal=20%
HALLMARK_CHOLESTEROL_HOMEOSTASIS	68	-0.548560807	-1.668260357	0.001477391	0.002763106	0.001047072	2443	tags=47%, list=10%, signal=42%
HALLMARK_GLYCOLYSIS	187	-0.444271712	-1.507184662	0.001492077	0.002763106	0.001047072	4567	tags=40%, list=19%, signal=32%
HALLMARK_XENOBIOTIC_METABOLISM	189	-0.434517696	-1.476402142	0.001755408	0.003134656	0.00118787	3909	tags=33%, list=16%, signal=28%
HALLMARK_WNT_BETA_CATENIN_SIGNALING	41	0.536388636	1.74398709	0.002325471	0.004009434	0.001519364	1498	tags=29%, list=6%, signal=28%
HALLMARK_ANDROGEN_RESPONSE	91	-0.50101427	-1.581007544	0.002826262	0.004710437	0.001785008	2800	tags=33%, list=11%, signal=29%
HALLMARK_ALLOGRAFT_REJECTION	186	-0.413677412	-1.401314341	0.009797813	0.015802924	0.005988476	4587	tags=28%, list=19%, signal=23%
HALLMARK_PI3K_AKT_MTOR_SIGNALING	98	-0.453102918	-1.444475416	0.010245909	0.016009233	0.006066657	5144	tags=44%, list=21%, signal=35%

NMIBC, non-muscle-invasive bladder cancer.