

**Table e-1: EBNA2 alleles and HLA aptotypes (a complete HLA typing was obtained in a random subset of the entire sample) in MS and HD.**

n	MS/HD	F/M	aa134	aa236	aa245	aa 256	aa267	Alleles	HLA-A	HLA-A	HLA-B	HLA-B	HLA-Cw	HLACw	HLA-DR	HLA-DR
		---	L(CTT)	T(ACC)	P	D	T	B95-8	---	---	---	---	---	---	---	---
1	HD1	F	L(CTT)	T(ACC)	P	D	T	1.3B	A24*2402	A31*3101	B51*5101	B51*5101	Cw15*1502	Cw15*1502	DR16*1601	DR12*1201
2	HD2	F	L(CTT)	T(ACC)	P	D	T	1.3B	A26*2601	A11*1101	B7*0702	B37*3701	Cw6*0602	Cw7*0702	DR10*1001	DR11*1101
3 <sup>a</sup>	HD3-1	M	L(CTT)	T(ACC)	P	D	T	1.3B	A2*0201	A2*0201	B40*4001	B51*5101	Cw15*1503	Cw12*1202	DR1*0101	DR10*1001
	HD3-2		L(CTT)	T(ACC)	P	D	T	1.3B								
4	HD4	F	L(CTT)	T(ACC)	P	D	T	GD1	A24*2402	A33*3301	B8*0801	B44*4401	Cw6*0602	Cw7*0702	DR3*0301	DR11*1101
5 <sub>a</sub>	HD5-1	M	L(CTG)	T(ACT)	P	N	I	1.2	A2*0201	A26*2601	B18*1801	B38*3801	Cw5*0501	Cw12*1202	DR1*0101	DR17*0301
	HD5-2		L(CTG)	T(ACT)	P	N	I	1.2								
	HD5-3		no seq	T(ACT)	P	D	I	1.2								
6	HD6	M	L(CTT)	T(ACC)	P	D	T	GD1	A2*0201	A2*0201	B18*1801	B51*5101	Cw14*1402	Cw12*1202	DR11*1101	DR11*1103
7 <sub>a</sub>	HD7-1	M	L(CTG)	T(ACT)	T	D	no seq	1.2	A2*0201	A32*3201	B18*1801	B50*5001	Cw7*0701	Cw6*0602	DR4*0403	DR16*1601
	HD7-2		L(CTT)	T(ACC)	P	D	T	1.3B								
8	HD8	F	L(CTT)	T(ACC)	P	D	T	1.3B	A2*0201	A3*0301	B8*0801	B55*5501	Cw3*0301	Cw7*0702	DR4*0402	DR13*1301
9	HD9	F	L(CTT)	T(ACC)	P	D	T	1.3B	A24*2402	A24*2402	B35*3504	B13*1301	Cw6*0602	Cw6*0602	DR7*0701	DR11*1101
10	HD10	F	L(CTT)	T(ACC)	P	D	T	1.3B	A3*0301	A26*2601	B35*3501	B18*1801	Cw12*1202	Cw12*1202	DR15*1501	DR11*1103
11	HD11	F	L(CTT)	T(ACC)	P	D	T	1.3B	A1*0101	A24*2402	B13*1301	B35*3502	Cw4*0401	Cw6*0602	DR11*1101	DR7*0701
12	HD12	M	L(CTT)	T(ACC)	P	D	T	1.3B	A2*0201	A32*3201	B15*1501	B51*5101	Cw3*0302	Cw4*0437	DR16*1601	DR14*1401
13	HD13	F	L(CTG)	T(ACT)	T	N	I	1.2	A3*0301	A26*2601	B7*0702	B27*2701	Cw1*0102	Cw7*0702	DR8*0801	DR11*1101
14	HD14	M	L(CTT)	T(ACC)	P	N	T	1.3B	A3*0330	A26*2601	B7*0702	B27*2701	Cw1*0102	Cw7*0702	DR16*1601	DR11*1101
15	HD15	F	L(CTT)	T(ACC)	P	N	T	1.3B	A3*0301	A68*6801	B55*5501	B53*5301	Cw4*0401	Cw1*0102	DR11*1101	DR14*1401
16	HD16	F	L(CTT)	T(ACC)	P	N	T	GD1	A23*2301	A24*2402	B49*4901	B49*4901	Cw7*0701	Cw7*0701	DR14*1401	DR13*1301
17	HD17	M	L(CTG)	no seq	no seq	no seq	no seq	1.2	A30*3001	A30*3001	B49*4901	B53*5301	Cw7*0701	Cw4*0401	DR3*0301	DR1*0124
18	HD18	F	L(CTT)	T(ACC)	P	D	T	1.3B	A2*0201	A29*2901	B18*1801	B35*3501	Cw1*0104	Cw12*1221	DR1*0101	DR12*1201
19	HD19	M	L(CTG)	T(ACT)	S	D	I	1.2	A2*0201	A34*3401	B35*3501	B8*0801	Cw7*0701	Cw4*0401	DR7*0701	DR11*1101
20	HD20	F	L(CTT)	T(ACC)	P	D	T	1.3B	A29*2901	A32*3201	B27*2703	B44*4437	Cw1*0102	Cw16*1601	DR7*0701	DR12*1201
21	HD21	F	L(CTG)	T(ACT)	P	D	I	1.2	A11*1101	A24*2402	B49*4901	B49*4901	Cw7*0701	Cw7*0701	DR11*1101	DR11*1101
22	HD22	F	L(CTT)	T(ACC)	P	D	T	1.3B	A3*0301	A33*3301	B7*0702	B14*1402	Cw7*0701	Cw8*0801	DR15*1501	DR1*0101

23	HD23	F	L(CTT)	T(ACC)	P	N	T	1.3B	A11*1101	A32*3201	B55*5501	B54*5405	Cw4*0401	Cw3*0303	DR3*0301	DR7*0701
24	HD24	F	L(CTT)	T(ACC)	P	D	T	1.3B	A3*0301	A30*3001	B15*1501	B35*3501	Cw3*0304	Cw4*0401	DR4*0402	DR4*0402
25	HD25	M	L(CTT)	T(ACC)	P	N	T	1.3B	A2*0201	A1*0101	B8*0801	B51*5101	Cw14*1402	Cw7*0701	DR16*1601	DR3*0301
26	HD26	F	L(CTT)	T(ACC)	P	D	T	1.3B	A2*0201	A11*1101	B39*3901	B52*5201	Cw12*1221	Cw7*0702	DR15*1501	DR8*0801
27	HD27	F	L(CTT)	T(ACC)	P	D	T	1.3B	A32*3201	A24*2402	B14*1402	B15*1517	Cw7*0702	Cw8*0801	DR7*0701	DR13*1301

28	HD28	F	L(CTT)	T(ACC)	P	D	T	GD1	A3*0301	A30*3001	B35*3501	B18*1801	Cw2*0202	Cw5*0501	DR3*0301	DR11*1101
29	HD29	F	L(CTT)	T(ACC)	P	D	T	1.3B	A24*2402	A24*2402	B15*1501	B7*0705	Cw3*0303	Cw15*1502	DR11*1101	DR10*1001
30	HD30	F	L(CTT)	T(ACC)	P	D	T	1.3B	A26*2601	A11*1101	B51*5101	B51*5101	Cw15*1502	Cw12*1202	DR4*0403	DR14*1401
31	HD31	F	L(CTT)	T(ACC)	P	N	T	1.3B	A2*0201	A23*2301	B7*0702	B7*0757	Cw4*0401	Cw7*0702	DR11*1101	DR8*0808
32	HD32	F	L(CTT)	T(ACC)	P	D	T	1.3B	A2*0201	A32*3201	B18*1801	B18*1801	Cw2*0201	Cw7*0701	DR16*1601	DR11*1101
33	HD33	M	L(CTT)	T(ACC)	P	N	T	GD1	A3*0301	A2*0201	B15*1501	B15*1501	Cw7*0704	Cw3*0303	DR7*0701	DR4*0403
34	HD34	F	L(CTT)	T(ACC)	P	D	T	1.3B	--	--	--	--	--	--	--	--
35	HD35	F	L(CTT)	T(ACC)	P	D	T	1.3B	--	--	--	--	--	--	--	--
36	HD36	F	L(CTG)	T(ACT)	T	D	I	1.2	--	--	--	--	--	--	--	--
37	HD37	M	L(CTT)	T(ACC)	P	D	T	1.3B	--	--	--	--	--	--	--	--
38	HD38	M	L(CTT)	T(ACC)	P	D	T	1.3B	--	--	--	--	--	--	--	--

1a	MS1-1	F	L(CTG)	T(ACT)	S	D	I	1.2	A26*2601	A32*3201	B51*5185	B44*4402	Cw3*0302	Cw16*1602	DR1*0101	DR7*0701
	MS1-2		L(CTG)	T(ACT)	S	D	I	1.2								
	MS1-3		no seq	T(ACT)	S	D	I	1.2								
2	MS2	F	L(CTT)	T(ACC)	T	D	T	1.3A	A24*2402	A31*3101	B35*3501	B7*0714	Cw7*0702	Cw12*1202	DR4*0403	DR7*0701
3	MS3	M	L(CTT)	T(ACC)	P	N	T	GD1	A23*2301	A30*3001	B18*1801	B7*0702	Cw7*0702	Cw5*0501	DR15*1501	DR3*0301
4a	MS4-1	M	L(CTG)	T(ACT)	S	D	I	1.2	A1*0101	A32*3201	B35*3501	B7*0702	Cw7*0702	Cw4*0401	DR15*1501	DR1*0101
	MS4-2		L(CTG)	T(ACT)	S	D	I	1.2								
	MS4-3		L(CTG)	T(ACT)	S	D	I	1.2								
5a	MS5-1	M	L(CTG)	T(ACT)	S	D	I	1.2	A29*2901	A2*0201	B7*0740	B39*3901	Cw12*1202	Cw15*1502	DR16*1601	DR15*1501
	MS5-2		L(CTG)	T(ACT)	S	N	I	1.2								
	MS5-3		L(CTG)	T(ACT)	S	D	I	1.2								
6a	MS6-1	F	L(CTG)	T(ACT)	S	D	I	1.2	A2*0201	A24*2402	B35*3501	B7*0724	Cw4*0401	Cw7*0702	DR4*0401	DR12*1201
	MS6-2		L(CTT)	T(ACC)	P	D	T	1.3B								
	MS6-3		L(CTT)	T(ACC)	P	D	T	1.3B								
7a	MS7-1	F	L(CTG)	T(ACT)	P	D	I	1.2	A1*0101	A11*1101	B37*3701	B51*5101	Cw4*0401	Cw6*0602	DR15*1501	DR4*0403

	MS7-2		L(CTG)	T(ACT)	P	N	I	1.2									
8a	MS8-1	M	L(CTG)	T(ACT)	P	D	I	1.2	A26*2601	A24*2402	B50*5001	B55*5501	Cw3*0303	Cw6*0602	DR4*0401	DR7*0701	
	MS8-2		L(CTG)	T(ACT)	P	D	I	1.2									
	MS8-3		L(CTG)	T(ACT)	P	D	I	1.2									
9	MS9	F	L(CTT)	T(ACC)	P	D	T	1.3B	A3*0301	A3*0301	B15*1517	B35*3501	Cw4*0401	Cw7*0701	DR10*1001	DR13*1301	
10a	MS10-1	F	L(CTT)	T(ACC)	no seq	D	no seq	1.2	A3*0301	A33*3301	B58*5801	B40*4006	Cw15*1502	Cw3*0302	DR16*1601	DR13*1301	
	MS10-2		L(CTT)	T(ACC)	P	D	T	GD1									
	MS10-3		L(CTT)	T(ACC)	P	D	T	1.3B									
11	MS11	M	L(CTG)	T(ACT)	S	D	I	1.2	A1*0101	A31*3101	B15*1517	B58*5801	Cw7*0701	Cw7*0701	DR13*1301	DR8*0803	

25	MS12	F	L(CTT)	T(ACC)	P	D	T	1.3B	A1*0101	A66*6605	B8*0814	B58*5808	Cw7*0701	Cw7*0701	DR3*0301	DR11*1101
26	MS13	M	L(CTG)	T(ACC)	T	D	I	1.2	A1*0101	A30*3001	B7*0702	B8*0801	Cw7*0701	Cw7*0704	DR15*1501	DR3*0301
27	MS14	F	L(CTT)	T(ACC)	P	N	T	GD1	A11*1101	A11*1101	B35*3502	B8*0801	Cw3*0303	Cw7*0707	DR14*1401	DR16*1601
28	MS15	F	L(CTG)	T(ACC)	T	N	I	1.2	A24*2402	A24*2402	B58*5801	B7*0705	Cw7*0702	Cw3*0302	DR3*0301	DR11*1101
29	MS16	F	L(CTT)	T(ACC)	P	D	T	1.3B	A11*1101	A30*3001	B35*3501	B58*5828	Cw4*0401	Cw4*0401	DR11*1101	DR11*1101
30	MS17	F	L(CTT)	T(ACC)	P	D	T	1.3B	A26*2601	A32*3201	B35*3501	B50*5001	Cw4*0401	Cw4*0401	DR1*0101	DR3*0301
31	MS18	F	L(CTG)	T(ACT)	S	D	I	1.2	A24*2402	A26*2601	B8*0801	B41*4101	Cw17*1701	Cw7*0701	DR3*0301	DR11*1101
32	MS19	F	L(CTG)	T(ACT)	S	D	I	1.2	A2*0201	A23*2301	B15*1503	B44*4403	Cw7*0712	Cw12*1205	DR13*1301	DR7*0701
33	MS20	F	L(CTG)	T(ACT)	S	D	I	1.2	--	--	--	--	--	--	--	--
34	MS21	F	L(CTT)	T(ACC)	P	N	T	1.3B	A2*0201	A3*0301	B7*0702	B13*1301	Cw7*0702	Cw6*0602	DR3*0301	DR4*0403
35	MS22	F	L(CTG)	T(ACT)	S	N	I	1.2	A1*0101	A2*0201	B37*3701	B58*5801	Cw6*0602	Cw7*0701	DR11*1101	DR16*1601
36	MS23	F	L(CTT)	T(ACC)	P	N	T	1.3B	A1*0101	A3*0301	B7*0702	B8*0801	Cw7*0702	Cw7*0701	DR3*0301	DR11*1103
37	MS24	F	L(CTG)	T(ACT)	T	D	I	1.2	A2*0201	A3*0301	B41*4101	B40*4008	Cw17*1701	Cw2*0202	DR15*1501	DR16*1601
38	MS25	F	L(CTG)	T(ACT)	P	D	I	1.2	A2*0201	A2*0201	B41*4118	B37*3721	Cw17*1701	Cw6*0602	DR3*0301	DR3*0301
39	MS26	M	L(CTG)	T(ACT)	S	N	I	1.2	A1*0101	A1*0101	B7*0702	B13*1301	Cw6*0602	Cw7*0704	DR15*1501	DR15*1501
40	MS27	F	L(CTT)	T(ACC)	P	D	T	1.3A	A2*0201	A32*3201	B35*3503	B27*2708	Cw2*0202	Cw4*0401	DR15*1501	DR7*0701
41	MS28	M	L(CTT)	T(ACC)	P	N	T	1.3B	A3*0301	A3*0301	B14*1401	B15*1501	Cw3*0304	Cw8*0801	DR13*1301	DR4*0401
42	MS29	F	L(CTG)	T(ACT)	P	D	I	1.2	A1*0101	A2*0201	B35*3501	B57*5701	Cw7*0701	Cw6*0602	DR10*1001	DR7*0701

43	MS30	F	L(CTG)	T(ACT)	S	D	I	1.2	A26*2601	A11*1101	B51*5101	B51*5101	Cw15*1502	Cw12*1202	DR4*0403	DR14*1401
44	MS31	F	L(CTT)	T(ACC)	P	D	T	1.3B	A23*2301	A30*3001	B18*1807	B44*4403	Cw4*0401	Cw5*0501	DR3*0301	DR11*1101
45	MS32	F	L(CTT)	T(ACC)	P	N	T	1.3B	A2*0201	A23*2301	B7*0702	B7*0757	Cw4*0401	Cw7*0702	DR11*1101	DR8*0808
46	MS33	F	L(CTT)	T(ACC)	P	D	T	1.3B	A2*0201	A32*3201	B18*1801	B18*1801	Cw2*0201	Cw7*0701	DR16*1601	DR11*1101
47	MS34	F	L(CTG)	T(ACT)	T	N	I	1.2	A1*0101	A3*0301	B35*3501	B35*3501	Cw15*1502	Cw4*0401	DR7*0701	DR16*1601
48	MS35	F	L(CTT)	T(ACC)	P	D	T	1.3B	A24*2402	A32*3201	B51*5185	B18*1801	Cw15*1502	Cw12*1202	DR15*1501	DR11*1101
49	MS36	F	L(CTT)	T(ACC)	P	D	T	1.3A	A3*0301	A2*0201	B18*1807	B7*0702	Cw4*0401	Cw7*0702	DR15*1501	DR3*0301
50	MS37	M	L(CTT)	T(ACC)	P	D	T	GD1	A3*0301	A2*0201	B15*1501	B15*1501	Cw7*0704	Cw3*0303	DR7*0701	DR4*0403
51	MS38	F	L(CTT)	T(ACC)	P	D	T	GD1	A1*0101	A1*0101	B7*0705	B57*5701	Cw15*1502	Cw6*0602	DR1*0103	DR7*0701
52	MS39	F	L(CTT)	T(ACC)	P	D	T	1.3A	A2*0201	A30*3001	B44*4402	B51*5101	Cw2*0202	Cw14*1402	DR16*1601	DR4*0401
53	MS40	F	L(CTT)	T(ACC)	P	D	T	1.3B	--	--	--	--	--	--	--	--
54	MS41	F	L(CTT)	T(ACC)	P	D	T	1.3B	--	--	--	--	--	--	--	--
55	MS42	F	L(CTT)	T(ACC)	P	D	T	1.3B	--	--	--	--	--	--	--	--
56	MS43	M	L(CTT)	T(ACC)	P	D	T	1.3B	--	--	--	--	--	--	--	--
57	MS44	M	L(CTT)	T(ACC)	P	D	T	1.3B	--	--	--	--	--	--	--	--
58	MS45	F	L(CTG)	T(ACT)	P	D	I	1.2	--	--	--	--	--	--	--	--
59	MS46	F	L(CTG)	T(ACT)	P	D	I	1.2	--	--	--	--	--	--	--	--
60	MS47	F	L(CTG)	T(ACT)	P	D	I	1.2	--	--	--	--	--	--	--	--
61	MS48	F	L(CTG)	T(ACT)	P	D	I	1.2	--	--	--	--	--	--	--	--
62	MS49	F	L(CTG)	T(ACT)	T	D	I	1.2	--	--	--	--	--	--	--	--
63	MS50	M	L(CTT)	T(ACC)	P	D	T	1.3B	--	--	--	--	--	--	--	--
64	MS51	M	L(CTT)	T(ACC)	P	D	T	1.3B	--	--	--	--	--	--	--	--
65	MS52	F	L(CTG)	T(ACT)	P	D	I	1.2	--	--	--	--	--	--	--	--
66	MS53	F	L(CTT)	T(ACC)	P	D	T	1.3A	--	--	--	--	--	--	--	--

<sup>a</sup>Donors with samplings at multiple time points

EBNA2 = Epstein Barr Nuclear Antigen-2; HLA= Human leukocyte antigen; aa = amino acids; MS = multiple sclerosis; HD = healthy donors;

**Table e-2: Clinical data of patients with multiple sclerosis**

Disease type	50 RRMS, 2 PPMS 1 SPMS
Disease duration, years, range	1-29
Mean±SD	7.292 ± 0.9546
Median (IQR)	5 (2-11)
EDSS score range,	0-8
Mean±SD	2.033 ± 0.2875
Median (IQR)	1 (1-3)
Disease-modifying therapies	6 IFN-b, 1 GA, 4 Tysabri
Activity at MRI	13/53

RRMS = relapse–remitting; PPMS= primary progressive; SPMS = secondary progressive;

IQR= interquartile range; EDSS=Expanded Disability Status Scale; IFN-b= interferon beta;

GA= glatiramer acetate; MRI= Magnetic resonance imaging

**Table e-3: Variants of the EBV 1.1 allele detected in a post-mortem brain sample from a patient with MS by Illumina MiSeq platform.**

Nucleotide position <sup>a</sup>	1.1 (B95-8)	Variants	Frequency (%) <sup>b</sup>
412 (138)	AAT (Asn)	GAT (Asp)	100
529 (177)	ACC (Thr)	ATC (Iso)	99
531 (178)	CAC (His)	TAC (Tyr)	62
714 (238)	CTT (Leu)	CTG (Leu)	5

<sup>a</sup>Nucleotide position in the *EBNA2* coding sequence (amino acid positions are in parentheses) <sup>b</sup>Frequencies  $\geq 5\%$  were considered.