

Supplementary Table 1: Plasma cytokine concentration did not show significant difference among different types of multiple sclerosis compared with healthy control

Analytes	Kruskal-Wallis test	Median (25%-75% range)				Dunn's Multiplex Comparison (P value)					
						HC vs			RRMS vs		BMS
	P value	HC	RRMS	BMS	SPMS	RRMS	BMS	SPMS	BMS	SPMS	SPMS
IL-8/ CXCL8	0.0748	5.82 (2.14-18.90)	11.75 (2.78-26.79)	14.22 (8.69-40.44)	43.47 (6.85-140.00)	>0.9999	0.4122	0.119	>0.9999	0.7161	>0.9999
IFN γ	0.0812	6.55 (4.54-12.32)	5.7 (2.32-24.10)	16.61 (9.195-64.32)	6.55 (2.678-17.24)	>0.9999	0.7176	>0.9999	0.1656	>0.9999	0.1344
IL-4	0.0848	1.6 (1.6-25.13)	5.17 (0.58-30.73)	48.73 (12.48-228.30)	12.28 (1.6-249.00)	>0.9999	0.2718	>0.9999	0.1671	>0.9999	>0.8869
IL-15	0.0905	1.42 (0.42-2.20)	1.935 (0.75-18.39)	12.46 (2.83-33.60)	3.96 (0.42-35.53)	>0.9999	0.1059	0.43	0.7072	>0.9999	>0.9999
MIP-1 α / CCL3	0.1082	2.47 (1.12-6.09)	7.34 (0.48-15.66)	15.38 (4.94-22.68)	13.59 (4.07-27.44)	>0.9999	0.3139	0.1963	>0.9999	>0.9999	>0.9999
VEGF	0.1429	78.34 (43.20-114.50)	34.64 (4.49-85.82)	98.26 (48.14-123.70)	85.08 (60.55-133.10)	>0.9999	>0.9999	>0.9999	0.3293	0.1445	>0.9999
IL-6	0.1492	2.87 (0.39-7.97)	1.65 (0.35-26.07)	35.01(3.67-103.10)	8.16 (0.35-388.50)	>0.9999	0.5398	>0.9999	0.278	0.9537	>0.9999
IL-10	0.1630	1.28 (0.89-2.71)	1.54 (0.53-20.99)	8.60 (4.53-20.95)	2.47 (0.86-20.65)	>0.9999	0.2226	0.9612	0.7382	>0.9999	>0.9999
TNF α	0.1807	10.80 (7.52-16.72)	14.42 (12.11-18.98)	16.46 (13.80-24.55)	17.50 (13.58-28.08)	>0.9999	0.3852	0.3386	>0.9999	>0.9999	>0.9999
IL-7	0.1915	4.02 (1.96-10.35)	5.06 (3.19-6.53)	6.77 (3.55-11.41)	7.97 (5.01-14.94)	>0.9999	>0.9999	0.6851	>0.9999	0.5046	>0.9999
MDC/ CCL22	0.2003	1860 (804-2542)	1413 (904-1811)	672 (544-1531)	980 (664-2842)	>0.9999	0.4423	>0.9999	0.4992	>0.9999	>0.9999
IP-10/ CXCL10	0.2277	793 (447-1362)	442 (244-685)	598 (406-1234)	600 (463-928)	0.5512	>0.9999	>0.9999	>0.9999	0.3084	>0.9999
IFN α 2	0.2493	8.00 (8.00-52.14)	23.06 (8.75-49.08)	47.36 (21.80-80.65)	36.91 (11.10-108.2)	>0.9999	>0.9999	0.9474	0.9841	0.8055	>0.9999

FGF2	0.2967	58.12 (40.06-104.30)	52.48 (28.65-116.90)	106.20 (65.28-191.50)	62.95 (32.10-113.60)	>0.9999	0.9468	>0.9999	0.7486	>0.9999	0.6147
IL-17A	0.2990	1.48 (0.95-5.78)	4.67 (1.52-6.58)	5.73 (2.67-16.84)	2.53 (0.80-8.12)	>0.9999	0.7904	>0.9999	>0.9999	>0.9999	0.515
IL-9	0.3033	0.09 (0.09-0.33)	0.12 (0.12-9.96)	3.53 (0.0.20-11.28)	0.22 (0.09-9.04)	0.9181	0.3555	>0.9999	>0.9999	>0.9999	>0.9999
G-CSF	0.3325	8.59 (2.75-23.86)	15.40 (8.15-19.30)	28.17 (9.41-81.34)	18.67 (4.80-48.59)	>0.9999	0.5804	>0.9999	>0.9999	>0.9999	>0.9999
GM-CSF	0.3370	5.71 (1.87-7.61)	3.64 (2.28-14.12)	14.25 (4.85-22.72)	5.93 (3.16-16.39)	>0.9999	0.8835	>0.9999	0.7246	>0.9999	>0.9999
MIP-1β/CCL4	0.3894	28.58 (7.69-51.94)	41.85 (19.47-59.22)	46.87 (27.65-82.03)	56.15 (22.36-113.5)	>0.9999	>0.9999	0.771	>0.9999	>0.9999	>0.9999
IL-5	0.4140	0.75 (0.49-1.83)	0.87(0.69-1.19)	3.13 (0.85-9.32)	0.88 (0.52-11.48)	>0.9999	>0.9999	>0.9999	>0.9999	>0.9999	0.9388
IL-2	0.5540	1.52(0.84-2.85)	1.66 (0.97-2.90)	2.78 (1.29-5.57)	1.57 (0.63-4.06)	>0.9999	>0.9999	>0.9999	>0.9999	>0.9999	>0.9999
IL-3	0.6710	0.69 (0.39-1.08)	1.21 (0.79-1.37)	0.82 (0.57-1.52)	1.22 (0.13-2.20)	>0.9999	>0.9999	>0.9999	>0.9999	>0.9999	>0.9999
Groα/CXCL1	0.6864	1698 (890-2065)	892 (439-1671)	756 (530-1257)	1143 (447-2709)	>0.9999	>0.9999	>0.9999	>0.9999	>0.9999	>0.9999
IL-12p70	0.9800	2.87 (1.29-9.94)	3.29 (1.22-6.30)	2.77 (1.40-9.80)	2.87 (1.61-8.42)	>0.9999	>0.9999	>0.9999	>0.9999	>0.9999	>0.9999
Flt-3L	0.9968	0.39 (0.39-63.33)	2.73(1.60-5.12)	1.60 (0.39-40.63)	9.49 (0.39-29.76)	>0.9999	>0.9999	>0.9999	>0.9999	>0.9999	>0.9999

Plasma derived from healthy controls (HC, n=5), patients with RRMS (n=8), BMS (n=12), and patients with SPMS (n=32) were analyzed using Luminex kit from Millipore. Kruskal-Wallis test and multiple comparison with Dunn's modification between different groups were performed. Median of plasma concentration (pg/ml) are presented followed by 25-75% range in the brackets.

Supplementary Table 2: Circulating biomarkers that can discriminate among different MS types

	AUC	95% CI	p Value	Cut off (pg/ml)	Sensitivity	Specificity	Likelihood Ratio
RRMS vs SPMS							
MCP1/CCL2	0.8711	0.7218 to 1.000	0.0013	> 369.4	90.63	87.5	7.25
sCD40L	0.8594	0.7462 to 0.9725	0.0019	> 487.6	81.25	87.5	6.50
MCP1/CCL2 & sCD40L	0.9297	0.8475 to 1.000	0.0002	NA	NA	NA	NA
RRMS vs BMS							
MCP1/CCL2	0.8542	0.6651 to 1.000	0.0087	> 371.9	75	87.5	6.00
BMS VS SPMS							
sCD40L	0.7865	0.6408 to 0.9321	0.0037	> 2206	53.13	91.67	6.38
IFNγ	0.7109	0.5575 to 0.8644	0.0328	<7.805	56.25	83.33	3.38
sCD40L & IFNγ	0.8307	0.7078 to 0.9536	0.0008	NA	NA	NA	NA

ROC curve analysis and multiple logistic regression analysis were performed using the plasma level of these soluble factors from RRMS (n=8),

BMS (n=12), and SPMS (n=32), AUC: under curve value, 95% CI: 95% confidence interval.