

Cryo-EM structures of cotton wool plaques' amyloid β and of tau filaments in dominantly inherited Alzheimer disease

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Supplementary material.

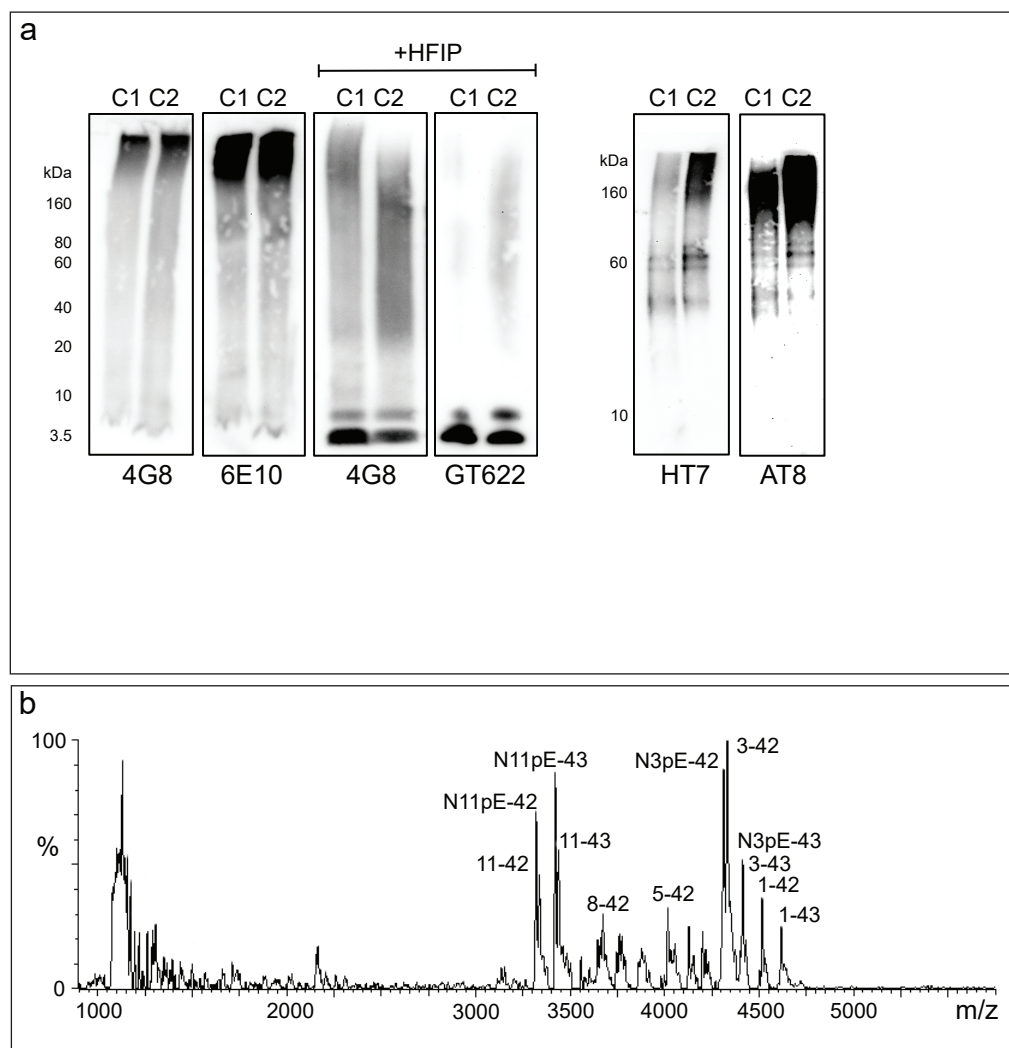
Supplementary Figures.

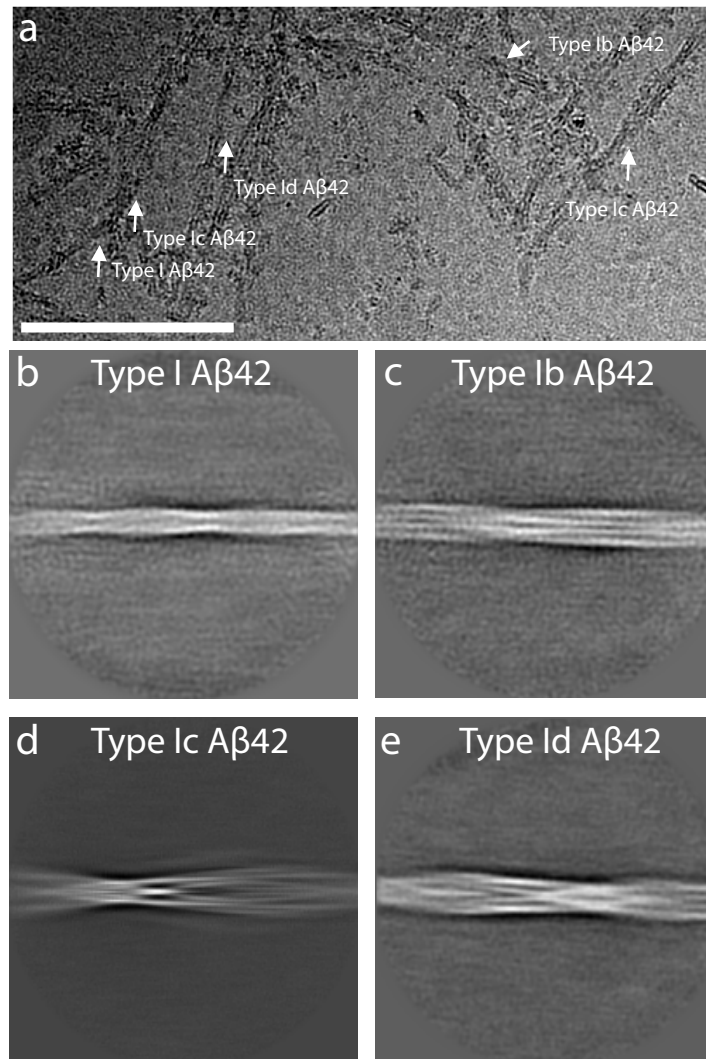
SFigure 1. Biochemical analysis of A β and tau in DIAD cases 1 and 2. (a) Western blot shows the presence of A β peptides and tau isolated from the cerebral cortex from cases #1 (V261I, C1) and #2 (A431E, C2). Presence of A β was assessed using antibodies 4G8 and 6E10. Samples were treated with HFIP (+HFIP) to disaggregate A β fibrils before western blot using 4G8 and GT622. Presence of tau was assessed using antibodies HT7 and AT8. Molecular masses are in kDa. (b) MALDI-TOF-MS of A β peptides isolated from frontal cortex of the V261I case.

SFigure 2. Representative cryo-EM images of filaments from sarkosyl-insoluble fractions. (a) Arrows indicate type I, Ib, Ic and Id A β filaments. (b-e) 2D class averages of type I, Ib, Ic and Id A β filaments. The scale bar represents 100 nm.

SFigure 3. (a) A β amino acid sequence showing the location of the β -strand regions in type I A β filaments. Type I A β filaments comprise from Gly₉ to Ala₄₂. (b) Cryo-EM map in transparent gray, with atomic model of a single molecule of type I A β filaments in CWPs.

SFigure 4. Fourier shell correlation curves. Fourier shell correlation (FSC) curves for independently refined two half maps and map vs model for A β filaments (a) and tau PHF and SF (b). The FSC threshold of 0.143 and 0.5 are shown as orange lines.

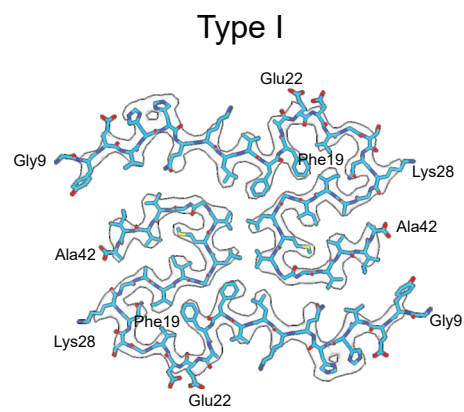




a



b



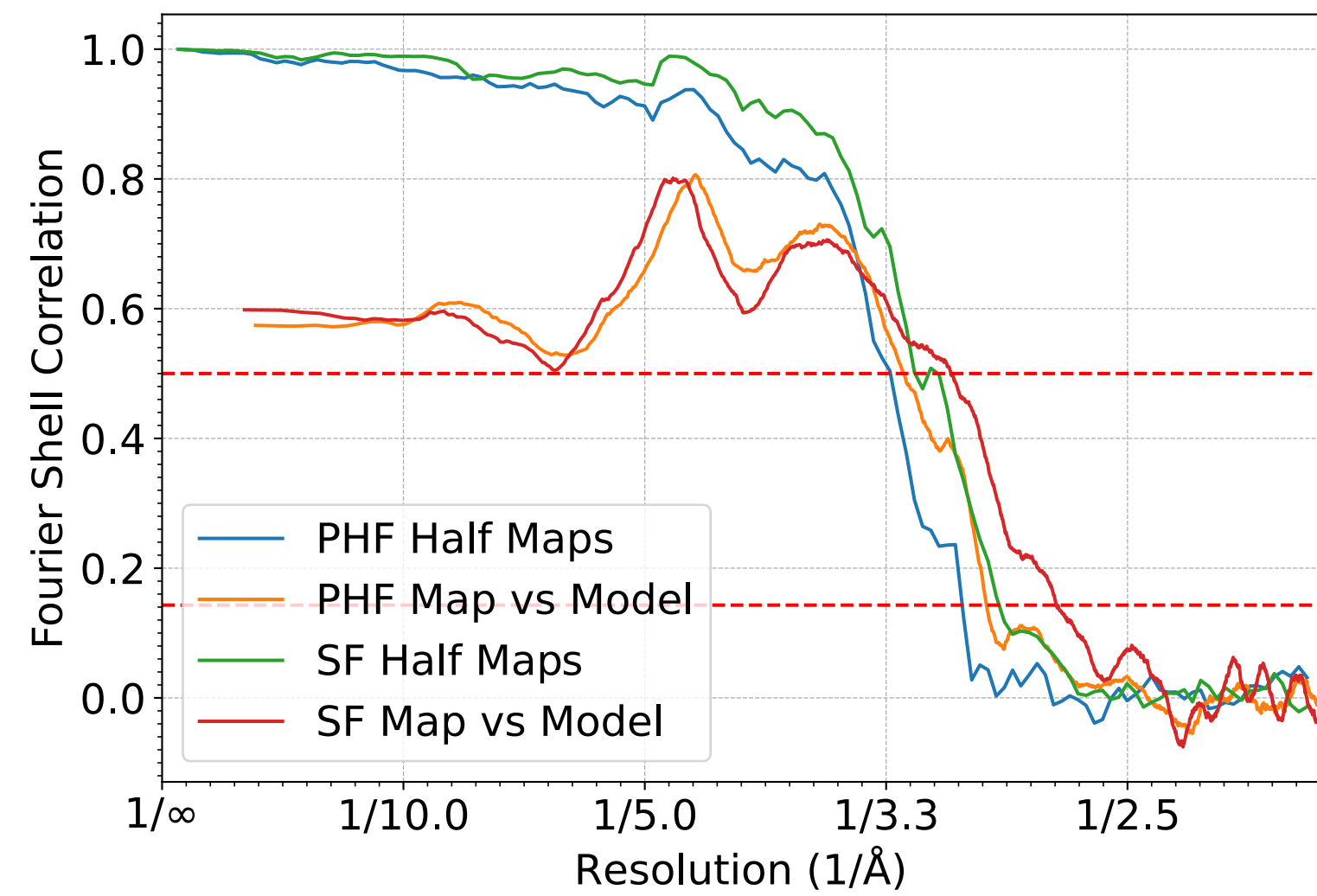
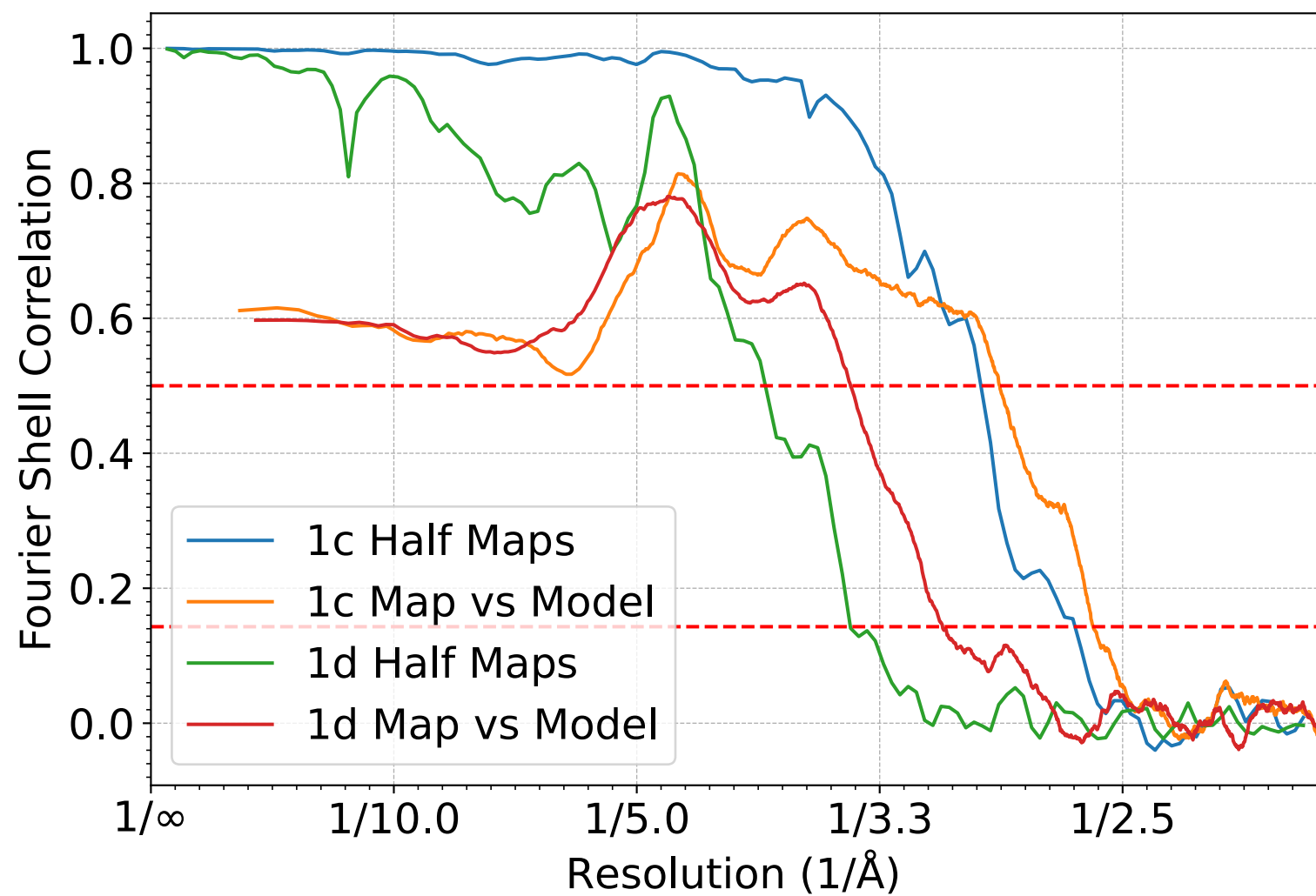


Table S1: Cryo-EM data collection and image processing

Data Collection and Processing	Case 1						Case 2					
Microscope	Krios											
Detector	K3											
Voltage (kV)	300											
Defocus range (μm)	-0.5 to -1.5											
Nominal magnification	x81,000											
Pixel size at detector (Å/pixel)	1.054											
Data collection software	EPU											
Total electron dose (e/Å ²)	57.79											
# Movies	6,183						17,581					
Reconstruction	PHF Tau	SF Tau	Type I Aβ42	Type Ib Aβ42	Type Ic Aβ42	Type Id Aβ42	PHF Tau	SF Tau	Type I Aβ42	Type Ib Aβ42	Type Ic Aβ42	Type Id Aβ42
# Initial particles	840,777		425,526				745,412		1,153,880			
# Final particles	40,114	10,372	6,937	3,417	14,083	3,014	20,710	24,819	3,499	2,815	16,128	2,590
Box size (pixel)	280	280	256	280	280	280	280	280	256	280	280	280
Symmetry imposed	C1	C1	C1	C2	C1	C1	C1	C1	C1	C2	C1	C1
Helical rise (Å)	2.38	4.78	2.38	4.76	2.39	4.77	2.38	4.78	2.38	4.76	2.39	4.770
Helical twist (°)	179.47	-0.90	178.51	-1.55	179.44	-1.741	179.457	-1.08	178.50	-1.55	179.44	-1.737
Resolution (Å) at FSC=0.143	3.0	4.5	3.8	8.0	2.9	3.6	3.0	2.9	3.8	8.0	2.7	3.6

Table S2: Atomic model validation statistics

	PHF Tau EMDB-46417 PDB- 9CZI	SF Tau EMDB- 46420 PDB- 9CZL	Type Ic A β 42 EMDB- 46422 PDB- 9CZN	Type Id A β 42 EMDB- 46424 PDB- 9CZP
Real-space model refinement				
Map vs Model resolution (Å) at FSC=0.5	3.0	3.1	2.7	3.5
Initial model used	5O3L	5O3T	7Q4B	7Q4B
Model composition				
Protein residues	730	740	680	680
Non-hydrogen atoms	5,570	5,660	5,020	5,020
R.M.S. deviations				
Bond lengths (Å)	0.0204	0.0225	0.0199	0.0210
Bond angles (°)	1.73	1.74	1.68	1.80
Model validation				
MolProbity score	1.20	1.06	0.83	1.09
Clashscore	0.79	0.52	0.00	0.40
Ramachandran plot				
Favored (%)	92.96	94.44	95.31	92.97
Allowed (%)	7.04	5.56	4.69	7.03
Disallowed (%)	0.00	0.00	0.00	0.00