

Integrating Host Genomics with Surveillance for Invasive Bacterial Diseases

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We tested the feasibility of linking Active Bacterial Core surveillance, a prospective, population-based surveillance system for invasive bacterial disease, to a newborn dried blood spot (nDBS) repository. Using nDBS specimens, we resequenced CD46, putative host gene receptor for *Neisseria meningitidis*, and identified variants associated with susceptibility to this disease.

Host genetic factors may help predict susceptibility to infectious diseases and could target high-risk populations for public health interventions such as vaccination. However, even with cost-effective genotyping technologies (1), small cohorts and limited associated epidemiologic data may lead to underpowered studies. Existing large population-based surveillance systems, if integrated with appropriate genetic material, could contribute crucial hypotheses and generate data to identify host factors underlying infectious diseases.

Active Bacterial Core surveillance (ABCs) is a network of state health departments, academic institutions, and local collaborators funded by the Centers for Disease Control and Prevention (CDC). This network conducts population-based surveillance for invasive bacterial pathogens, including encapsulated bacteria *Haemophilus influenzae*, *Neisseria meningitidis*, and *Streptococcus pneumoniae* (2); the Minnesota Department of Health has been involved in ABCs since 1995. Use of ABCs data to identify potential genetic risk factors could identify high-risk groups for vaccination with conjugated polysaccharide vaccines targeted

against encapsulated bacterial pathogens. In particular, *N. meningitidis*, the causative agent for meningococcal disease, has a baseline carriage rate of 5%–10% (3), a US incidence of 1 case/100,000 persons (2,4), and a 10%–15% case-fatality rate (2). Given the epidemiology of *N. meningitidis* and recent data suggesting a high sibling risk ratio (5), it is plausible that host factors (6) modify susceptibility or severity to meningococcal disease.

The Study

Although ABCs provides a unique epidemiologic context for assessing host genetic risk factors for *N. meningitidis*, host DNA is not collected. However, genetic material is collected prospectively from all infants through state-based newborn dried blood spot (nDBS) programs (7). We cross-referenced ABCs data to the state's nDBS repository to identify nDBSs from Minnesota ABCs case-patients and controls.

ABCs data were evaluated to identify cases of invasive encapsulated bacterial infection (*H. influenzae*, *N. meningitidis*, or *S. pneumoniae*) in persons born January 1, 1997, through December 31, 2000. Parents or guardians of case-patients were contacted by mail for written consent (and where needed, childhood consent). ABCs data from case-patients with parental consent and from case-patients who did not respond after 2 successive mailings were included in the study. Two controls, selected from among children with nDBSs, were matched per case by date of birth, race, and hospital of birth. ABCs data and case and control nDBSs were stripped of linkage to personal identifiers.

Human subject review and approval was obtained through CDC and the Minnesota Department of Health before study initiation. Once ABCs data and nDBSs were deidentified, the CDC institutional review board closed the project, which enabled genomic studies with unidentifiable nDBS specimens. The University of Washington human subjects division subsequently granted a certificate of exemption.

We identified 486 cases of invasive disease: 22 with *N. meningitidis*, 19 with *H. influenzae*, and 445 with *S. pneumoniae*. One case-patient refused consent and was dropped from the study; 88 case-patients (18.1%) gave written consent, and 397 (81.7%) did not respond after 2 mailings. The nDBSs were identified for 406 (84%) case-patients. Among controls, 812 (100%) were matched to case-patients by date of birth and race, and 674 (83%) were matched by date of birth, race, and hospital of birth. A total of 22 *N. meningitidis* case-patients and 44 controls with nDBSs defined the case-control (CC) study. Case-patient characteristics are shown in Table 1. No deaths were documented among the ABCs case-patients.

Genomic DNA was amplified from 3-mm punches of 1/2" nDBSs by using multiple displacement techniques (8)

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Table 1. Characteristics of 22 case-patients infected with *Neisseria meningitidis*

Characteristic	Value
Female, no. (%)	11 (50.0)
Race-ethnicity, no. (%)	
White	16 (72.7)
Black	3 (13.6)
Asian	2 (9.1)
Other	1 (4.6)
Mean age, d (range)	144 (9 d–3.4 y)
Bacteremia with focus, no. (%)	12 (54.6)
Meningitis, no. (%)	10 (45.5)
Serogroup, no. (%)	
B	10 (45.5)
C	5 (22.7)
Y	5 (22.7)
W135	1 (4.5)
Not groupable	1 (4.5)

(Molecular Staging, Inc., New Haven, CT, USA). We resequenced the *CD46* gene (9), a putative host gene receptor for *N. meningitidis* (10,11), in 143 samples from 66 CC study samples and 77 Coriell Cell Repository (CCR; Camden, NJ, USA) samples (online Technical Appendix, available from www.cdc.gov/EID/content/14/7/1138-Techapp.pdf) (GenBank accession no. AY916779). Standard dye primer and termination sequencing with sequence assembly and polymorphism discovery was performed through the Program for Genomic Applications (National Heart, Lung, and Blood Institute, Bethesda, MD, USA) (Seattle SNPs [single nucleotide polymorphisms]) (12). Of 269 diallelic sites (SNPs), 173 (64%) were in the CC study samples and 59 (34%) were unique to the CC study samples (Table 2, online Technical Appendix). Hardy-Weinberg equilibrium (HWE) was used to evaluate genotyping errors; most SNPs in CCR (97.6%) and CC study samples (96.5%) samples met HWE ($p \geq 0.05$).

The overall genotyping call rate for nDBS CC study samples was 89.5% compared with 96.7% for cell line–derived CCR DNAs ($p < 0.0001$, by χ^2 test). Among CC study samples, 62% had highly useable DNA quality as assigned by MSI after amplification. The DNA quality rating pre-

dicted genotyping call rate (generalized linear model $R^2 = 0.52$, $p < 0.0001$) with highly useable samples having a call rate of 93.9%.

Among 173 SNPs in the CC study samples, 116 (67%) were in case-patients, 146 (84.3%) in controls, and 89 (51.15%) in both groups (Table 2). We grouped SNPs (minor allele frequency $> 5\%$) from the European-American CCR samples into bins on the basis of linkage disequilibrium ($r^2 > 0.80$) by using the LDSelect algorithm (13). Among 17 CD46 tagSNPs tested (each representing 1 bin), site 6420 (rs41317049) was significantly associated with meningococcal disease (by Fisher exact test) assuming a general genotype model (separately comparing homozygous major, heterozygous, and homozygous minor alleles; $p = 0.0176$) and a dominant genetic model (homozygous major allele vs. all others; $p = 0.0440$) (online Technical Appendix). Logistic regression showed that, adjusting for age and sex, SNP 6420 had borderline significance ($p = 0.051$), with increased odds of disease (odds ratio 4.38) for GT/GG versus TT genotypes (95% confidence interval 0.99–19.30). Given a sample size of 16 case-patients and 32 controls, a general genotype model is powered ($\alpha = 0.05$, $\beta = 0.80$) to detect an odds ratio from 3.6 through 6.6, depending on the minor allele frequency of the risk-conferring SNP.

Conclusions

We integrated an active, population-based, prospective disease surveillance system post hoc with a population-based, prospective nDBS repository to combine disease surveillance information with genetic specimens. Although nDBSs have been used to establish prevalence (14), nDBSs have not been linked post hoc to an extensive clinical/epidemiologic database for genetic hypothesis generation.

To test use of these nDBS specimens for hypothesis generation, we resequenced a potential meningococcal risk factor, the putative meningococcal receptor CD46, for genetic variation discovery. Highly useable samples had genotyping call rates similar to those of cell-line extracted CCR DNA (94% vs. 97%). Furthermore, on the basis of

Table 2. Number of diallelic sites (SNPs) identified for CD46, by population*

Population	Sample size	No. SNPs† (population-specific SNPs)‡	No. common SNPs§
European American	23	93 (32)	58
African	24	130 (74)¶	68
Asian	24	88 (30)	46
Hispanic	6	56 (3)	56
Study samples	66	173 (59)	66
Case-patients	22	116 (27)	70
Controls	44	146 (57)	

*SNPs, single nucleotide polymorphisms.

†Includes SNPs and diallelic insertion/deletion polymorphisms (indels).

‡No. SNPs identified in only that racial/ethnic population.

§Common SNPs defined as having a minor allele frequency $> 5\%$.

¶Two SNPs (sites 18924 and 28122) were specific to the African cohort but in regions not resequenced sufficiently in other populations. Additional genotyping is needed to conclusively identify these as African specific.

HWE and similar allele frequencies between the CC study samples and CCR samples, we did not detect heterozygote bias. Ongoing studies are evaluating use of other technologies to genotype these samples.

We identified an association between an SNP (6420; rs41317049) in the candidate gene CD46 and case status for *N. meningitidis*. The intronic location of SNP 6420 and existence of CD46 splicing isoforms (15) suggest a possible role of altered splicing. However, the genetic association itself and any hypothesized mechanism require future replication studies to rule out alternative explanations of chance, population stratification, causality/susceptibility, or linkage disequilibrium.

Our results are novel, but this pilot study was powered for large genetic effects. Furthermore, the cohort was primarily of European descent, and results were not adjusted for multiple comparisons. Given the surveillance target period and duration that Minnesota retained nDBS specimens, our study cohort was children <5 years of age, the age range targeted for conjugate polysaccharide vaccines. With the growing importance of using nDBSs for genetic studies (7), future studies should assess whether this approach is generalizable. Use of existing large, surveillance databases linked to nDBS repositories will facilitate replication of the genetic association specifically, and more generally, evaluation of host genomics of susceptibility to infectious diseases.

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Dr Crawford is an assistant professor at the Center for Human Genetics Research at Vanderbilt University. Her research interests include the broad area of identifying genetic variations associated with complex human diseases or traits ranging from cardiovascular quantitative traits to infectious diseases.

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Technical Appendix

Table 1. Coriell cell repository DNA samples resequenced for single nucleotide polymorphisms in CD46

European-Americans (n = 23)	Yorubans (n = 24)	Asians (n = 24)	Hispanics (n = 6)
NA11995	NA18502	NA18526	NA17438
NA12892	NA19153	NA18562	NA17439
NA11882	NA19223	NA18545	NA17440
NA11994	NA19201	NA18609	NA17441
NA12815	NA18504	NA18566	NA17442
NA12891	NA18870	NA18621	NA17443
NA06985	NA19137	NA 18577	–
NA11840	NA19238	NA18635	–
NA11881	NA19144	NA18524	–
NA11993	NA19203	NA18537	–
NA12751	NA19200	NA18572	–
NA12814	NA18855	NA18552	–
NA06993	NA18505	NA18942	–
NA07056	NA18501	NA18945	–
NA11832	NA18861	NA18964	–
NA11839	NA19193	NA18961	–
NA11992	NA19143	NA18967	–
NA12057	NA18517	NA18981	–
NA12156	NA18856	NA18994	–
NA12239	NA19239	NA18998	–
NA12750	NA18871	NA18940	–
NA12813	NA19209	NA18949	–
NA07055	NA19152	NA18953	–
–	NA19210	NA18972	–

Table 2. Location, rs number, and sequence context of SNPs in CD46*

SNP (alleles)	Location within gene	rs no.	50 bases 5' flanking the SNP	50 bases 3' flanking the SNP
372 (A/T)	5' flanking	rs41266389	GAAAACTGAAAAGCATAAGGAAAAGTCAAATATCTGTAATCTT ATCAACCA	TGTTAATTTTGTCTGTATTCTTAGTTTCTTTTATACATATCAA TATGGTA
463 (G/A)	5' flanking	rs1970530	CAATATGGTACTTTTTGTTTTAATAAAAGGACTGCCAAAAGGC ACATGCCA	TTTGGACTCTGCTTTTTCCACTTACAATGATATCATAGTTTCT CATATTT
544 (C/A)	5' flanking	rs41266391	TATCATAGTTTCTCATATTTGGTATTCTTTTGAATATTTGCT GCATAGA	TTCCATCACACAAAGGTAAGTCCAGAAATTCTTTATTACTT TTGCTAGA
668 (G/C)	5' flanking	rs11118514	AAAATTAATCACATCAGAGTTTTGATCACATCAGAGCTTTGA TCACAGCT	TGATGATTTCTCTGGAACTGAGAGCCTAACACAAGTCATG TCCACTTTA
1303 (G/A)	5' flanking	rs2796267	aaccttgagattgtgaaaaaagacggccccgagacgatccagtagcag	cattcaagcaagaaaaactcaaatattgttcccaataatgcctgactaat
1362 (G/C)	5' flanking	rs41266393	caagaaaaactcaaatattgttcccaataatgcctgactaatgccaata	caagtaagggcccaggcagctctgacagcctgagctgccccaggataaaa
1589 (G/A)	5' flanking	rs2796268	ctccaccctgcctgggtcacaatatgacggcgagccagctcttccc	caggacgctcaggctccgggatggtaggccaaggcttagcaagaaaa
1685 (T/C)	5' flanking	rs41266395	gaaaaaagggcctcggggaacctgttctgtaggtccgcccaggcct	cccctgacctctgaaggccaaggctgcccgaacgcccaggctccgc
1758 (G/C)	5' flanking	rs41266397	gggctgcccgaacgcccaggctccgccccgcccggccgattggccc	agccgcccgtgactcgaagcactccgccccggcgccgctcgggcca
2637 (G/A)	Intron	rs41266399	CTGTGCGTAAGTGGCCTGTGTGCAGAGTTCCTGTGGGCA AGACAGCTCA	CTGTTTGTCTTGAATGGAGTGAGCGCGGACTCTGGGGCTA GGGAGGGCAT
2672 (C/G)	Intron	rs41268335	GGGCAAGACAGCTCAACTGTTTGTCTTGAATGGAGTGAGCG CGGACTCTG	GGCTAGGGAGGGCATGTTGAGTGAGAGCAGGCTCTCGGTG CCTGGGGTTA
2959 (G/A)	Intron	rs17048430	TTCTTCTTTTCTACTTTTGTGATCATATTTGAGAGATGTGAA ACAACCT	AAAAACAATGGTAGCCAAACCTAGTGAGAAATTAGTATCCTA ACAAAGGA
3014 (G/A)	Intron	rs41316813	ACAATGGTAGCCAAACCTAGTGAGAAATTAGTATCCTAACAA AGGAAGGC	gataatgtaactctgtttccctcagctcaTaaagtaagcttaagg
3048 (C/T)	Intron	rs41316815	CCTAACAAAGGAAGGCagataatgtaactctgtttccctcagctca	aagctaagcttaaggcctatcccactaaatattttgatttcattga
3550 (C/T)	Intron	rs35029161	atatttggcatattgttctgcctcatgtgcccgtcatgtgtatcta	gtccaaattatatttaggatacaataacatgatatttctacgttgc
3628(C/G)	Intron	rs41316817	catgtatagttctacgttgcatttttcttaggagcattcattcaac	aatatgggtctgtatgctgggtctattacactggttaggcaatacaaa
3687 (G/A)	Intron	rs41316819	tctgtatgtctgtgctattacactggtaggcaatacaaacaccattct	ttttctgatccttttctactattgtttacacacacattcatgcagga
3779 (C/G)	Intron	rs41316821	catgcaggaagataagcaggacttgtttgtcctaatgataagtgtca	tgccgggaacacagtagataaccaataaattattgtctaaatgtattgg
3905 (A/G)	Intron	rs41316823	cataatagtgacaataaattatgaaccaagggagtgctctggaggcaa	cagtataatttcagataataatctgacagcatttaacaaatgattggag
3996 (G/A)	Intron	rs41316825	atgattggagagagggaggctctctgctcatcaaacagactttggggc	tctgtgctgtgttccctcagccCaggaaacttctcctgacctgct
4021 (A/C)	Intron	rs41316827	ctgctcatcaaacagactttggggcAtctgtgctgctgttccctcagcc	aggaacattctcctcctgacctgctgcagaaacagctcctcctctgca
4257 (T/C)	Intron	rs41316829	TCTGTTCTTTGTCTCACCTGTGAGAATGCAGGGATCCTGT CTGTCTTGT	GCAC TTGTGGTTCCAAAAGCCGATTTGTTTACCTCTGTATC TGTTAAAT
4606 (C/T)	Intron	rs41316831	ATGGGAGTAGGGAGTAGTGGTGATAAGAAGAAAACAAAAG GACTTTTTTT	TTTTCTTTTAAAGATTAATGTTTAGaaTAAGCTTAGTgctagAaGT TCAGC
4965 (G/A)	Intron	rs41316833	TAGGAAGCTGAAGAAGATAATGAAAGCGATTTGAAATAGAG GAACATAGA	TTATGAAATGAATAGGGTGCAACATGAAAATAACAAAACCTA AGAATGAA
5032 (G/C)	Intron	rs2724382	GTGCAACATGGAAAATAACAAAACCTAAGAATGAAGAGAAGG AAAAGCAAG	TTAAGTTTGTAGGTTTATAAGGGTAAATCAAGACAGGTATGAA ACCTAGAG
5634 (T/A)	Intron	rs41316835	ttacaataatcttcacatgtttgtgttgacagcagtgatttga	taccaaaatttttgaatagctactctgagtgacatattgtctgggtg
5724 (G/A)	Intron	rs41316837	tggtctgggtgttggtccacatggatgaatggagttggcctgttaact	ttaaacacaaaaGcatgtgatagttacctgagagatccatgcaggggaga
5737 (A/G)	Intron	rs11118516	gtggccacatggatgaatggagttggcctgttaactAttaaacacaaaa	catgtgatagttacctgagagatccatgcaggggagagtcaggggaagg
5872 (A/G)	Intron	rs41316839	atgcttctggaggagatgatgggtgattaaggaagatgagttgagcag	agttgatgctaccagccaggaggaagggattcagagcagaggaagcaa

6181 (G/T)	Intron	rs41316841	tttgttgacttagcacaacatgaatccaaactagggtgtttgatt	cccaggcaggttagcagacaatttctgaatactattgcagatagagt
6254 (A/T)	Intron	rs41316843	ttctgaatacttattgcagatagagttgtcagtgtagcattctg	gcaccacaaggtgagtatagtagaaaaagaagaacatggtcttGaccc
6300 (C/G)	Intron	rs41317045	cttgTgcaccacaaggtgagtatagtagaaaaagaagaacatggtctt	acccccaggaactgaccttaagagaagacacctgaagtgacaagctg
6391 (T/C)	Intron	rs41317047	tgacaagctgtataagttagtgtttaaacatggaagaacaatctgag	aGagtacttatactgtagaagactctTagaggGgaagttactttgaa
6393 (A/G)	Intron	rs17048573	acaagctgtataagttagtgtttaaacatggaagaacaatctgagCa	agtacttatactgtagaagactctTagaggGgaagttactttgaaat
6420 (G/T)	Intron	rs41317049	actatggaagaacaatctgagCaGagtacttatactgtagaagactct	agaggGgaagttactttgaaatgaatttagaaaaatgtgggaaagatg
6426 (A/G)	Intron	rs2724383	gaagaacaatctgagCaGagtacttatactgtagaagactctTagagg	gaagttactttgaaatgaatttagaaaaatgtgggaaagatgcatcca
6564 (A/T)	Intron	rs12067460	tcagttattgtcgaatgttattccaaacaaacaaaagctaatagga	gttacttaaacatgcaagtcaccttctcactActatgagcactcag
6600 (G/A)	Intron	rs2724384	aaaagctaataggaTgttacttaaacatgcaagtcaccttctcact	ctatgagcactcaggtaaaagcatggaacagtcatttaaatctgccaa
6993 (G/A)	Intron	rs41317051	tagtaagtaaacaaacctcttttttctgctgctagagattg	tacatttggggtacatattccactacggtgatgatttctctgt
7644 (A/G)	Intron	rs41317053	tgttctgacaataagctgtgtaagcattaagaatgtagtaatcatga	aatttgcctcacaactgagtgCccctatttaaatctgccaactcta
7669 (T/C)	Intron	rs41317055	agcattaagaatgtagtaatcatgaGaattgtcttcacaactgagtg	ccctatttaaatctgccaactcttagagttgaagtagggctcacaataat
7756 (C/-)	Intron	rs41317057	gggctcacaataatgagaaatagaattgccaactaaagatacactgtat	cagatgactctgtaaagtgatcagacaaaactgacgcggttagcctt
7828 (T/C)	Intron	rs41317059	atcagacaaaactgacgcggttagccttaccatcaTGTTGATCAAAAT	TCTCAGTTGAAAAACCTTATTTTTGAGACTGCTACAGTGTGA AGCATCTC
7865 (A/G)	Intron	rs41317061	TGTTGATCAAAATCTCTCAGTTGAAAAACCTTATTTTTGAGA CTGCTACA	TGTGAAGCATCTCAAGAGCAGGACTGAGCCCTCGGTAATA GCCTTGT
7907 (A/G)	Intron	rs41317063	CTGCTACAGTGTGAAGCATCTCAAGAGCAGGACTGAGCCC TCGGTAATA	CCTTTGTTCTGTAGGGTTTTGAAGTTGTATATATTGGAGATA CTAGACAT
7925 (A/T)	Intron	rs2724385	TCTCAAGAGCAGGACTGAGCCCTCGGTAATAGCCTTTGTT CTGTAGGGT	TTGAAGTTGTATATATTGGAGATACTAGACATTTAAGATAAA TGTGCATT
8002 (G/A)	Intron	rs41317065	AGACATTTAAGATAAATGTGCATTTATAGAGTAAATGTAAGT ATTCTGCT	TAACAGAATACTTGAGGCTAGGCATTATAAAGAAAAAGAAAT GTATTTGG
8084 (A/G)	Intron	rs2724386	AGAAAAGAAATGTATTTGGCTCATATTTCTGGAGGCTGGAG AGTTCAAGG	GATGGCAGTAGTGTCTGGCAAGGGCTTTTGTGCTGCATCAT AACATGCTG
8203 (G/A)	Intron	rs41317067	TAGCATGTGCAAAAAAGACAAAGCACAAAGGGAGGGGGTTC TCGCTTTATA	CAACGTGCTCTTATGGTAATGAATCCAAGCCTACAAGAATG AGAACTCAT
8310 (G/A)	Intron	rs1891423	AAGAATTAATGAAGACCCTCTAGAAAGGCATTATACCTCTTA ATGACCTA	TCATTTCTTAAGGCCCCACCACCTCTCAATGCTGTTACACT GGCAATTA
8393 (T/A)	Intron	rs35677203	CTGTTACACTGGCAATTAATTTCAATATGAGTTTTGGTAGA GACAAACC	GATTCAAACAATAGCAGTAAACACCATAATATAGAAAAAGT AAGTGAGT
8455 (T/A)	Intron	rs41317069	TAGCAGTAACACACCATAATATAGAAAAAGTAAAGTGAAGTCTT GGAGGAAA	ATCAGCTGTGACTATGTAAGGCAACTGACAGTTTTTAAAATT TGGTCAAG
8693 (- /CTCT)	Intron	rs41317071	aaaATactaaATGAGAAATACCAATAAGTAGAATTATTCATGA TAATTA	AAGAGTCCAGAAGGAGGAGAGATTCTGTGAATTTAAATCA GGGAAGATT
8849 (T/C)	Intron	rs41317073	ATTCCTAGAAATACACTCTGTTCTAAATAATATTAATAGAAGC TAAAACT	ATGTAGCACTATCTATGTGCCAAATGCTAECTTATCTAATCC CCTAAACA
9014 (T/G)	Intron	rs2724387	TACCCAAGCTCAAGAACTAGATAAGTTGAGAAGCAGGGAC TTGAATCTA	CCATTCCAGCTCTAGGGCCTGTTCTCTCTACACAGTCCTTG TCCTTACTG
9620 (T/C)	Intron	rs41317075	ttctttatgtgggtatatactattggtattatcatattggaattcaaa	ggagaggttttaaataattTgattctttgtttgtttgttttc
9643 (G/T)	Intron	rs41317077	ttggtattatcatattggaattcaaaCggagaggttttaataattat	gattcttttggttttgttttcttaagacacggctcaggctatt
9717 (-/A)	Intron	rs34743953	ttcctaagacacggtctcaggctatttccaggctggggtcagtgcca	caatctcagctcaTgcagcctcagctctccaGtagctggggtcagg
9731 (C/T)	Intron	rs41317079	gtctcaggctatttccaggctggggtcagtgccaAcaatctcagctca	tgagcctcagcctctccaGtagctggggtcaggcatggtccatg
9751 (A/G)	Intron	rs41317081	ctggggtcagtgccaAcaatctcagctcaTgcagcctcagcctctcca	tagctggggtcaggcatggtccactatgctgcttttgaattttt

9975 (T/G)	Intron	rs2724388	taatttgaagaataaatgcaatacaaatcaacatgtaacataatfff	atgaaaaataataatffccaatcaaaataaaaattagtgagaatagtg
10046 (T/C)	Intron	rs2724389	aaatcaaaataaaatagtgagaatagtgcatgttccacatffffgca	atccttcaacatctggctaaagcaagattgtattggcctgtgtgt
10475 (T/C)	Intron	rs41317083	GCTGTACAGGAAGCATGGtctgcatctgctgggggttggtaggacct	gggaaacttaacaccattgggaaagacagaaggagagcaaggtgtctca
10885 (A/C)	Intron	rs2466572	gatataattgctcatagaaacctctttaaatacattgaattcacaa	cagcttgtagaaacctatattgacaaattattgaagacacagaaatff
10951 (T/A)	Intron	rs41258244	ctatattgacaaattattgaagacacagaaatffactaatgctgctt	atctttacatffcttctctttttctatttttaagaggtttgtg
11247 (G/A)	Intron	rs4844390	ttcaatttattcttctcatgtttaaactatgaaacatffttgtaa	tagtttcatctacagataaaacaaagcagggtgatgtcttctctctg
12104 (A/G)	Intron	rs2724359	aaaaagaaaagtctcaaatcaatgatctaatffccacctaagaact	aaaaagagcaagttaaatccaaactagcagatgaagaaatgataaaa
12455 (A/G)	Intron	rs41317085	agctttaccactgctggtggagccaaccactgccgagggctcatc	ccaacacgctggcagatccaagaggagatggcccaggatgagacGggc
12501 (A/G)	Intron	rs17006738	catcGccaacacgctggcagatccaagaggagatggcccaggatgagac	tggcacacacaggcaccgagaggtgggggtggcgtttccactgcct
12592 (C/A)	Intron	rs41317087	tcactgctggttctgagagacgctgctgctggcctgctgcccgc	tgtggaagccaggggggtgtgccatgcccccgttggacactgctgc
12752 (A/G)	Intron	rs41317089	tgaagacagcatctgggagacgagccctggggaaaatagaggagcc	ttcagaagtagctagatgagatattgaaatactgaaagacaaaacccc
12861 (T/C)	Intron	rs17006743	tgaagaactggcctcagatgtggtcagttcctatgatgacctggacaca	gggtctgaccacacgatggagggtggCctgcaagcattcagaggctt
12889 (G/C)	Intron	rs6671947	ttcctatgatgacctggacacaCgggtgctgaccacacgatggagggtg	cctgcaagcattcagaggcttgggctgctgccgtccgcccctccacct
13281 (T/C)	Intron	rs17006749	gacatccccacagccctgcccctcatcactttctgtctctcggaga	ggCgagctgcaactgcagcaatctgtttaaatttaggtaggtgaatttc
13284 (T/C)	Intron	rs2796269	atccccacagccctgcccctcatcactttctgtctctcggagaCgg	gagctgcaactgcagcaatctgtttaaatttaggtaggtgaattctta
13978 (T/C)	Intron	rs41317803	aggcacctgctctggcagcagactgagctcctgggggtgtcacggagctg	gggtgcccagctcacatgcttggaaacagcGtgtgctgctgattggaa
14010 (A/G)	Intron	rs2796270	gggggtgacagggagctgCgggtgccagctcacatgctggaacagc	tgtgctgctgattggaaatgctactgctgctgttaaattgggtgctg
14292 (C/T)	Intron	rs17041782	CTTCCCCCATCCCTTAGCCAAAAAGCTTTTATATTCTTTTGTGCATATGG	CATTCTTTAATATCAGTGATGTAAACTTTACTTGATTACTTTA CAAAAT
14626 (C/T)	Intron	rs2488252	TCCAGATGGCTTCACTGGGGAGTTCTACCAACCATCTAAGGAATAAATCA	AGCAATTTACACAAGCGTTTCAAGAAAGTGCAAGAGGAGG GAACACTTC
14634 (T/C)	Intron	rs7545126	GCTTCACTGGGGAGTTCTACCAACCATCTAAGGAATAAATCATAGCAATT	TACACAAGCGTTTCAAGAAAGTGCAAGAGGAGGGAACTT CTCATCCCA
14777 (-/A)	Intron	rs41317805	AAAAACATTATAAGAAAATTACAAATAATATCCTTGATGAACA CAGGACC	AAAATCTTCAACAAAATATTAGCAAACCAAATCCTGTGATAC ATAAAAAG
14954 (G/T)	Intron	rs41317807	tttgccacatcagtagactattaaggagaaaaaaatcatgtGGTTATCT	ATTAGATGCAAAAAACAAAGAAAATGTTTGACAGAATTCATC ATCTTATT
15107 (C/A)	Intron	rs2488253	TTACCCTGATAACAGACATCTACAAAAATCTCACAGCTAACA TTACACTT	ATGGTTCAAAAAAATTATACTTAGTGGTAAAAAGTAACATTG TACTTAGT
16004 (G/C)	Intron	rs41317809	ctttactatggtgtagttacatgattattgcatgtgcaaaactgata	agctgtacactgaaatggtgaatttactgtatgtaaattatccaat
16406 (G/A)	Intron	rs41317811	ataaatattaaaatffaccaccaccaccaccctgtagtattgggt	aaaactaccaacaaaaTttaaaagcagccagtgatggggaaacaa
16424 (G/T)	Intron	rs41317813	ccaccaccaccaccctgtagtattgggtAaaaactaccaacaaaa	tttaaaaagcagccagtgatggggaaaaacaacaaaaccCgtattacat
16444 (T/C)	Intron	rs2466571	cagtagtttggTAAAAactcaaaacaaaTtttaaaaagcagccagtgatga	tggggaaaaacaacaaaaccCgtattacatttaggagggcagggacaagt
16465 (T/C)	Intron	rs41317815	caaacaaaaTtttaaaaagcagccagtgatGtggggaaaaacaacaaaacc	gtattacatttaggagggcagggacaaglaagaatgacagccagccaagt
16878 (A/G)	Exon	rs17006830	aagcaacagttatgttgaatgagataaggggtttacctgtagggcagc	acacaattgtctgacagtaacagacttggatccccagttccaag
17080 (C/A)	Intron	rs41317817	caaaataactgaaaagaacaatttttagtatttaactctgctgtattc	tttctaTgccagatgaatgacacgaaattacataaaattctgctgtgtg
17087 (C/T)	Intron	rs41317819	actgaaaagaacaatttttagtatttaactctgctgtattcAttcta	gccagatgaatgacacgaaattacataaaattctgctgtgtgatttt
17183 (G/A)	Intron	rs41317821	tttttgtctttccagggcttctgacagctgtagacattgcatgggt	tatgcttttaatttttagtataaaaagtgaaattacaacaacttttg
17251 (A/T)	Intron	rs11118555	tatgtataaaaagtgaaattacaacaacttttgaattgaaacatgggca	ttttactaagtaagtcaaatggcataattcatataaatgaaatgaga
17314 (G/A)	Intron	rs17006838	aagtcaacaatggcataattcatataatgaaatgagagcaataactccc	agtgggtgAtcttcaacatttttttcttagtctgctcctcatcta
17323 (G/A)	Intron	rs41317823	atggcataattcatataatgaaatgagagcaataactcccAagtggtg	tcttcaacatttttttcttagtctgctcctcatctagtaaaaac
17526 (A/G)	Exon	rs17006843	actccaagtgtttggccaactcattatttttggttccagtgctc	acttcttccactacaaaatctccagcgtccagtgctcagggttagtaat
17589 (G/T)	Intron	rs2724374	acaaaatctccagcgtccagtgctcagggttagtaatttctgcttata	ttttcaaaaactcttaaatctggtgatttttataaaactcttcaa

17937 (A/G)	Intron	rs2488254	agcacttagcacagtgctggttagagaaagctcttagagctagccaat	tgactatcctacactaaattaatgttagggagggggaaggtcatgta
18116 (T/C)	Intron	rs41317825	tattttattctttcagaagtgatctgttgacaccttactgagittgtt	ctattgcaggactcttcattTctggaatgcaactagtttagctctct
18139 (C/T)	Intron	rs2488255	tctgtgacaccttactgagttgttCctattgcaggactctttcattt	ctggaatgcaactagtttagctctctctgtagtaaaacatttaaacagga
18325 (A/G)	Intron	rs2796271	tttttcttttagtgggcagtttatactggcaatagcaactcaatttat	gcaactgaaaggcaggaaaagctctatttactgaaataaaatagaagac
18696 (G/A)	Intron	rs41317827	tcctatccccaataatttaaaggatgcaagagaattatgcatgttaac	tagtaattaagataacctcttataaggctgggtgggtagctcacacctgt
18924 (G/C)	Intron	rs41317829	acttgaatcccagctgctcgggaggccgaggcaggagaatcgctgaac	cagtgggcagaggttgacagtgagccaagatgaccactgcactccagcc
19556 (C/T)	Intron	rs2724360	ttccctttttttttgagacagagcttgcctctgacccaggatgg	gtgcaGtggcggcttggctcactgcaacctccgctcccgggtcaa
19562 (C/G)	Intron	rs41317831	tttttttttgagacagagcttgcctctgacccaggatggTgtgca	tggcggcttggctcactgcaacctccgctcccgggtcaagcggf
20088 (T/C)	Intron	rs41317833	ttataaaatcaaacctattttctaggtcctaggcctactacaagcctc	agtctcaaattatccaggttggttaactcttactcactgataattgta
27144 (T/C)	Intron	rs12138764	tttagattgggggtacagggaaggtttgtacataagtaaacgtgtca	agggattgtgtacataaactattcatcaccaggatfaagcctagta
27328 (A/G)	Intron	rs41317835	gtgttcattagttcttaccatttagccccacttataagtgagaacatgc	gtattgggacgttctgtggaagacatgctgctcttttttagct
27384 (-/G)	Intron	rs41317837	tgggacgttctctggaagacatgctgctgtcttttttagctacgta	tattccacgggtatagtaccacattttcttaccagctgtcattga
27511 (C/T)	Intron	rs41317839	ttgctattgtgagcagtgctgaggaacattcatgtgcatatatactt	ggcagaatgattatatttctctgggtatataaccagtaatgggattgct
27609 (C/T)	Intron	rs41317841	gctgggtggaatgtagtctgttttaggtctttaggaatcgccatac	gctcccacaatgggtggaactaaatacactcccacgaacagcatataag
27852 (T/C)	Intron	rs41317843	tgtatgttttggccacatatatgtctctttttaaAAGTGTCTGTCA	GTGCTTTGCCACTTTTTAATGGAGTTGTTTTCTCTTGTAA ATTTTTT
27911 (G/A)	Intron	rs2796276	CCCACTTTTTAATGGAGTTGTTTTCTCTTGTAAATTTTTTA AGTTCcT	TAAATGCTAAATATTAaggccttgtcagatgcatagttgcaaaaatgtt
28122 (-/A)	Intron	rs41317945	TTTTTGATGCTTTGTGCATGAAATCTTTGTCTGTTATTATGTC CAGAGTG	TATTGCCTAGGTTGTCTTCCAGGGTTTTATAGTTTTGGGTT TTACATGC
29566 (G/A)	Intron	rs41317947	gcaccatttttgaataagttgtcttccccactgattgaaatgtca	ttgtatcatacattgattcataggtgttCcatcctctttctccttgg
29597 (A/C)	Intron	rs41317949	gcaccatttttgaataagttgtcttccccactgattgaaatgtca	catcctctttctccttgaacttggcattctctattctgCagcaa
29642 (T/C)	Intron	rs2724391	gtgttCcatcctctttctccttgaacttggcattctctattctgt	agcaaaagcaagtcttttttttttttactgtagtactatagt
29887 (A/C)	Intron	rs41317951	accatcagaccatcctctctagaatattataatcatcccacactgaat	tctactattaacagtaactctccattcctccatccccatcacctga
30647 (C/A)	Intron	rs41317953	atatcaaggcatggcactctgtgaggcccttctgttgcataatag	tggaggcatcacatggtggaaggaaaaagagacggtagagagagagta
30783 (G/C)	Intron	rs41317955	cccctgcaataacgacattagtcattcatgaggacagaccataatgac	caaacacctctaaaggcggccaccocaataacattacattgaCaataaa
30826 (A/C)	Intron	rs41317957	taatgacCcaaacacctctaaaggcggccaccocaataacattacattga	aattaaattcatcatgagtttgaaggggacattcaaacatagaccGt
30875 (A/G)	Intron	rs41317959	aCaattaaatttcatcatgagtttgaaggggacattcaaacatagacc	tcctaatagatatgaagttagatgcatactagatgcatctccataa
31008 (-/T)	Intron	rs41317961	cttattggtcattgtataatcttcttagagaacatcttttaagctt	tgccatttcaagttgggtgacattgttactgagtttaagagttat
31422 (T/C)	Intron	rs41317963	ttttgcatgtggataccagtttaccagcaccattgttagaagagact	ccttccccattgactgttctctgtcacgctgttgaacacgggtgac
31680 (-/TT)	Intron	rs34834365	aattgtggtccctgagattcatalgtatttggaaatggattttctat	cagaaaaaaaaaaccataaaataccatcatcaggatttcataggggtg
32125 (T/C)	Intron	rs41317965	gggatccttagggtttctaaataaaagatcatgtcatctgcaaacagag	Gaattttattctccttcaatttgaattcttttctacctaattg
32126 (A/G)	Intron	rs41317967	ggatccttagggtttctaaataaaagatcatgtcatctgcaaacagagC	aaattttattctccttcaatttgaattcttttctacctaattgc
32221 (C/A)	Intron	rs2796278	aattgctctgattagaacttcagtcctatgtcagatagaagtggaac	tggacacctgtcttctctgatctagggaagcctcattcatt
32282 (G/A)	Intron	rs41317969	gtctgttctgacttagggaaaaagcctcattcatttaacattgagt	tgatgtagctgtgggttttaatatatggccttattatgtgaggaag
32691 (T/C)	Intron	rs41317971	CTGCCTCGGCCTCCCAAAGTGTCTGGGATTACAGGCGTGAG CCACTGTGCC	GGCTAATCCCTCTATCTTTAATTTAATTAGAAATCACATTGG ATTTATA
32957 (A/G)	Intron	rs1962149	ATTATATTTAAAGGGATTTTCTACAAAGGTGAAAAAAATCA CCCTATGA	TTTAAAGGATTTAAGCTTTATATTTAATTCTTTCTCTTTTA TTAATT
33193 (C/G)	Intron	rs41258534	gagggtcccaaacataggatcctgttaggtaagataacttctaaat	ctgtgtgtatgtaggttaaataataaaacacaatttctccaca
33645 (G/A)	Intron	rs41317973	ctgttgccatctaaactgttaaaccctgataactgttatgagatgag	agagcagagttgaacatagcactttatgctttagcttagcaattaat
33891 (G/T)	Intron	rs41317975	tgttcatttattgggaatcctatggtatttaggactatgtctaat	tggggcagggcagagtaggaagtagagaggatgggaaggggattgata

33953 (C/T)	Intron	rs7541230	cagagatggaagtagagaggatggaagggtgataagataaagat	gtttggaagactttgaaataccatctgggcaatagaataatagaatt
34035 (A/G)	Intron	rs41317977	caatagaataatagaatttattatgactcactctacagatcacttttg	aggaaaaatacaaaataaatgctacaaaataagaaatgacagaatga
34492 (C/G)	Intron	rs11806810	agtctgcagggtcagagagcccccaggaactataatcatggaggaag	ggaagcaaacacattctctcacatgatggcaggaaggagaatgatgag
34563 (T/C)	Intron	rs41317979	tcacatgatggcaggaaggagaagatgagaaccaagtgaggaggaagc	gctataaaaccatcagatctcgtgagaacttactatcatgagaatgca
34844 (T/C)	Intron	rs35366573	ggaactgtttctctcagatgttggctcattgctgtgattgtattg	cataggtaatgatacaaaaatttgacaccacttaagtcaaaaaatttg
34997 (T/C)	Intron	rs41317981	tgtaaatggtaaacaccgatttaggaaaacctgacttttattgatata	ttaactacctacctgtgtatgtatttatactctgttattctgtat
35468 (C/T)	Intron	rs11118580	aagaagggttaaataaagcatgtttcttttaactcttggccttcta	acttaacatgctttgtgcagcttcagttgtaactgtattgcatgcta
36023 (T/G)	Intron	rs17007110	atccgattccctctatgttctcgaatttaccagattgcagtaaaact	atagggftaaagttaaaatgctgagaggggtAgatctGtaaggtacct
36057 (G/A)	Intron	rs41317983	agattgcagtaaaactGatagggftaaagttaaaatgctgagaggggtt	gatctGtaaggtacctcaattaaactgtctttaaataataaaaaatgta
36063 (A/G)	Intron	rs859705	cagtaaaactGatagggftaaagttaaaatgctgagaggggtAgatct	taaggtaacctcaattaaactgtctttaaataataaaaaatgtaaaagt
36502 (T/G)	Intron	rs6657476	cttactcataaggaactcaaaacttttcatattactgttattcttt	aaataccataatcccttactgtaactttaaactgttattatggaac
36871 (G/A)	Intron	rs41317985	tttgcctttttgtgatggagtctgctctgacccaggctggagtga	tggcgcaactctggctcgtgcaacctggcctctgggtcaagggtt
37106 (T/C)	Intron	rs4844619	ccgcccacctggcctcccaagggtgctaggattacaggcatgagccaccg	gcccggccttaatgggtctttaaagctcaacagttatctgactgttaca
37316 (G/C)	Intron	rs41317987	tgccattattaaatlttaaaatlttgggaaggtatgatactttag	caatgcaacataaataactgcaaatAgtagcacaactgaggaaaaat
37344 (C/A)	Intron	rs41317989	tggaaggatgatatactttagCcaatgcaacataaataactctgcaaat	gtagcacaactgaggaaaaatgctcagaaaaatgggtgagagacgaaa
37456 (G/A)	Intron	rs10449303	cttgaactttaaataataaactcgtgggaatctttagaatagatgtt	cccttttatgacaggaacatactcgtatggaaatcagcatatgtaatg
37896 (C/T)	Intron	rs41317991	tttctaataatgaagataatggaagtttaagattcctcatccatgtg	atccttaaaaaaggctatgggtaataaataagtagtactggctttcttac
38130 (A/G)	Intron	rs41317993	aaaccccgctcctactaaaaatacaaaaaaaataaagtgcc	ggcgctgtagcccagctactctggagggtgagggcaggaatggcgt
38668 (A/G)	Intron	rs859706	ggcaaaagggttaagatttctgccactttctgttcatagctctcagct	agaacagtataggataaccagtggtccgaaacaggtcccatccatgct
39497 (T/C)	Intron	rs41317995	Tggattgatacatactcaatgtatccctcaaaatgagggtgttaggc	gggtttgggtgctcacgcctgtaatcccagcaactttgtagggcaggcc
39986 (T/C)	Intron	rs41317997	Tcgttcttttgggttgaagtcactatttattcagccgtttctcttc	tctgttcagcacatacctaactgatgagaccacagagaagtaaaatgta
40399 (A/G)	Intron	rs41317999	tacctgtaaaacagctgtgaatccaaaagtaagaattgtgagccaact	Ggaaataaccacagaatcaactcattttagtgcaaggaggaataatgcc
40400 (A/G)	Intron	rs41318001	acctgtaaaacagctgtgaatccaaaagtaagaattgtgagccaactG	gaaataaccacagaatcaactcattttagtgcaaggaggaataatgcc
41263 (T/C)	Intron	rs41318003	acagctattgagtaaacaggcacatggtgcccacagcatgggtatgctgga	gaagggtgatttatatcccggagggtggaatggaagcaggtgagatt
41825 (A/G)	Intron	rs1142469	cagcactttgggaggccgaggcgggcatcactaaagttgagaccag	ttggccaaaatgggaaaccctgttctactaaaaatacaaacattagct
41991 (T/C)	Intron	rs41318005	ccggggaggagggtgcaagtgagccaagatcacaccacactgcactc	agcctgggtgacagagcaagactctgtctcaaaagaaaaataaagaa
42250 (G/C)	Intron	rs41318007	cgtttacgcctgagggtgcaatlttgaattttgcagtcagaccctgg	gatgacctgagcagtaggagataaattccacatgcttagcgttccagta
42791 (A/G)	Intron	rs12568382	tagaataataggtttataaagatgctattgttactactaaaagtgtagc	taaaacttagttataggagactcttagtgaatacatgatttctgta
42887 (G/A)	Intron	rs41318009	cttgacagtggggtagatgaggcatcacatactgaaacagtagaacc	ctatcttttaaaggctctgtgcccagagctacagctttaaataaggaggga
42951 (A/C)	Intron	rs41318011	ggttctgtgccagagctcagcctttaaagtgagggtcaggaagcatg	gttgtctccagcttcccaatggccctacatacaaaatgaggacatagt
43723 (G/A)	Intron	rs2724390	agtggtgaaatcttttgttcaaagattaatgccaactcctaagatt	ttcttccaactatagaatgattttatatactgttcaatgtaaaaag
44117 (C/T)	3' UTR	rs7144	ccataacaggagtgccactcattggtgcaagtgaaactgtagtctgt	gtttcccaagagaactccGtatgttcttaggttgtagtaaccactc
44138 (A/G)	3' UTR	rs6664092	atgggtgcaagtgaaactgtagtctgtTgtttcccaagagaaactcc	tatgttcttaggttgtagtaaccactcgaattctggttacctggtt
44655 (C/T)	3' UTR	rs14374	atgtttagttgcacaaatgggccaagaacatgacctgaggaagata	gattggaaaatcaagagtgtagaagaataaatactgtttactgtccaaa
45095 (G/T)	3' UTR	rs1237	caaattgttactaaatataagagaccagtttctctggaagttgtt	aaatgacagaagcgtatataaattcaagaaaatgagctgcaaaaatgt
46343 (-/T)	3' flanking	rs41318013	aactgaacaaggctagctgtttagaatacagaagcattgtctcaaa	aaacataaaaaacagaagcattctgtttaaataaacactaggtgaaaat
46403 (G/A)	3' flanking	rs41318015	aatacagaagcattctgtttaaataaacactaggtgaaaattatata	tgtgtgtgtgtatataatataatataatatacacacacacacaca
46532 (A/G)	3' flanking	rs41318017	gatggagttcgcattctgttccaggctggagtgaatggcactatctc	gctcaccacagctccacctctgggttcaagcGattctctgactcagc
46556 (A/G)	3' flanking	rs2745970	gcaatggcactatctcGgctcaccacagctccacctctgggttcaagc	attctctgactcagcctcctgagtagctgggattacaggcatgaccac
46777 (G/C)	3' flanking	rs41318019	gctgggattacaggcatgagccaccgcccggcctgaaaattatattga	tatgaatagagcattttgaaaaactttagtgcacctgagactgtaatgt

*SNPs, single nucleotide polymorphisms; UTR, untranslated region. SNPs are numbered based on GenBank accession no. AY916779. Nucleotides in upper case are unique flanking sequences and nucleotides in lower case are sequences in a repeat region.

Table 3. Single nucleotide polymorphisms in the coding region of CD46 in Coriell Cell Repository (CCR) reference samples and case-control study samples

Site* (rs no.)	Amino acid position	Residue	PolyPhen†/SIFT‡ predicted function	Population sample (minor allele frequency)
1992§	13	Serine to phenylalanine	Benign/tolerated	Asians from CCR (0.05)
9408 (rs12126088)	139	Leucine to leucine	Not applicable	Case-control study (0.02)
9444§	151	Serine to serine	Not applicable	Case-control study (0.01) and Asians from CCR (0.04)
16878 (rs17006830)	266	Aspartate to asparagine	Benign/tolerated	Africans from CCR (0.02)
20088 (rs41317835)	324	Proline to leucine	Probably damaging/tolerated	Africans from CCR (0.02) and case-control study (0.01)
34844 (rs35366573)	353	Alanine to valine	Benign/tolerated	European-Americans from CCR (0.02), Hispanics from CCR (0.08), and case-control study (0.02)

*Numbering based on reference sequence reported as GenBank accession no. AY916779.

†PolyPhen, polymorphism phenotyping (1).

‡SIFT, sorting tolerant from intolerant (2).

§Not reported in single nucleotide polymorphism database, but reported in the literature (3).

Table 4. Unadjusted p values for association test between case/control status and tag SNP genotypes in white case-control study samples*

SNP (rs no.) genotypes	No. cases	No. controls	General genotype model p value†	Dominant model p value‡
668 (rs11118514)			0.2305	0.4610
CC	13	26		
CG	0	1		
GG	1	0		
1303 (rs2796267)			0.0482	0.2817
AA	4	6		
AG	8	12		
GG	0	4		
6420 (rs41317049)			0.0176	0.0440
TT	10	28		
TG	6	3		
GG	0	1		
7925 (rs2724385)			0.0174	0.1437
TT	5	5		
TA	8	13		
AA	2	11		
8393 (rs35677203)			0.3199	0.3199
AA	15	26		
AT	1	4		
TT	0	0		
9751 (rs41317081)			0.2452	0.2452
GG	14	28		
GA	2	1		
AA	0	0		
10885 (rs2466572)			0.1383	0.2305
CC	4	10		
CA	9	11		
AA	2	3		
12104 (rs2724359)			0.0669	0.1775
GG	4	10		
GA	9	11		
AA	2	3		
13284 (rs2796269)			0.0296	0.2575
CC	0	3		
CT	6	15		
TT	10	11		
14777 (rs41317805)			0.2416	0.2416
A/A	12	21		
A/-	2	7		
-/-	0	0		

34492 (rs11806810)			0.3443	0.3443
GG	13	28		
GC	2	3		
CC	0	0		
36057 (rs41317983)			0.0902	0.1579
AA	11	23		
AG	3	3		
GG	1	0		
36063 (rs859705)			0.0586	0.1804
GG	4	11		
GA	8	11		
AA	3	5		
41825 (rs1142469)			0.0553	0.1623
GG	5	14		
GA	6	7		
AA	2	4		
42250 (rs41318007)			0.4637	0.4637
CC	9	21		
CG	1	2		
GG	0	0		

*SNP, single nucleotide polymorphism. Values in **boldface** for SNP 6420 were statistically significant ($p < 0.05$) in the general genotype and dominant models.

†Fisher exact test (2×3).

‡Fisher exact test (2×2).

References

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