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## Supplemental information

# Neoadjuvant immunotherapy, chemotherapy, and combination therapy in muscle-invasive bladder cancer: A multi-center real-world retrospective study

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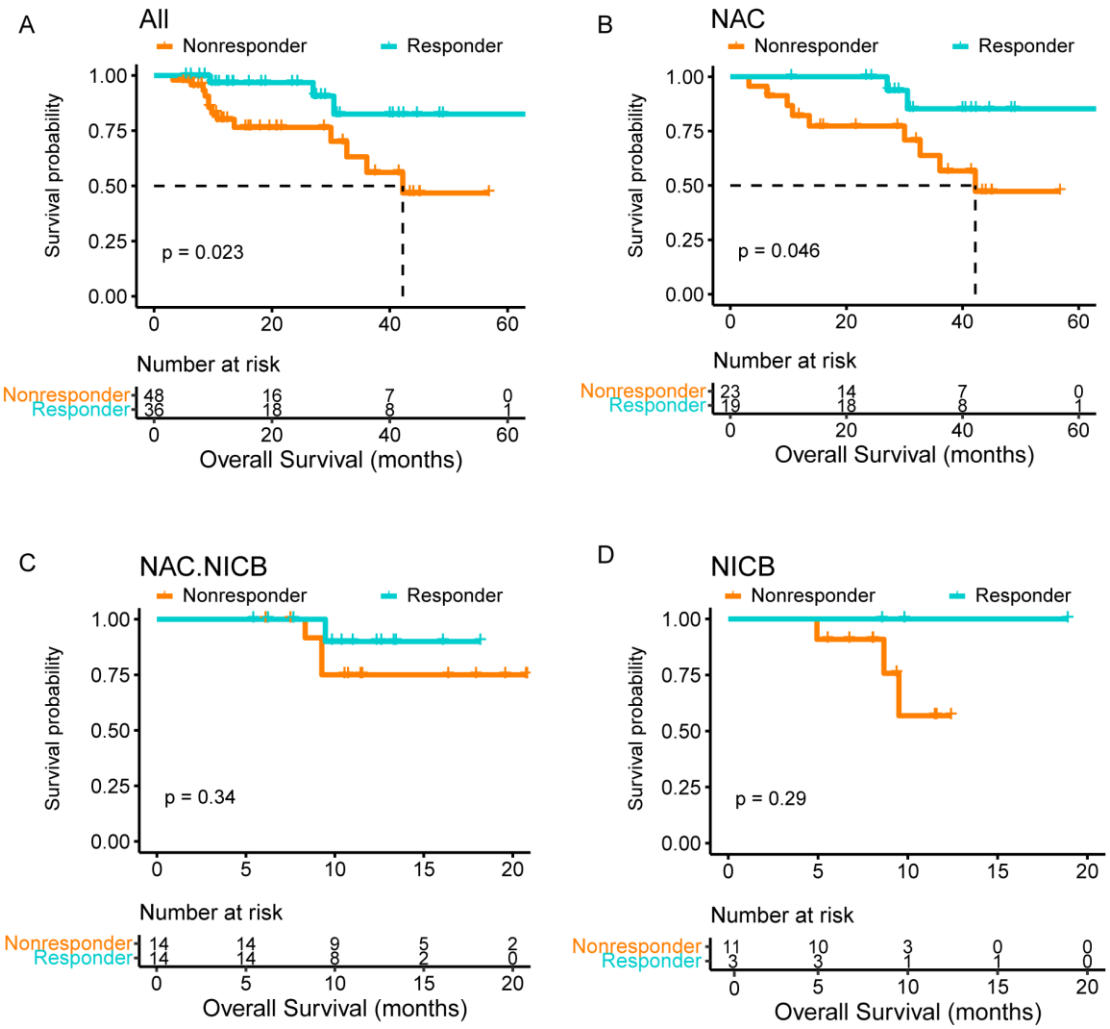


**Figure S1 related to Table 2. Overall survival of patients.**

(A) All cohort

(B) NAC cohort

(C) NAC.NICB cohort, and NICB cohort, stratified by pathologic response.

NAC.NICB: combination of neoadjuvant chemotherapy and immunotherapy; NAC: neoadjuvant chemotherapy; NICB: neoadjuvant immunotherapy;

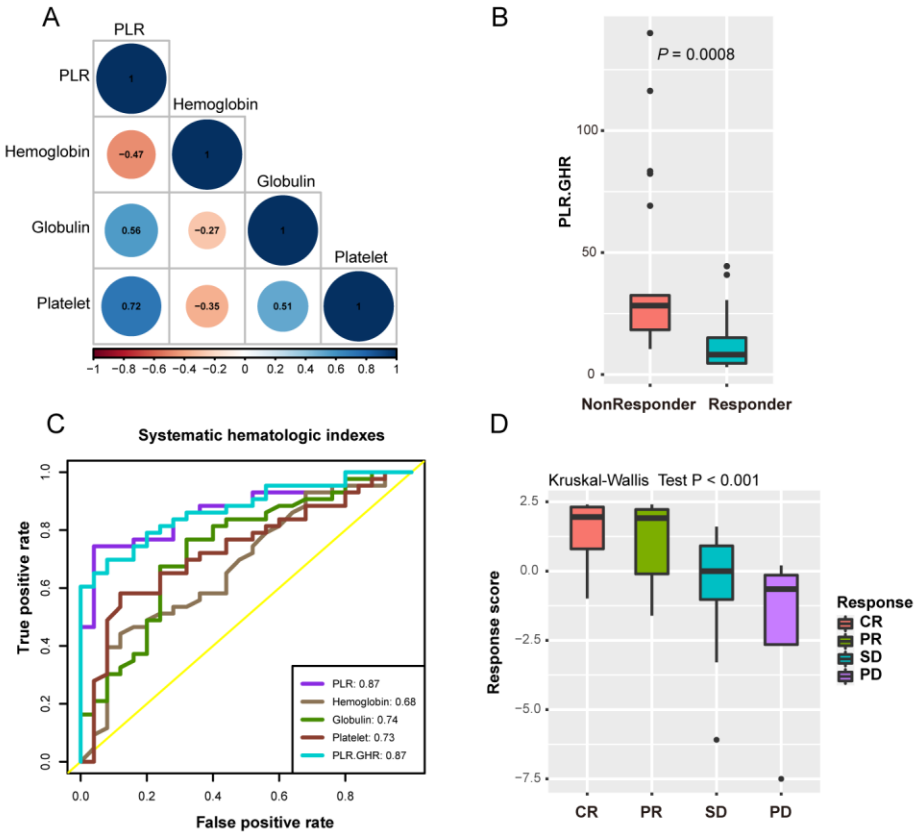


**Figure S2 related to Figure 2. Analysis of potential efficacy predictors during the validation stage.**

**(**A). The spearman correlations between four hematological indicators during the validation stage. brown color represents negative correlation, while blue color represents positive correlation. PLR: platelet-to-lymphocyte ratio.

(B). The PLR.GHR level in Responders and Nonresponders during the validation stage.

(C). ROC curves of five hematological indicators for predicting pathological response during the validation stage.

(D). The distribution of response score between different efficacy subgroups in the validation stage.

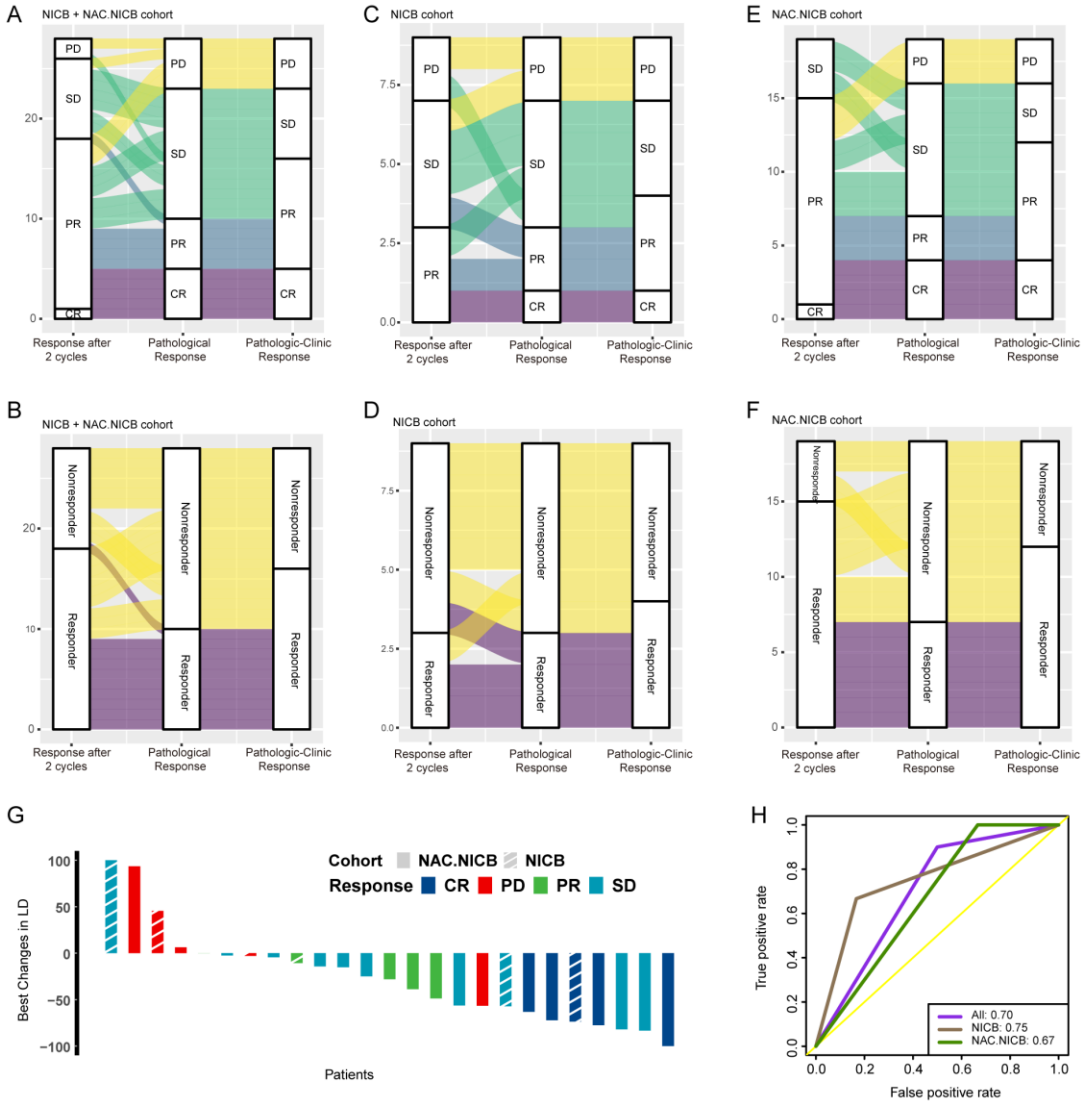


**Figure S3 related to Figure 2. Pathological response prediction with routine contrast-enhanced computed tomography (CT) after two neoadjuvant treatment cycles.**

(A-F) The one-to-one correspondence of radiographic response, pathological response, and pathologic-clinic response in NICB+NAC.NICB cohorts, NICB cohort, and NAC.NICB cohort during the discovery stage.

(G) The changes of the longest diameters during neoadjuvant treatments.

(H) ROC curves of the radiographic response after two treatment cycles for predicting pathological response.

NAC.NICB: combination of neoadjuvant chemotherapy and immunotherapy; NAC: neoadjuvant chemotherapy; NICB: neoadjuvant immunotherapy; CR: complete response; PR: partial response; SD: stable disease; PD: progression disease.

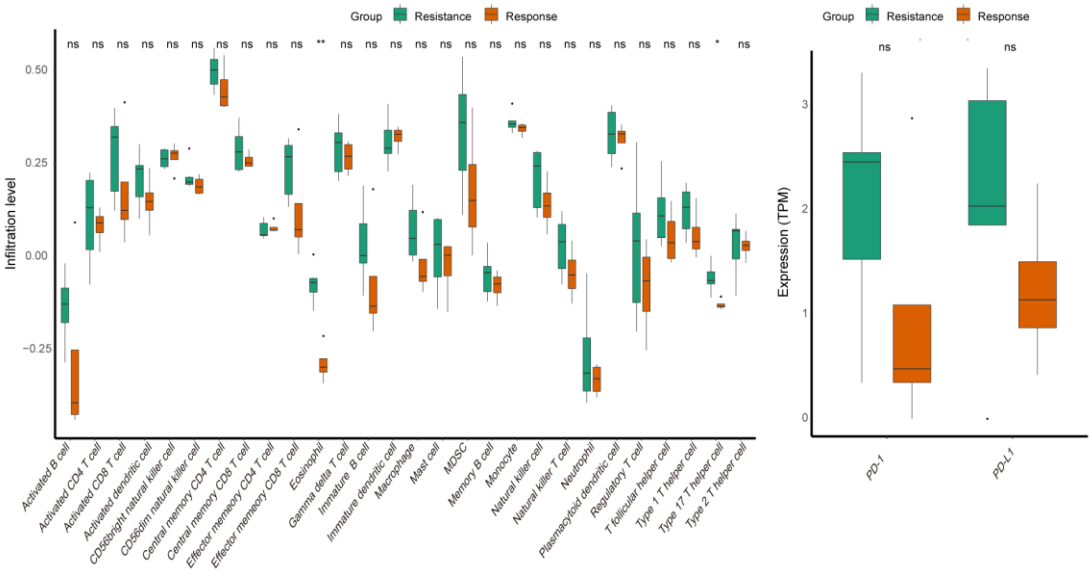


**Figure S4 related to Figure 3. Difference between response and resistance samples regarding the infiltration level of tumor-associated immune cells and the expression of PD-L1/PD-1.**

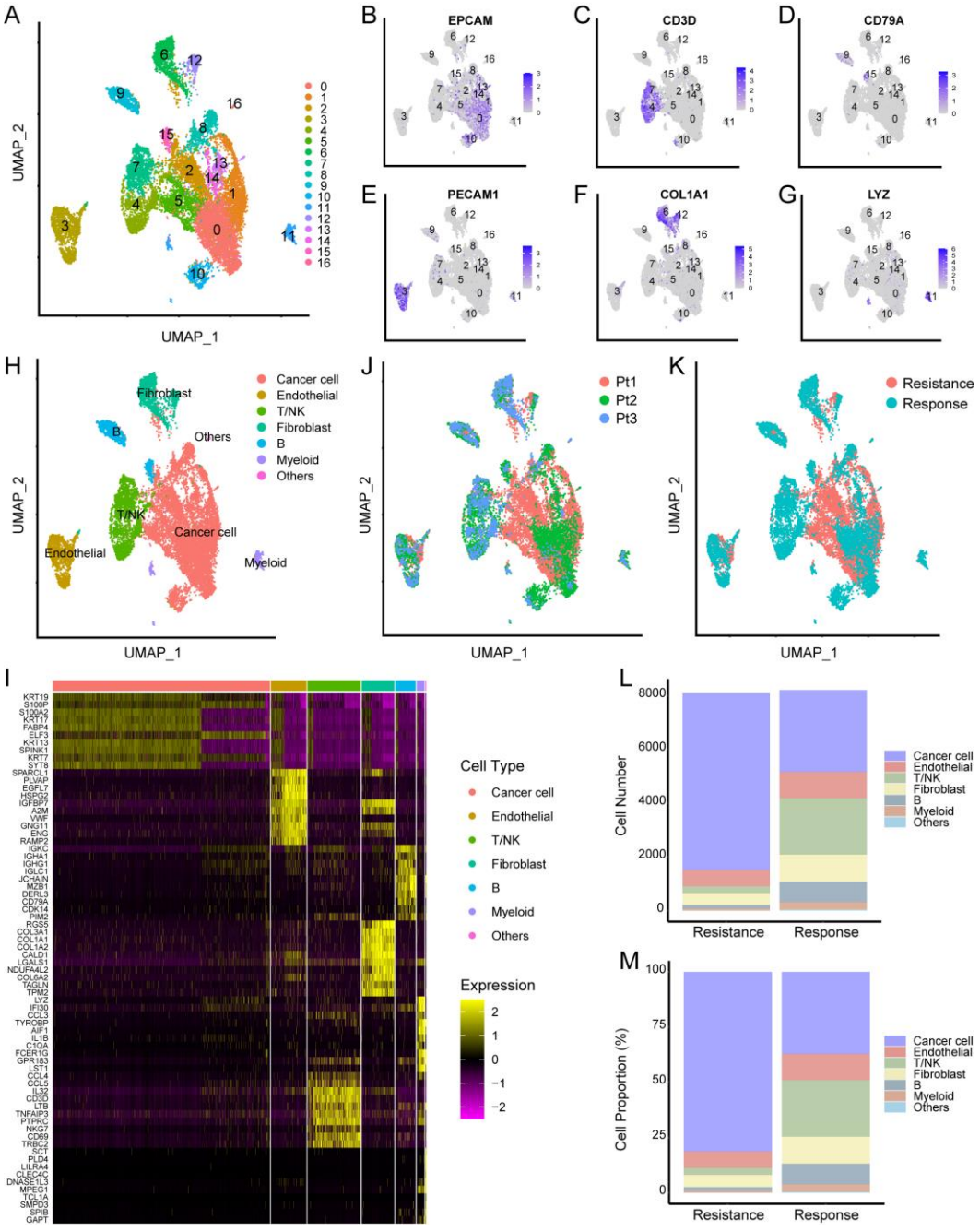


**Figure S5 related to Figure 4. Identifying cell types and comparing the difference on the proportions of cells between response and resistance groups.**

(A) UMAP plot of single cells profiled in the presenting work colored by clusters.

(B-G) Expression of marker genes for six major cell types. Bladder cancer epithelial cells: EPCAM; Endothelial cells: PECAM1; Fibroblasts: COL1A1; B cells: CD79A; Myeloid cells: LYZ; T/NK cells: CD3D.

(H-K) UMAP plot single cells colored by cell types, patients, and NICB efficacy. (I) Heatmap of top 10 marker genes of every major cell types.

(L-M) Histogram indicating the counts and proportions of main cell types in NICB resistance and

response groups.

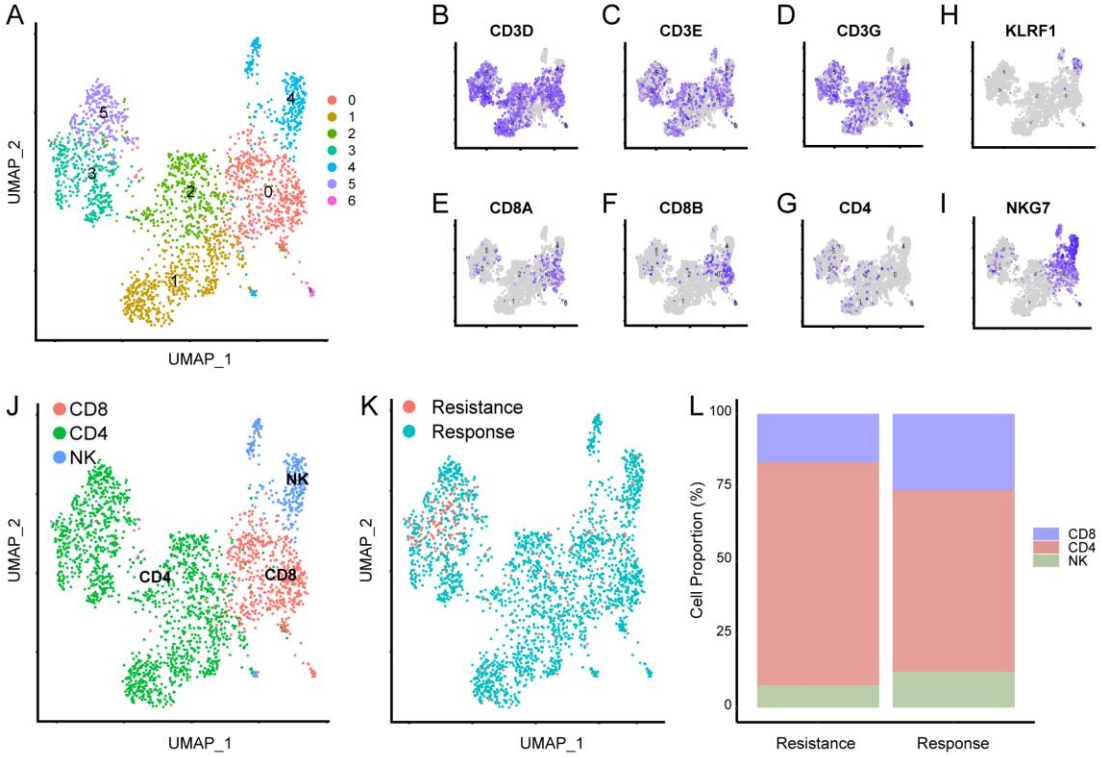


**Figure S6 related to Figure 4. Reclustering of T/NK cells in the NICB cohort.**

(A) UMAP plot of subgroups of T/NK cells.

(B-I) Expression of marker genes for three major cell types. T cells: CD3D, CD3E, CD3G; CD8 T cells: CD8A, CD8B; CD4 T cells: CD4; NK cells: KLRF1, NKG7.

(J-K) UMAP plot T/NK cells colored by cell types and NICB efficacy.

(L) Histogram indicating the proportions of three cell types in NICB resistance and response groups.

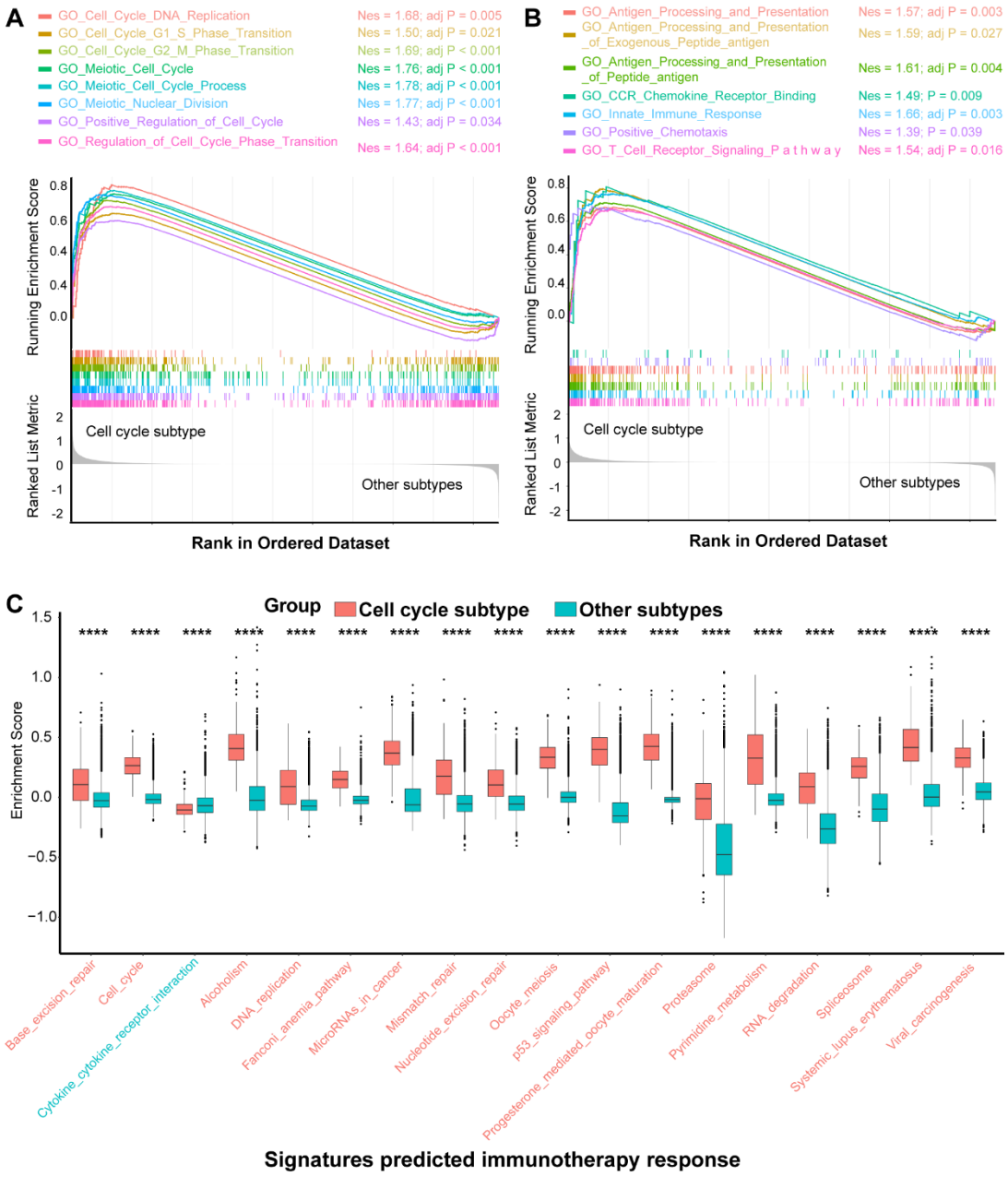


**Figure S7 related to Figure 4. GSEA analysis in the NICB cohort.**

(A) GSEA showed that several cell cycle related pathways and (B) several critical immune related pathways significantly enriched in Cell cycle subtype.
(C) The difference of enrichment scores of 19 immunotherapy efficacy associated signatures between Cell cycle subtype and other subtypes.

**Table S1. Treatment related adverse events during the discovery stage, Related to Table 2**

| | NAC.NICB (*n* = 21) | | NICB (*n* = 9) | |
|---|---|---|---|---|
| **Treatment Related Adverse Events** | **Grade 1-2** | **Grade 3** | **Grade 1-2** | **Grade 3** |
| Anemia | 4 (19%) | 2 ( 9.5%) | 0 | 0 |
| Decreased neutrophil count | 3 (14.3%) | 3 (14.3%) | 0 | 1 ( 11.1%) |
| Decreased white blood cell count | 6 (28.6%) | 0 | 0 | 0 |
| Decreased platelet count | 5 (23.8%) | 2 ( 9.5%) | 0 | 0 |
| Decreased appetite | 8 (38%) | 0 | 2 ( 22.2%) | 0 |
| Fatigue | 5 (23.8%) | 0 | 0 | 0 |
| Nausea | 8 (38.1%) | 2 ( 9.5%) | 1 ( 11.1%) | 0 |
| Pruritus | 9 ( 42.9%) | 0 | 1 ( 11.1%) | 0 |
| Hypothyroidism | 2 ( 9.5%) | 1 ( 4.8%) | 1 ( 11.1%) | 1 ( 11.1%) * |

Abbreviations: NAC.NICB: combination of neoadjuvant chemotherapy and immunotherapy; NICB: neoadjuvant immunotherapy;

*: Represents a grade 4 adverse event.

**Table S2. Associations between clinicopathological characteristics and pathological response in NAC.NICB cohort during the discovery stage, Related to Table 3**

| Characteristics | Level | Overall (N = 28) | Nonresponder (N = 14) | Responder (N = 14) | P value |
|---|---|---|---|---|---|
| Age (years) (mean (SD)) | | 59.89 (9.64) | 60.00 (11.75) | 59.79 (7.40) | 0.954 |
| Gender (%) | Female | 5 (17.9) | 4 (28.6) | 1 (7.1) | 0.326 |
| | Male | 23 (82.1) | 10 (71.4) | 13 (92.9) | |
| BMI (kg/m2) (mean (SD)) | | 23.51 (2.86) | 23.44 (2.83) | 23.58 (2.99) | 0.9 |
| Previous TURBT (%) | No | 23 (82.1) | 10 (71.4) | 13 (92.9) | 0.326 |
| | Yes | 5 (17.9) | 4 (28.6) | 1 (7.1) | |
| Previous NMIBC (%) | No | 24 (85.7) | 11 (78.6) | 13 (92.9) | 0.596 |
| | Yes | 4 (14.3) | 3 (21.4) | 1 (7.1) | |
| Previous BCG instillations (%) | No | 28 (100.0) | 14 (100.0) | 14 (100.0) | NA |
| Smoking status (%) | Nonsmoker | 9 (32.1) | 7 (50.0) | 2 (14.3) | 0.103 |
| | Smoker | 19 (67.9) | 7 (50.0) | 12 (85.7) | |
| Scr (umol/L) (median [IQR]) | | 84.00 [76.35, 88.75] | 84.60 [73.65, 97.60] | 81.05 [78.50, 87.45] | 0.713 |
| Concomitant Antibiotic Therapy (%) | No | 16 (57.1) | 9 (64.3) | 7 (50.0) | 0.414 |
| | Cephalosporin | 4 (14.3) | 1 (7.1) | 3 (21.4) | |
| | Quinolone | 2 (7.1) | 0 (0.0) | 2 (14.3) | |
| | Penicillin | 5 (17.9) | 3 (21.4) | 2 (14.3) | |
| | Quinolone and cephalosporin | 1 (3.6) | 1 (7.1) | 0 (0.0) | |
| Grade (%) | High grade | 24 (85.7) | 13 (92.9) | 11 (78.6) | 0.596 |
| | Low grade | 4 (14.3) | 1 (7.1) | 3 (21.4) | |
| History of systemic disease (%) | No | 12 (42.9) | 7 (50.0) | 5 (35.7) | 0.703 |
| | Yes | 16 (57.1) | 7 (50.0) | 9 (64.3) | |

| | | | | | |
|---|---|---|---|---|---|
| Hypertension (%) | No | 18 (64.3) | 10 (71.4) | 8 (57.1) | 0.695 |
| | Yes | 10 (35.7) | 4 (28.6) | 6 (42.9) | |
| Hydronephrosis (%) | No | 22 (78.6) | 9 (64.3) | 13 (92.9) | 0.165 |
| | Yes | 6 (21.4) | 5 (35.7) | 1 (7.1) | |
| Diabetes (%) | No | 25 (89.3) | 13 (92.9) | 12 (85.7) | 1 |
| | Yes | 3 (10.7) | 1 (7.1) | 2 (14.3) | |
| Urolithiasis (%) | No | 26 (92.9) | 13 (92.9) | 13 (92.9) | 1 |
| | Yes | 2 (7.1) | 1 (7.1) | 1 (7.1) | |
| WBC (median [IQR]) | | 6.80 [5.70, 7.90] | 6.20 [5.70, 7.78] | 6.90 [6.30, 8.80] | 0.576 |
| Neutrophil (median [IQR]) | | 4.05 [3.30, 5.05] | 3.65 [3.30, 4.95] | 4.20 [3.70, 5.00] | 0.528 |
| Lymphocyte (median [IQR]) | | 1.60 [1.30, 2.06] | 1.50 [1.30, 1.95] | 1.70 [1.30, 2.10] | 0.435 |
| Eosinophil (median [IQR]) | | 0.20 [0.14, 0.28] | 0.20 [0.20, 0.29] | 0.20 [0.10, 0.26] | 0.362 |
| Monocyte (median [IQR]) | | 0.70 [0.55, 0.70] | 0.70 [0.52, 0.77] | 0.60 [0.60, 0.70] | 0.603 |
| Albumin (mean (SD)) | | 38.39 (3.36) | 38.19 (4.02) | 38.60 (2.62) | 0.76 |
| Procalcitonin (median [IQR]) | | 0.04 [0.04, 0.06] | 0.04 [0.04, 0.06] | 0.05 [0.04, 0.06] | 0.914 |
| CA 125 (median [IQR]) | | 10.11 [7.90, 15.06] | 9.28 [7.95, 11.48] | 13.05 [8.51, 23.86] | 0.491 |
| CEA (median [IQR]) | | 2.83 [1.87, 5.36] | 2.50 [1.70, 5.31] | 3.30 [2.28, 5.05] | 0.368 |
| CA242 (median [IQR]) | | 6.04 [4.72, 7.06] | 6.57 [4.69, 8.06] | 4.83 [4.72, 6.54] | 0.643 |
| AFP (mean (SD)) | | 3.88 (1.87) | 3.26 (1.65) | 4.69 (1.95) | 0.135 |
| HCGβ (mean (SD)) | | 12.65 (6.29) | 11.59 (8.38) | 13.86 (2.72) | 0.508 |
| Cytokeratin 19 fragment (mean (SD)) | | 8.25 (5.13) | 9.89 (5.80) | 6.14 (3.44) | 0.154 |
| NLR (median [IQR]) | | 2.75 [2.00, 3.00] | 2.86 [2.30, 2.98] | 2.47 [1.92, 3.00] | 0.698 |
| MLR (median [IQR]) | | 0.36 [0.30, 0.47] | 0.41 [0.33, 0.47] | 0.32 [0.25, 0.41] | 0.207 |
| dNLR (median [IQR]) | | 1.59 [1.35, 1.89] | 1.60 [1.33, 1.89] | 1.56 [1.42, 1.83] | 0.827 |
| PIV (median [IQR]) | | 347.62 [214.91, 624.80] | 388.19 [241.31, 717.52] | 326.86 [150.82, 441.66] | 0.332 |
| CII (median [IQR]) | | 325.26 [251.85, 494.01] | 327.21 [231.68, 478.85] | 325.26 [270.69, 471.52] | 0.734 |

BMI: body mass index; TURBT: transurethral resection of the bladder tumor; NMIBC: non-muscle invasive bladder cancer ; BCG: Bacillus Calmette Guerin; WBC: white blood cell; NLR: neutrophil-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio; dNLR: derived neutrophil-to-lymphocyte ratio, equals to absolute neutrophil count/[white blood cell concentration - absolute neutrophil count]; PIV: Pan-Immune-Inflammation Value, equals to [neutrophil count × platelet count × monocyte count]/lymphocyte count; CII : cancer inflammation index, equals to BMI × serum albumin/NLR.

**Table S3. Baseline characteristics of patients who received bladder preservation therapy, Related to Table 2**

| | Overall | Recurrence | | P |
|---|---|---|---|---|
| | (N = 33) | No (N = 31) | Yes (N = 2) | value |
| Neoadjuvant treatment group | | | | 1 |
| NAC.NICB | 10 (30.3%) | 9 (29.0%) | 1 (50.0%) | |
| NAC | 15 (45.5%) | 14 (45.2%) | 1 (50.0%) | |
| NICB | 8 (24.2%) | 8 (25.8%) | 0 (0%) | |
| Follow up time (months) | | | | 0.081 |
| Median (IQR) | 13.00 (4.00, 16.00) | 11.00 (4.00, 14.50) | 21.50 (20.75, 22.25) | |
| Pathological Response | | | | **0.055** |
| CR | 17 (51.5%) | 17 (54.8%) | 0 (0%) | |
| PR | 14 (42.4%) | 13 (41.9%) | 1 (50.0%) | |
| SD | 2 (6.1%) | 1 (3.2%) | 1 (50.0%) | |
| Age (years) | | | | 0.455 |
| Mean (SD) | 63.3 (11.0) | 62.9 (10.9) | 69.0 (15.6) | |
| Gender | | | | 1 |
| Female | 4 (12.1%) | 4 (12.9%) | 0 (0%) | |
| Male | 29 (87.9%) | 27 (87.1%) | 2 (100%) | |
| BMI ($kg/m^2$) | | | | 0.285 |
| Mean (SD) | 23.7 (3.29) | 23.6 (3.32) | 26.2 (1.16) | |
| Previous NMIBC | | | | 1 |
| No | 28 (84.8%) | 26 (83.9%) | 2 (100%) | |
| Yes | 5 (15.2%) | 5 (16.1%) | 0 (0%) | |
| Previous BCG instillations | | | | 1 |
| No | 31 (93.9%) | 29 (93.5%) | 2 (100%) | |
| Yes | 2 (6.1%) | 2 (6.5%) | 0 (0%) | |
| Smoking status | | | | 1 |
| Nonsmoker | 12 (36.4%) | 11 (35.5%) | 1 (50.0%) | |
| Smoker | 21 (63.6%) | 20 (64.5%) | 1 (50.0%) | |
| Clinical Stage | | | | 0.208 |
| T2N0M0 | 19 (57.6%) | 19 (61.3%) | 0 (0%) | |
| T3N0M0 | 13 (39.4%) | 11 (35.5%) | 2 (100%) | |
| ≥T4N0M0 | 1 (3.0%) | 1 (3.2%) | 0 (0%) | |
| Grade | | | | 0.477 |
| High grade | 24 (72.7%) | 23 (74.2%) | 1 (50.0%) | |
| Low grade | 9 (27.3%) | 8 (25.8%) | 1 (50.0%) | |
| Histology variants | | | | NA |
| UC | 33 (100%) | 31 (100%) | 2 (100%) | |
| Neoadjuvant treatment sequence | | | | 0.125 |
| NAC | 10 (30.3%) | 9 (29.0%) | 1 (50.0%) | |
| NICB | 8 (24.2%) | 8 (25.8%) | 0 (0%) | |

| | | | | |
|---|---|---|---|---|
| NAC-before-NICB | 2 (6.1%) | 1 (3.2%) | 1 (50.0%) | |
| NICB-before-NAC | 3 (9.1%) | 3 (9.7%) | 0 (0%) | |
| NICB-concur-NAC | 10 (30.3%) | 10 (32.3%) | 0 (0%) | |
| Neoadjuvant treatment cycles | | | | 1 |
| Long course | 21 (63.6%) | 20 (64.5%) | 1 (50.0%) | |
| Short course | 12 (36.4%) | 11 (35.5%) | 1 (50.0%) | |
| Treatment maintenance after TURBT | | | | 1 |
| No | 6 (18.2%) | 6 (19.4%) | 0 (0%) | |
| Yes | 27 (81.8%) | 25 (80.6%) | 2 (100%) | |
| Dead | | | | 0.061 |
| No | 32 (97.0%) | 31 (100%) | 1 (50.0%) | |
| Yes | 1 (3.0%) | 0 (0%) | 1 (50.0%) | |

NAC.NICB: combination of neoadjuvant chemotherapy and immunotherapy; NAC: neoadjuvant chemotherapy; NICB: neoadjuvant immunotherapy; UC: urothelial carcinoma; NMIBC: non-muscle invasive bladder cancer; TURBT: transurethral resection of the bladder tumor; BMI: body mass index; BCG: Bacillus Calmette Guerin; CR: complete response; PR: partial response; SD: stable disease.

**Table S6. Correlations between neoadjuvant treatment cycles and efficacy, Related to Table 3**

| Neoadjuvant treatment group | | Nonresponder | Responder | P value |
|---|---|---|---|---|
| NAC.NICB | Long course | 26 (66.7%) | 42 (71.2%) | 0.802 |
| | Short course | 13 (33.3%) | 17 (28.8%) | |
| NAC | Long course | 11 (18.0%) | 13 (28.3%) | 0.307 |
| | Short course | 50 (82.0%) | 33 (71.7%) | |
| NICB | Long course | 15 (48.4%) | 7 (41.2%) | 0.860 |
| | Short course | 16 (51.6%) | 10 (58.8%) | |

Abbreviations: NAC.NICB: combination of neoadjuvant chemotherapy and immunotherapy; NICB: neoadjuvant immunotherapy;

**Table S7. Detailed information of signatures included in our study, Related to Figure 3**

| Signatures | Reference | Description | Genes |
|---|---|---|---|
| Alcoholism | PMID: 29443960 | Immunotherapy response signature | CREB3L4, H2AFV, H2AFZ, HIST1H2AB, HIST1H2AG, HIST1H2AH, HIST1H2AI, HIST1H2AM, HIST1H2BC, HIST1H2BD, HIST1H2BF, HIST1H2BJ, HIST1H2BK, HIST1H2BL, HIST1H2BN, HIST1H2BO, HIST1H3B, HIST1H3D, HIST1H3H, HIST1H4A, HIST1H4B, HIST2H2AB, HIST2H2AC, HIST2H2BE, HIST2H2BF, HIST2H3D, HIST3H2A |
| Base_excision_repair | PMID: 29443960 | Immunotherapy response signature | FEN1, LIG1, NEIL3, PARP1, PARP2, PCNA, POLE, POLE2, UNG |
| Cell_cycle | PMID: 29443960 | Immunotherapy response signature | BUB1, BUB1B, CCNA2, CCNB2, CCNE1, CCNE2, CDC20, CDC25A, CDC25C, CDC6, CDK1, CDK2, CDKN2A, DBF4, E2F1, E2F2, ESPL1, MAD2L1, MAD2L2, MCM2, MCM4, MCM6, MCM7, ORC1, ORC6, PCNA, PLK1, SKP2, SMC3, TFDP1, TTK, YWHAB |
| Cytokine-cytokine_receptor_interaction | PMID: 29443960 | Immunotherapy resistance signature | ACVR1, CCL24, FLT4, IFNGR1, IL4R, IL6ST, KIT, LIF, PDGFA, PDGFRB, TGFB1, TGFBR2, TNFRSF10B, TNFRSF14, TNFRSF1A |
| DNA_replication | PMID: 29443960 | Immunotherapy response signature | DNA2, FEN1, LIG1, MCM2, MCM4, MCM6, MCM7, PCNA, POLA2, POLE, POLE2, PRIM1, PRIM2, RFC2, RFC3, RFC4, RFC5, RNASEH2A, RPA1, RPA3 |
| Fanconi_anemia_pathway | PMID: 29443960 | Immunotherapy response signature | BLM, BRCA1, BRCA2, BRIP1, EME1, ERCC4, FANCA, FANCB, FANCD2, FANCI, PALB2, RAD51, RAD51C, RMI1, RMI2, RPA1, RPA3, TOP3A, UBE2T |
| Homologous_recombination | PMID: 29443960 | Immunotherapy response signature | BLM, BRCA2, EME1, RAD51, RAD51C, RAD54L, RPA1, RPA3, TOP3A, XRCC2, XRCC3 |
| MicroRNAs_in_cancer | PMID: 29443960 | Immunotherapy response signature | BRCA1, CCNE1, CCNE2, CDC25A, CDC25C, CDCA5, CDKN2A, DNMT1, E2F1, E2F2, EZH2, KIF23, STMN1, TRIM71 |
| Mismatch_repair | PMID: 29443960 | Immunotherapy response signature | EXO1, LIG1, PCNA, RFC2, RFC3, RFC4, RFC5, RPA1, RPA3 |
| Nucleotide_excision_repair | PMID: 29443960 | Immunotherapy response signature | CETN2, ERCC4, LIG1, PCNA, POLE, POLE2, RFC2, RFC3, RFC4, RFC5, RPA1, RPA3 |

| | | | |
|---|---|---|---|
| Oocyte_meiosis | PMID: 29443960 | Immunotherapy response signature | AURKA, BUB1, CCNB2, CCNE1, CCNE2, CDC20, CDC25C, CDK1, CDK2, ESPL1, FBXO5, MAD2L1, MAD2L2, PLK1, SGOL1, SMC3, YWHAB |
| p53_signaling_pathway | PMID: 29443960 | Immunotherapy response signature | CCNB2, CCNE1, CCNE2, CDK1, CDK2, CDKN2A, GTSE1, PPM1D, RFWD2, RRM2 |
| Progesterone-mediated_oocyte_maturation | PMID: 29443960 | Immunotherapy response signature | BUB1, CCNA2, CCNB2, CDC25A, CDC25C, CDK1, CDK2, MAD2L1, MAD2L2, PLK1 |
| Proteasome | PMID: 29443960 | Immunotherapy response signature | IFNG, PSMA4, PSMB2, PSMB4, PSMC4, PSMD4, PSMD7 |
| Pyrimidine_metabolism | PMID: 29443960 | Immunotherapy response signature | CTPS1, DTYMK, POLA2, POLE, POLE2, PRIM1, PRIM2, RRM2, TYMS |
| RNA_degradation | PMID: 29443960 | Immunotherapy response signature | CNOT10, EXOSC2, EXOSC8, LSM3, LSM4, LSM5, PARN |
| Spliceosome | PMID: 29443960 | Immunotherapy response signature | HNRNPM, LSM3, LSM4, LSM5, MAGOHB, PRPF19, SF3B2, SF3B3, SF3B4, SNRNP40, SNRPA1, SNRPC, USP39, WBP11 |
| Systemic_lupus_erythematosus | PMID: 29443960 | Immunotherapy response signature | H2AFV, H2AFZ, HIST1H2AB, HIST1H2AG, HIST1H2AH, HIST1H2AI, HIST1H2AM, HIST1H2BC, HIST1H2BD, HIST1H2BF, HIST1H2BJ, HIST1H2BK, HIST1H2BL, HIST1H2BN, HIST1H2BO, HIST1H3B, HIST1H3D, HIST1H3H, HIST1H4A, HIST1H4B, HIST2H2AB, HIST2H2AC, HIST2H2BE, HIST2H2BF, HIST |
| Viral_carcinogenesis | PMID: 29443960 | Immunotherapy response signature | CCNA2, CCNE1, CCNE2, CDC20, CDK1, CDK2, CDKN2A, CREB3L4, GTF2E1, HIST1H2BC, HIST1H2BD, HIST1H2BF, HIST1H2BJ, HIST1H2BK, HIST1H2BL, HIST1H2BN, HIST1H2BO, HIST1H4A, HIST1H4B, HIST2H2BE, HIST2H2BF, SKP2, YWHAB |

| | | | |
|---|---|---|---|
| NAC response signature | PMID: 26230923 | NAC response signature | ZNF486,ZNF321,ACAP3,C6ORF134,FMO9P,RHBG,GDPD3,SCNN1B,OSBPL11,ZNF107,WDR90,CRKL,RB1,ATM,FANCC,ERBB2,ERCC2 |
| NAC resistance signature | PMID: 26230923 | NAC resistance signature | HTRA1,RRAS,ANKH,KLF2,CCPG1,C9ORF125,SPRED1,TFEB,NRARP,SDR16C5,IPO7,SPRY1,LIN7C,SLC22A18,PNPO |
| EMT2 | PMID: 26997480 | Stromal signature | AXL, FAP, LOXL2, ROR2, TAGLN, TWIST2, WNT5A |
| EMT3 | PMID: 27321955 | Stromal signature | FOXF1, GATA6, SOX9, TWIST1, ZEB1, ZEB2 |
| Angiogensis | PMID: 29443960 | Stromal signature | CDH5, SOX17, SOX18, TEK |
| Pan-F-TBRS | PMID: 29443960 | Stromal signature | ACTA2,ACTG2,ADAM12,ADAM19, CNN1, COL4A1,CTGF,CTPS1,FAM101B,FSTL3,HSPB1,IGFBP3,PXDC1,SEMA7A,SH3PXD2A, TAGLN,TGFBI,TNS1,TPM1 |

NAC: neoadjuvant chemotherapy; EMT: epithelial interstitial transition; Pan-F-TBRS: panfibroblast TGFβ response signature.