Supplementary information

Amyloid-beta antibody binding to cerebral amyloid angiopathy fibrils and risk for amyloid-related imaging abnormalities

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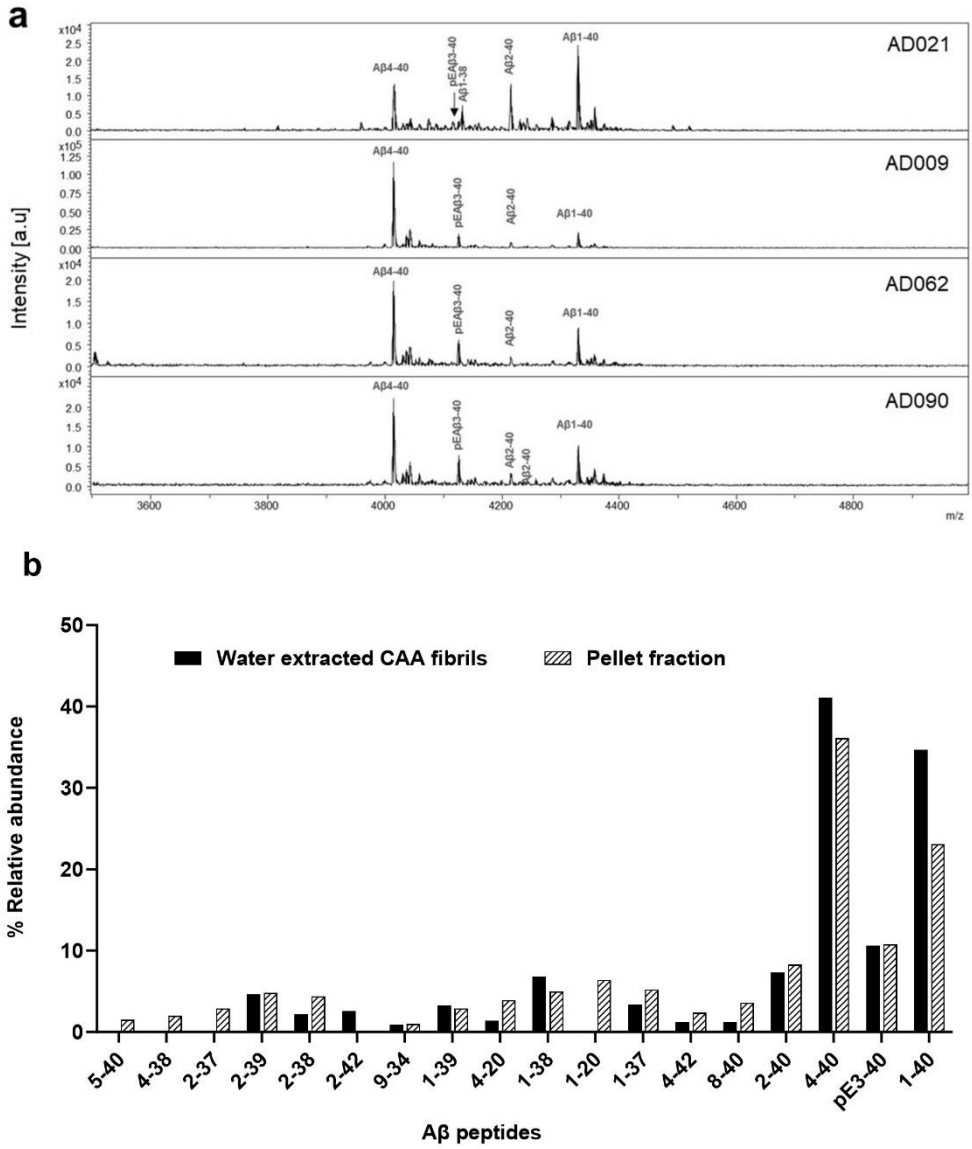
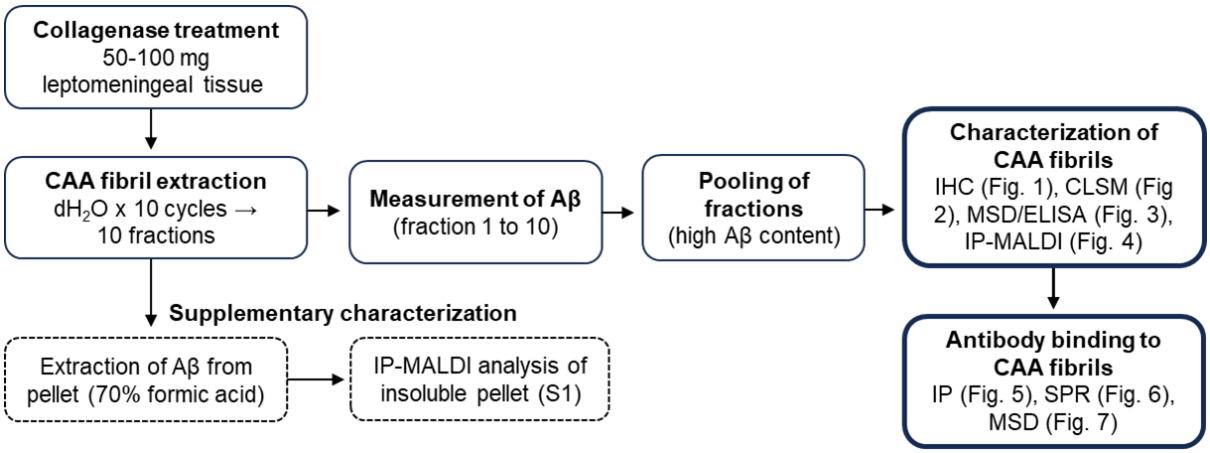
Supplementary Fig. 1



Supplementary Figure 1. IP-MALDI analyses of the FA-extracted pellet fractions from leptomeningeal tissues of AD subjects. **a,** Mass spectra for the indicated study subjects showing Aβ-assigned peaks. **b,** The relative abundance of the Aβ peptides identified in each pellet fraction sample (average of all subjects in **a**), as compared with the water-soluble extract from the same individual (data presented in Fig. 4).

Supplementary Fig. 2



Supplementary Figure 2. Schematic outline of the steps used to isolate and characterize CAA Aβ fibrils from human leptomeningeal tissue. Repeated water extraction of the tissue generated ten water fractions. The Aβ content of each fraction was analyzed using the V-PLEX® Aβ peptide panel 1 (4G8) assay (MSD). Fractions with high Aβ levels (usually fractions 2 to 6) were pooled, generating a representative sample from each subject for use in subsequent analyses. In a supplementary characterization, the final pellet that remained after all the water extractions had been completed was extracted in 70% formic acid prior to peptide characterization using immunoprecipitation (IP) matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI). IHC, immunohistochemistry; ELISA, enzyme-linked immunosorbent assay; CLSM, confocal laser scanning microscopy; SPR, surface plasmon resonance.

Supplementary Table 1: SPR kinetics of antibody binding to CAA Aβ fibrils

AD009			
Antibody	k_{a1} **($M^{-1}s^{-1}$)**	k_{d1} **(s^{-1})**	K_{D1} **(nM)**
Aducanumab	$3.36 \pm 1.20 \times 10^{5}$	$1.14 \pm 0.28 \times 10^{-1}$	358 ± 71.7
Bapineuzumab	$6.72 \pm 7.86 \times 10^{5}$	$1.31 \pm 0.83 \times 10^{-3}$	5.96 ± 4.96
Crenezumab	ND	ND	ND
Donanemab	$1.25 \pm 0.37 \times 10^{4}$	$3.08 \pm 0.39 \times 10^{-2}$	728 ± 119
Gantenerumab	$6.46 \pm 1.41 \times 10^{4}$	$3.01 \pm 0.71 \times 10^{-2}$	471 ± 57.0
Lecanemab	$5.36 \pm 2.73 \times 10^{4}$	$3.91 \pm 1.30 \times 10^{-2}$	764 ± 134
Solanezumab	ND	ND	ND

AD062			
Antibody	k_{a1} **($M^{-1}s^{-1}$)**	k_{d1} **(s^{-1})**	K_{D1} **(nM)**
Aducanumab	$8.53 \pm 3.47 \times 10^{4}$	$1.03 \pm 0.41 \times 10^{-1}$	1220 ± 282
Bapineuzumab	ND	ND	ND
Crenezumab	ND	ND	ND
Donanemab	ND	ND	ND
Gantenerumab	$3.29 \pm 0.40 \times 10^{4}$	$4.59 \pm 0.48 \times 10^{-2}$	1400 ± 92.6
Lecanemab	ND	ND	ND
Solanezumab	ND	ND	ND

AD090			
Antibody	k_{a1} **($M^{-1}s^{-1}$)**	k_{d1} **(s^{-1})**	K_{D1} **(nM)**
Aducanumab	$1.33 \pm 1.00 \times 10^{6}$	$5.48 \pm 3.01 \times 10^{-2}$	54.9 ± 31.3
Bapineuzumab	$9.93 \pm 10.1 \times 10^{5}$	$9.10 \pm 4.73 \times 10^{-5}$	0.17 ± 0.13
Crenezumab	ND	ND	ND
Donanemab	$2.28 \pm 1.23 \times 10^{4}$	$8.29 \pm 2.84 \times 10^{-3}$	465 ± 367
Gantenerumab	$7.71 \pm 4.23 \times 10^{4}$	$2.29 \pm 0.89 \times 10^{-2}$	347 ± 132
Lecanemab	$7.96 \pm 1.44 \times 10^{4}$	$8.35 \pm 1.14 \times 10^{-2}$	1060 ± 160
Solanezumab	ND	ND	ND

AD021			
Antibody	k_{a1} **($M^{-1}s^{-1}$)**	k_{d1} **(s^{-1})**	K_{D1} **(nM)**
Aducanumab	$2.52 \pm 0.18 \times 10^{5}$	$1.38 \pm 0.08 \times 10^{-1}$	548 ± 36.7
Bapineuzumab	$3.33 \pm 0.21 \times 10^{5}$	$9.83 \pm 4.70 \times 10^{-5}$	0.30 ± 0.16
Crenezumab	$8.30 \pm 2.62 \times 10^{3}$	$1.53 \pm 1.02 \times 10^{-2}$	2020 ± 1540
Donanemab	$2.53 \pm 1.43 \times 10^{4}$	$3.02 \pm 1.18 \times 10^{-2}$	1260 ± 192
Gantenerumab	$7.49 \pm 0.58 \times 10^{4}$	$2.92 \pm 0.34 \times 10^{-2}$	390 ± 22.0
Lecanemab	$1.28 \pm 0.11 \times 10^{5}$	$2.18 \pm 0.12 \times 10^{-2}$	170 ± 9.85
Solanezumab	ND	ND	ND

Data shown as mean ± SD. ND: not detected.
k_{a1}: association rate constant; k_{d1}: dissociation rate constant; K_{D1}: dissociation constant.