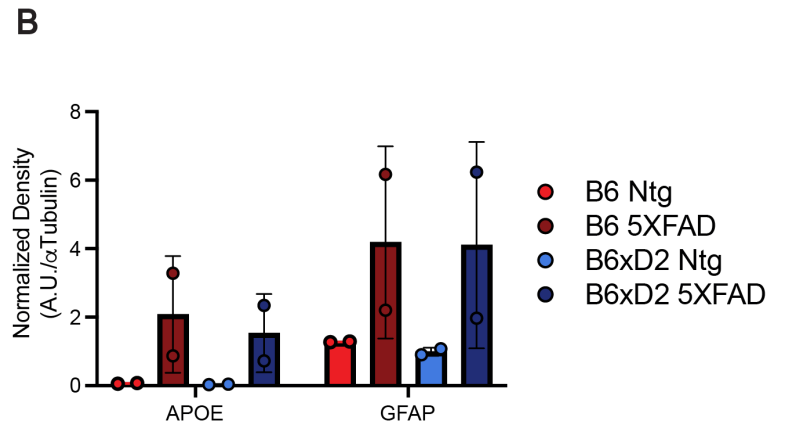
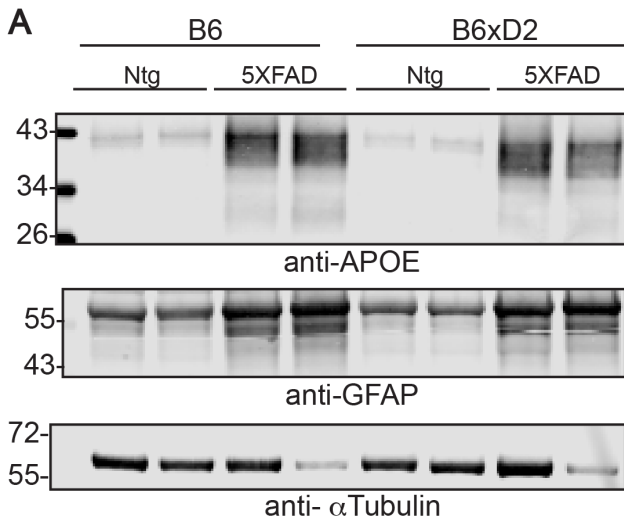
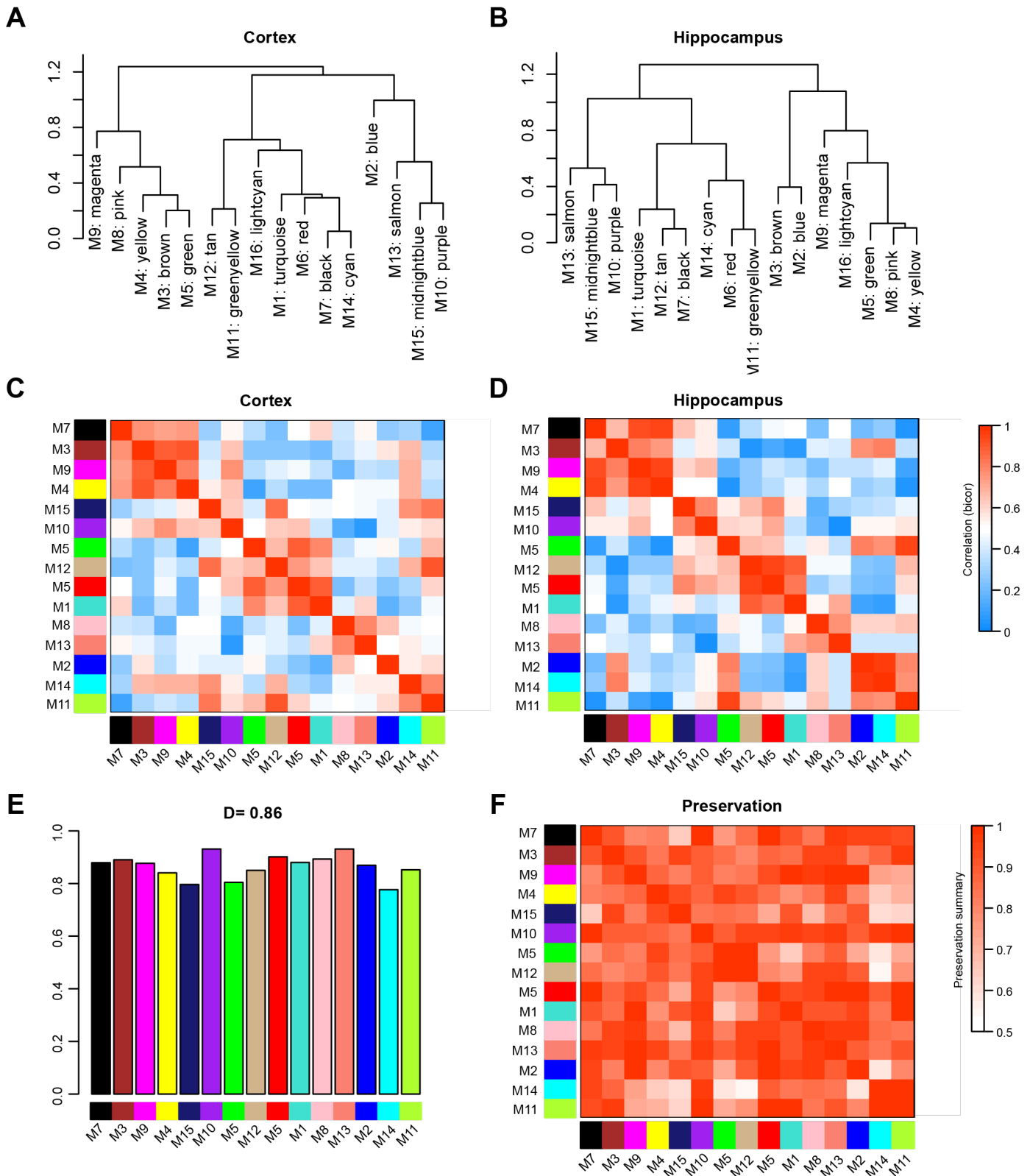


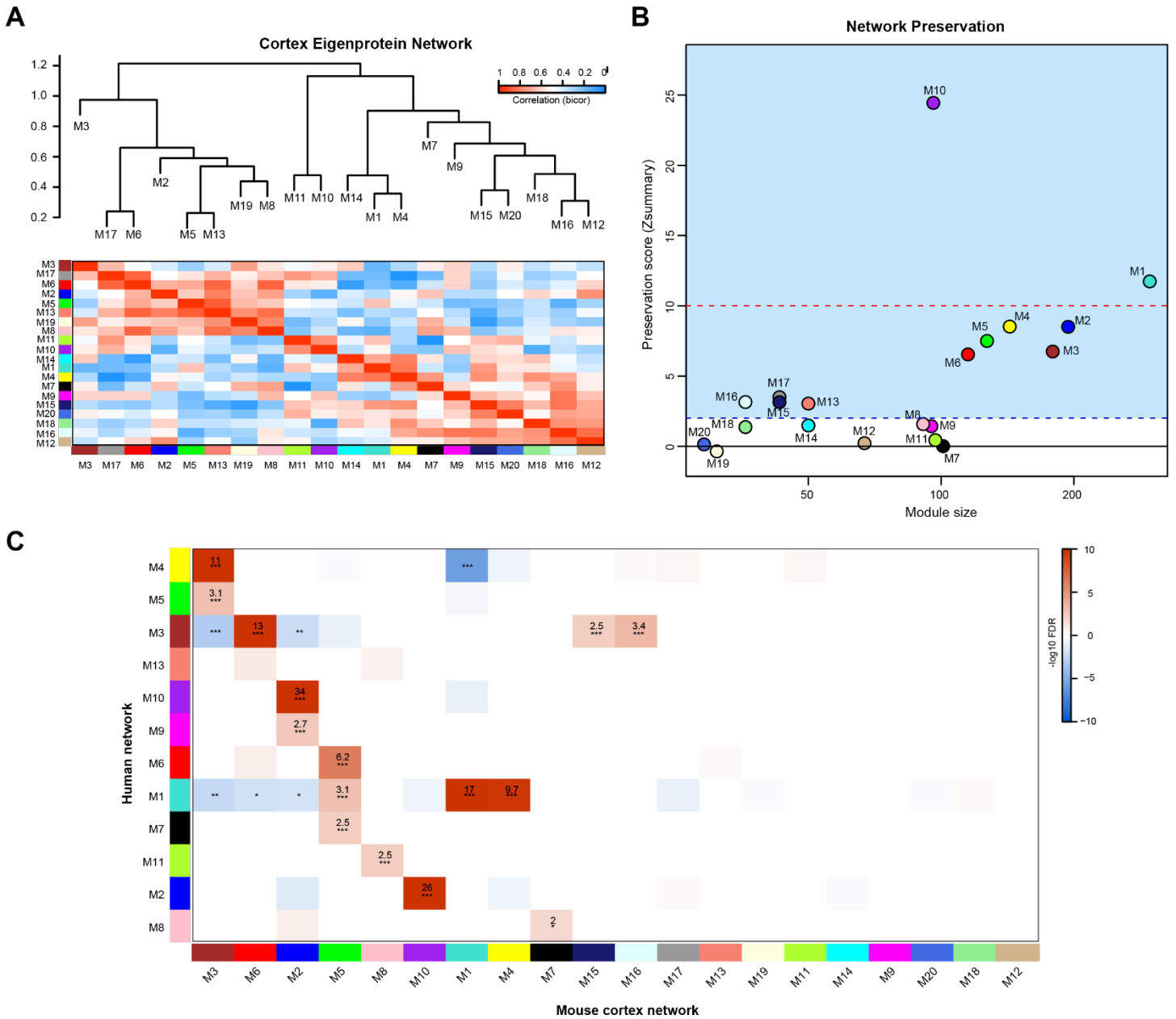
**Supplementary Figure 1.** Stacked bar plots illustrating the top 10 proteins explaining greatest variance for line, AD genotype and sex in cortex (**A**) and hippocampus (**B**). (**C**) Top variance explained proteins for line across cortex and hippocampus. (**D**) Top variance explained proteins for AD genotype across cortex and hippocampus.



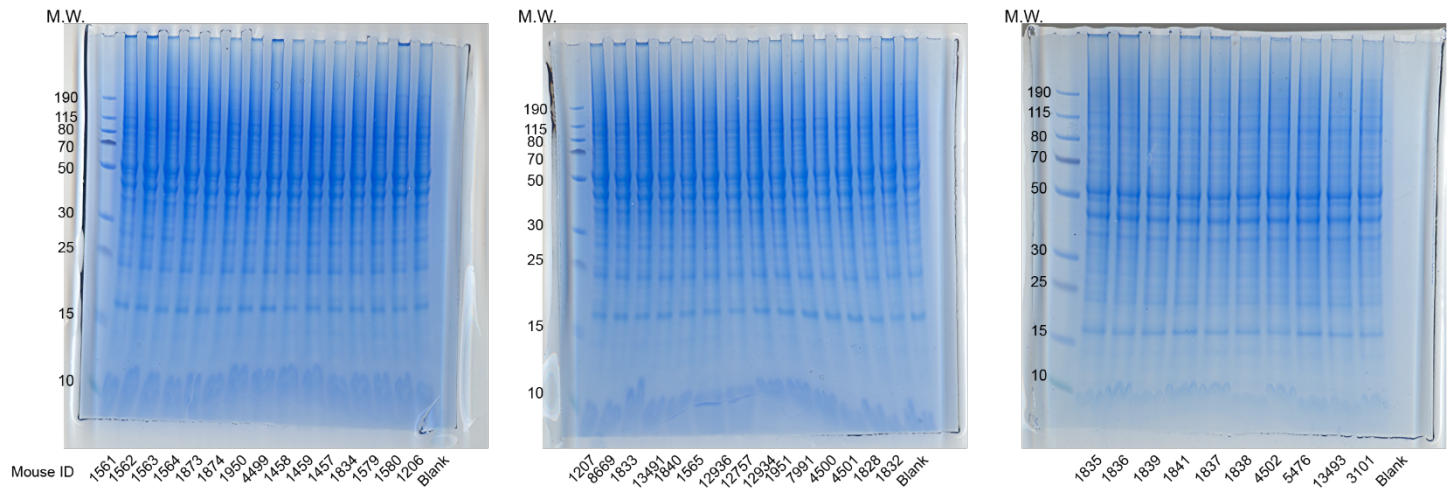
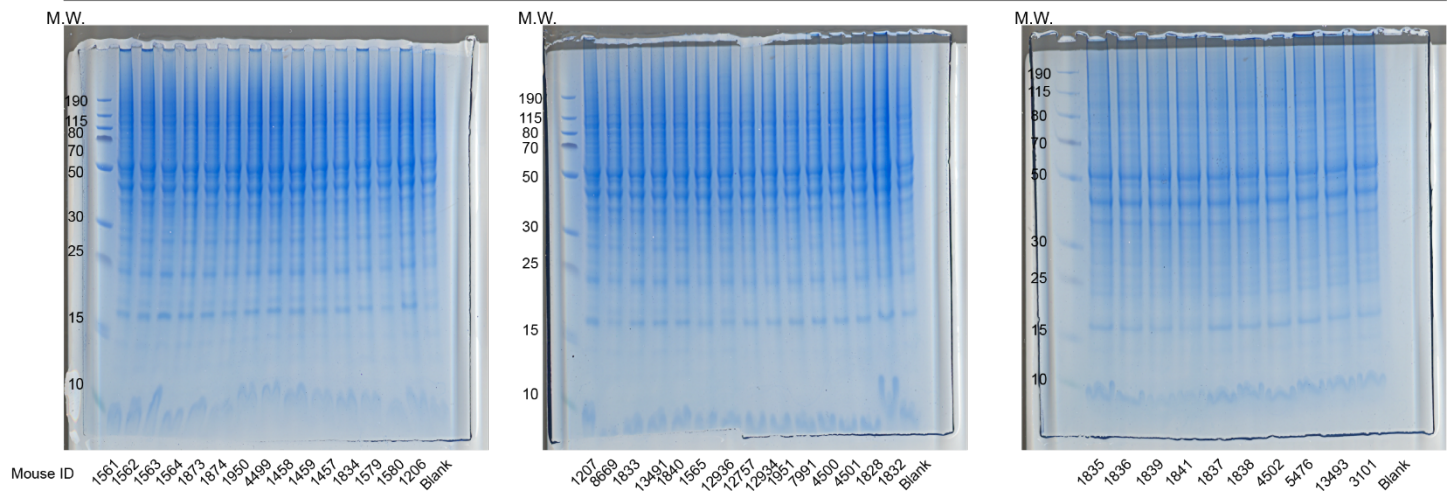
**Supplementary Figure 2. (A)** Levels of APOE and GFAP were assessed by Western blotting in nontransgenic (Ntg) and 5XFAD mice on the B6 and B6xD2 backgrounds in cortex.  $\alpha$ -tubulin was used as a loading control. **(B)** Quantification of protein levels in (A).



**Supplementary Figure 3.** (A-B) Consensus module eigene protein clustering represented as a dendrogram for cortex (A) and hippocampus (B). (C-D) Module eigenprotein correlation heatmap for cortex (C) and hippocampus (D). (E) Mean preservation relationship for each eigenprotein was calculated for the consensus network. Mean preservation was 0.83, indicating a high degree of preservation. (F) Preservation adjacency of the consensus network represented by heatmap. Most relationships were highly preserved across brain regions.



**Supplementary Figure 4.** (A) Eigenprotein network built using only cortex data showing module relatedness dendrogram and correlation (bicor). (B) Network preservation of mouse (cortex only) protein network in human frontal cortex network (Johnson et al., 2020). Modules with Zsummary greater than or equal to 1.96 ( $q=0.05$ , dashed blue line) are considered preserved, and modules with Zsummary of 10 or higher ( $q=1e-23$ , dashed red line) are considered highly preserved. The majority (11 out of 20) of consensus modules from the mouse (cortex only) proteome were found to be preserved in the human network. (C) Heatmap for the overrepresentation analysis (ORA) of mouse (cortex only) module members with human frontal cortex module members. Numbers in boxes are  $-\log_{10}$  FDR values.  $P^* < 0.05$ ,  $** < 0.01$ ,  $*** < 0.001$ . Heatmap threshold is set at 10% FDR (0.1).

**A****Cortex****B****Hippocampus**

**Supplementary Figure 5. (A-B)** Protein integrity was assessed by SDS-PAGE gel stained with Coomassie blue in the cortex (**A**) and hippocampus (**B**).