

Supplemental Table 1. Comparison of disease phenotypes between African American and Caucasian patients with ANCA disease

Characteristic	African American (n = 58)	Caucasian (n = 449)	P ^y
Age, years*	50.6±19.9	57.4±17.8	0.009
Time (months) follow-up	21.58	27.63	0.56
Male/Female	28/30	238/211	0.50
ANCA phenotype*			0.02
PR3 ANCA seropositive	18 (31%)	209 (48%)	
MPO ANCA seropositive	40 (69%)	230 (52%)	
Disease type [§]			0.13
Granulomatosis	15 (26%)	102 (23%)	
Microscopic polyangiitis	24 (41%)	242 (54%)	
Kidney-limited disease	19 (33%)	101 (23%)	
Serum creatinine level, mg/dL	5.3±3.9	4.5±3.4	0.16
Treatment resistance [†]	20 (40%)	92 (22%)	0.0008
Relapse (given a remission) [‡]	11 (37%)	132 (40%)	0.85
Renal biopsy [#] : Activity index	6.00	5.00	0.60
Renal biopsy: Chronicity index	3.00	6.00	0.05
Renal biopsy: Vascular sclerosis	1.00	1.00	0.35
Number (%) of patients with ESKD	22 (38%)	99 (22%)	0.01
Time (months) to ESKD [*]	4.6	13.6	0.01
Number (%) of deceased patients	4 (7%)	33 (7%)	0.90
Time (months) to death	30.9	33.0	0.77

*Descriptive data represented as mean±SD, median or n (%)

^y P-values were calculated using Wilcoxon rank sum test for continuous variables and Chi-square test or Fisher's exact test for categorical data.

* The group of patients with PR3-ANCA included those with PR3 and/or cytoplasmic ANCA.

MPO-ANCA included MPO and/or perinuclear ANCA. In Caucasian cohorts, four patients who had negative ANCA and six patients with target antigen specificities to both MPO and PR3 were excluded.

§ Four patients with Churg Strauss Syndrome in the Caucasian cohorts were excluded due to the small number.

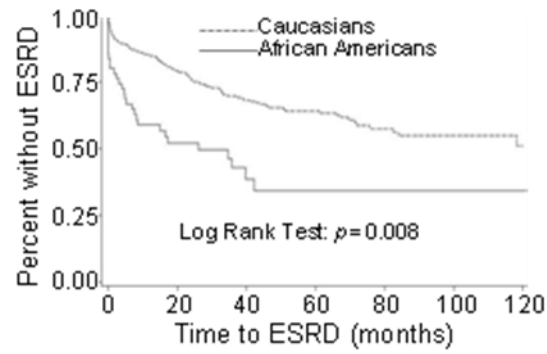
† In the African American cohort, 50 patients were treated; in the Caucasian cohort, 421 patients were treated.

‡ Percentages of patients who experienced a relapse are based on the numbers of patients in whom remission was achieved (30 in the African American cohort with 1 missing data and 329 in the Caucasian cohort with 2 missing data).

In the African American cohort, 46 patients had the renal biopsy data; In the Caucasian cohort, 354 had the renal biopsy data.

*Mean months to ESKD and death is among those who reached these endpoints.

All patients had biopsy-proven vasculitis with positive ANCA titers. Phenotypic comparisons between Caucasians and African Americans indicated that, for African American patients, disease onset occurs at an earlier age (50.6±19.9 versus 57.4±17.8, $p=0.009$), MPO-ANCA positivity is more frequent (69% vs. 52%, $p=0.02$), resistance to initial treatment is more common (40% versus 22%, $p=0.0008$), and progression to end-stage kidney disease (ESKD) is more frequent (38% vs. 22%, $p=0.01$) and on average 9-months faster ($p=0.01$). There were no substantial differences by race in gender, disease phenotype (or organ involvement, data not shown), disease relapse (given an initial response to treatment) or death (Table 1).



Supplemental Figure 1. Kaplan–Meier curve of kidney survival reflect a racial effect. Log-rank analysis tested the null hypothesis that survivor functions are statistically different between the two racial groups ($p=0.008$), with African Americans progressing to end-stage kidney disease faster than Caucasians.

Supplemental Table 2. Frequencies of *DRB1* and *DQB* haplotypes

<i>DRB1</i> genotype	HLA-DR serotype	DR-DQ haplotype	African American Allele frequency		Caucasian Allele frequency	
			PR3 ANCA (2n = 32) (%)	MPO ANCA (2n = 50) (%)	PR3 ANCA (2n = 148) (%)	MPO ANCA (2n = 44) (%)
<i>DRB1*01</i>	DR1	DR1-DQ5	3.1	8.0	10.1	15.9
		DR1-DQ7			0.7	
<i>DRB1*03</i>	DR17	DR17-DQ2	6.3	6.0	16.2	13.6
<i>DRB1*03</i>	DR18	DR18-DQ4		6.0	0.7	
<i>DRB1*04</i>	DR4	DR4-DQ2	3.1			
		DR4-DQ4		2.0	0.7	
		DR4-DQ7	9.4	6.0	10.8	20.5
		DR4-DQ8			6.8	6.8
<i>DRB1*07</i>	DR7	DR7-DQ2		8.0	8.1	4.5
		DR7-DQ9	3.1	2.0	4.1	4.5
<i>DRB1*08</i>	DR8	DR8-DQ4			2.0	4.5
		DR8-DQ7		10.0		
<i>DRB1*09</i>	DR9	DR9-DQ2	3.1	2.0		
		DR9-DQ9				2.3
<i>DRB1*10</i>	DR10	DR10-DQ5		2.0	0.7	2.3
<i>DRB1*11</i>	DR11	DR11-DQ5		2.0		
		DR11-DQ7	6.3	12.0	8.8	2.3
<i>DRB1*12</i>	DR12	DR12-DQ7		2.0	0.7	2.3
<i>DRB1*13</i>	DR13	DR13-DQ2		4.0		
		DR13-DQ5	3.1	2.0		
		DR13-DQ6	3.1	10.0	4.1	6.8
		DR13-DQ7	3.1	4.0	1.4	
<i>DRB1*14</i>	DR14	DR14-DQ5		2.0	4.1	2.3
<i>DRB1*15*</i>	DR15	DR15-DQ5		2.0		
		DR15-DQ6	56.3	4.0	20.3	9.1
<i>DRB1*16</i>	DR16	DR16-DQ5		2.0		2.3
		DR16-DQ7		2.0		

*Of note: *DRB1*15* homozygotes included 3 African Americans and 7 Caucasians

Supplemental Table 3. Relative Predispositional Effects (RPEs) analysis of *HLA-DRB1* alleles in ANCA disease compared to local community controls (Carolina Organ Donor Services).

(3a) African American patients (n=41)

DRB1 Allele	Patients	Controls	Round 1 of comparison		^a Round 2: *15 removed		^b Round 3: *15 and *16 removed	
			χ^2	P	χ^2	P	χ^2	P
*01	5	31	3.51	0.06	1.99	0.16	1.79	0.18
*03	8	29	0.72	0.40	0.11	0.74	0.06	0.81
*04	8	17	0.21	0.65	0.90	0.34	1.05	0.30
*07	6	19	0.19	0.66	0.00	0.99	0.01	0.94
*08	5	20	0.77	0.38	0.21	0.65	0.15	0.69
*09	2	5	0.00	0.97	0.08	0.77	0.11	0.74
*10	1	4	0.15	0.69	0.04	0.84	0.03	0.86
*11	9	25	0.03	0.85	0.12	0.73	0.19	0.66
*12	1	12	2.64	0.10	1.88	0.17	1.78	0.18
*13	13	28	0.30	0.59	1.37	0.24	1.61	0.20
*14	1	4	0.15	0.69	0.04	0.84	0.03	0.86
*15	21	18	13.06	0.0003	----	----	----	----
*16	2	0	5.17	0.02	6.36	0.01	----	----
Total	82	212	26.91	0.01	----	----	----	----
^a Total					13.1	0.29	----	----
					^b Total		6.81	0.74

^a Total minus the number of *15 alleles=61; ^b Total minus the number of *15 and *16 alleles=59

The overall χ^2 was significant ($p=0.01$), due to the *DRB1**15 ($p=0.0003$) and *DRB1**16 alleles ($p=0.02$). Removal of *DRB1**15 increased the significance of *DRB1**16 ($p=0.01$). Removal of *DRB1**15 and 16 produced non-significant results and the procedure was stopped.

(3b) Caucasian patients (n=96)

DRB1 Allele	Patients	Controls	Round 1 of comparison		^a Round 2: *15 removed		^b Round 3: *15 and *14 removed		^c Round 4: *15, *14 and *03 removed	
			χ^2	P	χ^2	P	χ^2	P	χ^2	P
*01	23	104	4.12	0.04	2.42	0.12	1.94	0.16	0.85	0.36
*03	31	57	3.88	0.05	6.07	0.01	6.95	0.01	----	----
*04	39	150	2.84	0.09	1.18	0.28	0.77	0.38	0.08	0.78
*07	22	71	0.27	0.60	0.01	0.94	0.01	0.94	0.26	0.61
*08	5	16	0.05	0.82	0.00	0.98	0.00	0.96	0.07	0.79
*09	1	6	0.50	0.48	0.36	0.55	0.32	0.57	0.21	0.64
*10	2	7	0.07	0.80	0.02	0.90	0.01	0.94	0.00	0.96
*11	14	34	0.25	0.62	0.70	0.40	0.91	0.34	1.69	0.19
*12	2	2	1.20	0.27	1.48	0.22	1.59	0.21	1.93	0.16
*13	11	43	0.89	0.34	0.39	0.53	0.27	0.61	0.04	0.84
*14	7	4	8.09	0.004	9.47	0.002	----	----	----	----
*15	34	46	11.29	0.0008	----	----	----	----	----	----
*16	1	6	0.50	0.48	0.36	0.55	0.32	0.57	0.21	0.64
Total	192	546	33.96	0.0006	----	----	----	----	----	----
^a Total					22.46	0.02	----	----	----	----
					^b Total		13.09	0.22	----	----
					^c Total		5.35	0.80	----	----

^a Total minus the number of *15 alleles=158; ^b Total minus the number of *15 and *14 alleles=151; ^c Total minus the number of *15, *14 and *03 alleles=120

Caucasian patients compared to local community controls also identified *DRB1**15 allele as a significant contributor to disease ($p=0.0008$) Other significant alleles included *DRB1**01, *03 and *14. *DRB1**01 frequency was significantly higher in the control group implying a protective effect. After *DRB1**15 was removed, *DRB1**03 and *14 remained significant.

(3c) African American patients with PR3-ANCA serology (n=16)

DRB1 Allele	Patients	Controls	Round 1 of comparison		^a Round 2: *15 removed		^b Round 3: *15 and *04 removed	
			χ^2	P	χ^2	P	χ^2	P
*01	1	31	2.80	0.09	0.66	0.42	0.31	0.58
*03	2	29	1.21	0.27	0.00	0.95	0.07	0.78
*04	4	17	0.65	0.42	5.07	0.02	----	----
*07	1	19	1.16	0.28	0.10	0.76	0.00	0.94
*08	0	20	3.02	0.08	1.44	0.23	1.13	0.29
*09	1	5	0.07	0.80	0.94	0.33	1.52	0.22
*10	0	4	0.60	0.44	0.29	0.59	0.23	0.63
*11	2	25	0.77	0.38	0.02	0.89	0.23	0.63
*12	0	12	1.81	0.18	0.87	0.35	0.68	0.41
*13	3	28	0.32	0.57	0.43	0.51	1.15	0.28
*14	0	4	0.60	0.44	0.29	0.59	0.23	0.63
*15	18	18	42.98	5.52×10⁻¹¹	----	----	----	----
*16	0	0	----	----	----	----	----	----
Total	32	212	55.99	5.09×10⁻⁸	----	----	----	----
^a Total					10.12	0.43	----	----
					^b Total		5.54	0.78

^a Total minus the number of *15 alleles=14; ^b Total minus the number of *15 and *04 alleles=10

Analysis of serological subgroups indicated that the allele with the greatest risk for PR3-ANCA disease in African Americans was *DRB1**15 ($p=5.52 \times 10^{-11}$). With exclusion of *DRB1**15, *DRB1**04 emerged as significant ($p=0.02$). A third round of analysis, removing both *DRB1**15 and *DRB1**04, indicated no significant deviations from previous values.

(3d) Caucasian patients with PR3-ANCA serology (n=74)

DRB1 Allele	Patients	Controls	Round 1 of comparison		^a Round 2: *15 removed		^b Round 3: *15 and *14 removed		^c Round 4: *15, *14 and *03 removed		^d Round 5: *15, *14, *03 and *11 removed	
			χ^2	P	χ^2	P	χ^2	P	χ^2	P	χ^2	P
*01	16	104	4.57	0.03	2.58	0.11	2.07	0.15	0.89	0.34	0.41	0.52
*03	25	57	4.10	0.04	6.89	0.01	7.95	0.005	----	----	----	----
*04	27	150	3.89	0.05	1.69	0.19	1.18	0.28	0.21	0.65	0.01	0.94
*07	18	71	0.06	0.80	0.07	0.79	0.19	0.66	0.88	0.35	1.55	0.21
*08	3	16	0.35	0.56	0.13	0.71	0.09	0.77	0.01	0.93	0.00	0.97
*09	0	6	1.63	0.20	1.42	0.23	1.35	0.24	1.19	0.28	1.10	0.30
*10	1	7	0.37	0.54	0.23	0.64	0.19	0.67	0.09	0.76	0.05	0.82
*11	13	34	1.12	0.29	2.23	0.14	2.67	0.10	4.21	0.04	----	----
*12	1	2	0.26	0.61	0.39	0.53	0.44	0.51	0.61	0.43	0.73	0.39
*13	8	43	0.97	0.33	0.38	0.54	0.25	0.61	0.03	0.87	0.00	0.96
*14	6	4	8.91	0.003	10.83	0.001	----	----	----	----	----	----
*15	30	46	14.92	0.0001	----	----	----	----	----	----	----	----
*16	0	6	1.63	0.20	1.42	0.23	1.35	0.24	1.19	0.28	1.10	0.30
Total	148	546	42.78	2.46×10⁻⁵	----	----	----	----	----	----	----	----
^a Total					28.26	0.003	----	----	----	----	----	----
					^b Total		17.74	0.06	----	----	----	----
					^c Total		9.31	0.41	----	----	----	----
					^d Total		4.95	0.76	----	----	----	----

^a Total minus the number of *15 alleles=118; ^b Total minus the number of *15 and *14 alleles=112; ^c Total minus the number of *15, *14 and *03 alleles=87; ^d Total minus the number of *15, *14, *03 and *11 alleles=74

*DRB1**15 was linked also with PR3-ANCA serology in Caucasians ($p=0.0001$). Also noted were *DRB1**01, *03, and *04. Exclusion of *DRB1**15 increased the significance of *DRB1**03 and *DRB1**14. Exclusion of *DRB1**15 and *DRB1**14 and *DRB1**03 revealed *DRB1**11 as significant.

(3e) African American patients with MPO-ANCA serology (n=25)

DRB1 Allele			Round 1 of comparison		^a Round 2: *16 removed	
	Patients	Controls	χ^2	P	χ^2	P
*01	4	31	1.33	0.25	1.15	0.28
*03	6	29	0.09	0.77	0.04	0.84
*04	4	17	0.00	1.00	0.00	0.94
*07	5	19	0.05	0.83	0.09	0.76
*08	5	20	0.01	0.91	0.04	0.84
*09	1	5	0.02	0.88	0.01	0.91
*10	1	4	0.00	0.96	0.01	0.93
*11	7	25	0.16	0.69	0.25	0.62
*12	1	12	1.09	0.30	1.00	0.32
*13	10	28	1.29	0.26	1.56	0.21
*14	1	4	0.00	0.96	0.01	0.93
*15	3	18	0.31	0.58	0.24	0.62
*16	2	0	8.48	0.004	----	----
Total	50	212	12.84	0.38	----	----
				^aTotal	4.4	0.96

^a Total minus the number of *16 alleles=48

(3f) Caucasian patients with MPO-ANCA serology (n=22)

DRB1 Allele			Round 1 of comparison	
	Patients	Controls	χ^2	P
*01	7	104	0.21	0.64
*03	6	57	0.39	0.53
*04	12	150	0.001	0.98
*07	4	71	0.49	0.48
*08	2	16	0.35	0.56
*09	1	6	0.47	0.49
*10	1	7	0.29	0.59
*11	1	34	1.07	0.30
*12	1	2	2.91	0.09
*13	3	43	0.06	0.81
*14	1	4	1.14	0.29
*15	4	46	0.02	0.88
*16	1	6	0.47	0.49
Total	44	546	7.89	0.79

Supplemental Table 4. Relative Predispositional Effects (RPE) of *HLA-DRB1* alleles in (a) African American and (b) Caucasian patients with ANCA disease compared to US database of African Americans-Bethesda and Caucasians-Bethesda

(4a) African American patients

<i>DRB1</i> Allele	Round 1 of comparison				Round 2: *15 removed	
	Patients	Controls	χ^2	<i>P</i>	χ^2	<i>P</i>
*01	5	10	0.33	0.57	0.71	0.40
*03	8	28	0.38	0.54	0.06	0.80
*04	8	11	2.27	0.13	3.41	0.06
*07	6	18	0.04	0.84	0.01	0.91
*08	5	13	0.01	0.93	0.14	0.71
*09	2	15	1.96	0.16	1.40	0.24
*10	1	5	0.31	0.58	0.18	0.67
*11	9	27	0.06	0.81	0.02	0.89
*12	1	12	2.42	0.12	1.90	0.17
*13	13	46	0.68	0.41	0.13	0.72
*14	1	2	0.07	0.80	0.14	0.71
*15	21	31	4.89	0.03	----	----
*16	2	6	0.01	0.91	0.00	0.95
Total	82	224	13.43	0.34	----	----
Total^a					8.10	0.70

^a Total minus the number of *15 alleles=61

(4b) Caucasian patients

<i>DRB1</i> Allele	Round 1 of comparison				Round 2: *15 removed		Round 3: *15 and *03 removed		Round 4: *15, *03 and *04 removed	
	Patients	Controls	χ^2	<i>P</i>	χ^2	<i>P</i>	χ^2	<i>P</i>	χ^2	<i>P</i>
*01	23	79	0.09	0.76	0.01	0.91	0.23	0.63	1.21	0.27
*03	31	68	3.06	0.08	4.88	0.03	----	----	----	----
*04	39	97	1.77	0.18	3.42	0.06	5.40	0.02	----	----
*07	22	89	0.98	0.32	0.33	0.56	0.04	0.84	0.16	0.69
*08	5	17	0.01	0.90	0.01	0.94	0.06	0.81	0.28	0.59
*09	1	10	1.32	0.25	1.08	0.30	0.89	0.34	0.63	0.43
*10	2	9	0.19	0.66	0.10	0.75	0.04	0.84	0.00	0.99
*11	14	63	1.35	0.25	0.69	0.41	0.28	0.60	0.00	0.97
*12	2	6	0.01	0.94	0.04	0.84	0.09	0.76	0.24	0.63
*13	11	74	5.54	0.02	4.14	0.04	3.06	0.08	1.65	0.20
*14	7	28	0.28	0.60	0.09	0.76	0.01	0.93	0.06	0.80
*15	34	57	9.20	0.002	----	----	----	----	----	----
*16	1	17	3.31	0.07	2.86	0.09	2.49	0.11	1.96	0.16
Total	192	614	27.11	0.01	----	----	----	----	----	----
Total^a					17.65	0.09	----	----	----	----
Total^b							12.60	0.25	----	----
Total^c									6.20	0.80

^a Total minus the number of *15 alleles=158; ^b Total minus the number of *15 and *03 alleles=127; ^c Total minus the number of *15, *03 and *04 alleles=88

(4c) African American patients - PR3-ANCA serology

DRB1 Allele	Round 1 of comparison				Round 2: *15 removed		Round 3: *15 and *04 removed	
	Patients	Controls	χ^2	P	χ^2	P	χ^2	P
*01	1	10	0.12	0.73	0.09	0.76	0.34	0.56
*03	2	28	0.93	0.33	0.00	0.98	0.13	0.72
*04	4	11	2.75	0.10	9.42	0.002	----	----
*07	1	18	0.91	0.34	0.07	0.79	0.00	0.99
*08	0	13	1.86	0.17	0.94	0.33	0.71	0.40
*09	1	15	0.57	0.45	0.01	0.93	0.04	0.85
*10	0	5	0.71	0.40	0.36	0.55	0.27	0.60
*11	2	27	0.83	0.36	0.00	0.98	0.17	0.68
*12	0	12	1.71	0.19	0.87	0.35	0.66	0.42
*13	3	46	1.82	0.18	0.03	0.86	0.08	0.77
*14	0	2	0.29	0.59	0.15	0.70	0.11	0.74
*15	18	31	26.31	2.90×10⁻⁷	----	----	----	----
*16	0	6	0.86	0.35	0.44	0.51	0.33	0.57
Total	32	224	39.68	8.13×10⁻⁵	----	----	----	----
Total^a					12.38	0.34	----	----
					Total^b		2.84	0.98

^a Total minus the number of *15 alleles=14; ^b Total minus the number of *15 and *04 alleles=10

(4d) Caucasian patients – PR3 ANCA serology

DRB1 Allele	Round 1 of comparison				Round 2: *15 removed		Round 3: *15 and *03 removed	
	Patients	Controls	χ^2	P	χ^2	P	χ^2	P
*01	16	79	0.40	0.52	0.03	0.87	0.04	0.84
*03	25	68	3.31	0.07	5.70	0.02	----	----
*04	27	97	0.44	0.51	1.58	0.21	3.00	0.08
*07	18	89	0.46	0.50	0.03	0.86	0.05	0.83
*08	3	17	0.25	0.62	0.09	0.77	0.02	0.90
*09	0	10	2.41	0.12	2.12	0.15	1.91	0.17
*10	1	9	0.57	0.45	0.39	0.53	0.27	0.60
*11	13	63	0.26	0.61	0.01	0.93	0.06	0.80
*12	1	6	0.12	0.73	0.05	0.82	0.02	0.90
*13	8	74	4.90	0.03	3.39	0.07	2.42	0.12
*14	6	28	0.07	0.79	0.00	0.98	0.06	0.80
*15	30	57	12.61	0.0004	----	----	----	----
*16	0	17	4.10	0.04	3.60	0.06	3.25	0.07
Total	148	614	29.89	0.003	----	----	----	----
Total^a					16.98	0.11	----	----
					Total^b		11.11	0.35

^a Total minus the number of *15 alleles=118; ^b Total minus the number of *15 and *03 alleles=93

Supplemental Table 5. Analysis of *DRB1*15* allelic variants within the African American cohort by high definition PCR-SSOP analysis

<i>DRB1*15</i> subgroup	[£] PR3-ANCA patients (n = 12)	[§] General population (n = 40)	<i>P</i> -value
1501	6 (50%)	5 (13%)	0.01 [*]
1502	0 (0%)	0 (0%)	--
1503	6 (50%)	32 (80%)	0.04 [*]
1504	0 (0%)	3 (8%)	-

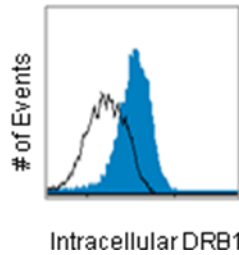
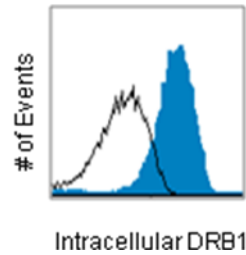
^{*} Fisher exact test

^{*} Chi-square test

[£] Allele sequencing was limited to 12 patients due to insufficient DNA, only one patient of the 12 was homozygous (*DRB1*1501*, 1501)

[§] Database from USA Southeast African American

*Note: DRB1*1501* refers to the first and *DRB1*1503* to the third identified allele of the *DRB1*15* family. These two variants differ at amino acid 58: *DRB1*1501* has a tyrosine at position 58 (FLDRYF-), while *DRB1*1503* has a histidine at that position (FLDRHF). This is particularly interesting since the *DRB1*1501* allelic variant is of Caucasian descent, while *DRB1*1503* is of African American descent and *DRB1*1502* & **1504* are of Asian/Pacific Islander descent.

A Haplotype: *DRB1**15,*15)B Haplotype: *DRB1**04,*14)

Supplemental Figure 2. Neutrophils contain intracellular pools of DRB1 protein. (A) *DRB1**15,*15 homozygous patient: Staining of intracellular DRB1 in neutrophils (overlay of negative control (normal mouse IgG) with anti-DRB1 antibody staining. (B) Neutrophils from a *DRB1**03,*14 patient showed similar results.

Supplemental Table 6. Neutrophil studies of *DRB1**15 cell surface expression and peptide binding post TNF- α exposure.

% Neutrophils (FACS analysis)			
<i>(a) Cells treated with sense PR3 peptide</i>			
Patients (1-4)	Positive for <i>DRB1</i> *15 surface expression	Positive for <u>sPR3¹⁴⁹⁻¹⁶³ Peptide</u> binding	Dual positivity
1	3.5%	9.5%	3.9%
2	7.2%	15.5%	7.1%
3	22.2%	12.9%	8.5%
4	14.2%	20.4%	10.1%
<i>(b) Cells treated with complementary PR3 peptide</i>			
	Positive for <i>DRB1</i> *15 surface expression	Positive for <u>cPR3¹⁴⁶⁻¹⁶¹ Peptide</u> binding	Dual positivity
1	3.3%	3.6%	3.2%
2	11.9%	13.3%	11.0%
3	25.6%	23.5%	13.0%
4	21.4%	30.8%	10.0%