

**Evaluation of PD-L1 and other immune markers in bladder urothelial carcinoma stratified by histologic variants and molecular subtypes**

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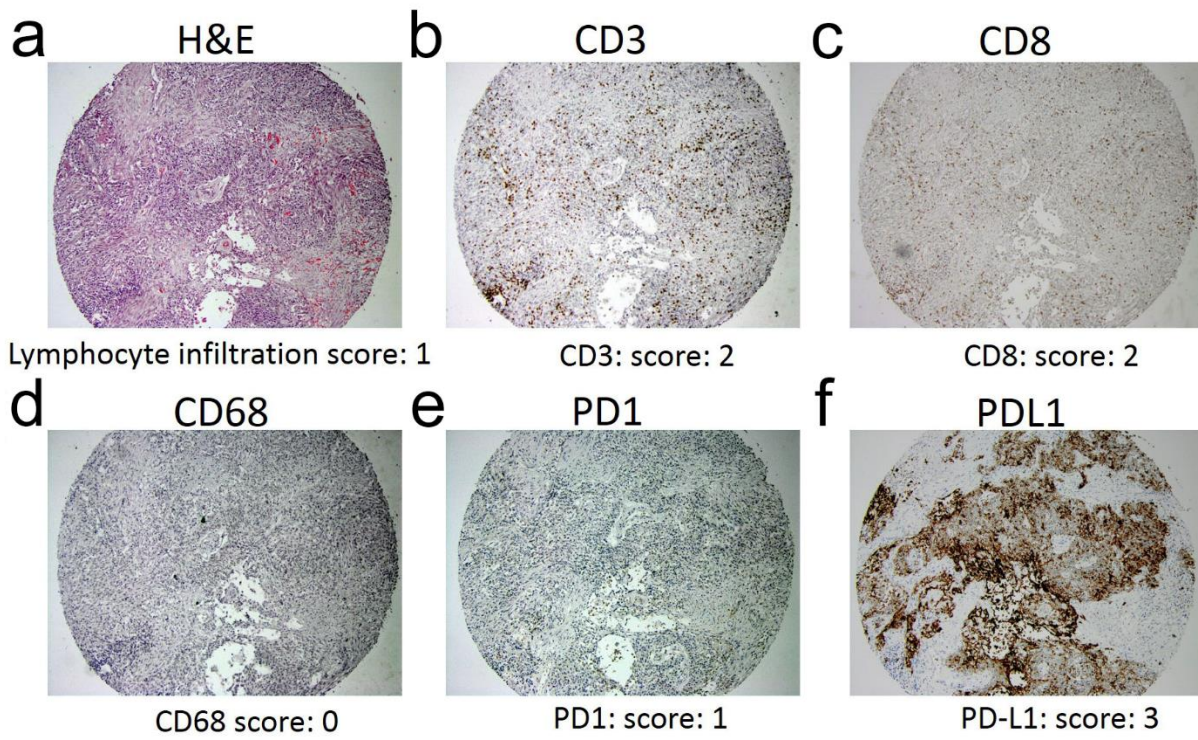
**Supplementary Table. S1.** Summary of histologic variants and molecular subtypes in this study.

CIS	77
NIPUC	40
UC, convention	52
UC, glandular	15
UC, micropapillary	14
UC, scc	39
UC, sarcomatoid	12
UC, nested	4
UC, plasmacytoid	4
UC, small cell	3
Basal-squamous	36
Urothelial-like	55
Genomically-unstable	27
mesenchymal	3
nontype	7

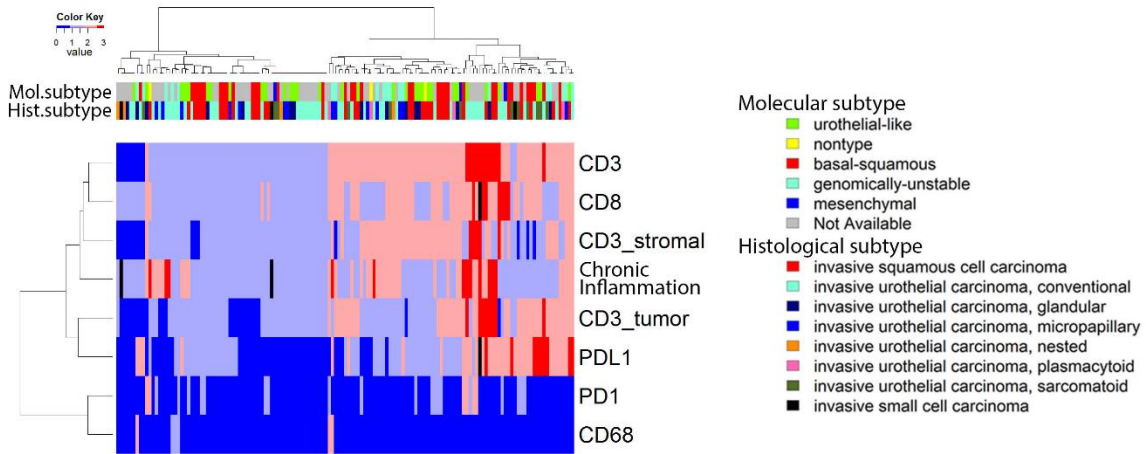
**Supplementary Table. S2.** Summary of scoring system for each marker by H&E and IHC stains.

<i>Immune Markers</i>	<i>IHC target</i>	<i>Function</i>	<i>Scoring System</i>			
			<i>0</i>	<i>1</i>	<i>2</i>	<i>3</i>
<b>HE</b>	lymphocytes	Chronic inflammation		<10% area	10-49% area	≥50% area
<b>CD3</b>	T cell	Immune response	no stain	<50% area, weak	<50% area, strong or ≥50% area, moderate	≥50% area, strong
<b>CD8</b>	Cytotoxic T cell	Immune response	no stain	<50% area, weak	<50% area, strong or ≥50% area, moderate	≥50% area, strong
<b>CD68</b>	Macrophage/monocytes	Immune suppression	no stain	<50% area, weak	<50% area, strong or ≥50% area, moderate	≥50% area, strong
<b>PD1</b>	Predominantly Lymphocytes	Immune suppression	no stain	<5% area	5-49% area	≥50% area
<b>PDL1</b>	Predominantly Tumor cells	Immune suppression	no stain	<5% area	5-49% area	≥50% area

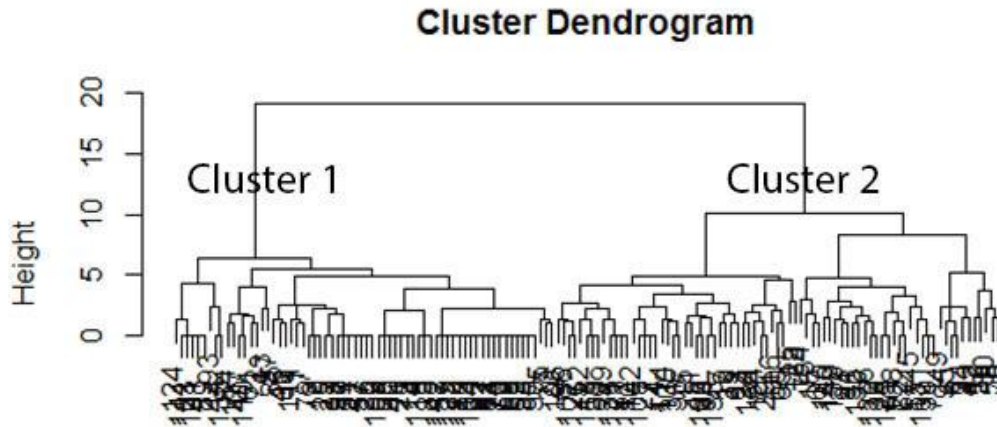
**Supplementary Figure. S1.** Representative H&E and immunohistochemically (IHC) stained sections for various markers. (A-F: 100x). The sections were evaluated by criteria described in Supplementary Table S2. A. H&E stain, score=1 for chronic inflammation; B. IHC stain, score=2 for CD3; C. IHC stain, score=2 for CD8; D. IHC stain, score=0 for CD68; E. IHC stain, score=1 for PD1; F. IHC stain, score=3 for PD-L1.



**Supplementary Figure. S2.** Immune high and immune low clusters in invasive UC by unsupervised hierarchical cluster. The same method from Figure 2 is applied to only invasive UC specimens. A similar immune high and immune low clustering pattern is identified.



**Supplementary Figure. S3.** Distribution of histologic variants of invasive UC in immune high and immune low clusters. The molecular subtypes and histology subtypes in the cluster dendrogram from spl. Fig. 1 are analyzed and compared. Within the invasive UC variants, sarcomatoid and squamous histologies show more case numbers in the immune high cluster, as compared to the other variants, but without statistical significance.



	<b>cluster1-66 specimen</b>		<b>cluster2-77-specimen</b>	
<b>Molecular subtypes</b>	urothelial-like	15	urothelial-like	17
	basal-squamous	15	basal-squamous	21
	nontype	1	nontype	2
	genomically-unstable	5	genomically-unstable	14
	mesenchymal	1	mesenchymal	2
<b>Histology subtypes</b>	convention	28	convention	24
	SCC	16	SCC	23
	glandular	7	glandular	8
	micropapillary	7	micropapillary	7
	sarcomatoid	3	sarcomatoid	9
	nested	3	nested	1
			plasmacytoid	4
	smallcell	2	smallcell	1