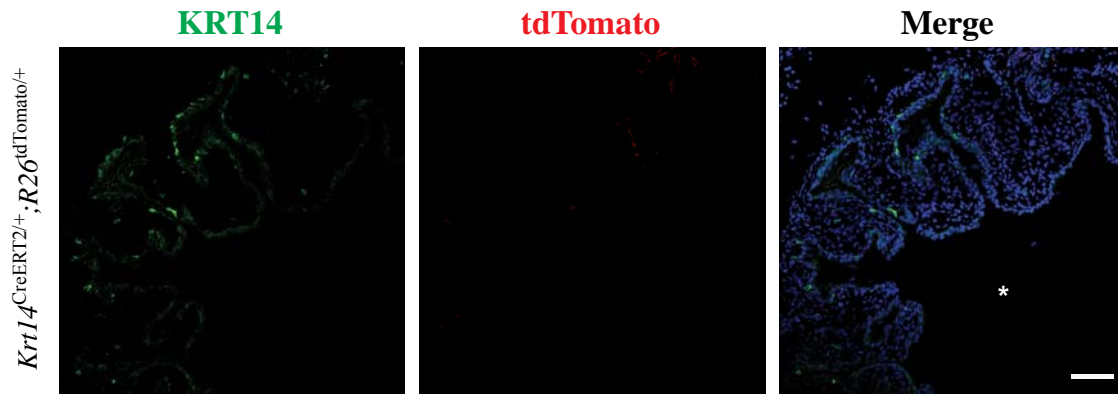
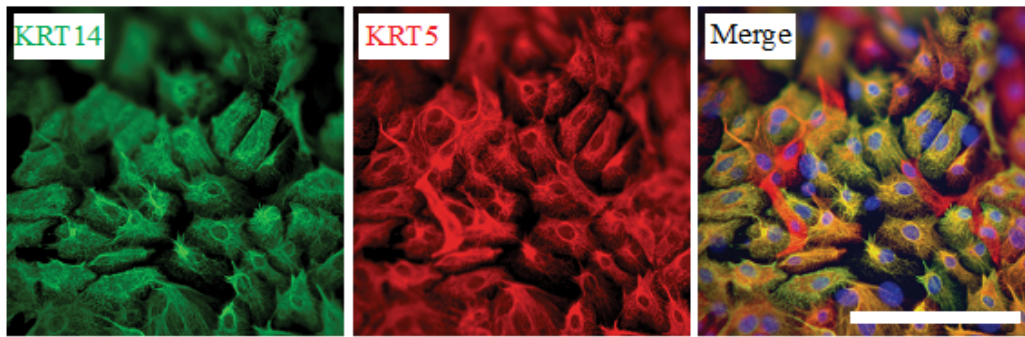


Supplementary Figure 1| Dynamic changes of bladder subpopulations during CPP-induced injury and repair. (a) IF against KRT14 and KRT5 in an 8 week-old wild type mouse. (b) IF against KRT5 and KRT20 at distinct time points during damage and repair at 20x and 40x magnifications. (c) IF against KRT14 and Ki67 at the above time points. Images for each time point in **a**, and **b**, come from adjacent 10 μ m sections and show equivalent regions wherever available. Dashed lines represent the basement membrane. Scale bars represent 100 μ m.

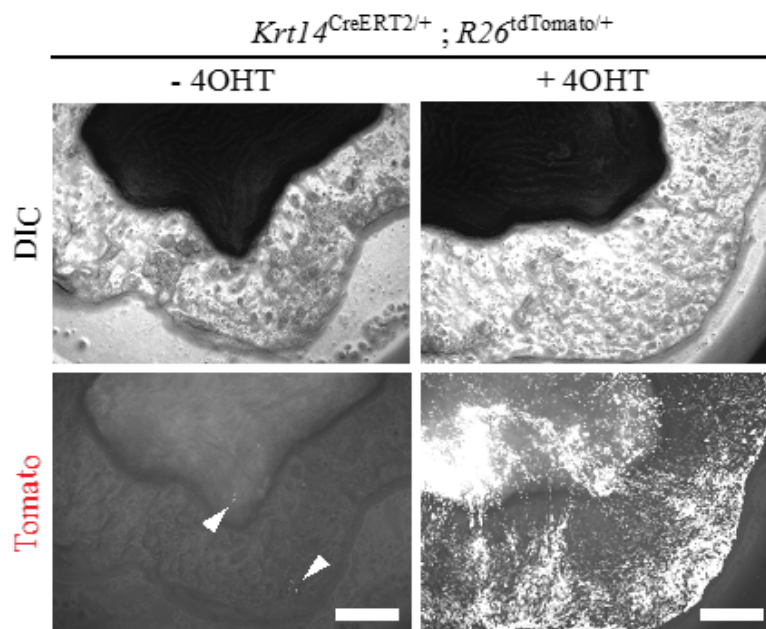


Supplementary Figure 2 | Genetic labeling of basal subtypes in mouse bladders. Section of a bladder from a *Krt14*^{CreERT2/+}; *R26*^{tdTomato/+} mouse without Tamoxifen activation, showing lack of tdTomato expression. Stars designate the bladder lumen. Scale bar represents 100 μ m.

a

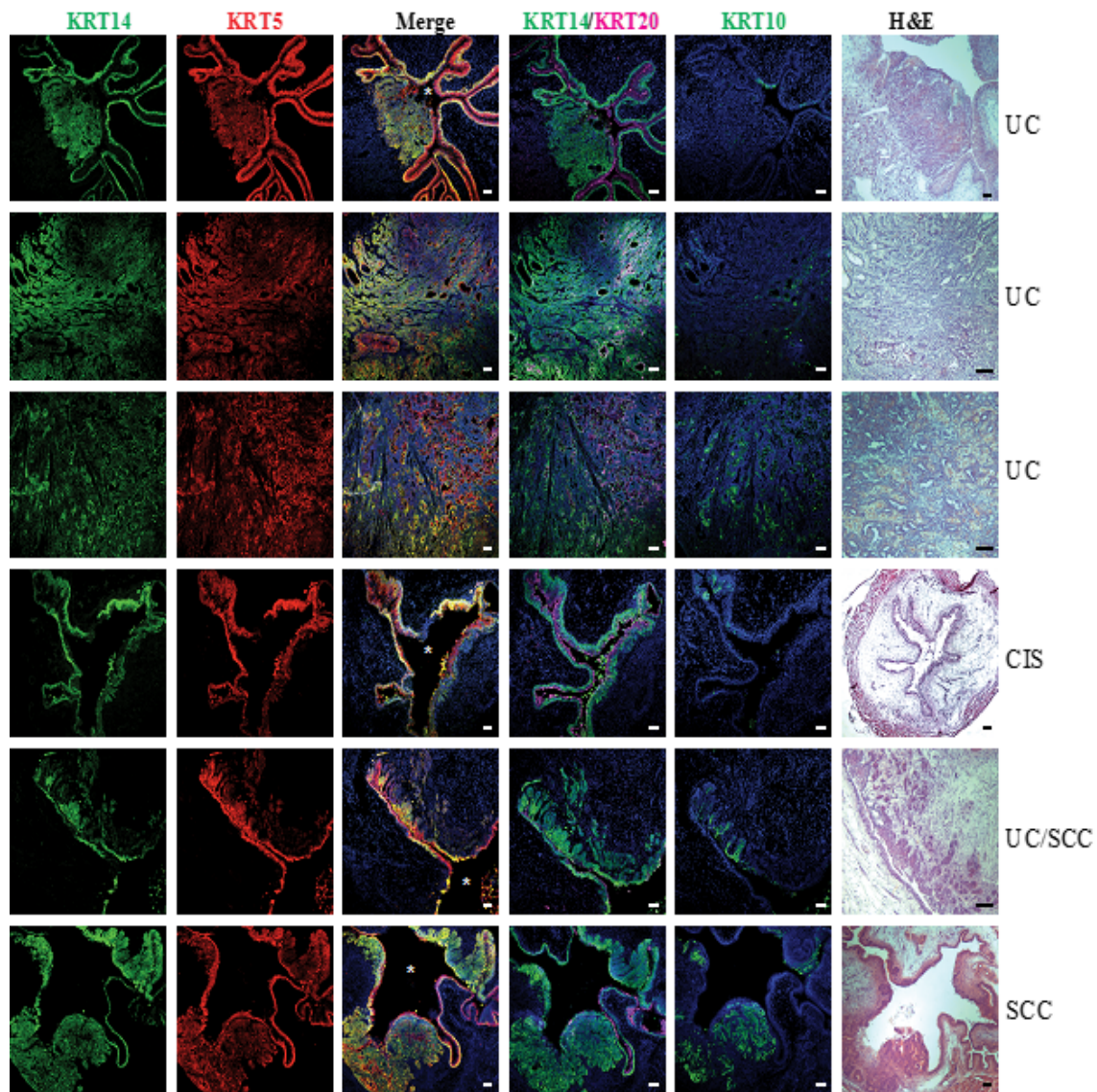


b



Supplementary Figure 3 | KRT14^{pos} cells support bladder explant growth ex vivo.

(a) Tamoxifen administration either *in vivo* or *ex vivo* is necessary for CreERT2 transgene activation and subsequent tomato expression. Arrowheads point to extremely sparse escapers. (b) Outgrowth cells are KRT14^{pos} and KRT5^{pos}. Scale bars represent 1 mm in **a**, and 100 μ m in **b**.



Supplementary Figure 4 | BBN-induced bladder tumors express KRT14.

BBN treatment induces development of different stage neoplasms. The majority co-express KRT5 and 14, while occasional KRT20 and KRT10 positivity is observed. UC: urothelial carcinoma; CIS: carcinoma in situ; SCC: Squamous cell carcinoma. Stars designate the bladder lumen. Scale bars represent 100 μ m.

Supplementary Table 1. Ki67^{pos} cell counts during CPP-induced injury and repair in total epithelial cells (Fig.1e)

	% total epithelial proliferation ± s.e.m.	Total cells counted	P value
N/T (n=5)	2.14 ± 0.92	1563	
6h (n=4)	0.49 ± 0.31	1879	<i>P</i> > 0.05
18h (n=3)	31.21 ± 7.26	839	<i>P</i> < 0.005
24h (n=6)	36.55 ± 7.03	1342	<i>P</i> < 0.005
48h (n=6)	66.26 ± 7.94	1532	<i>P</i> < 0.001
120h (n=6)	2.99 ± 0.81	1951	<i>P</i> > 0.05
240h (n=3)	1.33 ± 0.35	463	<i>P</i> > 0.05

Supplementary Table 2. Ki67^{pos} cell counts during CPP-induced injury and repair in the KRT14^{pos} and KRT14^{neg} subpopulations (Fig.1f)

	% KRT14^{pos} proliferation ±s.e.m.	KRT14^{pos} cells	% KRT14^{neg} proliferation ±s.e.m.	KRT14^{neg} cells	P value
N/T (n=5)	11.67 ± 7.26	34	1.91 ± 0.91	1529	<i>P</i> > 0.05
6h (n=4)	3.02 ± 1.07	112	0.32 ± 0.32	1767	<i>P</i> > 0.05
18h (n=3)	75.16 ± 8.27	124	24.27 ± 7.19	715	<i>P</i> < 0.01
24h (n=6)	71.25 ± 9.07	230	28.87 ± 6.78	1112	<i>P</i> < 0.005
48h (n=6)	85.7 ± 7.84	371	60.41 ± 8.21	1161	<i>P</i> < 0.05
120h (n=6)	10.15 ± 4.32	328	1.34 ± 0.46	1623	<i>P</i> > 0.05
240h (n=3)	3.04 ± 1.52	65	0.95 ± 0.51	398	<i>P</i> > 0.05

Supplementary Table 3. tdTomato^{pos} cell counts in untreated mice and after one round of CPP-induced injury and repair in the basal, intermediate and superficial cell populations in *Krt5*^{CreERT2/+}; *R26*^{tdTomato/+} mice (Fig. 3b)

Basal	% Tom^{pos} KRT5^{pos} / total KRT5^{pos} ± s.e.m.	Total KRT5^{pos} cells	P value
N/T (n=4)	63.54 ± 8.28	3887	
1 x CPP (n=4)	79.74 ± 4.92	3046	<i>P</i> > 0.05
Intermediate	% Tom^{pos} KRT5^{neg} KRT20^{neg} / total KRT5^{neg} KRT20^{neg} ± s.e.m.	Total KRT5^{neg} KRT20^{neg} cells	P value
N/T (n=4)	11.16 ± 5.2	853	
1 x CPP (n=4)	50.84 ± 5.67	783	<i>P</i> < 0.01
Superficial	% Tom^{pos} KRT20^{pos} / total KRT20^{pos} ± s.e.m.	Total KRT20^{pos} cells	P value
N/T (n=4)	2.24 ± 1.11	877	
1 x CPP (n=4)	27.4 ± 5.32	525	<i>P</i> < 0.01

Supplementary Table 4. Lineage tracing of KRT14^{pos} cells in BBN-induced tumours

BBN	4 months		6 months	
# mice	2		5	
tdTomato	+	-	+	-
Papillary	0	0	2	0
Hyp/Dysp¹	1	2	3	3
CIN/UC²	1	0	3	5
SCC³	0	0	2	2

¹Hyperplasia/Dysplasia

²Carcinoma In Situ/Urothelial Carcinoma

³Squamous Cell Carcinoma