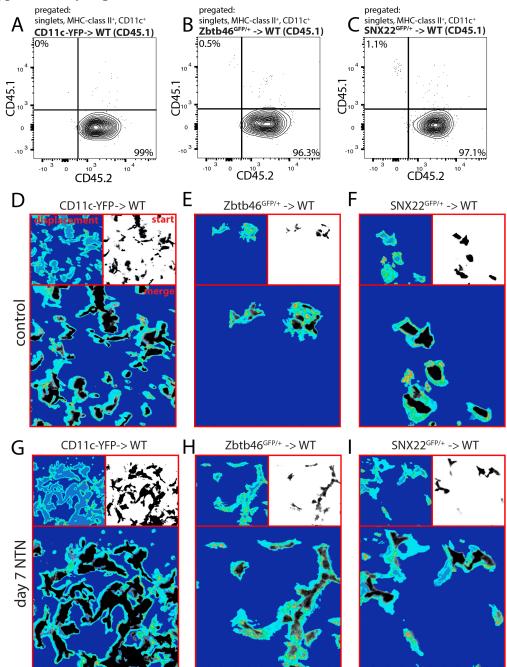
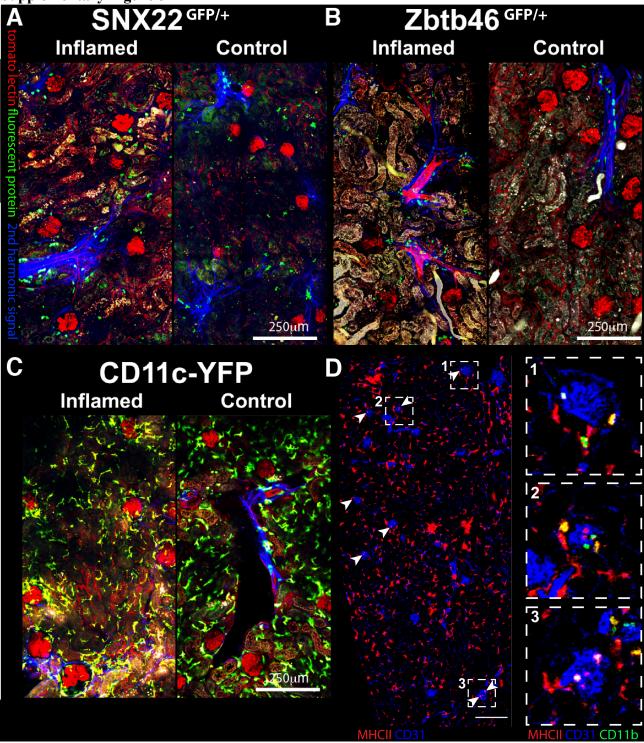


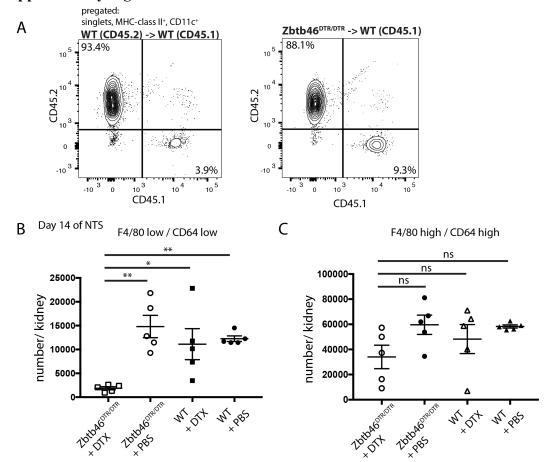
Generation and characterization of *Snx22*<sup>GFP</sup> knockin mice. (A) Shown is the *Snx22* genomic locus, targeting vector, and targeted allele after deletion of the floxed *Neo* by Cre recombinase. Exons are displayed as boxes. TK= thymidine kinase promoter; DTA= diphtheria toxin A expression cassette; triangles= LoxP sites. (B) Flow cytometry of kidney cells from a *Snx22*<sup>GFP/+</sup> mouse. Cells were pregated as indicated above the plots and analyzed for GFP expression. (C) CD45<sup>+</sup>/ *Snx22*-GFP<sup>HI</sup> cells were analyzed for expression of CD11c, MHC class II, CD103 and CD11b (D) *Snx22*<sup>GFP/+</sup> mice were analyzed for sensitivity and specificity of GFP expression. The percentage of *Snx22*<sup>GFP</sup> positive CD103<sup>+</sup> cDCs (gated as CD45+, MHC class II<sup>+</sup>, CD11c<sup>+</sup>, CD103<sup>+</sup>) was determined in 3 individual mice (sensitivity). The percentage of MHC class II<sup>+</sup>, CD11c<sup>+</sup>, CD103<sup>+</sup> cDCs of all CD45<sup>+</sup>, *Snx22*-GFP<sup>+</sup> cells was determined (specificity).



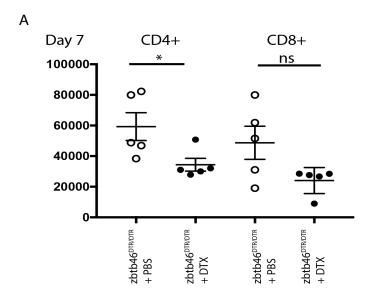
(A-C) Analysis of chimerism in MHC-class II<sup>+</sup>/CD11c<sup>+</sup> cells in the kidney, 8 weeks after transfer of Cd11c-YFP, *Zbtb46*<sup>GFP/+</sup> or *Snx22*<sup>GFP/+</sup> bone marrow (all CD45.2<sup>+</sup>) into lethally irradiated WT (CD45.1<sup>+</sup>) recipient mice. (D-F) Representative heatmaps of fluorescence intensity changes over time (images acquired every 30s for 15 minutes) in bone marrow chimeras at baseline (control). Each image shows the heatmap of the fluorescence intensity change and the shape of the cells in the start (time zero) images separately and also a merged image to demonstrate motility over time. (G-I) Representative heatmaps of fluorescence intensity changes over time (images acquired every 30s for 15 minutes) in bone marrow chimeras at day 7 after injection of NTS. The corresponding movies for all heatmaps in this figure are also present in the supplementary material.



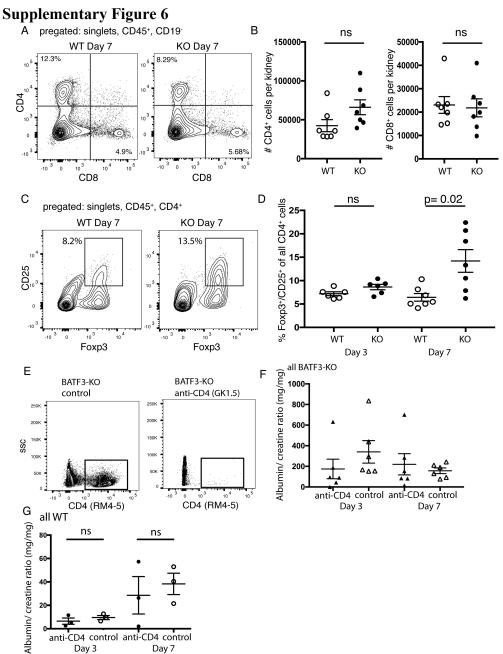
(A-C) Multiphoton tile-scans of kidney slices at baseline (control) and day 7 of NTN (inflamed) from (A)  $Snx22^{GFP/+}$ , (B)  $Zbtb46^{GFP/+}$ , and (C) CD11c-YFP bone marrow chimeras. Capillaries are depicted in red (tomato lectin), YFP or GFP in green, collagen fibers in blue (second harmonic signal), and the tubule system is visualized by auto-fluorescence (brown). (D) Immuno mass cytometry of a wildtype mouse kidney section shows MHC-class II<sup>+</sup> and CD11b<sup>+</sup> cells in healthy glomeruli (scale bar 200μm). Areas 1, 2 and 3 are also shown in higher magnification.



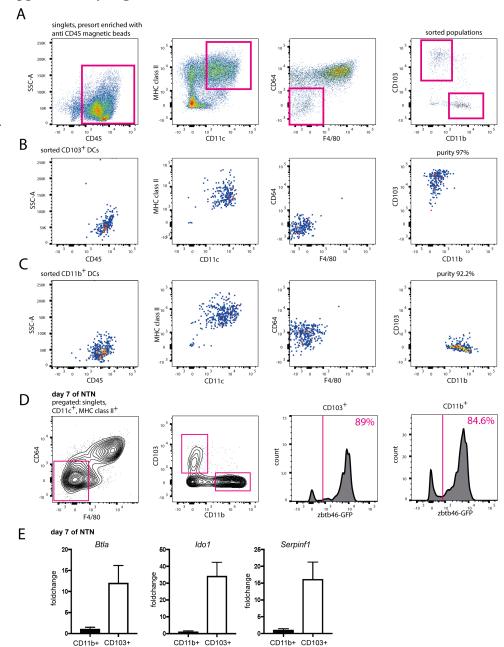
(A) Analysis of chimerism in MHC-class II<sup>+</sup>/CD11c<sup>+</sup> cells in the kidney 8 weeks after transfer of  $Zbtb46^{DTR/DTR}$  or WT bone marrow (both CD45.2<sup>+</sup>) into lethally irradiated WT (CD45.1<sup>+</sup>) recipient mice. (B) Absolute numbers of cDCs in chimeras 14 days after injection of NTS. cDCs were gated as being CD45<sup>+</sup>, MHC-class II<sup>+</sup>, CD11c<sup>+</sup>, CD64<sup>-</sup>, and F4/80<sup>-</sup>. Bone marrow chimeras created by transfer of  $Zbtb46^{DTR/DTR}$  or WT bone marrow were treated with either DTX or PBS every 48 hrs until the end of the experiment. Only the combination of  $Zbtb46^{DTR/DTR}$  + DTX led to a significant depletion of cDCs. (C) Absolute numbers of CD45<sup>+</sup>, MHC class II<sup>+</sup>, CD11c<sup>+</sup>, CD64<sup>+</sup>, F4/80<sup>+</sup> myeloid cells in  $Zbtb46^{DTR/DTR}$  or WT bone marrow chimeras treated with either DTX or PBS. The  $Zbtb46^{DTR/DTR}$  chimeras + DTX showed a trend towards lower numbers vs. controls, however this effect was not significant (this finding was confirmed in an independent experiment). Significance was determined by one-way-ANOVA followed by a Tukey's post-test. \* = P< 0.05, \*\* = P< 0.01.



**(A)** Quantification of absolute CD4<sup>+</sup> and CD8<sup>+</sup> T-cell numbers in kidneys of cDC-depleted and non-depleted mice at day 7 of NTN. The *Zbtb46*<sup>DTR/DTR</sup> chimeras + DTX showed a trend towards lower CD8<sup>+</sup> numbers vs. controls, however this effect was not significant (this finding was confirmed in an independent experiment).



(A) Representative FACS plot of CD4<sup>+</sup> and CD8<sup>+</sup> T-cells in *Batf*3-KO and WT mice at day 7 of NTN in kidney single cell suspensions. (B) Quantification of absolute CD4<sup>+</sup> and CD8<sup>+</sup> T-cell number per kidney in in *Batf*3-KO and WT mice. (C) Representative FACS plots of T-regulatory (Treg) cells in *Batf*3-KO and WT mice at day 7 of NTN in kidney single cell suspensions. Tregs were gated as CD45<sup>+</sup>, CD25<sup>+</sup>, and Foxp3<sup>+</sup>. (D) Quantification of Tregs at day 3 and day 7 of NTN; shown is the percentage of CD25<sup>+</sup>/Foxp3<sup>+</sup> cells of all CD45<sup>+</sup>/CD4<sup>+</sup> cells in *Batf*3-KO and WT mice. (E) Representative FACS plots of white blood cells from *Batf*3-KO mice treated with either anti-CD4 antibody (clone GK1.5) or isotype control. Cells were stained for CD4 (clone RM4-5). (F) Urinary albumin to creatinine ratios (mg/mg) of *Batf*3 KO mice treated with either anti-CD4 antibody or PBS before injection of NTS. (G) Urinary albumin to creatinine ratios (mg/mg) of WT mice treated with either anti-CD4 antibody or PBS before injection of NTS.



(A) Gating strategy for the sorting of CD11b<sup>+</sup> and CD103<sup>+</sup> cDCs. Kidney single cell suspensions were pre-sort enriched by anti-CD45 magnetic bead separation to increase sorting efficiency. After sorting, the purity of sorted CD103<sup>+</sup> (B) and CD11b<sup>+</sup> (C) cDCs was analyzed on a flow cytometer. The percentage of purity was calculated as percent CD45<sup>+</sup>, CD11c<sup>+</sup>, MHC class II<sup>+</sup>, F4/80<sup>-</sup>, CD64<sup>-</sup>, CD103<sup>+</sup> or CD11b<sup>+</sup> cells of all recorded events. (D) Flow cytometry of a zbtb46<sup>GFP/+</sup> mouse at day 7 of nephrotoxic nephritis. Cell were pregated as indicated. In the inflamed kidney, the majority of both CD103<sup>+</sup> and CD11b<sup>+</sup> cDCs were still zbtb46-GFP positive. (E) qPCR expression analysis of three potentially anti-inflammatory genes, that were identified as specifically upregulated in CD103<sup>+</sup> cDCs by RNAseq. qPCR confirmed the upregulation of *Btla, Ido1, Serpinf1* in CD103<sup>+</sup> cDCs at day 7 of NTN in comparison to CD11b<sup>+</sup> cDCs. Three biological replicates per group, CD11b<sup>+</sup> and CD103<sup>+</sup> cDCs were sorted from the same three animals.

#### Movie S1:

Time-lapse (interval = 30s) 3D reconstruction of a vibratome-cut kidney slice of a healthy CD11c-YFP bone marrow chimera demonstrates cell motility over time. The movie was overlaid with a heat map to demonstrate how change in fluorescence intensity over time was quantified. Most YFP<sup>+</sup> cells remained stationary, while their processes were extending and retracting.

#### Movie S2:

Time-lapse (interval = 30s) 3D reconstruction of a vibratome-cut kidney slice of a CD11c-YFP bone marrow chimera at day 7 of NTN. The movie was overlaid with a heat map to demonstrate how fluorescence intensity change over time was quantified. Although YFP<sup>+</sup> cell numbers in the periglomerular region increased, the majority of the cells remained stationary, with motile cell processes probing the surrounding tissue.

#### Movie S3:

Time-lapse (interval = 30s) 3D reconstruction of a vibratome-cut kidney slice of a healthy  $Zbtb46^{GFP/+}$  bone marrow chimera demonstrates cell motility over time. The movie was overlaid with a heat map to demonstrate how change in fluorescence intensity over time was quantified.  $GFP^+$  cells showed a more motile cell body but with only short processes.

#### Movie S4:

Time-lapse (interval = 30s) 3D reconstruction of a vibratome-cut kidney slice of a  $Zbtb46^{GFP/+}$  bone marrow chimera at day 7 of NTN. The movie was overlaid with a heat map to demonstrate how change in fluorescence intensity over time was quantified.  $GFP^+$  cell numbers were increased in comparison to those in movie S3, and most of the cells showed high cell motility.

### **Movie S5:**

Time-lapse (interval = 30s) 3D reconstruction of a vibratome-cut kidney slice of a healthy  $Snx22^{GFP/+}$  bone marrow chimera. The movie was overlaid with a heat map to demonstrate how change in fluorescence intensity over time was quantified.  $GFP^+$  cells showed rapid displacement of their cell bodies with short cell protrusions.

### **Movie S6:**

Time-lapse (interval = 30s) 3D reconstruction of a vibratome-cut kidney slice of a  $Snx22^{GFP/+}$  bone marrow chimera at day 7 of NTN. The movie was overlaid with a heat map to demonstrate how change in fluorescence intensity over time was quantified.  $GFP^+$  cells showed rapid displacement of their cell bodies, with a cell process in close proximity to structures of the glomerulus (circle).