

Description of Additional Supplementary Files

Supplementary Data 1. Data relating to Fig. 1A-E: Astrocyte TRAP-seq data relating to WT vs. $\text{Mapt}^{\text{P301S}}$ mice at early stage disease.

Supplementary Data 2. Data relating to Fig. 1A-E: Astrocyte TRAP-seq data relating to WT vs. $\text{Mapt}^{\text{P301S}}$ mice at late stage disease.

Supplementary Data 3. Data relating to Fig. 1F-J: Astrocyte TRAP-seq data relating to WT vs. APP/PS1 mice at early stage disease.

Supplementary Data 4. Data relating to Fig. 1F-J: Astrocyte TRAP-seq data relating to WT vs. APP/PS1 mice at late stage disease.

Supplementary Data 5. Data relating to Supplementary Fig. 2A-C: Illustration of the 'acute MCAO' gene set, the 'acute-LPS' gene set and the 'pan-reactive' gene sets.

Supplementary Data 6. Data relating to Fig. 3A and Supplementary Fig. 3: Set of genes significantly upregulated in both $\text{Mapt}^{\text{P301S}}$ and APP/PS1 models, and set of genes down-regulated in both $\text{Mapt}^{\text{P301S}}$ and APP/PS1 models.

Supplementary Data 7. Data relating to Fig. 4B. RNA-seq analysis of astrocytes sorted from GFAP-Nrf2 mice, vs. WT.

Supplementary Data 8. Data relating to Fig. 6A,B: RNA-seq analysis of the neocortex (WT, $\text{Mapt}^{\text{P301S}}$, GFAP-Nrf2, $\text{Mapt}^{\text{P301S}}$ _X_GFAP-Nrf2). Genes induced and repressed ($\text{Mapt}^{\text{P301S}}$ vs. WT) are shown.

Supplementary Data 9. Data relating to Fig. 9A,B: RNA-seq analysis of hippocampus (WT, APP/PS1, GFAP-Nrf2, APP/PS1_X_GFAP-Nrf2). Genes induced and repressed (APP/PS1 vs. WT) are shown.

Supplementary Data 10. Data relating to Supplementary Fig. 9A,B: RNA-seq analysis of cortex (WT, APP/PS1, GFAP-Nrf2, APP/PS1_X_GFAP-Nrf2). Genes induced and repressed (APP/PS1 vs. WT) are shown.

Supplementary Data 11. Data relating to Fig. 9G: Genes down-regulated by A β pathology (APP/PS1 vs. WT, $p_{\text{adj}} < 0.05$, Fig. 9A) that were also present in analysis of genes up-regulated by astrocytic Nrf2 in the APP/PS1 mouse (APP/PS1_X_GFAP-Nrf2 vs. APP/PS1, Fig. 9G).

Supplementary Data 12. Data relating to Fig. 9H. A β pathology induces tissue-wide deficits in four primary areas that are rescued by astrocytic Nrf2.