

Supplementary Information for

**Autoantibodies against CNS Antigens in a Subset of B Cell-Dominant Multiple Sclerosis Patients**

Stefanie Kuerten<sup>a,1,2</sup>, Tobias V. Lanz<sup>b,c,d,1,2</sup>, Nithya Lingampalli<sup>b,c</sup>, Lauren J. Lahey<sup>b,c</sup>, Christoph Kleinschnitz<sup>e</sup>, Mathias Mäurer<sup>f</sup>, Michael Schroeter<sup>g</sup>, Stefan Braune<sup>h</sup>, Tjalf Ziemssen<sup>i</sup>, Peggy P. Hoj, William H. Robinson<sup>b,c,3</sup>, Lawrence Steinman<sup>j,2,3</sup>

Paste Lawrence Steinman  
Email: [steinman@stanford.edu](mailto:steinman@stanford.edu)

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Supernatants  
ELISpot-neg vs. ELISpot-pos

overlap

Supernatants  
HC / OND vs. ELISpot-pos

AQP4 221-240	AQP4 61-80	ADCYAP1 27
CRYAB 91-110	AQP4 71-90	ADCYAP1 38
mMAG 97-112	AQP4 91-110	AQP4 1-20
MOBP 141-160	CRYAB 1-20	AQP4 11-30
NEFL	CRYAB 21-40	AQP4 231-250
OSP 161-180	CRYAB 71-91	BDNF
OSP 21-40	MBP	CNP 343-362
OSP 31-50	MBP 130-151	CRYAB 141-161
PLP 1-20	MBP 71-90	CRYAB 81-100
PLP 131-150	MBP 81-100	GFAP
PLP 211-230	MOBP 21-40	MBP 110-131
PLP 241-260	MOBP 61-80	MBP 160-181
PLP 89-106 acet	MOG 101-120	MBP 91-110
PRP	MOG 91-110	mMAG 121-136
PRPH	NEFH	MOBP 51-70
TRPV1	OSP 121-140	MOBP 71-90
	OSP 131-150	MOBP 81-100
	OSP 181-200	MOG 21-40
	OSP 51-70	MOG 61-80
	P0-MaIE	Neuropeptide K
	PLP 11-30	OSP 101-120
	PLP 141-160	OSP 11-30
	PLP 151-170	OSP 151-170
	PLP 161-180	OSP 171-190
	PLP 171-190	OSP 191-210
	PLP 181-200	PLP 21-40
	PLP 191-210	PLP 261-277
	PLP 231-250	PLP 41-60
	PLP 251-270	PLP 51-70
	PLP 61-80	PLP 91-110
	PLP 71-90	
	PMP2 2	
	S100B	
	SCN3A Cter	
	SCN8A Cter	
	SCN8A L1	
	SCN8A L3	
	SCN8A Nter	
	SNCG	
	TAU	
	TUBB3	

**Supplementary Figure S1: Comparison of IgG reactivity in B cell supernatants.** Venn diagram showing the names of significant antigens in the comparisons “ELISpot-neg vs. ELISpot-pos (supernatants)” (orange) and “HC/OND vs. ELISpot-pos (supernatants)” (green), corresponding to Fig. 2B.

Supernatants ELISpot-neg vs. ELISpot-pos	overlap	Plasma HC / OND vs. MS
AQP4 61-80	AQP4 221-240	AQP4 101-120
AQP4 91-110	AQP4 71-90	AQP4 11-30
CRYAB 1-20	CRYAB 21-40	AQP4 111-130
MBP	CRYAB 71-91	AQP4 121-140
MBP 130-151	CRYAB 91-110	AQP4 131-150
MBP 71-90	mMAG 97-112	AQP4 141-160
MBP 81-100	PLP 1-20	AQP4 151-170
MOBP 141-160	PLP 171-190	AQP4 171-190
MOBP 21-40	PLP 211-230	AQP4 181-200
MOBP 61-80		AQP4 191-210
MOG 101-120		AQP4 201-220
MOG 91-110		AQP4 21-40
NEFH		AQP4 231-250
NEFL		AQP4 261-280
OSP 121-140		AQP4 271-290
OSP 131-150		AQP4 281-300
OSP 161-180		AQP4 291-310
OSP 181-200		AQP4 301-320
OSP 21-40		AQP4 31-50
OSP 31-50		AQP4 41-60
OSP 51-70		AQP4 51-70
PO-MaIE		AQP4 prot 1
PLP 11-30		AQP4 prot 2
PLP 131-150		Bov ChromograninA
PLP 141-160		CNP prot
PLP 151-170		CNPase 356-375
PLP 161-180		CNPase 369-388
PLP 181-200		CRYAB 131-151
PLP 191-210		CRYAB 31-50
PLP 231-250		CRYAB 41-60
PLP 241-260		CRYAB 51-70
PLP 251-270		CRYAB 81-100
PLP 61-80		L1CAM 2
PLP 71-90		MBP 101-120
PLP 89-106 acet		MBP 111-129 iso5
PMP2 2		MBP 146-170 iso5
PRP		MBP 170-191
PRPH		MBP 21-40
S100B		MBP 83-99 iso5
SCN3A Cter		mMAG 105-120
SCN8A Cter		MOBP 51-70
SCN8A L1		MOG 11-30
SCN8A L3		MOG 31-50
SCN8A Nter		MOG 71-90
SNCG		MPZ
TAU		Neuropeptide g
TRPV1		Neuropeptide K
TUBB3		NRCAM
		NTRK1
		OSP 61-80
		OSP 71-90
		PLP 101-120
		PLP 178-197 acet
		PLP 261-277
		PLP 31-50

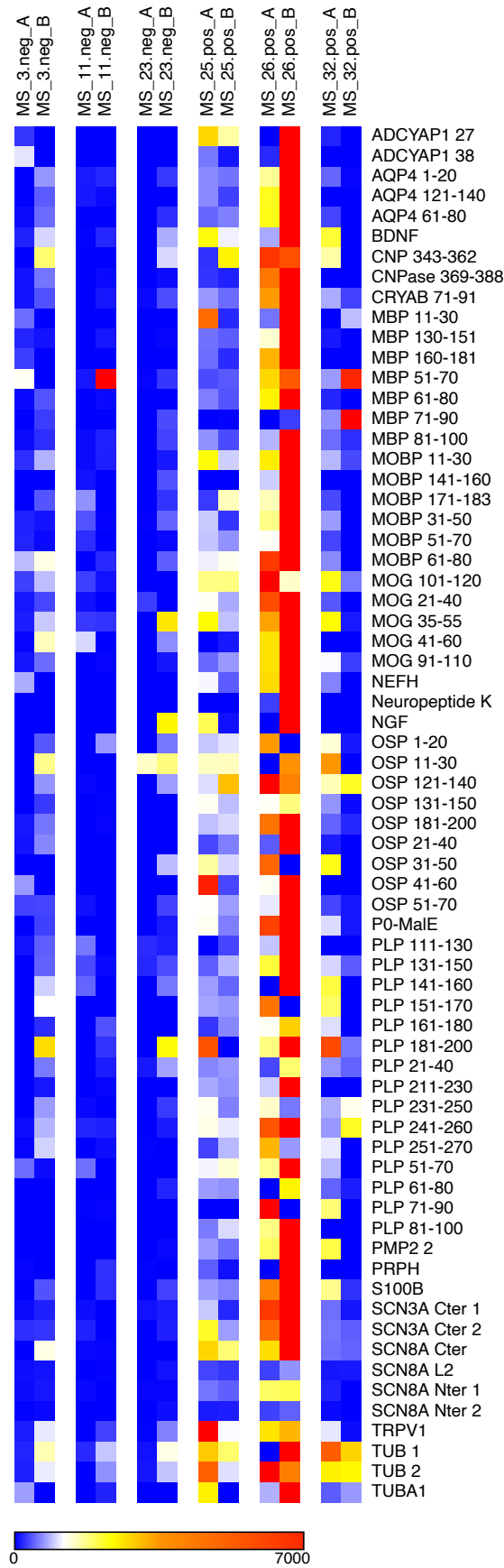
**Supplementary Figure S2: Comparison of IgG reactivity in B cell supernatants vs. plasma samples.** Venn diagram indicating the names of significant antigens in the comparisons “ELISpot-neg vs. ELISpot-pos (supernatants)” (orange) and “HC/OND vs. MS (plasma)” (blue), corresponding to Fig. 2C.

Plasma  
HC / OND vs. MS

<p>AQP4 101-120 AQP4 11-30 AQP4 111-130 AQP4 121-140 AQP4 131-150 AQP4 141-160 AQP4 151-170 AQP4 171-190 AQP4 181-200 AQP4 191-210 AQP4 21-40 AQP4 231-250 AQP4 271-290 AQP4 281-300 AQP4 291-310 AQP4 301-320</p>	<p>AQP4 31-50 AQP4 41-60 AQP4 51-70 AQP4 prot 1 AQP4 prot 2 Bov ChromograninA CNP prot CNPase 356-375 CNPase 369-388 CRYAB 131-151 CRYAB 31-50 CRYAB 51-70 CRYAB 81-100 L1CAM 2 MBP 111-129 iso5 MBP 146-170 iso5</p>	<p>MBP 170-191 MBP 83-99 iso5 mMAG 105-120 MOG 11-30 MOG 71-90 MPZ Neuropeptide g Neuropeptide K NRCAM NTRK1 OSP 61-80 OSP 71-90 PLP 101-120 PLP 178-197 acet PLP 261-277 PLP 31-50</p>
<p>AQP4 221-240 AQP4 71-90 CRYAB 71-91 CRYAB 91-110 mMAG 97-112 PLP 171-190</p>	<p>CRYAB 21-40 PLP 1-20 PLP 211-230</p>	<p>AQP4 201-220 AQP4 261-280 CRYAB 41-60 MBP 101-120 MBP 21-40 MOBP 51-70 MOG 31-50</p>
<p>AQP4 61-80 CRYAB 1-20 MBP MBP 130-151 MBP 71-90 MBP 81-100 MOBP 141-160 MOBP 61-80 MOG 101-120 NEFH NEFL OSP 121-140 OSP 131-150 OSP 161-180 OSP 181-200 OSP 21-40 OSP 31-50 P0-MalE PLP 11-30 PLP 131-150 PLP 151-170 PLP 161-180 PLP 181-200 PLP 191-210 PLP 231-250 PLP 241-260 PLP 251-270 PLP 61-80 PLP 71-90 PRP PRPH S100B SCN3A Cter SCN8A Cter SCN8A L1 SCN8A L3 SCN8A Nter SNCG TAU TRPV1 TUBB3</p>	<p>AQP4 91-110 MOBP 21-40 MOG 91-110 OSP 51-70 PLP 141-160 PLP 89-106 acet PMP2 2</p>	<p>ADCYAP1 38 AQP4 241-260 CRYAB 11-30 CRYAB 110-131 MBP 107-127 MBP 11-30 MBP 160-181 MBP 51-70 MBP 61-80 MBP 91-110 MOBP 1-20 MOBP 171-183 MOBP 51-70 MOG 41-60 MOG Nterm OSP 171-190 OSP 191-210 PLP 139-154 acet PLP 201-220 PLP 41-60 PLP 91-110 PMP2 1 TAC1</p>
		<p>Supernatants ELISpot-neg vs. ELISpot-pos Cohort 2</p>

Supernatants  
ELISpot-neg vs.  
ELISpot-pos  
Cohort 1

**Supplementary Figure S3: Comparison of IgG reactivity in B cell supernatants (2 cohorts) vs. plasma samples.** Venn diagram showing the names of significant antigens in the comparisons “ELISpot-neg vs. ELISpot-pos (supernatants, cohort 1)” (orange), “ELISpot-neg vs. ELISpot-pos (supernatants, cohort 2)” (green), and “HC/OND vs. MS (plasma)” (blue), corresponding to Fig. 3B.



**Supplementary Figure S4: Intra-individual comparison of IgG reactivity in B cell supernatants (2 timepoints).** Heatmap of antibody reactivity (MFI) against 57 myelin \_ntigens, determined significantly different between ELISpot-neg vs. ELISpot-pos B cell supernatants in SAM analysis. 2 timepoints are shown for each patient. Sample collection for time point \_B was performed 3 months after time point \_A.



Table S2.

**Demographics of healthy controls**

<b>Study ID</b>	<b>Gender</b>	<b>Age</b>
HC_1	f	54
HC_2	f	30
HC_3	f	58
HC_4	f	29
HC_5	f	24
HC_6	f	34
HC_7	f	27
HC_8	f	35
HC_9	f	40
HC_10	m	30

Table S3.

**Supplementary Table 3. Demographics of other neurological disease patients**

<b>Study ID</b>	<b>Gender</b>	<b>Age</b>	<b>Diagnosis</b>
OND_1	m	33	Stroke
OND_2	f	26	Migraine
OND_3	m	67	Transient ischemic attack
OND_4	f	78	Transient global amnesia
OND_5	m	71	Vestibular vertigo
OND_6	f	54	Parkinson's disease
OND_7	f	66	Parkinson's disease
OND_8	f	67	Myopathy
OND_9	m	44	Myopathy
OND_10	f	72	Trigeminal neuralgia
OND_11	m	74	Epilepsia
OND_12	f	72	Benign paroxysmal positional vertigo
OND_13	f	65	Epilepsia
OND_14	f	52	Polyneuropathy



Table S4.

Supplementary Table 4. Demographics of MS patients (cohort 1)

Study ID	Gender	Age	Disease Duration (yr)	EDSS	Treatment
MS_1.neg	f	25	1	2	None
MS_2.neg	f	33	1	2	None
MS_3.neg	f	35	11	7	Natalizumab
MS_4.neg	m	41	10	3.5	Natalizumab
MS_5.neg	f	34	9	2	Natalizumab
MS_6.neg	f	54	8	2	Glatiramer acetate
MS_7.neg	f	42	4.50	2	Glatiramer acetate
MS_8.neg	f	46	2.5	5.5	Natalizumab
MS_9.neg	m	32	6	2	Natalizumab
MS_10.neg	f	50	3	3.5	Interferon- $\beta$
MS_11.neg	f	43	16	4	Glatiramer acetate
MS_12.neg	m	54	18	5	None
MS_13.neg	f	33	1	2.5	None
MS_14.neg	f	36	2	0	Glatiramer acetate
MS_15.neg	f	28	2	1	Glatiramer acetate
MS_16.neg	f	32	2	2	Interferon- $\beta$
MS_17.neg	m	58	0.5	3	Interferon- $\beta$
MS_18.neg	f	30	1	4	Natalizumab
MS_19.neg	f	23	0	0	Glatiramer acetate
MS_20.neg	f	46	1	2	None
MS_21.neg	f	36	1	2	Interferon- $\beta$
MS_22.neg	f	51	13	6	Fingolimod
MS_23.neg	m	46	5	4	Natalizumab
MS_24.pos	m	35	6	3	Glatiramer acetate
MS_25.pos	m	25	3	2.5	Glatiramer acetate
MS_26.pos	f	33	11	6	Natalizumab
MS_27.pos	f	51	4.5	3	Natalizumab
MS_28.pos	m	28	5	2	Natalizumab
MS_29.pos	f	36	5	3	None
MS_30.pos	m	39	5.5	2	Natalizumab
MS_31.pos	f	30	3	0	Glatiramer acetate
MS_32.pos	f	18	3	1	Natalizumab
MS_33.pos	f	49	2	2	Interferon- $\beta$
MS_34.pos	f	63	15	6.5	Interferon- $\beta$
MS_35.pos	f	54	4	5.5	None
MS_36.pos	m	49	7	2	Natalizumab

Table S5.

Supplementary Table 5. Demographics of MS patients (cohort 2)

Study ID	Gender	Age	Disease Duration (yrs)	EDSS	Treatment
MS_1v.neg	m	39	13	1	Interferon- $\beta$
MS_2v.neg	f	50	8	2	Teriflunomide
MS_3v.neg	f	38	9	2.5	Dimethyl fumarate
MS_4v.neg	f	67	8.5	1	Glatiramer acetate
MS_5v.neg	f	45	6.5	1.5	Interferon- $\beta$
MS_6v.neg	f	31	6	0	Teriflunomide
MS_1v.pos	m	39	9	0	Interferon- $\beta$
MS_2v.pos	f	48	2.5	2	Glatiramer acetate
MS_3v.pos	m	38	6	0	Glatiramer acetate
MS_4v.pos	f	48	26	4	None
MS_5v.pos	f	51	6	2	Glatiramer acetate
MS_6v.pos	f	46	14	0	Glatiramer acetate
MS_7v.pos	f	47	12	2	Glatiramer acetate
MS_8v.pos	f	34	4	0	None