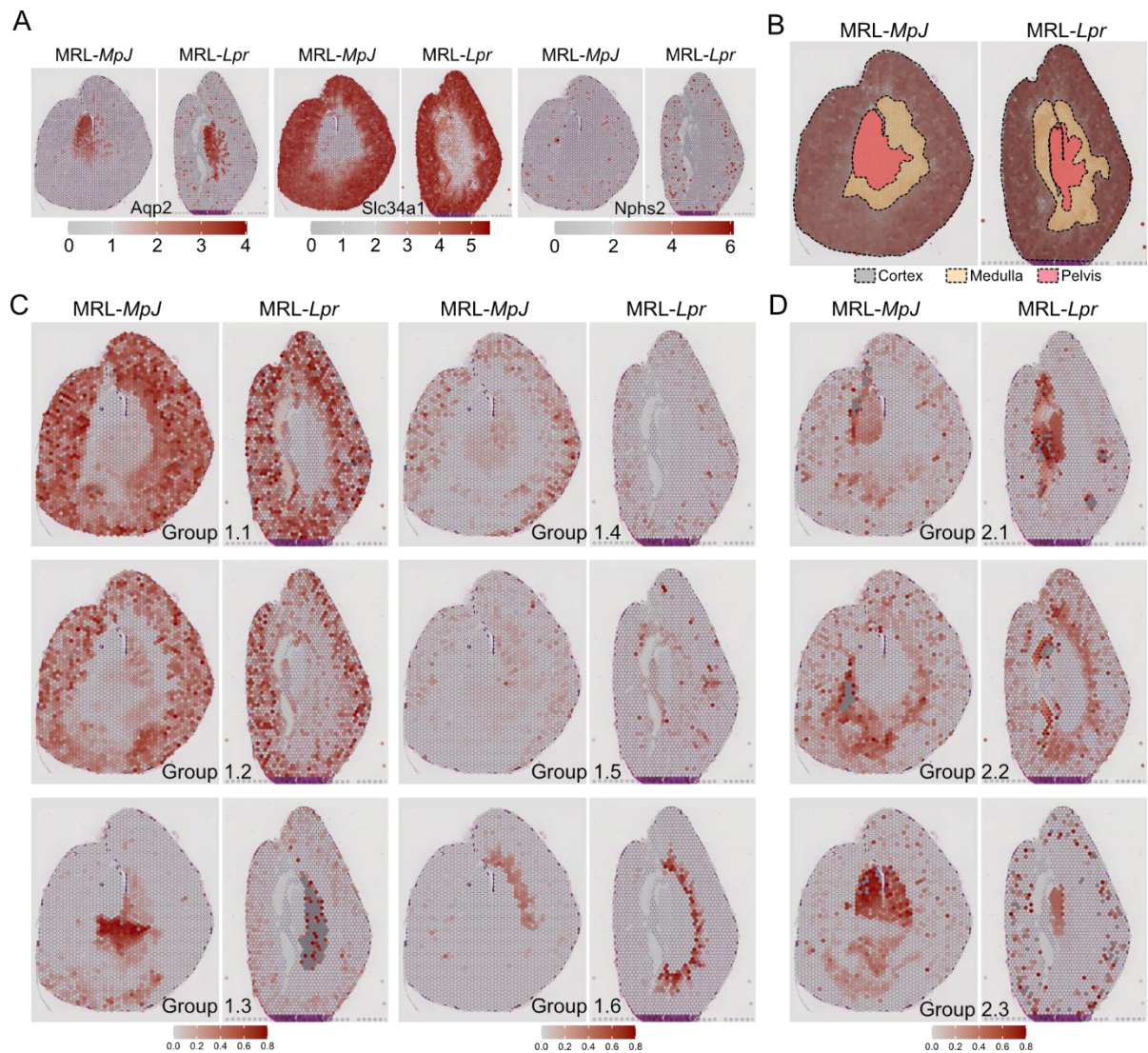


Supplemental figure 1: Macrophage populations expand with inflammation. (A)

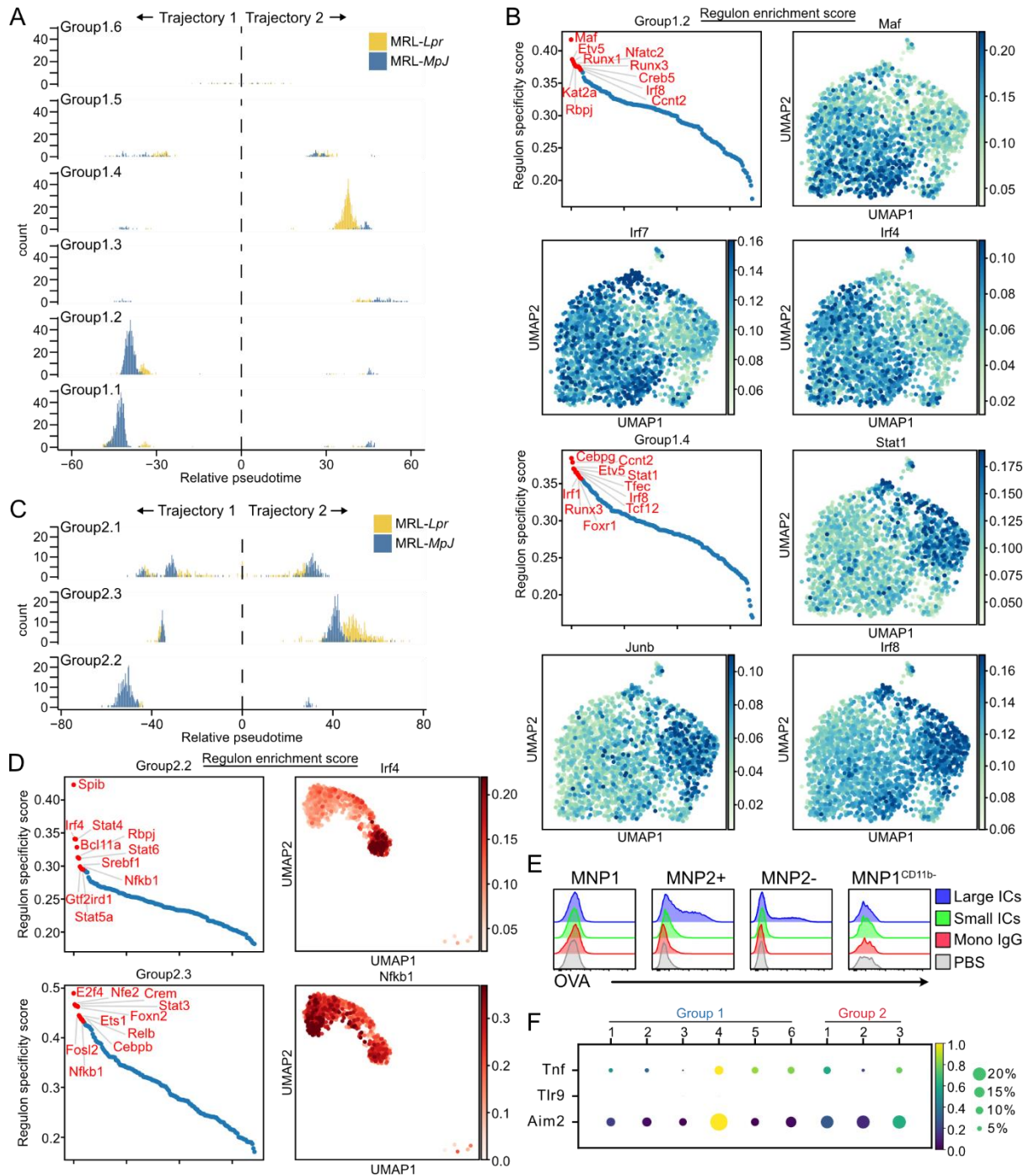
Representative iterative staining (n = 3) on murine C57BL/6 kidney showing MNP distribution throughout the tissue through expression of F4/80 (cyan), CD11b (yellow) and MHC II (magenta) (bottom) relative to blood vessels (CD31, red) and surrounding smooth muscles (α SMA, blue) and nerves (β III tubulin, green) (top). Scale bar = 350 μ m

(B) Representative confocal microscopy (n = 3 per group) showing MNP distribution in kidneys from 18-week-old MRL-*MpJ* (left) and MRL-*Lpr* (middle and right) mice through expression of F4/80 (cyan) and CD11b (yellow) relative to blood vessels (CD31, red). Scale bar = 150 μ m.



Supplemental figure 2: Spatial distribution of kidney macrophage populations. (A)

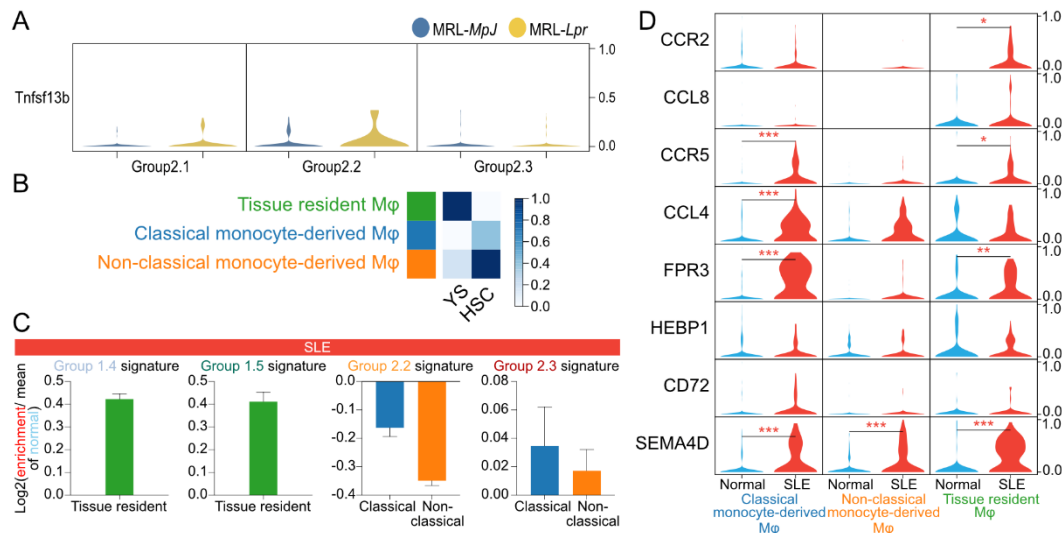
Spatial expression of markers used to delineate the anatomical regions in Visium Spatial Gene Expression data of MRL-*MpJ* and MRL-*Lpr* kidney sections (Aqp2 – pelvis; Slc34a1 = proximal tubules and Nphs2 – glomeruli). **(B)** Delineation of anatomical regions in MRL-*MpJ* and MRL-*Lpr* visium kidney sections based on (A). **(C)** Spatial transcriptomics of Group 1 macrophages signatures in MRL-*MpJ* and MRL-*Lpr* murine kidneys with annotated scRNAseq data above. Each spot / voxel denotes a prediction score of 0 – 1 for the location of each of the macrophage subgroups. **(D)** Spatial transcriptomics of Group 2 macrophages signatures in MRL-*MpJ* and MRL-*Lpr* murine kidneys with annotated scRNAseq data above. Each spot / voxel denotes a prediction score of 0 – 1 for the location of each of the macrophage subgroups.



Supplemental figure 3: Trajectory and regulon analysis of kidney macrophages. (A)

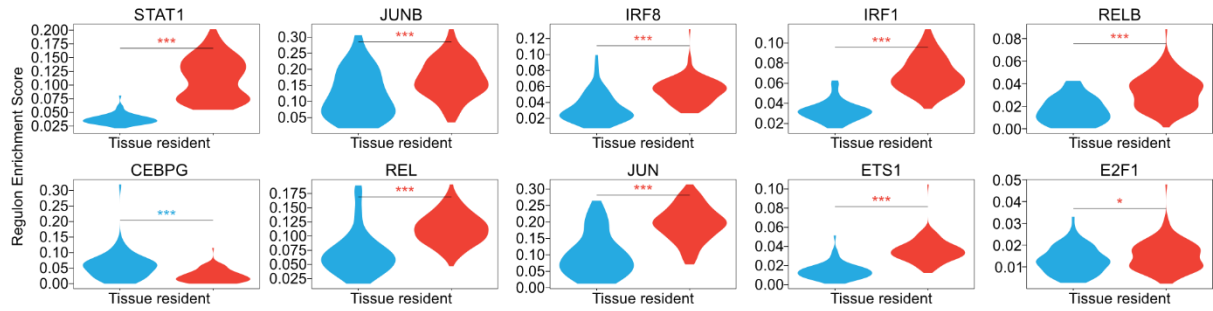
Proportion of cells from MRL-*MpJ* (blue) or MRL-*Lpr* (yellow) from each Group 1 cluster distributed along pseudotime scale. **(B)** (Top) Top ranked regulons in trajectory 1 for Group 1 (left) and enrichment UMAP of regulon activity of Maf, Irf7 and Irf4 in Group 1.2 trajectory (trajectory 1). (Bottom) Top ranked regulons in trajectory 2 for Group 1 (left) and enrichment UMAP of regulon activity of Stat1, Junb and Irf8 in Group 1.4 trajectory (trajectory 2). **(C)** Proportion of cells from MRL-*MpJ* (blue) or MRL-*Lpr* (yellow) from each Group 2 cluster distributed along pseudotime scale. **(D)** (Top left) Top ranked regulons in trajectory 1 for Group 2. (top right) Enrichment UMAP of regulon activity of Irf4 in Group 2.2 trajectory

(trajectory 1). (Bottom left) Top ranked regulons in trajectory 2 for Group 2. (Bottom right) Enrichment UMAP of regulon activity of Nfkb1 in Group 2.3 trajectory (trajectory 2). **(E)** Uptake of free and immune complexed AF647-OVA by kidney MNPs in vivo 2h following intravenous injection in C57BL/6 mice. 5:1 (large) and 1:1 (small) molar ratios of mouse IgGs:OVA were used. **(F)** Mean expression dot plot of genes Tnf, Tlr9 and Aim2.

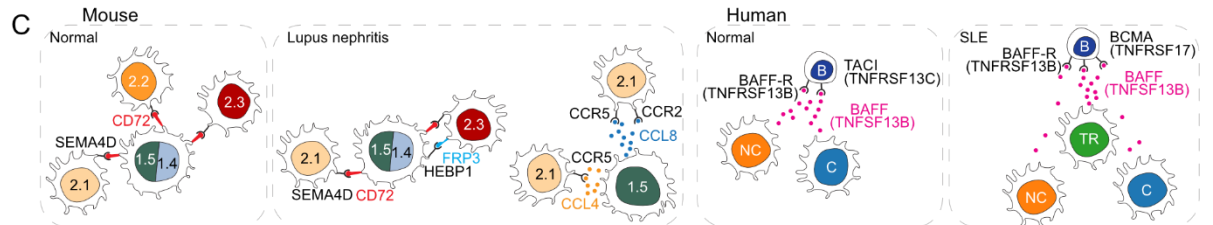
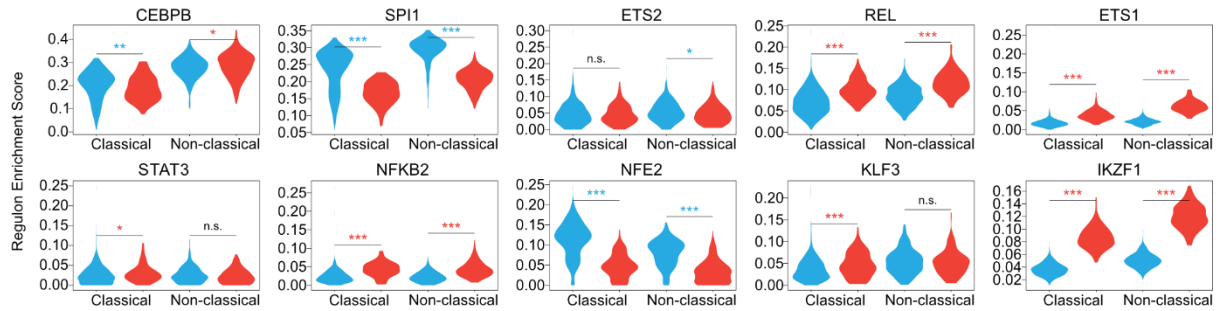


Supplemental figure 4: Kidney macrophages in human SLE. (A) Violin plot of Tnfsf13b (BAFF) in Group 2 clusters. (B) Heatmap of mean AUCell enrichment of F4/80hi/lo gene sets, corresponding to yolk sac (YS) vs hematopoetic stem-cell (HSC) lineage. Row enrichment value is scaled from 0 to 1 and presented as an increasing gradient from white to blue which corresponds to increasing enrichment score. (C) Bar charts showing relative log2 difference of AUCell enrichment of mouse Group1 and Group2 macrophage clusters in SLE compared to normal (mean of normal enrichment used as reference). (D) Violin plot of molecules, with significant interactions found in mouse macrophage in (A), in human macrophage clusters. Expression value is scaled from 0 to 1 across cell clusters. Significance was calculated using Wilcoxon rank sum test with BH post-test applied where * $p < 0.05$; *** $p < 0.001$. Colour of the p-value indicates which group has a higher value (red = SLE, blue = normal).

A Group1.4 Top 10 Regulons



B Group2.3 Top 10 Regulons



Supplemental figure 5: Top regulons in kidney macrophages. (A) Violin plot of regulon enrichment scores in human tissue resident macrophages split by normal (blue) or SLE (red) for Group1.4-related top 10 transcription factors. Significance was calculated using Wilcoxon rank sum test with BH post-test applied where $*p < 0.05$; $***p < 0.001$. Colour of the p-value indicates which group has a higher value (red = SLE, blue = normal). **(B)** Violin plot of regulon enrichment scores in human monocyte-derived macrophages split by normal (blue) or SLE (red) for Group2.3-related top 10 transcription factors. Significance was calculated using Wilcoxon rank sum test with BH post-test applied where $*p < 0.05$; $***p < 0.001$. Colour of the p-value indicates which group has a higher value (red = SLE, blue = normal). **(C)** Summary illustration of macrophage interactions in mouse and human kidneys.