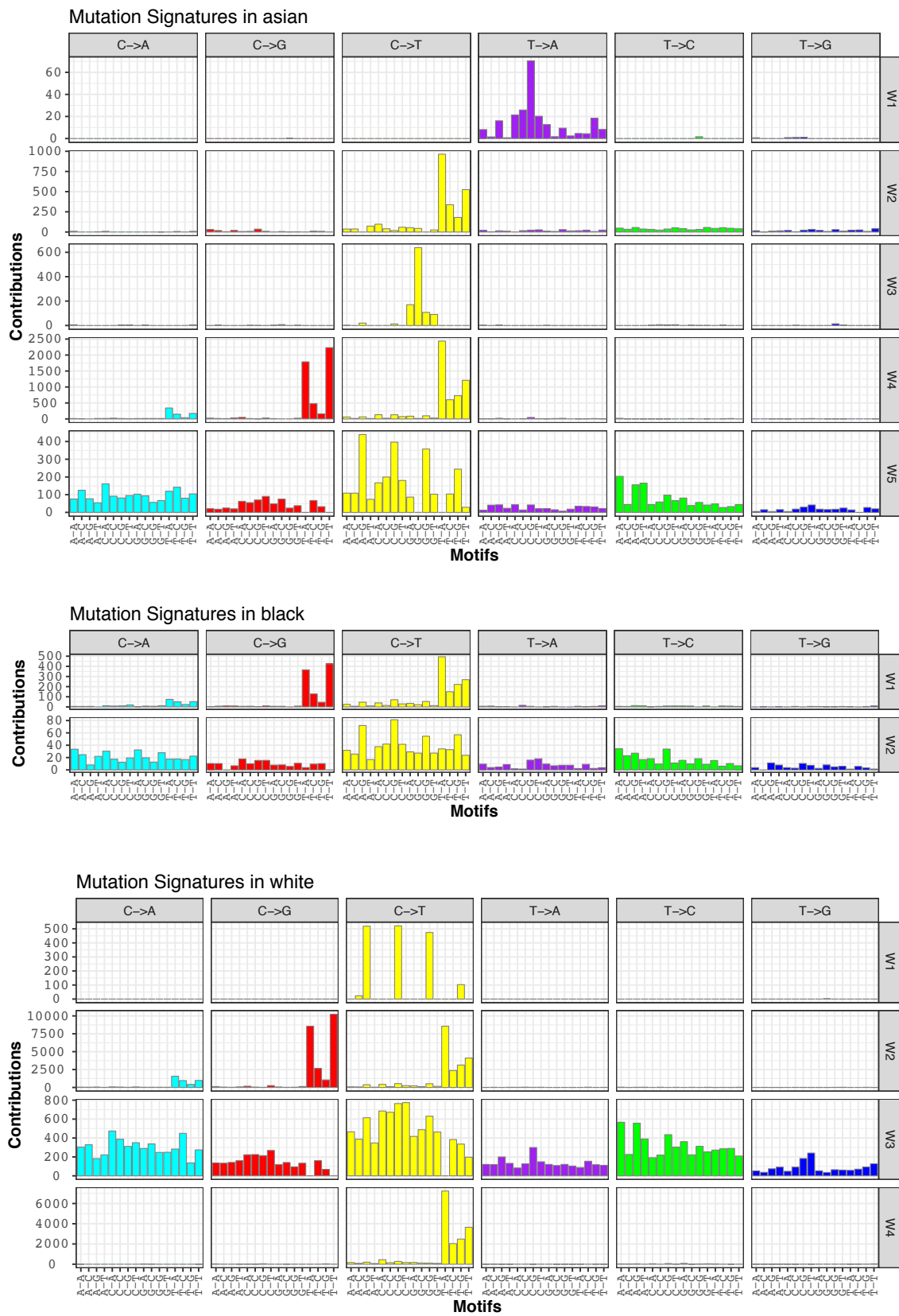


**Racial differences in genomic features and new trans-ancestry prognosis subtypes in
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Supplementary Fig 1



Supplementary Figure 1. Mutation signatures identified by the Bayesian NMF algorithm. From top to bottom: Asian, Black and White.

Supplementary Figure 2. The distribution of activities and fractions of the five mutation signatures in bladder cancer patients.

activity.zscore

signature

Racial origins

- Cohort 2 Asian (MIBC) (N = 60)
- Cohort 1 Asian (MIBC) (N = 37)
- Cohort 2 Asian (NMIBC) (N = 43)

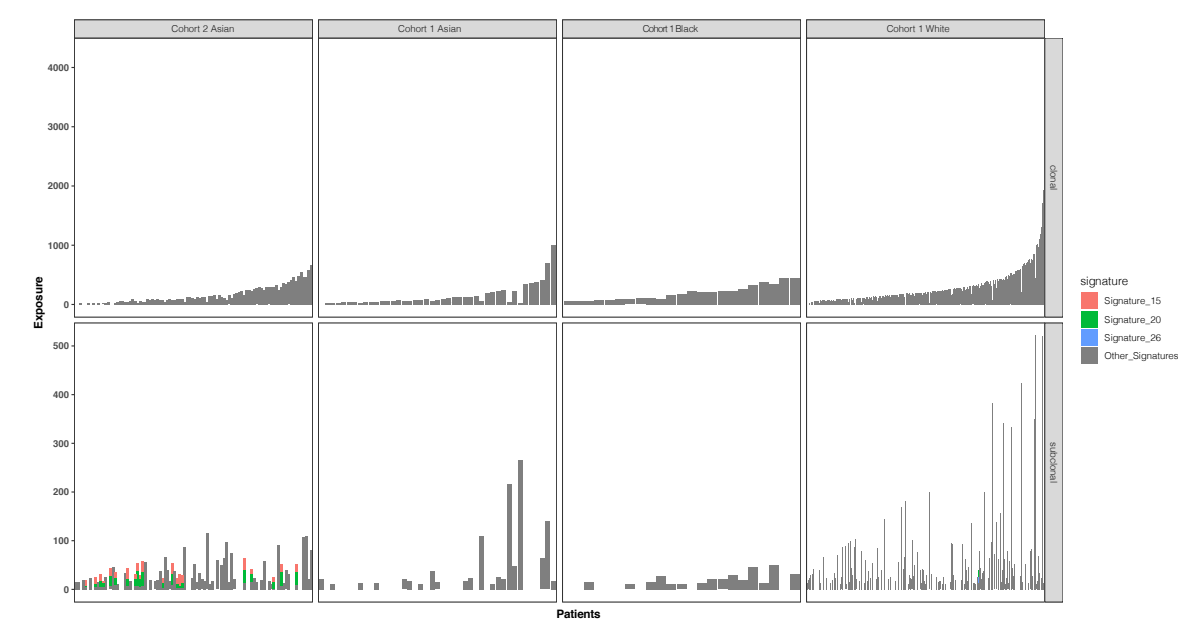
* $P < 0.05$

** $P < 0.01$

*** $P < 0.001$

Supplementary Figure 3. Comparison of the activities of the five mutation signatures in Asian bladder cancer patients from Cohort 1 and Cohort 2.

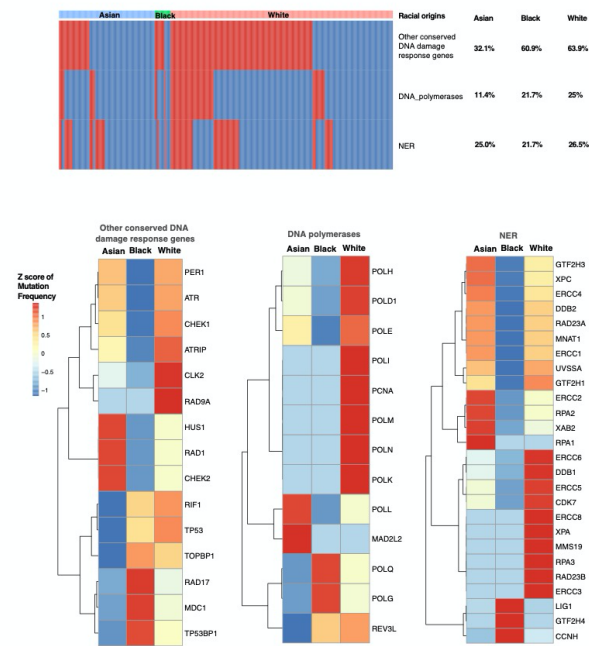
Supplementary Fig 4



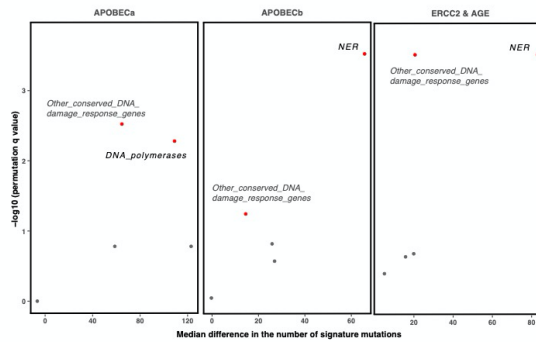
Supplementary Figure 4. The decomposition of mutation signatures in bladder cancer patients with the non-negative least square method.

Supplementary Fig 5

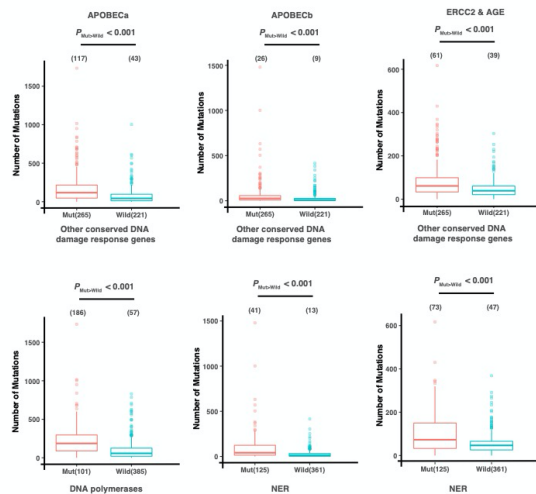
a



b

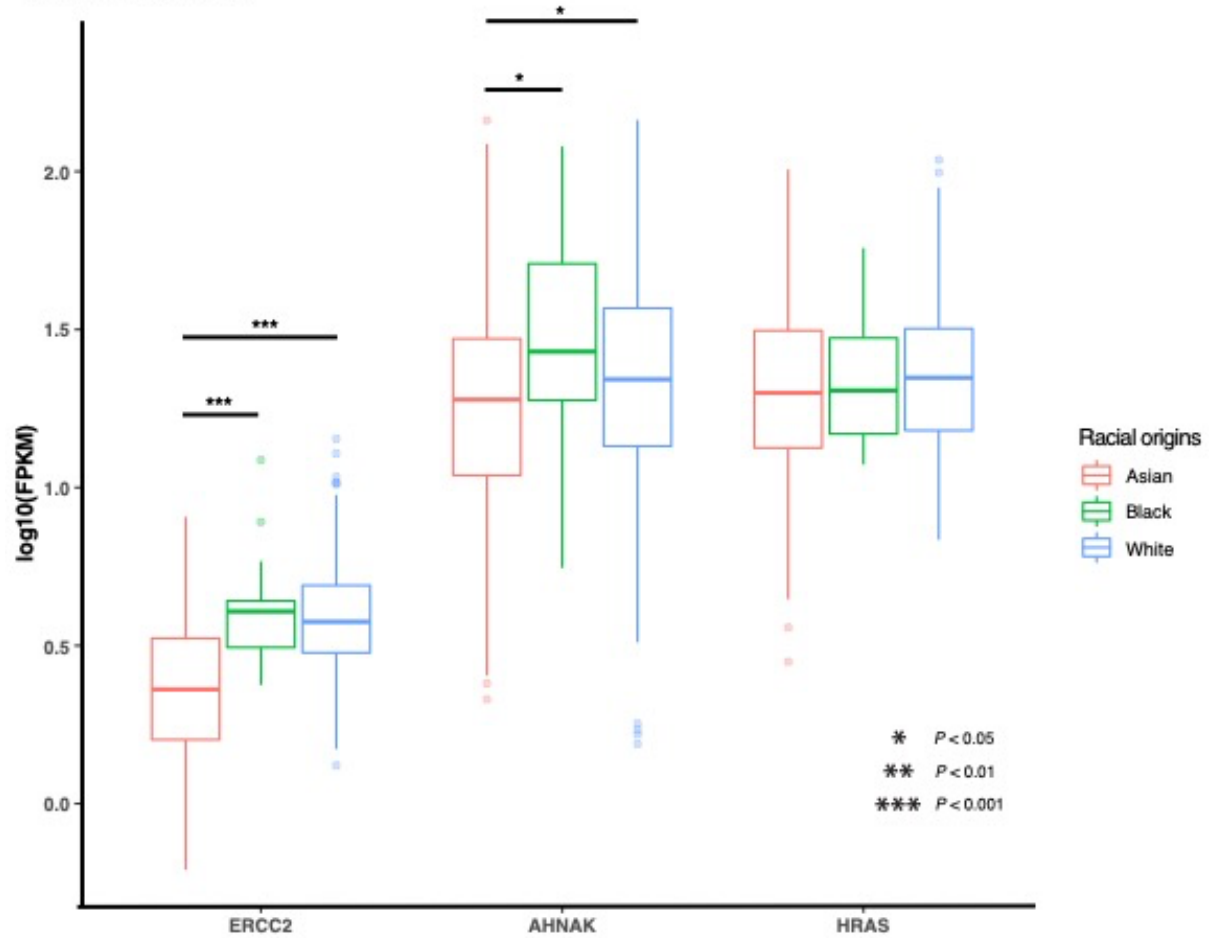


c



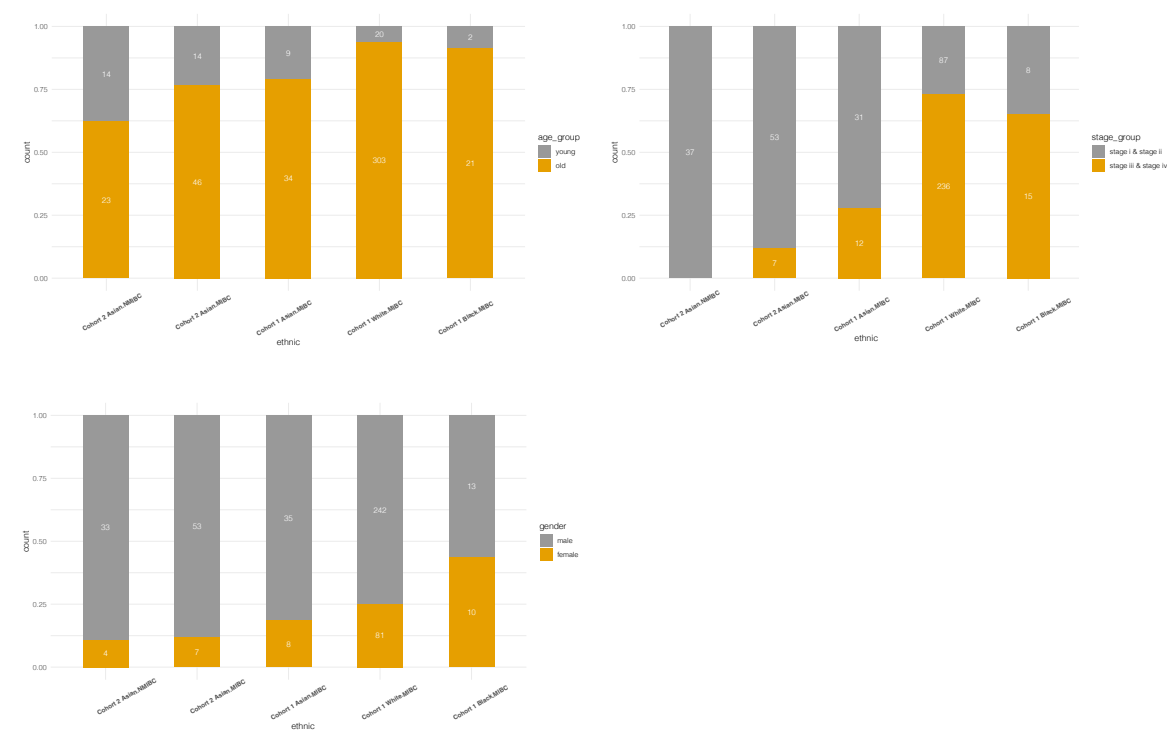
Supplementary Figure 5. Defects in DNA repair pathways associated with signature activities. (a) Differences in the mutation frequencies of the three pathways among Asian/Black/White populations. (b) Mutation enrichment analysis identifies associations between three pathways and signature activities. (c) Comparison of the estimated numbers of signature mutations in tumors with wild-type versus mutant genes in the three pathways.

Supplementary Fig 6



Supplementary Figure 6. The expression levels of *ERCC2/AHNAK/HRAS* genes in Asian/Black/White bladder cancer patients.

Supplementary Fig 7



Supplementary Figure 7. The distribution of age/TNM stage/gender in bladder cancer patients with different ethnicities.

a

Racial origins

- Cohort 2 Asian.NMIBC (N = 31)
- Cohort 2 Asian.MIBC (N = 41)
- Cohort 1 Black.MIBC (N = 7)
- Cohort 1 Asian.MIBC (N = 26)
- Cohort 1 White.MIBC (N = 87)

Sample fraction

SMG

jeuop

b

Groups (fisher.test $P < 0.05$)

- Cohort 2 Asian.MIBC vs Cohort 2 Asian.NMIBC
- Cohort 1 Asian.MIBC vs Cohort 2 Asian.MIBC
- Cohort 1 Black.MIBC vs Cohort 2 Asian.MIBC
- Cohort 1 Black.MIBC vs Cohort 1 Asian.MIBC
- Cohort 1 Black.MIBC vs Cohort 1 White.MIBC
- Cohort 1 White.MIBC vs Cohort 2 Asian.MIBC
- Cohort 1 White.MIBC vs Cohort 1 Asian.MIBC

$-\log_{10}(\text{pvalue})$

SMG

c

Racial origins

- Cohort 2 Asian.NMIBC (N = 35)
- Cohort 2 Asian.MIBC (N = 47)
- Cohort 1 Black.MIBC (N = 8)
- Cohort 1 Asian.MIBC (N = 28)
- Cohort 1 White.MIBC (N = 80)

Sample fraction

SMG

jeuop

d

Groups (fisher.test $P < 0.05$)

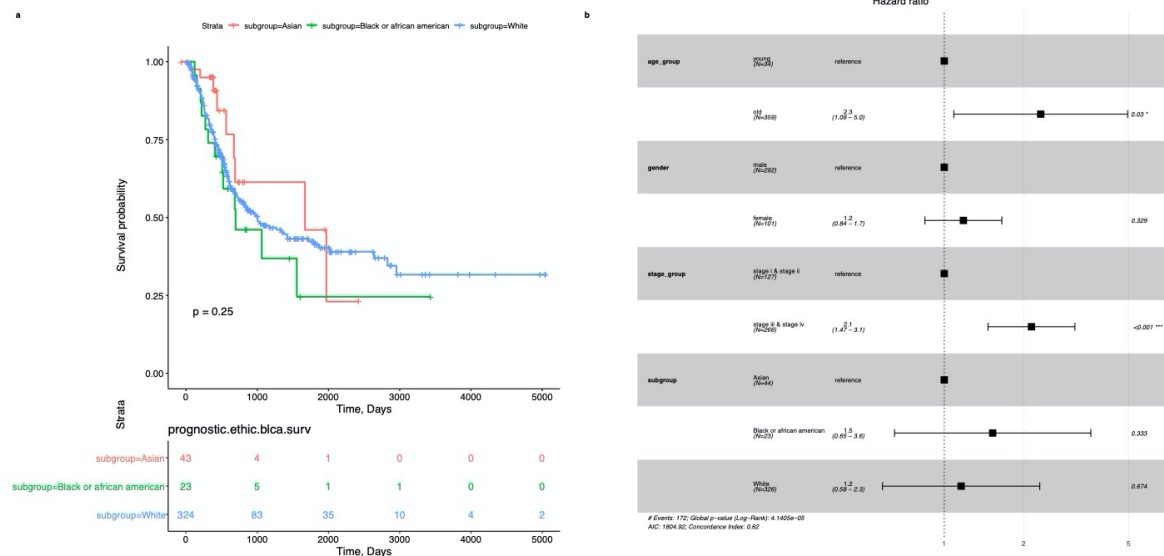
- Cohort 2 Asian.MIBC vs Cohort 2 Asian.NMIBC
- Cohort 1 Asian.MIBC vs Cohort 2 Asian.MIBC
- Cohort 1 White.MIBC vs Cohort 2 Asian.MIBC
- Cohort 1 White.MIBC vs Cohort 1 Asian.MIBC
- Cohort 1 Black.MIBC vs Cohort 2 Asian.MIBC
- Cohort 1 Black.MIBC vs Cohort 1 Asian.MIBC
- Cohort 1 Black.MIBC vs Cohort 1 White.MIBC

$-\log_{10}(\text{pvalue})$

SMG

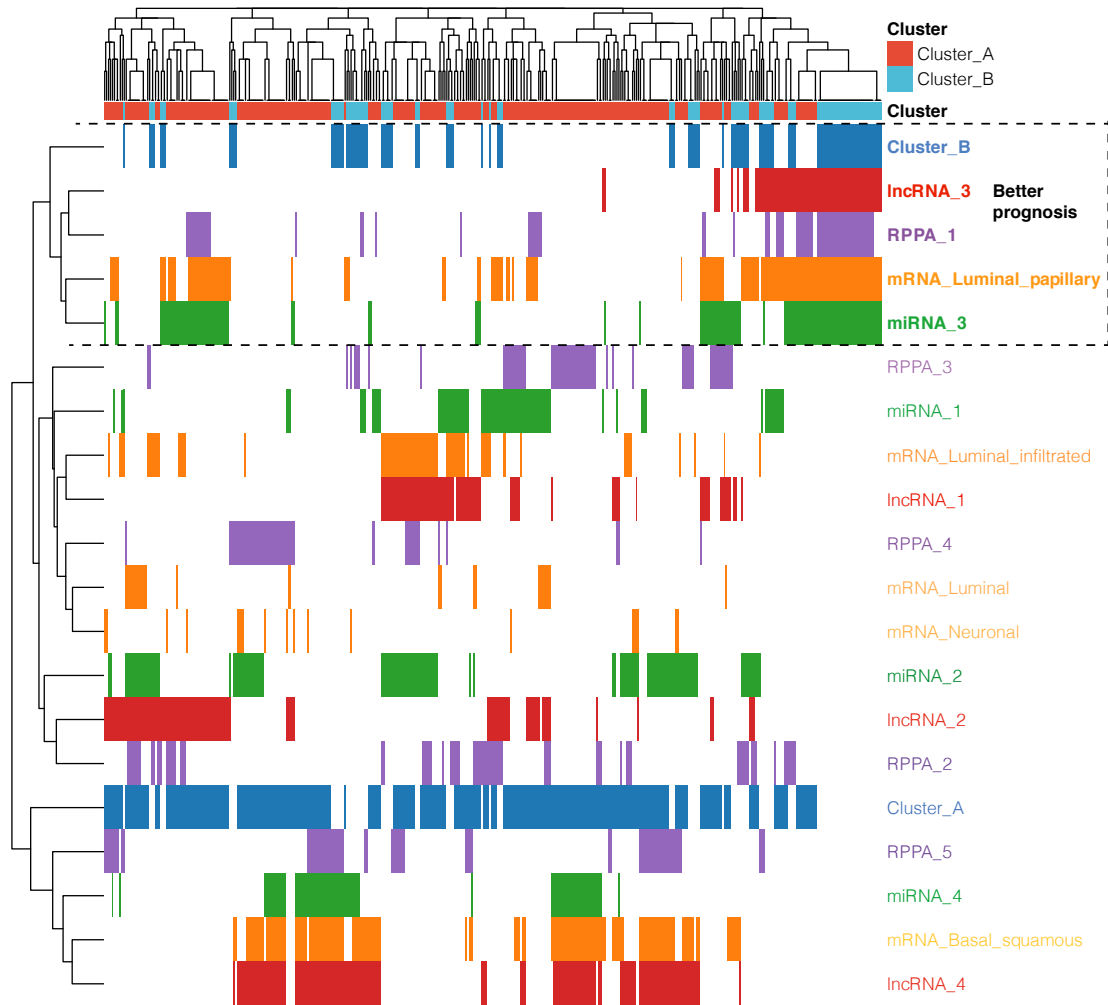
Supplementary Figure 8. Ethnic differences in SMG mutations and SCNAs in patients with Stage I & II disease. (a) The prevalence of mutations in SMGs across racial origins. (b) SMGs showing significantly different mutation frequencies in different racial origins. (c) The prevalence of SCNAs across racial origins. (d) Chromosome- or arm-level SCNAs showing great racial disparities.

Supplementary Fig 9



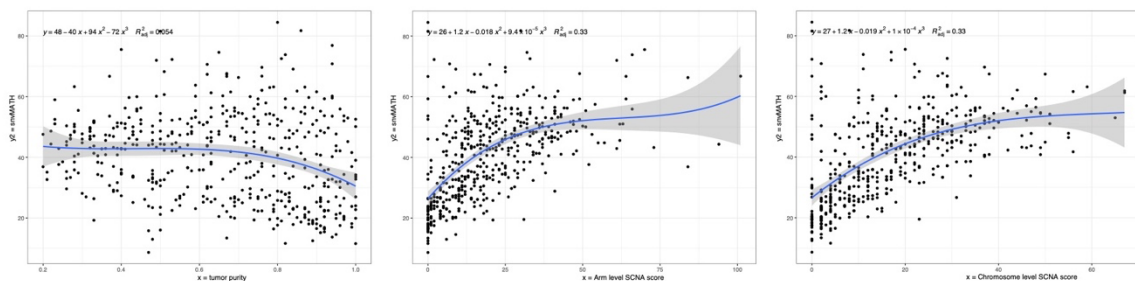
Supplementary Figure 9. Survival analysis of Asia/Black/White bladder cancer patients.
(a) Kaplan-Meier survival analysis. (b) Multivariate Cox regressions analysis of survival by including racial origins, age, gender and TNM stage.

Supplementary Fig 10



Supplementary Figure 10. Comparison of the two genomic subtypes (Cluster A and B) defined in our study with the molecular subtypes defined by TCGA at different expression levels.

Supplementary Fig 11



Supplementary Figure 11. The correlation analysis of MATH score with tumor purity, Arm/Chromosome level SCNA score.

Supplementary Table 1. Statistics of Somatic single nucleotide variants (SNVs), Insertions/deletions (Indels) and Somatic copy number alterations (SCNAs)

Clonal state	SNVs (n = 132, 100)	Indels (n = 4, 246)	SCNAs (n = 21, 779)
Clonal	117, 321 (88.8%)	2, 951 (69.5%)	12, 825 (58.9%)
Sub-clonal	14, 779 (11.2%)	1, 295 (30.5%)	8, 954 (41.1%)

Supplementary Table 2. Clinical characteristics of patients used for this study

Factor	Cohort 1 (TCGA-BLCA)	Cohort 2 (Chinese-BLCA)
<i>Cohort Size (Asian, Black, White, Not reported)</i>		
	408 (43, 23, 324, 18)	97 (97, 0, 0, 0)
<i>Histopathological subtype size (Asian, Black, White)</i>		
MIBC	390 (43, 23, 324)	60 (60, 0, 0)
NMIBC	0 (0, 0, 0)	37 (37, 0, 0)
<i>Follow up survival information</i>		
	Yes	Not available
<i>Smoking status (Yes, No)</i>		
	389 (180, 209)	Not available
<i>Age subgroup (Asian, Black, White in MIBC) (Asian, Black, White in NMIBC)</i>		
Young	31 (9, 20, 2) (0, 0, 0)	28 (14, 0, 0) (14, 0, 0)
Old	358 (34, 303, 21) (0, 0, 0)	69 (46, 0, 0) (23, 0, 0)
<i>Data type (used for analysis)</i>		
Mutation	Yes	Yes
SCNA	Yes	Yes
<i>Subclusters of clonal architectures (Asian, Black, White)</i>		
Cluster A	272 (21, 17, 234)	35 (35, 0, 0)
Cluster B	108 (22, 6, 80)	51 (51, 0, 0)
<i>Gender (Asian, Black, White in MIBC) (Asian, Black, White in NMIBC)</i>		
Male	290 (35, 242, 13) (0, 0, 0)	86 (53, 0, 0) (33, 0, 0)
Female	99 (8, 81, 10) (0, 0, 0)	11 (7, 0, 0) (4, 0, 0)
<i>TNM Stage (Asian, Black, White in MIBC) (Asian, Black, White in NMIBC)</i>		
Stage i & Stage ii	126 (31, 87, 8) (0, 0, 0)	90 (53, 0, 0) (37, 0, 0)
Stage iii & Stage iv	263 (12, 236, 15) (0, 0, 0)	7 (7, 0, 0) (0, 0, 0)

Supplementary Table 3. Clinical characteristics associated with the two subtypes of bladder cancer

Factor	Cluster A	Cluster B	P value
Cohort Size (MIBC, NMIBC)			
Chinese-BLCA	35 (27, 8)	51 (25, 26)	NMIBC patients enriched in Cluster B (< .001)
TCGA-BLCA	287 (287, 0)	111 (111, 0)	
Follow up survival information			
Chinese-BLCA	0	0	
TCGA-BLCA	284	110	
Age, median (range)			
Chinese-BLCA	69 (44 ~ 87)	62 (28 ~ 84)	
TCGA-BLCA	71 (35 ~ 91)	66 (39 ~ 89)	
Mutation Signature Cluster (MSig1, MSig2, MSig3, MSig4)			
Chinese-BLCA	35 (4, 29, 1, 1)	51 (10, 40, 1, 0)	
TCGA-BLCA	272 (189, 4, 22, 57)	107 (82, 2, 9, 14)	
Metastatic (No, Yes)			
TCGA-BLCA	198 (66, 132)	78 (41, 37)	non-metastatic patients enriched in Cluster B (< .001)
Whole Genome Doublings Number (0, 1, 2)			
Chinese-BLCA	35 (11, 17, 7)	51 (45, 5, 1)	
TCGA-BLCA	282 (63, 180, 39)	109 (87, 20, 2)	
Racial origins (Asian, Black, White)			
Chinese-BLCA	35 (35, 0, 0)	51 (51, 0, 0)	
TCGA-BLCA	272 (21, 17, 234)	108 (22, 6, 80)	
Gender (female, male)			
Chinese-BLCA	35 (6, 29)	51 (3, 48)	
TCGA-BLCA	282 (78, 208)	110 (25, 85)	
TNM Stage (stage I & stage II, stage III & stage IV)			

Chinese-BLCA	35 (34, 1)	51 (48, 3)
TCGA-BLCA	286 (84, 202)	110 (48, 62)

Legends for each Supplementary Data file:

Supplementary Data 1 Comparison of mutational signatures identified in our study to COSMIC mutational signatures.

Supplementary Data 2 Significantly mutated genes (SMGs) identified by MutSig2CV.

Supplementary Data 3 Kaplan-Meier survival analysis result of all SMGs and frequent SCNAs events according to their clonal or subclonal vs wild state.

Supplementary Data 4 Predominance of mutation acquisitions in patients with cluster A and B bladder cancer patients.