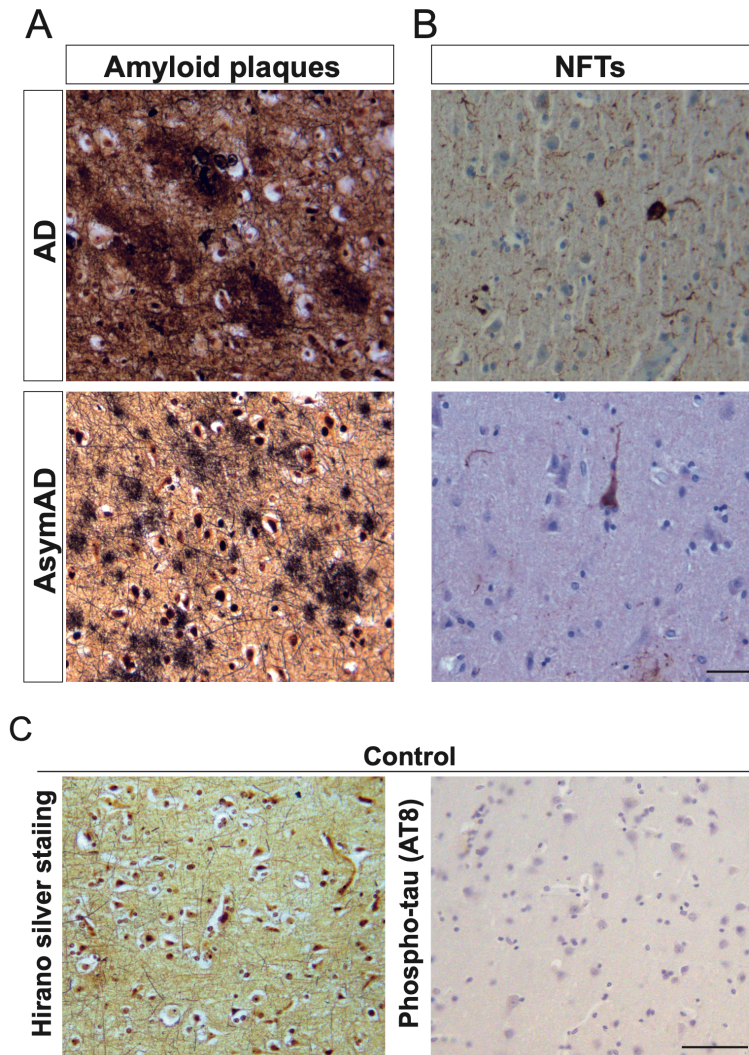858   **SUPPLEMENTAL FIGURES LEGENDS**

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861   **Supplementary Figure 1: Middle frontal gyrus autopsies in non-demented subjects with high**

862   **loads of Alzheimer's disease pathology. A-B** Histopathology performed in AD and AsymAD

863   cases confirmed the presence of amyloid plaques by Hirano silver staining (A) and neurofibrillary

864   tangles (NFTs) by AT8 **(B),** an antibody which recognizes the pathological phospho-sites in
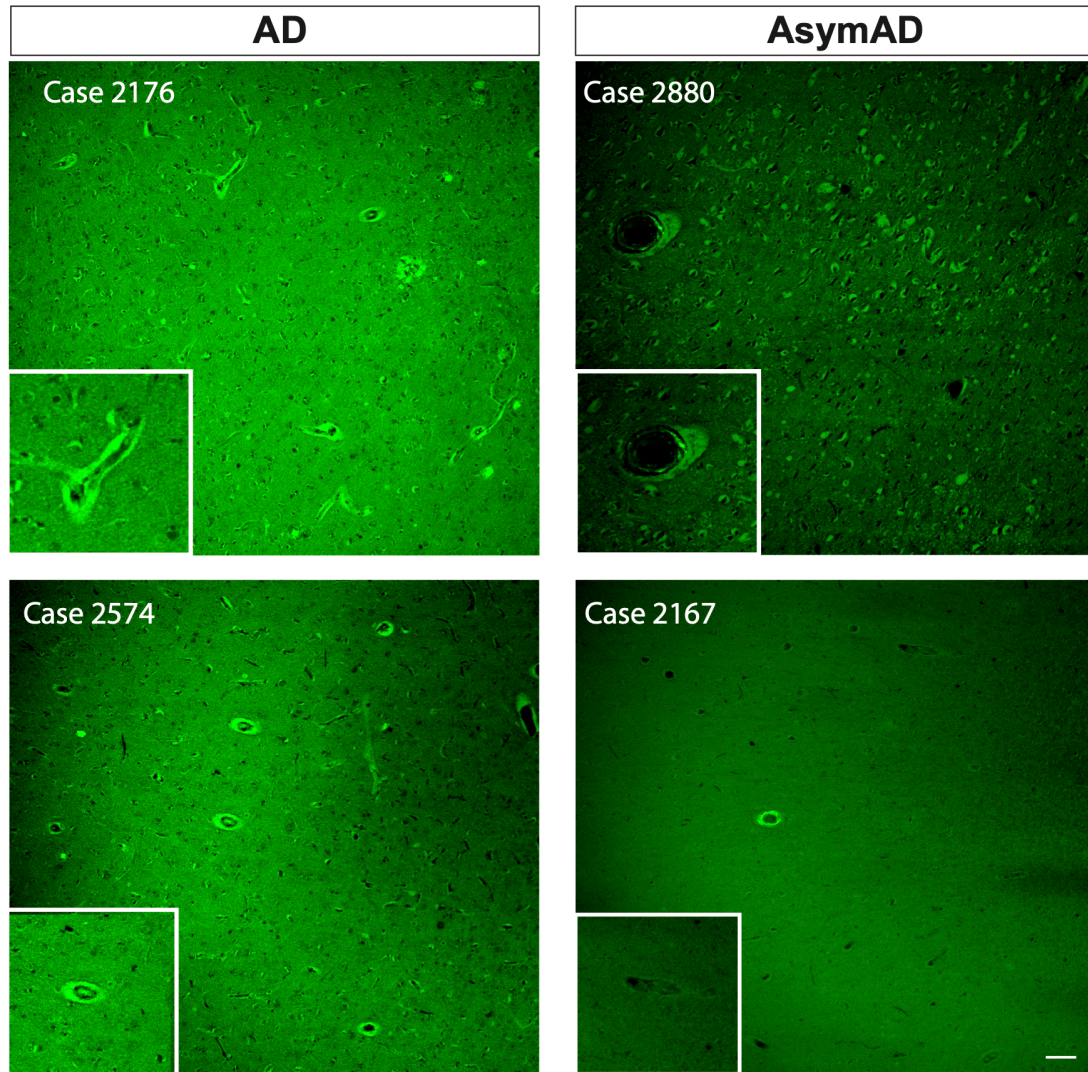
865   Ser202/Thr305 of tau protein. Representative images showing cases with a CERAD between B-C

866   and a Braak and Braak score of 4-6. Scale bar: 20 μm. **C.** No reactivity for none of these

867   pathological markers was found in age-matched control subjects. Scale bar: 50 μm.

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871 **Supplementary Figure 2:** Detection of vascular amyloid aggregation using Thioflavin S in AD

872 and AsymAD cases. The insets show structures recognizes as vasculature in the MFG of AD and
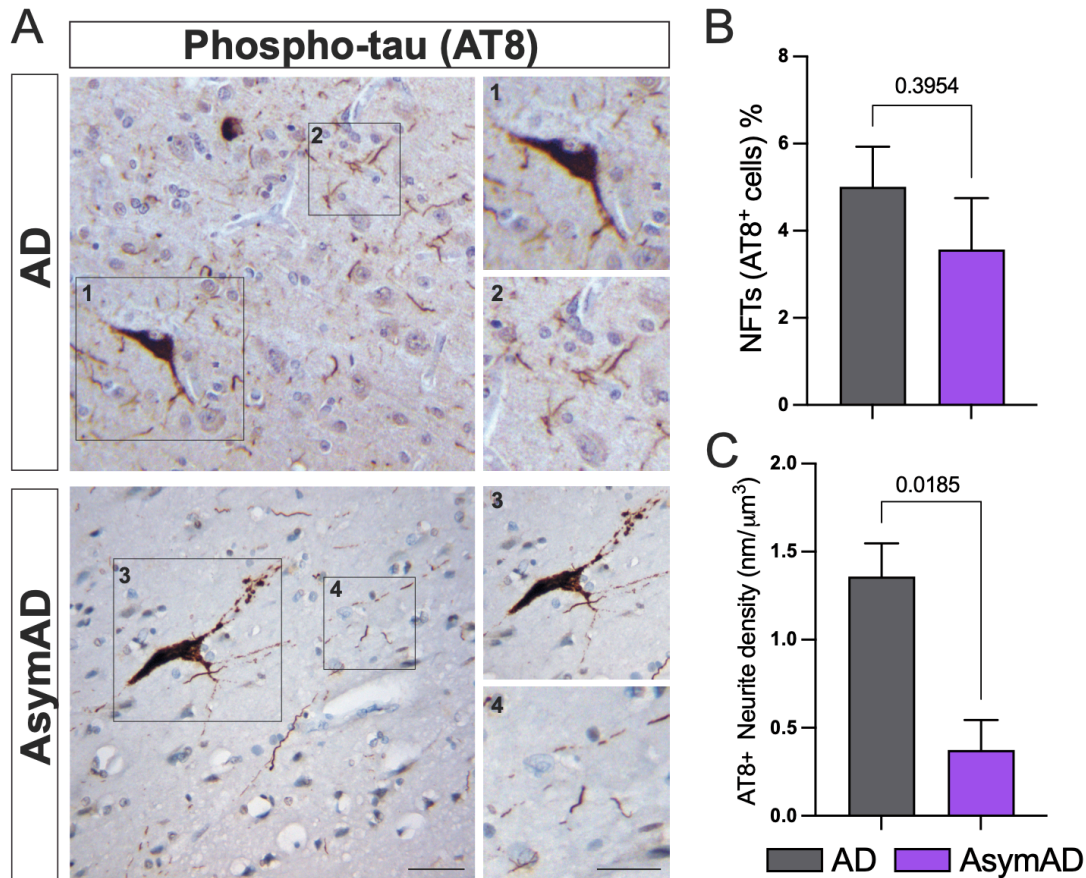
873 AsymAD cases. Scale bar: 50 μm.

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Supplementary Figure 3: AsymAD cases show similar numbers of NFTs compared to AD, but reduced AT8 positive (AT8+) neuritic staining. A. phospho-tau staining in AD and AsymAD subjects**.** Both representative figures were cases classified as CERAD C and Braak and Braak score of 6. Scale bar: 20 μm and 10 μm (insets) **B.** Quantification of AT8+ neurites and C. percentage of NFTs/AT8+ cell. Data is shown as mean ± *SEM,* Mann-Whitney test, *n=4-6* per condition.

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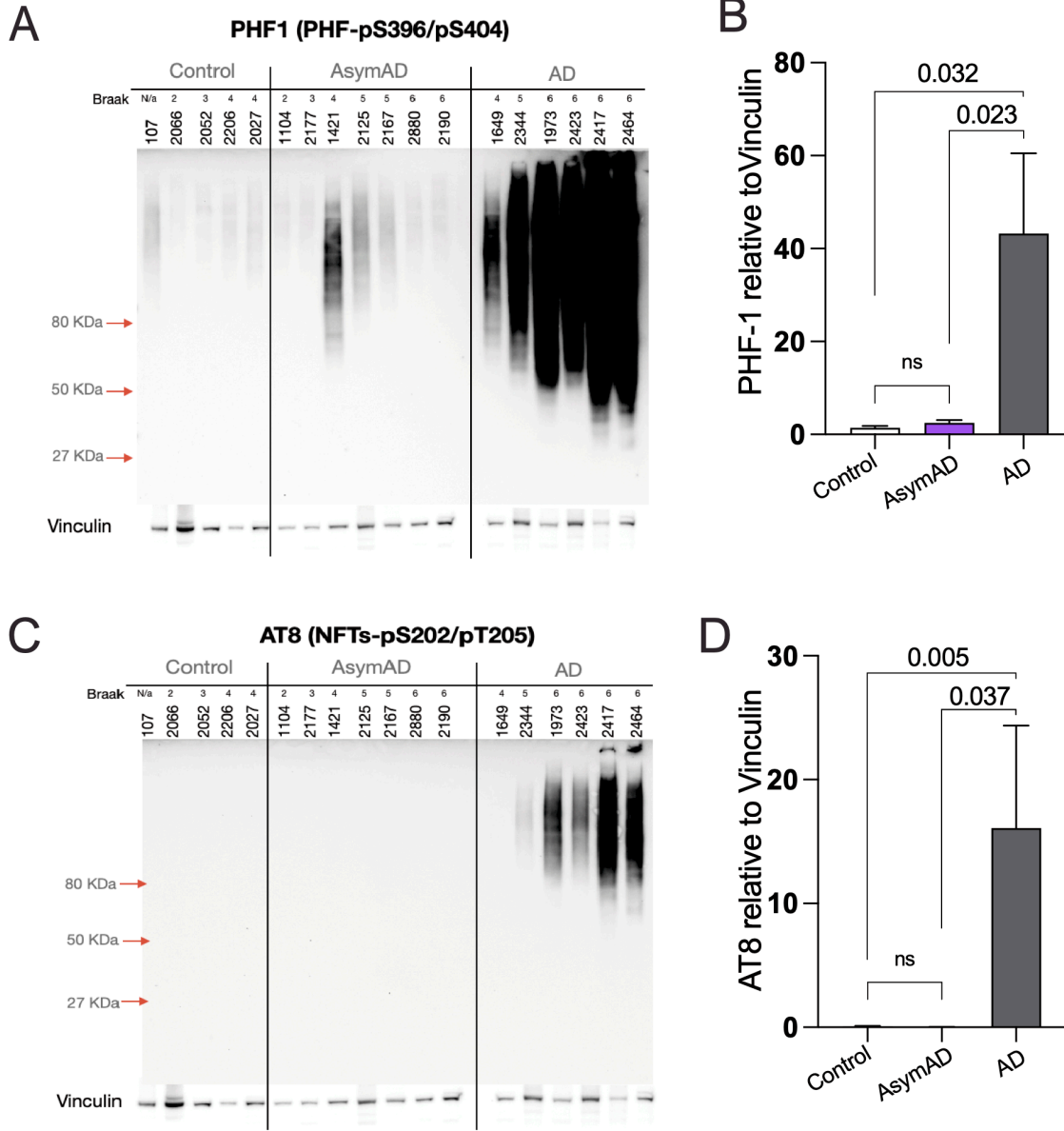**Supplementary Figure 4: Tau species in total soluble and insoluble extracts of AD, AsymAD and aged-matched controls. A-B.** Western blot against specific PHF1 (pTauS396/S404) (A) and AT8 (pTauS202/Thr305) (C) and its respective quantifications (B-D).
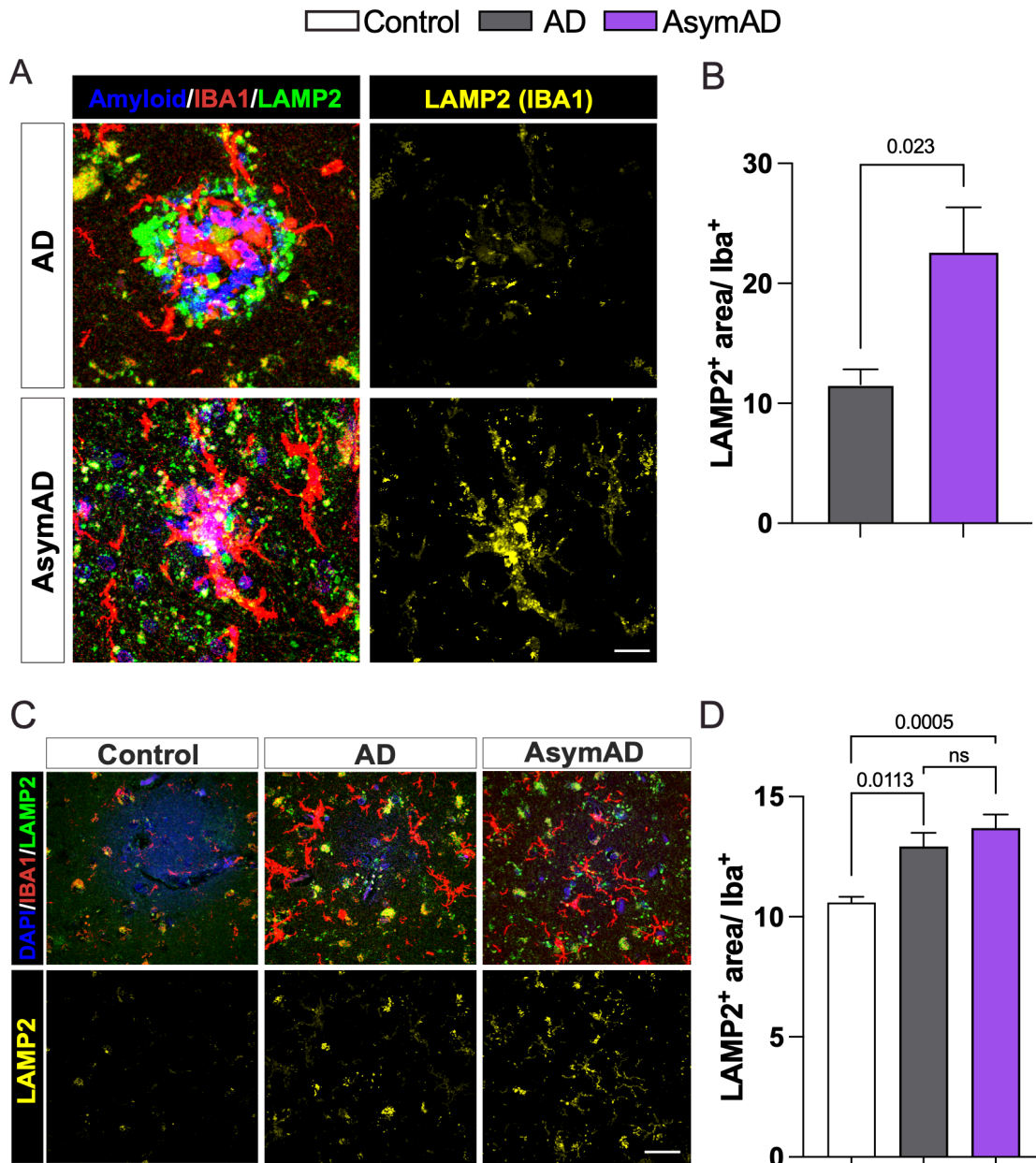
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909 **Supplementary Figure 5: Increased LAMP2 levels in plaque-AsymAD microenvironment.**

910 **A.** Staining against LAMP2 (green), IBA1 (red) and DAPI, to identify amyloid-plaques and cell

911 nuclei in AsymAD and AD cases **B.** Quantification of LAMP2 positive area within IBA1 area **C.**

912 LAMP2 and IBA1 immunostaining in areas free of amyloid plaques in control, AD and AsymAD

913 cases **D.** quantification of LAMP2 immunoreactivity in IBA1+ area. Data is shown as mean ±

914 *SEM.* In B, *n=6* cases, per condition and 22-28 plaques were analyzed. Significance was

915 determined by Mann-Whitney test. In F, $n=6$ cases, per condition were analyzed. Data is shown

916 as ±*SEM,* One-way ANOVA and Tukey's multiple comparisons test (n.s.; 0.5432)