

**HLA associations differ by ethnicity and aquaporin-4 antibody status in
neuromyelitis optica spectrum disorders**

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eTable 1: HLA frequencies in White AQP4-IgG-positive patients with NMOSD and NMDP healthy controls (2-field resolution)

HLA allele	Allele frequency, n/total n (%)		Two-sided Fisher exact test			
	White AQP4-IgG+ NMOSD patients	NMDP European Caucasian	<i>p</i> -value	<i>p</i> -value after Bonferroni correction	Odds ratio	Confidence interval (95%)
DRB1*03:01	101 / 346 (29.2)	303265 / 2485780 (12.2)	3.07e-17	2.73E-14	2.97	2.33 – 3.76
B*08:01	89 / 342 (26.0)	283379 / 2485780 (11.4)	7.93e-14	7.04E-11	2.73	2.12 – 3.49
C*07:01	100 / 342 (29.2)	126616 / 791352 (16)	8.23e-10	7.31E-07	2.17	1.7 – 2.75
DRB1*13:01	5 / 346 (1.4)	139204 / 2485780 (5.6)	1.53e-04	0.14	0.25	0.08 – 0.58
DRB1*07:01	25 / 346 (7.2)	333095 / 2485780 (13.4)	3.63e-04	0.32	0.50	0.32 – 0.76
A*01:01	82 / 344 (23.8)	410154 / 2485780 (16.5)	4.63e-04	0.41	1.58	1.22 – 2.04
C*03:04	12 / 342 (3.5)	59351 / 791352 (7.5)	3.75e-03	n.s.	0.45	0.23 – 0.79
B*40:01	7 / 342 (2.0)	131746 / 2485780 (5.3)	5.02e-03	n.s.	0.37	0.15 – 0.78
B*15:01	10 / 342 (2.9)	151633 / 2485780 (6.1)	0.01	n.s.	0.46	0.22 – 0.86
DRB1*04:01	18 / 346 (5.2)	218749 / 2485780 (8.8)	0.02	n.s.	0.57	0.33 – 0.91
B*44:03	8 / 342 (2.3)	116832 / 2485780 (4.7)	0.04	n.s.	0.49	0.21 – 0.97
A*11:01	12 / 344 (3.5)	151633 / 2485780 (6.1)	0.04	n.s.	0.56	0.28 – 0.99

The table lists all HLA alleles with uncorrected p -values <0.05 . HLA alleles with p -values <0.05 after Bonferroni correction are highlighted in bold.

AQP4-IgG = aquaporin-4 immunoglobulin G; NMDP = national marrow donor program; NMOSD = neuromyelitis optica spectrum disorders; n.s. = not significant ($p>1$)

eTable 2: HLA frequencies in White AQP4-IgG-positive patients with NMOSD and PopGen healthy controls (2-field resolution)

HLA allele	Allele frequency, n/total n (%)		Two-sided Fisher exact test			
	White AQP4-IgG+ NMOSD patients	Healthy controls (PopGen cohort)	<i>p</i> -value	<i>p</i> -value after Bonferroni correction	Odds ratio	Confidence interval (95%)
DQB1*02:01	104 / 348 (29.9)	284 / 2438 (11.6)	5.8e-17	5.15E-14	3.23	2.46 – 4.22
DRB1*03:01	101 / 346 (29.2)	280 / 2422 (11.6)	5.61e-16	4.98E-13	3.15	2.4 – 4.13
B*08:01	89 / 342 (26)	281 / 2436 (11.5)	1.21e-11	1.07E-08	2.70	2.03 – 3.56
C*07:01	100 / 342 (29.2)	359 / 2438 (14.7)	2.64e-10	2.34E-07	2.39	1.83 – 3.12
DQB1*06:03	7 / 348 (2.0)	181 / 2408 (7.5)	3.17e-05	0.03	0.25	0.1 – 0.54
B*15:01	10 / 342 (2.9)	219 / 2436 (9.0)	3.42e-05	0.03	0.31	0.14 – 0.58
C*03:04	12 / 342 (3.5)	232 / 2434 (9.5)	8.89e-05	0.08	0.35	0.17 – 0.62
DRB1*14:54	19 / 346 (5.5)	44 / 2406 (1.8)	1.52e-04	0.13	3.12	1.7 – 5.53
DQB1*03:02	18 / 348 (5.2)	266 / 2434 (10.9)	5.98e-04	0.53	0.44	0.26 – 0.73
DQB1*05:03	21 / 348 (6.0)	60 / 2438 (2.5)	8.62e-04	0.77	2.54	1.45 – 4.31
B*40:01	7 / 342 (2.0)	145 / 2426 (6.0)	1.4e-03	n.s.	0.33	0.13 – 0.7
A*01:01	82 / 344 (23.8)	415 / 2438 (17.0)	2.61e-03	n.s.	1.53	1.15 – 2.01
DQB1*02:02	13 / 348 (3.7)	193 / 2434 (7.9)	4.17e-03	n.s.	0.45	0.23 – 0.8

C*03:03	11 / 342 (3.2)	166 / 2434 (6.8)	8.92e-03	n.s.	0.45	0.22 – 0.85
DRB1*07:01	25 / 346 (7.2)	281 / 2418 (11.6)	0.01	n.s.	0.59	0.37 – 0.91
DRB1*04:01	18 / 346 (5.2)	207 / 2404 (8.6)	0.03	n.s.	0.58	0.33 – 0.96

The table lists all HLA alleles with uncorrected p -values <0.05 . HLA with p -values <0.05 after Bonferroni correction are highlighted in bold.

AQP4-IgG = aquaporin-4 immunoglobulin G; NMOSD = neuromyelitis optica spectrum disorders; n.s. = not significant ($p>1$)

eTable 3: HLA allele frequencies in Hispanic AQP4-IgG-positive patients with NMOSD and NMDP healthy controls (2-field resolution)

HLA allele	Allele frequency, n/total n (%)		Two-sided Fisher exact test			
	Hispanic AQP4-IgG+ NMOSD patients	Hispanic South or Central American healthy controls (NMDP)	<i>p</i> -value	<i>p</i> -value after Bonferroni correction	Odds ratio	Confidence interval (95%)
B*08:01	9 / 82 (11)	11444 / 293428 (3.9)	4.7e-03	n.s.	3.04	1.34 – 6.09
DRB1*16:02	6 / 82 (7.3)	6455 / 293428 (2.2)	9.58e-03	n.s.	3.51	1.25 – 8
DRB1*03:01	12 / 82 (14.6)	20540 / 293428 (7)	0.01	n.s.	2.28	1.12 – 4.24
DRB1*04:07	1 / 82 (1.2)	22007 / 293428 (7.5)	0.02	n.s.	0.15	0 – 0.87
A*30:02	6 / 82 (7.3)	7923 / 293428 (2.7)	0.02	n.s.	2.84	1.01 – 6.49
DQB1*03:02	8 / 82 (9.8)	2236 / 11528 (19.4)	0.02	n.s.	0.45	0.19 – 0.93
DQB1*05:02	4 / 82 (4.9)	161 / 11528 (1.4)	0.03	n.s.	3.62	0.95 – 9.82

The table lists all HLA alleles with uncorrected *p*-values <0.05.

AQP4-IgG = aquaporin-4 immunoglobulin G; NMDP = national marrow donor program; NMOSD = neuromyelitis optica spectrum disorder; n.s. = not significant (*p*>1)

eTable 4: HLA allele frequencies in Black AQP4-IgG-positive patients with NMOSD and NMDP healthy controls (2-field resolution)

HLA allele	Allele frequency, n/total n (%)		Two-sided Fisher exact test			
	Black AQP4-IgG+ NMOSD patients	USA African American pop 2 (NMDP)	<i>p</i> -value	<i>p</i> -value after Bonferroni correction	Odds ratio	Confidence interval (95%)
DRB1*08:04	17 / 88 (19.3)	1650 / 32356 (5.1)	2.12e-06	1.88e-03	4.46	2.45 – 7.66
DRB1*03:01	16 / 88 (18.2)	2297 / 32356 (7.1)	4.49e-04	0.40	2.91	1.58 – 5.06
B*08:01	10 / 88 (11.4)	31660 / 833162 (3.8)	1.9e-03	n.s.	3.25	1.5 – 6.29
DRB1*07:01	1 / 88 (1.1)	3171 / 32356 (9.8)	1.96e-03	n.s.	0.11	0 – 0.61
C*04:01	28 / 88 (31.8)	36980 / 199892 (18.5)	2.36e-03	n.s.	2.06	1.26 – 3.27
A*33:03	10 / 88 (11.4)	37492 / 833162 (4.5)	6.24e-03	n.s.	2.72	1.26 – 5.28
B*53:01	18 / 88 (20.5)	93314 / 833162 (11.2)	0.01	n.s.	2.04	1.14 – 3.46
A*68:01	8 / 88 (9.1)	30827 / 833162 (3.7)	0.02	n.s.	2.60	1.09 – 5.38
B*15:10	7 / 88 (8.0)	24995 / 833162 (3.0)	0.02	n.s.	2.79	1.09 – 6.03

The table lists all HLA alleles with uncorrected *p*-values <0.05. HLA alleles with *p*-values <0.05 after Bonferroni correction are highlighted in bold.

AQP4-IgG = aquaporin-4 immunoglobulin G; NMDP = national marrow donor program; NMOSD = neuromyelitis optica spectrum disorders; n.s. = not significant (*p*>1)

eTable 5: HLA frequencies in White AQP4-IgG-negative patients with NMOSD and INDIGO healthy controls (3-field resolution)

HLA allele	Allele frequency, n/total n (%)		Two-sided Fisher exact test			
	White AQP4-IgG- NMOSD patients	White healthy controls (INDIGO)	<i>p</i> -value	<i>p</i> -value after Bonferroni correction	Odds ratio	Confidence interval (95%)
C*07:01:01	25 / 96 (26)	655 / 4668 (14)	1.84e-03	n.s.	2.16	1.3 – 3.47
DRB4*01:01:01	8 / 96 (8.3)	80 / 2687 (3)	9.89e-03	n.s.	2.96	1.2 – 6.38
B*35:01:01	12 / 96 (12.5)	276 / 4700 (5.9)	1.41e-02	n.s.	2.29	1.12 – 4.28
DRB1*01:03	4 / 96 (4.2)	51 / 4590 (1.1)	2.54e-02	n.s.	3.87	0.99 – 10.86
B*49:01:01	5 / 96 (5.2)	79 / 4700 (1.7)	2.58e-02	n.s.	3.21	0.99 – 8.09
C*04:01:01	18 / 96 (18.8)	530 / 4668 (11.4)	3.40e-02	n.s.	1.80	1.01 – 3.07
B*18:01:01	9 / 96 (9.4)	214 / 4700 (4.6)	4.32e-02	n.s.	2.17	0.95 – 4.39

The table lists all HLA alleles with uncorrected *p*-values <0.05.

AQP4-IgG = aquaporin-4 immunoglobulin G; n = number; INDIGO = UCSF Multiple Sclerosis Biorepository, The Immunogenetics of Neurological Diseases working GrOup; NMOSD = neuromyelitis optica spectrum disorders; n.s. = not significant (*p*>1)

eTable 6: HLA frequencies in White AQP4-IgG negative NMOSD patients and NMDP healthy controls (2-field resolution)

HLA allele	Allele frequency, n/total n (%)		Two-sided Fisher exact test			
	White AQP4-IgG- NMOSD patients	European Caucasian healthy controls (NMDP)	<i>p</i> -value	<i>p</i> -value after Bonferroni correction	Odds ratio	Confidence interval (95%)
B*35:01	12 / 96 (12.5)	139204 / 2485780 (5.6)	0.01	n.s.	2.41	1.2 – 4.43
C*07:01	25 / 96 (26)	126616 / 791352 (16)	0.01	n.s.	1.85	1.12 – 2.95
C*04:01	18 / 96 (18.8)	83883 / 791352 (10.6)	0.02	n.s.	1.95	1.1 – 3.28
B*49:01	5 / 96 (5.2)	39772 / 2485780 (1.6)	0.02	n.s.	3.38	1.07 – 8.18
DRB1*01:03	4 / 96 (4.2)	29829 / 2485780 (1.2)	0.03	n.s.	3.58	0.96 – 9.48
C*06:02	3 / 96 (3.1)	73596 / 791352 (9.3)	0.03	n.s.	0.31	0.06 – 0.95
B*18:01	9 / 96 (9.4)	109374 / 2485780 (4.4)	0.04	n.s.	2.25	0.99 – 4.47

The table lists all HLA alleles with uncorrected *p*-values <0.05.

AQP4-IgG = aquaporin-4 immunoglobulin G; n = number; NMDP = National Marrow Donor Program; NMOSD = neuromyelitis optica spectrum disorders; n.s. = not significant ($p>1$)

eTable 7: Comparison of White AQP4-IgG-positive patients with NMOSD vs. INDIGO White controls restricted to HLA-DRB1*03:01:01 non-carriers

	Allele frequency in DRB1*03:01:01-negative individuals, n/total n (%)		Two-sided Fisher exact test			
HLA allele	White AQP4-IgG+ NMOSD patients	White healthy controls (INDIGO)	<i>p</i> -value	<i>p</i> -value after Bonferroni correction	Odds ratio	Confidence interval (95%)
DQA1*01:04:01	12 / 164 (7.0%)	88 / 3346 (3.0%)	2.1e-03	n.s.	2.92	1.42 – 5.51
DQB1*05:03:01	12 / 166 (7.0%)	93 / 3300 (3.0%)	3.9e-03	n.s.	2.69	1.31 – 5.06
DQB1*02:02:01	8 / 166 (5.0%)	376 / 3300 (11.0%)	7.2e-03	n.s.	0.39	0.17 – 0.80
DRB1*14:54:01	9 / 166 (5.0%)	78 / 3574 (2.0%)	0.01	n.s.	2.57	1.11 – 5.26
DPB1*104:01	7 / 166 (4.0%)	60 / 3376 (2.0%)	0.04	n.s.	2.43	0.92 – 5.44

The table lists all HLA alleles with uncorrected *p*-values <0.05 in DRB1*03:01:01-negative White AQP4-IgG+ patients with NMOSD with frequencies of ≥1% in patients and controls. *P*-values calculated using Fisher's exact test.

INDIGO = UCSF Multiple Sclerosis Biorepository, The Immunogenetics of Neurological Diseases working GrOup; AQP4-IgG = aquaporin-4 immunoglobulin G; n = number; NMOSD = neuromyelitis optica spectrum disorders

eTable 8: Comparison of Hispanic AQP4-IgG-positive patients with NMOSD vs. INDIGO Hispanic controls restricted to HLA-DRB1*03:01:01 non-carriers

	Allele frequency in DRB1*03:01:01-negative individuals, n/total n (%)		Two-sided Fisher exact test			
HLA allele	Hispanic AQP4-IgG+ NMOSD patients	Hispanic healthy controls (INDIGO)	<i>p</i> -value	<i>p</i> -value after Bonferroni correction	Odds ratio	Confidence interval (95%)
DPA1*01:03:01	37 / 58 (64.0%)	236 / 288 (82.0%)	4.20e-03	n.s.	0.39	0.20 – 0.76
DPB1*04:02:01	12 / 58 (21.0%)	116 / 288 (40.0%)	4.60e-03	n.s.	0.39	0.18 – 0.78
DRB1*04:07:01	1 / 58 (2.0%)	37 / 288 (13.0%)	0.01	n.s.	0.12	0.00 – 0.74
DQB1*03:02:01	7 / 58 (12.0%)	81 / 288 (28.0%)	0.01	n.s.	0.35	0.13 – 0.82
DQA1*03:01:01	7 / 58 (12.0%)	77 / 288 (27.0%)	0.02	n.s.	0.38	0.14 – 0.88
A*30:02:01	4 / 58 (7.0%)	4 / 288 (1.0%)	0.03	n.s.	5.22	0.94 – 28.96
DPA1*02:02:02	5 / 58 (9.0%)	7 / 288 (2.0%)	0.03	n.s.	3.77	0.91 – 14.39
DPB1*05:01:01	4 / 58 (7.0%)	5 / 288 (2.0%)	0.05	n.s.	4.17	0.80 – 20.05

The table lists all HLA alleles with uncorrected *p*-values <0.05 in DRB1*03:01:01-negative Hispanic AQP4-IgG+

patients with NMOSD with frequencies of $\geq 1\%$ in patients and controls. *P*-values calculated using Fisher's exact test.

INDIGO = UCSF Multiple Sclerosis Biorepository, The Immunogenetics of Neurological Diseases working GrOup; AQP4-IgG = aquaporin-4 immunoglobulin G; n = number; NMOSD = neuromyelitis optica spectrum disorders

eTable9: Relative Predisposition Effects (RPE) in White AQP4-IgG-positive patients with NMOSD and INDIGO White controls

Locus	Step	Allele	Direction	White AQP4-IgG+ NMOSD patients	White healthy controls (INDIGO)	Chi- square	p-value	Odd's ratio	CI (95%)	K alleles remaining
A	1	A*01:01:01	↑ (increased)	82 / 312 (26.3%)	752 / 4326 (17.4%)	22.18	0.02	1.69	1.28–2.22	12
B	1	B*08:01:01	↑ (increased)	89 / 295 (30.2%)	490 / 3953 (12.4%)	90.00	1.45e-11	3.05	2.31–4.01	19
C	1	C*07:01:01	↑ (increased)	95 / 328 (29.0%)	655 / 4444 (14.7%)	60.11	2.41e-07	2.36	1.81–3.05	16
DPA1	1	DPA1*02:01:02	↑ (increased)	26 / 336 (7.7%)	189 / 4490 (4.2%)	13.11	4.40e-03	1.91	1.20–2.94	4
DPB1	1	DPB1*05:01:01	↑ (increased)	14 / 316 (4.4%)	96 / 4131 (2.3%)	21.55	0.01	1.95	1.01–3.48	10
DPB1	2	DPB1*01:01:01	↑ (increased)	27 / 302 (8.9%)	229 / 4035 (5.7%)	16.46	0.04	1.63	1.03–2.49	9
DQA1	1	DQA1*05:01:01	↑ (increased)	104 / 308 (33.8%)	504 / 3702 (13.6%)	126.58	5.98e-23	3.23	2.48–4.20	10
DQA1	2	DQA1*01:04:01	↑ (increased)	21 / 204 (10.3%)	102 / 3198 (3.2%)	46.30	2.08e-07	3.48	2.02–5.77	9
DQA1	3	DQA1*01:03:01	↓ (decreased)	7 / 183 (3.8%)	306 / 3096 (9.9%)	19.82	5.97e-03	0.36	0.14–0.77	8
DQB1	1	DQB1*02:01:01	↑ (increased)	104 / 342 (30.4%)	510 / 4324 (11.8%)	138.07	4.03e-24	3.27	2.52–4.21	12
DQB1	2	DQB1*05:03:01	↑ (increased)	21 / 238 (8.8%)	107 / 3814 (2.8%)	51.56	1.38e-07	3.35	1.95–5.51	11
DQB1	3	DQB1*02:02:01	↓ (decreased)	13 / 217 (6.0%)	459 / 3707 (12.4%)	26.49	1.70e-03	0.45	0.23–0.80	10
DQB1	4	DQB1*06:03:01	↓ (decreased)	7 / 204 (3.4%)	281 / 3248 (8.7%)	17.46	0.03	0.38	0.15–0.80	9
DRB1	1	DRB1*03:01:01	↑ (increased)	101 / 311 (32.5%)	531 / 3885 (13.7%)	121.03	1.26e-19	3.04	2.33–3.94	14
DRB1	2	DRB1*14:54:01	↑ (increased)	19 / 210 (9.0%)	89 / 3354 (2.7%)	51.25	8.43e-07	3.65	2.05–6.19	13
DRB1	3	DRB1*01:01:01	↑ (increased)	36 / 191 (18.8%)	386 / 3265 (11.8%)	25.22	8.46e-03	1.73	1.15–2.55	12
DRBO	1	DRB3*01:01:02	↑ (increased)	97 / 284 (34.2%)	372 / 1952 (19.1%)	41.22	2.62e-07	2.20	1.66–2.91	7

The table shows the results of an RPE analysis, identifying HLA alleles sequentially enriched or decreased in White patients with AQP4-IgG-positive NMOSD compared to respective controls. A frequency filter ($\geq 1\%$ in patients and controls) was applied before testing to exclude rare alleles. Each step represents the allele with the largest residual deviation at the respective locus. Only alleles with $p < 0.05$ are listed. K alleles remaining denotes the number of alleles still included in the analysis at that step.

AQP4-IgG = aquaporin-4 immunoglobulin G; n = number; NMOSD = neuromyelitis optica spectrum disorders; INDIGO = UCSF Multiple Sclerosis Biorepository, The Immunogenetics of Neurological Diseases working GrOup; p-value calculated with Chi-square test.

eTable 10: Relative Predisposition Effects in Hispanic AQP4-IgG-positive patients with NMOSD vs. INDIGO Hispanic controls

Locus	Step	Allele	Direction	Hispanic AQP4-IgG+ NMOSD patients	Hispanic healthy controls (INDIGO)	Chi-square	p-value	Odd's ratio	CI (95%)	K alleles remaining
A	1	A*03:01:01	↑ (increased)	11 / 76 (14.5%)	13 / 266 (4.9%)	27.65	0.03	3.28	1.27–8.35	17
DQA1	1	DQA1*05:01:01	↑ (increased)	14 / 81 (17.3%)	12 / 299 (4.0%)	41.99	6.58e-05	4.97	2.03–12.36	14
DQA1	2	DQA1*03:01:01	↓ (decreased)	8 / 67 (11.9%)	82 / 287 (28.6%)	26.65	8.69e-03	0.34	0.13–0.76	13
DQB1	1	DQB1*02:01:01	↑ (increased)	14 / 81 (17.3%)	12 / 297 (4.0%)	39.81	1.83e-05	4.93	2.02–12.27	11
DQB1	2	DQB1*03:02:01	↓ (decreased)	8 / 67 (11.9%)	86 / 285 (30.2%)	24.45	3.64e-03	0.31	0.12–0.70	10
DRB1	1	DRB1*03:01:01	↑ (increased)	12 / 64 (18.8%)	11 / 251 (4.4%)	41.96	3.99e-04	5.00	1.90–13.28	17
DRB1	2	DRB1*04:07:01	↓ (decreased)	1 / 52 (1.9%)	37 / 240 (15.4%)	29.21	0.02	0.11	0.00–0.67	16
DRBO	1	DRB4*01:03:01	↓ (decreased)	8 / 80 (10.0%)	96 / 289 (33.2%)	25.94	5.17e-04	0.22	0.09–0.49	8

The table shows the results of an RPE analysis, identifying HLA alleles sequentially enriched or decreased in Hispanic patients with AQP4-IgG-positive NMOSD compared to respective controls. A frequency filter ($\geq 1\%$ in patients and controls) was applied before

testing to exclude rare alleles. Each step represents the allele with the largest residual deviation at the respective locus. Only alleles with $p < 0.05$ are listed. K alleles remaining denotes the number of alleles still included in the analysis at that step.

AQP4-IgG = aquaporin-4 immunoglobulin G; n = number; NMOSD = neuromyelitis optica spectrum disorders; INDIGO = UCSF Multiple Sclerosis Biorepository, The Immunogenetics of Neurological Diseases working GrOup; p-value calculated with Chi-square test.

eTable 11: Relative Predisposition Effects in Black AQP4-IgG-positive patients with NMOSD vs. INDIGO Black controls

Locus	Step	Allele	Direction	Black AQP4-IgG+ NMOSD patients	Black healthy controls (INDIGO)	Chi-square	p-value	Odd's ratio	CI (95%)	K alleles remaining
B	1	B*08:01:01	↑ (increased)	10 / 76 (13.2%)	15 / 361 (4.2%)	30.86	0.02	3.48	1.34–8.70	18
DPB1	1	DPB1*17:01	↑ (increased)	7 / 80 (8.8%)	7 / 354 (2.0%)	18.17	0.03	4.73	1.37–16.33	10
DQA1	1	DQA1*04:01:02	↑ (increased)	14 / 86 (16.3%)	18 / 459 (3.9%)	41.87	3.50e-05	4.74	2.08–10.61	13
DQA1	2	DQA1*05:01:01	↑ (increased)	18 / 72 (25.0%)	34 / 441 (7.7%)	24.07	0.01	3.98	1.97–7.83	12
DQB1	1	DQB1*03:19:01	↑ (increased)	18 / 88 (20.5%)	34 / 448 (7.6%)	33.86	7.10e-04	3.12	1.57–6.06	13
DQB1	2	DQB1*02:01:01	↑ (increased)	17 / 70 (24.3%)	33 / 414 (8.0%)	22.14	0.02	3.69	1.80–7.38	12
DRB1	1	DRB1*08:04:01	↑ (increased)	17 / 81 (21.0%)	28 / 420 (6.7%)	42.11	1.72e-03	3.71	1.79–7.48	20
DRBO	1	DRB3*01:01:02	↑ (increased)	16 / 59 (27.1%)	53 / 390 (13.6%)	13.20	0.02	2.36	1.16–4.65	6

The table shows the results of an RPE analysis, identifying HLA alleles sequentially enriched or decreased in Black patients with AQP4-IgG-positive NMOSD compared to respective controls. A frequency filter ($\geq 1\%$ in patients and controls) was applied before testing to exclude rare alleles. Each step represents the allele with the largest residual deviation at the respective locus. Only alleles with $p < 0.05$ are listed. K alleles remaining denotes the number of alleles still included in the analysis at that step.

AQP4-IgG = aquaporin-4 immunoglobulin G; n = number; NMOSD = neuromyelitis optica spectrum disorders; INDIGO = UCSF Multiple Sclerosis Biorepository, The Immunogenetics of Neurological DIseases working GrOup; p-value calculated with Chi-square test.

eTable 12: Genotypes in White AQP4-IgG-positive patients with NMOSD vs. INDIGO White controls

model	allele(s)	Genotype freq., n/total n (%) pts.	Genotype freq., n/total n (%) cls.	Odds Ratio	95% CI	p-value (FE)	Exp. AA (pts.)	Exp. AA (cls.)
Homozygous	DRB1*03:01:01	11 / 173 (6.4)	28 / 2295 (1.2)	5.49	2.42 - 11.63	4.35e-5	14.74	30.71
Heterozygous	DRB1*03:01:01	79 / 173 (45.7)	475 / 2295 (20.7)	3.22	2.31 - 4.47	2.20e-12		
Homozygous	B*08:01:01	7 / 171 (4.1)	20 / 2350 (0.9)	4.97	1.75 - 12.45	0.0016	11.58	25.54
Heterozygous	B*08:01:01	75 / 171 (43.9)	450 / 2350 (19.1)	3.30	2.36 - 4.59	1.66e-12		
Co-occurrence (unphased)	DRB1*03:01:01~DQA1*05:01:01 ~DQB1*02:01:01	90 / 172 (52.3)	460 / 2103 (21.9)	3.92	2.82 - 5.45	9.54e-17		
Co-occurrence (unphased)	A*01:01:01~B*08:01:01~ C*07:01:01~DRB1*03:01:01~ DQA1*05:01:01~DQB1*02:01:01 ~DRB3*01:01:02	50 / 169 (29.6)	137 / 1066 (12.9)	2.85	1.91 - 4.20	1.97e-7		

Genotype associations of DRB1*03:01:01, B*08:01:01 shown as homozygous (AA) and heterozygous (Aa), and unphased co-occurrences of DRB1*03~DQA1*05~DQB1*02 haplotype and the extended ancestral haplotype 8.1 in White AQP4-positive patients. Co-occurrence indicates presence of at least 1 allele per respective locus.

INDIGO = UCSF Multiple Sclerosis Biorepository, The Immunogenetics of Neurological Diseases working GrOup; pts. = patients; cls. = controls; AQP4-IgG = aquaporin-4 immunoglobulin G; AA = homozygote; Aa= heterozygote; n = number; NMOSD = neuromyelitis optica spectrum disorders; FE = Fisher's exact test; Exp. AA = expected number of homozygotes under Hardy-Weinberg equilibrium.