**SUPPLEMENTARY INFORMATION**

# Meta-analysis of Genome-wide Association Studies of Asthma In Ethnically Diverse North American Populations

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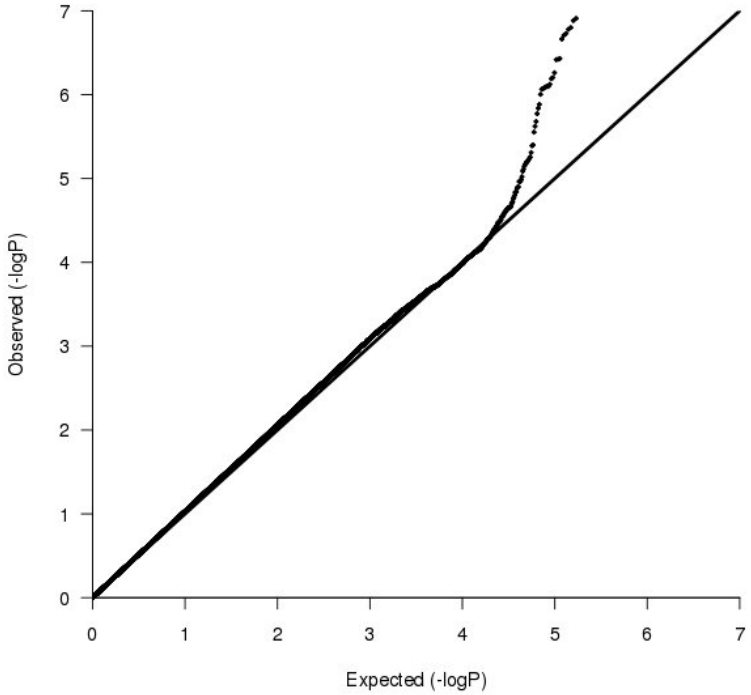
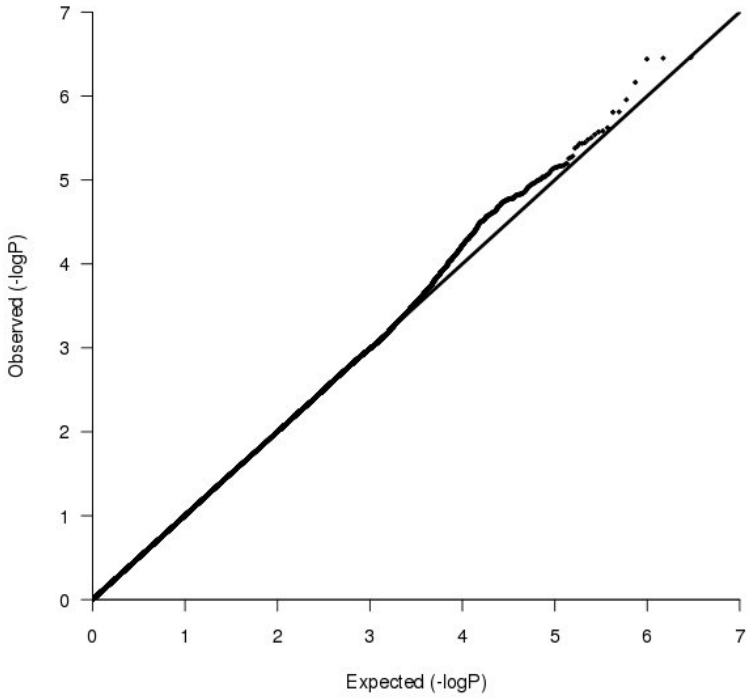
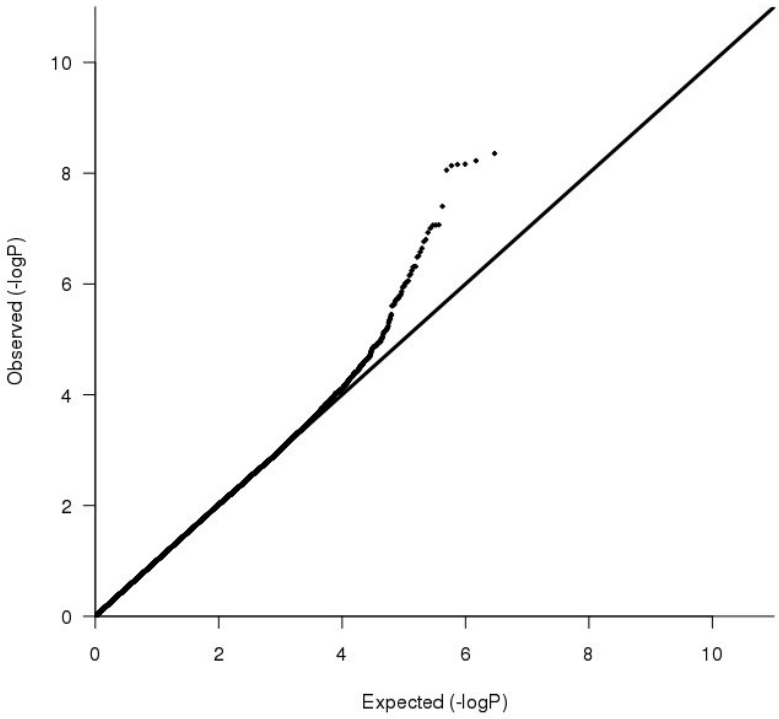
**Supplementary Figure 1.** QQ plot for the European American meta-analysis. The inflation factor, $\lambda_{GC}$ is 1.05.



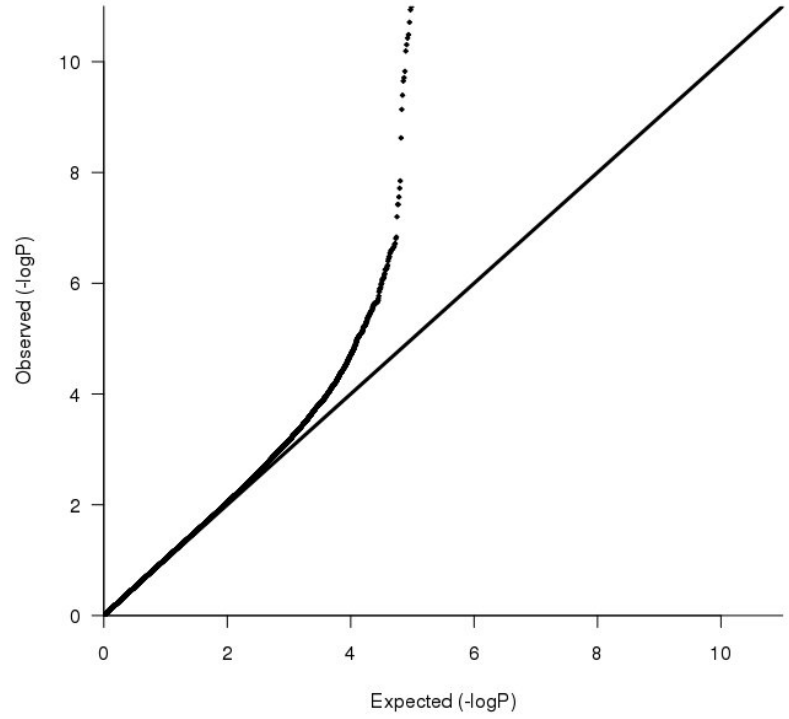
**Supplementary Figure 2.** QQ plot for the African American/African Caribbean meta-analysis. $\lambda_{GC}$=1.003.

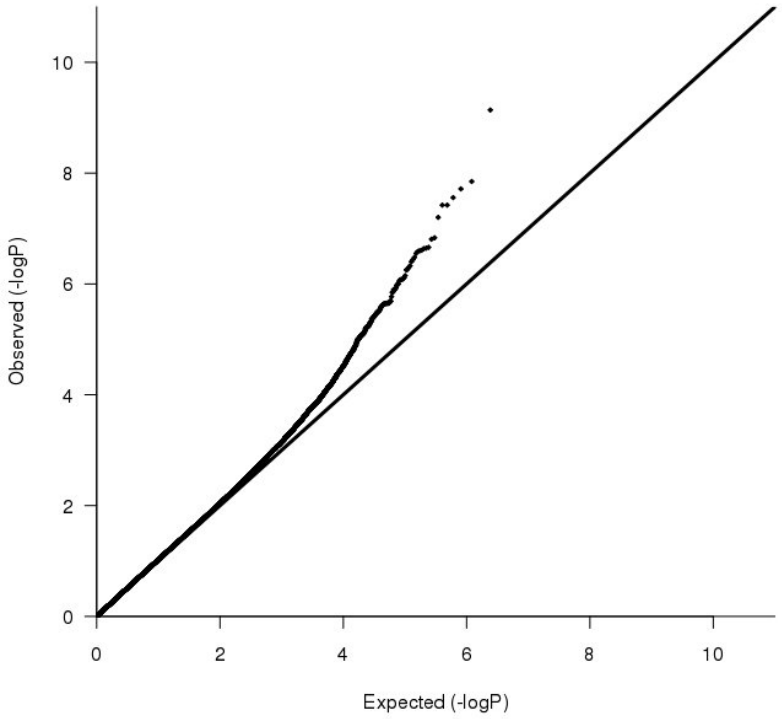


**Supplementary Figure 3**. QQ plot for the Latino meta-analysis. $\lambda_{GC}$=1.03.

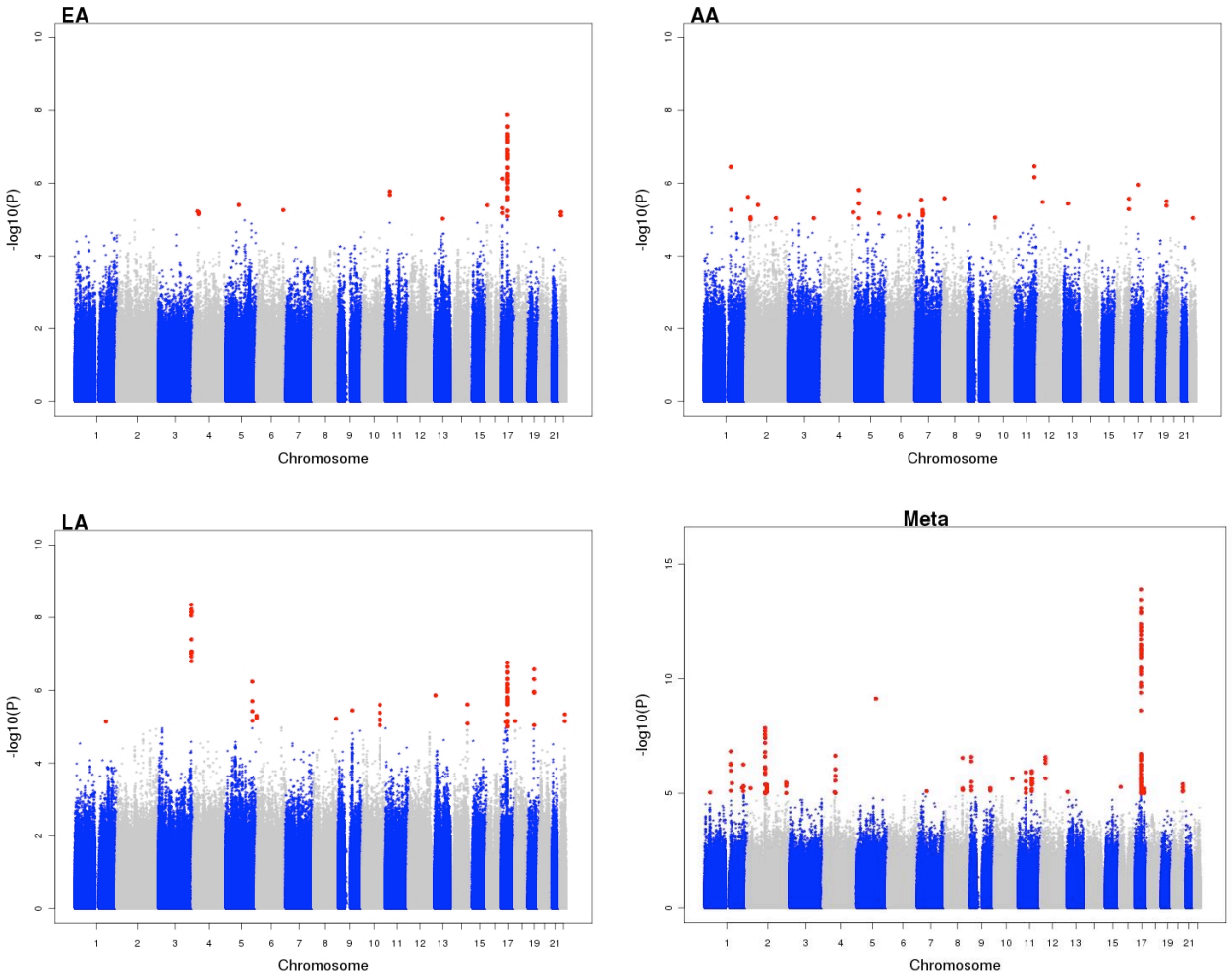


**Supplementary Figure 4**. QQ plots for the Overall meta-analysis (above**,** $\lambda_{GC}$=1.04), and the Overall meta-analysis excluding SNPs on 17q (below).

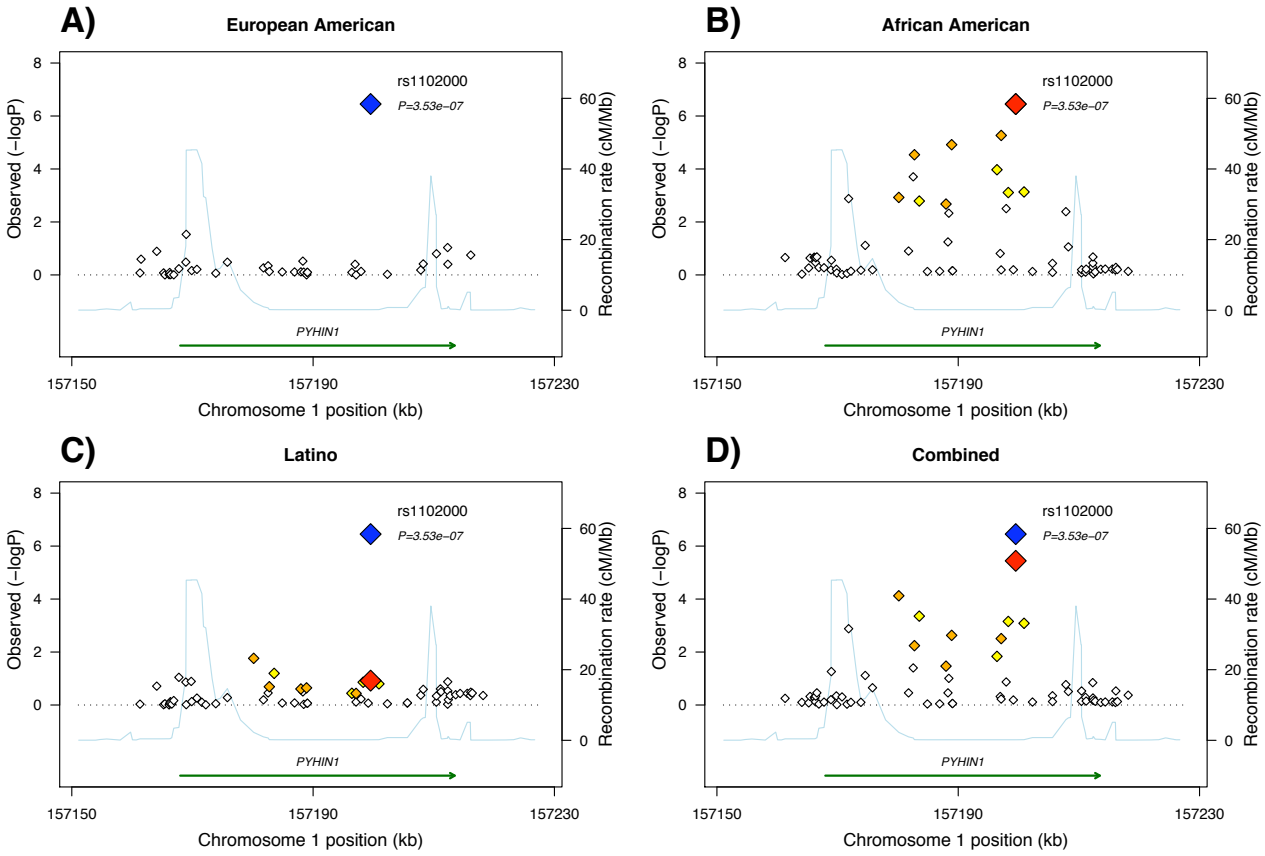


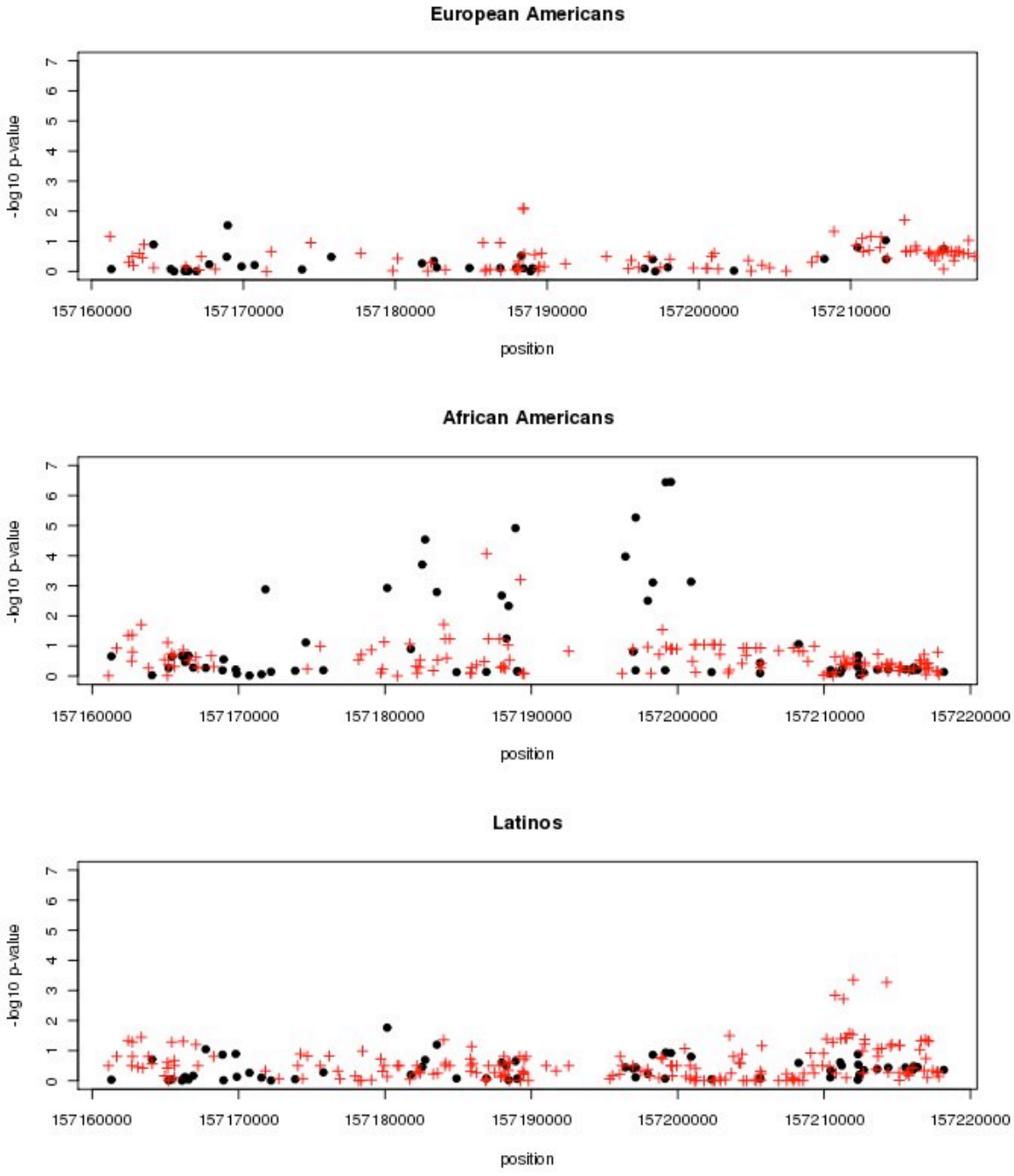
**Supplementary Figure 5:** Manhattan Plots of Meta-Analyses GWAS Results for the European American (EA), African American/African Caribbean (AA), Latinos (LA), and in the Combined sample (Meta). X-axis shows chromosome position and Y-axis shows the $-\log_{10}$(P-value); points in red indicate SNPs with association p-values $< 10^{-5}$.



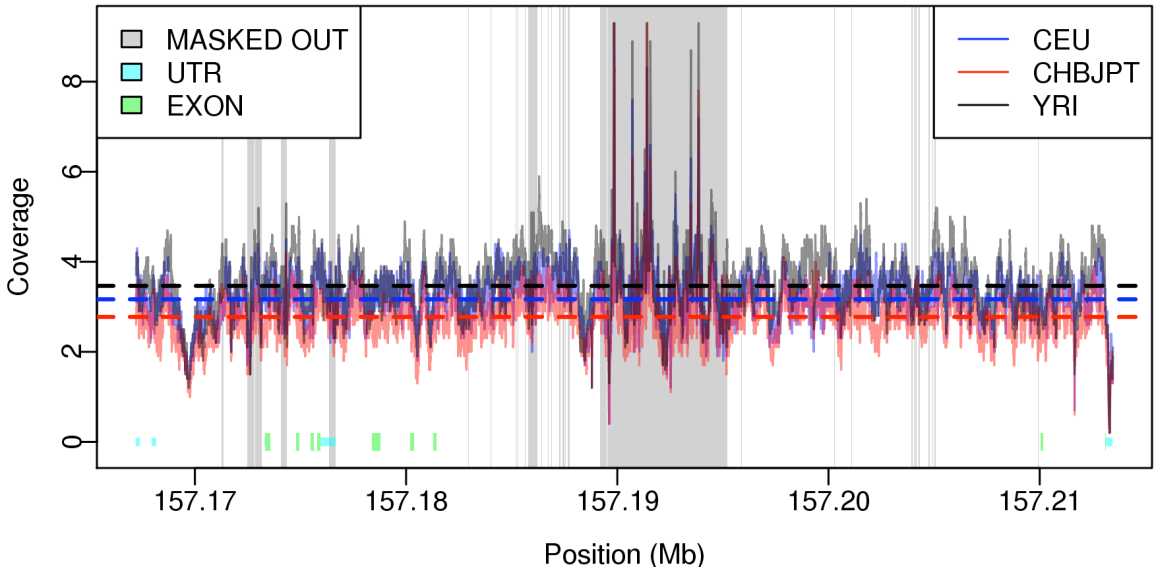
**Supplementary Figure 6**. Association results for the chromosome 1 region around *PYHIN1*. Panels A-D correspond to the GWAS results in the *PYHIN1* region on chromosome 1 in European Americans, African American/African Caribbeans, Latinos, and the Combined sample, respectively. The relative location and structure of the *PYHIN1* gene and direction of transcription are shown in the lower portion of each figure, and the chromosomal position on the x-axis. The light blue line shows the recombination rate across the region (right y-axis), and the left y-axis shows the significance of the associations in each panel. The large blue diamonds in panels A, C, and D show the top signal, rs1102000, in the African American/African Caribbean sample. The large red diamond in panels B, C, and D shows the p-value for rs1102000 in each of the samples (note that this SNP in not polymorphic in European Americans). The small diamonds in panels A-D show the p-values for all other SNPs, color-coded according to the level of LD with rs1102000 in the HapMap YRI (red, $r^2 >$ 0.9; orange, $r^2$ = 0.7-0.9; yellow, $r^2$ = 0.5-0.7).



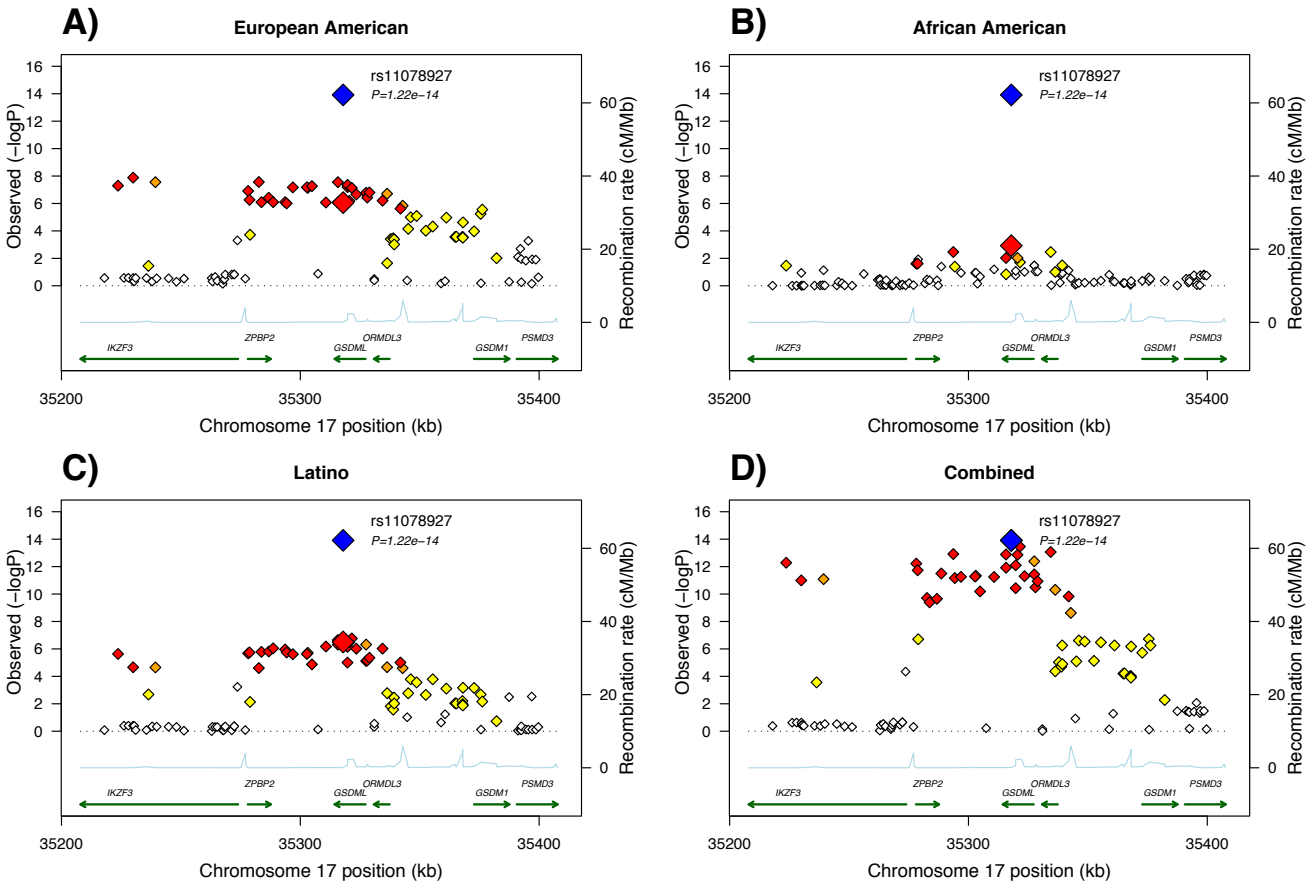
**Supplementary Figure 7**. Association results for additional imputed SNPs in the chromosome 1 region around *PYHIN1* using pilot data from the 1000 Genomes Project [1]. Shown is the same region as in Supplementary Figure 10, with "black dots" showing the results for the SNPs in the original meta-analysis and "red crosses" displaying association results for the additional SNPs obtained from the 1000 Genome Project imputation.



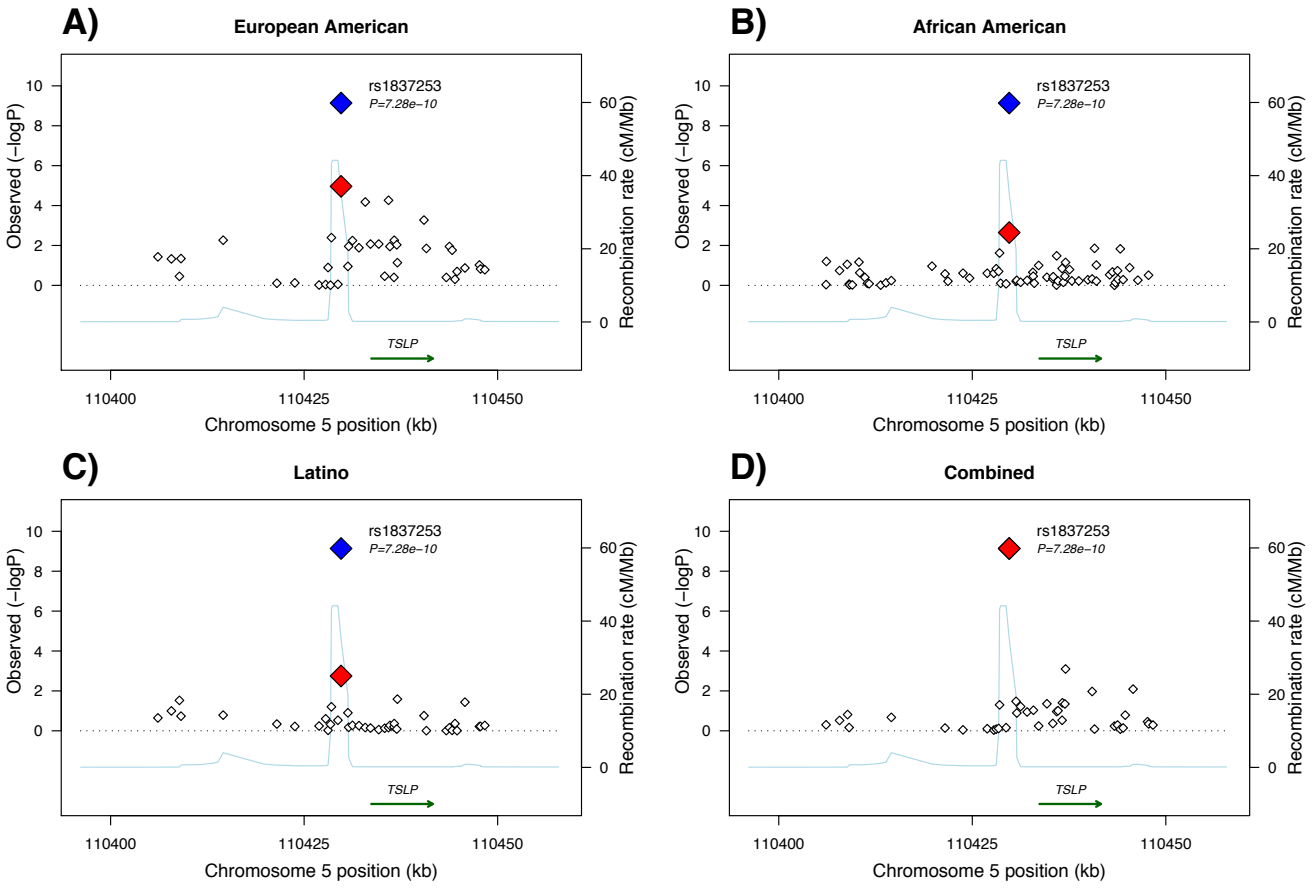
**Supplementary Figure 8**. Coverage of the *PYHIN1* gene in pilot data from the 1000 Genomes Project [1]. Solid lines represent the coverage at each position, and dashed lines represent the average coverage across chromosome 1. Shaded areas are regions of *PYHIN1* that were masked out, which were predominantly due to poor mapping quality (19% of all sites within the window). Coding exons (EXON) and UTRs are annotated according to the union of all transcripts, positions are reported according to hg18.



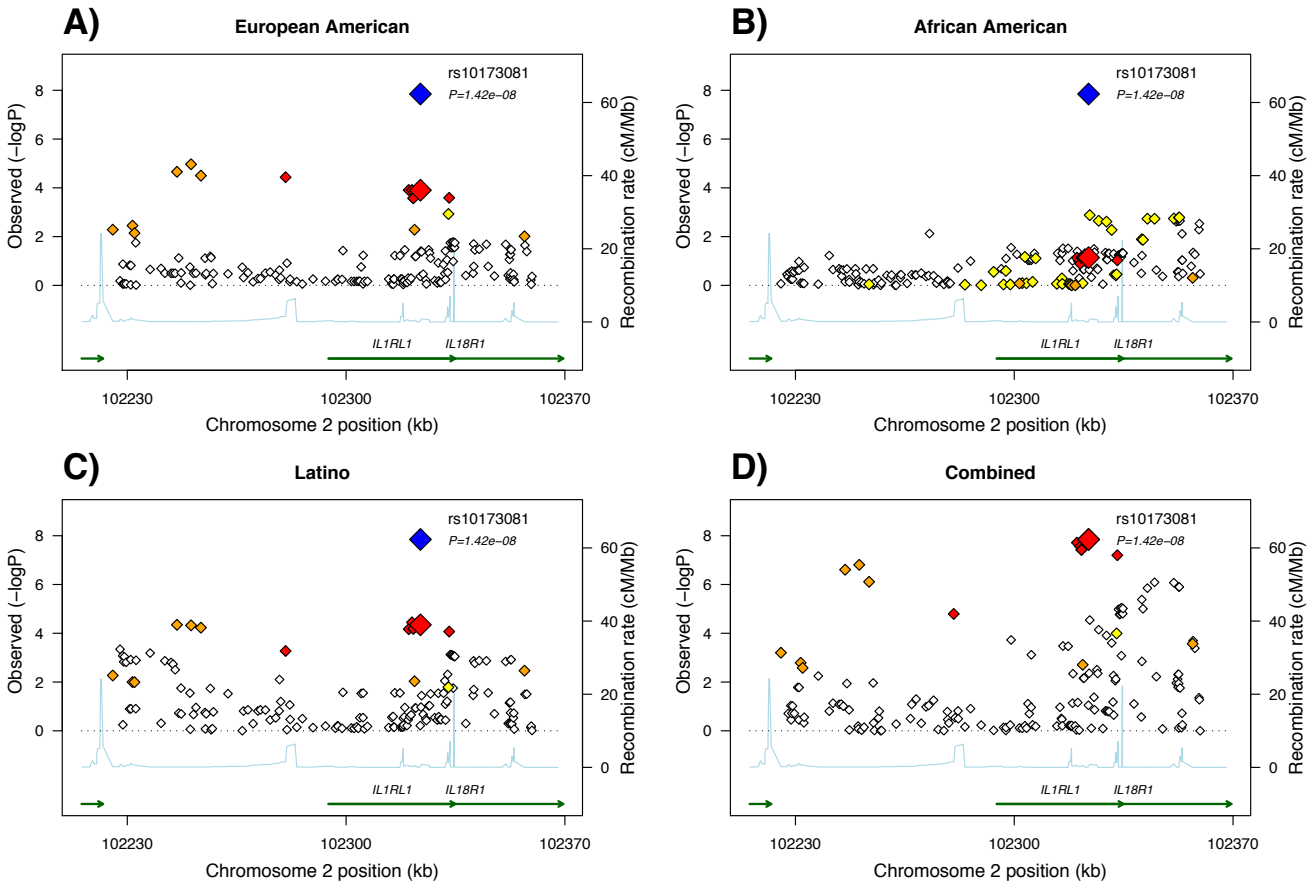
**Supplementary Figure 9**. Association results for the chromosome 17 region around *ORMDL3*. Panels A-D correspond to the GWAS results in the *ORMDL3* region on chromosome 17 in European Americans, African American/African Caribbeans, Latinos, and the Combined sample, respectively. The relative location and structure of the *ORMDL3* gene and direction of transcription are shown in the lower portion of each figure, and the chromosomal position on the x-axis. The light blue line shows the recombination rate across the region (right y-axis), and the left y-axis shows the significance of the associations in each panel. The large blue diamonds in panels A, B, and C show the top signal, rs11078927, in the African American/African Caribbean samples. The large red diamond in panels A, B, and C shows the p-value for rs11078927 in each of the samples. The small diamonds in panels A-D show the p-values for all other SNPs, color-coded according to the level of LD with rs11078927 in the HapMap CEU (red, $r^2 > 0.9$; orange, $r^2 = 0.7$-$0.9$; yellow, $r^2 = 0.5$-$0.7$).



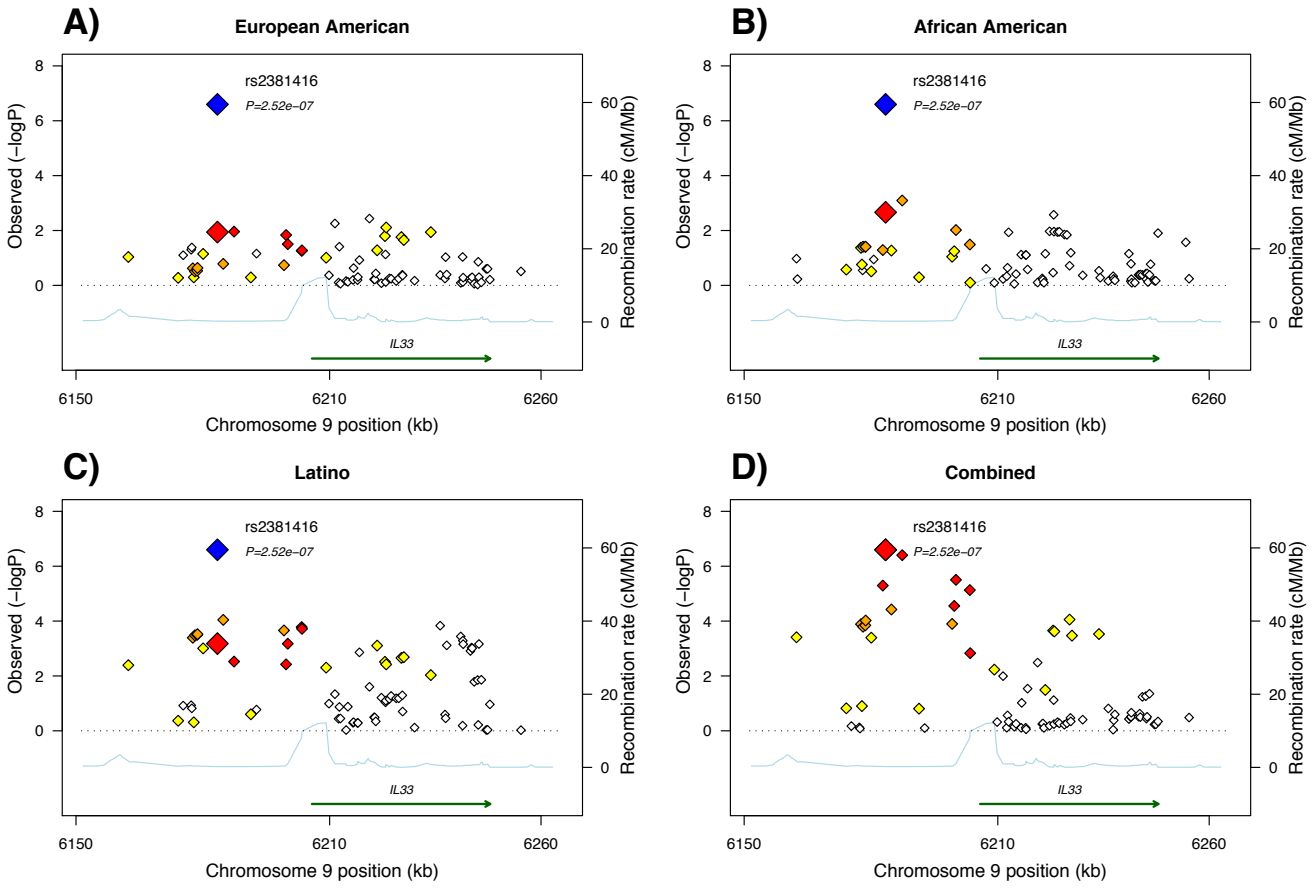
**Supplementary Figure 10**. Association results for the chromosome 5 region around *TSLP*. Panels A-D correspond to the GWAS results in the *TSLP* region on chromosome 5 in European Americans, African American/African Caribbeans, Latinos, and the Combined sample, respectively. The relative location and structure of the *TSLP* gene and direction of transcription are shown in the lower portion of each figure, and the chromosomal position on the x-axis. The light blue line shows the recombination rate across the region (right y-axis), and the left y-axis shows the significance of the associations in each panel. The large blue diamonds in panels A, B, and C show the top signal, rs1837253, in the combined meta-analysis. The large red diamond in panels A-D shows the p-value for rs1837253 in each of the samples. The small diamonds in panels A-D show the p-values for all other SNPs, color-coded according to the level of LD with rs1837253 in the HapMap CEU (red, $r^2 > 0.9$; orange, $r^2 = 0.7$-0.9; yellow, $r^2 = 0.5$-0.7).



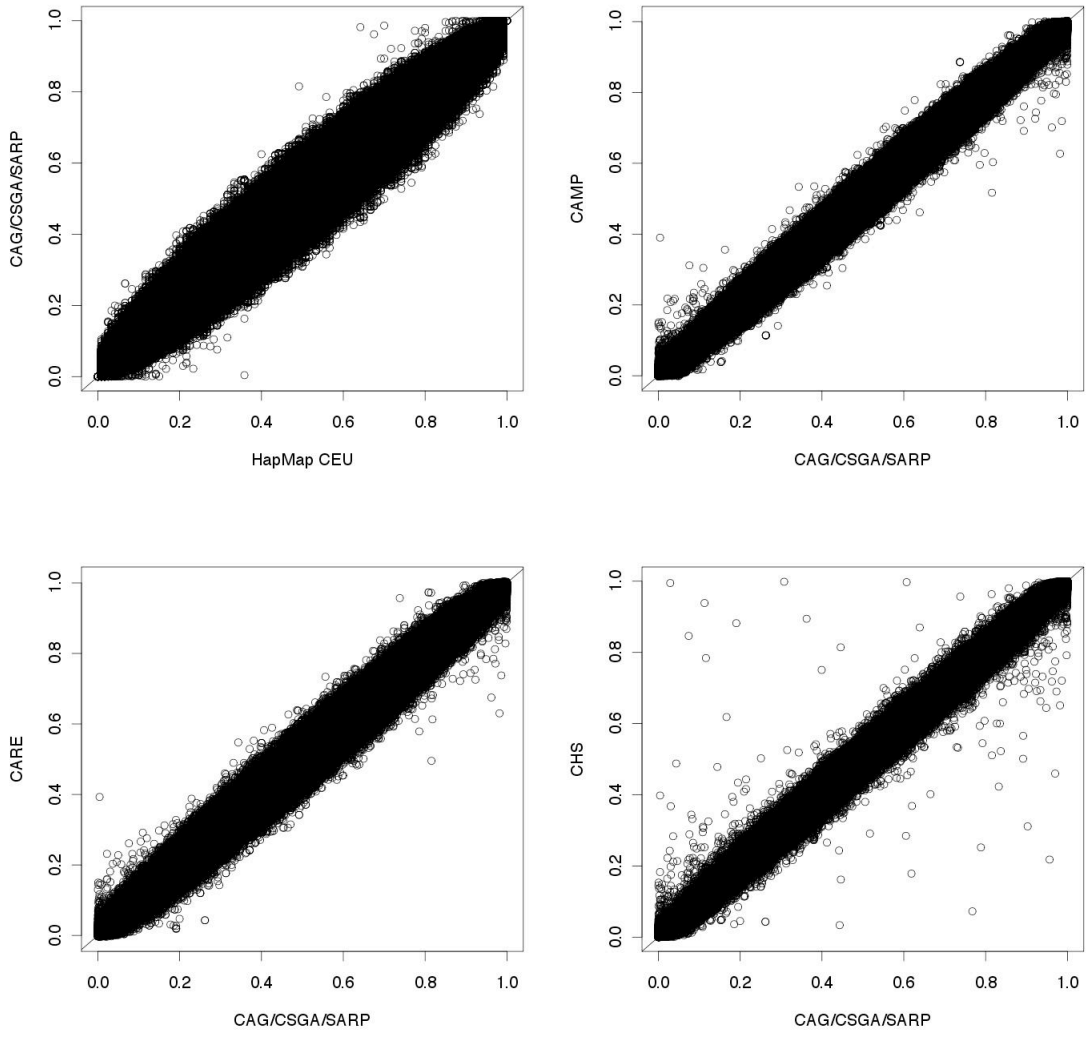
**Supplementary Figure 11**. Association results for the chromosome 2 region around *IL1RL1*. Panels A-D correspond to the GWAS results in the *IL1RL1* region on chromosome 2 in European Americans, African American/African Caribbeans, Latinos, and the Combined sample, respectively. The relative location and structure of the *IL1RL1* gene and direction of transcription are shown in the lower portion of each figure, and the chromosomal position on the x-axis. The light blue line shows the recombination rate across the region (right y-axis), and the left y-axis shows the significance of the associations in each panel. The large blue diamonds in panels A, B, and C show the top signal, rs10173081, in the combined meta-analysis. The large red diamond in panels A-D shows the p-value for rs10173081 in each of the samples. The small diamonds in panels A-D show the p-values for all other SNPs, color-coded according to the level of LD with rs10173081 in the HapMap CEU (red, $r^2 > 0.9$; orange, $r^2 = 0.7$-$0.9$; yellow, $r^2 = 0.5$-$0.7$).



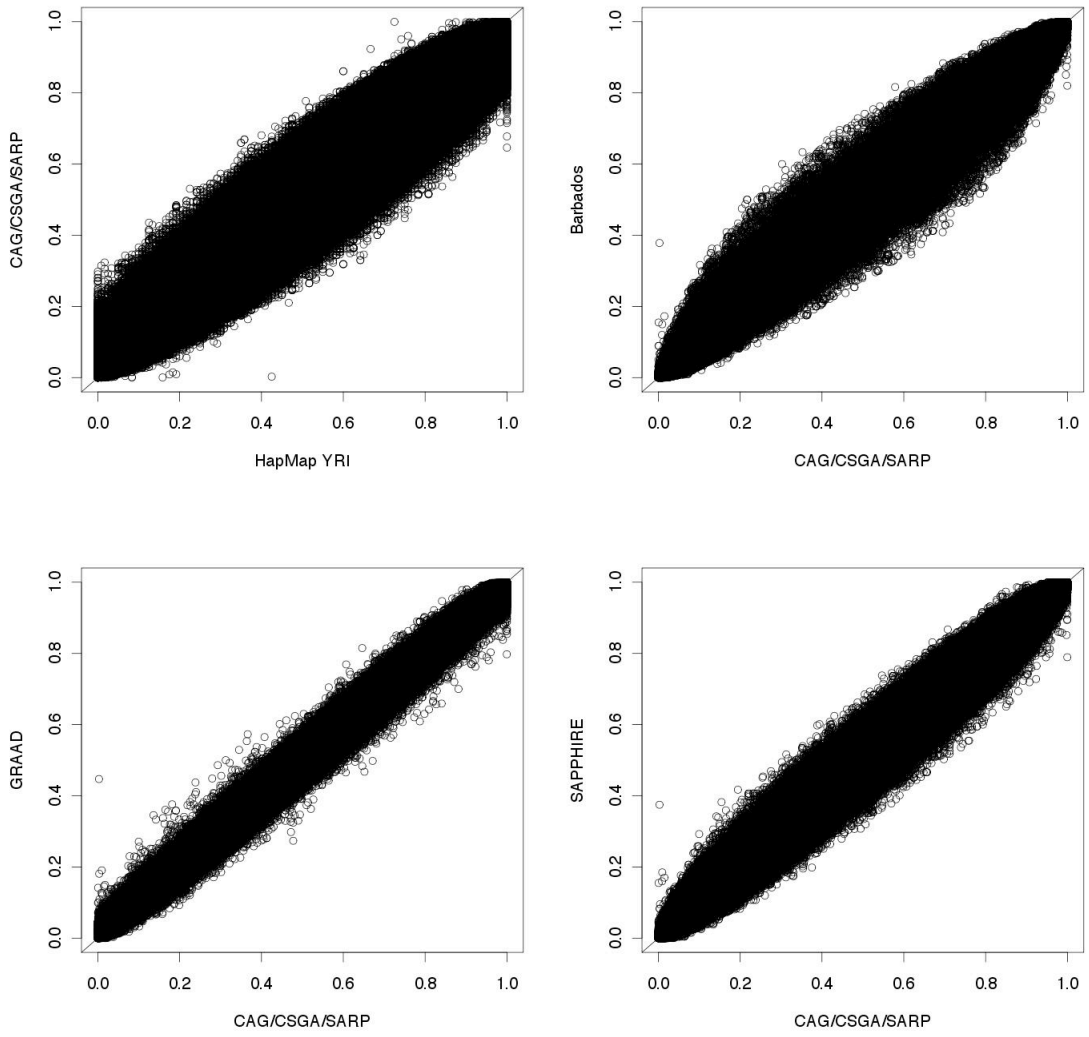
**Supplementary Figure 12**. Association results for the chromosome 9 region around *IL33*. Panels A-D correspond to the GWAS results in the *IL33* region on chromosome 9 in European Americans, African American/African Caribbeans, Latinos, and the Combined sample, respectively. The relative location and structure of the *IL33* gene and direction of transcription are shown in the lower portion of each figure, and the chromosomal position on the x-axis. The light blue line shows the recombination rate across the region (right y-axis), and the left y-axis shows the significance of the associations in each panel. The large blue diamonds in panels A, B, and C show the top signal, rs2381416, in the combined meta-analysis. The large red diamond in panels A-D shows the p-value for rs2381416 in each of the samples. The small diamonds in panels A-D show the p-values for all other SNPs, color-coded according to the level of LD with rs2381416 in the HapMap CEU (red, $r^2 > 0.9$; orange, $r^2 = 0.7$-$0.9$; yellow, $r^2 = 0.5$-$0.7$).



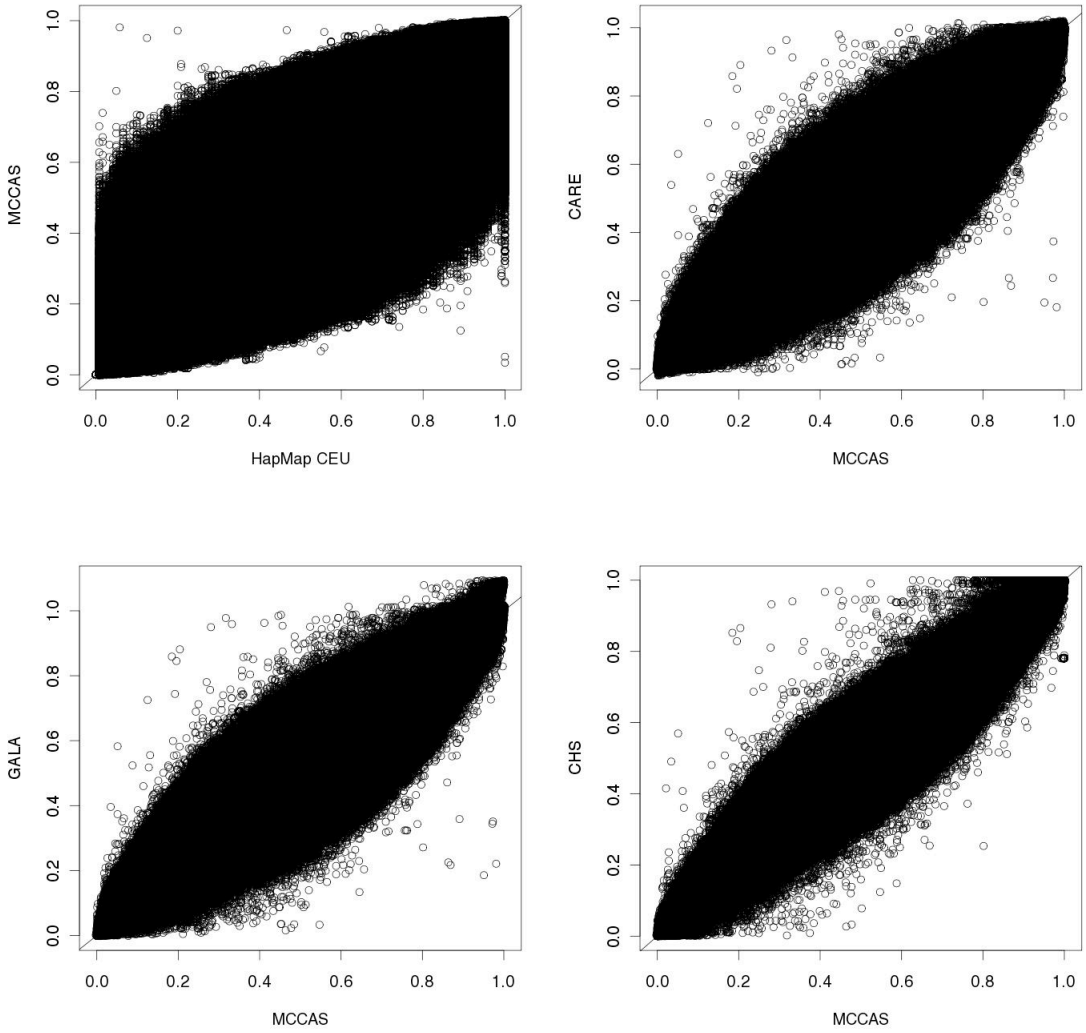
**Supplementary Figure 13.** Comparison of allele frequencies in the controls/untransmitted chromosomes across groups for Allele 1 in European American studies. Outliers in CHS allele frequencies did not appear to be caused by strand or allele orientation issues, and were therefore included in the meta-analysis; however, none of the SNPs with frequency difference > 0.2 were among the top signals of association in either the overall meta-analysis or the European American meta-analysis



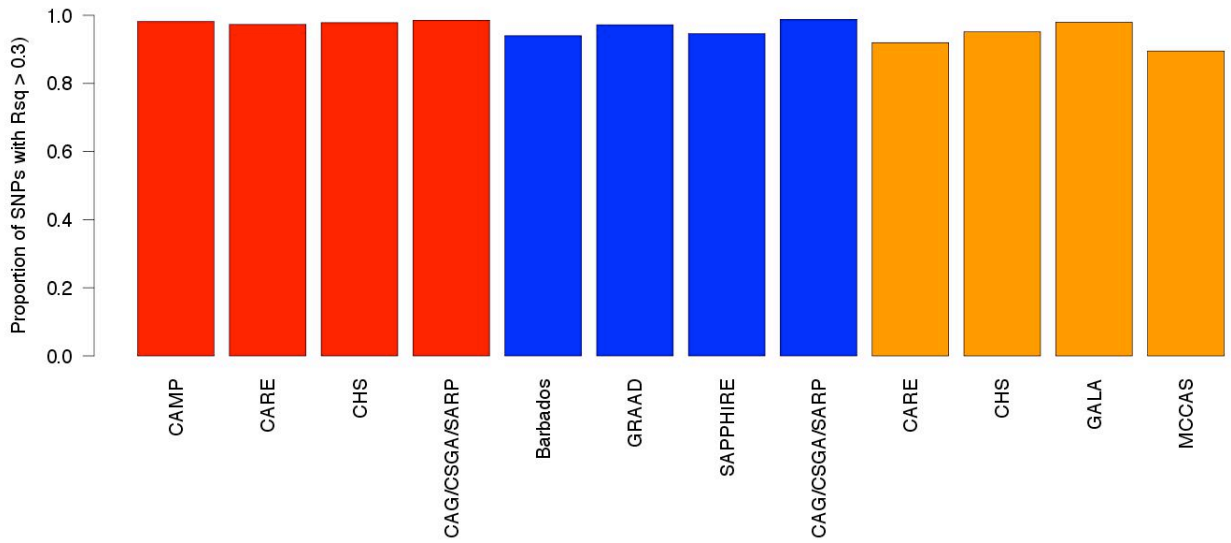
**Supplementary Figure 14.** Comparison of allele frequencies in the controls/untransmitted chromosomes across groups for Allele 1 in African American studies and Barbados.



**Supplementary Figure 15.** Comparison of allele frequencies in the controls/untransmitted chromosomes across groups for Allele 1 in Latino studies.



**Supplementary Figure 16.** The proportion of SNPs with Rsq imputation quality scores > 0.3 across each study. A threshold of Rsq > 0.5 was used for the Barbados study after adjusting for extended pedigrees. European American studies are in red, African American and Barbados studies are in blue, and Latino studies are in orange. Genotype imputation performed consistently well across studies, with the proportion of imputed genotypes with Rsq > 0.3 over 90% for all studies.



**Supplementary Table 1:** Frequencies of the most significant SNP in each of the regions with at least one SNP associated with asthma at $p<1x10^{-6}$ (see Table 2 in main text).

| | | | | | European American | | African American/African Caribbean | | Latino | |
|---|---|---|---|---|---|---|---|---|---|---|
| **SNP** | **Chr.** | **Position** | **A1** | **A2** | **Controls** | **Cases** | **Controls** | **Cases** | **Controls** | **Cases** |
| rs4845783 | 1 | 150,759,183 | G | A | 0.269 | 0.300 | 0.080 | 0.101 | 0.196 | 0.217 |
| rs1102000 | 1 | 155,745,980 | T | C | 1.000 | 1.000 | 0.719 | 0.770 | 0.981 | 0.980 |
| rs4653433 | 1 | 224,041,154 | A | G | 0.406 | 0.436 | 0.564 | 0.582 | 0.323 | 0.360 |
| rs10173081 | 2 | 102,323,780 | C | T | 0.856 | 0.886 | 0.736 | 0.748 | 0.889 | 0.913 |
| rs2017908 | 3 | 188,900,662 | A | C | 0.134 | 0.127 | 0.329 | 0.331 | 0.087 | 0.129 |
| rs11735820 | 4 | 66,181,611 | G | T | 0.302 | 0.338 | 0.335 | 0.366 | 0.208 | 0.230 |
| rs1837253 | 5 | 110,429,771 | C | T | 0.741 | 0.785 | 0.731 | 0.760 | 0.689 | 0.719 |
| rs10064618 | 5 | 153,752,482 | G | A | 0.590 | 0.593 | 0.269 | 0.281 | 0.358 | 0.423 |
| rs2453626 | 8 | 101,207,073 | C | T | 0.539 | 0.569 | 0.662 | 0.700 | 0.709 | 0.729 |
| rs2381416 | 9 | 6,183,455 | C | A | 0.262 | 0.296 | 0.563 | 0.603 | 0.227 | 0.262 |
| rs11214966 | 11 | 113,736,465 | C | T | 0.073 | 0.075 | 0.201 | 0.246 | 0.125 | 0.131 |
| rs16929496 | 12 | 25,885,071 | T | C | 0.785 | 0.814 | 0.740 | 0.757 | 0.836 | 0.854 |
| rs9891949 | 17 | 8,039,908 | A | G | 0.627 | 0.676 | 0.576 | 0.589 | 0.688 | 0.687 |
| rs11078927 | 17 | 35,317,931 | C | T | 0.552 | 0.606 | 0.865 | 0.887 | 0.682 | 0.730 |
| rs335016 | 19 | 35,065,232 | A | C | 0.425 | 0.440 | 0.418 | 0.421 | 0.443 | 0.495 |

**Supplementary Table 2:** Results of the meta-analyses for SNPs with p-values < $10^{-6}$ in at least one population or the combined populations. EA = European American, AA = African American/Caribbean American, LA = Latino, Meta = meta-analysis across all populations.

| SNP | Chr | Position (hg18) | A1/A2 | EA p-value | AA p-value | LA p-value | Meta p-value |
|---|---|---|---|---|---|---|---|
| rs4845783 | 1 | 149305632 | A/G | 2.29E-003 | 2.33E-004 | 4.78E-002 | 5.60E-007 |
| rs1538084 | 1 | 149309085 | A/C | 1.29E-003 | 6.44E-004 | 3.71E-002 | 5.01E-007 |
| rs6587688 | 1 | 149342695 | C/T | 1.37E-003 | 9.41E-005 | 4.10E-002 | 1.47E-007 |
| rs1231172 | 1 | 155745628 | T/C | NA | 3.62E-007 | 1.16E-001 | NA |
| rs1102000 | 1 | 155745980 | A/G | NA | 3.53E-007 | 1.20E-001 | NA |
| rs4653433 | 1 | 222281266 | A/G | 2.61E-003 | 2.68E-002 | 6.17E-004 | 5.44E-007 |
| rs949963 | 2 | 102228304 | C/T | 1.71E-003 | 1.91E-002 | 2.56E-003 | 8.32E-007 |
| rs871657 | 2 | 102229859 | C/T | 1.69E-003 | 1.82E-002 | 2.28E-003 | 7.08E-007 |
| rs10189629 | 2 | 102337982 | A/C | 2.20E-005 | 7.15E-001 | 4.50E-005 | 2.48E-007 |
| rs11692065 | 2 | 102342493 | C/T | 1.08E-005 | 7.22E-001 | 4.74E-005 | 1.56E-007 |
| rs11674302 | 2 | 102345646 | C/T | 3.16E-005 | 9.03E-001 | 5.90E-005 | 7.75E-007 |
| rs3771180 | 2 | 102412135 | G/T | 1.23E-004 | 7.33E-002 | 6.78E-005 | 1.93E-008 |
| rs13431828 | 2 | 102413171 | C/T | 1.23E-004 | 1.30E-001 | 3.56E-005 | 2.77E-008 |
| rs13408569 | 2 | 102413574 | C/G | 2.67E-004 | 7.36E-002 | 6.54E-005 | 3.79E-008 |
| rs13408661 | 2 | 102413600 | A/G | 2.66E-004 | 7.38E-002 | 6.50E-005 | 3.78E-008 |
| rs10173081 | 2 | 102415866 | C/T | 1.25E-004 | 7.29E-002 | 4.51E-005 | 1.42E-008 |
| rs10197862 | 2 | 102425067 | A/G | 2.57E-004 | 9.39E-002 | 8.52E-005 | 6.31E-008 |
| rs3755276 | 2 | 102436977 | C/T | 2.07E-002 | 1.85E-003 | 1.35E-003 | 8.10E-007 |
| rs1362348 | 2 | 102443142 | C/G | 2.08E-002 | 1.81E-003 | 1.44E-003 | 8.46E-007 |
| rs954470 | 3 | 188894973 | C/T | 1.19E-001 | 4.24E-001 | 9.89E-008 | 1.36E-002 |
| rs6770600 | 3 | 188898436 | A/G | 2.12E-001 | 6.60E-001 | 6.97E-009 | 6.29E-003 |
| rs11928175 | 3 | 188900416 | C/T | 1.50E-001 | 4.98E-001 | 7.32E-009 | 6.23E-003 |
| rs2017908 | 3 | 188900670 | A/C | 2.37E-001 | 6.66E-001 | 4.42E-009 | 4.92E-003 |
| rs9848804 | 3 | 188902018 | A/C | 1.59E-001 | 6.30E-001 | 8.81E-009 | 8.48E-003 |
| rs9812190 | 3 | 188902430 | A/G | 2.45E-001 | 6.80E-001 | 6.86E-009 | 5.55E-003 |
| rs7616923 | 3 | 188903921 | G/T | 1.70E-001 | 7.33E-001 | 5.96E-009 | 8.92E-003 |
| rs4254648 | 3 | 188911388 | A/G | 1.37E-001 | 4.39E-001 | 3.97E-008 | 7.82E-002 |
| rs9878204 | 3 | 188918390 | A/G | 8.31E-002 | 6.23E-001 | 8.56E-008 | 9.27E-002 |
| rs9865102 | 3 | 188918869 | C/T | 1.45E-001 | 6.38E-001 | 8.66E-008 | 6.23E-002 |
| rs6786702 | 3 | 188929433 | C/T | 1.52E-001 | 9.94E-001 | 8.71E-008 | 3.34E-002 |
| rs6762932 | 3 | 188931699 | A/G | 1.98E-001 | 9.69E-001 | 1.58E-007 | 2.92E-002 |
| rs9827569 | 3 | 188935184 | G/T | 1.83E-001 | 7.26E-001 | 1.18E-007 | 4.83E-002 |
| rs7659227 | 4 | 66324936 | A/G | 3.57E-004 | 5.41E-003 | 3.59E-002 | 8.89E-007 |
| rs11735820 | 4 | 66327782 | G/T | 1.48E-004 | 2.96E-003 | 3.30E-002 | 2.27E-007 |
| rs1837253 | 5 | 110429771 | C/T | 1.09E-005 | 2.25E-003 | 1.79E-003 | 7.28E-010 |
| rs10064618 | 5 | 153752482 | A/G | 7.62E-001 | 3.57E-001 | 5.75E-007 | 4.44E-004 |
| rs2453626 | 8 | 101207073 | C/T | 4.37E-003 | 2.14E-004 | 1.60E-002 | 2.82E-007 |
| rs2381416 | 9 | 6183455 | A/C | 1.14E-002 | 2.17E-003 | 6.62E-004 | 2.52E-007 |
| rs1888909 | 9 | 6187392 | C/T | 1.10E-002 | 8.06E-004 | 2.99E-003 | 3.97E-007 |
| rs11214966 | 11 | 113736465 | C/T | 7.59E-001 | 3.46E-007 | 5.85E-001 | 1.20E-003 |
| rs4938096 | 11 | 113740940 | C/T | 9.64E-001 | 6.87E-007 | 6.40E-001 | 3.07E-003 |
| rs16929496 | 12 | 25885071 | C/T | 3.19E-004 | 2.53E-002 | 2.70E-003 | 2.60E-007 |
| rs11048311 | 12 | 25913405 | A/C | 1.05E-004 | 1.77E-002 | 1.81E-002 | 4.70E-007 |

| SNP | Chr | Position (hg18) | A1/A2 | EA p-value | AA p-value | LA p-value | Meta p-value |
|---|---|---|---|---|---|---|---|
| rs11048317 | 12 | 25919674 | G/T | 2.05E-004 | 2.22E-002 | 6.07E-003 | 3.32E-007 |
| rs9891949 | 17 | 8039908 | A/G | 7.52E-007 | 6.78E-001 | 7.34E-001 | 4.47E-004 |
| rs2517955 | 17 | 35097207 | C/T | 6.08E-004 | 1.44E-001 | 6.81E-005 | 2.19E-007 |
| rs2952155 | 17 | 35115244 | C/T | 4.18E-004 | 9.78E-002 | 4.34E-004 | 3.63E-007 |
| rs1810132 | 17 | 35119531 | C/T | 4.88E-004 | 2.06E-001 | 4.41E-005 | 2.31E-007 |
| rs1058808 | 17 | 35137563 | C/G | 3.55E-004 | 7.23E-001 | 9.69E-006 | 8.33E-007 |
| rs907092 | 17 | 35175785 | A/G | 1.31E-006 | 2.22E-002 | 1.65E-006 | 3.24E-012 |
| rs2313430 | 17 | 35183342 | C/T | 5.14E-008 | 8.90E-002 | 2.41E-005 | 1.94E-011 |
| rs10445308 | 17 | 35191573 | C/T | 1.31E-007 | 3.18E-002 | 1.82E-006 | 8.39E-013 |
| rs9909593 | 17 | 35223675 | A/G | 5.06E-008 | 3.41E-002 | 2.33E-006 | 5.23E-013 |
| rs9303277 | 17 | 35229995 | C/T | 1.31E-008 | 1.15E-001 | 2.18E-005 | 1.01E-011 |
| rs3816470 | 17 | 35239327 | A/G | 2.79E-008 | 7.36E-002 | 2.23E-005 | 8.22E-012 |
| rs11557466 | 17 | 35278152 | C/T | 1.23E-007 | 2.46E-002 | 2.10E-006 | 6.02E-013 |
| rs11078925 | 17 | 35278734 | C/T | 5.48E-007 | 2.42E-002 | 1.81E-006 | 1.86E-012 |
| rs12150079 | 17 | 35278943 | A/G | 1.92E-004 | 1.18E-002 | 7.36E-003 | 1.98E-007 |
| rs12936231 | 17 | 35282646 | C/G | 2.73E-008 | 3.48E-001 | 2.50E-005 | 1.95E-010 |
| rs11870965 | 17 | 35283731 | A/T | 8.09E-007 | 3.98E-001 | 1.64E-006 | 4.04E-010 |
| rs1054609 | 17 | 35286803 | A/C | 3.82E-007 | 4.03E-001 | 1.55E-006 | 2.23E-010 |
| rs9907088 | 17 | 35288642 | A/G | 7.97E-007 | 3.98E-002 | 9.08E-007 | 3.16E-012 |
| rs12452894 | 17 | 35290112 | A/G | 3.78E-007 | 4.01E-002 | 8.78E-007 | 1.63E-012 |
| rs12232497 | 17 | 35293645 | C/T | 7.97E-007 | 3.46E-003 | 1.10E-006 | 1.21E-013 |
| rs2872507 | 17 | 35294289 | A/G | 9.92E-007 | 4.05E-002 | 1.83E-006 | 6.84E-012 |
| rs9901146 | 17 | 35296869 | A/G | 6.72E-008 | 1.15E-001 | 2.43E-006 | 5.57E-012 |
| rs12950743 | 17 | 35302759 | C/T | 6.55E-008 | 1.15E-001 | 2.35E-006 | 5.30E-012 |
| rs7359623 | 17 | 35303115 | C/T | 7.32E-008 | 1.11E-001 | 1.93E-006 | 4.64E-012 |
| rs8067378 | 17 | 35304874 | A/G | 5.42E-008 | 2.13E-001 | 1.34E-005 | 6.43E-011 |
| rs8069176 | 17 | 35310723 | A/G | 8.49E-007 | 6.39E-002 | 6.66E-007 | 5.66E-012 |
| rs2305480 | 17 | 35315722 | A/G | 8.30E-007 | 9.45E-003 | 2.27E-007 | 1.31E-013 |
| rs2305479 | 17 | 35315743 | C/T | 2.79E-008 | 1.44E-001 | 4.90E-007 | 1.21E-012 |
| rs11078927 | 17 | 35317931 | C/T | 8.62E-007 | 1.19E-003 | 3.12E-007 | 1.22E-014 |
| rs2290400 | 17 | 35319766 | C/T | 6.42E-008 | 1.74E-001 | 9.89E-006 | 3.75E-011 |
| rs1008723 | 17 | 35319793 | G/T | 4.44E-008 | 8.27E-002 | 7.05E-007 | 7.96E-013 |
| rs4795400 | 17 | 35320546 | C/T | 6.45E-007 | 9.39E-003 | 3.28E-007 | 1.38E-013 |
| rs869402 | 17 | 35321569 | C/T | 7.37E-008 | 1.94E-002 | 1.72E-007 | 3.46E-014 |
| rs7216389 | 17 | 35323475 | C/T | 2.17E-007 | 9.69E-002 | 9.67E-007 | 4.99E-012 |
| rs9303280 | 17 | 35327557 | C/T | 1.86E-007 | 3.32E-002 | 4.83E-007 | 4.09E-013 |
| rs9303281 | 17 | 35327572 | A/G | 1.66E-007 | 3.33E-002 | 7.65E-006 | 3.67E-012 |
| rs7219923 | 17 | 35328044 | C/T | 3.71E-007 | 9.04E-002 | 6.86E-006 | 3.25E-011 |
| rs7224129 | 17 | 35328952 | A/G | 1.58E-007 | 9.08E-002 | 4.42E-006 | 1.16E-011 |
| rs8076131 | 17 | 35334438 | A/G | 6.25E-007 | 3.47E-003 | 9.49E-007 | 8.62E-014 |
| rs12603332 | 17 | 35336333 | C/T | 1.96E-007 | 8.90E-002 | 2.14E-005 | 4.93E-011 |
| rs4795403 | 17 | 35339248 | C/T | 4.14E-004 | 3.25E-002 | 3.59E-003 | 5.58E-007 |
| rs4795405 | 17 | 35341943 | C/T | 2.39E-006 | 7.58E-002 | 9.84E-006 | 1.49E-010 |
| rs4794820 | 17 | 35342870 | A/G | 1.45E-006 | 2.86E-001 | 2.53E-005 | 2.38E-009 |
| rs8079416 | 17 | 35346239 | C/T | 1.02E-005 | 6.14E-001 | 1.64E-004 | 2.42E-007 |
| rs6503525 | 17 | 35348700 | C/G | 8.18E-006 | 5.97E-001 | 2.77E-004 | 2.88E-007 |
| rs4065985 | 17 | 35355458 | C/G | 4.79E-005 | 4.25E-001 | 1.63E-004 | 3.32E-007 |
| rs4795408 | 17 | 35361153 | A/G | 1.08E-005 | 5.11E-001 | 7.83E-004 | 5.55E-007 |

| SNP | Chr | Position (hg18) | A1/A2 | EA p-value | AA p-value | LA p-value | Meta p-value |
|---|---|---|---|---|---|---|---|
| rs6503526 | 17 | 35368124 | C/T | 2.39E-005 | 4.49E-001 | 6.81E-004 | 6.63E-007 |
| rs3894194 | 17 | 35375519 | A/G | 5.76E-006 | 2.41E-001 | 2.09E-003 | 1.92E-007 |
| rs7212938 | 17 | 35376206 | G/T | 2.80E-006 | 3.12E-001 | 6.93E-003 | 5.68E-007 |
| rs34724 | 19 | 35060850 | G/T | 5.16E-001 | 1.14E-001 | 4.96E-007 | 1.63E-002 |
| rs335016 | 19 | 35065232 | A/C | 1.57E-001 | 6.78E-001 | 2.65E-007 | 5.78E-005 |

**Supplementary Table 3:** Allele frequencies of allele 1 (FreqA1) in the controls/untransmitted chromosomes, cases/transmitted chromosomes, and the squared correlation between imputed and true genotypes (Rsq, imputation quality scores) for SNPs with meta-analysis p-values < $10^{-6}$ in at least one population or the combined populations. Genotyped SNPs are indicated with a "-" in the Rsq column. NA, SNP not polymorphic.

## a) European Americans:

| | | | | CAMP: | | | CARE: | | | CHS: | | | CAG/CSGA/SARP: | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SNP | Chr | Position (hg18) | A1/A2 | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq |
| rs4845783 | 1 | 149305632 | A/G | 0.724 | 0.686 | 1 | 0.724 | 0.696 | 1 | 0.741 | 0.705 | 0.99 | 0.723 | 0.705 | 1 |
| rs1538084 | 1 | 149309085 | A/C | 0.266 | 0.295 | 0.94 | 0.259 | 0.288 | 0.93 | 0.245 | 0.28 | 0.92 | 0.264 | 0.281 | 0.93 |
| rs6587688 | 1 | 149342695 | C/T | 0.722 | 0.685 | 0.98 | 0.72 | 0.694 | - | 0.736 | 0.701 | 0.97 | 0.723 | 0.702 | 0.98 |
| rs1231172 | 1 | 155745628 | T/C | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| rs1102000 | 1 | 155745980 | A/G | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA | NA |
| rs4653433 | 1 | 222281266 | A/G | 0.382 | 0.439 | - | 0.4 | 0.422 | 0.87 | 0.423 | 0.443 | - | 0.397 | 0.433 | - |
| rs949963 | 2 | 102228304 | C/T | 0.836 | 0.845 | - | 0.803 | 0.843 | 1 | 0.816 | 0.834 | - | 0.794 | 0.848 | - |
| rs871657 | 2 | 102229859 | C/T | 0.836 | 0.845 | 1 | 0.803 | 0.843 | - | 0.816 | 0.834 | - | 0.794 | 0.848 | 1 |
| rs10189629 | 2 | 102337982 | A/C | 0.136 | 0.097 | 1 | 0.138 | 0.094 | - | 0.138 | 0.116 | 0.98 | 0.144 | 0.104 | 1 |
| rs11692065 | 2 | 102342493 | C/T | 0.864 | 0.903 | 1 | 0.863 | 0.906 | 1 | 0.861 | 0.884 | 0.98 | 0.856 | 0.896 | - |
| rs11674302 | 2 | 102345646 | C/T | 0.136 | 0.097 | - | 0.137 | 0.094 | 0.99 | 0.139 | 0.116 | 0.98 | 0.143 | 0.104 | - |
| rs3771180 | 2 | 102412135 | G/T | 0.866 | 0.896 | 1 | 0.848 | 0.908 | 1 | 0.856 | 0.874 | 1 | 0.854 | 0.886 | - |
| rs13431828 | 2 | 102413171 | C/T | 0.866 | 0.896 | - | 0.848 | 0.908 | 1 | 0.856 | 0.874 | 1 | 0.854 | 0.886 | - |
| rs13408569 | 2 | 102413574 | C/G | 0.134 | 0.104 | 1 | 0.152 | 0.092 | 1 | 0.144 | 0.126 | 1 | 0.146 | 0.114 | 1 |
| rs13408661 | 2 | 102413600 | A/G | 0.134 | 0.104 | 1 | 0.152 | 0.092 | 1 | 0.144 | 0.126 | 1 | 0.146 | 0.114 | 1 |
| rs10173081 | 2 | 102415866 | C/T | 0.866 | 0.896 | 1 | 0.848 | 0.908 | 1 | 0.856 | 0.874 | 1 | 0.854 | 0.885 | 1 |
| rs10197862 | 2 | 102425067 | A/G | 0.865 | 0.893 | 1 | 0.848 | 0.908 | - | 0.854 | 0.872 | 0.99 | 0.852 | 0.883 | 0.99 |
| rs3755276 | 2 | 102436977 | C/T | 0.601 | 0.674 | 1 | 0.6 | 0.645 | 1 | 0.609 | 0.624 | 1 | 0.639 | 0.641 | - |
| rs1362348 | 2 | 102443142 | C/G | 0.601 | 0.674 | 1 | 0.6 | 0.645 | - | 0.609 | 0.624 | 1 | 0.639 | 0.641 | 1 |
| rs954470 | 3 | 188894973 | C/T | 0.857 | 0.855 | 0.95 | 0.877 | 0.882 | - | 0.839 | 0.869 | 0.93 | 0.862 | 0.851 | 0.95 |
| rs6770600 | 3 | 188898436 | A/G | 0.137 | 0.133 | 0.96 | 0.119 | 0.107 | 0.99 | 0.147 | 0.122 | 0.95 | 0.131 | 0.145 | 0.96 |
| rs11928175 | 3 | 188900416 | C/T | 0.864 | 0.868 | 0.97 | 0.88 | 0.894 | 1 | 0.856 | 0.88 | 0.98 | 0.875 | 0.862 | 0.96 |
| rs2017908 | 3 | 188900670 | A/C | 0.136 | 0.132 | 0.97 | 0.12 | 0.106 | 1 | 0.144 | 0.119 | 0.98 | 0.123 | 0.137 | 0.97 |
| rs9848804 | 3 | 188902018 | A/C | 0.864 | 0.869 | 0.97 | 0.88 | 0.894 | - | 0.856 | 0.881 | 0.98 | 0.88 | 0.867 | 0.99 |
| rs9812190 | 3 | 188902430 | A/G | 0.134 | 0.129 | 0.98 | 0.12 | 0.106 | 1 | 0.143 | 0.119 | 0.98 | 0.118 | 0.132 | - |
| rs7616923 | 3 | 188903921 | G/T | 0.867 | 0.873 | - | 0.88 | 0.894 | 1 | 0.858 | 0.882 | - | 0.882 | 0.868 | - |
| rs4254648 | 3 | 188911388 | A/G | 0.867 | 0.873 | - | 0.879 | 0.891 | 0.99 | 0.856 | 0.882 | - | 0.882 | 0.868 | - |
| rs9878204 | 3 | 188918390 | A/G | 0.868 | 0.873 | 0.99 | 0.866 | 0.873 | - | 0.858 | 0.882 | 0.99 | 0.855 | 0.852 | - |
| rs9865102 | 3 | 188918869 | C/T | 0.132 | 0.128 | 0.99 | 0.134 | 0.127 | - | 0.141 | 0.118 | 0.99 | 0.145 | 0.149 | 1 |
| rs6786702 | 3 | 188929433 | C/T | 0.133 | 0.128 | 1 | 0.138 | 0.127 | - | 0.14 | 0.116 | 0.99 | 0.142 | 0.15 | 0.99 |
| rs6762932 | 3 | 188931699 | A/G | 0.133 | 0.128 | 1 | 0.137 | 0.127 | - | 0.14 | 0.116 | 0.99 | 0.132 | 0.143 | 0.95 |
| rs9827569 | 3 | 188935184 | G/T | 0.867 | 0.873 | - | 0.881 | 0.889 | - | 0.86 | 0.884 | - | 0.882 | 0.867 | - |
| rs7659227 | 4 | 66324936 | A/G | 0.708 | 0.675 | 1 | 0.671 | 0.59 | - | 0.705 | 0.663 | 0.99 | 0.689 | 0.673 | 1 |
| rs11735820 | 4 | 66327782 | G/T | 0.292 | 0.325 | 1 | 0.325 | 0.41 | 1 | 0.295 | 0.337 | 0.99 | 0.31 | 0.326 | - |
| rs1837253 | 5 | 110429771 | C/T | 0.737 | 0.798 | - | 0.76 | 0.797 | - | 0.737 | 0.765 | - | 0.745 | 0.792 | - |
| rs10064618 | 5 | 153752482 | A/G | 0.421 | 0.384 | - | 0.38 | 0.408 | - | 0.405 | 0.413 | - | 0.422 | 0.415 | - |
| rs2453626 | 8 | 101207073 | C/T | 0.52 | 0.546 | - | 0.526 | 0.541 | 0.99 | 0.537 | 0.585 | - | 0.561 | 0.575 | - |
| rs2381416 | 9 | 6183455 | A/C | 0.702 | 0.694 | 0.98 | 0.75 | 0.697 | 0.97 | 0.737 | 0.722 | 0.97 | 0.759 | 0.697 | 0.98 |

| SNP | Chr | Position (hg18) | A1/A2 | CAMP: | | | CARE: | | | CHS: | | | CAG/CSGA/SARP: | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq |
| rs1888909 | 9 | 6187392 | C/T | 0.705 | 0.695 | 0.98 | 0.751 | 0.699 | 0.97 | 0.738 | 0.723 | 0.97 | 0.759 | 0.697 | - |
| rs11214966 | 11 | 113736465 | C/T | 0.081 | 0.08 | 0.99 | 0.078 | 0.078 | - | 0.072 | 0.07 | 0.99 | 0.068 | 0.074 | 0.99 |
| rs4938096 | 11 | 113740940 | C/T | 0.919 | 0.92 | 1 | 0.925 | 0.922 | - | 0.928 | 0.93 | 1 | 0.931 | 0.925 | 1 |
| rs16929496 | 12 | 25885071 | C/T | 0.223 | 0.179 | 0.84 | 0.199 | 0.184 | 0.92 | 0.22 | 0.188 | 0.83 | 0.207 | 0.188 | 0.93 |
| rs11048311 | 12 | 25913405 | A/C | 0.787 | 0.833 | 1 | 0.801 | 0.825 | 1 | 0.792 | 0.826 | 1 | 0.799 | 0.82 | 1 |
| rs11048317 | 12 | 25919674 | G/T | 0.213 | 0.168 | 1 | 0.198 | 0.175 | - | 0.208 | 0.174 | 0.99 | 0.202 | 0.18 | - |
| rs9891949 | 17 | 8039908 | A/G | 0.617 | 0.676 | 0.96 | 0.673 | 0.73 | - | 0.617 | 0.677 | 0.95 | 0.634 | 0.661 | 0.96 |
| rs2517955 | 17 | 35097207 | C/T | 0.373 | 0.404 | 0.95 | 0.387 | 0.363 | 0.8 | 0.346 | 0.39 | 0.88 | 0.323 | 0.376 | - |
| rs2952155 | 17 | 35115244 | C/T | 0.734 | 0.714 | 0.96 | 0.745 | 0.733 | 0.81 | 0.76 | 0.725 | 0.88 | 0.769 | 0.722 | 0.97 |
| rs1810132 | 17 | 35119531 | C/T | 0.338 | 0.366 | - | 0.334 | 0.318 | 0.83 | 0.318 | 0.353 | 0.91 | 0.288 | 0.343 | - |
| rs1058808 | 17 | 35137563 | C/G | 0.357 | 0.394 | 0.98 | 0.37 | 0.347 | 0.83 | 0.334 | 0.377 | 0.91 | 0.309 | 0.359 | 0.98 |
| rs907092 | 17 | 35175785 | A/G | 0.43 | 0.39 | - | 0.452 | 0.38 | - | 0.464 | 0.412 | - | 0.466 | 0.406 | - |
| rs2313430 | 17 | 35183342 | C/T | 0.53 | 0.575 | 0.99 | 0.515 | 0.586 | 0.99 | 0.505 | 0.556 | 0.98 | 0.485 | 0.558 | 1 |
| rs10445308 | 17 | 35191573 | C/T | 0.566 | 0.611 | 0.99 | 0.544 | 0.62 | 0.99 | 0.533 | 0.585 | 0.98 | 0.524 | 0.589 | - |
| rs9909593 | 17 | 35223675 | A/G | 0.558 | 0.611 | 0.99 | 0.542 | 0.62 | - | 0.528 | 0.581 | 0.99 | 0.523 | 0.588 | - |
| rs9303277 | 17 | 35229995 | C/T | 0.521 | 0.573 | - | 0.511 | 0.589 | - | 0.494 | 0.547 | - | 0.483 | 0.555 | - |
| rs3816470 | 17 | 35239327 | A/G | 0.522 | 0.566 | 0.98 | 0.507 | 0.583 | 0.97 | 0.491 | 0.545 | 0.98 | 0.461 | 0.528 | - |
| rs11557466 | 17 | 35278152 | C/T | 0.567 | 0.615 | 0.99 | 0.548 | 0.625 | 0.98 | 0.535 | 0.587 | 0.99 | 0.524 | 0.587 | 0.99 |
| rs11078925 | 17 | 35278734 | C/T | 0.433 | 0.385 | 0.99 | 0.452 | 0.374 | 0.98 | 0.465 | 0.413 | 0.99 | 0.463 | 0.407 | 0.99 |
| rs12150079 | 17 | 35278943 | A/G | 0.305 | 0.256 | - | 0.318 | 0.271 | - | 0.321 | 0.289 | - | 0.324 | 0.274 | - |
| rs12936231 | 17 | 35282646 | C/G | 0.534 | 0.575 | 1 | 0.517 | 0.596 | 1 | 0.496 | 0.55 | 0.99 | 0.488 | 0.559 | 1 |
| rs11870965 | 17 | 35283731 | A/T | 0.429 | 0.384 | 1 | 0.449 | 0.37 | 1 | 0.464 | 0.413 | 1 | 0.462 | 0.406 | 1 |
| rs1054609 | 17 | 35286803 | A/C | 0.571 | 0.617 | 1 | 0.551 | 0.63 | 1 | 0.536 | 0.587 | 1 | 0.538 | 0.594 | 1 |
| rs9907088 | 17 | 35288642 | A/G | 0.429 | 0.383 | 1 | 0.449 | 0.37 | 1 | 0.464 | 0.413 | 1 | 0.462 | 0.406 | 1 |
| rs12452894 | 17 | 35290112 | A/G | 0.571 | 0.617 | 1 | 0.552 | 0.63 | 1 | 0.536 | 0.587 | 1 | 0.538 | 0.594 | 1 |
| rs12232497 | 17 | 35293645 | C/T | 0.429 | 0.383 | 1 | 0.448 | 0.37 | 1 | 0.464 | 0.413 | 1 | 0.462 | 0.406 | 1 |
| rs2872507 | 17 | 35294289 | A/G | 0.429 | 0.383 | - | 0.448 | 0.37 | - | 0.465 | 0.414 | - | 0.462 | 0.406 | - |
| rs9901146 | 17 | 35296869 | A/G | 0.466 | 0.425 | 1 | 0.482 | 0.404 | 1 | 0.504 | 0.45 | 1 | 0.511 | 0.441 | - |
| rs12950743 | 17 | 35302759 | C/T | 0.466 | 0.425 | 1 | 0.482 | 0.404 | 1 | 0.504 | 0.45 | 1 | 0.511 | 0.441 | 1 |
| rs7359623 | 17 | 35303115 | C/T | 0.547 | 0.584 | 0.97 | 0.528 | 0.603 | 0.97 | 0.507 | 0.559 | 0.96 | 0.498 | 0.568 | 0.97 |
| rs8067378 | 17 | 35304874 | A/G | 0.534 | 0.575 | - | 0.519 | 0.597 | 0.99 | 0.498 | 0.549 | - | 0.488 | 0.559 | - |
| rs8069176 | 17 | 35310723 | A/G | 0.428 | 0.383 | 1 | 0.446 | 0.368 | 0.99 | 0.459 | 0.409 | 0.99 | 0.452 | 0.397 | - |
| rs2305480 | 17 | 35315722 | A/G | 0.423 | 0.377 | - | 0.446 | 0.368 | 0.99 | 0.457 | 0.407 | - | 0.451 | 0.396 | - |
| rs2305479 | 17 | 35315743 | C/T | 0.54 | 0.582 | 1 | 0.523 | 0.599 | - | 0.502 | 0.554 | 0.99 | 0.498 | 0.57 | - |
| rs11078927 | 17 | 35317931 | C/T | 0.578 | 0.622 | 1 | 0.558 | 0.634 | - | 0.542 | 0.589 | 1 | 0.549 | 0.604 | 1 |
| rs2290400 | 17 | 35319766 | C/T | 0.459 | 0.419 | - | 0.481 | 0.403 | 1 | 0.501 | 0.449 | - | 0.504 | 0.431 | - |
| rs1008723 | 17 | 35319793 | G/T | 0.541 | 0.581 | 1 | 0.519 | 0.597 | - | 0.501 | 0.551 | 0.99 | 0.496 | 0.569 | - |
| rs4795400 | 17 | 35320546 | C/T | 0.575 | 0.619 | 0.99 | 0.543 | 0.621 | 0.99 | 0.539 | 0.586 | 0.99 | 0.545 | 0.602 | 0.99 |
| rs869402 | 17 | 35321569 | C/T | 0.544 | 0.58 | 1 | 0.507 | 0.585 | - | 0.5 | 0.549 | 0.99 | 0.493 | 0.567 | 0.99 |
| rs7216389 | 17 | 35323475 | C/T | 0.456 | 0.421 | - | 0.493 | 0.415 | 0.99 | 0.5 | 0.452 | - | 0.509 | 0.435 | - |
| rs9303280 | 17 | 35327557 | C/T | 0.553 | 0.594 | 0.98 | 0.52 | 0.603 | 0.95 | 0.511 | 0.558 | 0.98 | 0.506 | 0.572 | 0.99 |
| rs9303281 | 17 | 35327572 | A/G | 0.544 | 0.579 | 1 | 0.507 | 0.585 | 0.99 | 0.499 | 0.547 | 1 | 0.489 | 0.558 | - |
| rs7219923 | 17 | 35328044 | C/T | 0.456 | 0.421 | 1 | 0.493 | 0.415 | 0.99 | 0.501 | 0.453 | 0.99 | 0.511 | 0.442 | - |
| rs7224129 | 17 | 35328952 | A/G | 0.543 | 0.579 | 1 | 0.506 | 0.585 | 0.99 | 0.499 | 0.547 | 0.99 | 0.489 | 0.558 | - |
| rs8076131 | 17 | 35334438 | A/G | 0.581 | 0.623 | 0.98 | 0.55 | 0.63 | 0.95 | 0.539 | 0.586 | 0.97 | 0.544 | 0.6 | - |
| rs12603332 | 17 | 35336333 | C/T | 0.56 | 0.599 | 0.99 | 0.528 | 0.612 | 0.94 | 0.516 | 0.564 | 0.98 | 0.51 | 0.576 | 0.99 |

| SNP | Chr | Position (hg18) | A1/A2 | CAMP: | | | CARE: | | | CHS: | | | CAG/CSGA/SARP: | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq |
| rs4795403 | 17 | 35339248 | C/T | 0.809 | 0.823 | 1 | 0.788 | 0.838 | - | 0.785 | 0.813 | 1 | 0.8 | 0.819 | 1 |
| rs4795405 | 17 | 35341943 | C/T | 0.588 | 0.633 | - | 0.559 | 0.648 | 0.93 | 0.549 | 0.594 | - | 0.563 | 0.61 | - |
| rs4794820 | 17 | 35342870 | A/G | 0.404 | 0.355 | 0.95 | 0.436 | 0.341 | 0.92 | 0.44 | 0.397 | 0.95 | 0.427 | 0.378 | 0.95 |
| rs8079416 | 17 | 35346239 | C/T | 0.49 | 0.518 | - | 0.441 | 0.518 | 0.82 | 0.458 | 0.491 | - | 0.454 | 0.515 | - |
| rs6503525 | 17 | 35348700 | C/G | 0.491 | 0.518 | 1 | 0.441 | 0.518 | 0.82 | 0.457 | 0.492 | 0.99 | 0.454 | 0.515 | 1 |
| rs4065985 | 17 | 35355458 | C/G | 0.619 | 0.656 | 0.92 | 0.581 | 0.676 | 0.8 | 0.594 | 0.619 | 0.89 | 0.597 | 0.652 | 0.94 |
| rs4795408 | 17 | 35361153 | A/G | 0.488 | 0.515 | 0.99 | 0.433 | 0.514 | 0.81 | 0.455 | 0.49 | 0.98 | 0.453 | 0.511 | 0.99 |
| rs6503526 | 17 | 35368124 | C/T | 0.51 | 0.485 | 0.99 | 0.568 | 0.487 | 0.8 | 0.546 | 0.51 | 0.98 | 0.546 | 0.489 | 0.99 |
| rs3894194 | 17 | 35375519 | A/G | 0.482 | 0.516 | - | 0.436 | 0.512 | 0.81 | 0.452 | 0.488 | - | 0.452 | 0.507 | - |
| rs7212938 | 17 | 35376206 | G/T | 0.484 | 0.516 | 0.86 | 0.443 | 0.532 | 0.78 | 0.452 | 0.481 | 0.82 | 0.474 | 0.537 | - |
| rs34724 | 19 | 35060850 | G/T | 0.553 | 0.523 | - | 0.569 | 0.54 | 0.76 | 0.548 | 0.559 | - | 0.566 | 0.547 | - |
| rs335016 | 19 | 35065232 | A/C | 0.419 | 0.455 | 0.76 | 0.413 | 0.443 | 0.76 | 0.437 | 0.426 | 0.78 | 0.415 | 0.444 | 0.86 |

## b) African Americans and African Caribbeans

| SNP | Chr | Position (hg18) | A1/A2 | Barbados: | | | GRAAD: | | | SAPPHIRE: | | | CAG/CSGA/SARP: | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq |
| rs4845783 | 1 | 149305632 | A/G | 0.921 | 0.907 | 0.64 | 0.923 | 0.876 | 0.76 | 0.899 | 0.877 | 0.86 | 0.922 | 0.917 | 0.92 |
| rs1538084 | 1 | 149309085 | A/C | 0.07 | 0.083 | 0.66 | 0.069 | 0.108 | 0.74 | 0.076 | 0.091 | 0.94 | 0.071 | 0.077 | 0.9 |
| rs6587688 | 1 | 149342695 | C/T | 0.909 | 0.887 | 0.66 | 0.902 | 0.861 | 0.78 | 0.901 | 0.877 | - | 0.907 | 0.901 | 0.92 |
| rs1231172 | 1 | 155745628 | T/C | 0.724 | 0.776 | 1 | 0.708 | 0.774 | 0.91 | 0.735 | 0.785 | 0.42 | 0.723 | 0.757 | 0.97 |
| rs1102000 | 1 | 155745980 | A/G | 0.724 | 0.776 | 1 | 0.708 | 0.774 | 0.91 | 0.735 | 0.785 | 0.42 | 0.723 | 0.757 | 0.97 |
| rs4653433 | 1 | 222281266 | A/G | 0.614 | 0.627 | - | 0.575 | 0.601 | - | 0.475 | 0.478 | 0.63 | 0.534 | 0.56 | - |
| rs949963 | 2 | 102228304 | C/T | 0.698 | 0.716 | - | 0.705 | 0.703 | - | 0.667 | 0.758 | 1 | 0.684 | 0.716 | - |
| rs871657 | 2 | 102229859 | C/T | 0.698 | 0.716 | 1.14 | 0.703 | 0.703 | 0.98 | 0.667 | 0.758 | - | 0.683 | 0.715 | 0.98 |
| rs10189629 | 2 | 102337982 | A/C | 0.171 | 0.204 | 0.88 | 0.189 | 0.189 | 0.99 | 0.243 | 0.257 | 0.83 | 0.185 | 0.166 | 1 |
| rs11692065 | 2 | 102342493 | C/T | 0.831 | 0.796 | - | 0.812 | 0.812 | - | 0.756 | 0.742 | 0.83 | 0.815 | 0.835 | - |
| rs11674302 | 2 | 102345646 | C/T | 0.21 | 0.247 | - | 0.216 | 0.234 | - | 0.282 | 0.297 | 0.8 | 0.228 | 0.194 | - |
| rs3771180 | 2 | 102412135 | G/T | 0.745 | 0.748 | 0.91 | 0.74 | 0.744 | 1 | 0.697 | 0.701 | 1 | 0.736 | 0.765 | - |
| rs13431828 | 2 | 102413171 | C/T | 0.717 | 0.729 | - | 0.72 | 0.721 | - | 0.661 | 0.666 | 0.96 | 0.722 | 0.747 | - |
| rs13408569 | 2 | 102413574 | C/G | 0.255 | 0.252 | 0.91 | 0.26 | 0.256 | 1 | 0.303 | 0.299 | 1 | 0.264 | 0.235 | 1 |
| rs13408661 | 2 | 102413600 | A/G | 0.255 | 0.252 | 0.91 | 0.26 | 0.256 | 1 | 0.303 | 0.299 | 1 | 0.264 | 0.235 | 1 |
| rs10173081 | 2 | 102415866 | C/T | 0.745 | 0.748 | 0.91 | 0.739 | 0.743 | 0.99 | 0.697 | 0.701 | 1 | 0.736 | 0.765 | 1 |
| rs10197862 | 2 | 102425067 | A/G | 0.745 | 0.746 | 0.9 | 0.735 | 0.741 | 0.99 | 0.692 | 0.691 | 0.97 | 0.734 | 0.761 | 0.98 |
| rs3755276 | 2 | 102436977 | C/T | 0.299 | 0.324 | 0.94 | 0.333 | 0.38 | 1 | 0.319 | 0.309 | 1 | 0.326 | 0.371 | - |
| rs1362348 | 2 | 102443142 | C/G | 0.299 | 0.324 | 0.94 | 0.333 | 0.38 | 1 | 0.319 | 0.309 | - | 0.326 | 0.371 | 1 |
| rs954470 | 3 | 188894973 | C/T | 0.809 | 0.806 | 0.73 | 0.844 | 0.832 | 0.75 | 0.856 | 0.869 | - | 0.825 | 0.821 | 0.76 |
| rs6770600 | 3 | 188898436 | A/G | 0.364 | 0.348 | 0.75 | 0.323 | 0.34 | 0.8 | 0.357 | 0.38 | 0.83 | 0.341 | 0.343 | 0.87 |
| rs11928175 | 3 | 188900416 | C/T | 0.684 | 0.676 | 0.84 | 0.7 | 0.698 | 0.87 | 0.669 | 0.647 | 0.88 | 0.701 | 0.693 | 0.98 |
| rs2017908 | 3 | 188900670 | A/C | 0.334 | 0.338 | 0.84 | 0.329 | 0.316 | 0.9 | 0.355 | 0.378 | 0.85 | 0.317 | 0.325 | 0.95 |
| rs9848804 | 3 | 188902018 | A/C | 0.685 | 0.676 | 0.85 | 0.698 | 0.703 | 0.94 | 0.669 | 0.648 | 0.89 | 0.704 | 0.695 | 1 |
| rs9812190 | 3 | 188902430 | A/G | 0.307 | 0.312 | 0.83 | 0.296 | 0.284 | 0.94 | 0.32 | 0.34 | 0.87 | 0.294 | 0.304 | - |
| rs7616923 | 3 | 188903921 | G/T | 0.685 | 0.677 | - | 0.696 | 0.706 | - | 0.669 | 0.649 | 0.89 | 0.705 | 0.697 | - |
| rs4254648 | 3 | 188911388 | A/G | 0.564 | 0.596 | - | 0.607 | 0.623 | - | 0.609 | 0.588 | 0.96 | 0.616 | 0.602 | - |
| rs9878204 | 3 | 188918390 | A/G | 0.562 | 0.592 | 0.88 | 0.611 | 0.625 | 0.96 | 0.614 | 0.591 | - | 0.637 | 0.615 | - |

| SNP | Chr | Position (hg18) | A1/A2 | Barbados: | | | GRAAD: | | | SAPPHIRE: | | | CAG/CSGA/SARP: | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq |
| rs9865102 | 3 | 188918869 | C/T | 0.438 | 0.408 | 0.88 | 0.389 | 0.376 | 0.96 | 0.384 | 0.409 | 0.99 | 0.363 | 0.385 | 1 |
| rs6786702 | 3 | 188929433 | C/T | 0.436 | 0.405 | 0.9 | 0.38 | 0.366 | 0.96 | 0.368 | 0.401 | - | 0.344 | 0.383 | 0.98 |
| rs6762932 | 3 | 188931699 | A/G | 0.328 | 0.306 | 0.95 | 0.29 | 0.28 | 0.91 | 0.268 | 0.285 | - | 0.248 | 0.274 | 0.91 |
| rs9827569 | 3 | 188935184 | G/T | 0.501 | 0.539 | - | 0.58 | 0.602 | - | 0.581 | 0.558 | 0.79 | 0.614 | 0.579 | - |
| rs7659227 | 4 | 66324936 | A/G | 0.613 | 0.564 | 0.88 | 0.613 | 0.594 | 0.99 | 0.683 | 0.612 | 0.95 | 0.628 | 0.614 | 1 |
| rs11735820 | 4 | 66327782 | G/T | 0.347 | 0.392 | - | 0.343 | 0.372 | - | 0.277 | 0.358 | 0.96 | 0.333 | 0.343 | - |
| rs1837253 | 5 | 110429771 | C/T | 0.74 | 0.742 | - | 0.72 | 0.761 | - | 0.754 | 0.803 | - | 0.727 | 0.761 | - |
| rs10064618 | 5 | 153752482 | A/G | 0.743 | 0.748 | - | 0.731 | 0.713 | - | 0.695 | 0.673 | 0.52 | 0.732 | 0.715 | - |
| rs2453626 | 8 | 101207073 | C/T | 0.692 | 0.724 | - | 0.657 | 0.681 | - | 0.649 | 0.696 | 0.87 | 0.641 | 0.698 | - |
| rs2381416 | 9 | 6183455 | A/C | 0.405 | 0.358 | 1.01 | 0.468 | 0.401 | 0.98 | 0.439 | 0.442 | 0.87 | 0.433 | 0.412 | 0.98 |
| rs1888909 | 9 | 6187392 | C/T | 0.457 | 0.418 | 0.99 | 0.52 | 0.457 | 0.95 | 0.491 | 0.488 | 0.88 | 0.512 | 0.479 | - |
| rs11214966 | 11 | 113736465 | C/T | 0.221 | 0.224 | 0.79 | 0.192 | 0.258 | 0.89 | 0.169 | 0.262 | - | 0.201 | 0.249 | 0.93 |
| rs4938096 | 11 | 113740940 | C/T | 0.776 | 0.769 | 0.8 | 0.803 | 0.739 | 0.87 | 0.823 | 0.735 | - | 0.794 | 0.745 | 0.94 |
| rs16929496 | 12 | 25885071 | C/T | 0.248 | 0.22 | 0.77 | 0.276 | 0.262 | 0.76 | 0.22 | 0.238 | 0.77 | 0.267 | 0.245 | 0.82 |
| rs11048311 | 12 | 25913405 | A/C | 0.803 | 0.836 | 0.81 | 0.777 | 0.79 | 0.94 | 0.821 | 0.803 | 0.95 | 0.787 | 0.819 | 0.97 |
| rs11048317 | 12 | 25919674 | G/T | 0.266 | 0.234 | 0.83 | 0.287 | 0.281 | 0.92 | 0.223 | 0.248 | - | 0.256 | 0.22 | - |
| rs9891949 | 17 | 8039908 | A/G | 0.593 | 0.593 | 1.05 | 0.575 | 0.585 | 0.97 | 0.553 | 0.592 | - | 0.57 | 0.589 | 0.99 |
| rs2517955 | 17 | 35097207 | C/T | 0.808 | 0.815 | 0.98 | 0.753 | 0.75 | 0.88 | 0.745 | 0.741 | 0.82 | 0.773 | 0.799 | - |
| rs2952155 | 17 | 35115244 | C/T | 0.618 | 0.618 | 1.01 | 0.664 | 0.617 | 0.94 | 0.635 | 0.619 | 0.83 | 0.64 | 0.627 | 0.96 |
| rs1810132 | 17 | 35119531 | C/T | 0.447 | 0.463 | - | 0.403 | 0.43 | - | 0.448 | 0.436 | 0.8 | 0.453 | 0.454 | - |
| rs1058808 | 17 | 35137563 | C/G | 0.918 | 0.904 | 0.87 | 0.854 | 0.853 | 0.72 | 0.803 | 0.8 | 0.7 | 0.849 | 0.854 | 0.87 |
| rs907092 | 17 | 35175785 | A/G | 0.12 | 0.106 | - | 0.166 | 0.155 | - | 0.175 | 0.168 | - | 0.159 | 0.132 | - |
| rs2313430 | 17 | 35183342 | C/T | 0.446 | 0.416 | 1.07 | 0.38 | 0.417 | 0.91 | 0.441 | 0.433 | 0.96 | 0.392 | 0.423 | 0.97 |
| rs10445308 | 17 | 35191573 | C/T | 0.845 | 0.852 | 0.99 | 0.799 | 0.812 | 0.96 | 0.757 | 0.798 | 0.96 | 0.797 | 0.823 | - |
| rs9909593 | 17 | 35223675 | A/G | 0.846 | 0.853 | 0.99 | 0.799 | 0.811 | 0.97 | 0.754 | 0.799 | 0.97 | 0.798 | 0.823 | - |
| rs9303277 | 17 | 35229995 | C/T | 0.448 | 0.416 | - | 0.372 | 0.416 | - | 0.432 | 0.43 | - | 0.394 | 0.42 | - |
| rs3816470 | 17 | 35239327 | A/G | 0.424 | 0.402 | 1.04 | 0.353 | 0.397 | 0.97 | 0.386 | 0.405 | 0.96 | 0.366 | 0.393 | - |
| rs11557466 | 17 | 35278152 | C/T | 0.895 | 0.916 | 1.12 | 0.856 | 0.856 | 0.98 | 0.839 | 0.835 | 0.97 | 0.851 | 0.879 | 0.99 |
| rs11078925 | 17 | 35278734 | C/T | 0.105 | 0.084 | 1.12 | 0.144 | 0.144 | 0.98 | 0.161 | 0.165 | 0.97 | 0.149 | 0.121 | 0.99 |
| rs12150079 | 17 | 35278943 | A/G | 0.055 | 0.031 | - | 0.068 | 0.066 | - | 0.068 | 0.074 | - | 0.072 | 0.056 | - |
| rs12936231 | 17 | 35282646 | C/G | 0.484 | 0.474 | 1.03 | 0.428 | 0.452 | 0.98 | 0.503 | 0.467 | - | 0.438 | 0.475 | 0.99 |
| rs11870965 | 17 | 35283731 | A/T | 0.253 | 0.258 | 1.03 | 0.305 | 0.292 | 0.98 | 0.259 | 0.293 | 0.99 | 0.308 | 0.271 | 1 |
| rs1054609 | 17 | 35286803 | A/C | 0.747 | 0.742 | 1.03 | 0.695 | 0.708 | 0.98 | 0.741 | 0.707 | 0.99 | 0.692 | 0.729 | 1 |
| rs9907088 | 17 | 35288642 | A/G | 0.228 | 0.221 | 1 | 0.283 | 0.26 | 1 | 0.231 | 0.272 | 1 | 0.278 | 0.241 | 1 |
| rs12452894 | 17 | 35290112 | A/G | 0.772 | 0.779 | 1 | 0.716 | 0.74 | 1 | 0.769 | 0.728 | 1 | 0.722 | 0.759 | 1 |
| rs12232497 | 17 | 35293645 | C/T | 0.103 | 0.075 | 1.12 | 0.14 | 0.141 | 0.99 | 0.155 | 0.141 | 1 | 0.146 | 0.111 | 1 |
| rs2872507 | 17 | 35294289 | A/G | 0.228 | 0.221 | - | 0.284 | 0.261 | - | 0.231 | 0.272 | - | 0.278 | 0.241 | - |
| rs9901146 | 17 | 35296869 | A/G | 0.366 | 0.386 | 0.96 | 0.443 | 0.416 | 0.99 | 0.348 | 0.395 | 0.96 | 0.41 | 0.362 | - |
| rs12950743 | 17 | 35302759 | C/T | 0.366 | 0.386 | 0.96 | 0.443 | 0.416 | 0.99 | 0.348 | 0.394 | 0.96 | 0.41 | 0.362 | 1 |
| rs7359623 | 17 | 35303115 | C/T | 0.661 | 0.652 | 0.96 | 0.581 | 0.619 | 0.99 | 0.681 | 0.629 | 0.96 | 0.621 | 0.668 | 0.99 |
| rs8067378 | 17 | 35304874 | A/G | 0.492 | 0.476 | - | 0.429 | 0.459 | - | 0.504 | 0.478 | 0.95 | 0.447 | 0.481 | - |
| rs8069176 | 17 | 35310723 | A/G | 0.336 | 0.343 | 0.99 | 0.413 | 0.372 | 0.99 | 0.321 | 0.353 | 0.93 | 0.373 | 0.323 | - |
| rs2305480 | 17 | 35315722 | A/G | 0.106 | 0.082 | - | 0.147 | 0.143 | - | 0.166 | 0.162 | 0.97 | 0.147 | 0.118 | - |
| rs2305479 | 17 | 35315743 | C/T | 0.864 | 0.876 | 1.07 | 0.823 | 0.812 | 0.98 | 0.801 | 0.804 | 0.97 | 0.818 | 0.843 | - |
| rs11078927 | 17 | 35317931 | C/T | 0.897 | 0.927 | 1.11 | 0.858 | 0.859 | 0.98 | 0.841 | 0.862 | - | 0.85 | 0.887 | 0.97 |
| rs2290400 | 17 | 35319766 | C/T | 0.444 | 0.437 | - | 0.466 | 0.464 | - | 0.438 | 0.452 | 0.93 | 0.491 | 0.467 | - |

| SNP | Chr | Position (hg18) | A1/A2 | Barbados: | | | GRAAD: | | | SAPPHIRE: | | | CAG/CSGA/SARP: | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq |
| rs1008723 | 17 | 35319793 | G/T | 0.734 | 0.738 | 0.96 | 0.685 | 0.699 | 0.97 | 0.727 | 0.708 | - | 0.692 | 0.724 | - |
| rs4795400 | 17 | 35320546 | C/T | 0.891 | 0.912 | 1.09 | 0.848 | 0.85 | 0.97 | 0.826 | 0.83 | - | 0.845 | 0.877 | 0.94 |
| rs869402 | 17 | 35321569 | C/T | 0.882 | 0.901 | 1.02 | 0.836 | 0.832 | 0.95 | 0.817 | 0.81 | - | 0.822 | 0.856 | 0.92 |
| rs7216389 | 17 | 35323475 | C/T | 0.148 | 0.14 | - | 0.199 | 0.207 | - | 0.226 | 0.225 | 0.92 | 0.225 | 0.192 | - |
| rs9303280 | 17 | 35327557 | C/T | 0.796 | 0.8 | 0.93 | 0.726 | 0.738 | 0.94 | 0.746 | 0.75 | 0.84 | 0.734 | 0.759 | 0.96 |
| rs9303281 | 17 | 35327572 | A/G | 0.521 | 0.523 | 1.04 | 0.471 | 0.47 | 0.96 | 0.471 | 0.506 | 0.91 | 0.452 | 0.494 | - |
| rs7219923 | 17 | 35328044 | C/T | 0.398 | 0.39 | 1.03 | 0.433 | 0.436 | 0.96 | 0.422 | 0.419 | 0.89 | 0.465 | 0.434 | - |
| rs7224129 | 17 | 35328952 | A/G | 0.603 | 0.61 | 1.03 | 0.567 | 0.564 | 0.96 | 0.578 | 0.581 | 0.89 | 0.535 | 0.566 | - |
| rs8076131 | 17 | 35334438 | A/G | 0.876 | 0.898 | 1.09 | 0.831 | 0.837 | 0.91 | 0.806 | 0.816 | 0.88 | 0.806 | 0.848 | - |
| rs12603332 | 17 | 35336333 | C/T | 0.462 | 0.423 | 1.04 | 0.377 | 0.418 | 0.97 | 0.395 | 0.427 | 0.93 | 0.395 | 0.415 | 0.97 |
| rs4795403 | 17 | 35339248 | C/T | 0.935 | 0.945 | 1.18 | 0.906 | 0.901 | 0.93 | 0.902 | 0.895 | 0.83 | 0.902 | 0.934 | 0.96 |
| rs4795405 | 17 | 35341943 | C/T | 0.691 | 0.66 | - | 0.607 | 0.638 | - | 0.646 | 0.66 | 0.84 | 0.624 | 0.655 | - |
| rs4794820 | 17 | 35342870 | A/G | 0.438 | 0.45 | 1.03 | 0.498 | 0.485 | 0.94 | 0.491 | 0.459 | 0.85 | 0.505 | 0.47 | 0.93 |
| rs8079416 | 17 | 35346239 | C/T | 0.459 | 0.465 | - | 0.42 | 0.431 | - | 0.467 | 0.489 | 0.63 | 0.434 | 0.429 | - |
| rs6503525 | 17 | 35348700 | C/G | 0.459 | 0.465 | 0.94 | 0.418 | 0.428 | 0.98 | 0.467 | 0.489 | 0.63 | 0.434 | 0.43 | 0.99 |
| rs4065985 | 17 | 35355458 | C/G | 0.81 | 0.829 | 0.88 | 0.768 | 0.776 | 0.93 | 0.804 | 0.785 | 0.53 | 0.777 | 0.789 | 0.97 |
| rs4795408 | 17 | 35361153 | A/G | 0.359 | 0.349 | 1.04 | 0.316 | 0.34 | - | 0.366 | 0.403 | 0.68 | 0.338 | 0.331 | 0.96 |
| rs6503526 | 17 | 35368124 | C/T | 0.673 | 0.686 | 1.04 | 0.703 | 0.67 | 0.98 | 0.662 | 0.619 | 0.7 | 0.687 | 0.695 | 0.97 |
| rs3894194 | 17 | 35375519 | A/G | 0.32 | 0.308 | - | 0.288 | 0.319 | - | 0.324 | 0.364 | 0.69 | 0.29 | 0.295 | - |
| rs7212938 | 17 | 35376206 | G/T | 0.216 | 0.199 | 0.79 | 0.196 | 0.218 | 0.75 | 0.239 | 0.257 | 0.48 | 0.184 | 0.195 | - |
| rs34724 | 19 | 35060850 | G/T | 0.342 | 0.365 | - | 0.362 | 0.357 | - | 0.4 | 0.43 | 0.33 | 0.364 | 0.39 | - |
| rs335016 | 19 | 35065232 | A/C | 0.411 | 0.416 | 0.81 | 0.421 | 0.427 | 0.7 | 0.449 | 0.448 | 0.31 | 0.413 | 0.411 | 0.83 |

## c) Latinos

| SNP | Chr | Position (hg18) | A1/A2 | CHS: | | | CARE: | | | MCCAS: | | | GALA: | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq |
| rs4845783 | 1 | 149305632 | A/G | 0.794 | 0.793 | 0.98 | 0.833 | 0.736 | 0.98 | 0.831 | 0.793 | 0.94 | 0.791 | 0.768 | 0.98 |
| rs1538084 | 1 | 149309085 | A/C | 0.202 | 0.207 | 0.91 | 0.141 | 0.249 | 0.94 | 0.159 | 0.193 | 0.88 | 0.209 | 0.218 | 0.94 |
| rs6587688 | 1 | 149342695 | C/T | 0.781 | 0.774 | 0.8 | 0.809 | 0.721 | - | 0.815 | 0.791 | 0.41 | 0.786 | 0.766 | 0.96 |
| rs1231172 | 1 | 155745628 | T/C | NA | NA | NA | 0.955 | 0.979 | 0.77 | 0.979 | 0.982 | 0.46 | 0.957 | 0.956 | 0.8 |
| rs1102000 | 1 | 155745980 | A/G | NA | NA | NA | 0.955 | 0.979 | 0.77 | 0.979 | 0.982 | 0.45 | 0.957 | 0.956 | 0.8 |
| rs4653433 | 1 | 222281266 | A/G | 0.333 | 0.369 | - | 0.346 | 0.301 | 0.78 | 0.231 | 0.285 | - | 0.391 | 0.423 | 0.82 |
| rs949963 | 2 | 102228304 | C/T | 0.869 | 0.879 | - | 0.836 | 0.904 | 1 | 0.925 | 0.948 | - | 0.864 | 0.871 | 1 |
| rs871657 | 2 | 102229859 | C/T | 0.869 | 0.879 | - | 0.836 | 0.904 | - | 0.923 | 0.946 | 0.95 | 0.864 | 0.872 | - |
| rs10189629 | 2 | 102337982 | A/C | 0.114 | 0.095 | 0.93 | 0.169 | 0.087 | - | 0.068 | 0.037 | 0.94 | 0.143 | 0.117 | - |
| rs11692065 | 2 | 102342493 | C/T | 0.886 | 0.904 | 0.92 | 0.832 | 0.914 | 0.99 | 0.934 | 0.965 | 0.97 | 0.869 | 0.883 | 1 |
| rs11674302 | 2 | 102345646 | C/T | 0.115 | 0.096 | 0.92 | 0.171 | 0.088 | 0.98 | 0.068 | 0.035 | - | 0.148 | 0.126 | 0.97 |
| rs3771180 | 2 | 102412135 | G/T | 0.885 | 0.894 | 0.98 | 0.856 | 0.923 | 1 | 0.931 | 0.967 | 0.95 | 0.861 | 0.882 | 1 |
| rs13431828 | 2 | 102413171 | C/T | 0.885 | 0.894 | 0.98 | 0.846 | 0.923 | 1 | 0.932 | 0.968 | - | 0.857 | 0.881 | 0.99 |
| rs13408569 | 2 | 102413574 | C/G | 0.115 | 0.106 | 0.98 | 0.144 | 0.077 | 1 | 0.068 | 0.032 | 1 | 0.152 | 0.118 | 1 |
| rs13408661 | 2 | 102413600 | A/G | 0.115 | 0.106 | 0.98 | 0.144 | 0.077 | 1 | 0.068 | 0.032 | 1 | 0.152 | 0.118 | 1 |
| rs10173081 | 2 | 102415866 | C/T | 0.886 | 0.898 | 0.99 | 0.856 | 0.923 | 1 | 0.929 | 0.965 | 0.92 | 0.861 | 0.881 | 1 |
| rs10197862 | 2 | 102425067 | A/G | 0.877 | 0.884 | 0.98 | 0.856 | 0.923 | - | 0.929 | 0.966 | 0.93 | 0.86 | 0.88 | - |
| rs3755276 | 2 | 102436977 | C/T | 0.73 | 0.737 | 1 | 0.702 | 0.769 | 1 | 0.844 | 0.884 | 0.99 | 0.657 | 0.674 | 1 |

| | | | | CHS: | | | CARE: | | | MCCAS: | | | GALA: | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| SNP | Chr | Position (hg18) | A1/A2 | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq |
| rs1362348 | 2 | 102443142 | C/G | 0.733 | 0.739 | 0.99 | 0.702 | 0.769 | - | 0.844 | 0.884 | 0.99 | 0.657 | 0.674 | - |
| rs954470 | 3 | 188894973 | C/T | 0.914 | 0.868 | 0.88 | 0.952 | 0.875 | - | 0.93 | 0.908 | 0.85 | 0.923 | 0.874 | 0.94 |
| rs6770600 | 3 | 188898436 | A/G | 0.083 | 0.128 | 0.88 | 0.045 | 0.134 | 0.92 | 0.081 | 0.108 | 0.83 | 0.117 | 0.159 | 0.93 |
| rs11928175 | 3 | 188900416 | C/T | 0.917 | 0.873 | 0.89 | 0.949 | 0.866 | 0.94 | 0.924 | 0.897 | 0.88 | 0.906 | 0.849 | 0.96 |
| rs2017908 | 3 | 188900670 | A/C | 0.079 | 0.123 | 0.96 | 0.05 | 0.135 | 0.98 | 0.077 | 0.106 | 0.9 | 0.111 | 0.155 | 0.99 |
| rs9848804 | 3 | 188902018 | A/C | 0.921 | 0.877 | 0.96 | 0.952 | 0.865 | - | 0.926 | 0.898 | 0.92 | 0.909 | 0.852 | - |
| rs9812190 | 3 | 188902430 | A/G | 0.079 | 0.123 | 0.96 | 0.047 | 0.135 | 0.98 | 0.072 | 0.1 | 0.93 | 0.102 | 0.148 | 0.99 |
| rs7616923 | 3 | 188903921 | G/T | 0.922 | 0.879 | - | 0.954 | 0.858 | 0.98 | 0.93 | 0.901 | - | 0.909 | 0.85 | 0.99 |
| rs4254648 | 3 | 188911388 | A/G | 0.914 | 0.866 | - | 0.949 | 0.855 | 0.98 | 0.923 | 0.896 | - | 0.893 | 0.838 | 0.99 |
| rs9878204 | 3 | 188918390 | A/G | 0.912 | 0.868 | 0.95 | 0.923 | 0.846 | - | 0.911 | 0.885 | 0.88 | 0.88 | 0.822 | - |
| rs9865102 | 3 | 188918869 | C/T | 0.088 | 0.132 | 0.95 | 0.077 | 0.154 | - | 0.089 | 0.115 | 0.88 | 0.133 | 0.178 | - |
| rs6786702 | 3 | 188929433 | C/T | 0.089 | 0.133 | 0.94 | 0.077 | 0.173 | - | 0.09 | 0.114 | 0.88 | 0.132 | 0.178 | - |
| rs6762932 | 3 | 188931699 | A/G | 0.089 | 0.133 | 0.94 | 0.077 | 0.173 | - | 0.08 | 0.103 | 0.85 | 0.125 | 0.165 | - |
| rs9827569 | 3 | 188935184 | G/T | 0.915 | 0.867 | - | 0.934 | 0.846 | - | 0.924 | 0.897 | - | 0.885 | 0.832 | - |
| rs7659227 | 4 | 66324936 | A/G | 0.774 | 0.741 | 0.98 | 0.779 | 0.654 | - | 0.822 | 0.808 | 0.95 | 0.769 | 0.745 | - |
| rs11735820 | 4 | 66327782 | G/T | 0.223 | 0.257 | 0.97 | 0.204 | 0.338 | 0.96 | 0.171 | 0.186 | 0.92 | 0.219 | 0.23 | 0.97 |
| rs1837253 | 5 | 110429771 | C/T | 0.687 | 0.699 | - | 0.736 | 0.712 | - | 0.668 | 0.702 | - | 0.707 | 0.757 | - |
| rs10064618 | 5 | 153752482 | A/G | 0.597 | 0.545 | - | 0.571 | 0.52 | - | 0.735 | 0.679 | - | 0.629 | 0.526 | - |
| rs2453626 | 8 | 101207073 | C/T | 0.681 | 0.69 | - | 0.598 | 0.617 | 0.99 | 0.783 | 0.808 | - | 0.695 | 0.713 | 0.97 |
| rs2381416 | 9 | 6183455 | A/C | 0.776 | 0.75 | 0.94 | 0.699 | 0.658 | 0.96 | 0.832 | 0.81 | 0.89 | 0.723 | 0.665 | 0.94 |
| rs1888909 | 9 | 6187392 | C/T | 0.78 | 0.752 | 0.95 | 0.692 | 0.667 | 0.96 | 0.837 | 0.82 | 0.91 | 0.732 | 0.684 | 0.95 |
| rs11214966 | 11 | 113736465 | C/T | 0.102 | 0.108 | 0.97 | 0.106 | 0.135 | - | 0.143 | 0.14 | 0.93 | 0.143 | 0.148 | - |
| rs4938096 | 11 | 113740940 | C/T | 0.898 | 0.892 | 0.98 | 0.895 | 0.865 | - | 0.854 | 0.859 | 0.94 | 0.869 | 0.852 | - |
| rs16929496 | 12 | 25885071 | C/T | 0.177 | 0.161 | 0.76 | 0.126 | 0.146 | 0.85 | 0.146 | 0.122 | 0.56 | 0.166 | 0.149 | 0.85 |
| rs11048311 | 12 | 25913405 | A/C | 0.858 | 0.869 | 0.99 | 0.875 | 0.865 | 1 | 0.902 | 0.93 | 0.96 | 0.871 | 0.863 | 1 |
| rs11048317 | 12 | 25919674 | G/T | 0.142 | 0.131 | 0.99 | 0.125 | 0.135 | - | 0.106 | 0.076 | 0.91 | 0.162 | 0.147 | - |
| rs9891949 | 17 | 8039908 | A/G | 0.668 | 0.668 | 0.96 | 0.696 | 0.606 | - | 0.709 | 0.743 | 0.97 | 0.698 | 0.666 | - |
| rs2517955 | 17 | 35097207 | C/T | 0.421 | 0.441 | 0.85 | 0.373 | 0.511 | 0.82 | 0.429 | 0.454 | 0.86 | 0.463 | 0.532 | 0.83 |
| rs2952155 | 17 | 35115244 | C/T | 0.652 | 0.643 | 0.76 | 0.685 | 0.581 | 0.75 | 0.649 | 0.62 | 0.88 | 0.669 | 0.61 | 0.75 |
| rs1810132 | 17 | 35119531 | C/T | 0.432 | 0.452 | 0.73 | 0.335 | 0.498 | 0.64 | 0.387 | 0.415 | - | 0.429 | 0.483 | 0.67 |
| rs1058808 | 17 | 35137563 | C/G | 0.625 | 0.622 | 0.66 | 0.527 | 0.665 | 0.57 | 0.634 | 0.66 | 0.49 | 0.635 | 0.697 | 0.58 |
| rs907092 | 17 | 35175785 | A/G | 0.318 | 0.284 | - | 0.376 | 0.289 | - | 0.311 | 0.273 | - | 0.33 | 0.262 | - |
| rs2313430 | 17 | 35183342 | C/T | 0.643 | 0.672 | 0.97 | 0.539 | 0.648 | 0.99 | 0.618 | 0.661 | 0.85 | 0.598 | 0.637 | 0.99 |
| rs10445308 | 17 | 35191573 | C/T | 0.67 | 0.706 | 0.97 | 0.617 | 0.696 | 0.99 | 0.682 | 0.717 | 0.91 | 0.669 | 0.725 | 0.99 |
| rs9909593 | 17 | 35223675 | A/G | 0.657 | 0.695 | 0.98 | 0.615 | 0.692 | - | 0.688 | 0.722 | 0.95 | 0.668 | 0.724 | - |
| rs9303277 | 17 | 35229995 | C/T | 0.61 | 0.64 | - | 0.538 | 0.644 | - | 0.639 | 0.684 | - | 0.597 | 0.638 | - |
| rs3816470 | 17 | 35239327 | A/G | 0.622 | 0.648 | 0.96 | 0.545 | 0.649 | 0.96 | 0.633 | 0.681 | 0.92 | 0.592 | 0.63 | 0.97 |
| rs11557466 | 17 | 35278152 | C/T | 0.673 | 0.71 | 0.98 | 0.643 | 0.709 | 0.98 | 0.687 | 0.72 | 0.96 | 0.681 | 0.74 | 0.99 |
| rs11078925 | 17 | 35278734 | C/T | 0.326 | 0.289 | 0.99 | 0.356 | 0.29 | 0.98 | 0.311 | 0.276 | 0.98 | 0.333 | 0.26 | 0.99 |
| rs12150079 | 17 | 35278943 | A/G | 0.217 | 0.201 | - | 0.233 | 0.2 | - | 0.202 | 0.177 | - | 0.213 | 0.183 | - |
| rs12936231 | 17 | 35282646 | C/G | 0.619 | 0.652 | 0.99 | 0.559 | 0.655 | 0.99 | 0.639 | 0.685 | 0.98 | 0.607 | 0.643 | - |
| rs11870965 | 17 | 35283731 | A/T | 0.325 | 0.286 | 1 | 0.356 | 0.298 | 0.99 | 0.319 | 0.281 | 0.98 | 0.354 | 0.281 | 1 |
| rs1054609 | 17 | 35286803 | A/C | 0.675 | 0.714 | 1 | 0.644 | 0.702 | 1 | 0.681 | 0.719 | 0.98 | 0.66 | 0.719 | 1 |
| rs9907088 | 17 | 35288642 | A/G | 0.325 | 0.286 | 1 | 0.355 | 0.298 | 1 | 0.318 | 0.28 | 0.99 | 0.35 | 0.273 | 1 |
| rs12452894 | 17 | 35290112 | A/G | 0.675 | 0.714 | 1 | 0.644 | 0.702 | 1 | 0.682 | 0.72 | 0.99 | 0.664 | 0.727 | 1 |
| rs12232497 | 17 | 35293645 | C/T | 0.325 | 0.286 | 1 | 0.356 | 0.289 | 1 | 0.313 | 0.276 | 0.99 | 0.333 | 0.259 | 1 |

| SNP | Chr | Position (hg18) | A1/A2 | CHS: | | | CARE: | | | MCCAS: | | | GALA: | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq | Control FreqA1 | Case FreqA1 | Rsq |
| rs2872507 | 17 | 35294289 | A/G | 0.328 | 0.294 | - | 0.356 | 0.298 | - | 0.318 | 0.279 | - | 0.35 | 0.273 | - |
| rs9901146 | 17 | 35296869 | A/G | 0.381 | 0.348 | 0.99 | 0.432 | 0.327 | 0.99 | 0.354 | 0.306 | 0.99 | 0.385 | 0.319 | 0.99 |
| rs12950743 | 17 | 35302759 | C/T | 0.381 | 0.348 | 0.99 | 0.432 | 0.327 | 0.99 | 0.354 | 0.306 | 0.99 | 0.385 | 0.319 | 0.99 |
| rs7359623 | 17 | 35303115 | C/T | 0.624 | 0.656 | 0.98 | 0.572 | 0.675 | 0.98 | 0.651 | 0.699 | 0.98 | 0.637 | 0.691 | 0.98 |
| rs8067378 | 17 | 35304874 | A/G | 0.617 | 0.65 | - | 0.557 | 0.645 | 0.99 | 0.639 | 0.687 | - | 0.609 | 0.649 | 0.99 |
| rs8069176 | 17 | 35310723 | A/G | 0.323 | 0.284 | 0.99 | 0.376 | 0.307 | 0.99 | 0.32 | 0.279 | 0.99 | 0.358 | 0.285 | 0.99 |
| rs2305480 | 17 | 35315722 | A/G | 0.319 | 0.281 | - | 0.356 | 0.298 | 1 | 0.308 | 0.269 | - | 0.334 | 0.253 | 1 |
| rs2305479 | 17 | 35315743 | C/T | 0.623 | 0.657 | 0.99 | 0.587 | 0.673 | - | 0.662 | 0.707 | 0.99 | 0.655 | 0.718 | - |
| rs11078927 | 17 | 35317931 | C/T | 0.677 | 0.717 | 0.99 | 0.644 | 0.712 | - | 0.693 | 0.73 | 1 | 0.682 | 0.748 | - |
| rs2290400 | 17 | 35319766 | C/T | 0.379 | 0.342 | - | 0.428 | 0.35 | 0.97 | 0.349 | 0.306 | - | 0.406 | 0.346 | 0.98 |
| rs1008723 | 17 | 35319793 | G/T | 0.622 | 0.657 | 0.98 | 0.587 | 0.673 | - | 0.657 | 0.701 | 0.99 | 0.641 | 0.703 | - |
| rs4795400 | 17 | 35320546 | C/T | 0.673 | 0.711 | 0.98 | 0.633 | 0.712 | 0.99 | 0.691 | 0.726 | 0.99 | 0.68 | 0.748 | - |
| rs869402 | 17 | 35321569 | C/T | 0.62 | 0.656 | 0.98 | 0.568 | 0.683 | - | 0.661 | 0.703 | 0.99 | 0.656 | 0.722 | 0.97 |
| rs7216389 | 17 | 35323475 | C/T | 0.36 | 0.328 | - | 0.432 | 0.32 | 0.99 | 0.342 | 0.301 | - | 0.367 | 0.293 | 0.96 |
| rs9303280 | 17 | 35327557 | C/T | 0.625 | 0.662 | 0.97 | 0.564 | 0.694 | 0.96 | 0.657 | 0.698 | 0.99 | 0.643 | 0.702 | 0.94 |
| rs9303281 | 17 | 35327572 | A/G | 0.62 | 0.656 | 0.98 | 0.536 | 0.653 | 0.98 | 0.642 | 0.686 | 0.98 | 0.602 | 0.642 | 0.95 |
| rs7219923 | 17 | 35328044 | C/T | 0.381 | 0.345 | 0.98 | 0.445 | 0.346 | 0.98 | 0.352 | 0.312 | 0.98 | 0.405 | 0.345 | 0.95 |
| rs7224129 | 17 | 35328952 | A/G | 0.61 | 0.647 | 0.95 | 0.552 | 0.649 | 0.96 | 0.639 | 0.679 | 0.94 | 0.604 | 0.65 | 0.93 |
| rs8076131 | 17 | 35334438 | A/G | 0.664 | 0.698 | 0.96 | 0.626 | 0.717 | 0.96 | 0.691 | 0.721 | 0.97 | 0.675 | 0.739 | 0.95 |
| rs12603332 | 17 | 35336333 | C/T | 0.621 | 0.656 | 0.97 | 0.524 | 0.672 | 0.95 | 0.647 | 0.683 | 0.97 | 0.592 | 0.63 | 0.95 |
| rs4795403 | 17 | 35339248 | C/T | 0.755 | 0.79 | 0.98 | 0.793 | 0.828 | - | 0.761 | 0.78 | 0.96 | 0.801 | 0.816 | - |
| rs4795405 | 17 | 35341943 | C/T | 0.65 | 0.683 | - | 0.608 | 0.723 | 0.94 | 0.668 | 0.702 | - | 0.645 | 0.696 | 0.95 |
| rs4794820 | 17 | 35342870 | A/G | 0.345 | 0.311 | 0.95 | 0.409 | 0.297 | 0.92 | 0.343 | 0.304 | 0.94 | 0.382 | 0.334 | 0.91 |
| rs8079416 | 17 | 35346239 | C/T | 0.573 | 0.597 | - | 0.435 | 0.681 | 0.78 | 0.621 | 0.655 | - | 0.555 | 0.585 | 0.98 |
| rs6503525 | 17 | 35348700 | C/G | 0.571 | 0.592 | 0.99 | 0.399 | 0.625 | 0.65 | 0.621 | 0.651 | 0.98 | 0.548 | 0.579 | - |
| rs4065985 | 17 | 35355458 | C/G | 0.674 | 0.694 | 0.9 | 0.588 | 0.777 | 0.79 | 0.695 | 0.72 | 0.9 | 0.661 | 0.706 | 0.94 |
| rs4795408 | 17 | 35361153 | A/G | 0.562 | 0.586 | 0.97 | 0.395 | 0.593 | 0.64 | 0.618 | 0.646 | 0.95 | 0.508 | 0.528 | 0.94 |
| rs6503526 | 17 | 35368124 | C/T | 0.435 | 0.415 | 0.97 | 0.611 | 0.396 | 0.65 | 0.378 | 0.352 | 0.97 | 0.512 | 0.476 | 0.94 |
| rs3894194 | 17 | 35375519 | A/G | 0.562 | 0.578 | - | 0.385 | 0.589 | 0.63 | 0.62 | 0.642 | - | 0.489 | 0.508 | 0.83 |
| rs7212938 | 17 | 35376206 | G/T | 0.51 | 0.528 | 0.64 | 0.329 | 0.521 | 0.49 | 0.563 | 0.567 | 0.64 | 0.422 | 0.433 | 0.61 |
| rs34724 | 19 | 35060850 | G/T | 0.546 | 0.496 | - | 0.503 | 0.553 | 0.67 | 0.448 | 0.399 | - | 0.534 | 0.455 | 0.81 |
| rs335016 | 19 | 35065232 | A/C | 0.429 | 0.461 | 0.78 | 0.424 | 0.407 | 0.66 | 0.486 | 0.539 | 0.68 | 0.428 | 0.501 | 0.76 |

**Supplementary Table 4.** Baseline characteristics of subjects in replication studies. NA, data not available.

| Sample[^] | EVE Center | N Asthma Cases | Sex Ratio (M:F) | AGE OF ONSET (YRS) (ASTHMA) | | AGE AT ENROLLMENT (YRS) | | % Atopic[*] |
|---|---|---|---|---|---|---|---|---|
| | | | | Mean (SD) | Median (range) | Mean (SD) | Median (range) | |
| European Americans | | | | | | | | |
| CARE | Arizona | 85 | 60:25 | 3.7 (2.9) | 3 (0-16) | 10.2 (2.9) | 10.2 (6-17) | 77.4 |
| CHS | USC | 265 | 127:138 | 7.8 (5.3) | 7 (0-18) | 11.8 (2.9) | 10.6 (5-17) | NA |
| Freiburg | Chicago | 459 | 302:157 | NA | NA | 9.9 (2.9) | 9.5 (2-18) | 96.0 |
| iCAP | Harvard | 1731 | 389:1342 | NA | NA | 35.8 (8.7) | 37.0 (5-48) | NA |
| Madison | Chicago | 187 | 118:69 | 4.5 (2.4) | 5 (0-12) | 5.1 (4.4) | 6.4 (0-13) | 67.2 |
| African American/Caribbean Americans | | | | | | | | |
| CARE | Arizona | 11 | 5:6 | 3.7 (2.7) | 3.3 (0-9) | 9.2 (3.3) | 8.2 (6-17) | 90.9 |
| iCAP | Harvard | 183 | 35:148 | NA | NA | 35.8 (7.4) | 36.0 (7- 48) | NA |
| SAGE | UCSF | 791 | 402:389 | 4.9 (5.5) | 3 (0-39) | 14.9 (6.4) | 14.0 (7-40) | 71.2 |
| SAPPHIRE | Henry Ford | 1162 | 409:753 | 13.4 (13.5) | 9 (0-55) | 32.9 (14.0) | 33.0 (12-56) | NA |
| Latino | | | | | | | | |
| CARE | Arizona | 60 | 35:25 | 4.4 (3.3) | 4 (0-15) | 10.6 (2.9) | 10.3 (6-17) | 77.6 |
| CHS | USC | 337 | 187:150 | 4.3 (4.5) | 2.5 (0-18) | 9.0 (2.9) | 9.8 (4-18) | NA |
| Costa Rica | Harvard | 591 | 351:240 | 2.5 (2.3) | 2 (0-12) | 9.0 (1.8) | 8.7 (6-14) | 85.4 |
| GALA2 | UCSF | 1237 | 699:534 | 3.2 (3.4) | 2 (0-20) | 11.8 (3.1) | 11.0 (6-23) | 71.1 |
| HOLA | UCSF | 74 | 35:39 | 5.5 (7.1) | 2 (0-31) | 15.8 (10.5) | 13 (5-40) | NA |

[^]CARE, Clinical Asthma Research Network; CHS, Children's Health Study, iCAP, The i2b2 Crimson Asthma Project; SAGE, Study of African Americans, Asthma, Genes and Environment; SAPPIRE, Study of Asthma Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity; GALA 2, Genes-Environment & Admixture in Latino Americans; HOLA, Honduran Latino Asthma Study

[*]1 or more positive allergen skin tests or specific IgE

**Supplementary Table 5.** Association p-values in EVE samples for SNPs reported in previous GWAS of asthma. References in the third column refer to the initial report. The SNPs near HLA-DQ in Moffat et al. [2] and Li et al. [3] were not genotyped or imputed in the EVE samples; instead five tag SNPs for HLA-DQ from Leslie et al. [4] are included here. P-values <0.05 are shown in bold font.

| Locus | SNP | Ref. | Ethnicity of Discovery Sample in Original Study | P-values in EVE Meta-Analyses | | | |
|---|---|---|---|---|---|---|---|
| | | | | Eur Am | Afr Am/ Afr Carib | Latino | Combined |
| *HLA-DQ* | rs6906021 | [2,3] | European | 0.72 | 0.50 | 0.0099 | 0.041 |
| *HLA-DQ* | rs4947342 | [2,3] | European | 0.036 | 0.032 | 0.99 | 0.014 |
| *HLA-DQ* | rs6457617 | [2,3] | European | 0.69 | 0.77 | 0.73 | 0.84 |
| *HLA-DQ* | rs2647012 | [2,3] | European | 0.35 | 0.25 | 0.77 | 0.17 |
| *HLA-DQ* | rs3997854 | [2,3] | European | 0.025 | 0.64 | 0.0037 | 0.62 |
| *17q21* | rs2305480 | [2] | European | $8.3 \times 10^{-7}$ | 0.0094 | $2.3 \times 10^{-7}$ | $1.3 \times 10^{-13}$ |
| *17q21* | rs3894194 | [2] | European | $5.8 \times 10^{-6}$ | 0.24 | 0.0021 | $1.9 \times 10^{-7}$ |
| *IL18R1* | rs3771166 | [2] | European | 0.034 | 0.0017 | 0.0012 | $1.3 \times 10^{-6}$ |
| *IL33* | rs1342326 | [2] | European | 0.071 | 0.31 | $9.9 \times 10^{-4}$ | $4.0 \times 10^{-4}$ |
| *SMAD3* | rs744910 | [2] | European | $1.9 \times 10^{-4}$ | 0.14 | 0.68 | 0.0037 |
| *IL2RB* | rs2284033 | [2] | European | 0.064 | 0.48 | 0.56 | 0.062 |
| *RORA* | rs11071559 | [2] | European | 0.0021 | 0.080 | 0.84 | 0.0059 |
| *SLC22A5* | rs2073643 | [2] | European | 0.19 | 0.17 | 0.18 | 0.021 |
| *IL13* | rs20541 | [2,3] | European | 0.15 | 0.41 | 0.86 | 0.15 |
| *RAD50* | rs2706347 | [3] | European | 0.59 | 0.15 | 0.17 | 0.0058 |
| *RAD50* | rs2040704 | [3] | European | 0.68 | 0.049 | 0.16 | 0.035 |
| *RAD50* | rs2244012 | [3] | European | 0.67 | 0.060 | 0.20 | 0.045 |
| *DENND1B* | rs2786098 | [5] | European American | 0.67 | 0.12 | 0.79 | 0.67 |
| *DENND1B* | rs1775456 | [5] | European American | 0.67 | 0.46 | 0.60 | 0.86 |

**Supplementary Table 6:** Comparisons of local ancestry in cases and controls in the African American/African Caribbean studies at *PYHIN1*. We estimated local ancestry in the African American/African Caribbean studies using LAMP[6] under a 2-population model of 80% African ancestry and 20% European ancestry, 7 generations of admixture, and a constant recombination rate of 1e-8. Windows were offset by 0.2, and a cutoff for LD was set to 0.1. Only genotyped SNPs on chromosome 1 were used to infer local ancestry at *PYHIN1*. Local ancestry was compared between cases and controls using logistic regression (CAG/CSGA/SARP, GRAAD, and SAPPHIRE) and the MQLS method[7] (for Barbados families). There was no significant difference in local ancestry between cases and controls for any of the studies, with a combined p-value across the studies of 0.77.

| Study | Mean Cases | Mean Controls | P-value |
|---|---|---|---|
| Barbados | 0.867 | 0.873 | 0.76 |
| CAG/CSGA/SARP | 0.803 | 0.788 | 0.36 |
| GRAAD | 0.789 | 0.797 | 0.63 |
| SAPPHIRE | 0.795 | 0.818 | 0.50 |

**Supplementary Table 7.** Number of genotyped and imputed SNPs included in the meta-analysis from each study following quality control filtering.

| Population | Study | Total SNPs that passed QC filters |
|---|---|---|
| **European American:** | CAG/CSGA/SARP | 2,371,955 |
| | CAMP (trios) | 2,359,837 |
| | CARE (trios) | 2,343,139 |
| | CHS | 2,355,787 |
| **African American:** | CAG/CSGA/SARP | 2,942,270 |
| | GRAAD | 2,935,690 |
| | Barbados (sibships) | 2,804,265 |
| | SAPPHIRE | 2,829,080 |
| **Latino:** | CARE (trios) | 2,749,626 |
| | MCCAS (trios) | 2,755,385 |
| | CHS | 2,448,134 |
| | GALA (trios) | 2,870,376 |

**Supplementary Table 8**. CARE Clinical trials included in EVE Meta-Analysis and replication. ICS=inhaled corticosteroids.

| Trial | Full Name | Phenotype | Age (yrs) |
|---|---|---|---|
| PEAK | Prevention of Early Asthma in Kids | High risk of asthma | 2-4 |
| CLIC | Characterizing the Response to a Leukotriene Receptor Antagonist and an Inhaled Corticosteroid | Mild/moderate persistent asthma | 6-18 |
| PACT | Pediatric Asthma Controller Trial | Mild/moderate persistent asthma | 6-14 |
| AIMS | Acute Intervention Management Strategies | History of moderate/severe wheezing | 1-5 |
| MARS | Montelukast or Azithromycin for Reduction of Inhaled Corticosteroids in Childhood Asthma | Moderate/severe persistent asthma | 8-16 |
| TREXA | TReating Children to Prevent EXacerbations of Asthma | Mild persistent asthma controlled on low dose ICS | 6-17 |
| BADGER | Best ADd-on Therapy Giving Effective Response | Mild-to-moderate persistent asthma not controlled with low dose of ICS | 6-18 |

## Supplementary Note: Description of GWAS and Replication Studies

### a. Childhood Asthma Research and Education (CARE)

**Subjects:** Five clinical trials including children with physician-diagnosed asthma or those at high risk for asthma from the Childhood Asthma Research and Education (CARE) network that were part of the SHARe-Asthma Resource Project (SHARP) were included in the EVE meta-analysis: PEAK, PACT, CLIC, AIMS and MARS (Supplementary Table 8), contributing in total 217 European American and 52 Latino trios. Detailed descriptions of each trial and SHARP are available at http://www.asthma-carenet.org/trials.html, and http://www.ncbi.nlm.nih.gov/projects/gap/cgi-bin/study.cgi?study_id=phs000166.v2.p1, respectively.

**Genotyping and QC:** Genotyping was performed for the SHARP CARE subjects on the Affymetrix SNP Array 6.0. Markers were filtered based on 95% call rates, Hardy-Weinberg equilibrium p-values > $10^{-6}$, allele frequencies similar between the parents of trios and the HapMap CEU or MEX (for Caucasian and Hispanic/Latino populations respectively, $p > 10^{-6}$), fewer than 5 Mendelian errors, no evidence of plate effects ($p > 10^{-6}$), and unique mapping positions of the probes to a single location in hg18. Subjects were excluded unless the following criteria were met: call rate > 95%, a comparison to parental genotypes identified fewer than 5 Mendelian errors, genetic sex was consistent to reported sex, a principal component analysis including the 11 HapMap phase III populations suggested a general consistency with self-reported ethnicity, no unexpected excess in homozygosity or heterozygosity levels, and no unexpected relatedness or identity between subjects.

**Data Analysis:** Genotype Imputation was performed using MACH using the phase 2 release 21 consensus haplotypes for the CEU (for imputing genotypes in the Caucasian trios), and the combined CEU, YRI, and CHB/JPT haplotypes (for imputing genotypes in the Hispanic trios). Allele frequencies in transmitted and untransmitted chromosomes were estimated by summing the dosages of the children of complete trios and taking the average (i.e. transmitted allele frequency), and summing the dosages of the parents of complete trios, subtracting the dosages of the children, and then taking the average (i.e. untransmitted allele frequency). Association testing for CARE was performed on complete trios using a modified version of PBAT[8].

### b. Chicago Asthma Genetics Study, Collaborative Studies on the Genetics of Asthma, and the Severe Asthma Research Program (CAG/CSGA/SARP)

**Subjects:** Subjects were from the Chicago Asthma Genetics Study (CAG), the NHLBI Collaborative Studies on the Genetics of Asthma (CSGA), and the Severe Asthma Research Program (SARP).

**CAG** included both European American and African American subjects collected at the

University of Chicago from a) families ascertained through affected sib pairs, b) affected children and their parents, c) adults and children with severe persistent asthma, and d) non-asthmatic control subjects (over the age of 18 years). Samples a-c were recruited in the adult and/or pediatric asthma clinics at University of Chicago Hospital; controls were recruited from the medical center at large. Asthma was defined based on the following criteria, 1) a physician's diagnosis (with no conflicting diagnosis), 2) the presence of at least 2 self-reported symptoms (cough, wheeze, shortness of breath), 3) current use of asthma medications, and 4) either bronchial hyperresponsiveness, defined as a ≥20% decrease in FEV1 after inhalation of ≤25 mg/mL methacholine, or reversibility to inhaled bronchodilator, defined as a ≥15% increase in baseline FEV1 after inhalation of a bronchodilator (albuterol) or after treatment. Subjects with a birthweight below 4.4 lb or with > 3 pack-years of cigarette smoking were excluded. Controls had no self-reported personal or family history of asthma among first-degree relatives.

**SARP and CSGA** included both European American and African American subjects. Control subjects and subjects with mild to severe asthma were recruited at the NHLBI funded Severe Asthma Research Program (SARP) centers and the NHLBI Collaborative Studies on the Genetics of Asthma (CSGA) and met the American Thoracic Society (ATS) definition of severe persistent asthma[9]. Subjects were characterized according to asthma severity (see[10,11]). Controls were recruited from the same medical centers, and had no personal or first-degree relative family history of asthma. SARP, and CSGA studies were approved by the appropriate Institutional Review Board at the participating sites including appropriate informed consent.

**Genotyping and QC:** Genotyping was performed on the Illumina 1Mv1 platform, with individual genotypes called using clustering algorithms as implemented in the BeadStudio software by Illumina. The resulting number of markers was 1,033,467 prior to additional QC measures. Markers were filtered based on 95% call rates, Hardy-Weinberg equilibrium p-values > $10^{-5}$, consistency in allele frequency from the HapMap ASW (chi-square p-value > $10^{-5}$), and < 5 heterozygous genotype calls in males for X-linked markers. The total number of markers following QC was 1,025,129. Subjects were filtered based on 95% call rates, matching genetic and reported sex (Fstat on X chromosome between -0.2 and 0.3 for females, and between 0.8 and 1 for males), consistency in self-reported ethnicity based on a principal component analysis in Eigenstrat (no obvious clustering with the HapMap CEU for African Americans, and the HapMap YRI for European Americans), and high or low heterozygosity (Fstat < 0.5 and > -0.2). Samples were flagged for unexpected pairwise relatedness (IBD > 30%) or genetic identity (IBS > 90%), with subsequent filtering performed by selecting a single sample from the pair (or group) having the highest call rate.

**Data Analysis:** Imputation of the phase 2, release 21 HapMap SNPs was performed using MACH[12], with the consensus CEU haplotypes used as a reference for the European American cases and controls, and the combined consensus CEU and YRI haplotypes for the African American cases and controls. Tests of allelic association were performed on dosages for both genotyped and imputed SNPs using logistic regression in R (http://CRAN.R-project.org/). For the set of African American cases and controls, local ancestry was used as a covariate at the

SNP level as estimated using the set of genotyped SNPs in the program LAMP - Local Ancestry in adMixed Populations[6]. Admixture in African Americans was modeled under 7 generations of admixture with a 2-population model of 81% ancestry from Africa and 19% ancestry from Europe as estimated based on the first principal component in a PCA analysis using EIGENSTRAT[13]). Windows were offset by a factor of 0.2, the cutoff for linkage was set to 0.1, and a constant recombination rate was set to $10^{-8}$. Local ancestry for imputed SNPs was obtained from the next closest genotyped SNP.

### c. Childhood Asthma Management Program (CAMP)

**Subjects:** The Childhood Asthma Management Program (CAMP) population is composed of non-Hispanic white subjects from a multi-center clinical trial that followed 1,041 children with asthma for four years and 84% of the original participants for 12 years[14]. Stringent inclusion criteria ensured that participants had mild to moderate asthma, which was assessed as having asthma symptoms at least twice per week, using asthma medication daily, or using an inhaled bronchodilator twice per week for six or more months of the year prior to recruitment. CAMP subjects had increased airway responsiveness, as established by a bronchoprovocation test of up to 12.5mg/dl of methacholine resulting in 20% or greater forced expiratory volume in one second ($FEV_1$) reduction.

**Genotyping and QC:** Genome-wide SNP genotyping of 422 Caucasian CAMP subjects and their families was performed on Illumina's HumanHap550v3 Genotyping BeadChip (Illumina, Inc., San Diego, CA). Details of the quality control (QC) criteria used to screen the genome-wide SNP data have been provided previously[15]. Briefly, of the 1,215 CAMP subjects and parents who were genotyped, 1,170 had genotyping call rates > 95% and were used in subsequent analyses. A total of 486,706 SNPs remained after excluding those having low clustering scores (n=6,257), flanking sequences that did not map to a unique position on the HG17 reference genome (n=1,329), 5 or more Mendel errors (n=2,445), a genotyping rate < 95% (n=2396), being monomorphic (n=3790), having minor allele frequency (MAF) < 5% (n=44,468), failing Hardy-Weinberg Equilibrium at a threshold of p<=0.001 (n=582), and having MAF that differed by more than 0.20 from the corresponding HapMap Phase 2 Release 21 MAF in CEU (n=403).

**Data Analysis:** Imputation of the HapMap Phase 2 Release 21 SNPs was performed using MACH[12] with the CEU phased haplotypes as a reference. Family-based association statistics for 385 complete CAMP trios, based on imputed genotype dosages, and assuming an additive model of inheritance were calculated using PBAT version 3.61[8].

### d. The Children's Health Study (CHS)

**Subjects:** The Children's Health Study (CHS) is an ongoing cohort study in southern California investigating both genetic and environmental factors related to childhood asthma and lung

function growth. The CHS GWAS was based on a nested case-control sample of 1249 asthmatics and 1751 controls selected from within the cohort. All subjects in this GWAS sample were either Hispanic white (HW) (n=1398) or non-Hispanic white (NHW) (n=1602). Based on questionnaire responses, children were characterized as having physician diagnosed asthma at study entry or during active follow-up (cases), or as never having a diagnosis of asthma (controls).

**Genotyping and QC:** Study samples were genotyped at the USC Epigenome Center using the Illumina HumanHap550, HumanHap550-Duo or Human610-Quad BeadChip microarrays. Individuals were excluded from analysis with call rates < 90% (n=155). The HumanHap550, HumanHap550-Duo and Human610-Quad contained 366, 366 and 418 SNPs respectively that overlapped with a candidate gene study containing a large number of the subjects in this study (n=2,905). The average concordance rate between matching subjects for these overlapping SNPs was > 99.69% for > 99% of the samples having a call rate > 90%. Subjects with poor concordance with genotypes from the candidate gene study were excluded (n=19). SNPs were excluded prior to imputation if they were not concordant between Illumina genotyped HapMap samples and HapMap2_r21 (< 95% in any population) or not concordant between Illumina genotyped HapMap samples on the HumanHap550 and Human610 (< 95% in any population) (n=8,616). Additionally, SNPs were filtered if they had a call rate < 95% (n=84,381) or departed from Hardy-Weinberg equilibrium ($p < 10^{-5}$) in controls in HW and NHW samples separately (n=762 and 766 respectively).

**Data analysis:** Imputation was performed with MACH v1.0.16[12] using the HapMap phase 2 release 21 consensus CEU haplotypes as a reference for the NHW subjects and CEU+ASN haplotypes for the HW subjects. Tests of allelic association were performed on dosages for both genotyped and imputed SNPs using logistic regression using R (www.R-project.org), adjusting for age, community of residence, sex, and ancestry covariates derived from the program STRUCTURE[16] applied to 557 ancestrally informative markers.

### e. Genetics of Asthma in Latino Americans (GALA)

**Subjects:** The Genetics of Asthma in Latino American's (GALA) Study [17] includes children (probands) and their biological parents recruited from schools, clinics and hospitals that cared for Latino patients at four sites: San Francisco Bay Area, New York City, Puerto Rico and Mexico City. In all health care centers, medical records were reviewed to identify patients with physician-diagnosed mild or moderate-severe asthma based on medical billing records (ICD 9 codes). Patients were contacted to participate in the study if approved by their primary physician. Bilingual and bicultural physicians specialized in asthma were present at all interviews, and all forms and questionnaires for subjects were available in English and Spanish. Based on interviews and questionnaire data, children were included in the study if they were between the ages of 8-40 with physician diagnosed mild to moderate-severe asthma and had experienced two or more symptoms in the previous two years at time of recruitment (including wheezing, coughing and/or shortness of breath). Trios were enrolled if both parents

and 4 sets of grandparents of the proband self-identified as either Puerto Rican or Mexican ethnicity.

**Genotyping and QC*:*** Genotyping was performed on the Affymetrix 6.0 GeneChip Array containing > 900,000 SNPs prior to QC measures. Subjects were filtered based on 95% call rates, complete trios, and Mendelian errors. Markers were filtered based on 95% call rates, Hardy-Weinberg equilibrium p-values $>10^{-6}$, < 1% Mendelian inconsistencies, unambiguous mapping to the human reference genome, and no evidence for previous plate effects. The total number of trios passing QC was 538 (n=1,614), and the total number of markers passing QC was 729,685.

**Data Analyses:** Imputation was performed using MACH[12] using the phased CEU, YRI, and ASN phase 2, release 21 consensus HapMap genotypes as a reference. Allele frequencies in transmitted and untransmitted chromosomes were estimated by summing the dosages of the children of complete trios and taking the average (i.e. transmitted allele frequency), and summing the dosages of the parents of complete trios, subtracting the dosages of the children, and then taking the average (i.e. untransmitted allele frequency). Family-based association statistics were calculated using allelic dosages assuming an additive model in PBAT version 6.4.0[8].

### f. Genomic Research on Asthma in the African Diaspora (GRAAD) and Barbados

**Subjects (GRAAD):** The Genomic Research on Asthma in the African Diaspora study consists of 498 asthma cases and 500 non-asthmatic controls from the Baltimore-Washington, D.C. metropolitan area who self-reported as African American. Because asthma is often characterized by onset during childhood, there was a deliberate decision to favor adults in the control group to minimize including controls with the potential for developing asthma. A standardized questionnaire based on either the American Thoracic Society[18] or International Study of Asthma and Allergy in Childhood (ISAAC) [19] was administered by a clinical coordinator. Asthma was defined as both a self-reported history of asthma, and a documented history of physician-diagnosed asthma (past or current). All controls (except 50, see below) were likewise administered a standardized questionnaire and were determined to be negative for a history of asthma. Asthma status on 50 controls participating in a study of the genetics of human pigmentation[20] was not explicitly determined, although “known clinical disease” was among the exclusion criteria. The study protocol was approved by the institutional review board at either the Johns Hopkins University or Howard University.

**Subjects (Barbados):** A population of 163 African Caribbean families were ascertained through asthmatic probands from Barbados containing a total of 1,028 individuals. Probands and their extended family members were recruited through referrals at local polyclinics or the Accident and Emergency Department at the Queen Elizabeth Hospital. Asthma was defined as both a self-reported history of asthma and documented history of physician-diagnosed asthma (past or current), plus a history of wheezing without an upper respiratory infection

(URI) for two out of four hallmark symptoms (wheezing with a URI, cough without a URI, shortness of breath, and tightness in the chest). The study protocol was approved by the institutional review board at either the Johns Hopkins University or Howard University.

**Genotyping and QC:** Details of genotyping and quality control (QC) have been previously described[21]. Briefly, genotypes were generated at the Center for Inherited Disease Research (CIDR) for 665,352 SNPs on the Illumina HumanHap650Y Versions 1 and 3 BeadChips and the Illumina Infinium II assay protocol. Genotypes were released for 994 GRAAD samples, 948 Barbados samples on Version 1 arrays and 61 Barbados samples typed on Version 3 arrays for SNPs with < 5% missing data, no replicate error or Mendelian error in the HapMap control trios, among other standard QC protocols. Relationships between individuals within each study were verified using PLINK[22] and RELPAL[23], and Mendelian inconsistencies in the family-based sample, and marker-level QC parameters (including minor allele frequency, differential missing rates between cases and controls, and Hardy Weinberg Equilibrium) were evaluated in PLINK[22]. The genetic structure of African American cases and controls was evaluated using unrelated individuals from the three HapMap "continental" ancestral populations (CEU, YRI, and ASN; www.hapmap.org) using 416 SNPs identified as ancestry informative markers (AIMs) selected for maximal difference between African and European populations in STRUCTURE[16].

**Data Analysis:** Genotypes were imputed at all HapMap phase 2, release 21 SNPs using MACH[12], and using a combined panel of the HapMap CEU, YRI and ASN phased haplotypes for both the African American (GRAAD) and African Caribbean (Barbados) samples. For the family-based dataset (Barbados), association tests were performed with the MQLS method[7] using imputed allele dosage. For the case-control sample (GRAAD), a two sample t-test was used to compare the allele dosage between cases and controls.

### g. Mexico City Childhood Asthma Study (MCCAS)

**Subjects:** The study population, genotyping and quality control have been previously described[24,25]. Briefly, children between the ages of 5-17 with asthma, and their biological parents were recruited between June 1998 and November 2003 from a pediatric allergy specialty clinic at a large public hospital in central Mexico City. Children were diagnosed with asthma by a pediatric allergist at the referral clinic based on clinical symptoms and response to treatment, using guidelines from the British Thoracic Society and Scottish Intercollegiate Guidelines Network[26]. The protocol was approved by the Institutional Review Boards of the National Institute of Environmental Health Sciences, US and the National Institute of Public Health, Mexico.

**Genotyping and QC:** Peripheral blood lymphocytes were isolated from whole blood, and DNA was extracted using Gentra Puregene kits (Gentra Systems, Minneapolis, Minnesota). A total of 498 complete trios with previously confirmed parentage and sufficient amounts of DNA were genotyped at 561,466 SNPs using the Illumina HumanHap 550K BeadChip, version 3

(Illumina, San Diego, California) at the University of Washington, Department of Genome Sciences. Genotypes were determined using the Illumina BeadStudio Genotyping Module, following the manufacturer's recommended conditions. Quality control was conducted primarily using PLINK[22]. SNPs were excluded due to poor chromosomal mapping, call rates < 95%, minor allele frequencies < 1%, HWE p-value (in parents only) < $1x10^{-10}$ (N=557), Mendelian errors in more than two families, and one or more discordant genotypes across the 14 HapMap replicate samples identified using the Genotyping Library and Utilities application (http://code.google.com/p/glu-genetics/). The final number of autosomal SNPs included was 520,767. Subjects were excluded based on unexpected relatedness between trios and call rates < 95%, and were tested for unusual autosomal homozygosity and inconsistencies between reported and genetic sex. The final number of subjects included 492 complete case-parent trios (1,468 study subjects).

**Data Analysis:** Genotype Imputation was performed using MACH with the combined CEU, YRI, and ASN phase 2 release 21 consensus haplotypes as a reference. Allele frequencies in transmitted and untransmitted chromosomes were estimated by summing the dosages of the children of complete trios and taking the average (i.e. transmitted allele frequency), and summing the dosages of the parents of complete trios, subtracting the dosages of the children, and then taking the average (i.e. untransmitted allele frequency). Family-based association statistics for 492 complete trios was performed on genotype dosages assuming an additive model of inheritance using PBAT version 3.61[8].

### h. The Study of Asthma Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity (SAPPHIRE)

**Subjects:** Study participants received their care through a large health system serving southeast Michigan. Cases were part of the Study of Asthma Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity (SAPPHIRE) (n=149), and met the following criteria: age 12-56 years, had a diagnosis of asthma (based on both patient report and documentation in the medical record), and did not have a prior diagnosis of chronic obstructive pulmonary disease or congestive heart failure (CHF), a baseline $FEV_1$ between 40-90% predicted, >12% baseline bronchodilator reversibility, no smoking in the preceding year or <10 pack-year smoking history total, no oral or inhaled corticosteroid use in the 4 weeks preceding screening, and not pregnant at the time of enrollment and not intending to get pregnant during the study period. Controls were obtained from a separate cohort, the Wayne County Health Environment Allergy and Asthma Longitudinal Study. All were women ≥ 21 years of age who also resided in the Detroit metropolitan area and received their care from the same health system. The analytic group for the meta-analysis was restricted to individuals who reported being African American. The Institutional Review Board of Henry Ford Health System approved all of the components of this study.

**Genotyping and QC:** Genotyping for the cases was performed on the Affymetrix Genome-Wide Human SNP Array 6.0, whereas control individuals were genotyped on either the

Mapping 500K Array and the Genome-Wide Human SNP Array 5.0 (Affymetrix, Inc., Santa Clara, California). Genotyping calls and the chip quality control (QC) call rate were assessed using Affymetrix Genotyping Console. Subjects with the following were excluded from the analysis: missing information for one chip (i.e., for those genotyped on the 2 chip Mapping 500K Array), genetic sex inconsistent with reported sex, chips which did not meet the manufacture's recommended QC call rate, and <90% overall call rate. In order to appropriately match cases and controls, genetic ancestry was estimated in all individuals using markers informative for African and European ancestry and the program PSMIX[27]. We restricted the control set to individuals with ≥30% African ancestry (n=132), which was the lower limit of African ancestry among the cases. Single nucleotide polymorphisms (SNPs) common to all genotyping platforms were selected and subjected to the following additional criteria: call rate ≥ 95% and an exact Hardy-Weinberg equilibrium test with p-value $>10^{-5}$ among the controls.

**Data Analysis:** A total of 404,088 SNPs were used to impute the HapMap phase 2, release 21 SNPs using MACH[12] with the phased HapMap CEU and YRI haplotypes as a reference. Case/control association tests for asthma status were performed using logistic regression in R (http://CRAN.R-project.org/) on genotype dosages, and adjusting for the first principal component from EIGENSTRAT[13].

**Description of replication studies**

**a. Harvard - CR and iCAP**

**i. Genetics of Asthma in Costa Rica Study (CR):** This cohort consists of 591 probands from the Genetics of Asthma in Costa Rica Study (CR), which is comprised of Costa Rican schoolchildren with asthma and their parents[28,29]. Children had a high probability of having at least six great-grandparents born in the Central Valley of Costa Rica and were defined as having asthma if they had a doctor's diagnosis of asthma and at least two respiratory symptoms or asthma attacks in the year prior to enrollment in the study. Genotyping was performed with Taqman PCR assays with an ABI Prism 7900 machine (Applied Biosystems, Foster City, CA). Standard PCR conditions, as recommended by the manufacturer, were used. Family-based association statistics for asthma affection status under an additive model were calculated using Golden Helix PBAT version 6.4.0[8].

**ii. i2b2 Crimson Asthma Project (iCAP):** The i2b2 Crimson Asthma Project (iCAP) consists of Partners Healthcare System, Inc. (Boston, MA) patients who were selected based on extracted de-identified electronic medical record (EMR) data and whose DNA was obtained via discarded clinical samples [30]. Using "Informatics for Integrating Biology to the Bedside" (i2b2) resources, a large set of asthmatic patients was identified on the basis of International Classification of Diseases, Ninth Revision (ICD-9) codes for asthma (i.e. 493*) recorded between 1/1/80 and 11/30/06 within Partners' EMRs. Controls were identified on the basis of absence of asthma ICD-9 codes recorded between 1/1/80 and 8/9/07, being between 17 and

40 years of age, and having been seen as a Brigham and Women's Hospital outpatient in at least one of over 850 clinics between 5/1/2004 and 5/1/2007. The last requirement was to help ensure that patients would be available for Crimson Project sample collection. Recruitment criteria for the collection of blood from cases included a restriction of age to be <50 years. In order to conduct genomic studies of these patients, clinical samples that are routinely collected at healthcare visits were obtained via the Crimson Project (http://www.crimsonproject.org). For this study, samples corresponding to 3,610 European American (1,731 cases; 1,879 controls) and 368 African American (183 cases; 185 controls) patients were available. Genotyping was performed with Taqman PCR assays with an ABI Prism 7900 machine (Applied Biosystems, Foster City, CA). Standard PCR conditions, as recommended by the manufacturer, were used. Case-control associations were performed using Cochran-Armitage trend tests in PLINK[22].

**b. Henry Ford Health System – SAPPHIRE**

**i. Study of Asthma Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity (SAPPHIRE):** Cases included in the replication study were part of the Study of Asthma Phenotypes and Pharmacogenomic Interactions by Race-Ethnicity (SAPPHIRE) cohort but were not enrolled in the treatment trial (and hence constituted an independent set of individuals from those included in the meta-analysis). Cases were between the ages of 12-56 years, had a diagnosis of asthma (based on both patient report and documentation in the medical record), and did not have a prior diagnosis of chronic obstructive pulmonary disease or congestive heart failure (CHF). Controls for the replication study were recruited from the same geographic area, were between the ages of 12-56 years, and had no prior diagnosis of asthma, COPD, or CHF. The analytic group for the replication analysis was restricted to individuals who reported being African American. Genotyping was performed using Taqman SNP genotyping assays (Applied Biosystems, Foster City, California), and association testing was performed using logistic regression in R (http://CRAN.R-project.org/).

**c. University of Arizona – CARE**

**i. Childhood Asthma Research and Education (CARE):** Two additional clinical trials from the Childhood Asthma Research and Education (CARE) network were included in the replication analysis: Effective Response (BADGER) and Treating Children to Prevent Exacerbations of Asthma (TREXA) (Supplementary Table 8). Detailed descriptions of each trial are available at http://www.asthma-carenet.org/trials.html. Genotyping was performed using Taqman PCR assays for each SNP, and TDT tests were performed using PLINK[22].

**d. University of California San Francisco - GALA II, SAGE and HOLA**

**i. Genes-Environment & Admixture in Latino Asthmatics (GALA II):** The Genes-Environment & Admixture in Latino Asthmatics Study (GALA II) is an ongoing study recruiting

Latino children who are at high risk (Puerto Rican), intermediate risk (Dominican) and low risk (Mexican) for asthma. A total of 2,531 subjects (1,244 cases and 1,287 controls) from the GALA II study were included in the replication. Cases and controls were recruited concurrently at community clinics and hospitals and were administered a detailed questionnaire. Asthma was defined as a history of physician diagnosed asthma, 12% improvement in $FEV_1$ after the administration of albuterol and/or positive methacholine provocation challenge, and a self-reported presence of coughing, wheezing, or shortness of breath in the 2 years preceding enrollment. Cases were between the ages of 8-21 from New York, Chicago, San Francisco, Houston, and Puerto Rico. Controls were recruited concurrently at each clinic, and were of similar age, sex, and ethnicity but had no reported history of asthma, allergies, lung disease, chronic illness or medication use, coughing, wheezing or shortness of breath in the preceding 2 years, and < 10 pack-years of smoking history.

**ii. The Study of African Americans, Asthma, Genes and Environments (SAGE):** The Study of African Americans, Asthma, Genes and Environments (SAGE) includes African American asthmatics and controls recruited from clinics in the San Francisco Bay Area. Subjects were enrolled in the study if they self-identified as African Americans, and if both biological parents and all biological grandparents were identified as African Americans. Participants were administered a detailed questionnaire. Two phases of recruitment were included in the replication. From the first phase, a total of 561 subjects (283 cases and 278 controls) were included. Cases were between the ages of 8-40 with a history of physician-diagnosed asthma, and a self-reported history of two or more asthma symptoms (wheezing, coughing, and/or shortness of breath) in the preceding two years. Controls were recruited concurrently at each clinic, and were of similar age (8-40) and sex as the cases, but had no reported history of asthma, allergies, lung disease, chronic illness or medication use, coughing, wheezing or shortness of breath in the preceding 2 years, < 10 pack-years of smoking history, and had not smoked in the year preceding enrollment. From the second phase, a total of 760 subjects (508 cases and 252 controls) were included. Cases and controls were between the ages of 8-21 and were recruited from multiple centers in the San Francisco Bay Area under the same protocol as the GALA2 study in Latinos.

**iii. Honduran Latino Asthma Study (HOLA):** The HOnduran Latino Asthma (HOLA) Study is an ongoing study of Honduran children and young adults. A total of 172 subjects, including 74 cases and 98 controls were included in the replication. Subjects were between the ages of 5-40 and were recruited from the Honduran province of Olancho during a respiratory medical mission. Cases were recruited during an annual, week-long pulmonary and allergy clinic in Juticalpa, Honduras and were referred to the study by specialists working in the clinic. Subjects were included if they met the following criteria: a) they carried a physician diagnosis of asthma; b) they reported two or more symptoms of asthma within the year prior to enrollment (wheeze, cough, dyspnea, or nocturnal awakening) or were taking medication to control asthma (albuterol or other short- or long- acting bronchodilators, inhaled corticosteroids, oral corticosteroids, or theophylline); c) they consented to enrollment (or in the case of a minor, the subject assented and a parent consented). Potential subjects were excluded if a) they carried a diagnosis of any other cardiac or pulmonary disease, b) were

active smokers, or had a total lifetime history of smoking of greater than 5 total pack-years, c) were unable to complete any part of the study. The control group was recruited from the local community of Juticalpa and included subjects who had never been diagnosed with asthma, had no asthmatic symptoms (wheezing, cough, dyspnea, or nocturnal awakenings), and were not taking any medication to treat asthma, but otherwise met all other criteria for inclusion.

**e. University of Chicago – Madison and Freiburg**

**i. Madison:** The Madison cohort included European American children who participated in one or more of the following three studies conducted in Madison, Wisconsin: Childhood Origins of Asthma (COAST) [31], COAST+, Treg, and RhinoGen. The samples in the replication included 209 children from COAST, 20 from COAST+, 29 from Treg, and 135 from RhinoGen. The COAST sample consists of children participants in a birth cohort study of the origins of asthma in Madison, Wisconsin. The parents of children in this study were recruited in their ninth month of pregnancy with the study child if at least one parent had asthma (assessed by current or past medication use or a doctor's diagnosis) or allergy (assessed by skin prick test) [31]. At age 6 and yearly thereafter, COAST children were diagnosed with asthma if they met at least one of the following criteria: 1) doctor-diagnosed asthma, 2) doctor-prescribed albuterol use for coughing or wheezing episodes more than once between 60 and 72 months of age, 3) daily controller medication, 4) implemented a step-up plan as prescribed by an MD including the use of albuterol or short term use of inhaled corticosteroids during illness, and/or 5) use of prescribed prednisone for asthma exacerbation. COAST+ consists of a population of children born in the Madison area who had parental histories of asthma and/or allergies identical to those of the original COAST cohort, and who met the same criteria for asthma diagnoses as the COAST children. Their ages ranged from 10 to 12 years at enrollment. Children in the Treg study were 6-8 years at enrollment and were not required to have a parent with asthma or allergies. Asthma diagnosis was the same as for COAST. The RhinoGen study included two groups of children, both ages 4-12 years, recruited in Madison, WI. The control group included healthy boys and girls ages 4-12 years in whom allergy status was characterized. For the asthma group, children were in addition required to have: 1) a physician diagnosis of asthma, 2) a history of symptoms of cough, wheeze, or shortness of breath in the past year that required treatment with a bronchodilator, 3) a current treatment plan that includes use of albuterol or asthma controller medication (ICS, LTRA), and a step-up plan for asthma exacerbations. All protocols were approved by the University of Wisconsin Institutional Review Board and written informed consent was obtained for all subjects.

**ii. Freiburg:** The Freiburg sample consists of 459 children with asthma and 294 non-asthmatic control children, who were recruited from clinics at the Children's University Hospital in Freiburg, Germany. Asthma was defined by the presence of self-reported symptoms (cough, wheeze, or shortness of breath), current use of asthma medications, a doctor's diagnosis, and BHR (15% fall in baseline FEV1 after either inhalation of ≤8 mg/dL histamine or ≤6 minutes of exercise provocation). The controls are children without a history of asthma, recurrent wheezing, or atopy who were recruited from the Children's Hospital in Freiburg (similar to the

cases) and a large GP practice with specialization in asthma and allergy in the Freiburg area. The control children had various non-allergic complaints typical for a pediatric practice, and did not have any current or past smoking history. All protocols were approved by the University of Chicago Institutional Review Board and written informed consent (or assent) was obtained on all subjects.

**f. University of Southern California - CHS**

**i. Children's Health Study (CHS):** Two cohorts in the Children's Health Study (CHS) including a total of 1,221 children (765 from cohort 1, and 456 from cohort 2) who were either Hispanic (n=683) or non-Hispanic white (n=538) were included in the replication. The first cohort included children between the ages of 5-18 years recruited from schools in 12 southern California communities in 1993, 1996 and 2000. The second cohort included children between the ages of 4-12 years recruited from kinder gardens and schools in a single community in 2007. A total of 602 cases were classified as having asthma if the adult completing the questionnaire reported that a doctor had "ever diagnosed the child as having asthma". A total of 619 controls were selected using frequency matching with cases on sex, ethnicity, cohort, and follow-up time from children without the asthma outcome. Genomic DNA was extracted from buccal mucosal cells by using PUREGENE$^{TM}$ DNA purification kit (Gentra Systems, Minneapolis, MN). Genotypes for the 14 SNPs were determined by the TaqMan Allelic Discrimination (AD) assay (Applied Biosystems, Foster City, CA) using the study materials and protocol. Association testing between genotype and asthma status was performed using logistic regression, considering age, cohort, sex, ethnicity, and community of residence as potential confounders.

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