Supplemental Figure Legends

Figure S1. *Evidence of advanced intestinalized SPEM in stomachs of gastritis-prone SAMP mice*. *(A)* Representative histologic image of 4-wk-old SAMP shows early hyperproliferation of gastric glands compared to age-matched AKR (*left panels*), while in 20-wk-old SAMP, Alcian blue/PAS staining highlights acidic mucin-secreting cells (a*rrows*) replacing parietal (*arrowheads*) and chief cells as SPEM progresses, which is absent in age-matched AKR (*right panels*). Original magnification: X20+1.25; scale bars: 100μm (N=6-8). (*B*) Representative IF images of full-thickness corpus from 4-wk-old SAMP display early, aberrant staining of GSII (green) and Clu (red), characteristic of SPEM (*left lower panels*) compared to age-matched AKR (*left upper panels*) that becomes more evident in 20-wk-old SAMP with established gastritis, with clear abundance of $GSII^+$ cells and increased CD44v and Clu (both red), localizing to base of gastric glands (*arrows*, *right lower panels*) when compared to age-matched AKR controls (*right upper panels*). Original magnification: X20; scale bars: 100μm.

Figure S2. *Molecular profiling indicates advanced SPEM in SAMP corpus that progresses with age.* Relative expression of *(A) Gif*, *Atp4a*, *Tff1*, *(B) Tff2, Mist1*, *(C) He4*, *Clu*, *Lyz*, *Gpx2*, and *(D) Cftr*, *Dmbt1*, *Etv5* in young SAMP vs. SAMP with established disease and vs. age-matched AKR controls. Data is expressed as fold-change vs. 4-wk-old AKR (with mean arbitrarily set as 1); **P*<0.05, ***P*<0.01, ****P*<0.001 vs. age-matched AKR, and $^{\#\#}P$<0.01, $^{\#\#\#}P$<0.001 vs. 4-wk-old AKR/SAMP (N=6-9).

Figure S3. *Increased circulating levels of IL-33 in SAMP mice*. Serum levels of total IL-33 protein in 4-, 10- and 20-wk-old SAMP vs. age-matched control AKR; **P*<0.05, ****P*<0.001 vs. age-matched AKR. $^{\#}$*P*<0.05 vs. 4-wk-old SAMP (N=3-6).

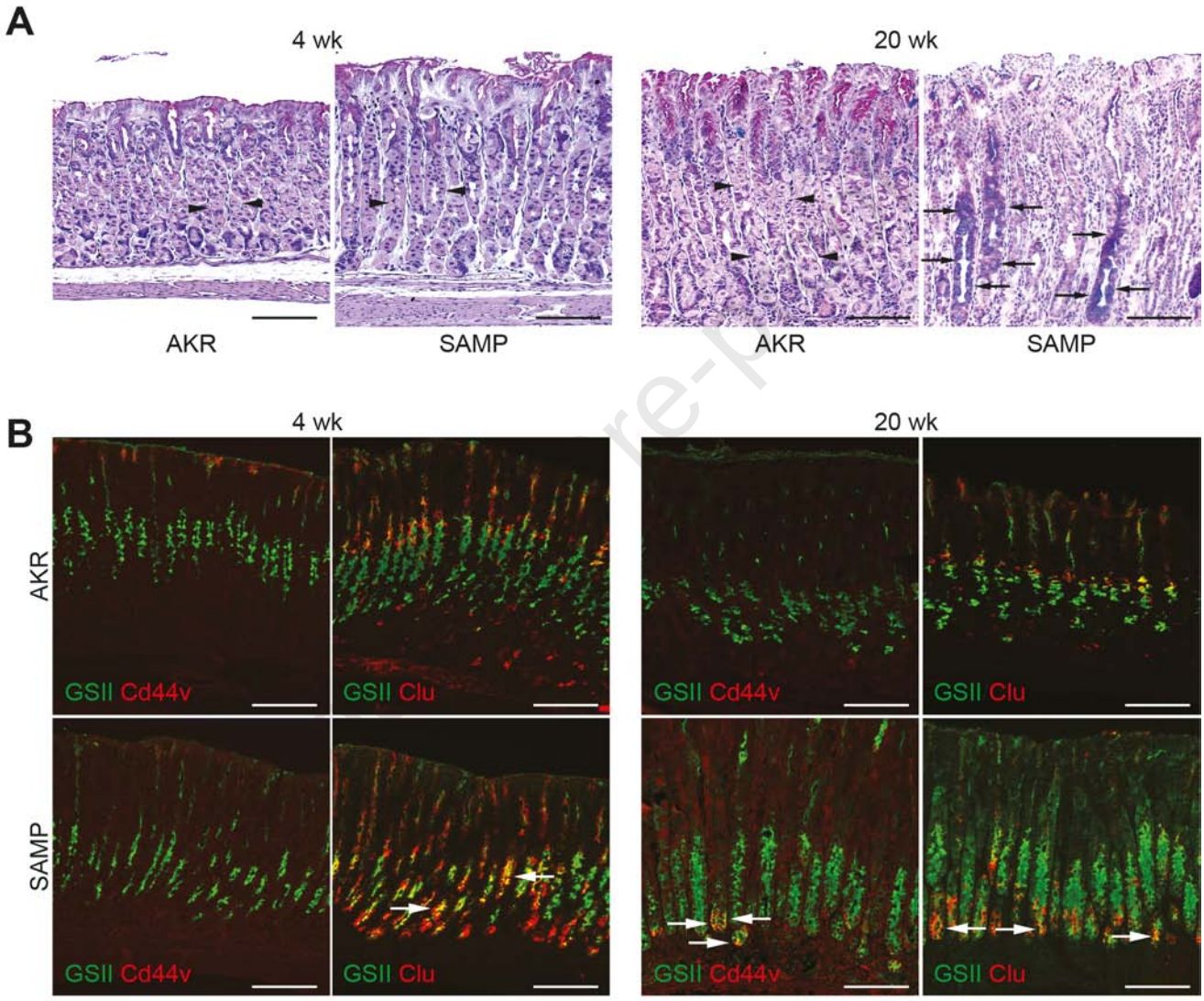
Figure S4. *Gating strategy for distinguishing M1 vs. M2 macrophages by flow cytometry.* Representative 2D dot plots (shown here for BM) for SAMP depict, from left to right: 1) SSC vs. FSC (gating on general cells), 2) FSC-A vs. FSC-H (gating on singlets), 3) SSC-A vs. live/dead (gating on live cells), 4) CD11b vs. SSC-A (gating on granulocytes), 5) Ly6G vs. SSC-A (gating on $Ly6G^-$ cells), 6) CD163 vs. F4/80 (gating on macrophages, Mph), 7) TNF vs. MHCII (gating on M1 macrophages), and Arg1 vs. CD163 (gating on M2 macrophages).

Figure S5. *Strong prominence of M2- vs. M1-associated gene markers expressed in macrophages from SAMP vs. AKR mice.* Relative transcript levels of M1- vs. M2-associated molecules (defined in Sica and Mantovani, Trends Immunol 2002 and Murray, Immunity 2017) in isolated macrophages from 10-wk-old SAMP, normalized by *36B4* and expressed as % fold-change of age-matched AKR controls. Data is presented as mean±SD (N=6).

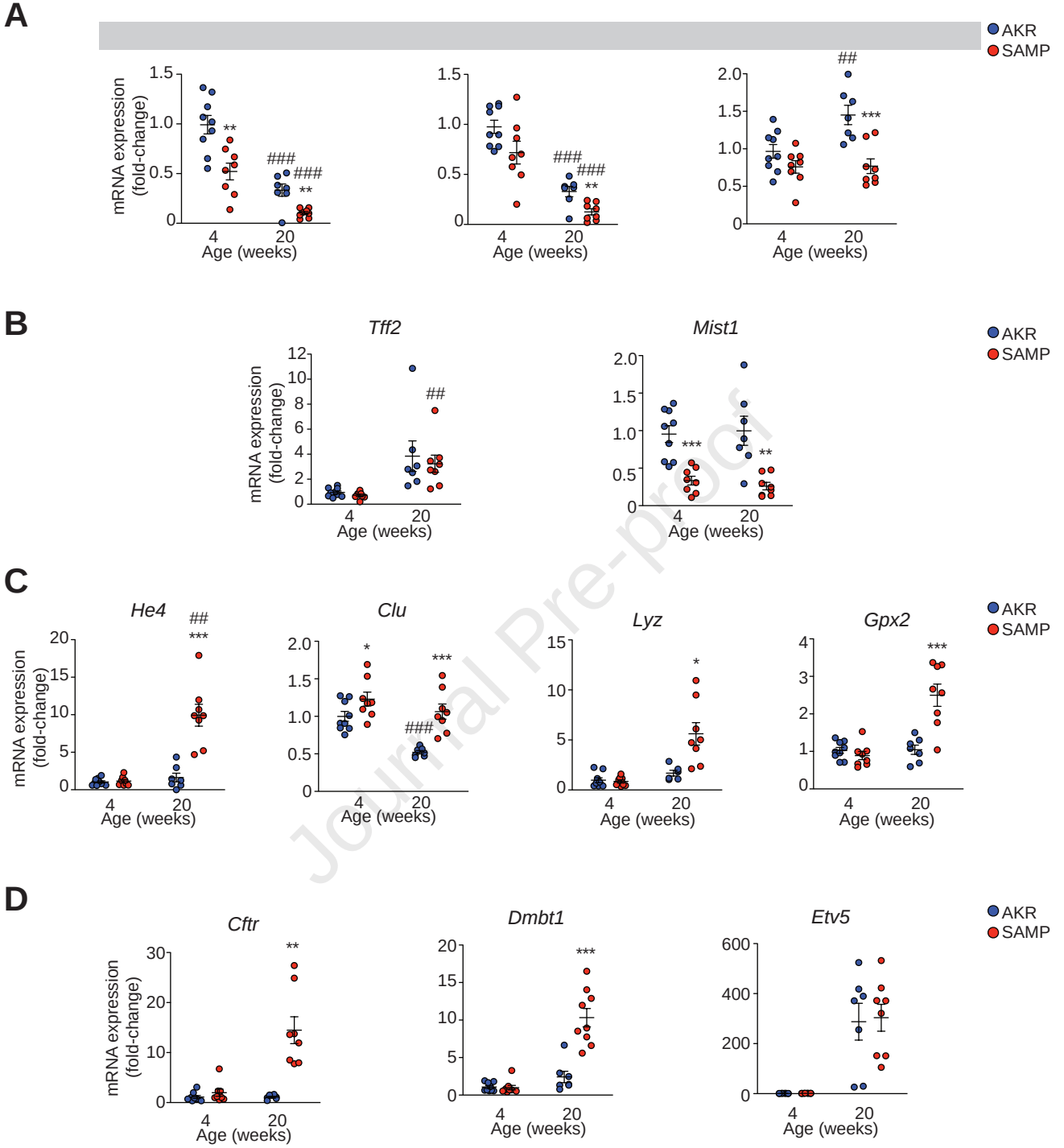
Figure S6. *Gating strategy for detecting eosinophils by flow cytometry*. Representative 2D dot plots (shown here for BM) for control AKR depict, from left to right: 1) SSC vs. FSC (P1, gating on general cells), 2) FSC-A vs. FSC-H (P2, gating on singlets), 3) SSC-A vs. live/dead (gating on live cells), and 4) CD11b vs. Siglec-F (gating on EOS).

Figure S7. *Eosinophil depletion is effective in decreasing peripheral (BM) and local (gastric) eosinophils, and reduces M2 macrophages and expression of M2-associated genes in SAMP stomachs. (A)* Frequency of peripheral (BM)-derived eosinophils (*left panel*) and eosinophil count (*right panel*), *(B)* M2 macrophage frequency (*left panel*), and M2 macrophage count (*right panel*, defined as IL-33^{+}CD163^{+} cells shown in **Fig. 6A**, middle panels) in SAMP corpus after eosinophil depletion by administration of anti-IL-5 and anti-CCR3, alone and in combination, vs. IgG-treated controls (N=4-9). *(C)* Relative transcript levels of M2-associated molecules, normalized by *36B4* and expressed as fold-change vs. IgG-treated controls (with mean set arbitrarily as 1) (N=6), and *(D)* representative IHC images localizing IL-33 (N=4). Original magnification: X10+1.25; scale bars: 100μm. **P*<0.05, ***P*<0.01, ****P*<0.001, *****P*<0.0001.

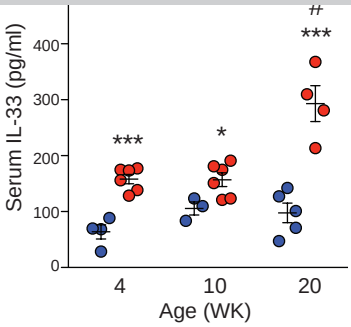
Figure S8. *Evidence that aberrant adaptive immune responses, and not increased ILC2 frequency, is essential for development of gastritis/SPEM in SAMP mice.* Corpus tissues were excised from stomachs of SAMP and AKR, processed into single-cell suspensions for flow cytometric analysis of ILC2s using the following gating strategy: (*A*) live cells were gated on CD45^{+}, then on CD127^{+} cells negative for lineage markers CD3 (T cells), CD11c (DCs), B220 (B cells), CD11b (myeloid cells), Ly6g, Ter-119 (granulocytes), and positive for the transcription factor, GATA3, (*B*) with ILC2s reported as both percentages and absolute numbers; **P*<0.05, ***P*<0.01 (N=3-7). (C) Epithelial hyperplasia (*left panels*) and total inflammation (*right panels*) in corpus from SAMP x RAG2$^{-/-}$ mice vs. WT controls; **P*<0.05, ***P*<0.01, ****P*<0.001 (N=7-15).



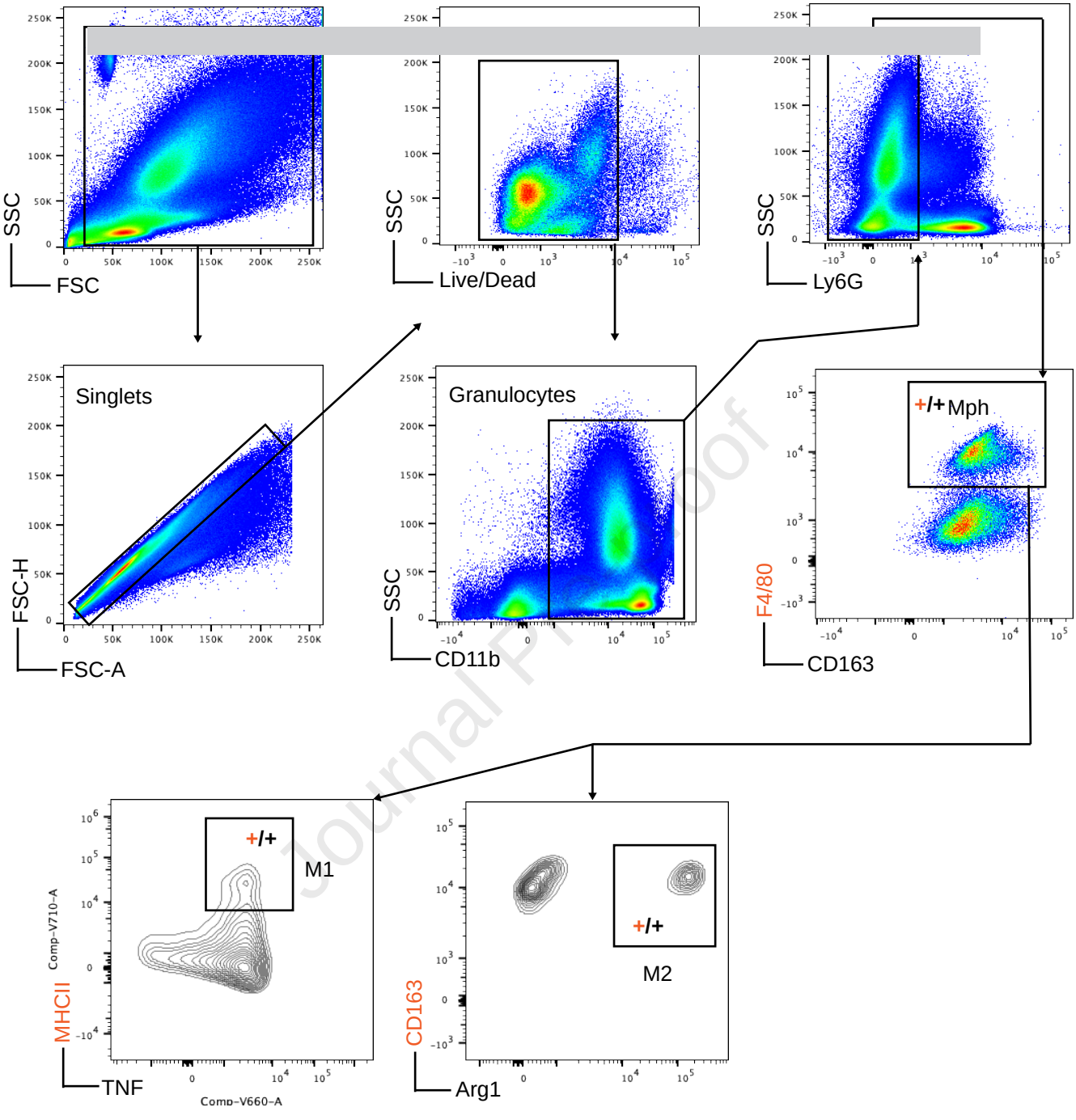
Supplemental Figure 1



Supplemental Figure 2



Supplemental Figure 3



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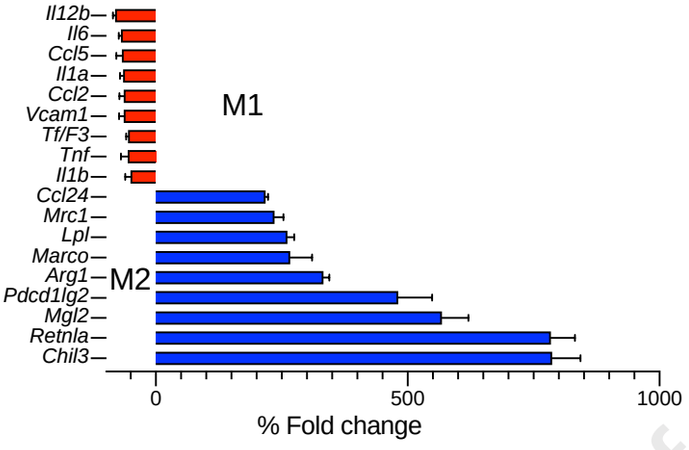

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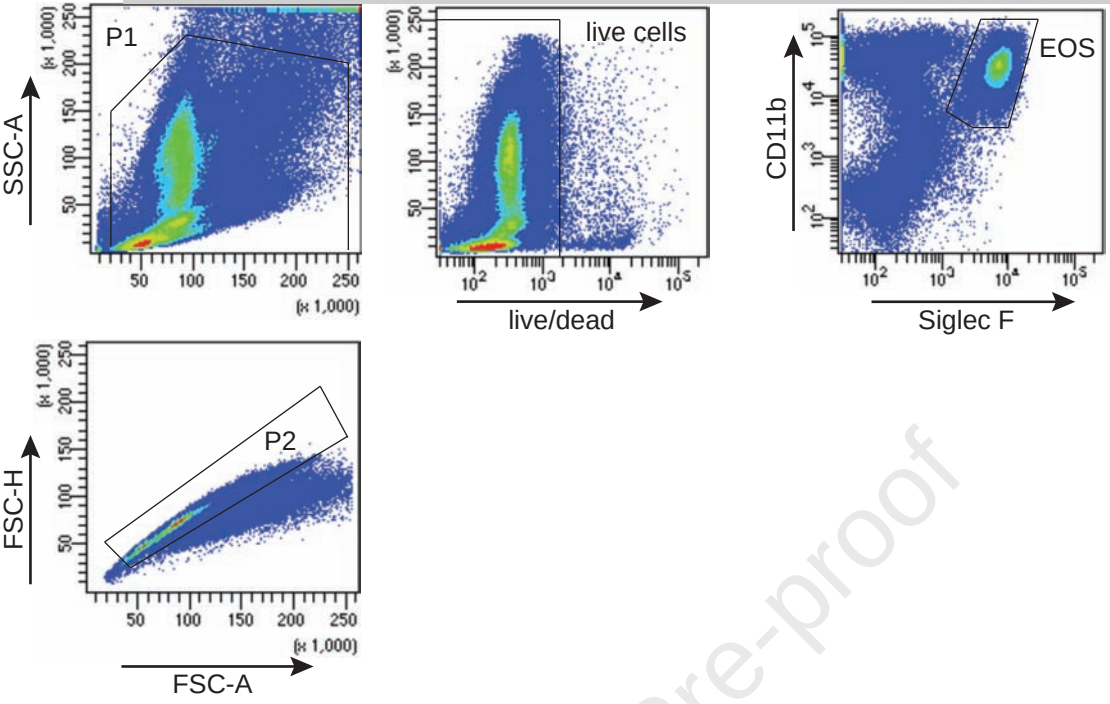
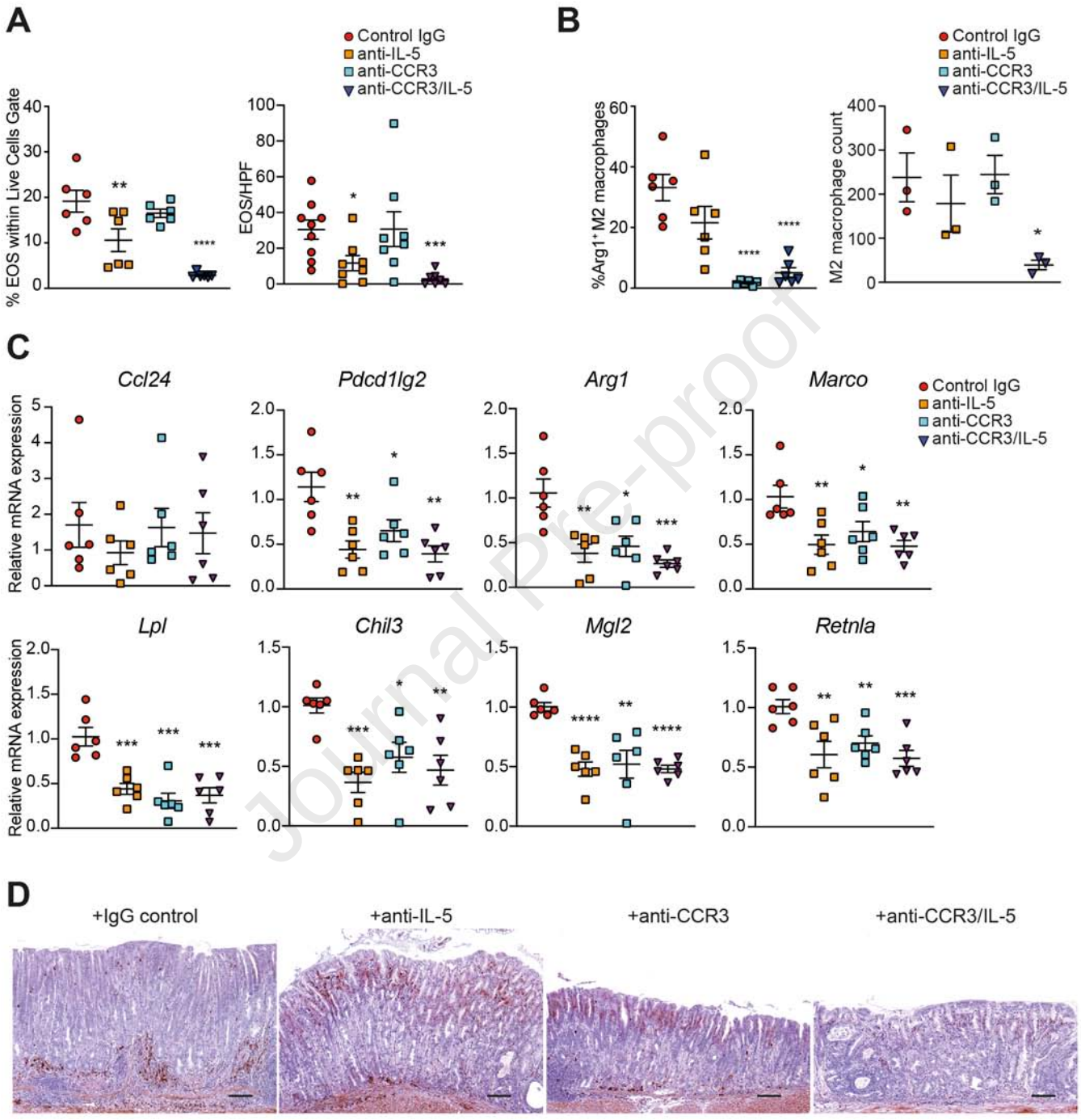
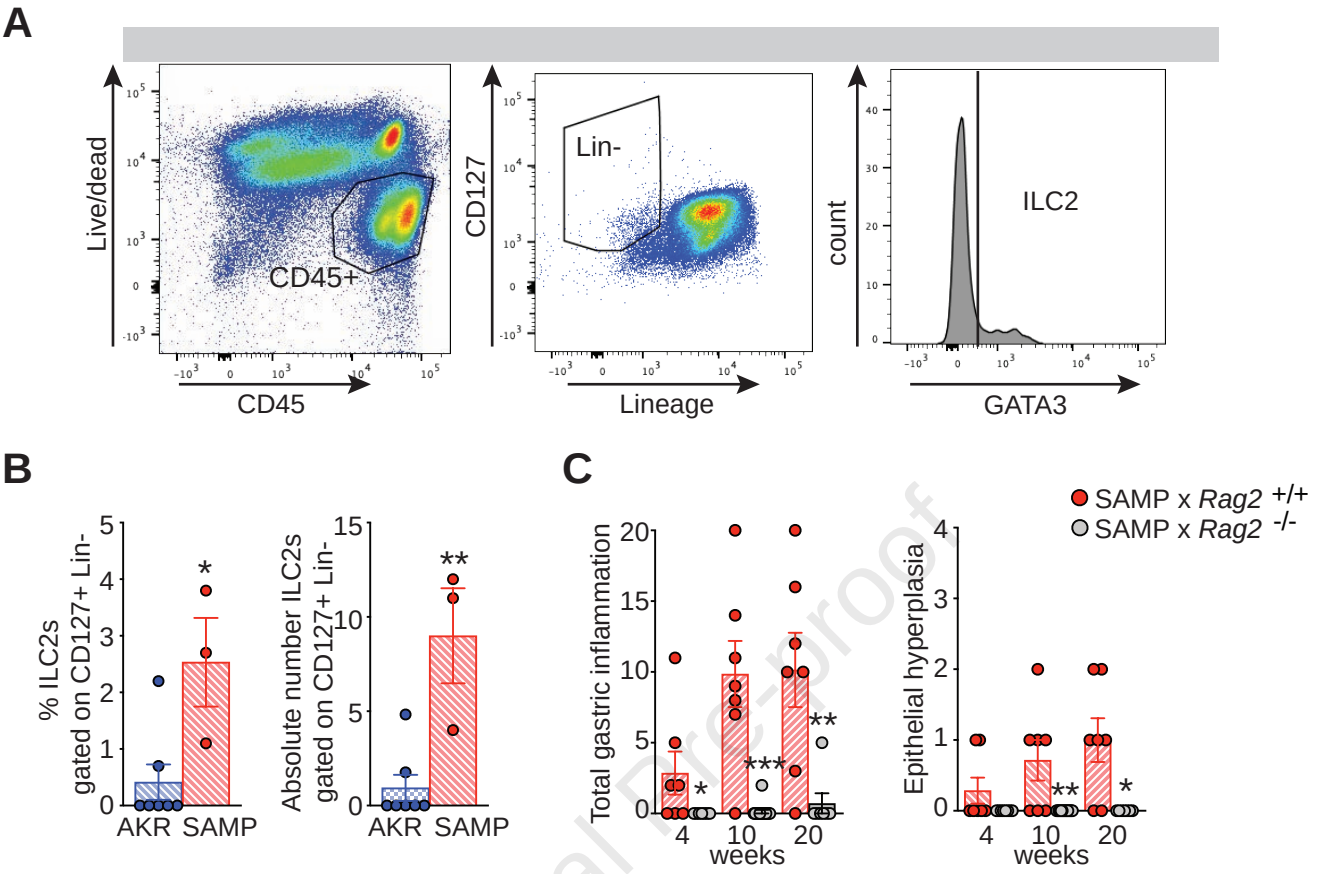


Supplemental Figure 6



Supplemental Figure 7



Supplemental Figure 8

Supplemental Table 1. *Primer sequences for qPCR analyses*

Target	Sequence fwd	Sequence rev
Actinb	5'-CAGGGTGTGATGGTGGGAATG-3'	5'-GTAGAAGGTGTGGTGCCAGATC-3'
Tff1	5'-AGCACAAGGTGATCTGTGTCC-3'	5'-GGAAGCCACAATTTATCCTCTCC-3'
Tff2	5'-TGCTCTGGTAGAGGGCGAG-3'	5'-CGACGCTAGAGTCAAAGCAG-3'
Mist1	5'-TGGTGGCTAAAGCTACGTGTC-3'	5'-GACTGGGGTCTGTCAGGTGT-3'
Atp4a	5'-TCTGCTTTGCGGGACTTGTA-3'	5'-CGGCATTTGAGCACAGCAT-3'
Lyz	5'-GAGACCGAAGCACCGACTATG-3'	5'-CGGTTTTGACATTGTGTTCGC-3'
Gif	5'-CCCTCTACCTCCTAAGTGTTCTC-3'	5'-CTGAGTCAGTCACCGAGTTCT-3'
He4	5'-AACCAATTACGGACTGTGTGTT-3'	5'-TCGCTCGGTCCATTAGGCT-3'
Dmbt1	5'-ACCTCCTCACGGTGCTACAG-3'	5'-GCTTCTTCACATCCTCCACTG-3'
Cftr	5'-CTGGACCACACCAATTTTGAGG-3'	5'-GCGTGGATAAGCTGGGGAT-3'
Gpx2	5'-CAGGGCTGTGCTGATTGAG-3'	5'-CGGACATACTTGAGGCTGTTC-3'
Clu	5'-CCAGCCTTTCTTTGAGATGA-3'	5'-CTCCTGGCACTTTTCACACT-3'
Etv5	5'-GCTCTTGGTGCTAAGTAGGA-3'	5'-TCTGATGGGTGGGTGACA-3'
Il33	5'-TCCTTGCTTGGCAGTATCCA-3'	5'-TGCTCAATGTGTCAACAGACG-3'
Il1rl1(ST2L)	5'-TGCGTACATCATTTACCCTCGGGTC-3'	5'-TCTTGTGCCACAAGAGTGAAGTAGG-3'
Il1rl1(sST2)	5'-ACGCTCGACTTATCCTGTGG-3'	5'-CAGGTCAATTGTTGGACACG-3'
Ccl24	5'-ATTCTGTGACCATCCCCTCAT-3'	5'-TGTATGTGCCTCTGAACCCAC-3'
Pdcd1lg2	5'-TGTGCTGCCTTTTCTGTGTC-3'	5'-GCAGCATGGTCTGTGTCAAT-3'
Arg1	5'-TTTTAGGGTTACGGCCGGTG-3'	5'-CCTCGAGGCTGTCCTTTTGA-3'
Marco	5'-GCACTGCTGCTGATTCAAGTTC-3'	5'-AGTTGCTCCTGGCTGGTATG-3'
Lpl	5'-GTGGCCGAGAGCGAGAAC-3'	5'-AAGAAGGAGTAGGTTTTATTTGTGGA-3'
Chil3	5'-CAGGTCTGGCAATTCTTCTGAA-3'	5'-GTCTTGCTCATGTGTGTAAGTGA-3'
Mgl2	5'-TTAGCCAATGTGCTTAGCTGG-3'	5'-GGCCTCCAATTCTTGAAACCT-3'
Retnla	5'-CCCTCCACTGTAACGAAGACTC-3'	5'-CACACCCAGTAGCAGTCATCC-3'
Mrc1	5'-GGACGAGCAGGTGCAGTT-3'	5'-CAACACATCCCGCCTTTC-3'
Il1a	5'-GCACCTTACACCTACCAGAGT-3'	5'-AAACTTCTGCCTGACGAGCTT-3'
Il1b	5'-GCAACTGTTCCTGAACTCAACT-3'	5'-ATCTTTTGGGGTCCGTCAACT-3'
Tnf	5'-CCCTCACACTCAGATCATCTTCT-3'	5'-GCTACGACGTGGGCTACAG-3'
Vcam1	5'-ACGTCAGAACAACCGAATCC-3'	5'-GTGGTGCTGTGACAATGACC-3'
Il12b	5'-TGGTTTGCCATCGTTTTGCTG-3'	5'-ACAGGTGAGGTTCACTGTTTCT-3'
Il6	5'-TAGTCCTTCCTACCCCAATTTCC-3'	5'-TTGGTCCTTAGCCACTCCTTC-3'
Ccl5	5'-GCTGCTTTGCCTACCTCTCC-3'	5'-TCGAGTGACAAACACGACTGC-3'
Ccl2	5'-TTAAAAACCTGGATCGGAACCAA-3'	5'-GCATTAGCTTCAGATTTACGGGT-3'
Tf/F3	5'-CCGAGCAATGGAAGAGTTTC-3'	5'-CGCTTGCACAGAGATATGGA-3'
36B4	5'-GCTCCAAGCAGATGCAGCA-3'	5'-CCGGATGTGAGGCAGCAG-3'

Supplemental Table 2. *Antibodies utilized for flow cytometry*

Antigen	Label	Catalog #	Source
CD11c	PECy7	561241	BD Biosciences, San Jose, CA
CD11b	PE-CF594	562287	BD Biosciences
F4/80	Alexa-488	564227	BD Biosciences
Ly6G	BUV396	563978	BD Biosciences
Siglec F	BV610	740280	BD Biosciences
MHCII	BV711	563414	BD Biosciences
Arginase 1	APC	17-3697-82	ThermoFisher, Waltham, MA
TNF	BV650	563943	BD Biosciences
CD163	BV421	155309	Biolegend, San Diego, CA
IL33	PE	MA5-23640	ThermoFisher