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Supplemental Information

Memory B Cells Activate Brain-Homing, Autoreactive $CD4^+$ T Cells in Multiple Sclerosis

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Table S1. Demographic characteristics of the study population, Related to Figure 1-4, Figure 7, Figure S1-S4, Figure S7 and Table S2-S3.

cohort	donors	treatment	n	age (mean ± SD)	age (range)	F:M ratio	treatment duration months (mean; range)	Genotype (HLA/SNP)	*In vitro* CFSE	*Ex vivo* B/T cell subsets	*In vitro* Multiplex cytokine	*In vitro* CFSE RNAseq	RASGRP2 reactivity
1st	HD	---	32	32.6 ± 6.8	25-49	1.7	none	HLA/SNP	X[d]		X		X[h]
	RRMS (REL)	none/nihil[+]	18	33.1 ± 7.5	20-45	2.0	none	HLA	X	X			
	RRMS (REM)	none/nihil[+]	32	37.4 ± 8.1	22-54	1.1	none	HLA/SNP	X[abcd]	X	X[ac]	X[f]	X[h]
	Psoriasis	none/topic*	10	34.3 ± 6.4	25-47	0.4	none/topic*		X				
	Morbus Crohn	none	7	41.3 ± 9.9	25-53	1.3	none		X				
	RRMS	rituximab	14	47.3 ± 8.3	30-59	1.3	7.1; 3-21		X		X		
	RRMS	natalizumab	15	36.6 ± 7.7	23-50	4.0	17.9; 11-30		X	X	X		
	RRMS	fingolimod	10	39.8 ± 7.8	24-47	1.5	12.7; 3-36		X		X		
2nd	HD	---	14	31.4 ± 4.8	25-41	0.8	none		X[e]		X[e]		
	RRMS (REM)	none/nihil[+]	14	33.8 ± 9.5	22-54	1.8	none		X[e]		X[e]		
3rd	RRMS/SPMS	before/after rituximab	179	42.3 ±10.0	19-65	2.0	10.1; 0 and 3-29			X (counts)			
	RRMS	before/after rituximab	9	41 ± 6.8	33-54	3.5	6.2; 0 and 5-7			X (frequency)			
	RRMS	before/after rituximab	9	46.4 ± 9.2	32-59	0.8	3; 0 and 3		X[ac]				
4th	RRMS	natalizumab	8	35.8 ± 8.4	24-53	0.6	20.5; 3-62	HLA					X[g]
	RRMS	natalizumab	20	38.2 ± 8.6	21-56	0.8	61.3; 11-124	HLA					X[h]

HD = healthy donors; RRMS = relapsing remitting multiple sclerosis; SPMS = secondary progressive multiple sclerosis; REL = relapse; REM = remission; nihil = untreated; F = female; M = male; [+]no glucocorticoids for at least 4 weeks and no other immunomodulatory treatments for at least 12 weeks; [*]only topic therapy to the skin; [a]blocking; [b]intracellular signaling/cytokine; [c]B cell depletion/transfer/co-cultures; [d]in vitro CFSE^{dim} expansion and EBV B cell transformation; [e]various stimulations; [f]RNA sequencing of sorted CFSE^{dim} (proliferating) and CFSE^{hi} (resting) CD4^{+} T and B cells upon 7-day in vitro autoproliferation (only in RRMS (REM)) [g]RASGRP2 reactivity using thymidine incorporation assay (7 days); [h]RASGRP2 reactivity using Fluorospot assay (2 days)