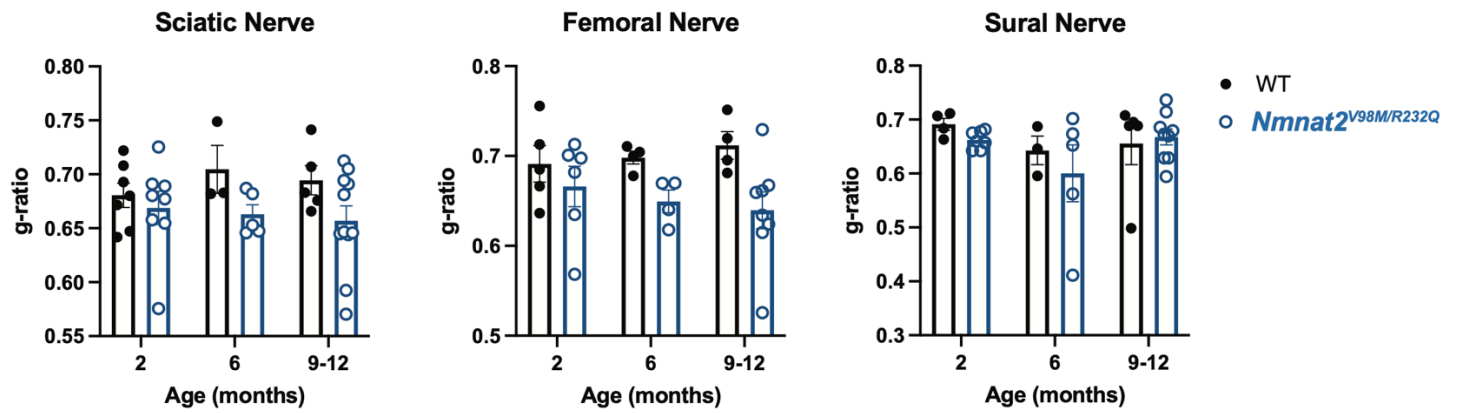
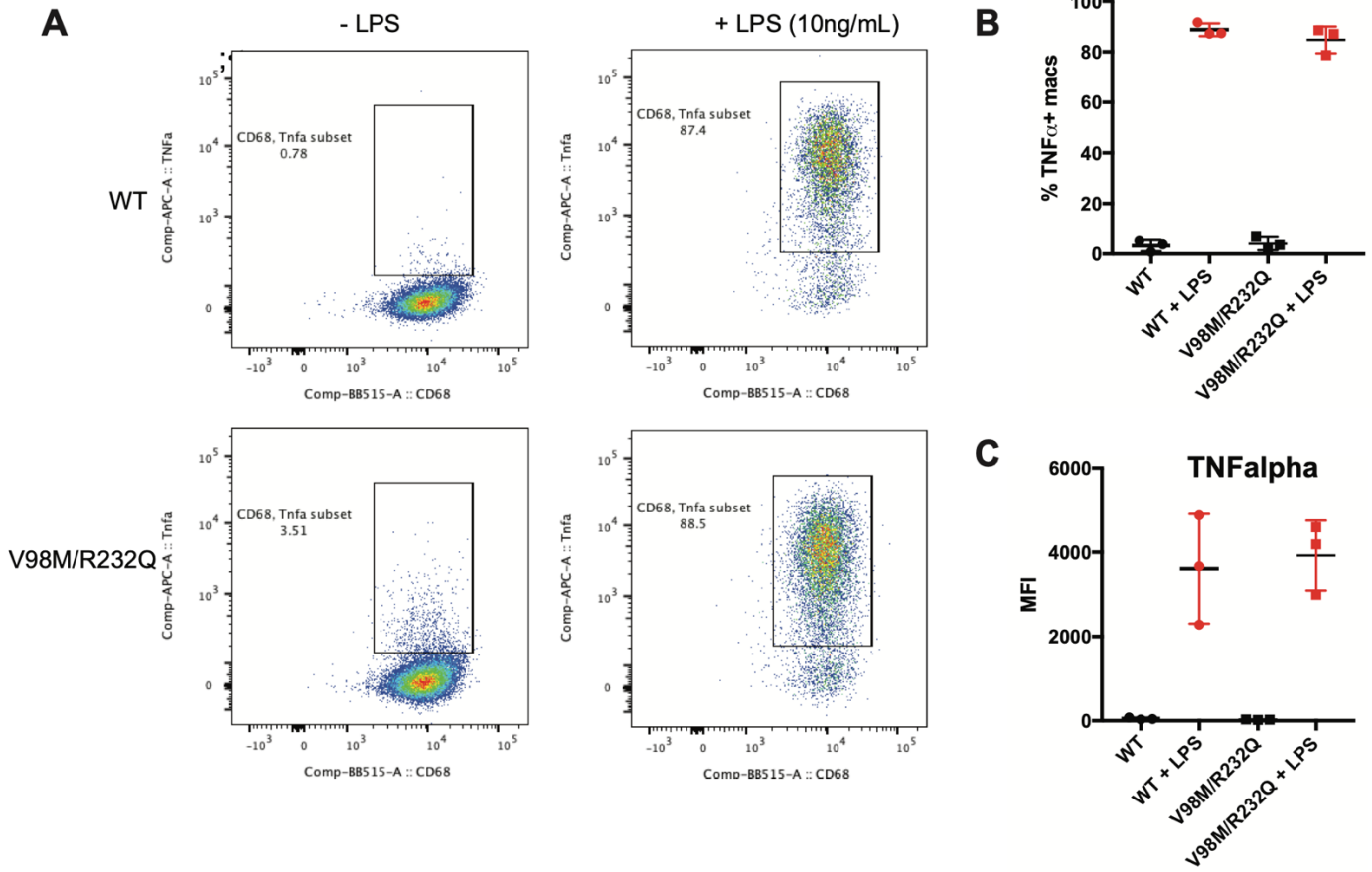


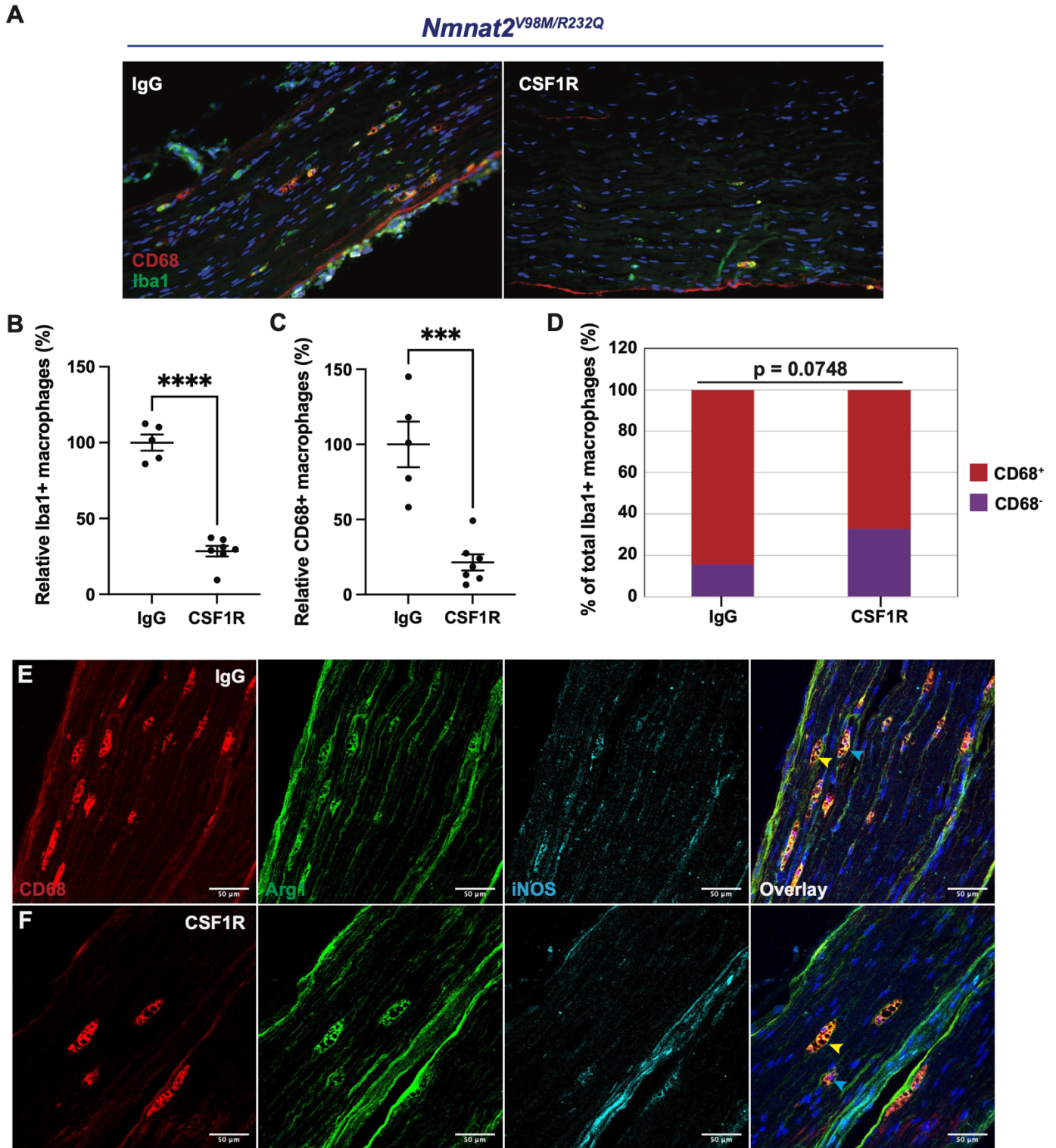
Supplemental Figure 1: Intraepidermal nerve fiber density is unaffected in *Nmnat2*^{V98M/R232Q} mice. Intraepidermal nerve fiber density of footpad skin of 12-month-old *Nmnat2*^{V98M/R232Q}; *Sarm1* KO (n=4) and *Nmnat2*^{V98M/R232Q} (n=3) mice. All data are presented as mean ± SEM. Statistical significance was determined by Student's unpaired t-test. ns: not significant.



Supplemental Figure 2: Myelin thickness is preserved in *Nmnat2*^{V98M/R232Q} mice. Average g-ratio in sciatic, femoral, and sural nerves at 2, 6, and 9-12 months of age, comparing *Nmnat2*^{V98M/R232Q} mice (n=3-7) to WT mice (n=4-7). All data are presented as mean ± SEM.



Supplemental Figure 3: Macrophage activation assay. **A-B**, Representative scatter plots (A) and quantification (B) of CD68⁺ TNF- α ⁺ *Nmnat2*^{V98M/R232Q} or WT peritoneal macrophages in the presence or absence of LPS (10ng/mL) stimulation for 4hrs (n=3). **C**, Mean fluorescence intensity (MFI) of TNF- α cell surface expression on CD68⁺TNF α ⁺ peritoneal macrophages in the presence or absence of LPS (10ng/mL) stimulation for 4hrs. All data are presented as mean \pm SEM.



Supplemental Figure 4: Macrophage depletion quantification. **A**, Representative images of Iba1⁺ and CD68⁺ cells in *Nmnat2*^{V98M/R232Q} sciatic nerves after 3 months of IgG or CSF1R injections. **B-C**, Quantification of (B) Iba1⁺ and (C) CD68⁺ macrophages in the sciatic nerves of CSF1R-injected (n=7) or IgG-injected (n=5) *Nmnat2*^{V98M/R232Q} mice (reported as a percentage of the IgG control). **D**, Quantification of the relative distribution of CD68⁻ and CD68⁺ total macrophages (Iba1⁺) in the sciatic nerves of CSF1R-injected (n=7) or IgG-injected (n=5) *Nmnat2*^{V98M/R232Q} mice. **E**, Representative images of CD68, Arg1, and iNOS immunofluorescence in *Nmnat2*^{V98M/R232Q} sciatic nerves after 3 months of (E) IgG or (F) CSF1R injections. Scale bar represents 50 μm. Yellow arrows indicate Arg1/CD68 co-localization and blue arrows represent Arg1/iNOS/CD68 co-localization. All data are presented as mean ± SEM. Statistical significance was determined by Student's unpaired t-test. ***p<0.001, ****p<0.0001.