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Supplementary information

Advances in bladder cancer biology and therapy

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Supplementary Table 1.

	Nomenclatures					
UNC	**Luminal**		**Claudin-low**		**Basal-like**	
	luminal markers (UPK2, UPK1B, UPK3A); mutation of FGFR3 , KDM6A ; TSC1 mutation & deletion		amplification of EGFR, PPARG; mutations of RB1, EP300 and NCOR1; immune gene signature (CD274, IDO1, FASLG, CTLA4, PD1, LAG3, HAVCR2, PDCD1LG2, IL10)		Basal markers (CD44, KRT14, KRT5, KRT6B, KRT20); RB1 mutations& deletion; amplification of CCND1, E2F3 and CCNE1;	
MDA	**Luminal**		**TP53-like**			**Basal**
	PPARγ activation; luminal markers (CD24, FOXA1, GATA3, ERBB2, ERBB3, XBP1, and KRT20); estrogen receptor transcription; FGFR3 mutations		P53 pathway genes; resistant to neoadjuvant chemotherapy		P63 activation; basal markers (CD44, KRT5, KRT6, KRT14, and CDH3); sequmouse differentiation; aggressvie	
TCGA	**Cluster I**		**Cluster II**	**Cluster III**		**Cluster IV**
	focally amplified; PPARG, and EGFR amplification; MLL2 mutations; DNA hypermethylation; miR-200a-3P; miR200b-3P		Papillary-like FGFR3 mutation; CDKN2A deletion	TP53/cell-cycle-mutant; squamouse features (KRT5, KRT6A, KRT14); TP53 mutation; RB1 mutations; E2F3 and CCND1 amplification		miR-99a-5p; miR-100-5P
TCGA	**Luminal Papillary**	**Luminal**	**Neuronal**	**Luminal Infiltrated**	**Basal/squamous**	
	luminal marker (high UPK2, UPK1A); differentiaion marker (FOXA1, GATA3, PPARG); sonic Hedgehog (SHH, BMP5); high CDH1, ERBB2 expression; FGFR3 mutations; Papillary histology; Low CIS	Luminal markers (KRT20+, GATA3+, FOXA1+); TP53 mutation; CDKN2A deletion	Neuronal-differentiation; typical neuroendocrine markers; TP53 and RB1 loss ; E2F3/SOX4 amp p53/cell-cycle pathway; SOX2; DLX6; MSI1; PLEKHG4B	Luminal markers(KRT20+, GATA3+, FOXA1+); Wild type p53; Low purity; EMT markers (TWIST1, ZEB1); miR-200 family; Medium CD274 (PD-L1), CTLA-4; Myofibroblast markers	basal and stem cell markers (CD44, KRT5, KRT6A, KRT14) and squamous differentiation markers (TGM1, DSC3, PI3); Immune markers (High CD274 (PD-L1), CTLA4); high Immune infiltrates; ; TP53 mutations; loss of SHH signaling; high EGFR expression	
LUND	**Urothelial-like (Uro,)**	**Genomically unstable (GU)**	**Epithelial-infiltrated (Epi-Inf)**	**Basal/SCC**	**Mesenchymal-like**	**Small-cell /Neuroendorine-like (Sc/NE)**
	urothelial differentiation signature (RXRA, PPARG, FOXA1, GATA3); FGFR3+, CCND1+, RB1+, and E2F3−; CDKN2A deletions/mutations	urothelial differentiation signature; FGFR3−, CCND1−, RB1−, and E2F3+	urothelial differentiation signature (RXRA, PPARG, FOXA1, GATA3); Uro and GU tumour-cell phenotypes	Basal markers KRT5/KRT14-high; high CDH3	strong ECM signature; high ZEB2 and VIM	overexpression of E2F3, CDKAL1, SOX4, and MBOAT1

Supplementary Table 1. Summary of Major Bladder Cancer Subtype Classification Studies: Summary of major bladder cancer subtype classification studies including the University of North Carolina (UNC)[8,34], MD Anderson Cancer Center (MDA)[10], The Cancer Genome Atlas Network (TCGA)[7,35], and LUND taxonomy[12]. Classifications, differentiation markers, gene expression signatures, and genetic alterations (including mutation, deletion and amplifications) in various systems are displayed. "+" highly expressed; "-" not expressed or not detected.