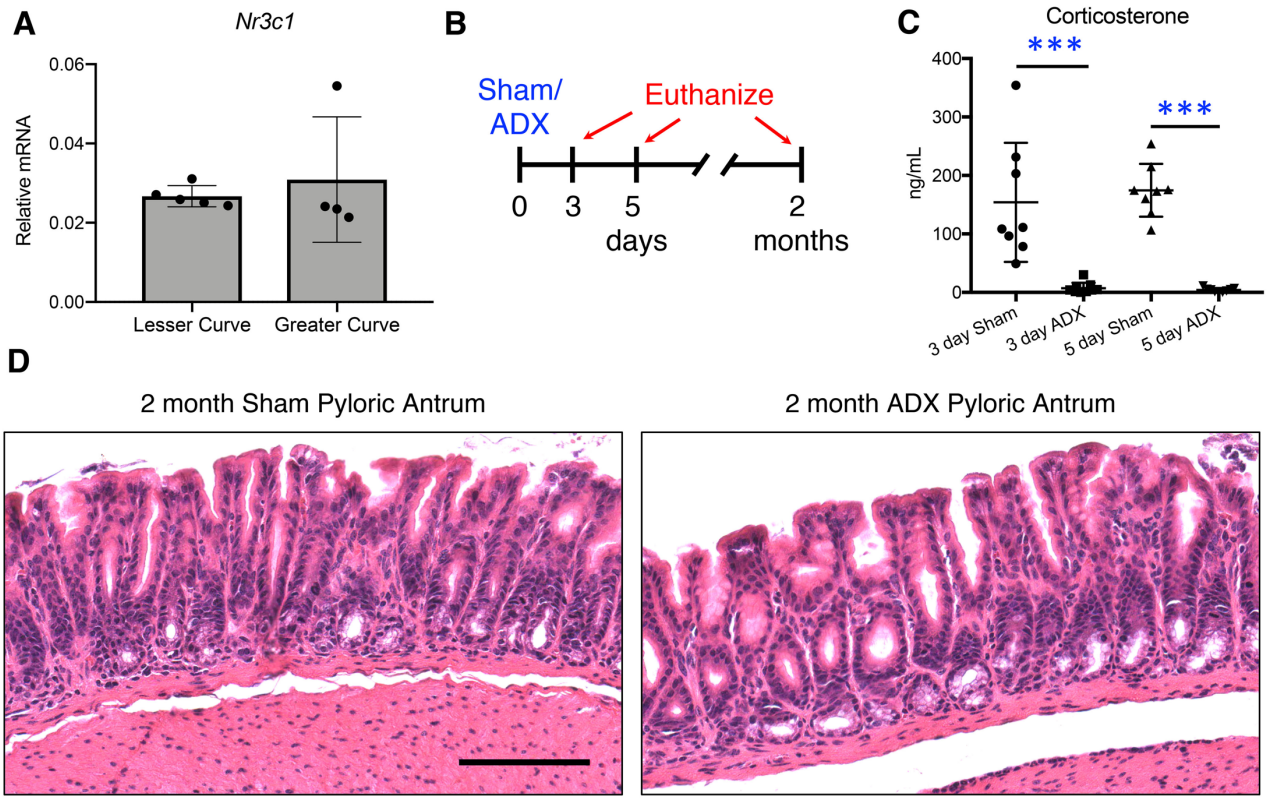
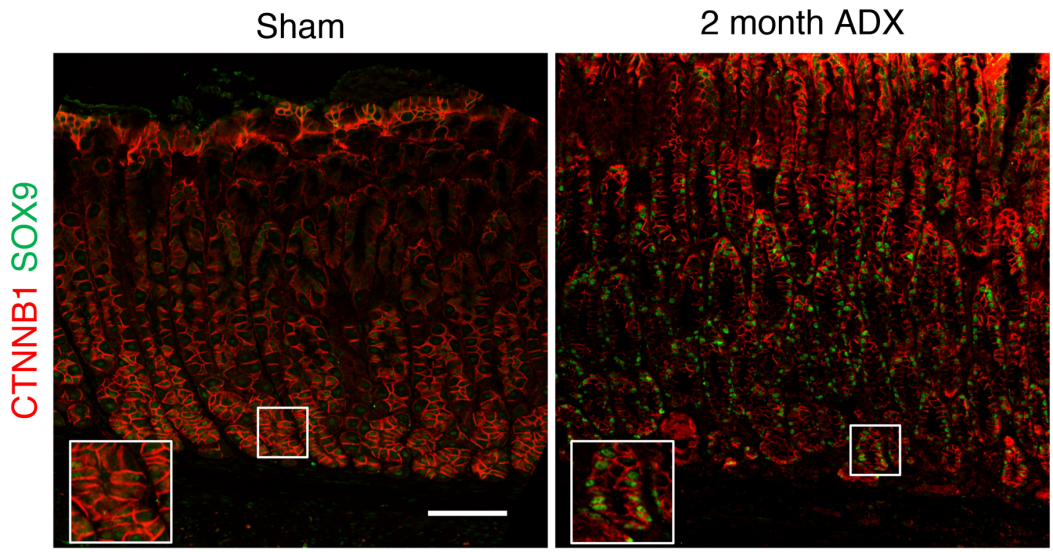
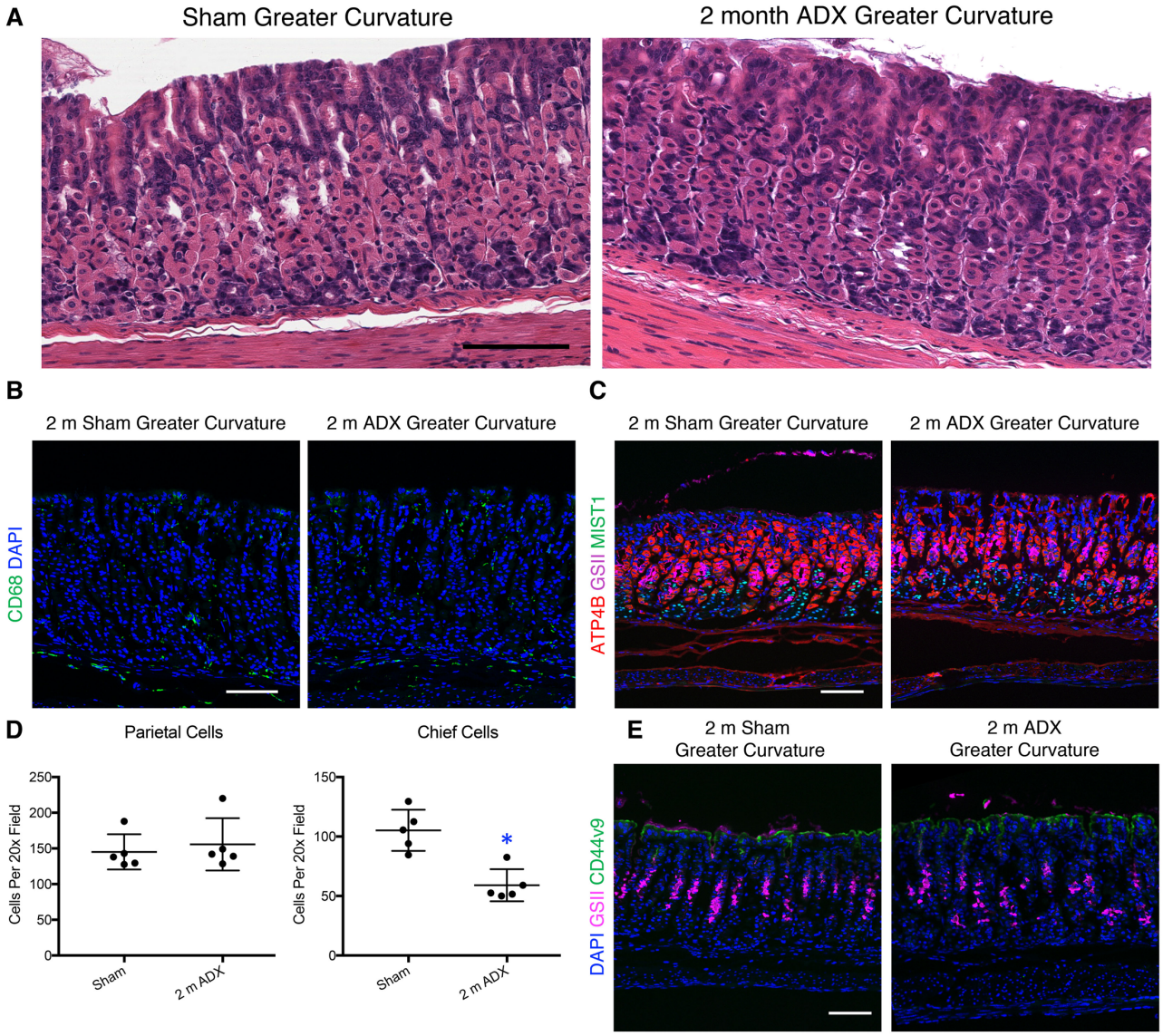


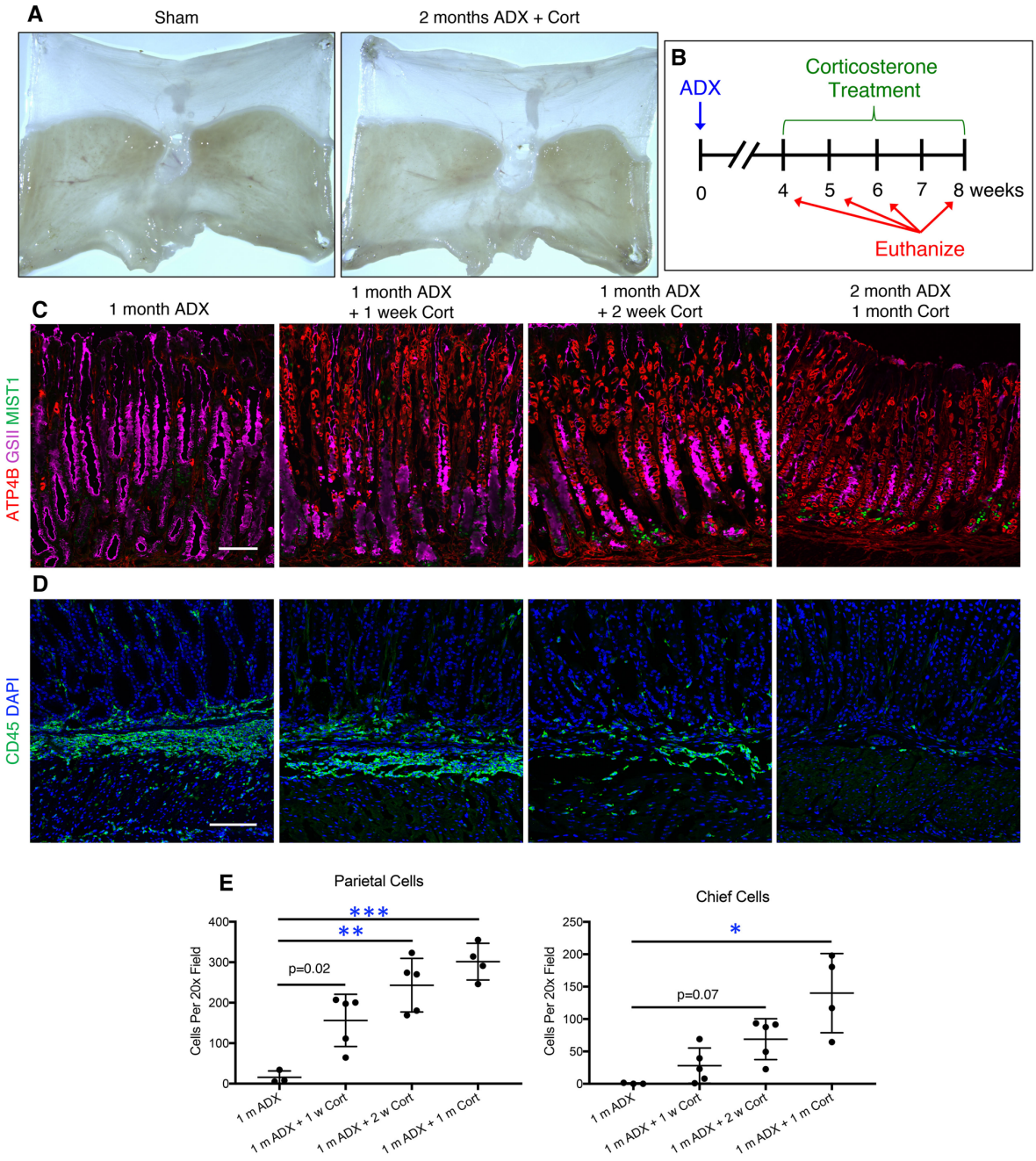
Supplementary Figure 1. Circulating glucocorticoids are depleted 3 days post adrenalectomy. (A) Quantitative RT-PCR using RNA isolated from the lesser curvature and greater curvature of the gastric corpus from adrenal-intact mice. *P*-values were determined by paired *t*-test; $n \geq 4$. (B) Schematic of experimental model system. (C) Commercial ELISA assay for serum corticosterone in sham mice or mice euthanized 3 days post-adrenalectomy. ($n=8$ mice/group); *P*-values were determined by one-way ANOVA with post hoc Tukey's *t*-test ***$P \leq 0.0001$. Data are mean ± SD (in both A and C) (D) Hematoxylin and eosin staining of tissue sections from the gastric pyloric antrum. Scale bar are 100 μm; $n=5$ mice/group.



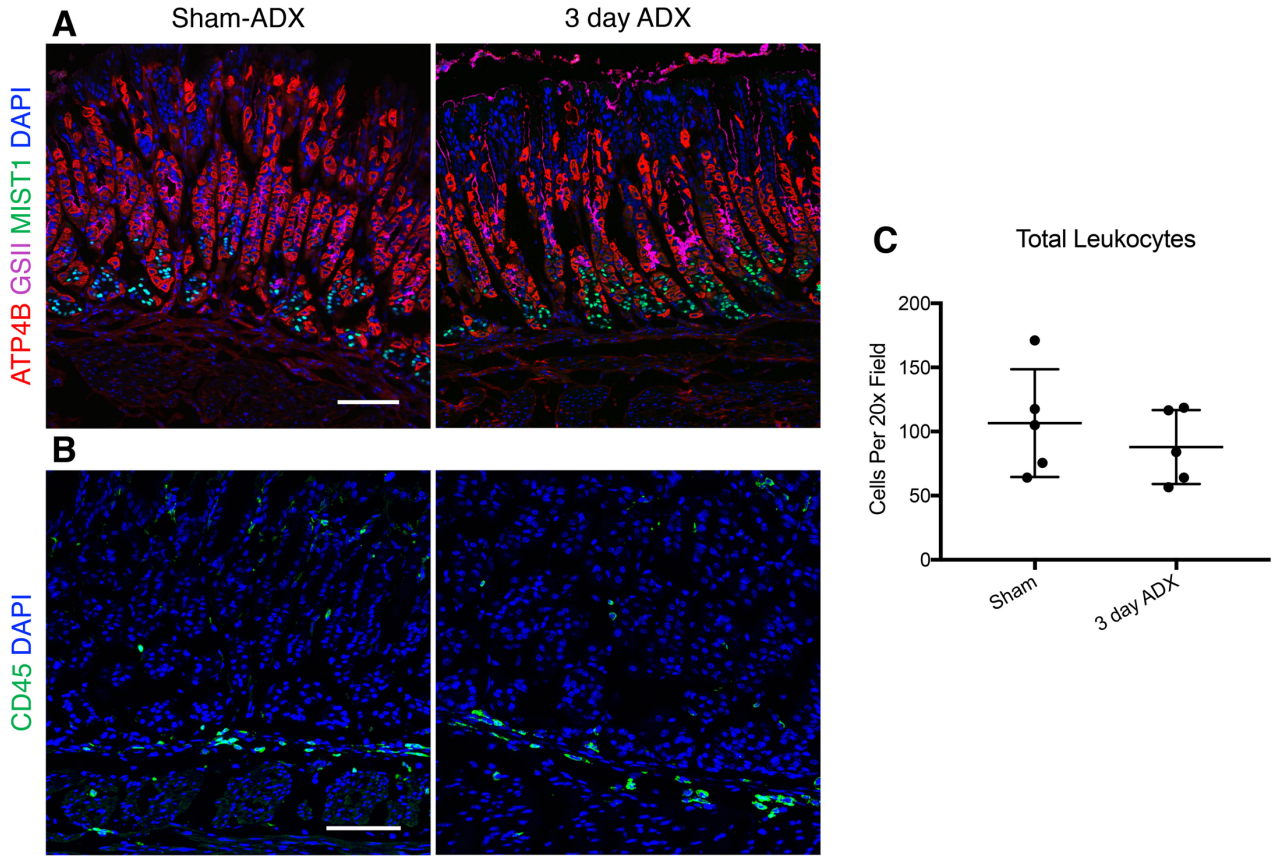
Supplementary Figure 2. Adrenalectomy induces expression of the SPEM marker gene SOX9. Stomach sections from the gastric corpus lesser curvature from mice euthanized 2 months after sham surgery or adrenalectomy probed for the SPEM marker SOX9 (green) and the epithelial cell marker CTNNB1 (red). Scale bars are 100 μm; *n*=6 mice/group.



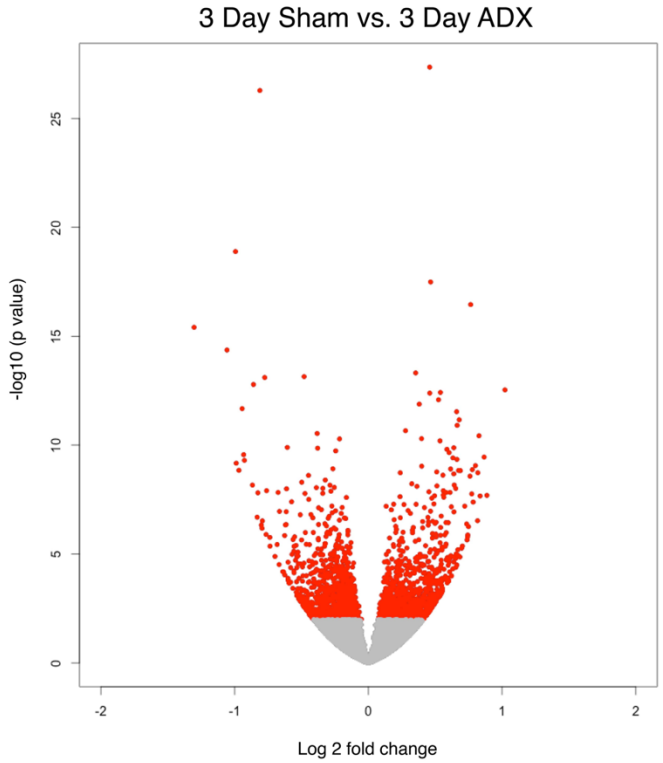
Supplementary Figure 3. Adrenalectomy does not trigger inflammation or SPEM within the gastric corpus greater curvature. (A) H&E micrograph of the gastric corpus from mice euthanized 2 months after sham surgery or adrenalectomy. (B-C) Tissue sections of the gastric corpus greater curvature probed for CD68 (green, macrophages) or (C) for ATP4B (parietal cells, red), GSII lectin (mucous neck cells, pink), and MIST1 (chief cells, green). (D) Quantitation of the number of parietal cells and chief cells per 20x field within the greater curvature. Data are mean ± SD; *P*-values were determined by unpaired two-tailed *t*-test; * $P \leq 0.01$ (E) Stomach sections probed for the SPEM marker CD44v9 (green) and for the MNC marker GSII (pink). Scale bars are 100 μm; *n*=5 mice/group for all experiments.



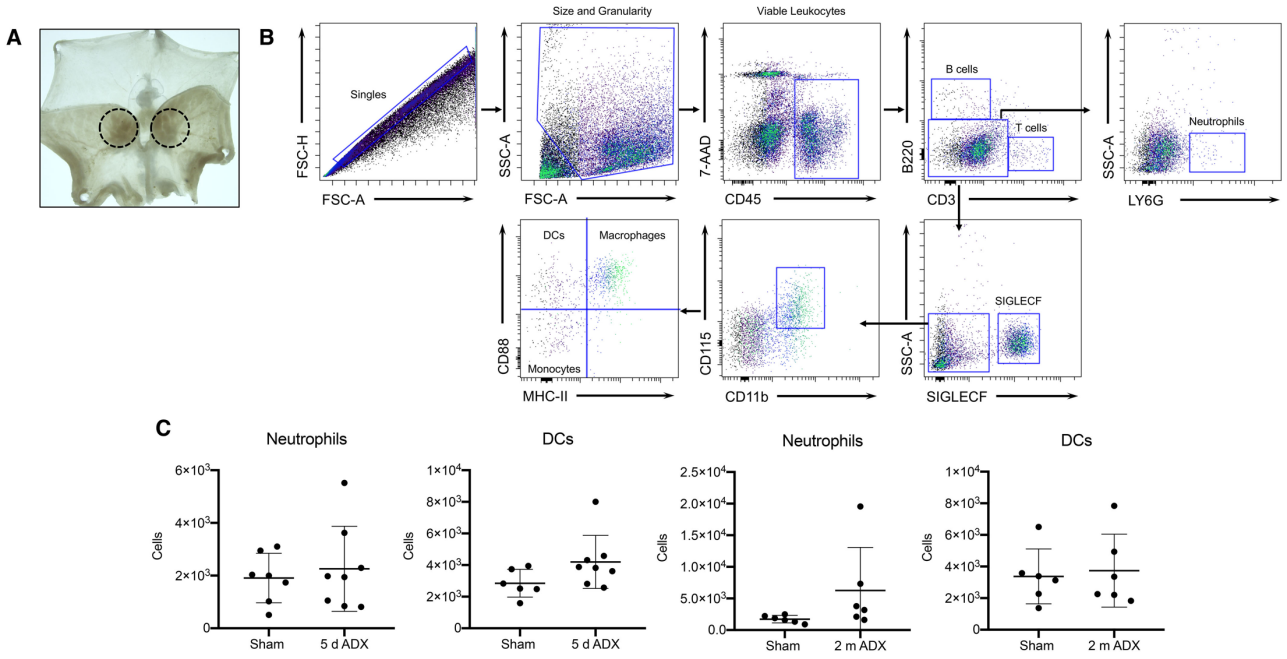
Supplementary Figure 4. Treatment with endogenous glucocorticoids reverses SPEM and gastric inflammation. (A) Representative image of the internal stomach from mice euthanized 2 months after sham surgery or from adrenalectomized mice treated with corticosterone for 2 months (*n*=5 mice/group). (B) Mice were adrenalectomized at 8 weeks of age. Corticosterone treatment was initiated 1 month after surgery and mice were euthanized 1 week, 2 weeks, or 1 month of continuous treatment. Control mice were euthanized 1 month after adrenalectomy. (C-D) Section from the gastric corpus lesser curvature were probed for (C) ATP4B (parietal cells, red), GSII lectin (mucous neck cells, pink), and MIST1 (chief cells, green) or for (D) CD45 (leukocytes, green). Nuclei were stained with DAPI (blue). Scale bars are 100 μm. (E) Quantitation of the number of parietal cells and chief cells observed per 20x field in the lesser curvature. *n*≥3 mice/group; experiment was performed one time. Data are mean ± SD; *P*-values were determined by one-way ANOVA with post hoc Tukey's *t*-test. **P*≤0.01 ***P*≤0.001 ****P*≤0.0001.



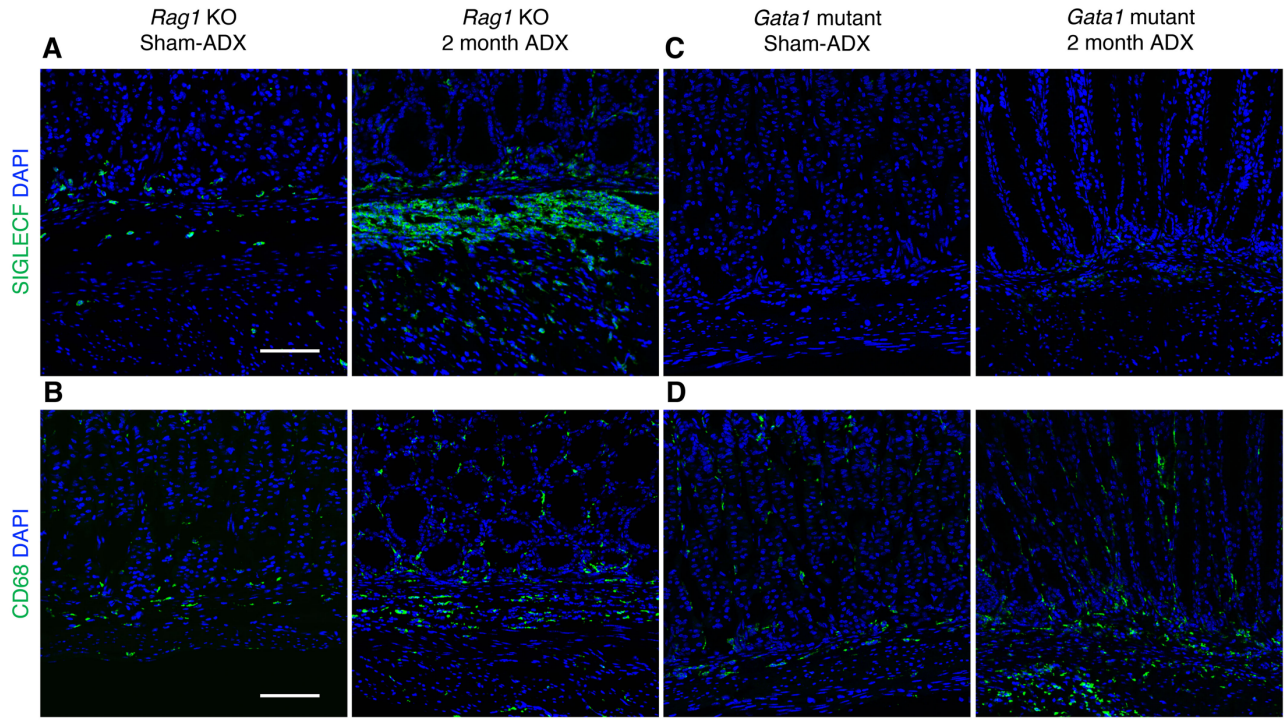
Supplementary Figure 5. The gastric mucosa is histologically normal 3 days post-adrenalectomy. Immunostaining of the gastric corpus lesser curvature from mice euthanized 3 days after sham surgery or adrenalectomy. Sections were probed for (A) ATP4B (parietal cells, red), GSII lectin (mucous neck cells, pink), and MIST1 (chief cells, green) or for (B) CD45 (leukocytes, green). Nuclei were stained blue with DAPI. Scale bars are 100 μm. (C) Quantitation of the number of CD45+ leukocytes within the lesser curvature (*n*=5 mice/group). Data are mean ± SD; *P*-values were determined by unpaired two-tailed *t*-test.



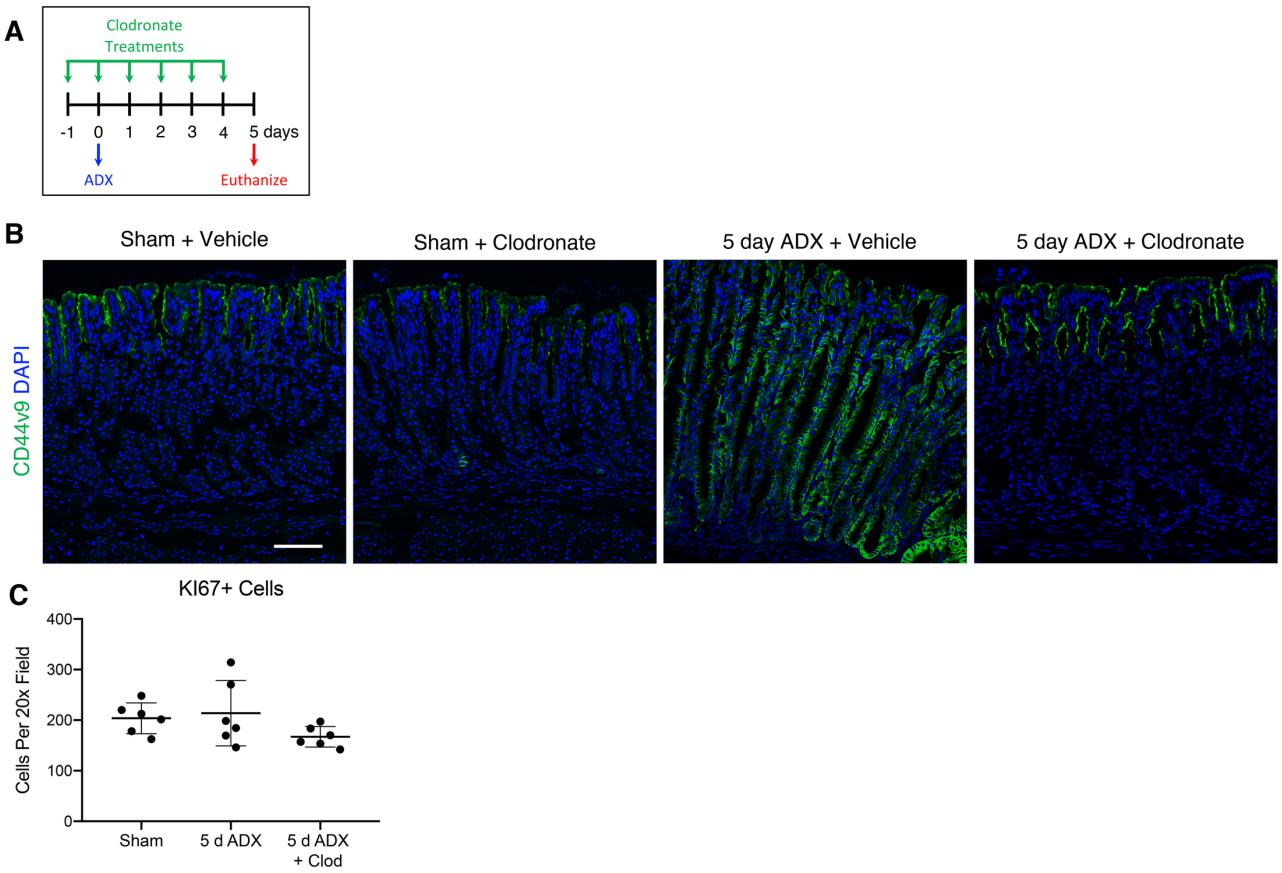
Supplementary Figure 6. Adrenalectomy induces transcriptional changes of a large number of genes in the gastric corpus. A volcano plot of the differentially regulated genes identified by RNAseq in the gastric corpus lesser curvature 3 days after adrenalectomy compared to mice euthanized 3 days after sham surgery. The dots in red are statistically significant with $P<0.01$; $n=4$ mice/group.



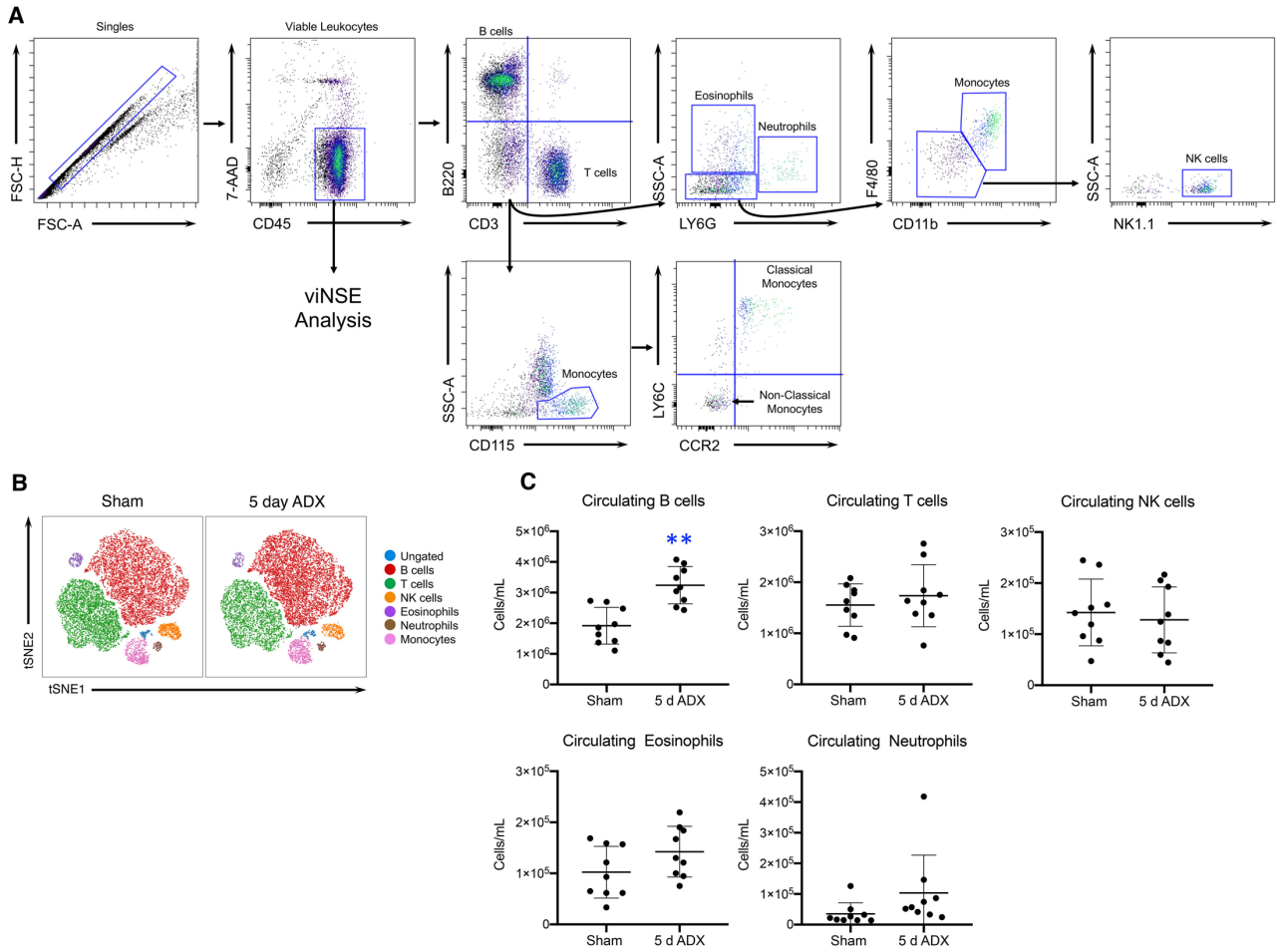
Supplementary Figure 7. Adrenalectomy does not lead to changes in the number of stomach neutrophils. (A) Leukocytes were isolated from the gastric corpus lesser curvature for analysis by flow cytometry. (B) The gating strategy use to identify the indicated cell populations. (C) Quantitation of the number of neutrophils and dendritic cells within the gastric corpus lesser curvature of mice euthanized 5 days or 2 months after sham surgery or adrenalectomy; *n*=9 mice/group.



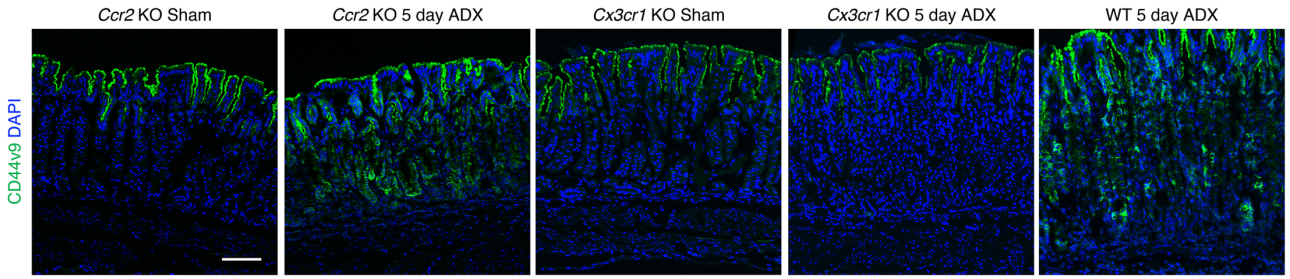
Supplementary Figure 8. Removal of B cells and T cells and eosinophils does not prevent adrenalectomy induced gastric inflammation. Representative stomach sections from *Rag1* knockout mice (A-B) or *Gata1* mutant mice (C-D) euthanized 2 months after sham surgery or adrenalectomy. Sections were probed for (A and C) SIGLECF (eosinophils, green) or for (B and D) CD68 (macrophages, green). Nuclei were labeled with DAPI (blue). Scale bars are 100 μm; *n*=6 mice/group.



Supplementary Figure 9. Macrophage depletion prevents SPEM development. (A) Schematic of experimental design. Mice were treated with vehicle or clodronate loaded liposomes daily for 6 consecutive days beginning 24 hours before sham surgery or adrenalectomy and were euthanized 5 days after surgery. (B) Representative images of tissue sections from the gastric corpus lesser curvature from mice treated with vehicle or clodronate euthanized 5 days after sham surgery or adrenalectomy (*n*≥7 mice/group). Sections were probed for the SPEM marker CD44v9 (green) and nuclei were labeled blue with DAPI. Scale bar is 100 μm. (C) Quantitation of KI67/CTNNB1 double positive cells within the gastric corpus lesser curvature 5 days after sham surgery or adrenalectomy or in adrenalectomized mice treated with clodronate liposomes; *n*=6 mice/group.



Supplementary Figure 10. Adrenal insufficiency does not trigger general leukocytosis in peripheral blood. (A) The gating strategy used to analyze peripheral blood leukocytes. (B) Representative tSNE analysis of peripheral blood leukocytes isolated from mice euthanized 5 days after sham surgery or adrenalectomy. (C) Quantitation of peripheral blood leukocytes by flow cytometric analysis. *P*-values were determined by unpaired *t*-test. ***P*≤0.001; *n*=9 mice/group.



Supplementary Figure 11. Adrenalectomy does not induce SPEM in *Cx3cr1* KO mice. Stomach sections from *Ccr2* KO or *Cx3cr1* KO mice euthanized 5 days after sham surgery or adrenalectomy or from WT mice euthanized 5 days after adrenalectomy. Sections were probed for the SPEM marker CD44v9 (green). Nuclei were stained blue with DAPI. Scale bars are 100 μm; $n \geq 6$ mice/group.

Supplementary Table 1: Antibodies

Antibody	Concentration	Catalog #	Application	Supplier
MIST1	1:100	14896	Histology	Cell Signaling Technologies (Danvers, MA)
NR3C1	1:400	3660		
KI67	1:200	12202		
ATP4B	1:1000	MA3-923		ThermoFisher Scientific (Waltham, MA)
Griffonia simplicifolia (GSII) lectin	1:1000	L21416		
7AAD	1:4000	A1310	Flow Cytometry	BioLegend (San Diego, CA)
CD45.2	1:100	109832		
NK1.1	1:100	108723		
CD3	1:100	100210		
F4/80	1:100	123116		
B220	1:100	103222		
Ly6g	1:100	127616		
CD115	1:100	135510		
CD88	1:100	135809		
CD16/32	1:500	101301		
CD45	1:100	103101	Histology	
CD68	1:100	137001		
CTNNB1	1:400	610153		BD Bioscience (San Jose, CA)
CD11b	1:100	562128	Flow Cytometry	
SIGLECF	1:100	562068		
CCL2	1:100	FAB5538P-025		R&D Systems (Minneapolis, MN)
SOX9	1:100	AB5535	Histology	Millipore Sigma (Burlington, MA)
MHC II	1:100	11-5320-82	Flow Cytometry	eBioscience (Santa Clara, CA)
SIGLECF	1:100	14170280	Histology	
CD44v9	1:100	CAC-LKG-M002		Cosmo Bio (Tokyo, Japan)

Supplementary Table 2: PCR Primers

Primer	Assay ID	Supplier
Wfdc2	Mm00509434_m1	ThermoFisher Scientific (Waltham, MA)
Tff2	Mm00447491_m1	
Olfm4	Mm01320260_m1	
Cftr	Mm00445197_m1	
Ccl2	Mm00441242_m1	
Cx3cl1	Mm00436454_m1	