

Supplementary material

Table S1. List of the biomarkers measured by means of PEA technique (inflammation panel) in the CSF of recruited patients. Biomarkers are listed according to the alphabetical order of the abbreviations. Proteins with a call rate <95% (excluded from further analysis) are indicated.

Abbreviations	Full or alternative names	Call rate < 95%
ADA	Adenosine deaminase or adenosine aminohydrolase	
ARTN	Artemin or enovin or neurobastin	X
AXIN1	Axin-1	X
βNGF	β-nerve growth factor	
BDNF	Brain-derived neurotrophic factor	X
CASP-8	Caspase 8	X
CCL4	Chemokine (C-C motif) ligand 4 or or macrophage inflammatory protein 1β (MIP-1β)	
CCL11	Chemokine (C-C motif) ligand 11 or eosinophil chemotactic protein or eotaxin-1	
CCL19	Chemokine (C-C motif) ligand 19 or EBI1 ligand chemokine (ELC) or macrophage inflammatory protein protein-3-β (MIP-3-β)	
CCL20	Chemokine (C-C motif) ligand 20 or liver activation regulated chemokine (LARC) or macrophage inflammatory protein-3 (MIP3A)	X
CCL23	Chemokine (C-C motif) ligand 23 or macrophage inflammatory protein 3 (MIP-3) or myeloid progenitor inhibitory factor 1 (MPIF-1)	X
CCL25	Chemokine (C-C motif) ligand 25	X
CCL28	Chemokine (C-C motif) ligand 28 or mucosae associated epithelial chemokine (MEC)	X
CD5	Cluster of differentiation 5	
CD6	Cluster of differentiation 6	X
CD40	Cluster of differentiation 40	
CD244	Cluster of differentiation 244	X
CDCP1	CUB domain-containing protein 1 or cluster of differentiation 318 (CD318) or transmembrane and associated with src kinases (Trask)	
CX3CL1	Chemokine (C-X3-C motif) ligand 1 or fractalkine	
CXCL1	Chemokine (C-X-C motif) ligand 1 or neutrophil-activating protein 3 (NAP-3)	
CXCL5	Chemokine (C-X-C motif) ligand 5 or epithelial-derived neutrophil-activating protein 78 (ENA-78)	
CXCL6	Chemokine (C-X-C motif) ligand 6	
CXCL9	Chemokine (C-X-C motif) ligand 9 or monokine induced by gamma-interferon (MIG)	
CXCL10	Chemokine (C-X-C motif) ligand 10 or interferon gamma-inducible protein 10 (IP-10) or small inducible cytokine B10	
CXCL11	Chemokine (C-X-C motif) ligand 11 or interferon-inducible T-cell α chemoattractant (I-TAC) or interferon-gamma-inducible protein 9 (IP-9)	
CSF1	Colony stimulating factor 1 or macrophage colony-stimulating factor (M-CSF)	
CST5	Cystatin D	
DNER	Delta and Notch-like epidermal growth factor-related receptor	
EIF4EBP1	Eukaryotic translation initiation factor 4E-binding protein 1	
EN-RAGE	Extracellular newly identified receptor for advanced glycation end-products binding protein or S100 calcium-binding protein A12 (S100A12) or calgranulin C	X
FGF-5	Fibroblast growth factor 5	
FGF-19	Fibroblast growth factor 19	

FGF-21	Fibroblast growth factor 21	X
FGF-23	Fibroblast growth factor 23	X
Flt3L	FMS-like tyrosine kinase 3 ligand	
GDNF	Glial cell-derived neurotrophic factor	X
IFN γ	Interferon γ	X
HGF	Hepatocyte growth factor or scatter factor (SF)	
IL-1α	Interleukin 1 α or hematopoietin 1	X
IL-2	Interleukin 2	X
IL-2RB	Interleukin 2 receptor subunit β	X
IL-4	Interleukin 4	X
IL-5	Interleukin 5	X
IL-6	Interleukin 6	X
IL-7	Interleukin 7	X
IL-8	Interleukin 8	
IL-10	Interleukin 10	X
IL-10RA	Interleukin 10 receptor α subunit or cluster of differentiation W210A (CDW210A)	X
IL-10RB	Interleukin 10 receptor β subunit or cluster of differentiation W210B (CDW210A)	
IL-12B	Interleukin 12 β subunit	
IL-13	Interleukin 13	X
IL-15RA	Interleukin 15 receptor α subunit	X
IL-17A	Interleukin 17 A	X
IL-17 C	Interleukin 17 C	X
IL-18	Interleukin 18 or interferon gamma inducing factor	
IL-18R1	Interleukin-18 receptor-1 or cluster of differentiation w218a (CDw218a)	
IL-20	Interleukin 20	X
IL-20RA	Interleukin 20 receptor α subunit	X
IL-22 RA1	Interleukin 22 receptor α 1 subunit	X
IL-24	Interleukin 24	X
IL-33	Interleukin 33	X
LIF	Leukemia inhibiting factor	X
LIFR	Leukemia inhibiting factor receptor or cluster of differentiation 118 (CD118)	
MCP-1	Monocyte chemoattractant protein 1 or chemokine (C-C motif) ligand 2 (CCL2) or small inducible cytokine A2	
MCP-2	Monocyte chemoattractant protein 2 or chemokine (C-C motif) ligand 8 (CCL8)	
MCP-3	Monocyte chemoattractant protein 3 or chemokine (C-C motif) ligand 7 (CCL7)	X
MCP-4	Monocyte chemoattractant protein 4 or chemokine (C-C motif) ligand 13 (CCL13)	X
MIP-1α	Macrophage inflammatory protein 1- α or chemokine (C-C motif) ligand 3 (CCL3)	
MMP1	Matrix metalloproteinase 1 or interstitial collagenase or fibroblast collagenase	
MMP10	Matrix metalloproteinase 10 or stromelysin 2 or transin-2	
NRTN	Neurturin	X
NT-3	Neurotrophin 3	X
OPG	Osteoprotegerin	
OSM	Oncostatin M	X
PDL1	Programmed death-ligand 1 or cluster of differentiation 274 (CD274) or B7 homolog 1 (B7-H1)	
SCF	Stem cell factor or KIT-ligand (KL) or steel factor	
SIRT2	NAD-dependent deacetylase sirtuin-2	

SLAMF1	Signaling lymphocytic activation molecule 1 or cluster of differentiation 150 (CD150)	X
ST1A1	Sulfotransferase 1A1	X
STAMBP	STAM binding protein	X
TGFα	Transforming growth factor α	
TGFβ1	Transforming growth factor β 1	
TNF	Tumor necrosis factor or tumor necrosis factor α (TNF α) or cachectin	X
TNFβ	Tumor necrosis factor β or lymphotoxin	X
TNFSF14	Tumor necrosis factor superfamily member 14 or homologous to lymphotoxin, exhibits inducible expression and competes with HSV glycoprotein D for binding to herpesvirus entry mediator, a receptor expressed on T lymphocytes (LIGHT)	
TNFRSF9	Tumor necrosis factor receptor superfamily member 9 or cluster of differentiation 137 (CD137) or induced by lymphocyte activation (ILA)	
TRAIL	TNF-related apoptosis-inducing ligand	
TRANCE	TNF-related activation-induced cytokine or receptor activator of nuclear factor kappa-B ligand (RANKL) or tumor necrosis factor ligand superfamily member 11 (TNFSF11) or osteoprotegerin ligand (OPGL) or osteoclast differentiation factor (ODF)	X
TSLP	Thymic stromal lymphopoietin	X
TWEAK	TNF-related weak inducer of apoptosis or tumor necrosis factor ligand superfamily member 12 (TNFSF12)	
uPA	Urokinase type plasminogen activator	
VEGFA	Vascular endothelial growth factor A	

Figure S1. Scatter plots showing the NPX value of the proteins with a q-value < 0.05 in the comparison between RRMS and OND. The RRMS group is further splitted into MS OCB+ and MS OCB—. The bars indicate mean and standard deviations. (A) CD5, (B) IL-12B, (C) TNFB, (D) TNFSF14, (E) TNFRSF9, (F) MIP-1-alpha.

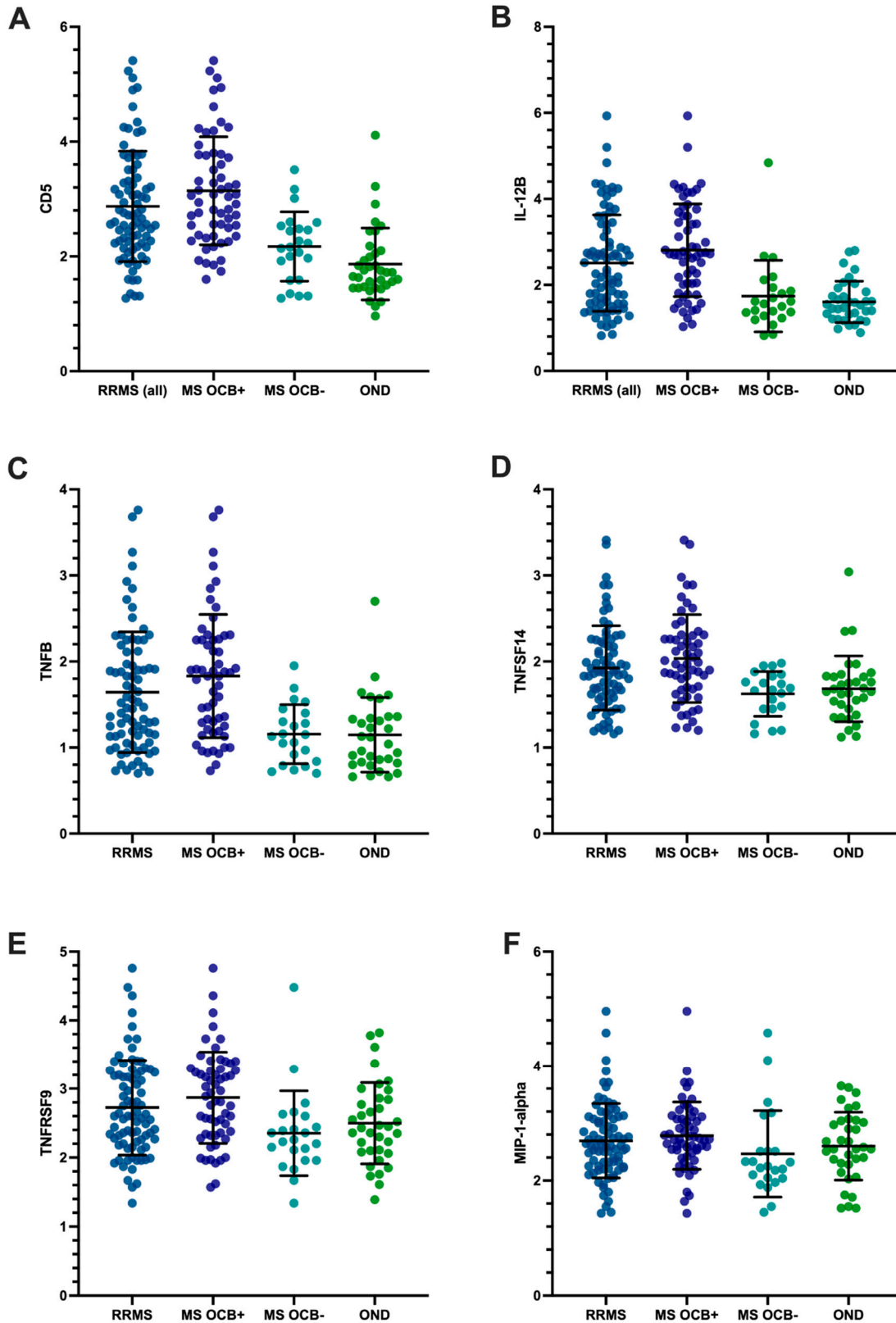


Figure legend. MS OCB+: multiple sclerosis with cerebrospinal fluid IgG oligoclonal bands. MS OCB—: multiple sclerosis without cerebrospinal fluid IgG oligoclonal bands. NPX: normalized protein expression. OND: other neurological diseases. PEA: proximity extension assay. RRMS: relapsing remitting multiple sclerosis.

Table S2. Coefficients relative to not z-scored NPX values in multivariate analysis of PEA-tested proteins in MS OCB+ vs. OND and MS OCB— vs. OND.

Coefficients	
MS OCB+ vs. OND	
Intercept	-5.68
IL-12B	1.24
CD5	0.92
CX3CL1	-0.20
FGF-19	-0.20
CST5	0.04
MCP-1	-0.13
MS OCB— vs. OND	
Intercept	2.2
CX3CL1	-1.04
CD5	0.42
NfL	0.00017
CCL4	0.15
OPG	-0.083

Table legend. MS OCB+: multiple sclerosis with cerebrospinal fluid IgG oligoclonal bands. MS OCB—: multiple sclerosis without cerebrospinal fluid IgG oligoclonal bands. NPX: normalized protein expression. OND: other neurological diseases. PEA: proximity extension assay.