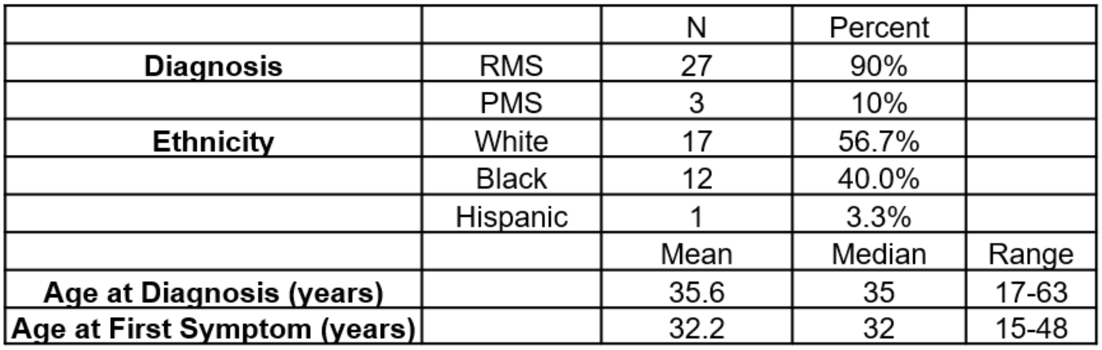
Wang, Y. et al. Supplementary Table 1

Table 1. Information on MS Patient Population.



		N	Percent	
Diagnosis	RMS	27	90%	
	PMS	3	10%	
Ethnicity	White	17	56.7%	
	Black	12	40.0%	
	Hispanic	1	3.3%	
		Mean	Median	Range
Age at Diagnosis (years)		35.6	35	17-63
Age at First Symptom (years)		32.2	32	15-48

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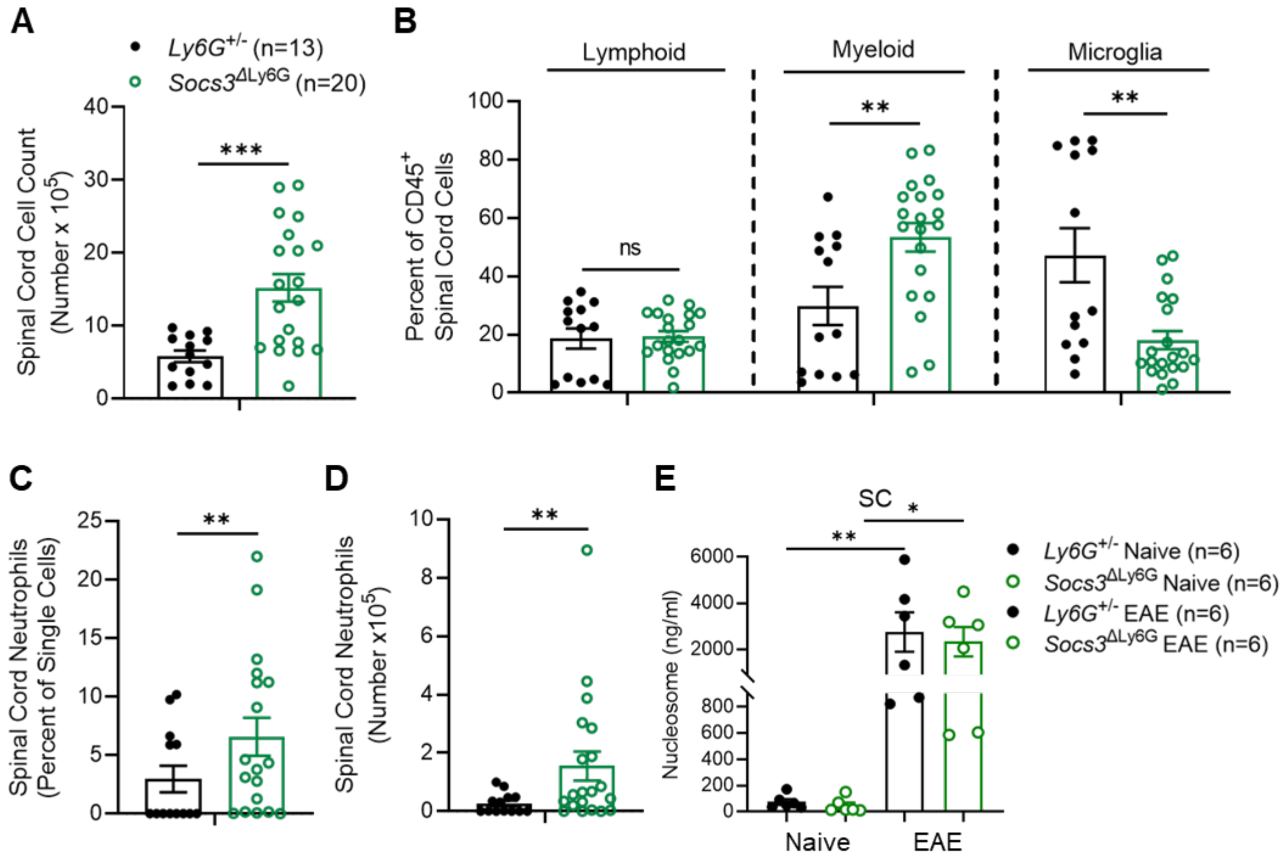
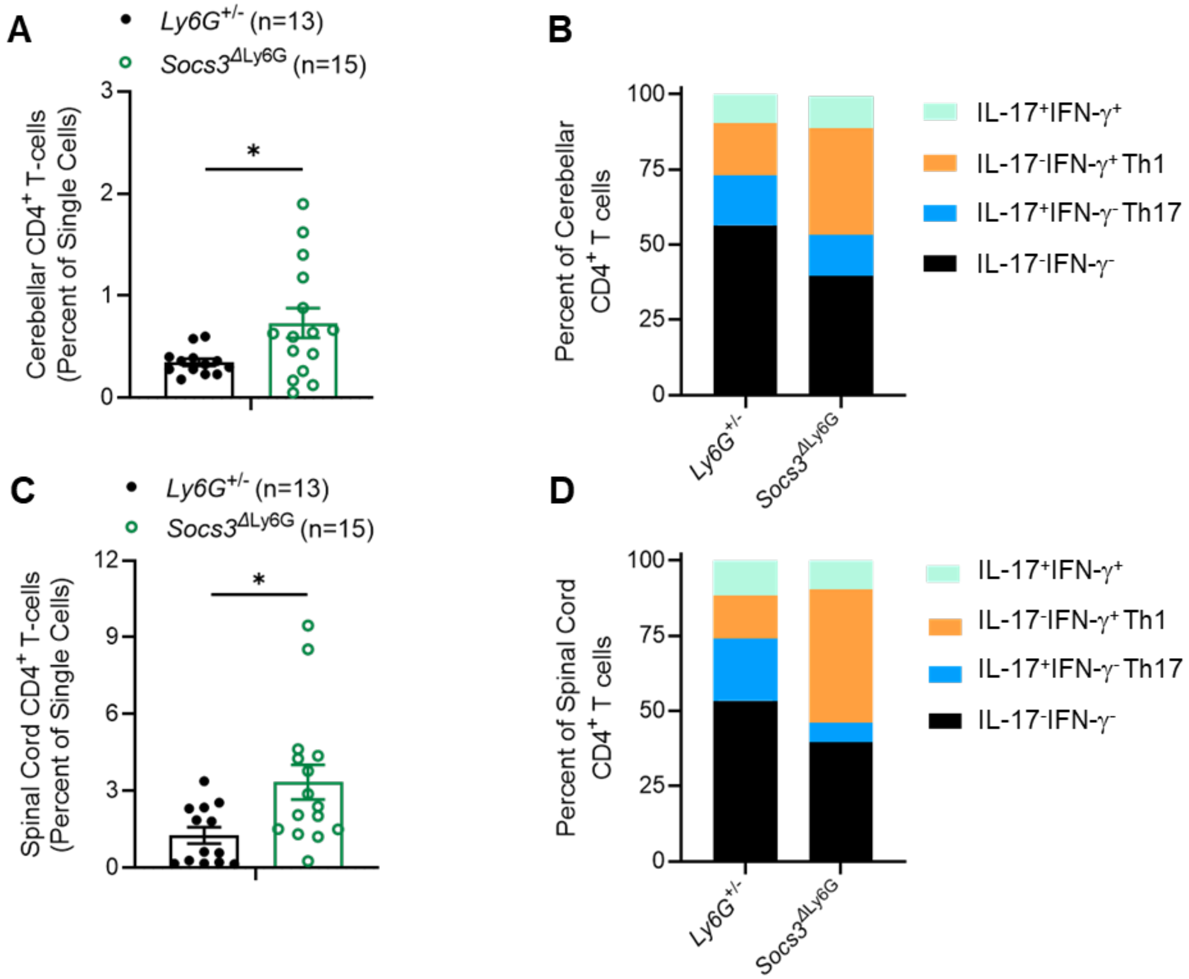


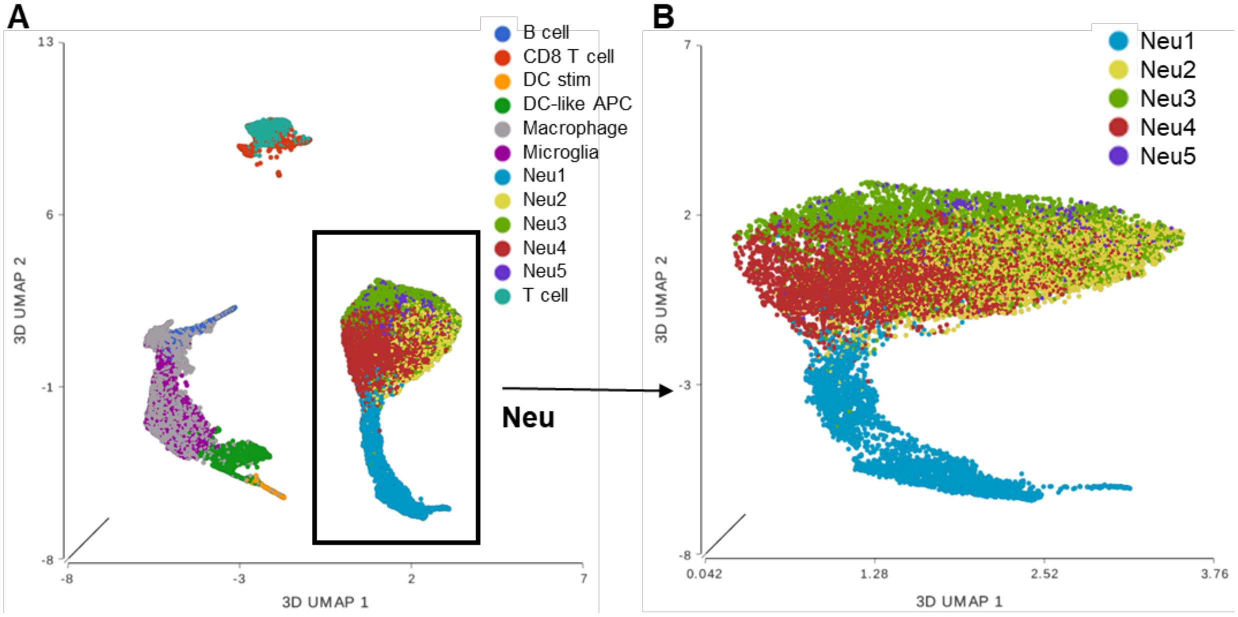
Supplementary Figure 1. *Socs3*$^{\Delta Ly6G}$ Mice Exhibit Increased Spinal Cord Myeloid Cell and Neutrophil Infiltration. EAE was induced in *Ly6G*$^{+/-}$ and *Socs3*$^{\Delta Ly6G}$ mice. At the peak of cEAE and btEAE, respectively, the spinal cord (SC) was collected to determine cell counts and percentages of immune cell populations, including lymphoid (CD45^{+}CD11b^{-}), myeloid (CD45^{hi}CD11b^{+}), and microglia (CD45^{lo}CD11b^{+}) **(A and B)**. **(C)** Percent of SC neutrophils (CD45^{+}CD11b^{+}Ly6G^{+}Ly6C^{low}). **(D)** Total number of SC-infiltrating neutrophils. **(E)** At the peak of cEAE and btEAE in *Ly6G*$^{+/-}$ and *Socs3*$^{\Delta Ly6G}$ mice, respectively, SC homogenate samples were collected. H3.1-nucleosome expression was quantified by ELISA. *p<0.05, **p<0.01 and ***p<0.001. ns: not significant.

Wang, Y. et al. Supplementary Figure 2



Supplementary Figure 2. *Socs3*$^{\Delta Ly6G}$ Mice Exhibit Increased CD4$^+$ T-cells that Skew to Th1. EAE was induced in *Ly6G*$^{+/-}$ and *Socs3*$^{\Delta Ly6G}$ mice. CB and SC tissues were collected at the peak of cEAE and btEAE, respectively, and analyzed by flow cytometry. CB and SC cells were stimulated for 4 h with PMA (25 ng/ml) and ionomycin (1 μg/ml) in the presence of GolgiStop. **(A)** Percent of CB CD4$^+$ T-cells. **(B)** The proportion of IL-17 and IFN-γ expression as a percent of total CB CD4$^+$ T-cells. **(C)** Percent of SC CD4$^+$ T-cells. **(D)** The proportion of IL-17 and IFN-γ expression as a percent of total SC CD4$^+$ T-cells. $^*p<0.05$.

Wang, Y. et al. Supplementary Figure 3



Supplementary Figure 3. UMAP of All CD45$^+$CD11b$^+$ Cells by scRNA-Seq. EAE was induced in *Ly6G*$^{+/-}$ and *Socs3*$^{\Delta Ly6G}$ mice, and then SC and/or CB were collected at the peak of EAE (days 12-14). Live CD45$^+$CD11b$^+$ cells from the SC of *Ly6G*$^{+/-}$ mice with EAE (n=3), from the SC and CB of *Socs3*$^{\Delta Ly6G}$ mice with EAE (n=3), and from the combined SC of naïve Ly6G$^{+/-}$ mice (n=3) and naïve *Socs3*$^{\Delta Ly6G}$ mice (n=4) were subjected to scRNA-Seq. **(A)** All cell clusters are shown by UMAP. **(B)** UMAP of neutrophil clusters.

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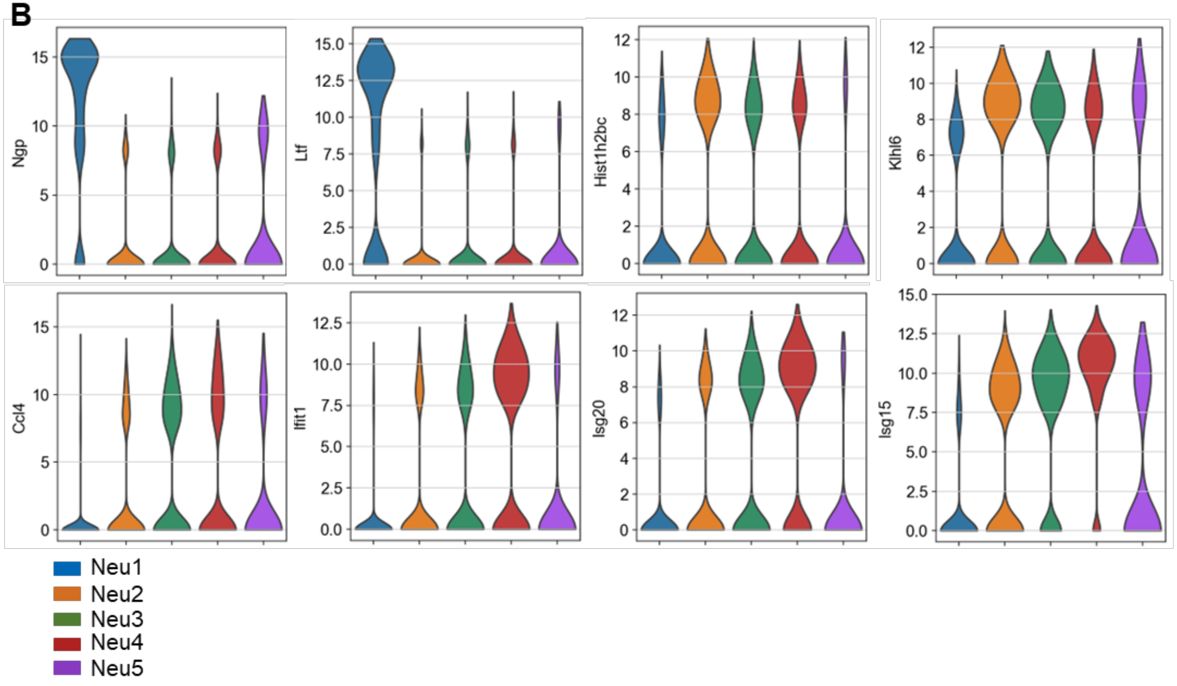
A

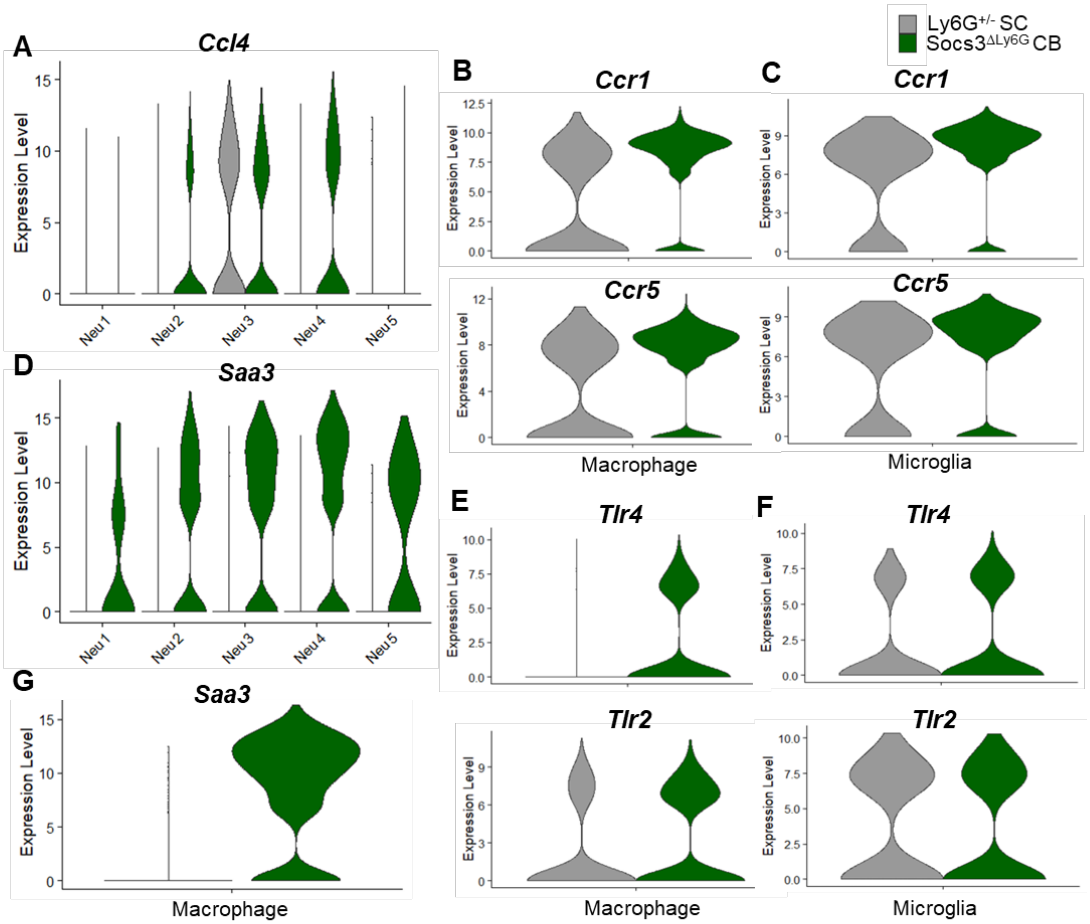
Neu1	Neu2	Neu3	Neu4	Neu5
Stfa3	Hist1h2bc	Rab15	Cxcl3	A430057M04Rik
Ngp	Entpd3	Ccl3	Lipg	Rnd2
Camp	Igfbp6	Hcar2	Il1rap	Itpr2
Scrg1	Csf3r	Fnip2	Steap4	Rem2
Ltf	Il1r2	Ly6i	Cxcl2	Cxcl2
Itgb2l	Map1lc3b	Gadd45b	Ifit1	Gm15337
Retnlg	Mmp9	Ninj1	Slfn4	Gm13391
Gpr27	Cxcr2	Ccrl2	Il1b	Azi2
Padi4	Ifitm1	Pmaip1	Hdc	9130230L23Rik
Serpinb1a	Bcl2l15	Cd274	Ffar2	Mbnl2
Stfa2	Klhl6	Tmem140	Isg20	Rlf
1700047M11Rik	Hist1h4i	Csf1	Ier3	Shisa4
Tinagl1	Pnpla2	E230032D23Rik	Trem1	Neat1
Pglyrp1	Hp	Cstb	Qsox1	Vmp1
Adpgk	Prnp	Il1rn	Ifitm1	Arid5b
Mgst2	Trp53inp1	Cd24a	Isg15	Tgoln1
Bmx	Cd300lf	Acod1	Cstdc4	Gm42696
Anxa1	Klhl24	Basp1	Acod1	Vwa1
Orm1	Cd63	Fth1	Upp1	Gadd45g
Chil5	Grina	Clec4d	Rsad2	Frrs1

B



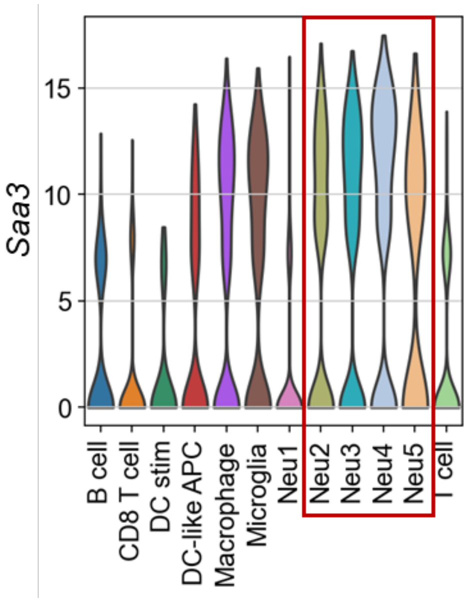
Supplementary Figure 4. Top 20 Marker Genes from Each Neutrophil Cluster. Live CD45$^+$CD11b$^+$ cells from the SC of *Ly6G*$^{+/-}$ mice with EAE (n=3), from the SC and CB of *Socs3*$^{\Delta Ly6G}$ mice with EAE (n=3), and from the combined SC of naïve *Ly6G*$^{+/-}$ mice (n=3) and naïve *Socs3*$^{\Delta Ly6G}$ mice (n=4) were subjected to scRNA-Seq. **(A)** The top 20 marker genes are listed for each neutrophil cluster. **(B)** Violin plots colored for differential cluster-defining genes.

Wang, Y. et al. Supplementary Figure 5



Supplementary Figure 5. Ligand and Receptor Expression in Neutrophils and Macrophages/Microglia in Mice with EAE (*Socs3*$^{\Delta Ly6G}$ CB vs. *Ly6G*$^{+/-}$ SC). EAE was induced in *Ly6G*$^{+/-}$ and *Socs3*$^{\Delta Ly6G}$ mice, and then SC or CB were collected at the peak of EAE (days 12-14). Live CD45^{+}CD11b^{+} cells from the SC of *Ly6G*$^{+/-}$ mice with EAE (n=3) and the CB of *Socs3*$^{\Delta Ly6G}$ mice with EAE (n=3) were subjected to scRNA-Seq. Ligand and receptor expression were compared between *Socs3*$^{\Delta Ly6G}$ CB and *Ly6G*$^{+/-}$ SC groups. **(A)** Violin plot of *Ccl4* expression (ligand) in neutrophil clusters in *Socs3*$^{\Delta Ly6G}$ CB (green) vs. *Ly6G*$^{+/-}$ SC (gray). **(B)** Violin plots of *Ccr1* and *Ccr5* (receptors) expression in macrophages. **(C)** Violin plots of *Ccr1* and *Ccr5* (receptors) expression in microglia. **(D)** Violin plot of *Saa3* (ligand) expression in neutrophils. **(E)** Violin plots of *Tlr4* and *Tlr2* (receptors) expression in macrophages. **(F)** Violin plots of *Tlr4* and *Tlr2* (receptors) expression in microglia. **(G)** Violin plot of *Saa3* (ligand) expression in macrophages.

Wang, Y. et al. Supplementary Figure 6



Supplementary Figure 6. Expression of *Saa3* in Different Cell Clusters. EAE was induced in *Ly6G*$^{+/-}$ and *Socs3*$^{\Delta Ly6G}$ mice, and then SC and/or CB were collected at the peak of EAE (days 12-14). Live CD45^{+}CD11b^{+} cells from the SC of *Ly6G*$^{+/-}$ mice with EAE (n=3), from the SC and CB of *Socs3*$^{\Delta Ly6G}$ mice with EAE (n=3), and from the combined SC of naïve *Ly6G*$^{+/-}$ mice (n=3) and naïve *Socs3*$^{\Delta Ly6G}$ mice (n=4) were subjected to scRNA-Seq. Violin plot of *Saa3* expression in different clusters of scRNA-Seq dataset.