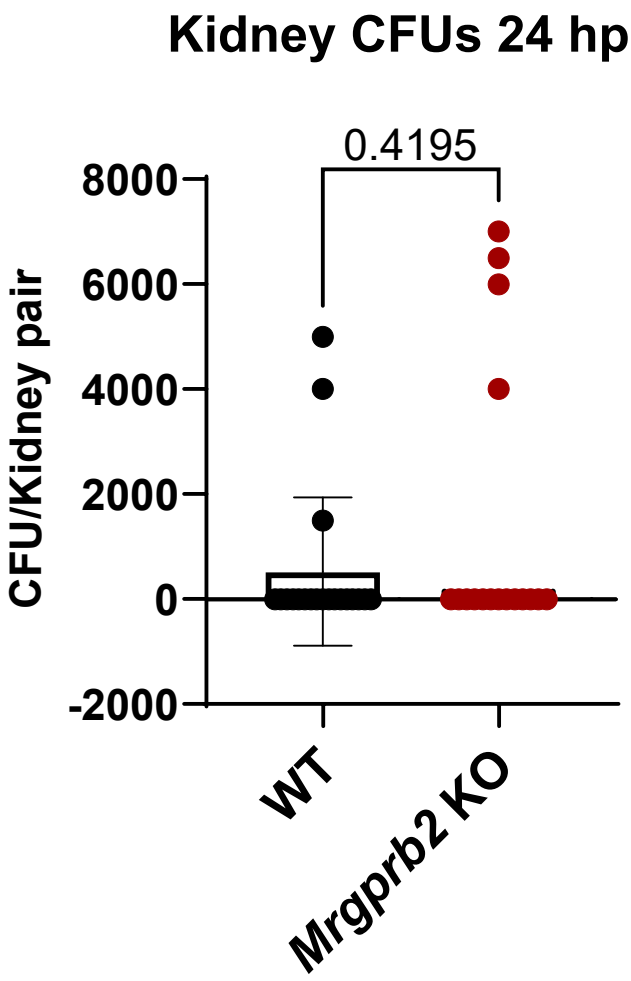

Figure S1: Kidney CFUs are unchanged in WT and Mrgprb2 KO mice

Kidney CFUs in WT and *Mrgprb2* KO mice 24 hpi. Graph shows median with 95% CI. p-values are calculated using two-tailed Mann-Whitney U test.

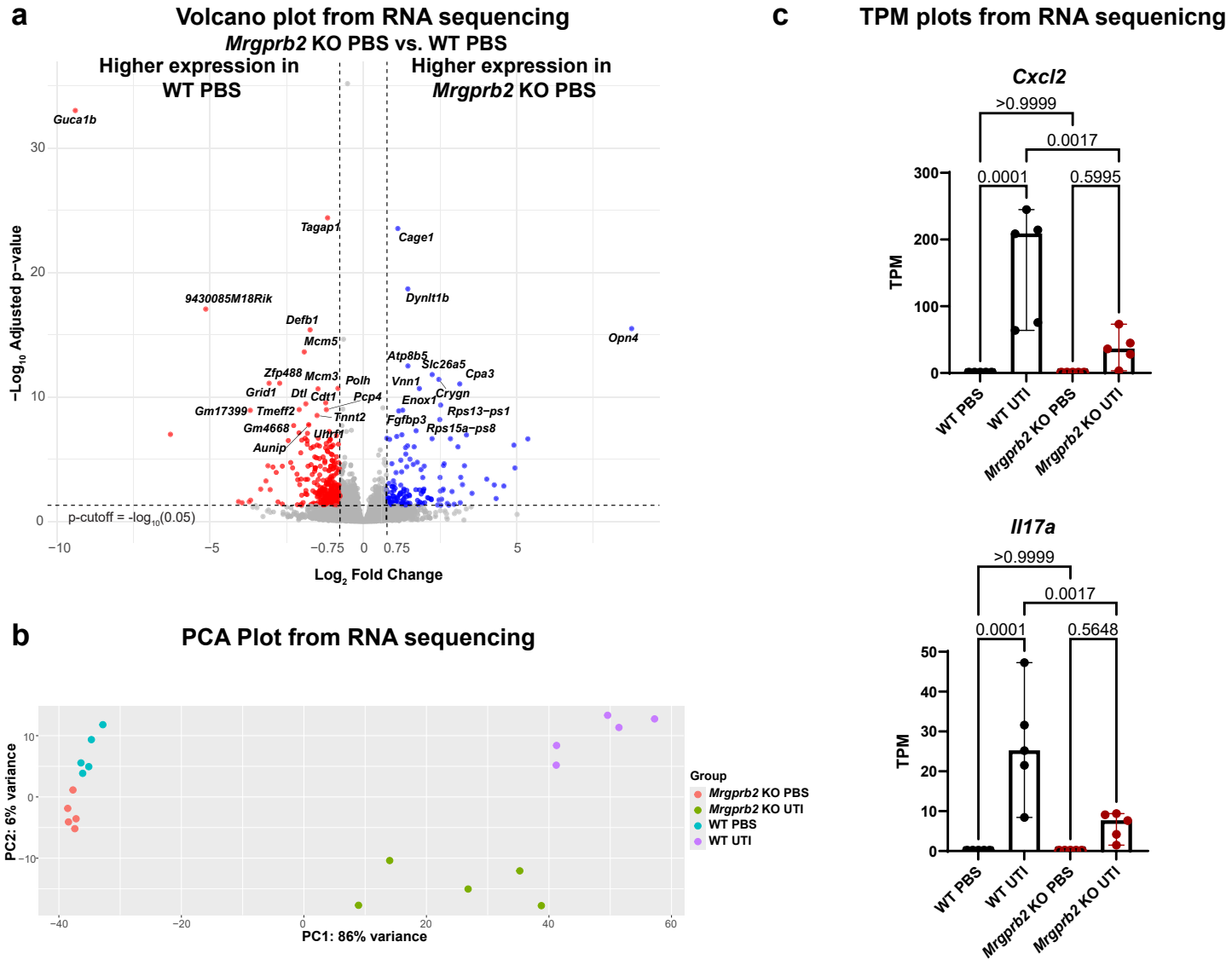

Figure S2: Minimal transcriptional changes are observed in PBS treated WT and Mrgprb2 KO bladders

a) Volcano plot from RNAseq data showing differentially expressed genes in WT PBS versus *Mrgprb2* KO PBS bladders. Top 30 differentially expressed genes are labelled on the volcano plot. Log_2foldchange > 0.75 represents genes with higher expression in *Mrgprb2* KO PBS bladder. Log_2foldchange < -0.75 represents genes with higher expression in WT PBS. p-value cutoff is $-log_{10}(0.05)$. **b**) PCA plot showing sample clustering based on gene expressions from WT PBS, WT UTI, *Mrgprb2* KO PBS, and *Mrgprb2* KO UTI bladder (n = 5 each). **c**) Transcripts Per Million (TPM) plots show expression of *Cxcl2* and *Il17a* in WT and *Mrgprb2* KO bladder in PBS and UTI conditions. Graph shows median with 95% CI. p-values are calculated using ordinary one-way ANOVA.

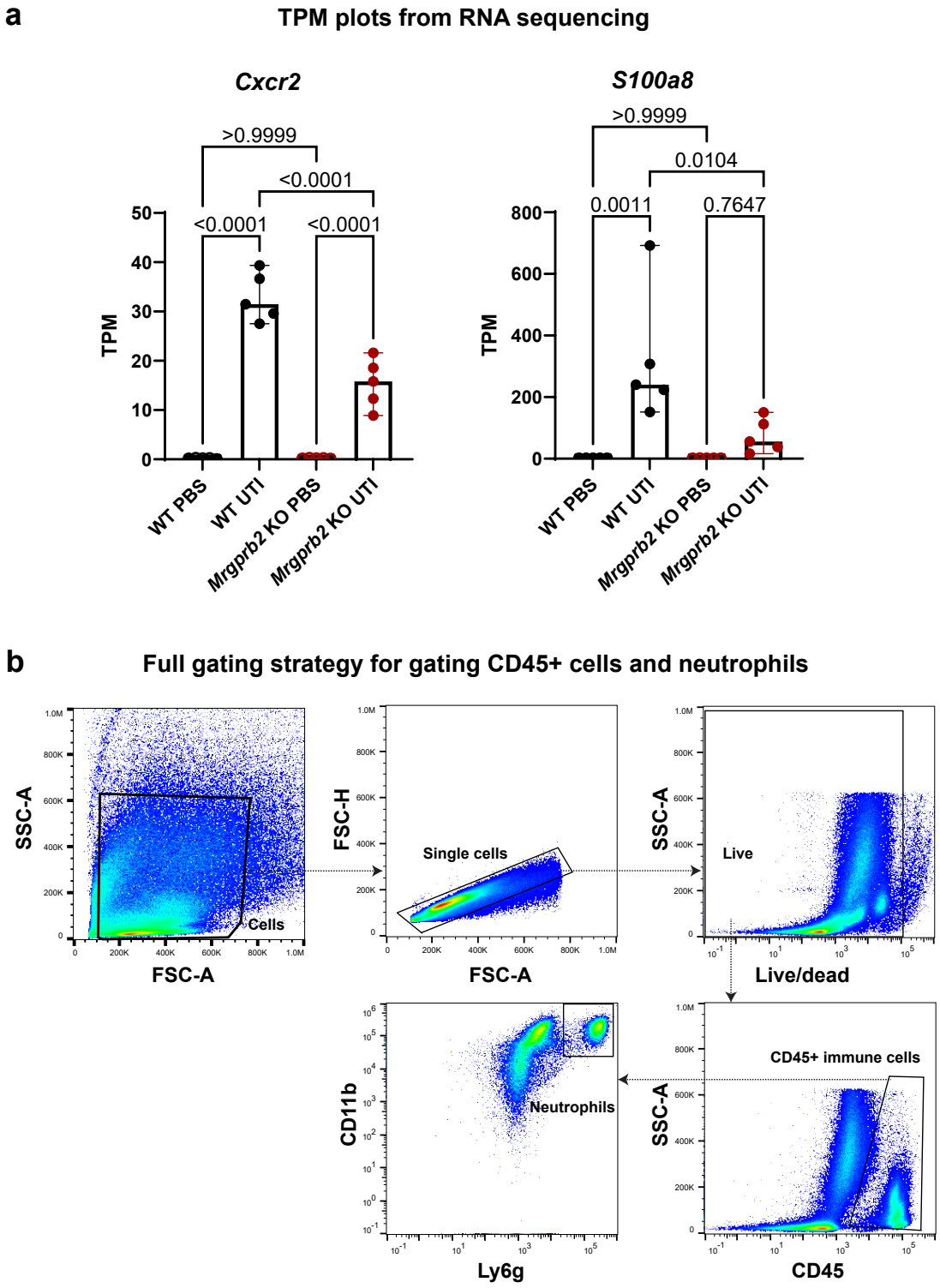

Figure S3: Mrgprb2 promotes neutrophil and immune cell infiltration into the bladder during UTI

a) Transcripts Per Million (TPM) plots from RNAseq data show expression of *Cxcr2* and *S100a8* in WT and *Mrgprb2* KO bladder in PBS and UTI conditions. Graph shows median with 95% CI. p-values are calculated using ordinary one-way ANOVA. **b**) Representative gating strategy used to gate CD45+ immune cells and neutrophils. Cells were gated on SSC-A and FSC-A. Single cells were gated from cells on FSC-A and FSC-H. Live cells were identified as single cells negative for Live/dead dye on SSC-A. CD45+ immune cells were identified as live cells positive for CD45 on SSC-A. Neutrophils were identified as CD45+ cells positive for CD11b and Ly6g. Representative gating is from a WT UTI bladder sample.

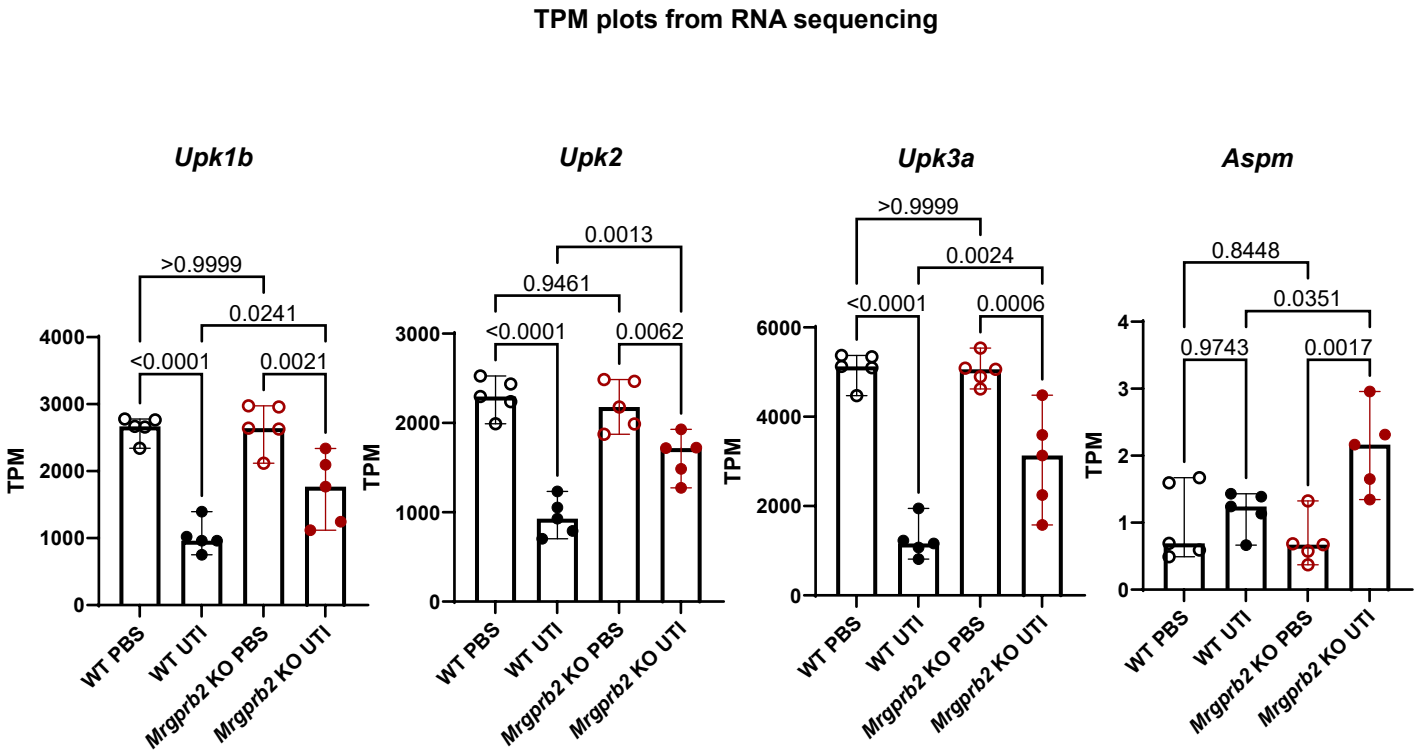

Figure S4: *Mrgprb2* KO mice suffer less epithelial damage during UTI

Transcripts Per Million (TPM) plots from RNAseq data show expression of *Upk1b*, *Upk2*, *Upk3a*, and *Aspm* in WT and *Mrgprb2* KO bladder in PBS and UTI conditions. Graph shows median with 95% CI. p-values are calculated using ordinary one-way ANOVA.

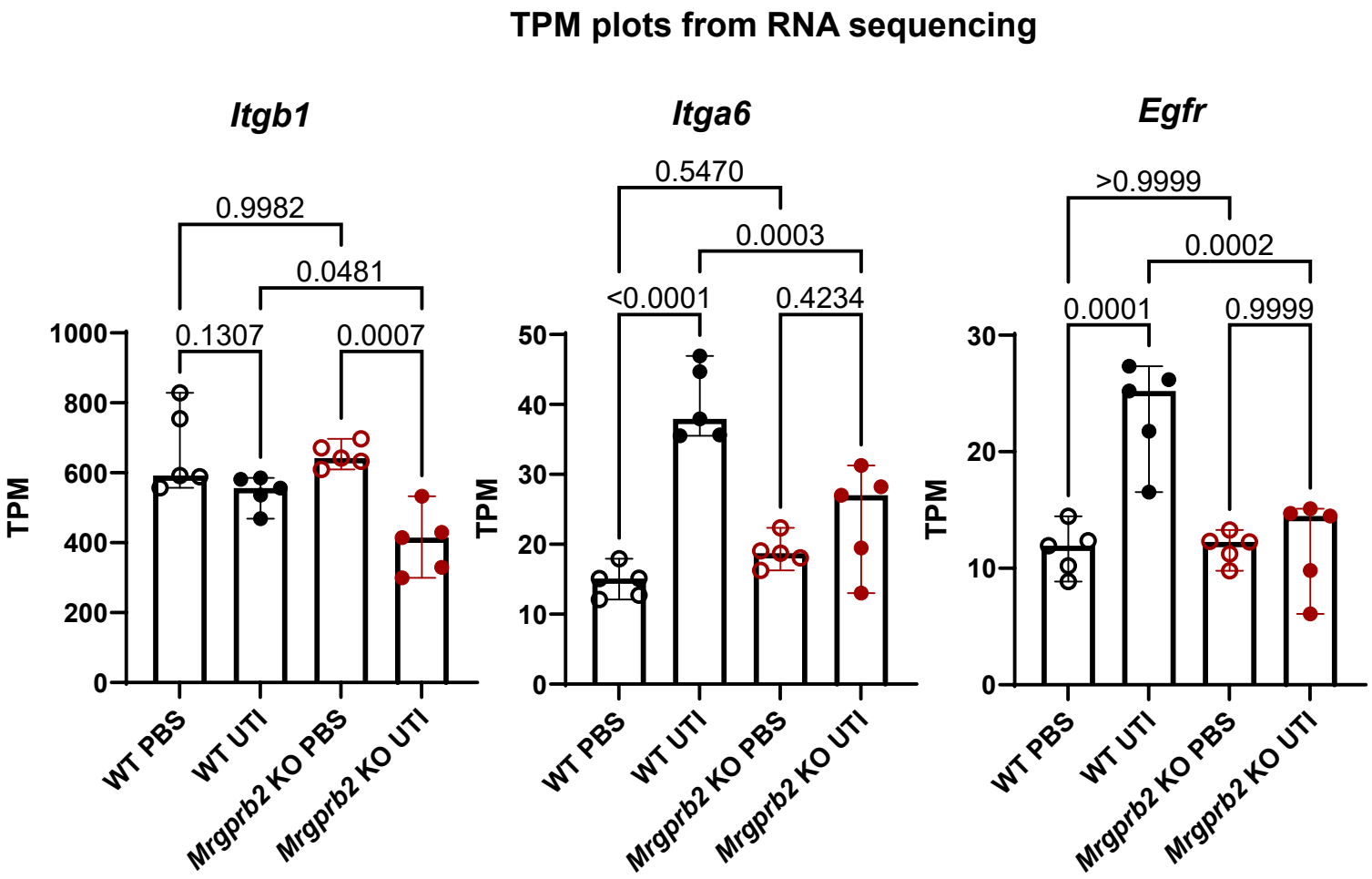

Figure S5: Mrgprb2 promotes transcriptional changes that increases epithelial receptivity

Transcripts Per Million (TPM) plots from RNAseq data show expression of *Egfr*, *Itgb1*, and *Itga6* in WT and *Mrgprb2* KO bladder in PBS and UTI conditions. Graph shows median with 95% CI. p-values are calculated using ordinary one-way ANOVA.

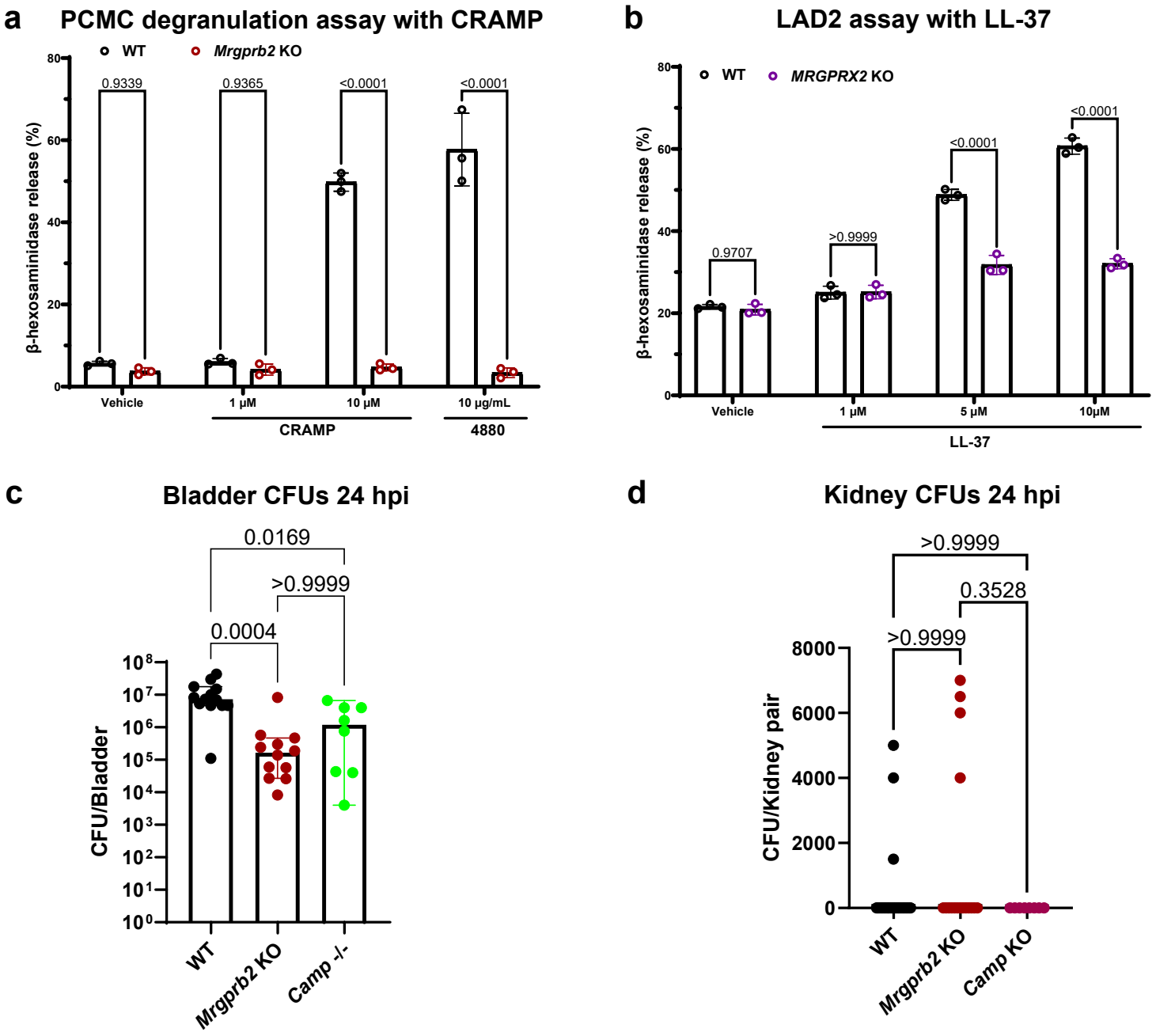

Figure S6: Mrgprb2 signals via cathelicidin interaction

a) Graph showing percentage of β-Hexosaminidase release in response to vehicle, CRAMP (1 μM, and 10μM), and 10μg/mL 4880 (positive control) in PCMCs obtained from WT and *Mrgprb2* KO mice. **b**) Graph showing percentage of β-Hexosaminidase release in response to vehicle and LL-37 (1 μM, 5 μM, and 10μM) in WT and *MRGPRX2* KO LAD2 mast cells. (**a-b**) Graph shows median with 95% CI. p-values are calculated using ordinary one-way ANOVA. **c**) Bladder CFUs 24 hpi in WT, *Mrgprb2* KO, and *Camp* KO mice. **d**) Kidney CFUs 24 hpi in WT, *Mrgprb2* KO, and *Camp* KO mice. (**c-d**) Graph shows median with 95% CI. p-values are calculated using Kruskal-Wallis test.

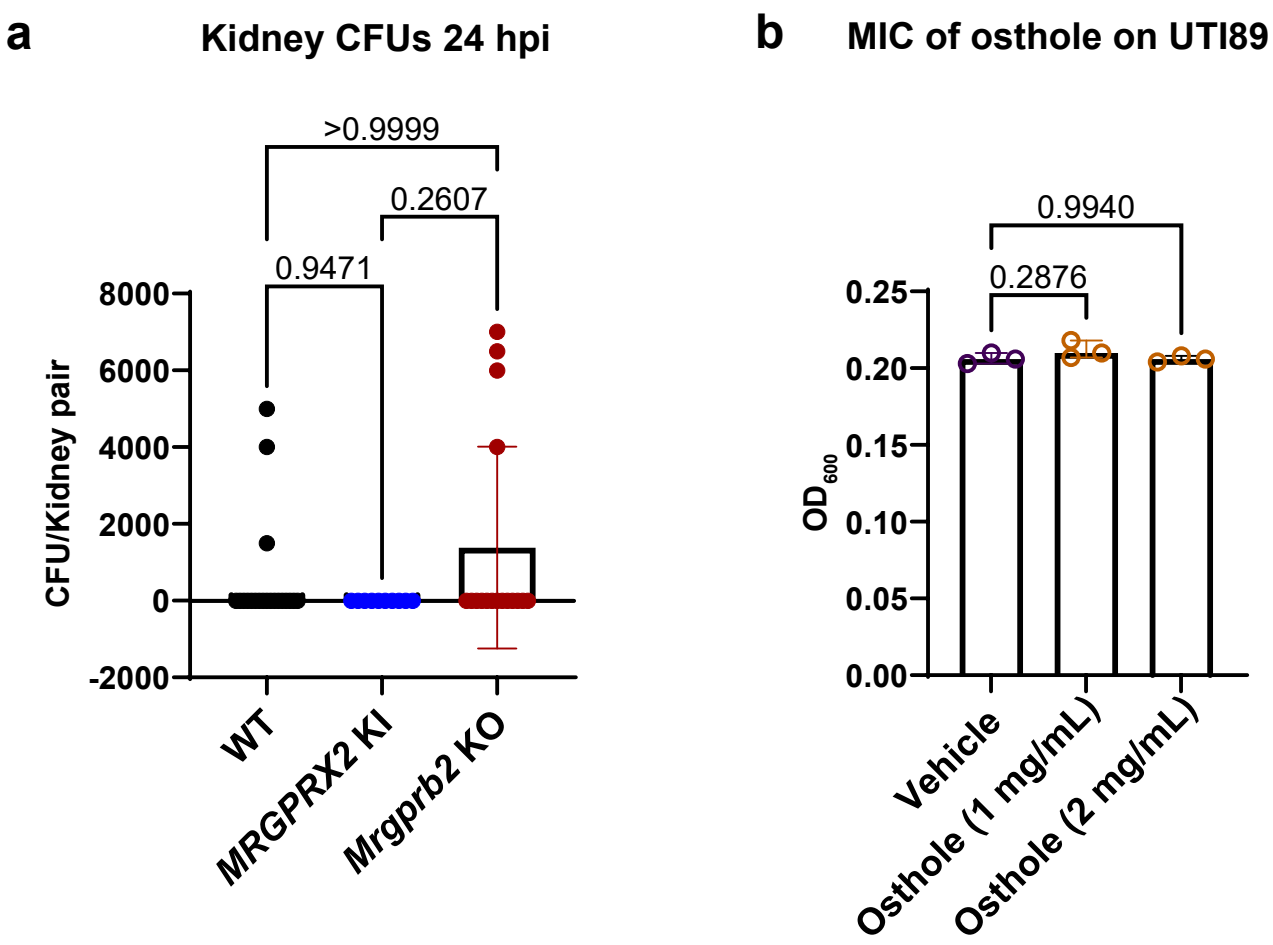

Figure S7: Osthole does not affect bacterial viability upon administration

a) Kidney CFUs 24 hpi in WT, *MRGPRX2* KI, and *Mrgprb2* KO. Graph shows median with 95% CI. p-values are calculated using Kruskal-Wallis test. **b**) Results from MIC assay showing the there is no difference in OD_{600} of UTI89 grown in vehicle (10% Tween 80 and 10% DMSO in LB), and with osthole (1 mg/mL and 2 mg/mL in LB containing 10% Tween 80 and 10% DMSO). Graph shows median with 95% CI. p-values are calculated using ordinary one-way ANOVA.