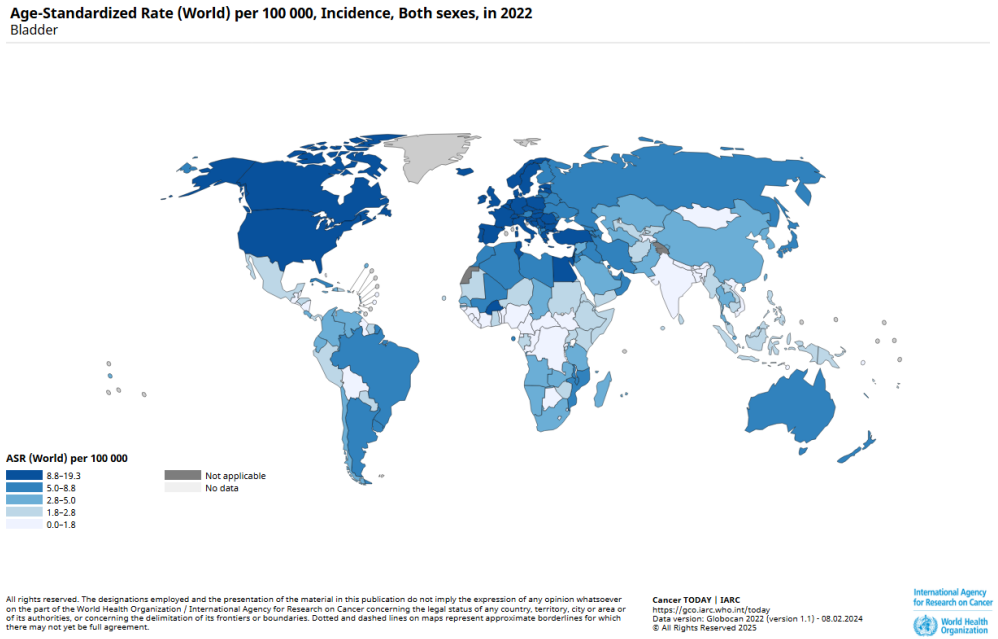
Neoadjuvant immunotherapy driven bladder preservation for muscle invasive bladder cancer

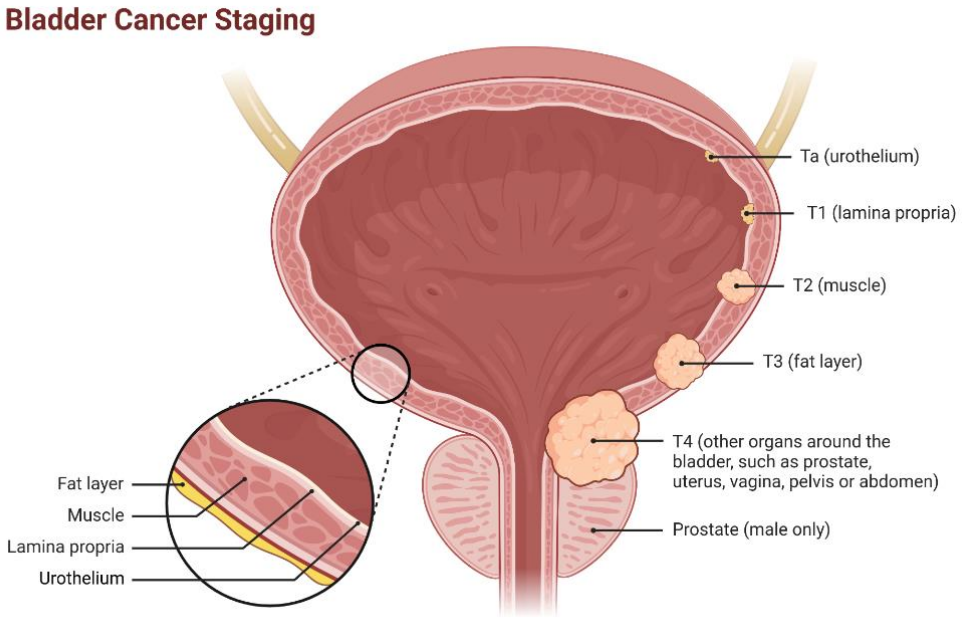
Jiao Hu[1,2,17,#], Luzhe Yan[1,2,17,#], Jinhui Liu[1,2,17,#], Minfeng Chen[1,2,17,#], Yunbo He[1,2,17,#], Benyi Fan[1,2,17], Bo Peng[3], Long Wang[4], Weibin Hou[4], Chao Li[4], Bosen You[5], Meng Zhang[6], Wenze Li[7,17], Jiaxing Wang[7], Hongzhou Cai[8], Shenglin Gao[9], Yang Liu[10], Dingshan Deng[1,2,17], Huihuang Li[1,2,17], Guanghui Gong[11], Jiansheng Tang[12], Chengyong Wang[13], Xiaofeng Yang[14], Liang Wei[14], Guangzheng Lin[15], Ruizhe Wang[1,2,17], Xiao Guan[1,2,17], Shiyu Tong[1,2,17], Yangle Li[1,2,17], Wei He[1,2,17], Zhiyong Cai[1,2,17], Peihua Liu[1,2,17], Yu Gan[1,2,17], Yu Cui[1,2,17], Yuanqing Dai[1,2,17], Yi Cai[1,2,17], Zefu Liu[1,2,17], Jiatong Xiao[1,2,17], Zhenyu Nie[1,2,17], Zhenyu Ou[1,2,17], Jinbo Chen[1,2,17,], Xi Guo[16,], Xiongbing Zu[1,2,16,17,*]

1Department of Urology, Xiangya Hospital, Central South University, Changsha, China
2National Clinical Research Center for Geriatric Disorders, Xiangya Hospital, Central South University, Changsha, China
3Department of Urology, Zhangjiajie People's Hospital, Zhangjiajie, China
4Department of Urology, The Third Xiangya Hospital, Central South University, Changsha,China
5Department of Urology, The Second Affiliated Hospital of Harbin Medical University, Harbin, China
6Department of Urology, The First Affiliated Hospital of Anhui Medical University, China
7Department of Urology, The First People's Hospital of Xiangtan City, Xiangtan, China
8Department of Urology, Jiangsu Cancer Hospital & The Affiliated Cancer Hospital of Nanjing Medical University & Jiangsu Institute of Cancer Research, Nanjing Medical University, Nanjing, China
9Department of Urology, The Affiliated Changzhou Second People's Hospital of Nanjing Medical University, Changzhou, China
10Department of Urology and Guangdong Key Lab of Urology, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China
11Department of Pathology, Xiangya Hospital, Central South University, Changsha, China
12Department of Urology, The Affiliated Hospital of Xiangnan University, Xiangnan University, Chenzhou, China
13Department of Urology, The First Affiliated Hospital of Bengbu Medical College, Anhui, Bengbu,China
14Department of Urology, First Hospital of Shanxi Medical University, Taiyuan, China
15Department of Urology, The Second Hospital of Anhui Medical University, Hefei, China
16Department of Urology, Hunan Provincial People's Hospital, the First Affiliated Hospital of Hunan Normal University, Changsha, China
17Furong Laboratory, Changsha, China

Jiao Hu, Luzhe Yan, Jinhui Liu, Minfeng Chen, Yunbo He, Benyi Fan, Bo Peng, et al. 2025. Neoadjuvant immunotherapy driven bladder preservation for muscle invasive bladder cancer. ***iMeta*** 4: e70063. https://doi.org/10.1002/imt2.70063

Background

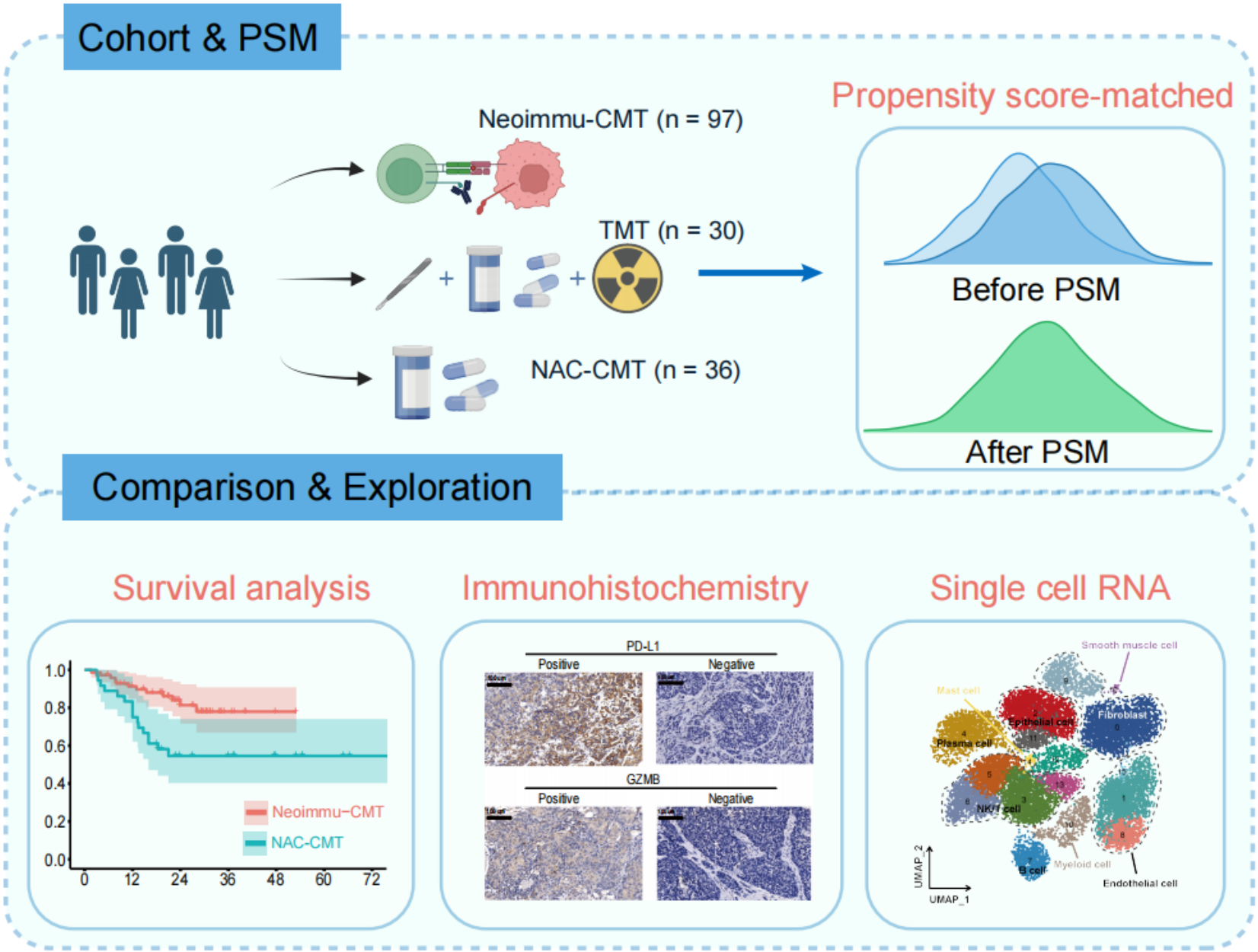




- Bladder cancer is one of the ten most common cancers worldwide.
- Radical cystectomy significantly impacts patients' quality of life.
- In recent years, multimodal treatment approaches aimed at bladder preservation have gained increasing attention.
- Bladder-preserving strategies based on neoadjuvant immunotherapy have shown promising potential.

Nature reviews Urology. 2011, 8(11): 631-42.

Highlight



- **Bladder-preserving therapy driven by neoadjuvant immunotherapy for muscle-invasive bladder cancer demonstrates significant clinical application potential in the field of bladder-sparing treatments.**
- **A systematic and feasible immune therapy-based bladder-sparing treatment protocol has been proposed.**
- **This is the first article in the field of bladder-sparing treatment that explores the tumor microenvironment using single-cell sequencing to identify sensitive patients.**

Outcome

Study Design and Patient Inclusion and Exclusion Criteria

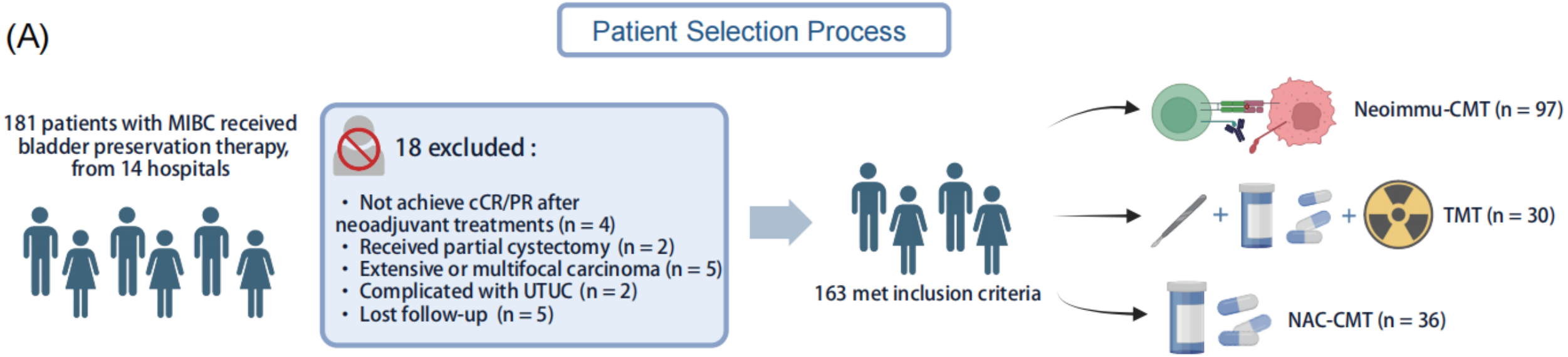


Figure 1. (A) Patient selection process.

Outcome

Efficacy comparison of Neoimmu-CMT VS TMT / NAC-CMT

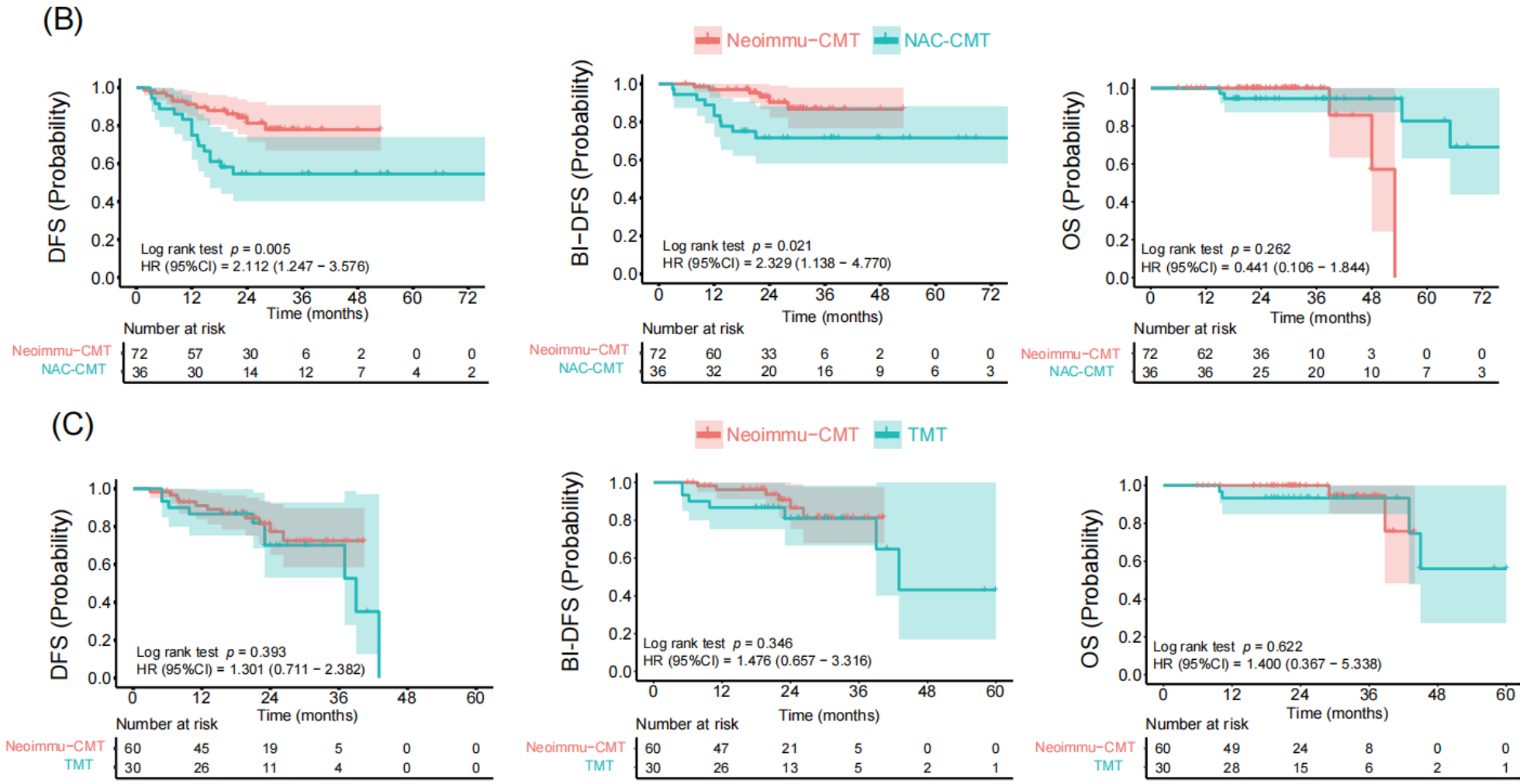


Figure 1. (B) Neoimmu-CMT demonstrates superiority over NAC-CMT; (C) Neoimmu-CMT shows comparability to TMT.

Outcome

Cox Analysis of Efficacy-Related Factors in Neoimmu-CMT

Variable	Univariable Cox DFS				Multivariable Cox DFS			
	HR	95% CI Lower	95% CI Upper	P value	HR	95% CI Lower	95% CI Upper	P value
Neoadjuvant therapy								
Immunotherapy	Reference				Reference			
Chemoimmunotherapy	0.660	0.222	1.967	0.456	0.769	0.255	2.323	0.642
ADC combined with Immunotherap	0.967	0.189	4.936	0.968	1.283	0.224	7.359	0.780
Clinical T stage								
Low stage	Reference				Reference			
High stage	2.463	0.873	6.953	**0.089**	3.238	1.036	10.118	**0.043**
Response to neoadjuvant therapy								
cCR	Reference				Reference			
cPR	9.105	2.565	32.325	**0.001**	9.657	2.697	34.583	**<0.001**
Smoking status								
Non-smoker	Reference							
Smoker	1.840	0.628	5.396	0.266				
Tumor associated hydronephrosis								
No	Reference				Reference			
Yes	1.373	0.179	10.547	0.761	1.120	0.139	9.052	0.915
Tumor number								
Single	Reference							
Multiple	1.203	0.406	3.567	0.739				
Age	1.034	0.977	1.095	0.247				
BMI	0.995	0.843	1.174	0.950				
Gender								
Male	Reference							
Female	0.955	0.269	3.386	0.943				
Histology variants								
UC	Reference							
Others	1.956	0.438	8.728	0.379				
KPS	0.998	0.927	1.076	0.967				
Tumor diameter	1.011	0.972	1.051	0.597				

Table S3. Prognostic factors of DFS.

Variable	Univariable Cox BI-DFS				Multivariable Cox BI-DFS			
	HR	95% CI Lower	95% CI Upper	P value	HR	95% CI Lower	95% CI Upper	P value
Neoadjuvant therapy								
Immunotherapy	Reference				Reference			
Chemoimmunotherapy	1.313	0.313	5.505	0.710	1.153	0.262	5.086	0.851
ADC combined with Immunotherap	0.000	0.000	Inf	0.999	0.000	0.000	Inf	0.999
Clinical T stage								
Low stage	Reference				Reference			
High stage	6.835	1.619	28.859	**0.009**	7.526	1.557	36.379	**0.012**
Response to neoadjuvant therapy								
cCR	Reference				Reference			
cPR	15.888	1.950	129.462	**0.010**	20.016	2.360	169.787	**0.006**
Smoking status								
Non-smoker	Reference							
Smoker	5.942	0.729	48.420	0.096				
Tumor associated hydronephrosis								
No	Reference				Reference			
Yes	0.000	0.000	Inf	0.998	0.000	0.000	Inf	0.999
Tumor number								
Single	Reference							
Multiple	0.940	0.186	4.754	0.940				
Age	1.047	0.968	1.132	0.252				
BMI	0.992	0.793	1.240	0.943				
Gender								
Male	Reference							
Female	0.692	0.139	3.431	0.652				
Histology variants								
UC	Reference							
Others	1.542	0.189	12.608	0.686				
KPS	0.960	0.893	1.032	0.265				
Tumor diameter	1.017	0.965	1.073	0.524				

Table S4. Prognostic factors of BI-DFS.

Outcome

Baseline Characteristics Comparison in Neoimmu-CMT

Variable	Total (n = 97)	NICB.ADC (n = 23)	NICB.NAC (n = 39)	NICB (n = 35)	P value
Age, Mean ± SD	66.64 ± 9.43	66.83 ± 8.09	63.92 ± 7.80	69.54 ±	0.036
BMI, Mean ± SD	23.33 ± 2.96	24.11 ± 2.88	23.65 ± 3.12	22.46 ± 2.67	0.079
KPS, Mean ± SD	97.58 ± 6.89	98.48 ± 4.38	97.82 ± 6.47	96.71 ± 8.57	0.614
Gender, n(%)					0.596
Female	18 (18.56)	3 (13.04)	9 (23.08)	6 (17.14)	
Male	79 (81.44)	20 (86.96)	30 (76.92)	29 (82.86)	
Smoking status, n(%)					0.141
Nonsmoker	50 (51.55)	16 (69.57)	18 (46.15)	16 (45.71)	
Smoker	47 (48.45)	7 (30.43)	21 (53.85)	19 (54.29)	
Tumor associated hydronephrosis, n(%)					0.003
No	89 (91.75)	17 (73.91)	38 (97.44)	34 (97.14)	
Yes	8 (8.25)	6 (26.09)	1 (2.56)	1 (2.86)	
Tumor number, n(%)					<.001
Multiple	35 (36.08)	16 (69.57)	10 (25.64)	9 (25.71)	
Single	62 (63.92)	7 (30.43)	29 (74.36)	26 (74.29)	

Table S5. Baseline characteristics of patients in the immunotherapy group.

Outcome

Immune Phenotype and Biomarker Analysis

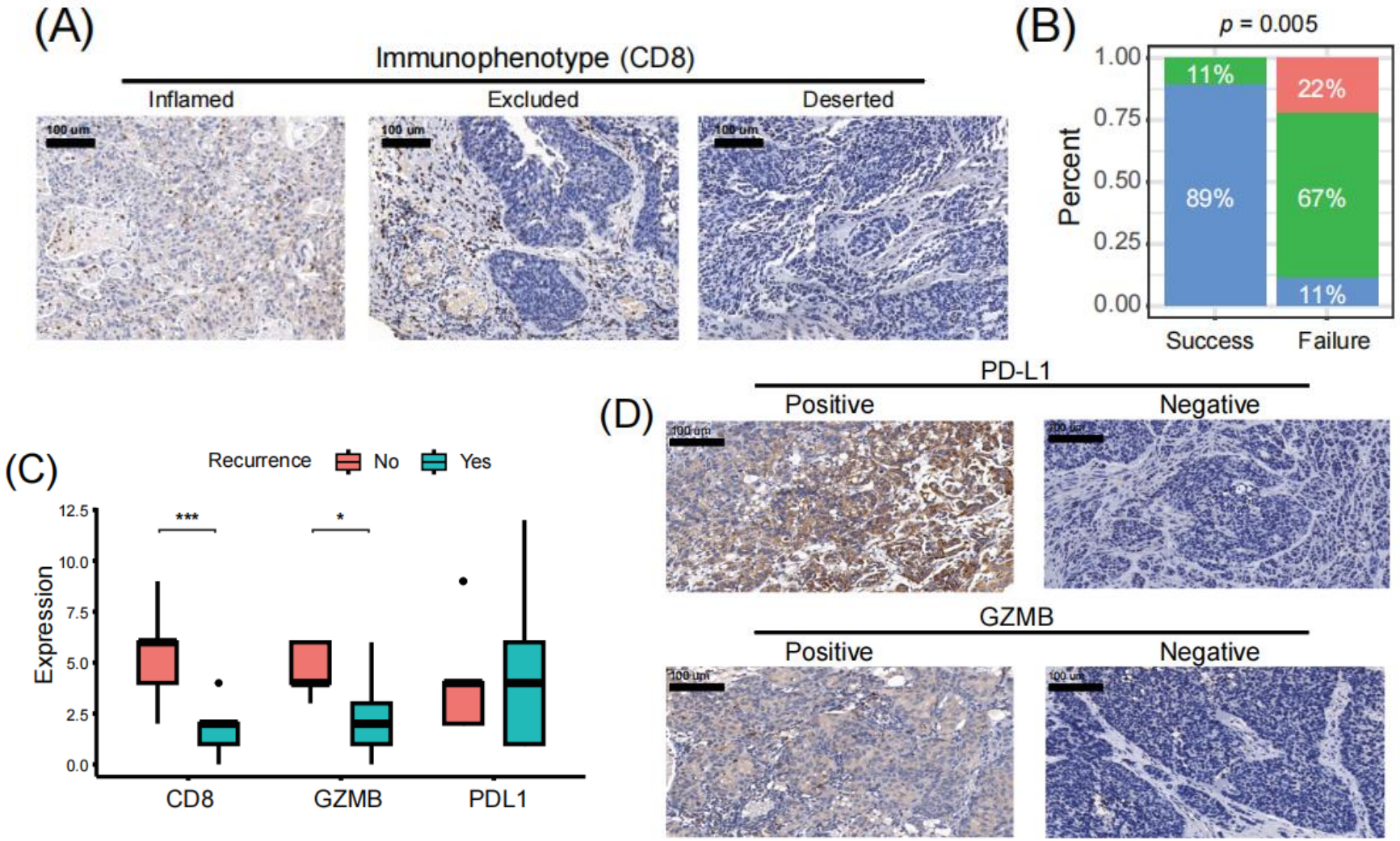


Figure 2. (A) Representative images of three immune phenotypes were displayed; (B) The associations between immune phenotypes and Neoimmu-CMT outcomes; (C) Differences in the expression of CD8, GZMB, and PD-L1 between bladder preservation success and failure groups; (D) Representative images of GZMB and PD-L1 staining were displayed.

Outcome

Analysis of Tumor Microenvironment Cellular Composition

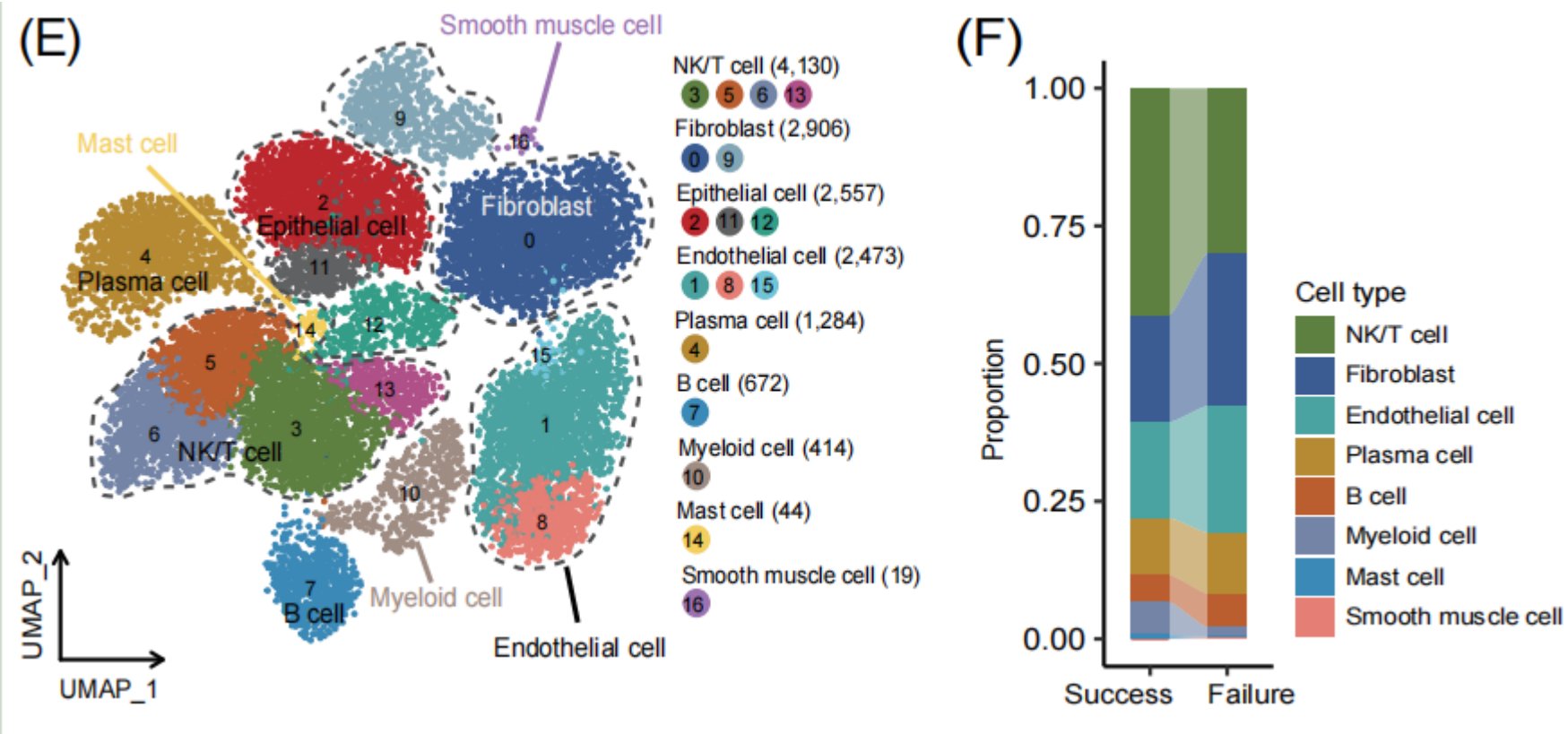


Figure 2. (E) UMAP plot of single cells profiled in the presenting work. All patients received Neoimmu-CMT based on neoadjuvant tislelizumab treatment; (F) Histogram indicating the counts and proportions of main cell types between groups (all cells).

Outcome

Analysis of Tumor Microenvironment Cell Subpopulation Distribution

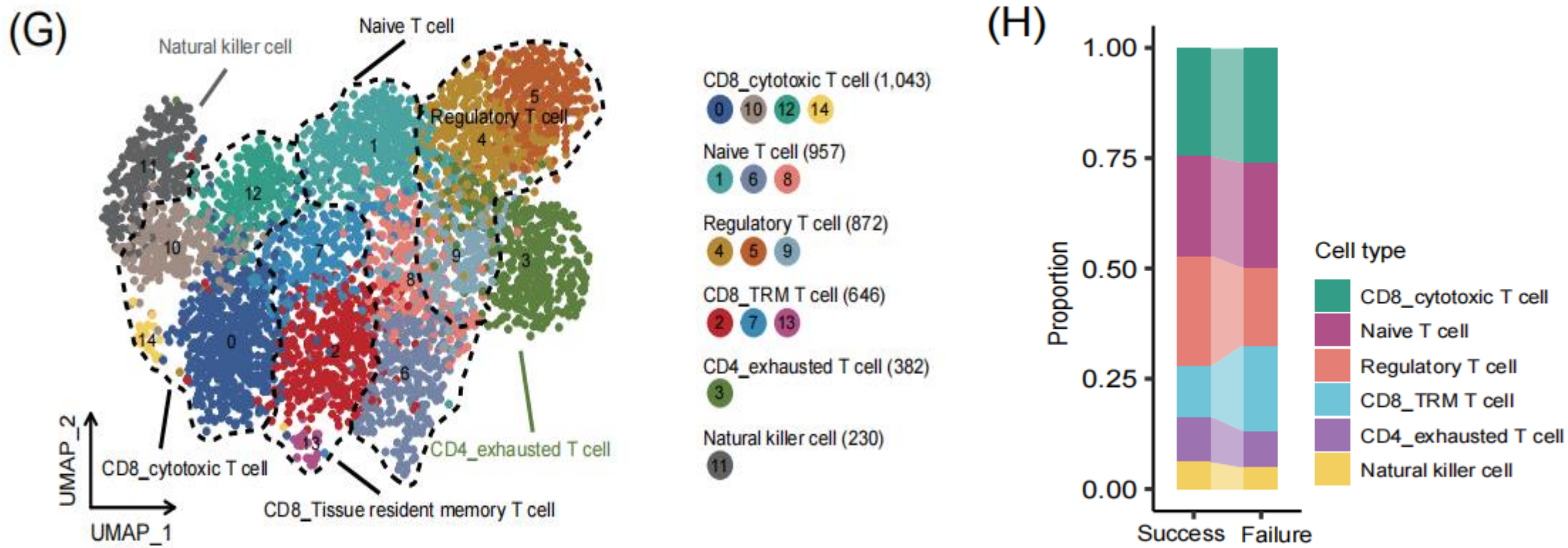


Figure 2. (G) UMAP plot of subgroups of T/NK cells; (H) Histogram indicating the counts and proportions of main cell types between groups (T/NK cells).

Outcome

Analysis of Tumor Microenvironment Cell Subpopulation Distribution

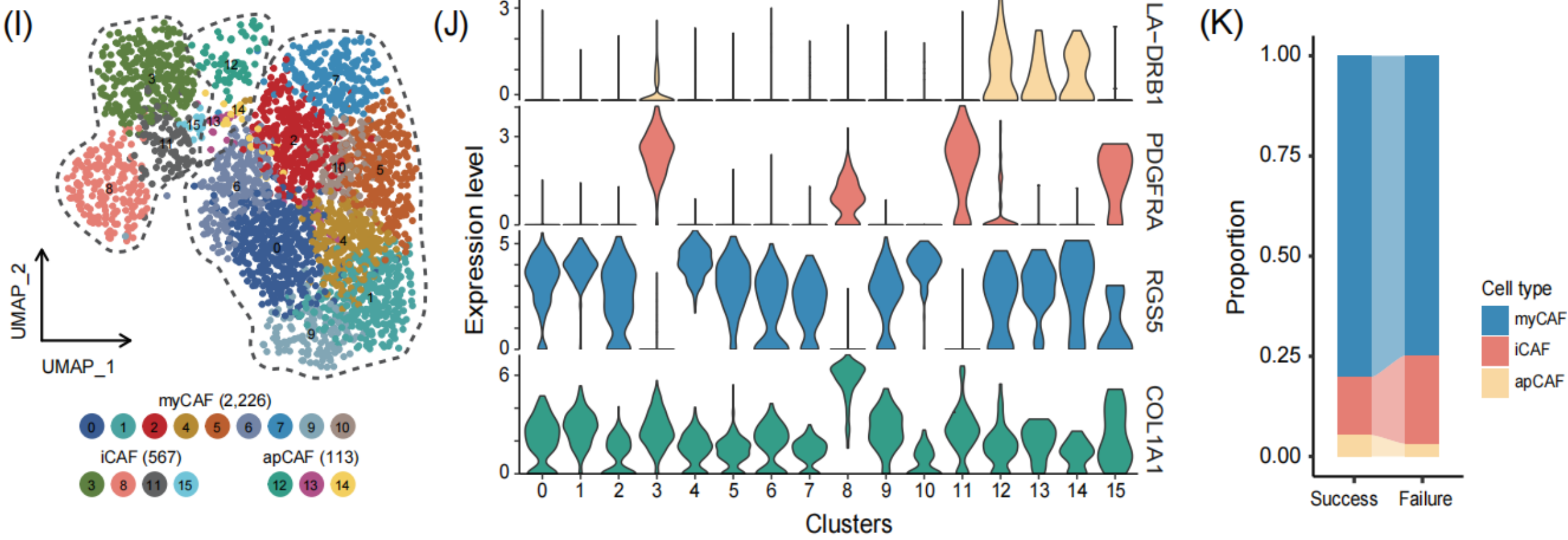


Figure 2. (I) UMAP plot of subgroups of fibroblast cells; (J) Marker genes of each subcluster and cell types; (K) Histogram indicating the counts and proportions of main cell types between groups (fibroblasts).

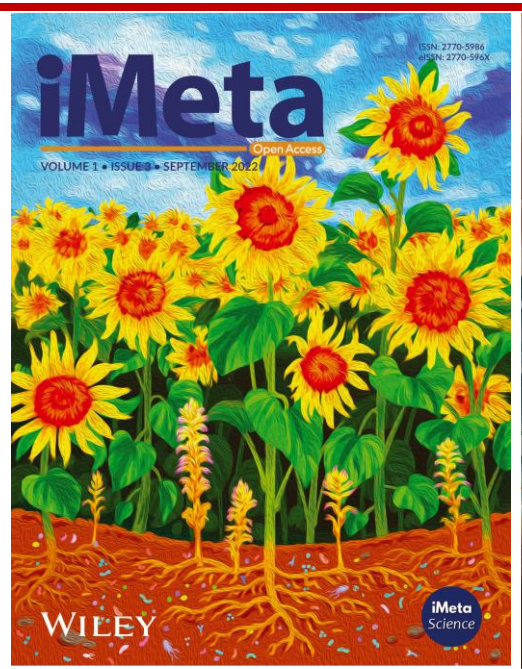
Summary

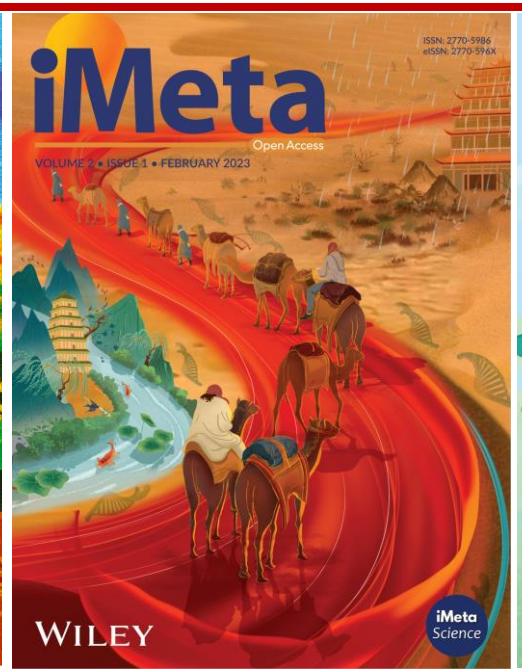
- Neoimmu-CMT demonstrates significantly better bladder-preserving efficacy in MIBC patients compared to traditional NAC-CMT, and shows comparable efficacy to conventional TMT with fewer side effects.
- Bladder-preserving outcomes based on different neoadjuvant immunotherapy regimens are similar among patients achieving clinical complete or partial response.
- The distribution and functional activity of CD8+ T cells in the tumor microenvironment may serve as important biomarkers for predicting treatment response.
- In patients with treatment failure, increased fibroblasts, reduced NK and T cells, particularly elevated inflammatory cancer-associated fibroblasts, are closely associated with poor prognosis.

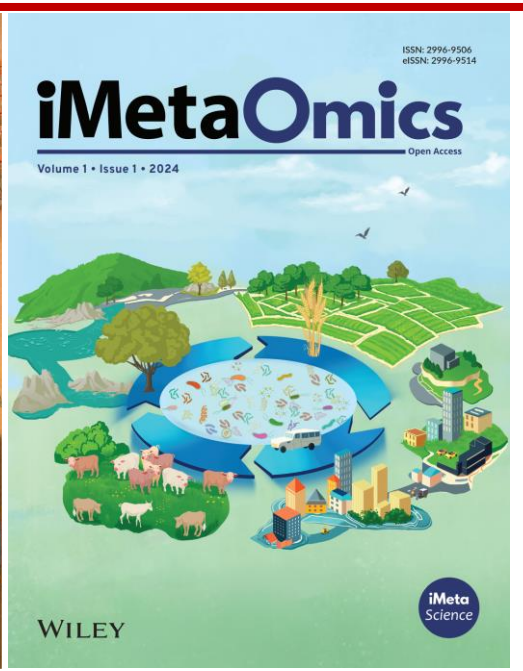
Jiao Hu, Luzhe Yan, Jinhui Liu, Minfeng Chen, Yunbo He, Benyi Fan, Bo Peng, et al. 2025. Neoadjuvant immunotherapy driven bladder preservation for muscle invasive bladder cancer. ***iMeta*** 4: e70063. https://doi.org/10.1002/imt2.70063

iMeta: Integrated metaomics to understand the biology, med and environment

WILEY







"***iMeta***" launched in 2022 by iMeta Science Society, impact factor (IF) **33.2**, ranking top 65/22249 in world and 2/161 in the microbiology. It aims to publish innovative and high-quality papers with broad and diverse audiences. **Its scope is similar to *Cell*, *Nature Biotechnology/Methods/Microbiology/Medicine/Food***. Its unique features include video abstract, bilingual publication, and social media with 600,000 followers. Indexed by **SCIE/ESI**, **PubMed**, **Google Scholar** etc.

"***iMetaOmics***" launched in 2024, with a **target IF>10, and its scope is similar to *Nature Communications*, *Cell Reports***, *Microbiome, ISME J, Nucleic Acids Research, Briefings in Bioinformatics,* etc.

"***iMetaMed***" launched in 2025, with a **target IF>15, similar to *Med, Cell Reports Medicine*, *eBioMedicine, eClinicalMedicine*** etc.

Society: http://www.imeta.science
Publisher: https://wileyonlinelibrary.com/journal/imeta
iMeta: https://wiley.atyponrex.com/journal/IMT2
Submission: iMetaOmics: https://wiley.atyponrex.com/journal/IMO2
iMetaMed: https://wiley.atyponrex.com/journal/IMM3

iMetaScience
iMetaScience

office@imeta.science
imetaomics@imeta.science

Promotion Video

Update 2025/6/18