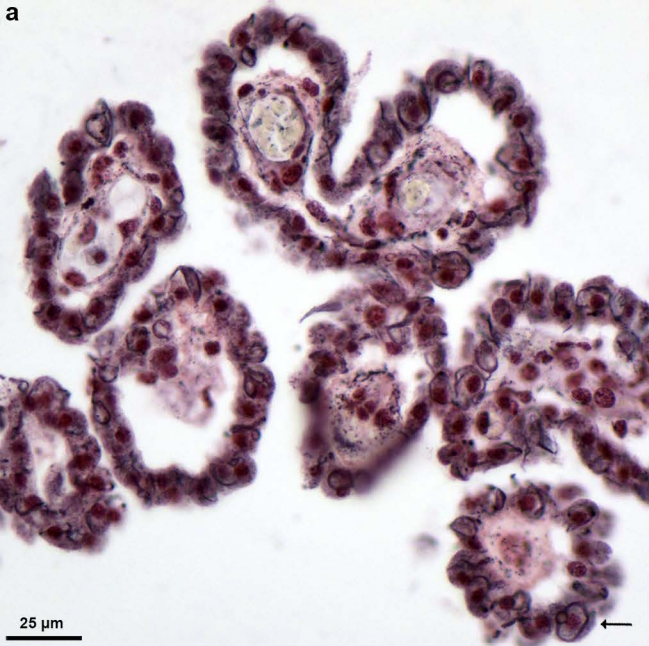
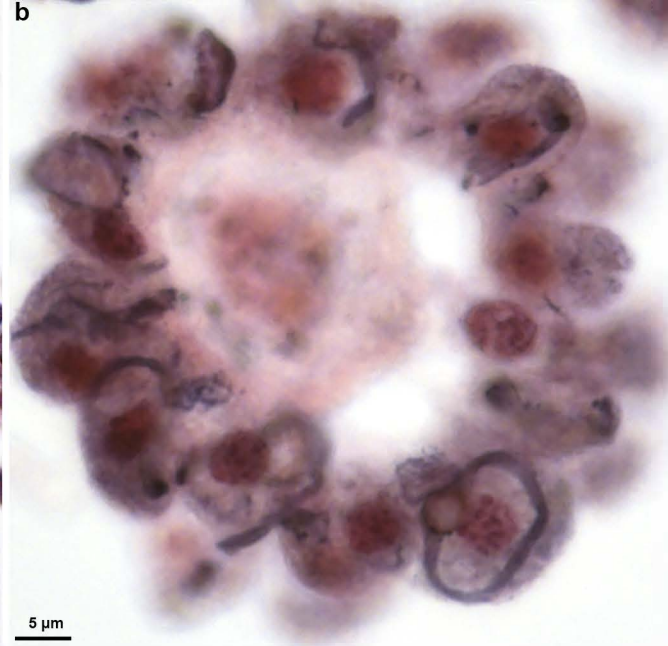
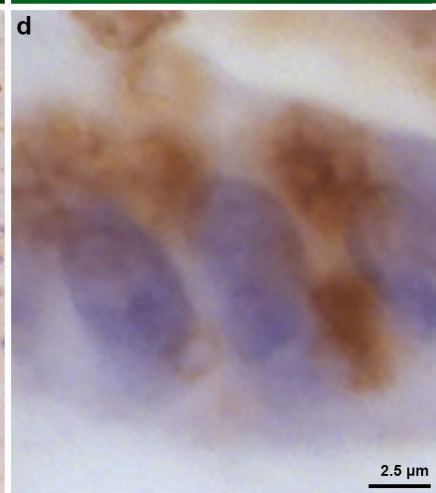
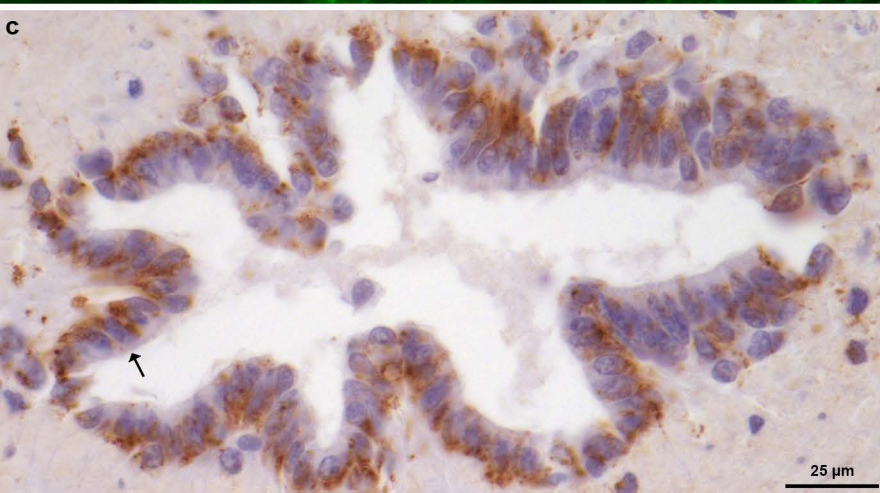
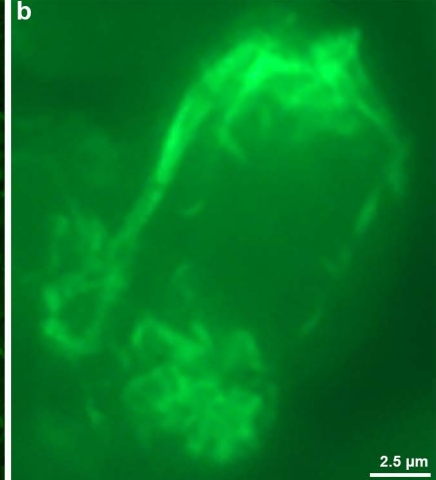
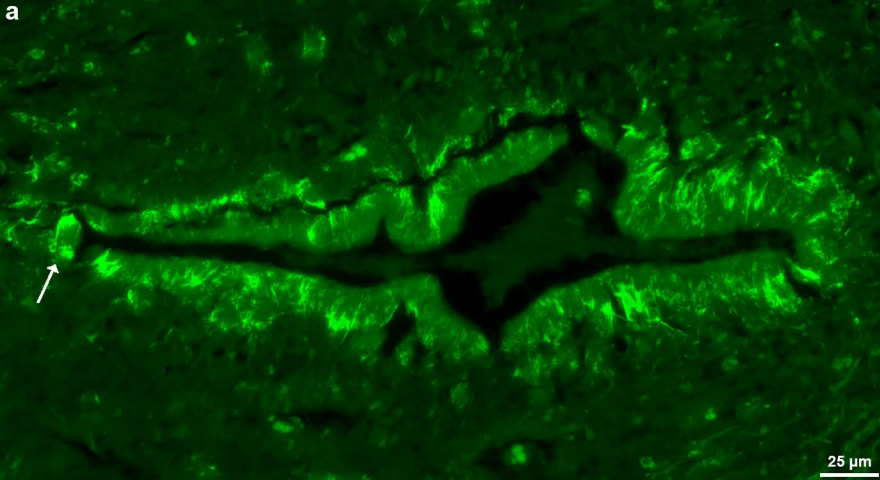


Supplementary Table 1. Cryo-EM data collection, refinement and validation statistics

	Case 3 Ependyma and Subependymal Tissue	Case 3 Ependyma and Subependymal Tissue	Case 14 Choroid plexus	Case 20 Choroid plexus
Data collection				
Magnification	96,000	96,000	96,000	96,000
Voltage (kV)	300	300	300	300
Detector	Falcon-4	Falcon-4	Falcon-4	Falcon-4
Electron dose (e-/Å ²)	30.0	30.0	30.0	30.0
Defocus range (µm)	1.7-2.4	1.7-2.4	1.7-2.4	1.7-2.4
Pixel size (Å)	0.824	0.824	0.824	0.824
Initial particle images (no.)	39,057	61,188	23,157	685,561
	TMEM106B	PHF	TMEM106B	TMEM106B
Processing				
Symmetry imposed	C1	2 ₁	C1	C1
Final particle images (no.)	5,990	30,897	10,971	38,763
Map resolution (Å)	3.36	3.04	3.58	2.64
FSC threshold = 0.143				
Helical rise (Å)	4.80	2.39	4.81	4.88
Helical twist (°)	-0.46	179.43	-0.49	-0.46
				Case 20
Model Refinement				
Initial model used (PDB)				7QVC
Model resolution (Å)				2.53
FSC threshold = 0.5				
Map sharpening <i>B</i> factor (Å ²)				-36.7
Model composition				
Non-hydrogen atoms				4,568
Protein residues				540
Ligands				16
<i>B</i> factors (Å ²)				
Protein				44.8
R.m.s. deviations				
Bond lengths (Å)				0.0066
Bond angles (°)				1.320
Validation				
MolProbity score				1.58
Clashscore				3.52
Poor rotamers (%)				0.00
Ramachandran plot				
Favored (%)				93.23
Allowed (%)				6.77
Disallowed (%)				0.00
PDB				9FNB
EMDB				EMD-50587

PHF = paired helical filaments; FSC = Fourier shell correlation; PDB = protein data bank; EMDB = electron microscopy data bank;

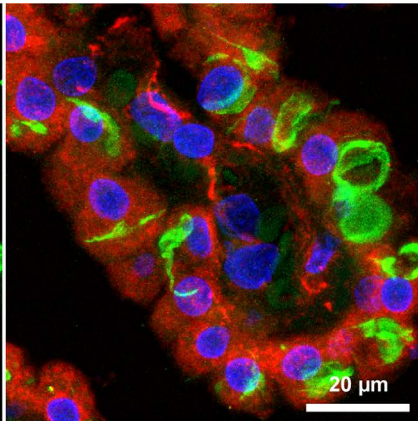
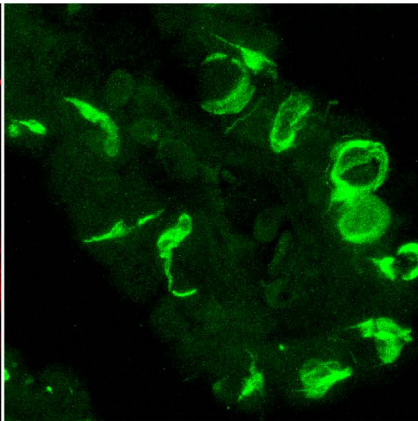
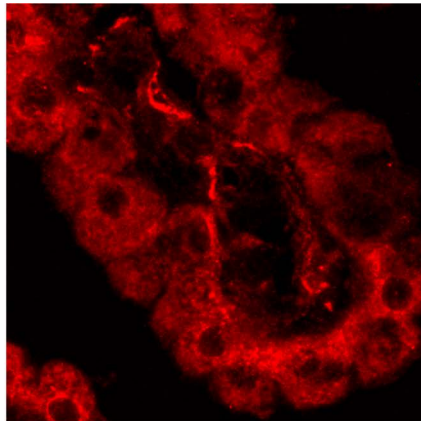
a**b**



A303-439A

pFTAA

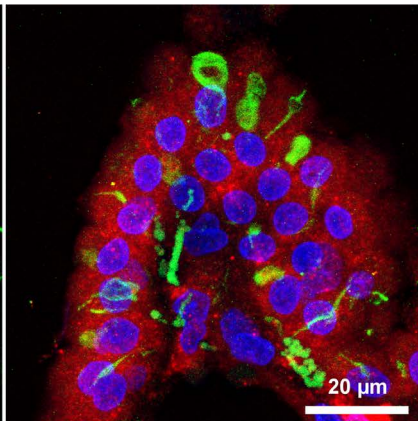
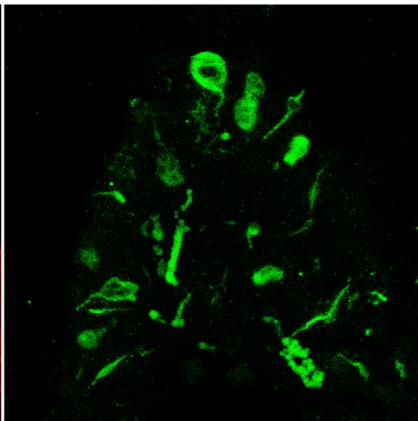
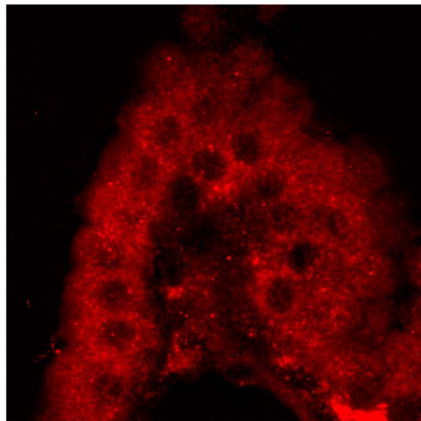
Hoechst Merged

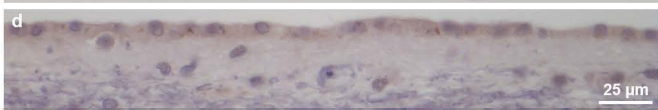
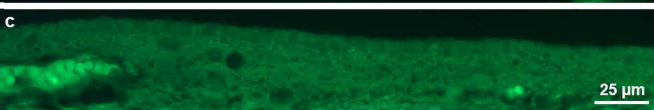
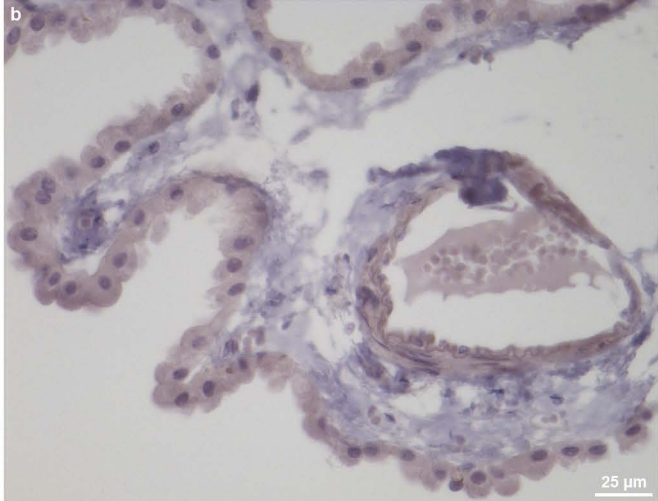
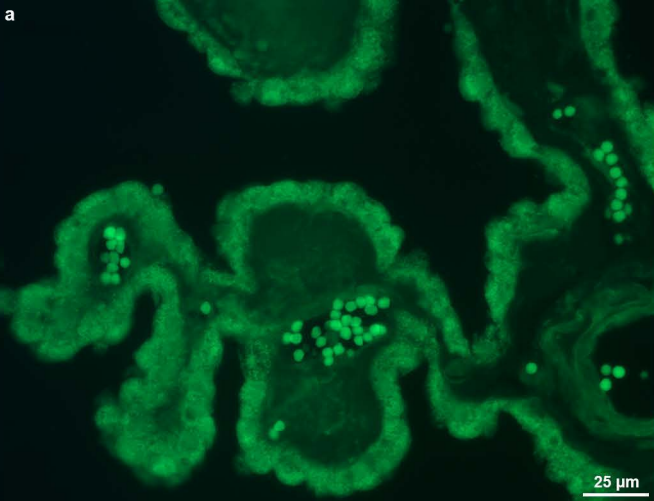


TMEM263

pFTAA

Hoechst Merged



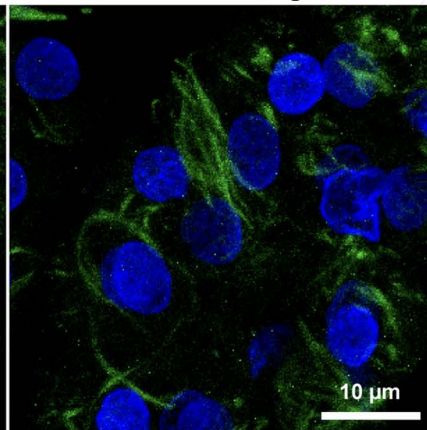
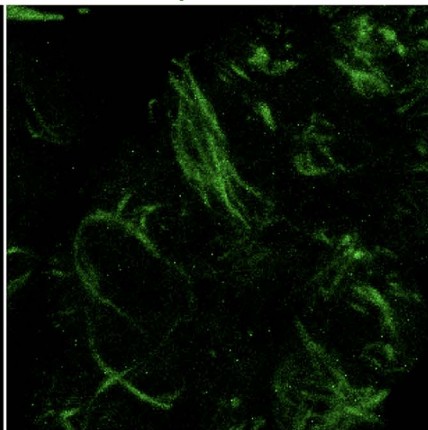


**No Primary Ab
Alexa Fluor 647**

pFTAA

Hoechst Merged

a



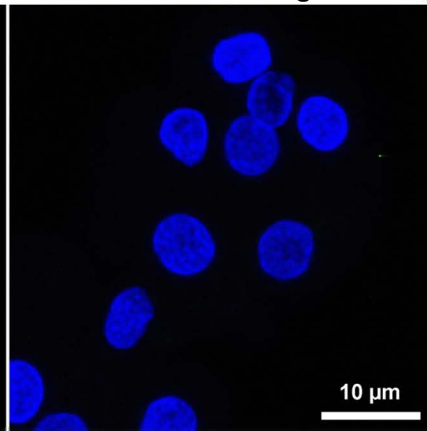
10 μm

**No Primary Ab
Alexa Fluor 568**

**No Primary Ab
Alexa Fluor 488**

Hoechst Merged

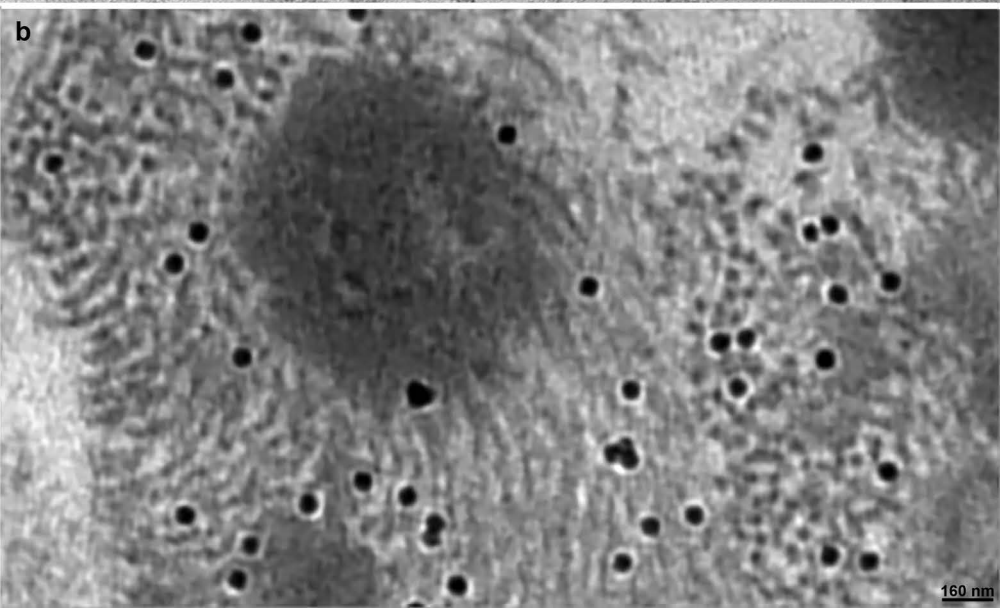
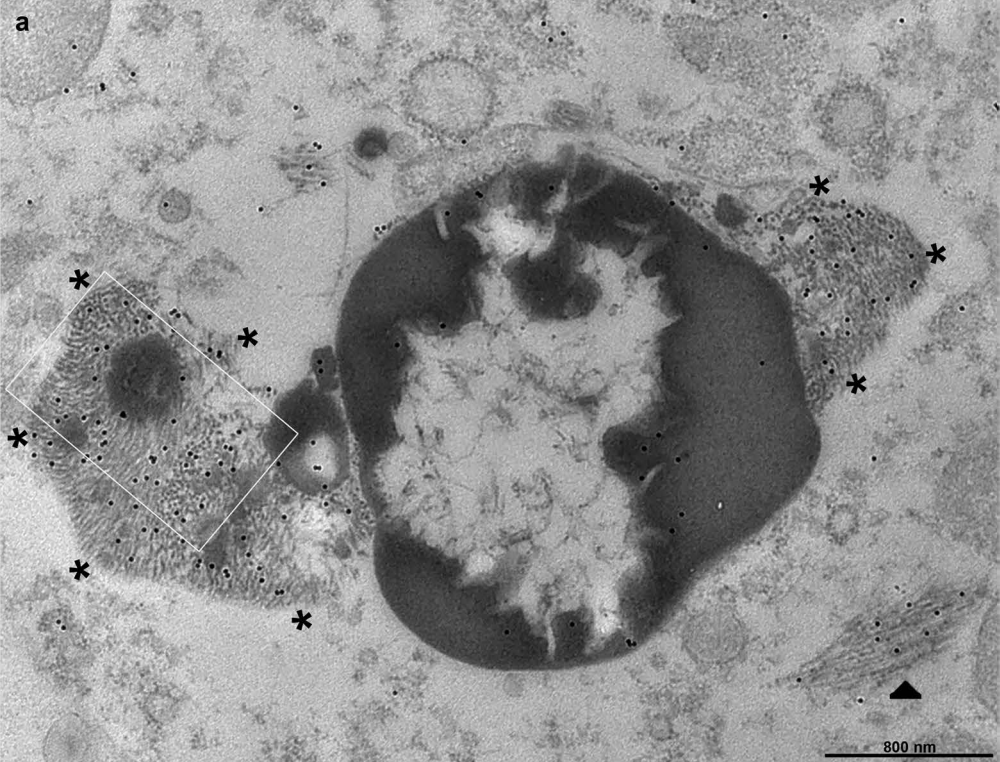
b

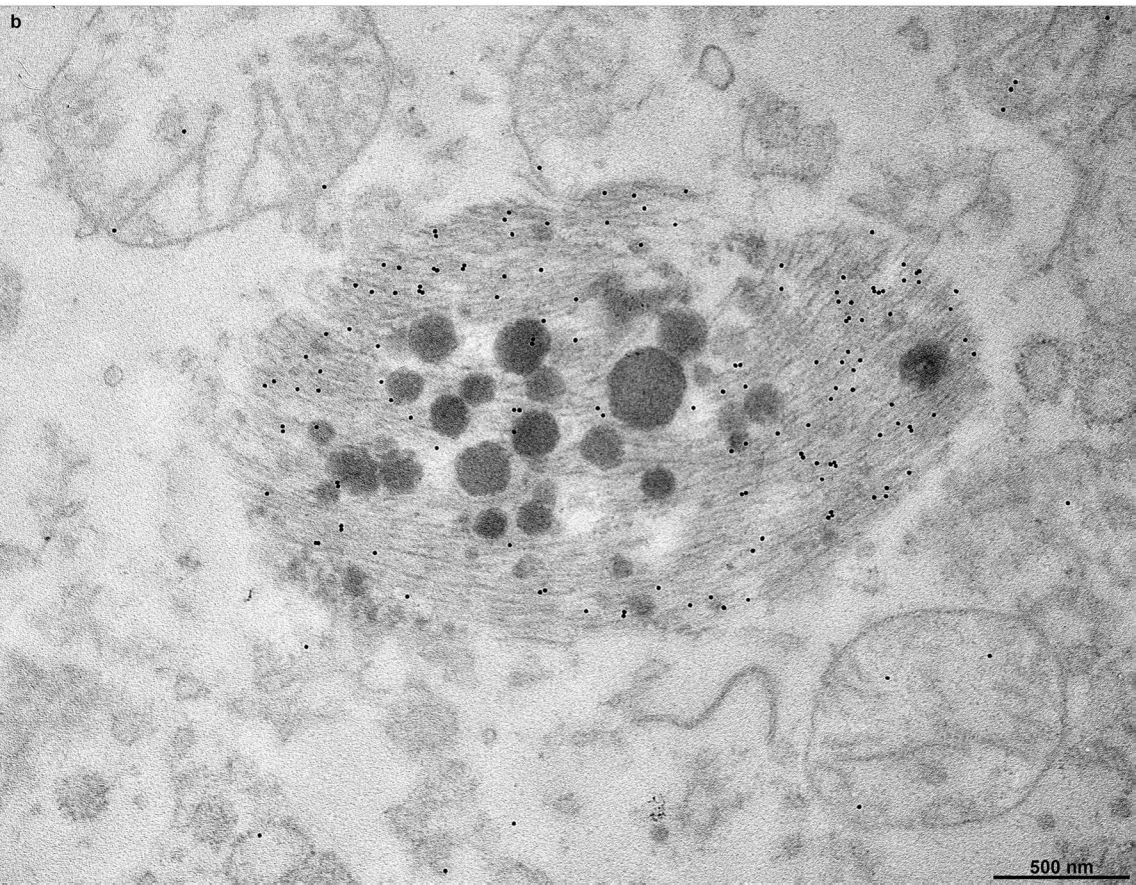
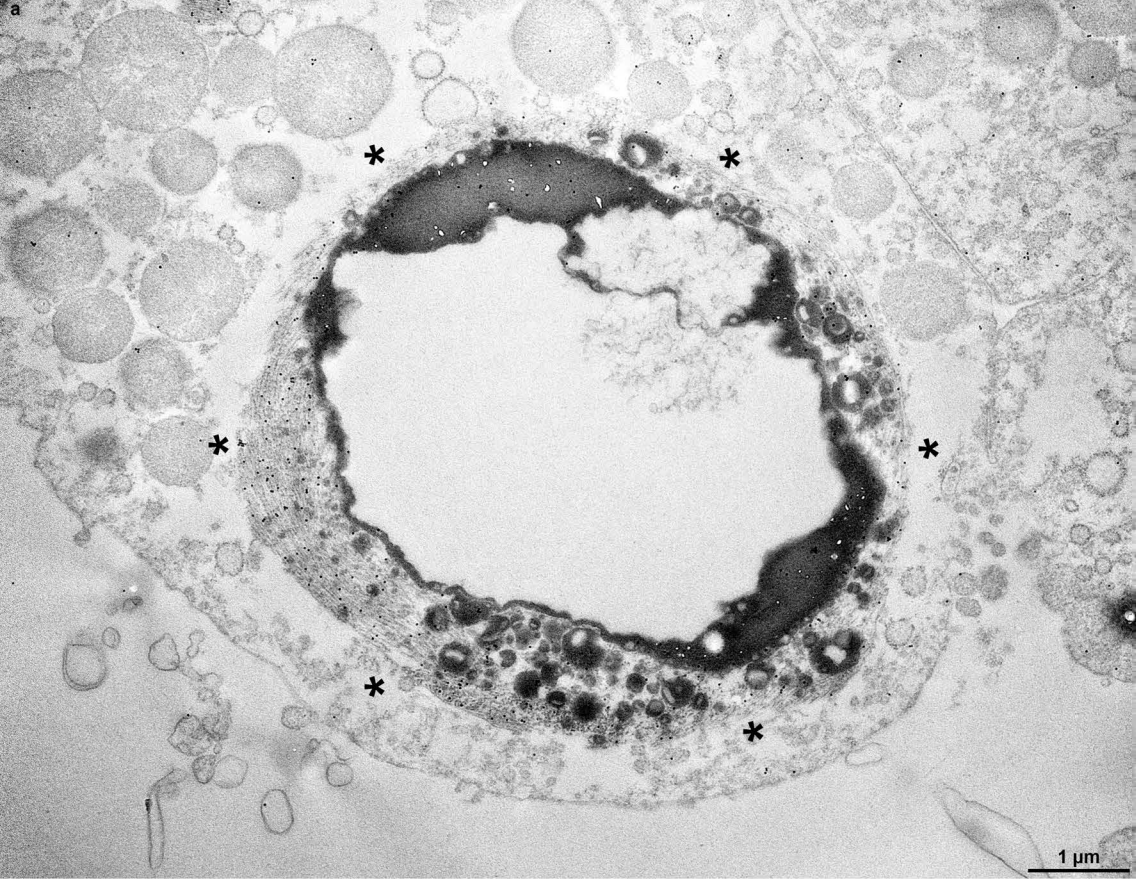


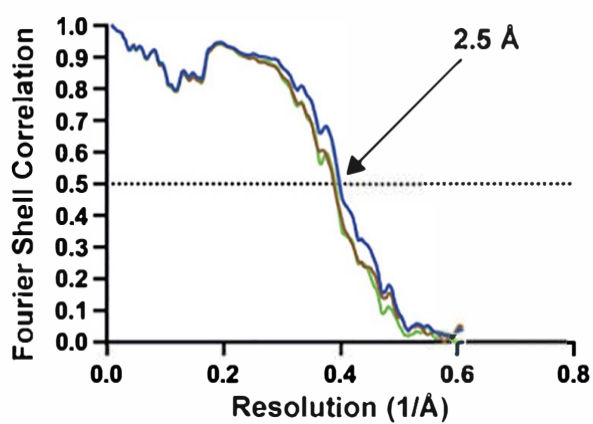
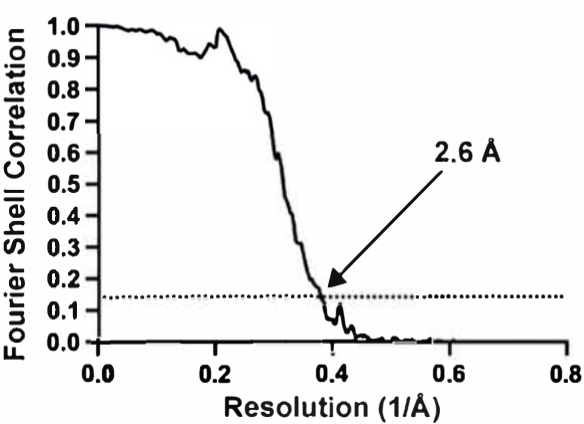
10 μm



1 μ m







1 Supplementary Figure Legends

2 Supplementary Figure 1

3 Histopathology of Biondi bodies with Bodian silver

4 Choroid plexuses from case 2.

5 a, b, Numerous argyrophilic Biondi bodies in the cytoplasm of ependymal
6 cells are seen in Bodian silver preparations. Enlargement of ependymal
7 cells (b) shows multiple shapes of Biondi bodies including one in the form
8 of a ring pointed to by an arrow in a. Scale bar, 25 μm (a) and 5 μm (b).

9

10 Supplementary Figure 2

11 Histopathology of Biondi bodies in the central canal of the spinal cord
12 using Thioflavin S and antibody TMEM239

13 Spinal cord from case 4.

14 a, b, Ependymal cells lining the central canal of the spinal cord were
15 stained with Thioflavin S. Numerous fluorescent Biondi bodies can be
16 seen. High magnification of fluorescent inclusions in b that are denoted by
17 an arrow in a. Scale bar, 25 μm (a) and 2.5 μm (b).

18 c, d, Ependymal cells lining the central canal of the spinal cord were
19 stained with antibody TMEM239. Numerous immunoreactive Biondi bodies
20 are seen. High magnification of TMEM239 immunopositive inclusions in d
21 that are denoted by an arrow in c. Scale bar, 25 μm (c) and 2.5 μm (d).

22

23

24

25 Supplementary Figure 3

26 Double-labelling of choroid plexuses with Biondi bodies using anti-
27 TMEM106B antibodies (A0303-439A and TMEM263) and amyloid dye
28 pFTAA

29 Choroid plexuses from cases 9 and 10.

30 The panels on the left show single-labelling immunofluorescence of the
31 choroid plexuses by antibody A303-439A (red) or antibody TMEM263
32 (red); the panels in the middle show single-labelling fluorescence of
33 Biondi bodies by pFTAA (green); the panels on the right show double-
34 labelling of choroid plexuses by A303-439A and pFTAA or TMEM263 and
35 pFTAA. Cell nuclei are labelled using Hoechst dye (blue). No co-labelling
36 of A303-439A or TMEM263 and pFTAA was observed. Scale bar, 20 μm .

37

38 Supplementary Figure 4

39 Choroid plexuses and ependymal cells lining the lateral ventricle that are
40 devoid of Biondi bodies

41 Choroid plexuses and ependymal cells lining the lateral ventricle of case
42 24.

43 a, The ependymal cells do not contain Biondi bodies; they show no
44 specific fluorescence in Thioflavin S preparations (a,c) and are
45 immunonegative for antibody TMEM239 (b,d). Scale bar, 25 μm .

46

47

48

49 Supplementary Figure 5

50 Negative controls for immunofluorescence of choroid plexuses with Biondi
51 bodies

52 Choroid plexuses from case 22. When anti-TMEM106B antibody TMEM239
53 was omitted and only Alexa Fluor conjugated secondaries (488, 568, or
54 647) were used, no specific signal was detected. pFTAA staining was
55 performed to confirm the presence of Biondi bodies. Nuclei were labelled
56 using Hoechst dye (blue). Scale bar, 10 μm .

57

58 Supplementary Figure 6

59 Immunoelectron microscopy of a Biondi body

60 Choroid plexuses from case 8 and anti-TMEM106B antibody TMEM239.

61 The cytoplasm of an ependymal cell shows a round body made of
62 osmiophilic material intimately related to a bundle of filaments decorated
63 by gold particles and reminiscent of the shape of a phrygian cap (outlined
64 by asterisks). The osmiophilic body has the appearance of a secondary
65 lysosome or a residual body. The nucleus of the cell and mitochondria are
66 seen around the inclusion. Scale bar, 1 μm .

67

68 Supplementary Figure 7

69 Immunoelectron microscopy of a Biondi body

70 Choroid plexuses from case 11 and anti-TMEM106B antibody TMEM239.

71 a, The cytoplasm of an ependymal cell contains bundles of filaments that
72 are decorated by gold particles. Two large bundles (outlined by asterisks)

73 are seen in association with a large, round dense osmiophilic structure.
74 Within this structure, an electron-lucent area can also be seen. A smaller
75 bundle of filaments decorated by gold particles is present in the lower
76 part of the picture (arrowhead). Scale bar, 800 nm.

77 b, Higher magnification of the filament bundle (denoted by the box in a)
78 decorated by gold particles. Scale bar, 160 nm.

79

80 Supplementary Figure 8

81 Immunoelectron microscopy of a Biondi body

82 Choroid plexuses from case 11.

83 a, Biondi body consisting of a ring of filaments (outlined by asterisks)
84 decorated by gold particles surrounding a large round osmiophilic and
85 electron-lucent inclusion. Mitochondria are seen in the vicinity. Scale bar,
86 1 μm .

87 b, A bundle of filaments, decorated by gold particles, is intermixed with
88 round osmiophilic bodies and is adjacent to mitochondria. Scale bar, 1
89 μm .

90

91 Supplementary Figure 9

92 Fourier shell correlation curves and resolution estimates

93 Solvent-corrected Fourier shell correlation (FSC) curves of cryo-EM half
94 maps (left panels) and model-to-map validation (right panels) for the

95 TMEM106B fold I Biondi variant from case 20 (Table 2). FSC curve

96 between a model refined in half-map 1 and half-map 2 is shown in brown

- 97 (model 1 versus half-map 1) and FSC curve between the same model and
- 98 half map 2 is shown in green (model 1 versus half-map 2).