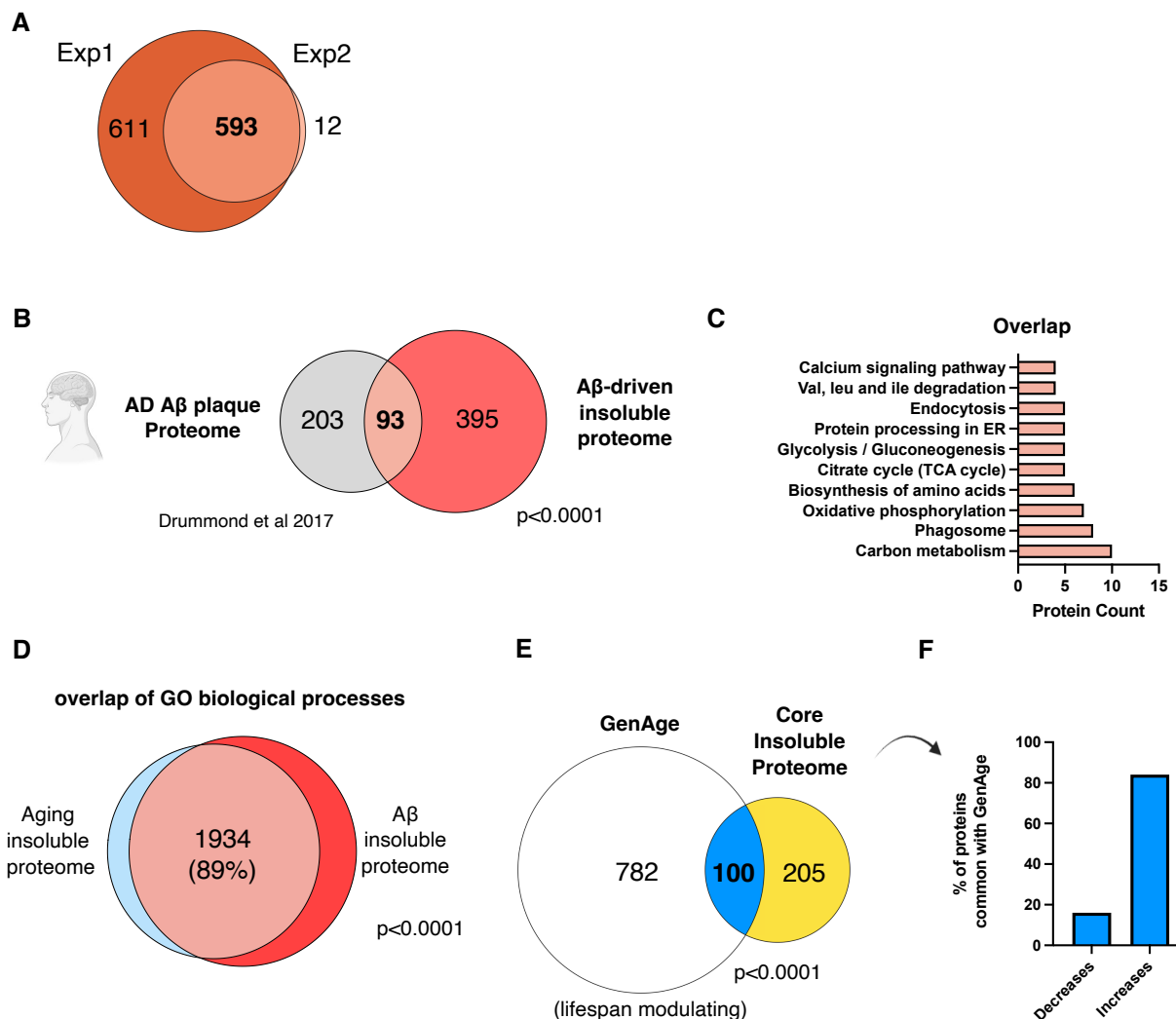
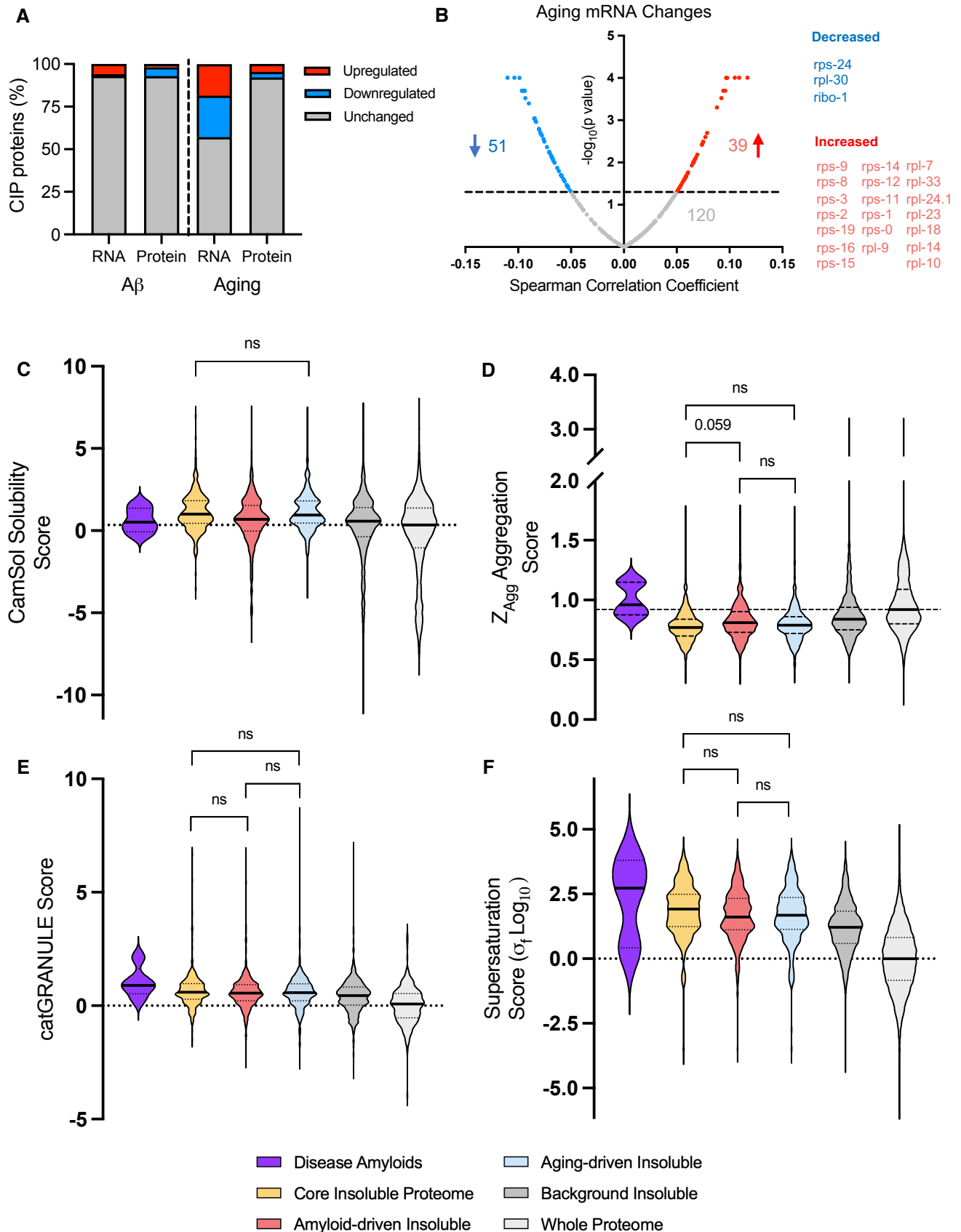


Supplementary Figure 1



A. Overlap of proteins which increased in abundance in the insoluble proteome after A β expression across independent experiments. **B.** Overlap of proteins reliably identified in A β -rich plaques from AD patient brains³⁷ and the A β -driven insoluble proteome, Fischer's exact test, image created with Biorender.com. **C.** Top 10 KEGG annotations by protein count for overlapping proteins between AD senile plaque proteome (Drummond et al. 2017) and the A β -driven insoluble proteome. **D.** Overlap of GO biological processes represented in the aging insoluble proteome and the A β -driven insoluble proteome, Fischer's exact test. **E.** Overlap of proteins which have been shown to modulate lifespan (from GenAge database) and proteins in the Core Insoluble Proteome, Fischer's exact test. **F.** Proportion of proteins in the CIP for which reduced or ablated expression leads to a decrease or increase in lifespan in *C. elegans*.

Supplementary Figure 2

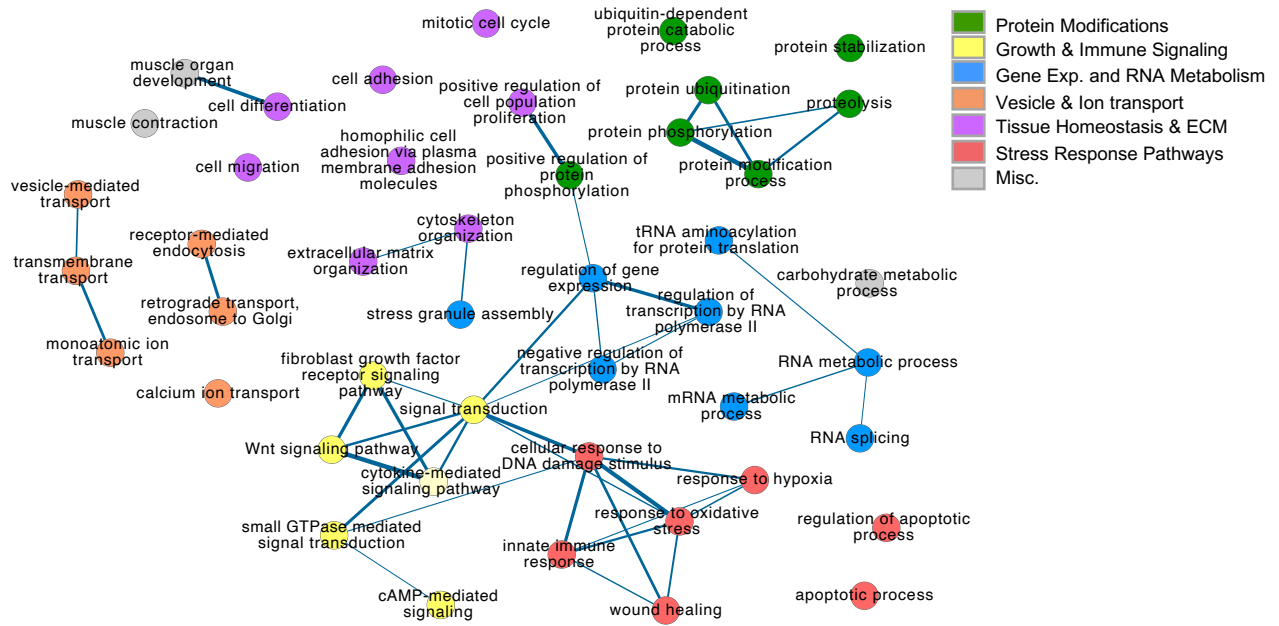


A. Proportion of CIP proteins differentially expressed after A β expression⁵⁰ or during wild-type aging in *C. elegans*^{51,52}. **B** Volcano plot of Spearman Correlation between mRNA expression of CIP encoding genes and aging, from Day 2 to Day 10, in wild-type *C. elegans* with ribosomal genes highlighted. **C.** Violin plot of CamSol intrinsic solubility score distribution for each proteome. **D.** Violin plot of catGRANULE RNA granule prediction score distribution for each proteome. **E.** Violin plot of Zyggregator aggregation propensity score distribution for each proteome. **F.** Violin plot of Supersaturation ($\sigma_f \log_{10}$) score distributions for each proteome. In each case the Background Insoluble is all proteins identified in any insoluble proteome across any experiment and the Whole Proteome is the *C. elegans* reference proteome. Disease Amyloids = A β precursor protein, α -Synuclein, prion protein, β -2 microglobulin, and amylin. For clarity, only comparisons that were not statistically significant are shown, all other pair-wise comparisons were significant with $p_{\text{adj}} < 0.05$, Kruskal Wallis Test with Dunn's correction.

Supplementary Figure 3

A

GO Biological Processes shared between the core insoluble proteome and all 5 ARD classes



A. ReviGo network representation of the non-redundant GO biological processes shared between the CIP and all 5 diverse CARD categories.