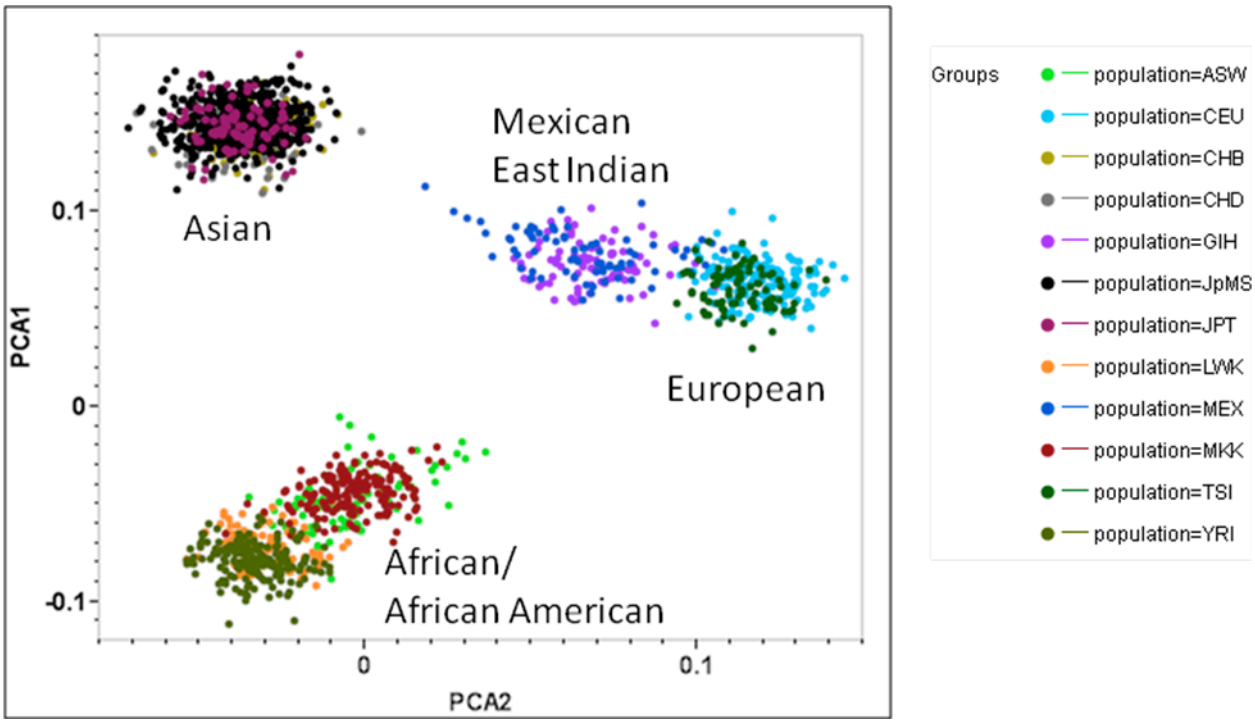
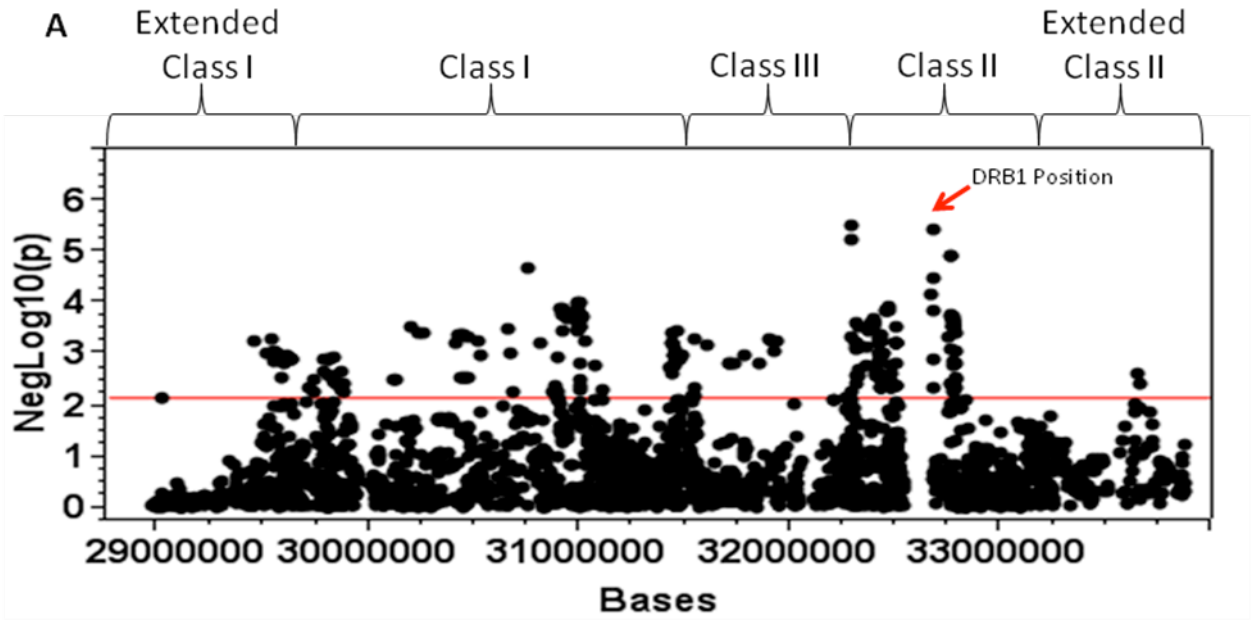
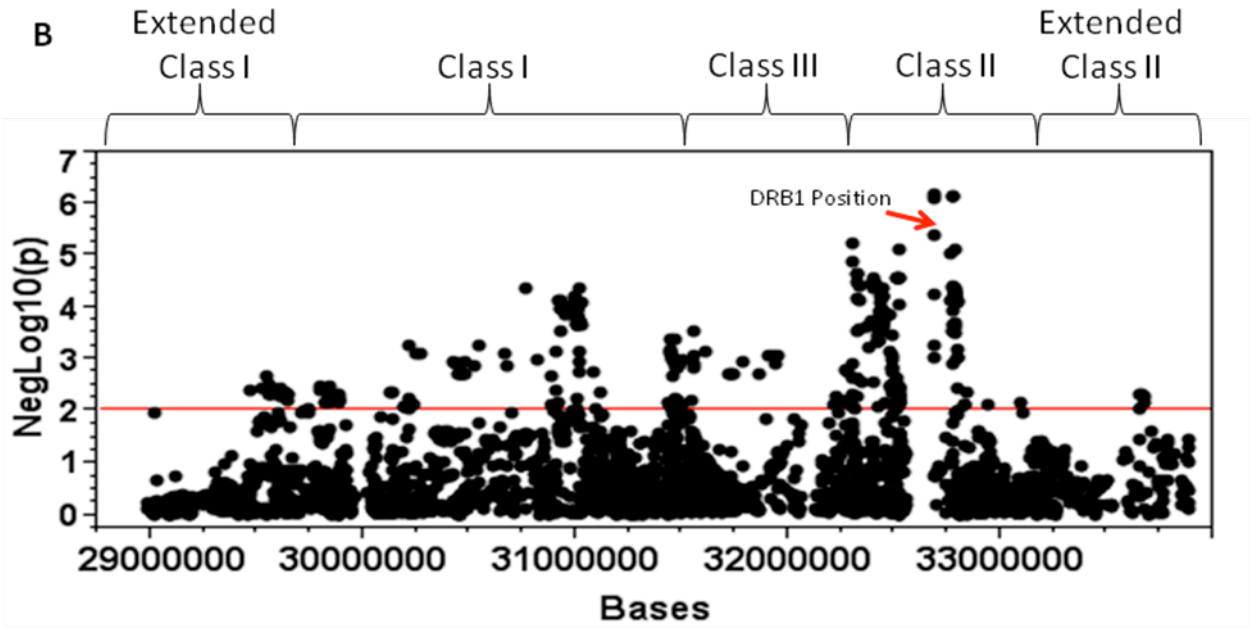
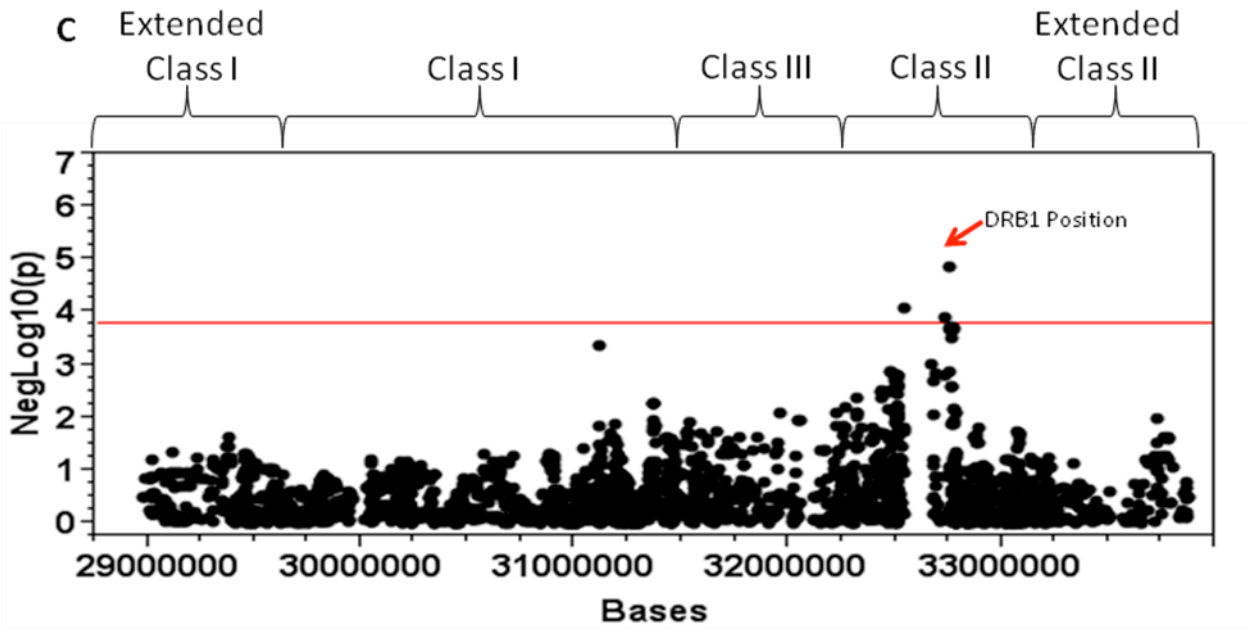
Supplementary Figure 1: Plot of the First Two Dimensions from MDS Analysis for the Japanese MS Sample and 11 HapMap Populations. Dimensions derived from 705 non-chromosome 6 SNPs common between all 12 populations. The Japanese MS Sample (JpMS) clusters well with the other three Asian populations. ASW = African ancestry in Southwest USA; CEU = CEPH (NW European); CHB = Han Chinese in Beijing, China; CHD = Chinese in Denver, Colorado; GIH = Gujarati Indians in Houston, Texas; JPT = Japanese in Tokyo, Japan; LWK = Luhya in Webuye, Kenya; MEX = Mexican ancestry in Los Angeles, California; MKK = Maasai in Kinyawa, Kenya; TSI = Tuscan in Italy; YRI = Yoruban in Ibadan, Nigeria.



Supplementary Figure 2: Negative Log10(p-value) for Each SNP Plotted onto SNP Position for A) MS vs. Healthy Control, B) AQP4- vs. Healthy Control, and C) AQP4- vs. AQP4+. No SNPs included in the models, and gender included in all models. Red line indicates FDRp = 0.1.






C
Extended
Class I
Class I
Class III
Class II
Extended
Class II
DRB1 Position
NegLog10(p)
0
1
2
3
4
5
6
7
29000000
30000000
31000000
32000000
33000000
Bases

Supplementary Table 1. Tagging Parameters of the MS Susceptible Significant SNP Haplotypes for DRB1. Results from analysis of 218 Japanese individuals (both patients and controls) for whom classical DRB1 data were available. The sensitivity is the percentage of a given DRB1 allele that is captured by a given SNP haplotype, and the positive predictive value is the percentage of a given SNP haplotype that captures the particular DRB1 allele. MSvs.Cont = All MS vs. healthy control; Ab-vsCont = AQP4- patients vs. controls; Ab-Ab+ = AQP4- patients vs. AQP4+ patients; Trait = trait for which SNPs making up haplotype were significant; DRB1--Hap = DRB1 allele--SNP haplotype.

Trait	DRB1--Hap	Freq DRB1 Allele	Freq Hap	Joint Freq	D'	Sensitivity	Specificity	Positive Predictive Value
MSvs.Cont	04:05--A-G	0.18	0.66	0.18	0.96	0.99	0.41	0.27
MSvs.Cont	15:01--A-G	0.10	0.66	0.10	1.00	1.00	0.38	0.16
MSvs.Cont	08:03--A-G	0.08	0.66	0.08	0.75	0.92	0.36	0.12
MSvs.Cont	08:02--A-G	0.06	0.66	0.05	0.84	0.95	0.36	0.08
MSvs.Cont	04:06--A-G	0.04	0.66	0.04	0.85	0.95	0.35	0.06
MSvs.Cont	04:03--A-G	0.03	0.66	0.03	1.00	1.00	0.35	0.05
MSvs.Cont	12:02--A-G	0.03	0.66	0.03	0.76	0.92	0.35	0.04
MSvs.Cont	14:01--A-G	0.03	0.66	0.02	0.11	0.70	0.34	0.03
MSvs.Cont	14:05--A-G	0.02	0.66	0.02	0.69	0.89	0.35	0.03
MSvs.Cont	12:01--A-G	0.05	0.66	0.02	0.41	0.39	0.33	0.03
MSvs.Cont	04:10--A-G	0.02	0.66	0.02	0.42	0.80	0.34	0.03
MSvs.Cont	11:01--A-G	0.02	0.66	0.01	0.18	0.72	0.34	0.02
MSvs.Cont	14:06--A-G	0.01	0.66	0.01	0.51	0.83	0.34	0.02
MSvs.Cont	13:02--A-G	0.05	0.66	0.01	0.70	0.20	0.32	0.01
MSvs.Cont	14:03--A-G	0.01	0.66	0.01	1.00	1.00	0.34	0.01
MSvs.Cont	09:01--A-G	0.08	0.66	0.01	0.86	0.09	0.29	0.01
MSvs.Cont	04:04--A-G	0.01	0.66	0.01	1.00	1.00	0.34	0.01
MSvs.Cont	16:02--A-G	0.01	0.66	0.01	1.00	1.00	0.34	0.01
MSvs.Cont	04:01--A-G	0.01	0.66	0.00	0.02	0.67	0.34	0.01
MSvs.Cont	01:01--A-G	0.06	0.66	0.00	0.94	0.04	0.30	0.00
MSvs.Cont	15:02--A-A	0.10	0.18	0.10	1.00	1.00	0.91	0.53
MSvs.Cont	09:01--A-A	0.08	0.18	0.03	0.33	0.45	0.84	0.19
MSvs.Cont	12:01--A-A	0.05	0.18	0.02	0.36	0.48	0.84	0.13
MSvs.Cont	08:03--A-A	0.08	0.18	0.01	0.53	0.08	0.81	0.04
MSvs.Cont	14:01--A-A	0.03	0.18	0.00	0.16	0.15	0.82	0.03
MSvs.Cont	12:02--A-A	0.03	0.18	0.00	0.53	0.08	0.82	0.01
MSvs.Cont	14:05--A-A	0.02	0.18	0.00	0.40	0.11	0.82	0.01
MSvs.Cont	11:01--A-A	0.02	0.18	0.00	0.22	0.14	0.82	0.01
MSvs.Cont	04:01--A-A	0.01	0.18	0.00	0.19	0.33	0.82	0.01
MSvs.Cont	03:01--A-A	0.00	0.18	0.00	1.00	1.00	0.82	0.01
MSvs.Cont	13:01--A-A	0.00	0.18	0.00	1.00	1.00	0.82	0.01

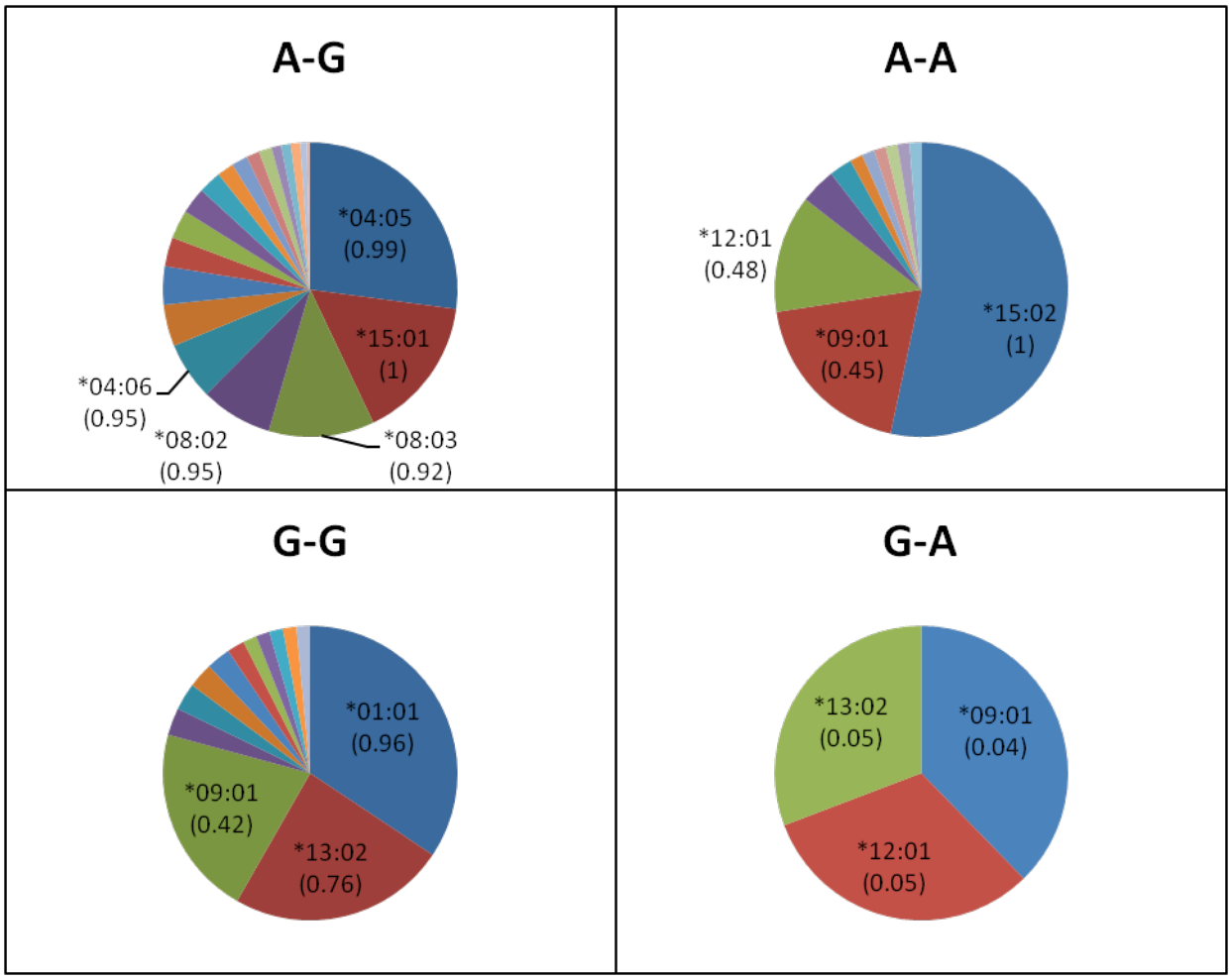
MSvs.Cont	01:01--G-G	0.06	0.16	0.05	0.95	0.96	0.89	0.34
MSvs.Cont	13:02--G-G	0.05	0.16	0.04	0.71	0.76	0.88	0.24
MSvs.Cont	09:01--G-G	0.08	0.16	0.03	0.32	0.42	0.87	0.21
MSvs.Cont	10:01--G-G	0.00	0.16	0.00	1.00	1.00	0.85	0.03
MSvs.Cont	14:01--G-G	0.03	0.16	0.00	0.01	0.15	0.84	0.03
MSvs.Cont	12:01--G-G	0.05	0.16	0.00	0.44	0.09	0.84	0.03
MSvs.Cont	04:10--G-G	0.02	0.16	0.00	0.05	0.20	0.85	0.03
MSvs.Cont	08:02--G-G	0.06	0.16	0.00	0.65	0.05	0.84	0.02
MSvs.Cont	04:05--G-G	0.18	0.16	0.00	0.92	0.01	0.81	0.01
MSvs.Cont	04:06--G-G	0.04	0.16	0.00	0.66	0.05	0.84	0.01
MSvs.Cont	11:01--G-G	0.02	0.16	0.00	0.10	0.14	0.84	0.01
MSvs.Cont	14:06--G-G	0.01	0.16	0.00	0.01	0.17	0.85	0.01
MSvs.Cont	04:07--G-G	0.00	0.16	0.00	1.00	1.00	0.85	0.01
MSvs.Cont	09:01--G-A	0.08	0.01	0.00	0.33	0.04	0.99	0.38
MSvs.Cont	12:01--G-A	0.05	0.01	0.00	0.28	0.05	0.99	0.31
MSvs.Cont	13:02--G-A	0.05	0.01	0.00	0.27	0.05	0.99	0.31
Ab-vs.Cont	04:05--G-G	0.18	0.38	0.17	0.93	0.95	0.75	0.46
Ab-vs.Cont	08:02--G-G	0.06	0.38	0.06	1.00	1.00	0.66	0.15
Ab-vs.Cont	04:06--G-G	0.04	0.38	0.04	1.00	1.00	0.65	0.12
Ab-vs.Cont	04:03--G-G	0.03	0.38	0.03	1.00	1.00	0.64	0.08
Ab-vs.Cont	12:02--G-G	0.03	0.38	0.03	1.00	1.00	0.64	0.08
Ab-vs.Cont	04:10--G-G	0.02	0.38	0.02	0.82	0.89	0.63	0.05
Ab-vs.Cont	04:01--G-G	0.01	0.38	0.01	1.00	1.00	0.63	0.02
Ab-vs.Cont	04:04--G-G	0.01	0.38	0.00	0.47	0.67	0.63	0.01
Ab-vs.Cont	08:03--G-G	0.08	0.38	0.00	0.93	0.03	0.59	0.01
Ab-vs.Cont	09:01--G-G	0.08	0.38	0.00	0.92	0.03	0.60	0.01
Ab-vs.Cont	13:02--G-G	0.05	0.38	0.00	0.87	0.05	0.61	0.01
Ab-vs.Cont	12:01--G-G	0.05	0.38	0.00	0.87	0.05	0.61	0.01
Ab-vs.Cont	14:06--G-G	0.01	0.38	0.00	0.56	0.17	0.62	0.01
Ab-vs.Cont	04:07--G-G	0.00	0.38	0.00	1.00	1.00	0.63	0.01
Ab-vs.Cont	15:01--A-G	0.10	0.57	0.10	1.00	1.00	0.48	0.18
Ab-vs.Cont	15:02--A-G	0.10	0.57	0.10	1.00	1.00	0.48	0.17
Ab-vs.Cont	08:03--A-G	0.08	0.57	0.08	0.78	0.91	0.47	0.13
Ab-vs.Cont	09:01--A-G	0.08	0.57	0.07	0.93	0.97	0.47	0.13
Ab-vs.Cont	01:01--A-G	0.06	0.57	0.06	1.00	1.00	0.46	0.10
Ab-vs.Cont	12:01--A-G	0.05	0.57	0.04	0.56	0.81	0.45	0.07
Ab-vs.Cont	14:01--A-G	0.03	0.57	0.03	1.00	1.00	0.45	0.05
Ab-vs.Cont	14:05--A-G	0.02	0.57	0.02	1.00	1.00	0.44	0.04
Ab-vs.Cont	11:01--A-G	0.02	0.57	0.02	1.00	1.00	0.44	0.03
Ab-vs.Cont	14:06--A-G	0.01	0.57	0.01	0.62	0.83	0.44	0.02
Ab-vs.Cont	13:02--A-G	0.05	0.57	0.01	0.66	0.20	0.41	0.02
Ab-vs.Cont	14:03--A-G	0.01	0.57	0.01	1.00	1.00	0.44	0.02
Ab-vs.Cont	16:02--A-G	0.01	0.57	0.01	1.00	1.00	0.44	0.01

Ab-vs.Cont	10:01--A-G	0.00	0.57	0.00	1.00	1.00	0.44	0.01
Ab-vs.Cont	04:05--A-G	0.18	0.57	0.00	0.98	0.01	0.31	0.00
Ab-vs.Cont	04:04--A-G	0.01	0.57	0.00	0.41	0.33	0.43	0.00
Ab-vs.Cont	03:01--A-G	0.00	0.57	0.00	1.00	1.00	0.44	0.00
Ab-vs.Cont	13:01--A-G	0.00	0.57	0.00	1.00	1.00	0.44	0.00
Ab-vs.Cont	13:02--A-A	0.05	0.05	0.04	0.74	0.76	0.99	0.75
Ab-vs.Cont	12:01--A-A	0.05	0.05	0.01	0.10	0.14	0.96	0.14
Ab-vs.Cont	08:03--A-A	0.08	0.05	0.01	0.03	0.07	0.95	0.11
Ab-vs.Cont	04:05--G-A	0.18	0.01	0.01	0.65	0.03	1.00	0.72
Ab-vs.Cont	04:10--G-A	0.02	0.01	0.00	0.27	0.11	0.99	0.28
Ab-Ab+	04:05--A	0.18	0.76	0.18	0.95	0.99	0.29	0.23
Ab-Ab+	15:01--A	0.10	0.76	0.10	0.86	0.97	0.26	0.13
Ab-Ab+	15:02--A	0.10	0.76	0.09	0.84	0.96	0.26	0.12
Ab-Ab+	08:03--A	0.08	0.76	0.08	0.88	0.97	0.26	0.11
Ab-Ab+	01:01--A	0.06	0.76	0.06	1.00	1.00	0.25	0.07
Ab-Ab+	08:02--A	0.06	0.76	0.06	1.00	1.00	0.25	0.07
Ab-Ab+	13:02--A	0.05	0.76	0.05	0.80	0.95	0.25	0.06
Ab-Ab+	04:06--A	0.04	0.76	0.04	1.00	1.00	0.25	0.06
Ab-Ab+	04:03--A	0.03	0.76	0.03	0.67	0.92	0.24	0.04
Ab-Ab+	04:10--A	0.02	0.76	0.02	1.00	1.00	0.24	0.03
Ab-Ab+	14:05--A	0.02	0.76	0.02	0.56	0.89	0.24	0.03
Ab-Ab+	14:01--A	0.03	0.76	0.01	0.69	0.24	0.22	0.01
Ab-Ab+	04:04--A	0.01	0.76	0.01	1.00	1.00	0.24	0.01
Ab-Ab+	09:01--A	0.08	0.76	0.00	0.92	0.06	0.18	0.01
Ab-Ab+	12:01--A	0.05	0.76	0.00	0.87	0.10	0.21	0.01
Ab-Ab+	04:01--A	0.01	0.76	0.00	0.12	0.67	0.24	0.01
Ab-Ab+	14:06--A	0.01	0.76	0.00	0.78	0.17	0.23	0.00
Ab-Ab+	10:01--A	0.00	0.76	0.00	0.34	0.50	0.24	0.00
Ab-Ab+	04:07--A	0.00	0.76	0.00	1.00	1.00	0.24	0.00
Ab-Ab+	13:01--A	0.00	0.76	0.00	1.00	1.00	0.24	0.00
Ab-Ab+	09:01--G	0.08	0.24	0.07	0.92	0.94	0.82	0.30
Ab-Ab+	12:01--G	0.05	0.24	0.04	0.87	0.90	0.79	0.18
Ab-Ab+	12:02--G	0.03	0.24	0.03	1.00	1.00	0.78	0.13
Ab-Ab+	14:01--G	0.03	0.24	0.02	0.69	0.76	0.78	0.10
Ab-Ab+	11:01--G	0.02	0.24	0.02	1.00	1.00	0.77	0.07
Ab-Ab+	14:06--G	0.01	0.24	0.01	0.78	0.83	0.77	0.05
Ab-Ab+	14:03--G	0.01	0.24	0.01	1.00	1.00	0.77	0.04
Ab-Ab+	16:02--G	0.01	0.24	0.01	1.00	1.00	0.77	0.03
Ab-Ab+	15:02--G	0.10	0.24	0.00	0.84	0.04	0.74	0.01
Ab-Ab+	15:01--G	0.10	0.24	0.00	0.86	0.03	0.74	0.01
Ab-Ab+	14:05--G	0.02	0.24	0.00	0.56	0.11	0.76	0.01
Ab-Ab+	04:03--G	0.03	0.24	0.00	0.67	0.08	0.76	0.01
Ab-Ab+	04:05--G	0.18	0.24	0.00	0.95	0.01	0.71	0.01

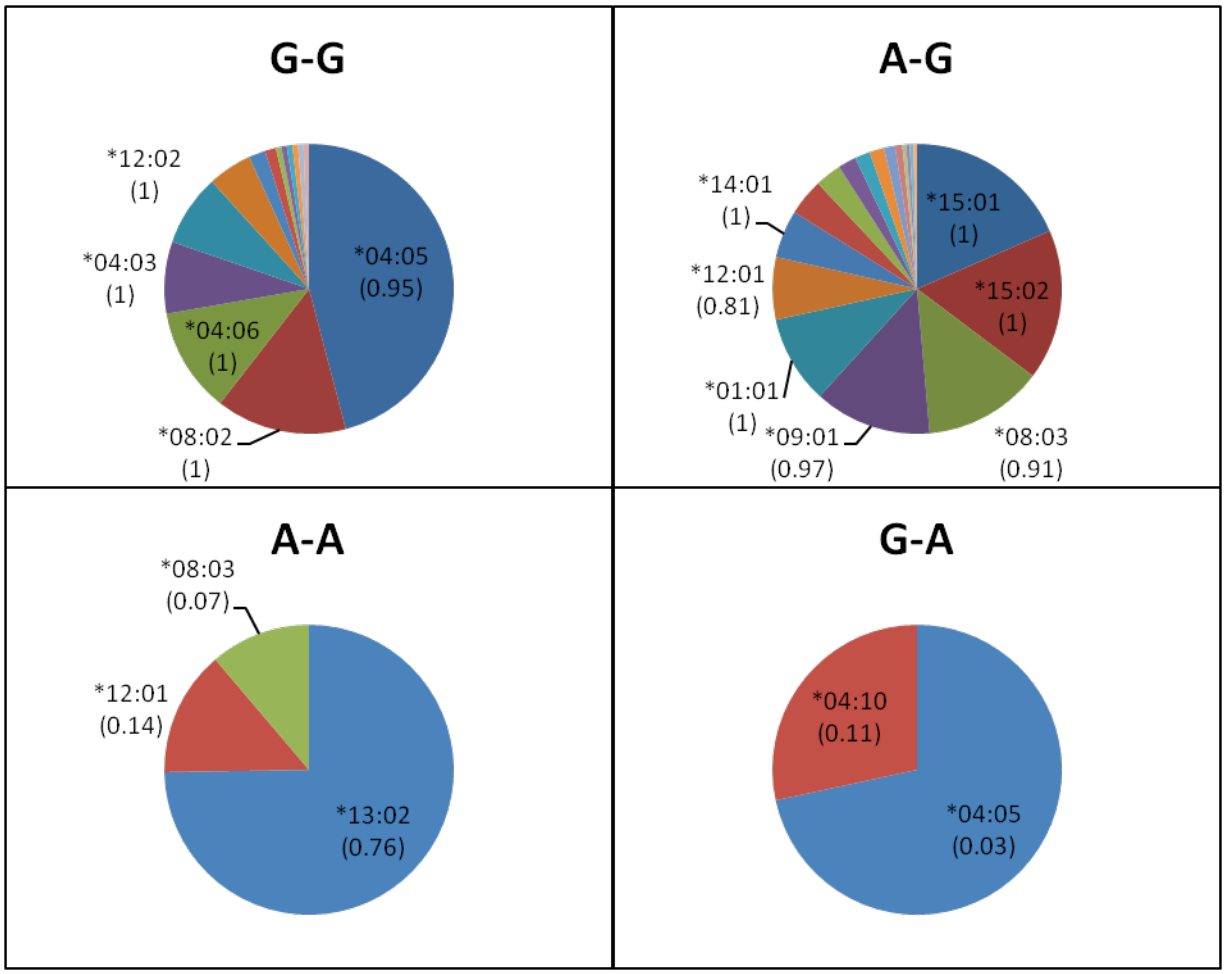
Ab-Ab+	08:03--G	0.08	0.24	0.00	0.88	0.03	0.74	0.01
Ab-Ab+	13:02--G	0.05	0.24	0.00	0.80	0.05	0.75	0.01
Ab-Ab+	04:01--G	0.01	0.24	0.00	0.12	0.33	0.76	0.01
Ab-Ab+	10:01--G	0.00	0.24	0.00	0.34	0.50	0.76	0.01
Ab-Ab+	03:01--G	0.00	0.24	0.00	1.00	1.00	0.76	0.01

Supplementary Figure 3. Distribution of DRB1 Alleles for Each MS Susceptible Significant Haplotype. The size of the slices indicates the positive predictive value for each haplotype. Each slice is labeled with the DRB1 allele and specificity (in parentheses). Haplotypes with positive predictive value < 5% not shown. A) All MS haplotypes. B) AQP4- haplotypes. C) AQP4- vs. AQP4+ SNP.

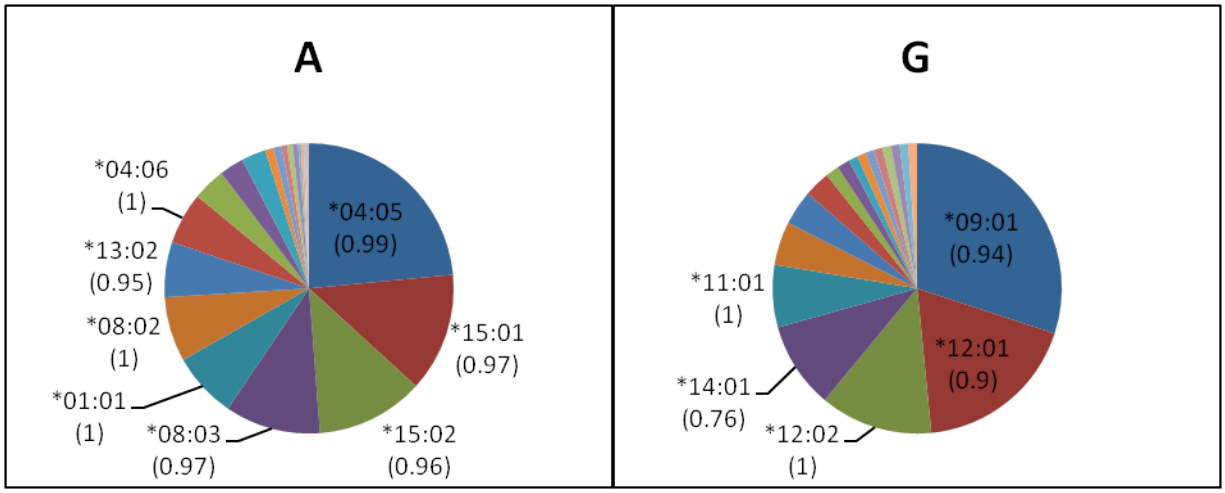
A



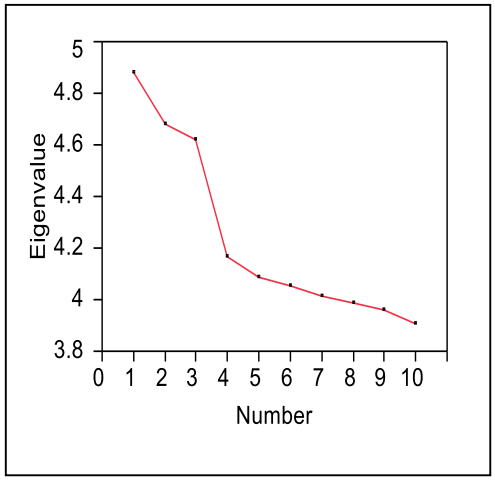
B


G-G
*12:02 (1)
*04:03 (1)
*04:06 (1)
*08:02 (1)
*04:05 (0.95)
A-G
*14:01 (1)
*12:01 (0.81)
*01:01 (1)
*09:01 (0.97)
*15:01 (1)
*15:02 (1)
*08:03 (0.91)
A-A
*08:03 (0.07)
*12:01 (0.14)
*13:02 (0.76)
G-A
*04:10 (0.11)
*04:05 (0.03)

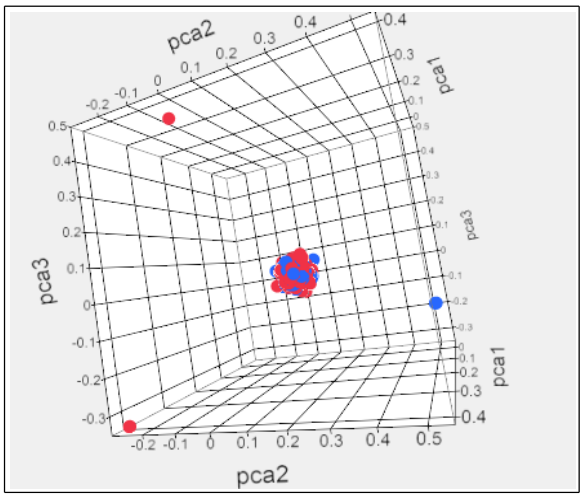
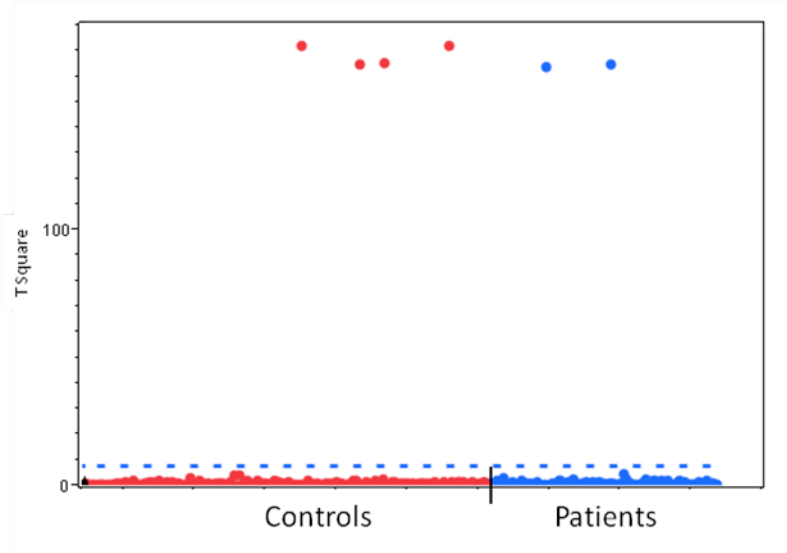
C


A
*04:06 (1)
*13:02 (0.95)
*08:02 (1)
*01:01 (1)
*08:03 (0.97)
*15:02 (0.96)
*15:01 (0.97)
*04:05 (0.99)
G
*11:01 (1)
*14:01 (0.76)
*12:02 (1)
*12:01 (0.9)
*09:01 (0.94)

Supplementary Figure 4: Scree Plot of the First Ten Principal Components for the Experimental Sample. Components were calculated using 3,668 non-chromosome 6 SNPs.



Supplementary Figure 5: Graph of Experimental Sample onto the First Three Components. Three obvious outliers were detected. Red dots are controls, Blue dots are patients.



Supplementary Figure 6: T^2 Statistic Plot of First Three Principal Components to Identify Outliers. Red dots are controls, blue dots are patients. The dotted line represents the upper control limit.