

Table S1. Demographics and diagnoses of the patient cohorts used in this study. Individually characterized brains in the University of Florida Neuromedicine Human Brain and Tissue Bank were used in the study. Experimental Group denotes the designation for this study. NP Dx1, primary diagnosis based on neuropathology; NP Dx2 and NP Dx3, secondary diagnoses based on neuropathology; Thal phase, burden of immunostained amyloid deposits in cortical and subcortical area; Braak stage, CERAD score, neuritic plaque frequency; AD, Alzheimer's disease; ARTAG, Aging-related tau astroglipathy; CAA, cerebral amyloid angiopathy; CVD, cardiovascular disease; HC, healthy control with no dementia; LATE, limbic-predominant age-related TDP-43 encephalopathy; PSP, Progressive supranuclear Palsy. N/A: Not applicable; ND, not done.

| Experimental Group | Post-mortem Diagnosis | NP Dx1  | NP Dx2                           | NP Dx3                      | Thal stage | Braak stage | CERAD score | APOE genotype | Sex | Age | PMI  |
|--------------------|-----------------------|---------|----------------------------------|-----------------------------|------------|-------------|-------------|---------------|-----|-----|------|
| AD-A               | AD                    | AD high | CAA widespread, mild             | N/A                         | 4          | V           | frequent    | 3/4           | m   | 77  | 5    |
| AD-B               | AD                    | AD high | CAA widespread, moderate         | N/A                         | 5          | VI          | frequent    | 3/4           | m   | 63  | 2    |
| AD-C               | AD                    | AD high | CAA widespread, mild to moderate | LATE stage 2                | 4          | VI          | frequent    | 3/4           | f   | 82  | 7    |
| AD-D               | AD                    | AD high | CAA (moderate to severe)         | Acute microinfarcts         | 4          | VI          | frequent    | 3/4           | m   | 73  | 6    |
| AD-E               | AD                    | AD high | CAA widespread, moderate         | N/A                         | 5          | VI          | frequent    | 3/4           | m   | 59  | 7    |
| AD-F               | AD                    | AD high | CAA widespread, moderate         | N/A                         | 5          | VI          | frequent    | 3/3           | m   | 83  | 7    |
| LN-13              | PSP                   | PSP     | AD low                           | N/A                         | 3          | I           | none        | 3/3           | f   | 77  | 10   |
| LN-A               | PSP                   | PSP     | AD low                           | CAA focal, mild to moderate | 3          | I           | none        | ND            | m   | 70  | 19.5 |
| LN-B               | PSP                   | PSP     | AD intermediate                  | CAA widespread, severe      | 5          | III         | moderate    | 4/4           | m   | 72  | 27   |
| LN-C               | PSP                   | PSP     | LATE Stage2                      | AD low                      | 1          | II          | none        | 3/3           | m   | 77  | 12   |
| LN-D               | PSP                   | PSP     | AD low                           | ARTAG                       | 3          | I           | none        | 3/3           | m   | 78  | 3    |
| LN-E               | PSP                   | PSP     | LATE Stage 1                     | N/A                         | 0          | 0           | none        | 3/3           | f   | 70  | 18   |
| LN-F               | PSP                   | PSP     | AD low                           | CAA focal, mild             | 1          | II          | sparse      | 3/3           | m   | 76  | 6    |
| HC-1               | Control               | N/A     | N/A                              | N/A                         | 0          | 0           | none        | 3/4           | f   | 55  | 12   |
| HC-2               | Low AD                | AD low  | CVD                              | N/A                         | 1          | II          | none        | ND            | m   | 88  | 4    |

Table S2. Antibodies used in this study

| Antibody name        | Specificity                              | Host Species      | Dilutions    | Source   |
|----------------------|--|-------------------|--------------|--|
| Recombinant anti-tau | Mouse and human tau                      | Rabbit monoclonal | 1:10000 (WB) | Abcam Cat# ab254256, RRID:AB_2894402                                 |
| Tau-5                | Mouse, human, rat, bovine, and sheep tau | Mouse monoclonal  | 1:1000 (WB)  | Innovative Research Cat# AHB0042, RRID:AB_1502093                    |
| DAKO                 | Human tau                                | Rabbit polyclonal | 1:2500 (IHC) | Agilent Cat# A0024, RRID:AB_10013724                                 |
| AT8                  | pSer202/pT205                            | Mouse monoclonal  | 1:1000 (WB)  | Thermo Fisher Scientific Cat#MN1020, RRID:AB_223647                  |
| PHF1                 | pSer396/pSer404                          | Mouse monoclonal  | 1:1000 (WB)  | Gift from Dr. Peter Davies (Greenberg et al., 1992; RRID:AB_2313687) |
| AT270                | pThr181                                  | Mouse monoclonal  | 1:1000 (WB)  | Thermo Fisher Scientific Cat#MN1050, RRID:AB_223651                  |
| AT100                | pThr212/pSer214                          | Mouse monoclonal  | 1:1000 (WB)  | Thermo Fisher Scientific Cat# MN1060, RRID:AB_223652                 |
| AT180                | pThr231                                  | Mouse monoclonal  | 1:1000 (WB)  | Thermo Fisher Scientific Cat# MN1040, RRID:AB_223649                 |
| pSer262              | pSer262                                  | Rabbit polyclonal | 1:1000 (WB)  | Thermo Fisher Scientific Cat# 44-750G, RRID:AB_2533743               |
| pSer422              | pSer422                                  | Rabbit polyclonal | 1:1000 (WB)  | Thermo Fisher Scientific Cat# 44-764G, RRID:AB_2533748               |
| Tau C3               | Tau cleaved at Asp421 and Asp422         | Mouse monoclonal  | 1:1000 (WB)  | Thermo Fisher Scientific Cat# AHB0061, RRID:AB_2536237               |
| GAPDH                | GAPDH                                    | Rabbit monoclonal | 1:1000 (WB)  | Abcam Cat# ab181602, RRID:AB_2630358                                 |
| TUB 2.1              | $\beta$ -tubulin                         | Mouse monoclonal  | 1:1000 (WB)  | Sigma-Aldrich Cat# T4026, RRID:AB_477577                             |
| actin                | $\beta$ -actin                           | Mouse monoclonal  | 1:1000 (WB)  | Sigma-Aldrich Cat# A5441, RRID:AB_476744                             |