Supplementary Data

Resequencing Candidate Genes Implicates

Rare Variants in Asthma Susceptibility

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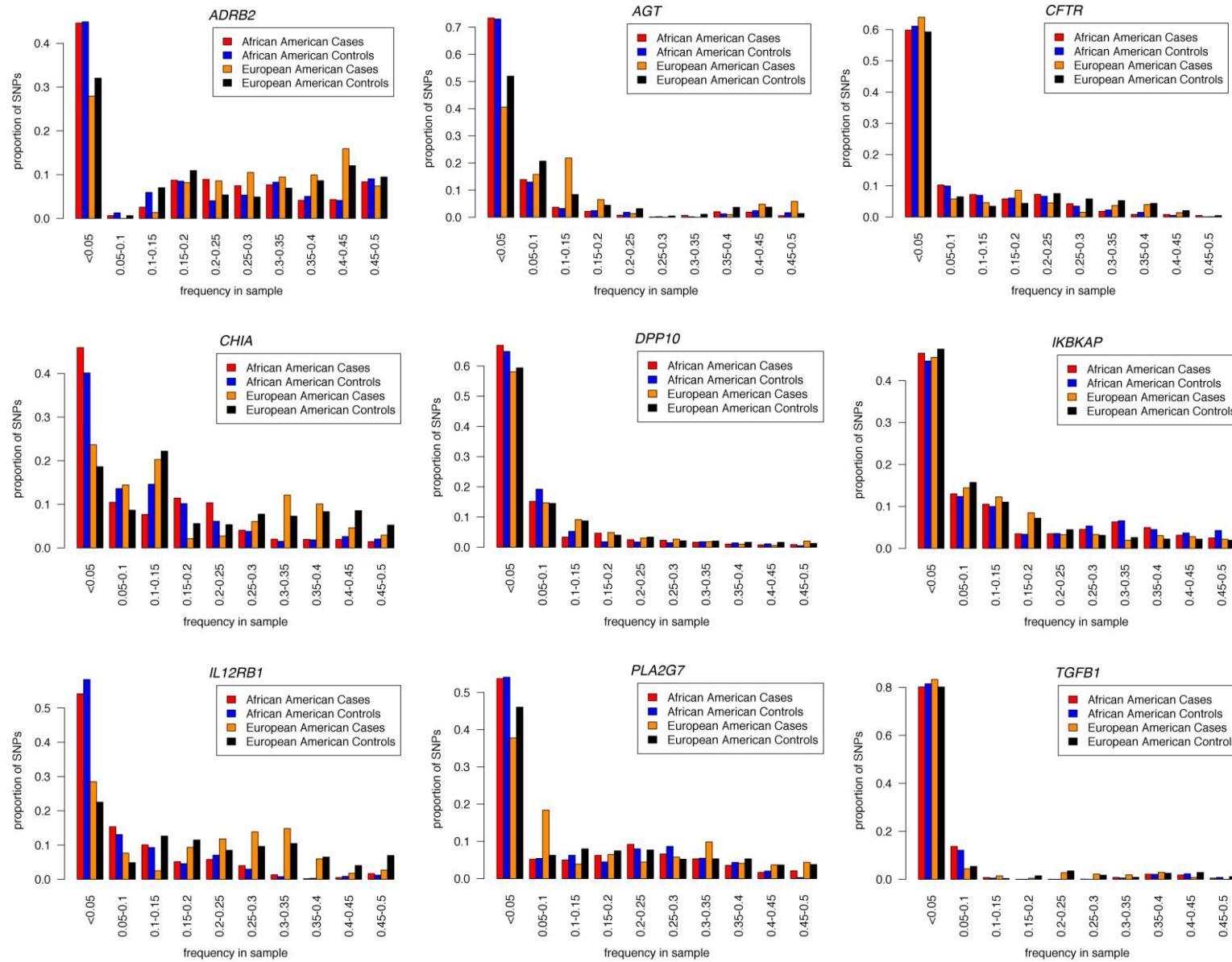
Figure S1. Individual Site Frequency Spectra by Gene

A total of 100 chromosomes were resampled in each of the European American and African American cases and controls to account for missing data and differences in sample size.
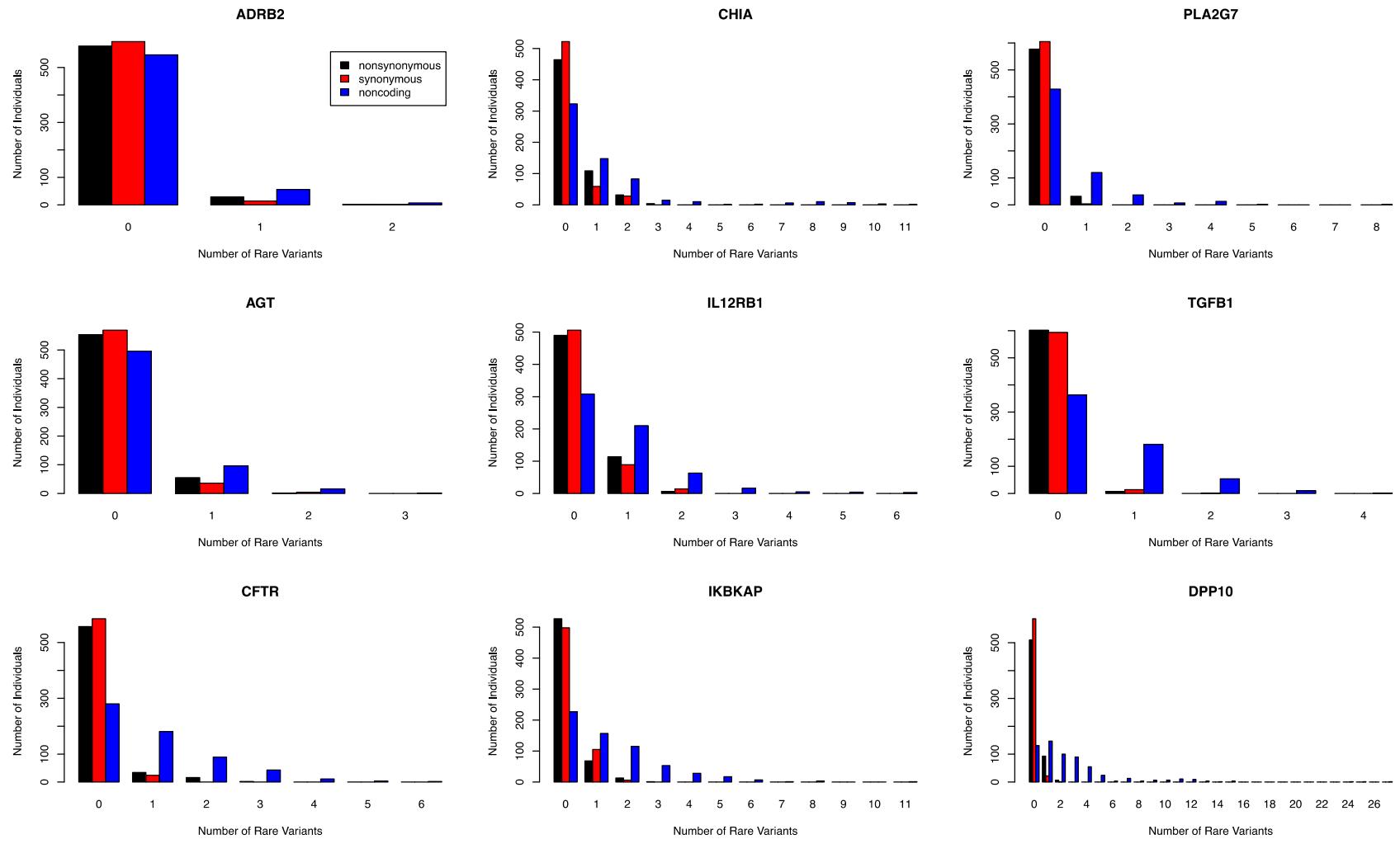
Figure S2. Distribution of the Number of Rare Variants Observed in African American Individuals Included in the Study
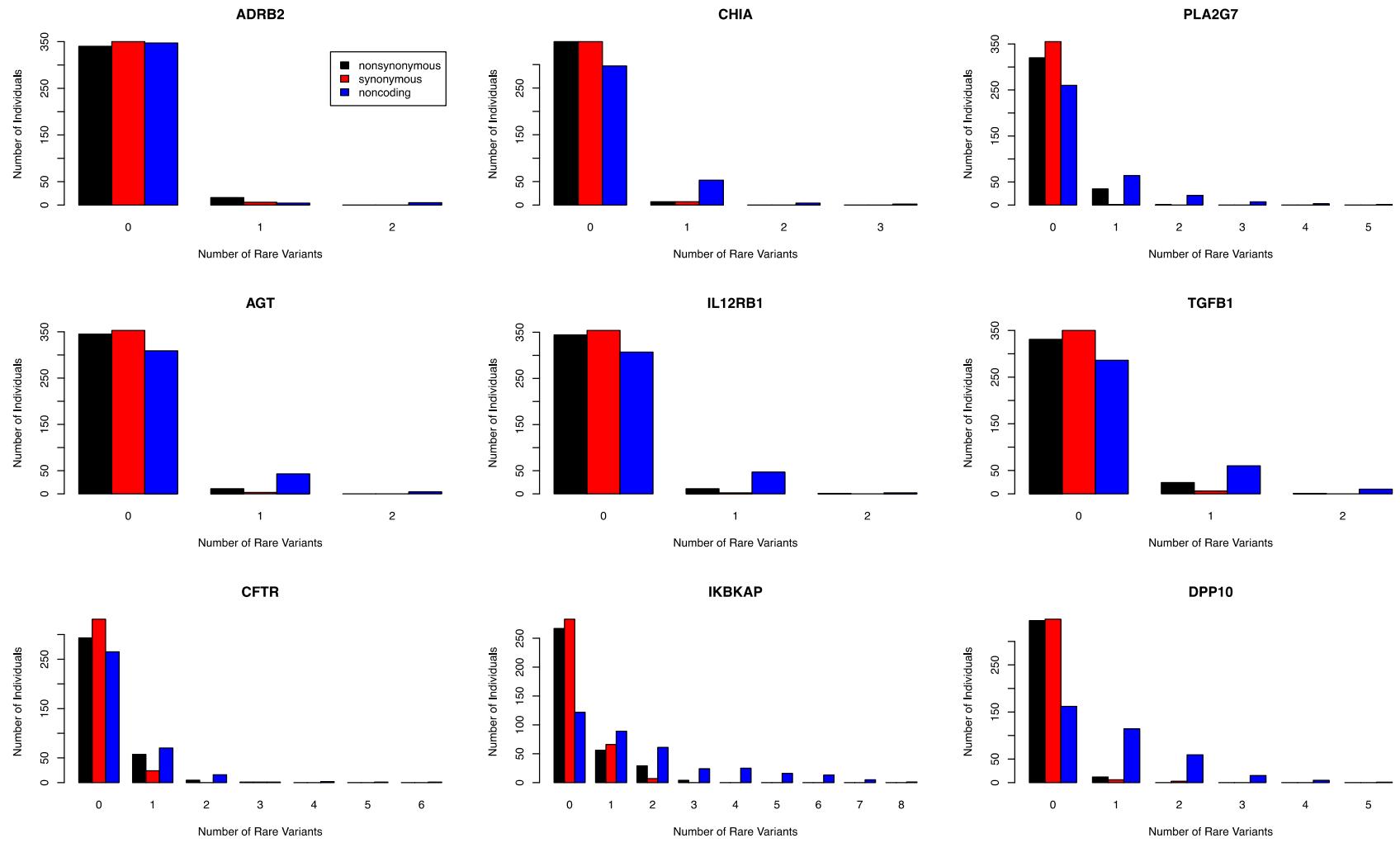
Figure S3. Distribution of the Number of Rare Variants Observed in European American Individuals Included in the Study
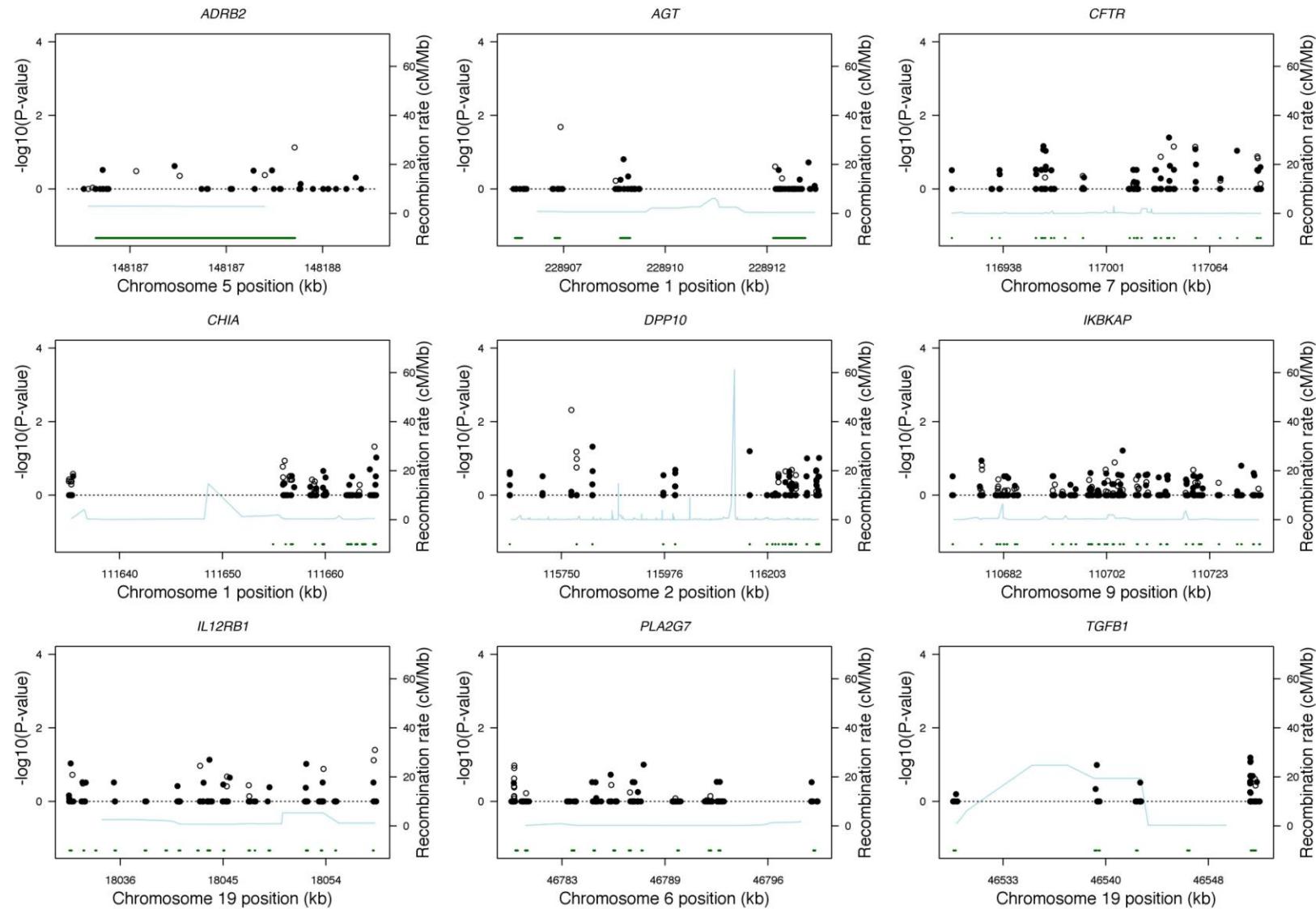
Figure S4. Individual Allelic Tests of Association for All Variants Identified in Each Gene in 342 African American Cases and 267 Controls

Rare variants are indicated by solid black points, coding exons are indicated by a green line, and the recombination rate is in light blue.

5
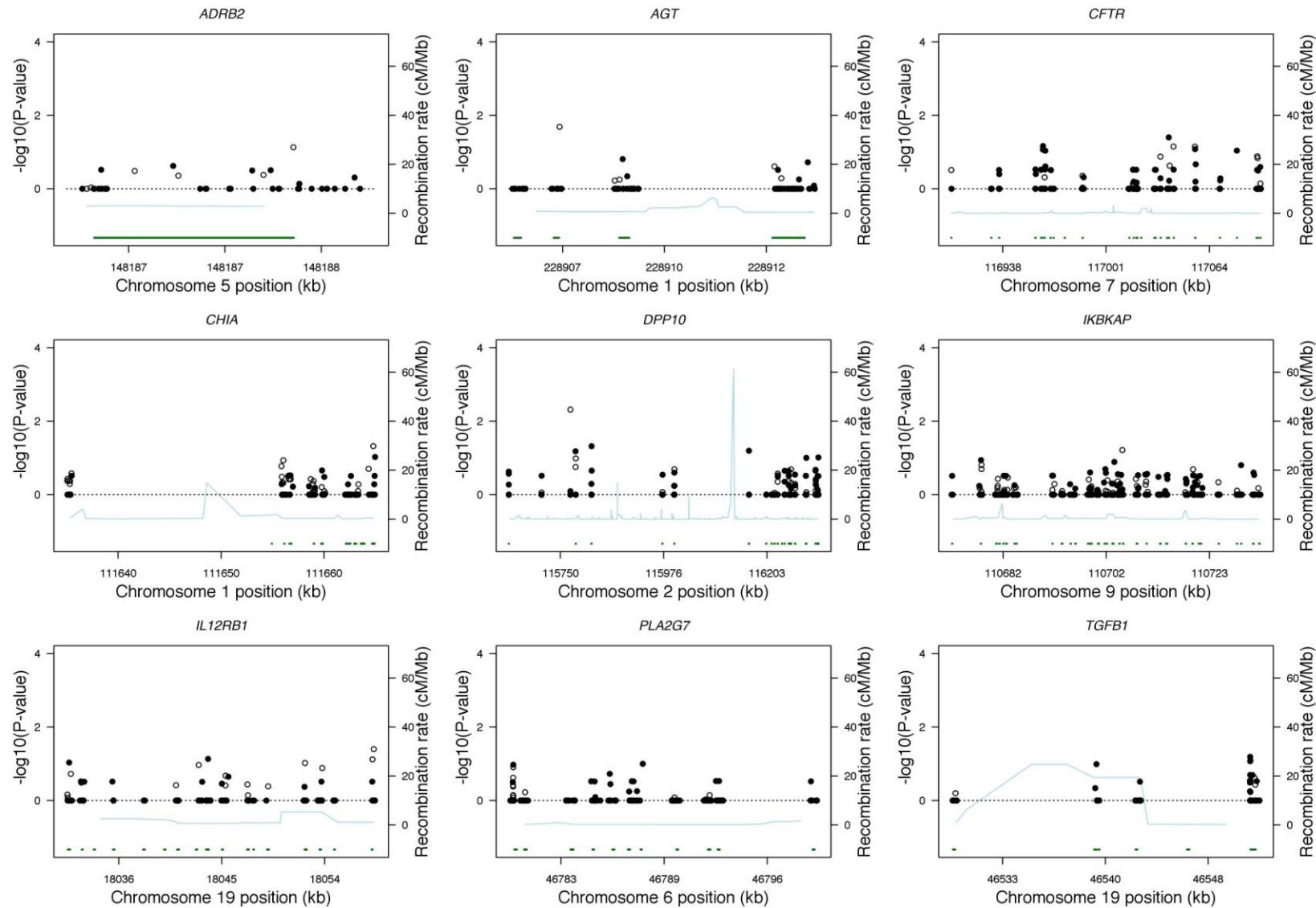
Figure S5. Individual Allelic Tests of Association for All Variants Identified in Each Gene in 108 European American Cases and 248 Controls

Rare variants are indicated by solid black points, coding exons are indicated by a green line, and the recombination rate is in light blue.

6
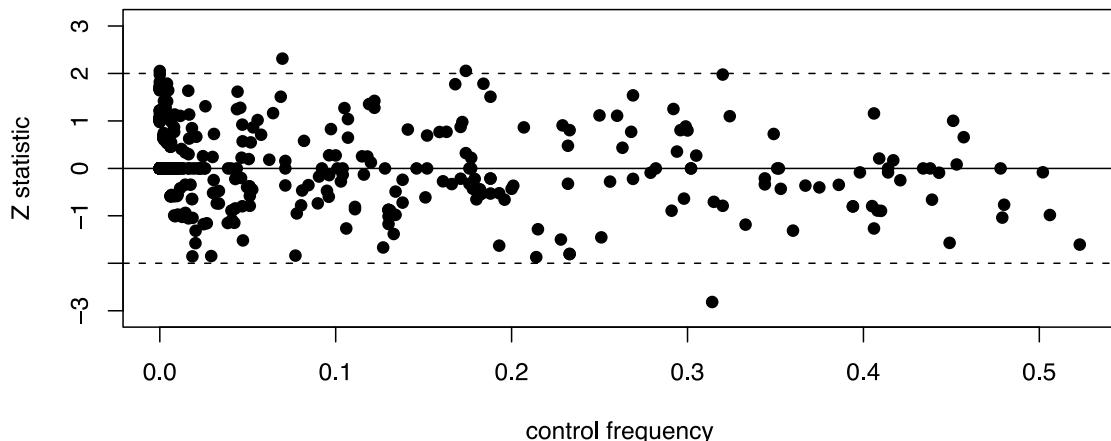
All genes EurAm

All genes AfAm
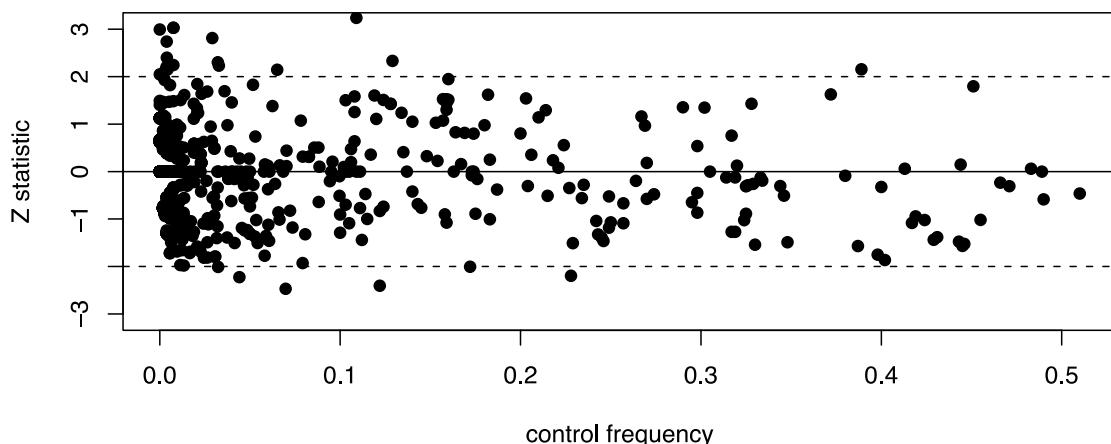
Figure S6. Z-statistics of Individual Tests of Allelic Association Versus Minor Allele Frequency in the European American Controls (EurAm, above), and African American Controls (AfAm, below)

Positive values indicate variants whereby the rare allele increases the risk of asthma. In African Americans there are qualitatively more rare variants that increase the risk of asthma as indicated by having a test statistic > 2 (above the dashed line).

Table S1. Estimates of the Probability of Negative Selection (Pr [γ < -0.5]) and the Population Scaled Selection Coefficient (γ=2N$_e$s) for Nonsynonymous Sites for Candidate Asthma-Associated Genes in African Americans (AA) and European Americans (EA)

Symbol	AA Pr[γ <-0.5]	AA γ	EA Pr[γ <-0.5]	EA γ
ACE	0.72	0.37	0.29	0.56
ADRB2	-2.23	0.88	-2.35	0.88
AGT	-2.18	0.89	-2.17	0.87
ALOX5	1.76	0.52	1.69	0.46
C3	2.13	0.21	3.54	0.24
C3AR1	5.38	0.21	-1.53	0.78
C5	-0.12	0.56	-0.53	0.64
CARD15	-1.17	0.71	-2.18	0.91
CCL11	-2.02	0.84	NA	NA
CCL24	-1.85	0.81	-1.38	0.77
CCL26	1.22	0.54	2.40	0.49
CD14	4.43	0.33	0.97	0.49
CFTR	-1.92	0.84	-3.01	0.96
CHIA	-2.14	0.89	-2.53	0.92
CHRM3	-1.50	0.76	4.12	0.56
CRHR1	1.37	0.47	-1.34	0.75
CRTH2	-1.32	0.72	NA	NA
CSF2	-0.73	0.65	-0.94	0.72
CYSLTR2	-0.16	0.54	-0.39	0.60
DPP10	-1.66	0.80	-2.35	0.89
EDN1	1.93	0.37	1.11	0.47
FCER1B	-1.18	0.71	2.35	0.38
GATA3	NA	NA	-1.47	0.78
IFNGR1	-0.83	0.66	0.76	0.53
IKAP	-2.46	0.96	-1.58	0.81
IL12RB1	-1.91	0.84	-2.56	0.91
IL13	-1.75	0.80	-1.57	0.78
IL1B	0.93	0.48	0.45	0.58
IL1RN	1.43	0.47	6.24	0.54
IL3	-0.69	0.64	-2.09	0.85
IL4	0.92	0.49	-0.03	0.59
IL4RA	-0.27	0.60	-0.44	0.64
ITGB3	-1.38	0.76	-0.97	0.73
KCNS3	-14.39	0.97	NA	NA
LTA	NA	NA	-2.85	0.91
MUC7	0.52	0.43	0.02	0.58
NOD1	-1.51	0.77	-1.70	0.80
NOS1	2.95	0.43	0.54	0.53

Symbol	AA Pr[γ <-0.5]	AA γ	EA Pr[γ <-0.5]	EA γ
NOS2A	-0.74	0.65	-1.08	0.72
PGDS	NA	NA	-5.37	0.90
PHF11	-0.57	0.67	NA	NA
PLA2G7	-2.17	0.88	-2.38	0.90
PTGDR	0.55	0.47	1.71	0.43
SELP	-0.49	0.60	-0.59	0.69
SPINK5	-1.56	0.79	-0.88	0.68
STAT6	1.09	0.44	1.83	0.49
TGFB1	-2.72	0.83	-6.53	0.95
TIM1	-1.09	0.69	-0.54	0.63
TLR2	1.83	0.36	-2.59	0.93
TLR4	-1.59	0.78	-2.22	0.87
TLR6	-1.55	0.80	2.87	0.24
TLR9	5.32	0.19	1.54	0.41
VDR	0.68	0.45	0.52	0.52

Table S2. Counts of the Number of Rare Nonsynonymous (NS), Synonymous (S), and Non-coding (NC) Variants in Cases and Controls

A. African Americans

Gene	Cases			Controls		
	NS	**S**	**NC**	**NS**	**S**	**NC**
ADRB2	5	4	8	5	3	7
AGT	16	6	24	9	5	21
CFTR	13	4	71	16	4	60
CHIA	15	12	39	11	6	31
DPP10	9	6	120	9	4	97
IKBKAP	18	15	130	15	11	119
IL12RB1	9	12	32	9	9	30
PLA2G7	5	3	47	5	1	46
TGFB1	3	6	28	2	2	28
TOTAL	**93**	**68**	**499**	**81**	**45**	**439**

B. European Americans

Gene	Cases			Controls		
	NS	**S**	**NC**	**NS**	**S**	**NC**
ADRB2	3	0	2	2	3	4
AGT	2	1	2	5	2	7
CFTR	11	2	26	18	4	30
CHIA	2	3	10	4	2	11
DPP10	3	2	33	4	1	56
IKBKAP	7	5	40	12	7	78
IL12RB1	3	0	7	4	2	11
PLA2G7	1	0	12	2	1	27
TGFB1	2	2	14	2	2	17
TOTAL	**34**	**15**	**146**	**53**	**24**	**241**

Table S3. Mann-Whitney *U* Tests Comparing Local European Ancestry at Each Gene in African American Cases and Controls

Gene	Mean African Ancestry in Cases	Mean African Ancestry in Controls	p-value
AGT	0.805	0.831	0.43
CFTR	0.799	0.819	0.39
CHIA	0.796	0.820	0.23
DPP10	0.782	0.822	0.11
IKBKAP	0.797	0.826	0.094
IL12RB1	0.803	0.842	0.056
PLA2G7	0.805	0.803	0.86
TGFB1	0.807	0.855	0.10

Local ancestry was estimated using the program LAMP using genotypes from the Illumina 1M and 650K chip.