

Analyte	Skogholt's disease Median (IQR)	Controls Median (IQR)	<i>p</i>	Ratio of medians	Source
	N=11	N=14			
CSF-Total protein g/L	1.57 (1.34–1.83)	0.36 (0.32–0.53)	<.001	3.5	(a)
CSF-Albumin mg/L	982 (830–1173)	238 (190–368)	<.001	3.4	(a)
CSF/S-Albumin ratio	25.8 (17.7–28.4)	6.4 (4.6–9)	<.001	3.3	(a)
	N=7	N=11			
CSF p-Tau pg/mL	464 (346–476)	36.5 (27.2–49.5)	<0.001	12.7	(b)
CSF t-Tau pg/mL	3160 (2814–3562)	342 (236–397)	<0.001	9.23	(b)
CSF Aβ1–42 pg/mL	1464 (950–1718)	921 (721–1068)	0.079	1.59	(b)
CSF Aβ1–40 pg/mL	38,528 (29,796–40,531)	10,614 (8788–12,940)	<0.001	3.63	(b)
CSF Aβx–38 pg/mL	5359 (5211–5829)	1628 (1370–2302)	<0.001	3.29	(b)
CSF Aβx–40 pg/mL	13106 (10829– 14016)	4326 (3820–4901)	<0.001	3.03	(b)
CSF Aβx–42 pg/mL	558 (340–663)	307 (266–361)	0.031	1.82	(b)
CSF Aβ1–42/1–40	0.034–0.0485	0.0885–0.0963	0.022	0.46	(b)
CSF GFAP pg/mL	52,373 (45,109–56,718)	16,974 (9830–22,089)	<0.001	3.09	(b)
CSF NfL pg/mL	4210 (2851–8818)	1200 (881–4027)	0.046	3.51	(b)
CSF PDGFRβ pg/mL	1936 (1752–2051)	410 (316–523)	<0.001	4.72	(b)
CSF βTP μg/mL	108 (107–120)	16 (15–18.8)	<0.001	6.75	(b)
	N=11	N=14			
Plasma t-Tau pg/mL	33.2 (28.7–39.2)	39.3 (24.6–47.7)	0.536	0.844	(b)
Plasma GFAP pg/mL	56.8 (35–81.2)	82 (68.6–153)	0.033	0.693	(b)
Plasma NfL pg/mL	9.49 (8.46–15.7)	30.1 (14.3–61.2)	0.025	0.316	(b)
Plasma Aβ40 pg/mL	92 (89–101)	94.6 (89.2–123)	0.647	0.973	(b)
Plasma Aβ42 pg/mL	6.47 (6.18–7.03)	6.97 (6.3–7.3)	0.501	0.928	(b)
Plasma pTau181 pg/mL	7.33 (5.92–9.34)	5.85 (5.45–10.8)	0.687	1.250	(b)
Plasma Aβ42/Aβ40	0.0705 (0.063–0.0761)	0.069 (0.0626–0.0766)	0.851	1.020	(b)

Supplementary Table S7. CSF and plasma biomarker concentrations in Skogholt's disease and control groups, as reported in (a) Aspli et al., 2022,¹ and (b) Aspli et al., 2023.² Values are shown as median (IQR), with *p*-values from Mann–Whitney U tests. Ratios reflect Skogholt/control group differences. Mean (SD) values with statistical comparisons are reported in the original publications.

1. Aspli KT, Holmøy T, Flaten TP, Whist JE, Aaseth JO. Skogholt's disease-A tauopathy precipitated by iron and copper? *J Trace Elem Med Biol.* 2022;70:126915. doi:10.1016/j.jtemb.2021.126915
2. Aspli KT, Aaseth JO, Holmøy T, et al. CSF, Blood, and MRI Biomarkers in Skogholt's Disease—A Rare Neurodegenerative Disease in a Norwegian Kindred. *Brain Sciences.* 2023;13(11):11. doi:10.3390/brainsci13111511

Trace metal	ATP-Dependent Transport at the ChP	CSF Change	CSF		Plasma	
			Skogholt's disease	Controls	Skogholt's disease	Controls
Copper (Cu)	Yes, export	↑	69.3 ± 7.7	21.7 ± 2.0	477 ± 23	478 ± 37
Iron (Fe)			106.2 ± 11.8	30.5 ± 9.7	440 ± 57	458 ± 36
Selenium (Se)			8.75 ± 1.21	2.48 ± 0.21	42.9 ± 2.3	41.1 ± 2.2
Zinc (Zn)			42.0 ± 4.4	24.6 ± 2.5	333 ± 17	342 ± 15
Manganese (Mn)	Yes, import	↓	0.79 ± 0.17	1.32 ± 0.14	2.7 ± 0.20	3.09 ± 0.35
Thallium (Tl)			0.046 ± 0.002	0.077 ± 0.005	0.008 ± .001	0.007 ± .001
Lead (Pb)	No	↔	0.28 ± 0.09	0.59 ± 0.07	0.51 ± 0.09	0.93 ± 0.21
Strontium (Sr)			15.4 ± 1.3	15.9 ± 1.4	11.1 ± 0.7	11.7 ± 1.0

Supplementary Table S8. Trace metal concentrations in CSF and plasma of patients with Skogholt's disease and controls.

CSF and plasma concentrations of selected trace elements in individuals with Skogholt's disease and matched controls, reanalyzed from Gellein et al.¹ Elements were selected based on known or hypothesized ATP-dependent transport at the choroid plexus. The table includes metals with ATP-dependent export (Cu, Fe, Se, Zn), ATP-dependent import (Mn, Tl), and two comparators lacking defined active transport mechanisms (Pb, Sr). "CSF Change" indicates the direction of between-group difference. All values in µg/L. These eight elements were prioritized for analysis based on mechanistic relevance and are the only ones discussed in the main text. Values significantly different from controls are indicated in bold. This selective, bidirectional pattern—retention of exported metals and depletion of imported ones—cannot be explained by barrier leak or diffusion stasis. It instead reflects transport-specific failure shaped by local ATP availability, reinforcing the model of mitochondrial ChP dysfunction.

1. Gellein K, Skogholt JH, Aaseth J, et al. Trace elements in cerebrospinal fluid and blood from patients with a rare progressive central and peripheral demyelinating disease. *J Neurol Sci.* 2008;266(1-2):70-78. doi:10.1016/j.jns.2007.08.042