

Supplementary Information Guide

Supplementary Table 1. Antibodies used in CITE-seq.

Supplementary Table 2. Differentially expressed genes in different B cell subclusters and genotype specific gene set enrichment analysis (GSEA) based on CITE-seq dataset.

Supplementary Table 3. DEGs of *wild type*, *C9orf72*^{-/-}, *Grn*^{-/-}, and *Grn*^{-/-};*C9orf72*^{-/-} splenic B cells after BCR ligation, cGMP treatment, TLR7 stimulation, or TLR9 stimulation.

Supplementary Table 4. Peptide epitopes identified in *C9orf72*^{-/-}, *Grn*^{-/-}, and *Grn*^{-/-};*C9orf72*^{-/-} sera via PhIP-seq.

Supplementary Table 5. Autoantigens detected by *C9orf72*^{-/-}, *Grn*^{-/-}, and *Grn*^{-/-};*C9orf72*^{-/-} sera using CDI proteomic microarray.

Supplementary Table 6. Autoantigens identified by both Proteomic Array and PhIP-Seq using *C9orf72*^{-/-}, *Grn*^{-/-}, and *Grn*^{-/-};*C9orf72*^{-/-} sera.

Supplementary Table 7. Demographic data and concentration IgG, Albumin, anti-ROBO3, C1q, and C3b in human CSF samples.

Supplementary Table 8. Differentially expressed genes and enriched GO terms and KEGG pathways identified by bulk RNA-seq in 7 and 12-month-old *C9orf72*^{-/-}, *Grn*^{-/-}, and *Grn*^{-/-};*C9orf72*^{-/-} mouse brain.

Supplementary Table 9. Meta-data for snRNA-seq in 12-month-old *C9orf72*^{-/-}, *Grn*^{-/-}, and *Grn*^{-/-};*C9orf72*^{-/-} mouse thalamus.

Supplementary Table 10. Differentially expressed genes, GO terms, and KEGG pathways enriched in microglia and astrocytes in 12-month-old *C9orf72*^{-/-}, *Grn*^{-/-}, and *Grn*^{-/-};*C9orf72*^{-/-} mouse thalamus.