The identification of a Distinct Astrocyte Subtype that Diminishes in Alzheimer's Disease

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Supplementary Figure 1. cell type clusters identified from analyzing single nuclei RNA-seq datasets from GSE143758 (A) and syn18485175 (B). For each dataset, UMAP plots of all nuclei and the expression of various cell markers. Dot size indicates the proportion of expressing cells, colored by standardized expression levels.



Supplementary Figure 2. Astrocyte subpopulations identified from analyzing dataset GSE143758. (A) The UMAP visualization of astrocyte lineage cells split into AD mice and controls. (B) The percentage of each Astrocyte subpopulations in control and AD samples. Colored according to cluster types. (C) UMAP plots of *GFAP* expression in astrocyte lineage cell populations. D, Violin plot showing scale log-normalized read counts of *GFAP* expression.



Supplementary Figure 3. The functional enrichment in ast_cluster1 cells from dataset syn18485175.



Supplementary Figure 4. cell type clusters identified from analyzing single nuclei RNA-seq datasets from GSE138852. (A) UMAP plots of all cells from dataset GSE138852. (B) The expression of neuron markers and proportion of clusters identified in control and AD samples. C, UMAP plots of astrocyte lineage cells separated by patient information. D, The expression of astrocyte specific marker in astrocyte lineage cells.



Supplementary Figure 5. The change of locations of AQP4 protein in the context of cerebral vessels in control and AD prefrontal cortex. Representative images of immunohistochemistry showing that more AQP4⁺/CD63⁺ (Green/Red) cells are located in the close vicinity of cerebral vessels marked by CD31⁺ expression (Magenta) in 27-months old control compared to the 20-Months old APP^{NL-F}/Knck-in (APP^{NL-F}) mouse brain (Scale bar 50 µm).



Supplementary Figure 6. A β plaque engulfed by GFAP^{low}/CD63⁺ cells *in vivo* and *in vitro*. (A) Immunohistochemistry of 20-months old APP^{NL-F/NL-F} knock-in (APP^{NL-F}) AD mouse brain prefrontal cortex showing colocalization of A β plaque with GFAP^{low}/CD63⁺ cells (upper panel), in contrast to GFAP^{high}/CD63⁺ cells (lower panel) (Scale bar 100 µm). (B) Immunocytochemistry of primary astrocyte culture with FAM labeled A β 42 showing engulfment of FAM-A β 42 by GFAP^{low}/CD63⁺ cells compared with GFAP^{high}/CD63⁺ cells (Scale bar 100 µm). Arrowheads indicate GFAP^{low}/CD63⁺ astrocytes and Arrows indicate GFAP^{high}/CD63⁺ astrocytes.