

Online Supplementary files

Distinct Molecular Signatures of Amyloid-beta and Tau in Alzheimer's Disease Associated with Down Syndrome

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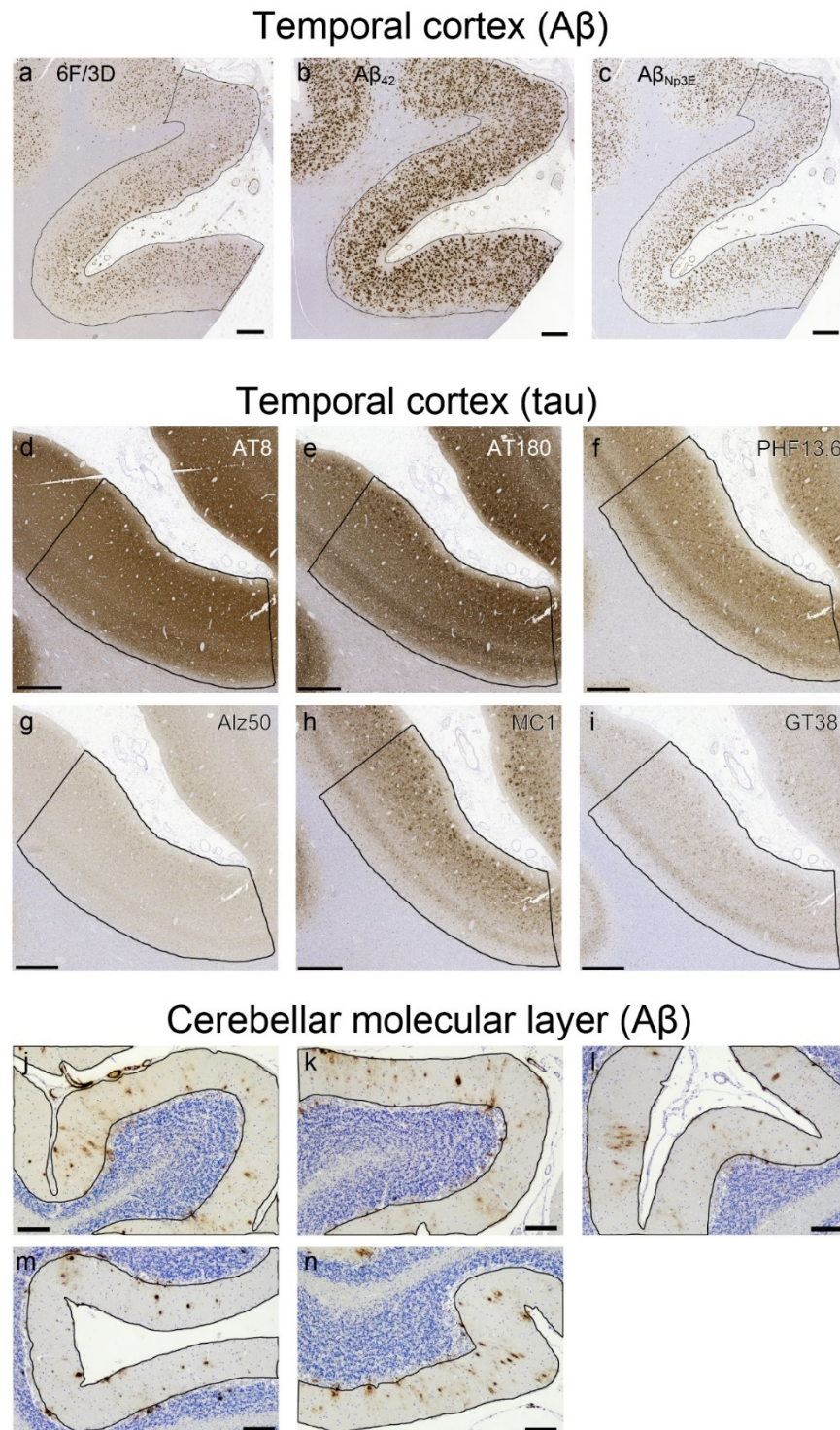
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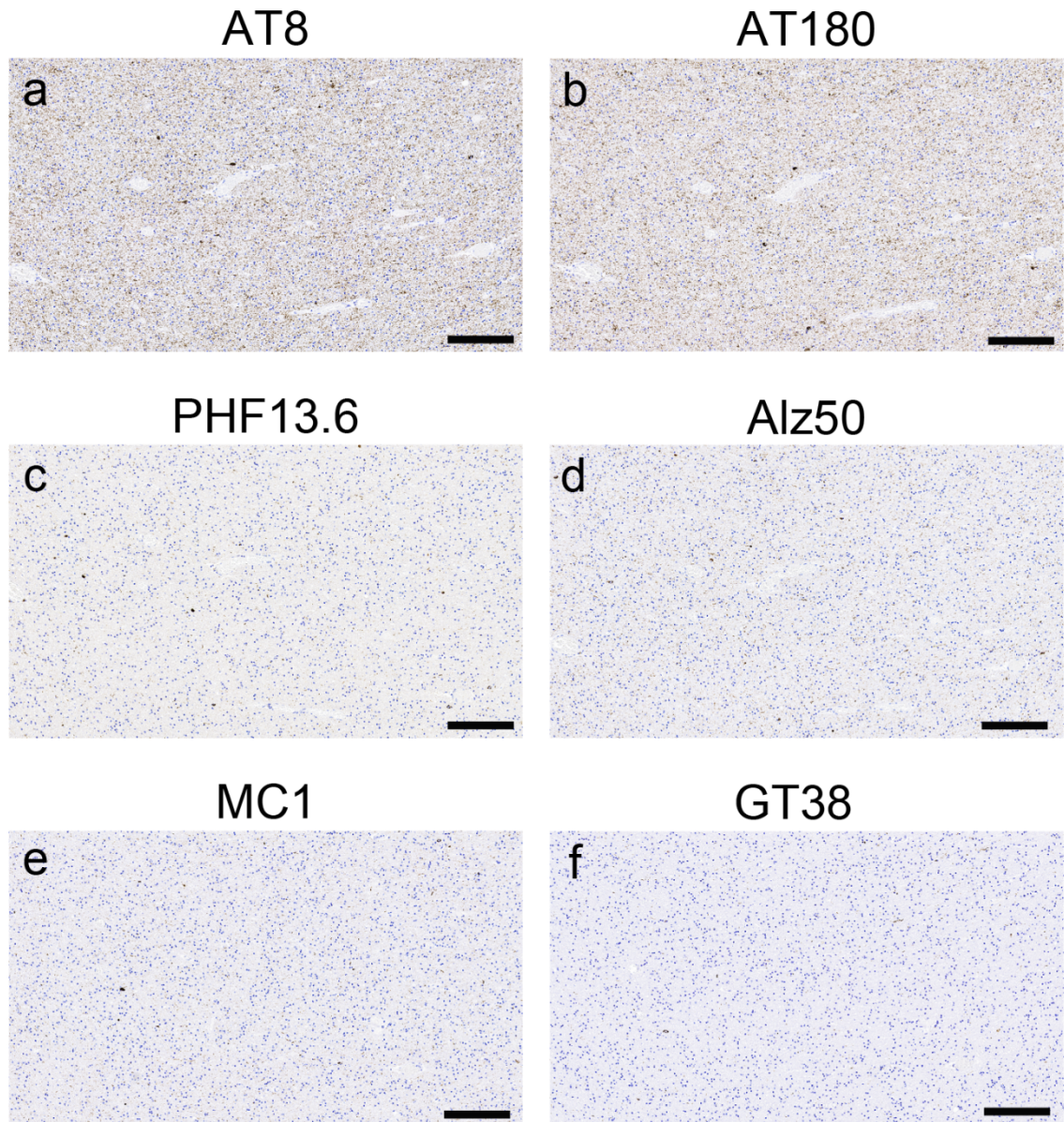
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Supplementary Figure S1. Representative microphotographs of the quantitative analysis areas in the neocortex and cerebellar molecular layer



(a–n) DS1. (j–n) Immunohistochemistry for pan-A β (6F/3D). In each image, the area surrounded by the black line is the region of interest. In the quantitative analysis of A β in the temporal cortex, we evaluated the cortex including the sulcal depth and gyral crests to evaluate all types of A β plaques. Scale bar = 1 mm (a–i), 200 μ m (j–n)

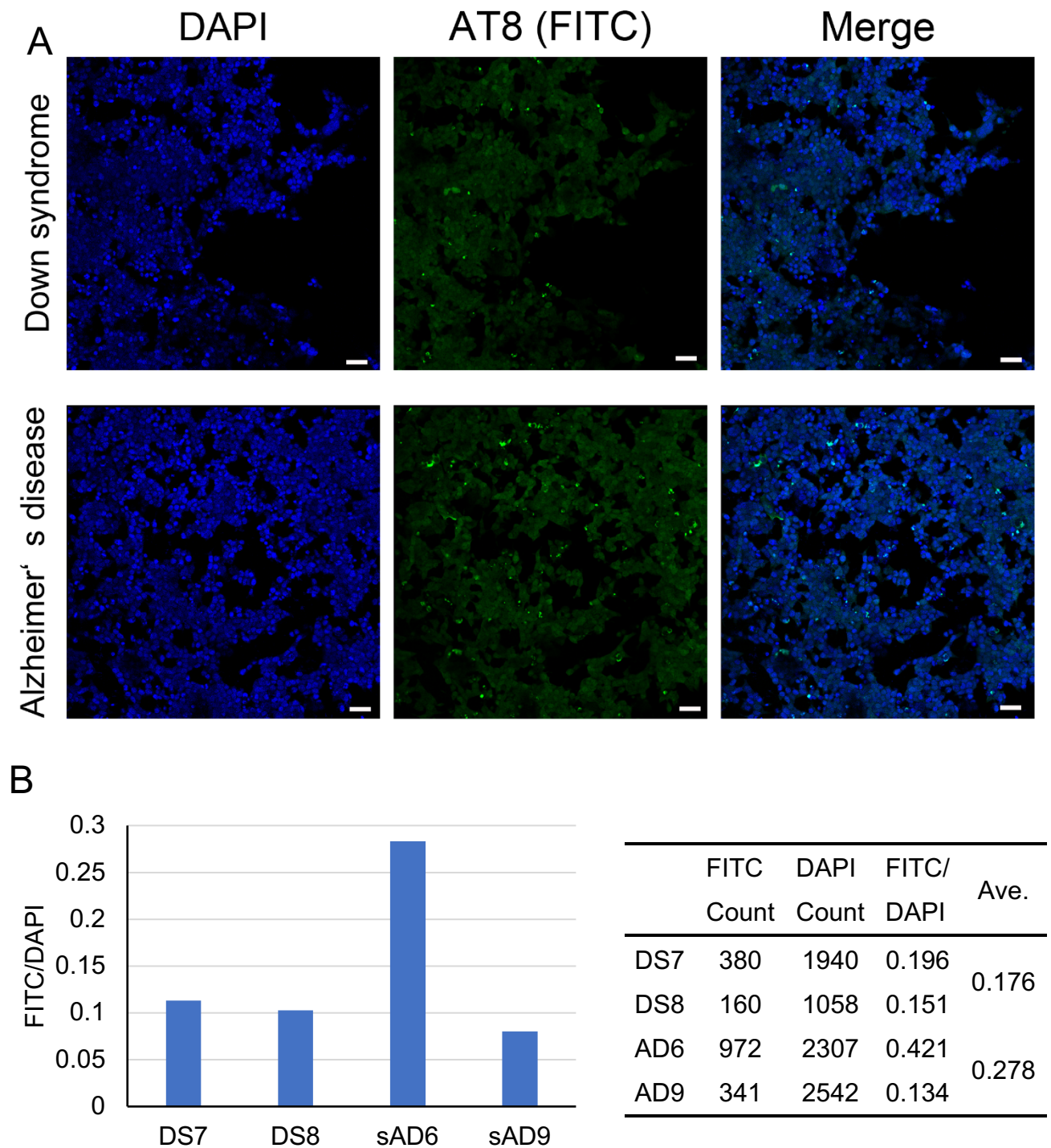
Supplementary Figure S2. Representative microphotographs of the quantitative analysis areas in the white matter.



(a–f) Same areas in DS1.

Scale bar = 200 μ m (a–f)

Supplementary Figure S3. Representative microphotographs and a summary of the results of tau seeding assay analysis



(A) Confocal images. (B) Summary of the results.

In the temporal cortex, both Down syndrome (DS) and sporadic Alzheimer's disease (sAD) cases show the seeding activity consistent with the Braak NFT stage (DS7/DS8, Braak NFT stage 6/5; sAD6/sAD9, Braak NFT stage 6/4). Scale bar = 50 μ m (A)

Supplementary Table S1. All results of quantitative analysis for A β

Case	Cerebrum (temporal cortex)						Cerebellum (molecular layer)					
	6F/3D		A β ₄₂		A β _{Np3E}		6F/3D		A β ₄₂		A β _{Np3E}	
	Ave- Size	P- Load	Ave- Size	P- Load	Ave- Size	P- Load	Ave- Size	P- Load	Ave- Size	P- Load	Ave- Size	P- Load
DS1	77.2	9.6	65.4	28.0	119.2	10.7	76.2	3.4	605.7	55.6	155.9	7.4
DS2	77.3	16.2	99.0	24.7	173.2	15.4	99.2	3.4	419.0	52.1	100.5	4.2
DS3	63.1	12.1	71.0	23.1	91.3	11.3	168.9	5.1	451.4	38.9	217.7	4.4
DS4	46.1	1.8	106.3	11.7	46.1	1.8	43.4	0.2	297.7	20.7	132.9	2.0
DS5	44.5	4.9	38.4	10.7	56.8	5.2	84.4	2.3	535.1	44.9	178.9	8.2
DS6	59.3	6.9	88.8	19.9	92.8	8.2	80.7	0.7	389.4	33.6	145.8	4.1
DS7	71.4	12.3	111.4	26.6	145.8	18.2	198.2	3.4	403.9	33.4	167.7	2.1
DS8	67.6	1.9	100.4	10.2	84.0	4.2	35.2	0.1	491.3	27.7	221.3	5.1
DS9	42.0	5.5	83.0	17.1	58.1	6.6	86.4	1.6	314.1	21.4	218.9	8.0
DS10	45.2	4.4	67.9	11.2	107.9	7.0	46.8	0.2	351.0	24.6	134.1	3.3
AD1	45.0	8.2	56.5	12.0	56.5	8.9	90.1	1.6	477.8	28.4	180.6	5.5
AD2	52.1	5.7	75.5	12.0	84.0	6.9	41.1	0.1	217.3	2.7	60.3	0.1
AD3	47.2	4.8	60.0	7.9	67.0	6.0	119.2	0.4	253.2	1.6	199.1	0.8
AD4	41.2	4.2	65.3	9.4	61.2	5.3	82.5	0.5	505.6	5.7	315.8	2.4
AD5	35.8	6.6	47.0	10.5	35.7	6.6	N/E	N/E	N/E	N/E	N/E	N/E
AD6	27.0	5.3	28.2	5.0	45.3	10.1	N/E	N/E	N/E	N/E	N/E	N/E
AD7	25.0	4.3	28.6	6.9	25.5	3.7	62.3	0.1	400.7	9.5	42.9	0.2
AD8	24.0	2.1	43.5	8.3	40.6	4.6	N/E	N/E	N/E	N/E	N/E	N/E
AD9	55.0	3.2	71.6	4.5	124.8	4.0	167.0	3.4	252.0	7.0	216.3	5.1
AD10	15.6	2.6	29.2	6.1	30.6	5.2	48.1	0.1	368.2	6.3	137.7	1.1

Abbreviations: AD, Alzheimer's disease; Ave, average; DS, Down syndrome; *N/E, not evaluated; P, plaque

* N/E means that we did not evaluate the A β burden in this case because the case did not show 6F/3D or A β ₄₂ or A β _{Np3E} deposition in the molecular layer.

Supplementary Table S2. All results of quantitative analysis for tau

Case	AT8		AT180		PHF13.6		Alz50		MC1		GT38	
	Cx	WM	Cx	WM	Cx	WM*	Cx	WM	Cx	WM	Cx	WM*
DS1	76.7	10.9	70.7	10.1	45.6	1.9	12.6	2.6	30.6	1.6	8.6	0.3
DS2	48.0	8.0	38.3	8.9	14.5	3.6	3.8	1.2	1.3	0.7	0.1	0.0
DS3	74.1	5.8	70.0	4.8	43.2	1.4	6.2	1.6	6.4	0.6	6.3	0.1
DS4	16.9	1.0	12.4	0.9	1.0	7.3	1.3	0.3	0.4	0.2	0.0	0.1
DS5	44.0	3.6	58.9	5.0	20.6	5.3	3.2	0.9	1.0	0.3	5.3	0.1
DS6	74.9	4.1	73.9	4.1	24.5	6.5	5.8	0.9	4.6	0.2	0.9	0.2
DS7	57.9	6.8	53.5	6.6	2.9	11.8	2.8	1.0	2.1	0.4	0.2	0.1
DS8	37.9	5.0	32.5	4.4	0.9	14.5	2.0	0.8	0.9	0.6	0.1	0.9
DS9	77.0	5.5	66.9	5.0	36.6	2.6	9.1	0.9	8.4	0.2	6.3	0.1
DS10	61.3	9.5	56.6	8.4	26.8	13.1	10.1	1.6	7.1	0.6	3.5	0.1
AD1	52.5	3.4	45.9	2.8	21.4	1.4	4.8	1.2	1.4	0.6	0.6	0.3
AD2	52.9	2.2	46.9	2.8	24.2	5.5	3.3	0.4	6.3	0.5	0.7	0.7
AD3	43.7	4.6	36.5	4.0	19.4	2.4	3.3	0.9	2.9	0.8	0.1	0.0
AD4	47.9	3.0	37.5	2.7	11.2	9.5	1.9	0.5	0.6	0.3	0.4	0.2
AD5	65.2	2.9	56.2	3.2	38.7	1.1	6.2	0.8	2.2	0.2	2.4	0.2
AD6	32.7	2.6	22.7	1.8	12.5	0.6	6.0	0.8	1.8	0.3	0.6	0.0
AD7	58.5	1.0	52.8	0.9	20.6	0.2	7.3	0.4	4.3	0.2	2.2	0.0
AD8	47.1	1.5	42.9	1.4	21.7	1.6	1.1	0.5	0.2	0.2	0.9	0.2
AD9	15.3	0.5	13.7	0.6	0.2	9.7	1.0	0.1	0.4	0.2	0.0	3.7
AD10 [†]	42.3	0.6	46.2	1.1	3.3	9.2	2.2	0.1	0.3	0.1	2.2	0.3

Abbreviations: AD, Alzheimer's disease; Cx, cortex; DS, Down syndrome; WM, white matter

* Data shown in grey are abnormally high compared to the bright-field observation, which may be due to nonspecific immunoreactivity in the background. These data were excluded from the statistical analysis in this study (GT38). Regarding the results of PHF13.6 in the WM, we did not statistically evaluate them because half of the results were abnormally high.

[†] The results of the tau deposition burden obtained from AD10 were excluded from the statistical analysis of tau pathology.