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Supplemental Data

BOOST: A Fast Approach to Detecting Gene-Gene Interactions in Genome-wide Case-Control Studies

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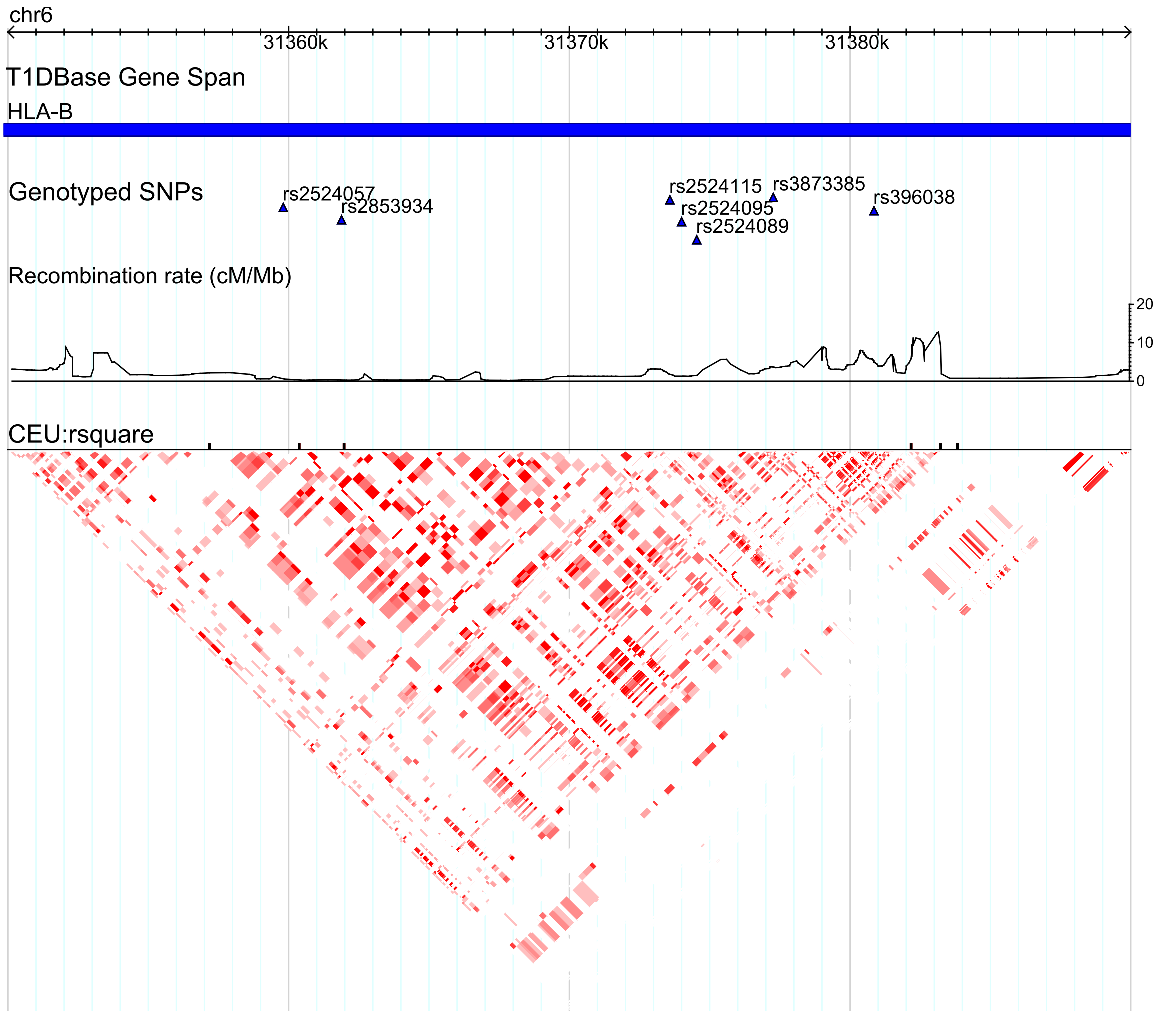

Figure S1. The Region 31350k–31390k of Chromosome 6, Where the Gene *HLA-B* in the MHC Class I Locates

The recombination rate and LD plot from HapMap show that a block structure spans from 31360k to 31380k. This region is mapped through the SNP rs2524057, rs2853934, rs2524115, rs396038, rs3873385, rs2524095 and rs2524089. The SNP rs2524095 and rs2524089 are involved in the interactions with the region 32930k - 32960k. The other five SNPs are involved in the interactions with the region 31360k to 31380k shown in Figure 5 of the main article.

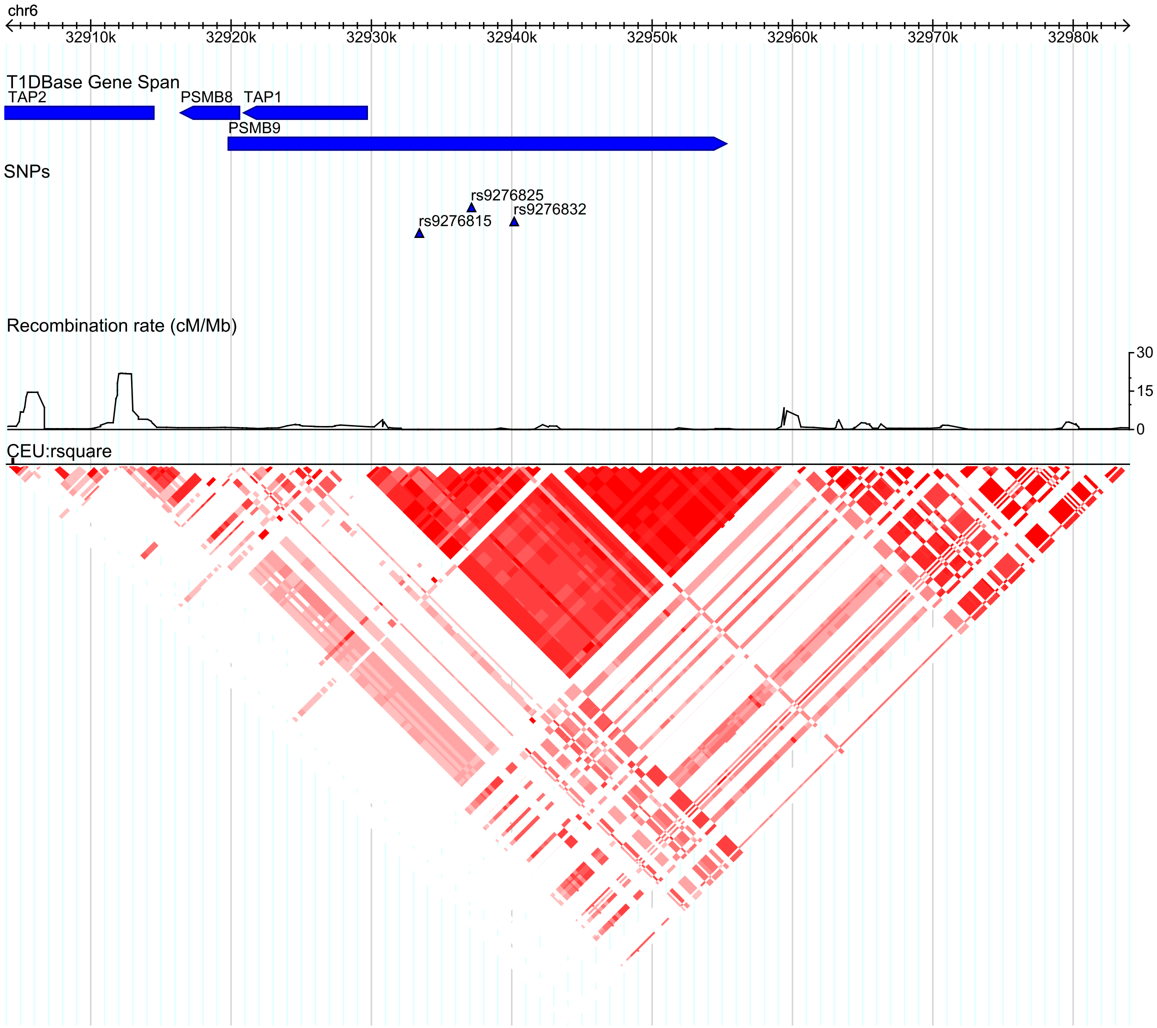

Figure S2. The Region 32900k–32990k of Chromosome 6, Where the Genes *TAP2*, *PSMB8*, *PSMB9* and *TAP1* in the MHC Class II Reside

The recombination rate and LD plot from HapMap show that a block structure exists from 32900k - 32990k. This region is mapped through the SNPs rs9276815, rs9276825 and rs9276832 whose single-locus P_{values} are not significant.

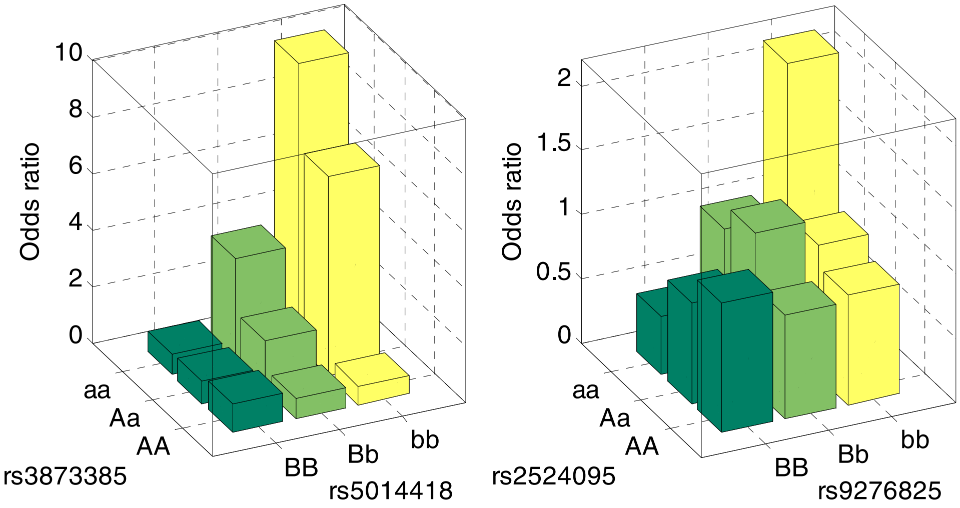

Figure S3. Odds Ratios of the Two Interaction Groups

Left panel: The odds ratio of the SNP pair (rs3873385, rs5014418). This odds ratio can be approximated by a multiplicative model

Right panel: The odds ratio of the SNP pair (rs2524095, rs9276825). It can be approximated by a joint recessive model.

Figure S4. The Performance Comparison between BOOST and PLINK on Models epi 1–20

For Models epi 1-5, h^2 = 0.4 and MAF = 0.2. For Models epi 6-10, h^2 = 0.4 and MAF = 0.4. For Models epi 11-15, h^2 = 0.3 and MAF = 0.2. For Models epi 16-20, h^2 = 0.3 and MAF = 0.4. Under each parameter setting, 100 data sets are generated. In each data set, 1000 SNPs are simulated. 400, 800 and 1600 samples with balanced design are simulated. The power is calculated as the proportion of the 100 data sets in which the interactions of the disease associated SNPs are detected. The absence of bars means no power. The comparison shows that our method significantly outperforms PLINK for most of these models.

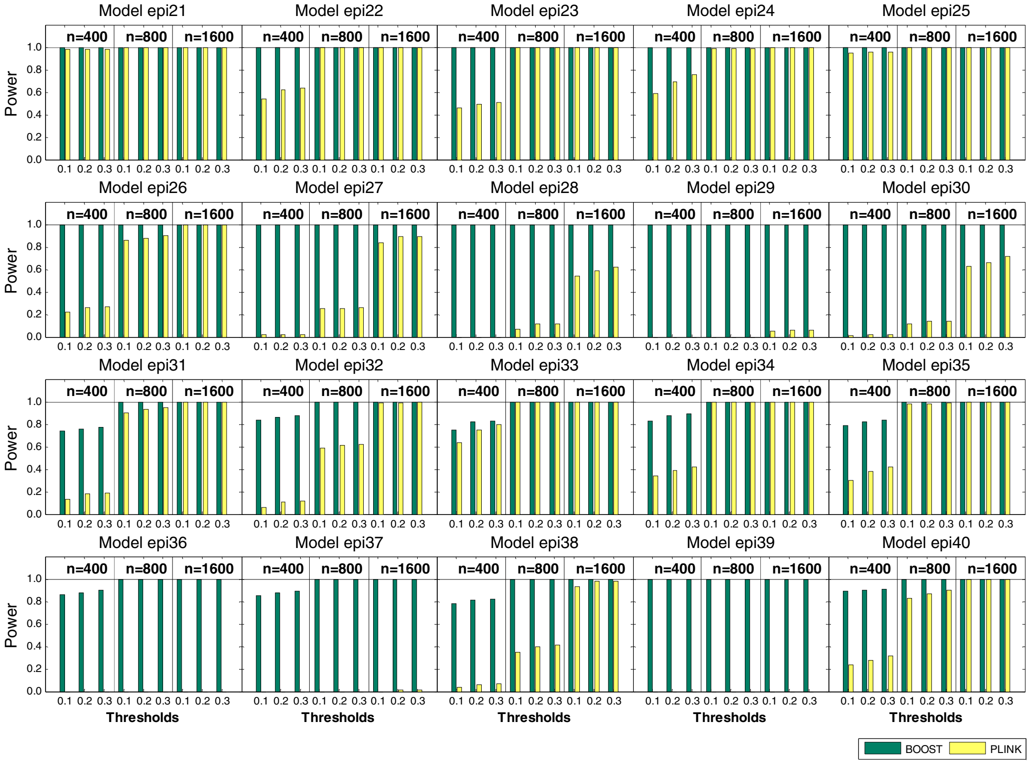

Figure S5. The Performance Comparison between BOOST and PLINK on Models epi 21–40

For Models epi 21-25, h^2 = 0.2 and MAF = 0.2. For Models epi 26-30, h^2 = 0.2 and MAF = 0.4. For Models epi 31-35, h^2 = 0.1 and MAF = 0.2. For Models epi 36-40, h^2 = 0.1 and MAF = 0.4. The numbers of data sets, SNPs and samples are the same as in Figure S4. The comparison shows that our method significantly outperforms PLINK for most of these models in terms of detection power.

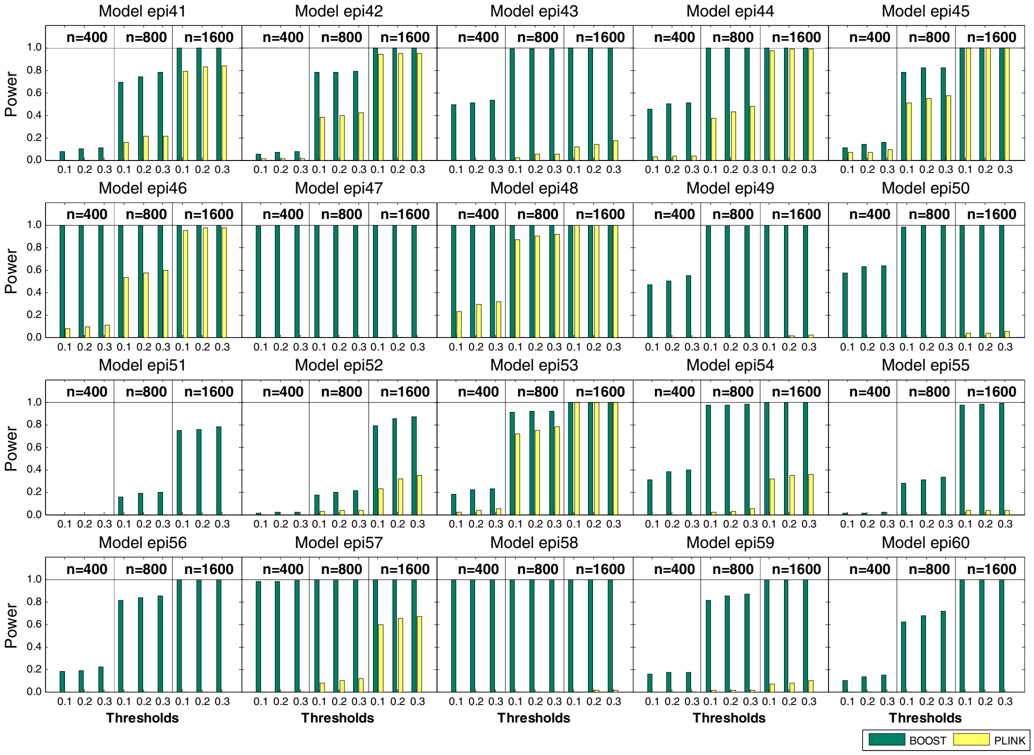

Figure S6. The Performance Comparison between BOOST and PLINK on Models epi41–60

For Models epi 41-45, h^2 = 0.05 and MAF = 0.2. For Models epi 46-50, h^2 = 0.05 and MAF = 0.4. For Models epi 51-55, h^2 = 0.025 and MAF = 0.2. For Models epi 56-60, h^2 = 0.025 and MAF = 0.4. The other parameters are the same as in Figure S4. Our method is superior over PLINK for most of these models.

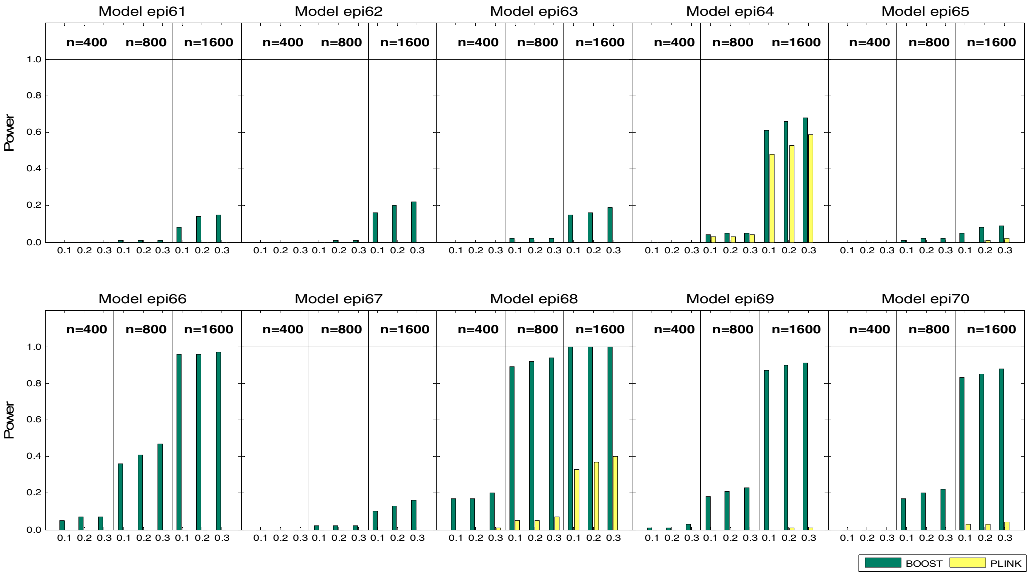

Figure S7. The Performance Comparison between BOOST and PLINK on Models epi 61–70

For Models epi 61-65, $h^2 = 0.01$ and MAF = 0.2. For Models epi 66-70, $h^2 = 0.01$ and MAF = 0.4. The other settings are the same as in Figure S4. Our method performs better than PLINK for most of these models.

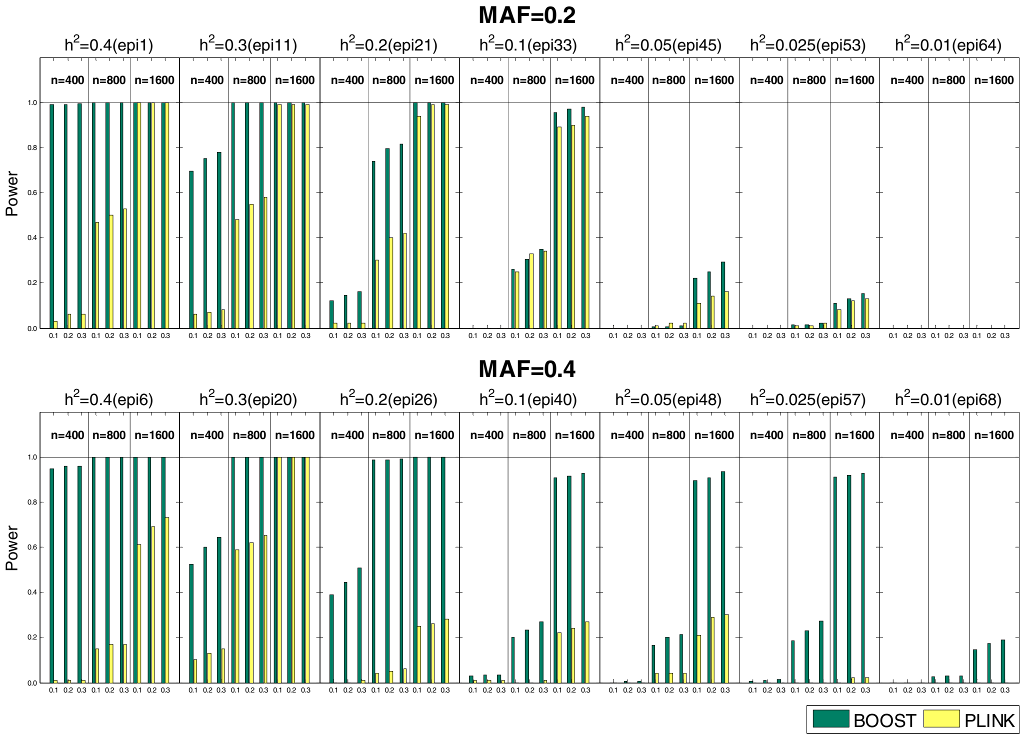

Figure S8. The Performance of BOOST and PLINK when Genetic Heterogeneity (GH) Is Present

The significance thresholds set as 0.1, 0.2 and 0.3 after the Bonferroni correction. We simulate 100 data sets under each model setting containing 1000 SNPs. Different sample sizes (n=400, 800 and 1600) are simulated. To simulate genetic heterogeneity, 50% case samples are generated at loci X_1 and X_2 and another 50% case samples are generated at loci X_3 and X_4. The distribution of case samples is based on a specific disease model given in Table S6.

Table S1. The Number of SNPs Passing Our Quality Control for the Seven Data Sets from the WTCCC

BD	CAD	CD	HT	RA	T1D	T2D
352,329	352,890	355,022	353,559	353,344	353,397	352,291

Table S2. The Interaction SNP Pairs in the Two Regions of Chromosome 6: The Region 31350k–31390k and the Region 32900k–32990k

SNP 1		SNP 2		Interaction
SNP	Single-locus P-value	SNP	Single-locus P-value	BOOST P-value
rs2524095	2.254×10^{-2}	rs9276815	1.926×10^{-1}	1.443×10^{-15}
rs2524095	2.254×10^{-2}	rs9276825	1.661×10^{-5}	9.259×10^{-14}
rs2524095	2.254×10^{-2}	rs9276832	1.064×10^{-1}	1.100×10^{-16}
rs2524089	1.796×10^{-2}	rs9276815	1.926×10^{-1}	4.441×10^{-16}
rs2524089	1.796×10^{-2}	rs9276825	1.661×10^{-5}	3.364×10^{-14}
rs2524089	1.796×10^{-2}	rs9276832	1.064×10^{-1}	1.100×10^{-16}

The first region is shown in Figure S1 and the second one is shown in Figure S2. The SNPs in the column ‘SNP 1’ reside in gene *HLA-B* and the SNPs in the column ‘SNP 2’ locate at the block 32930k - 32960k where gene *PSMB9* resides. They show strong interactions without displaying significant main effects.

Table S3. Odds Ratios for the Interactions Discussed in Table 4 in the Main Article

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Odds ratio (95% confidence interval) of the SNP pair (rs2524057, rs9276448)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.782257 (0.630619-0.959055)	0.719534 (0.215448-1.482213)
Aa	0.844810 (0.731690-0.969650)	1.638000 (1.247961-2.088884)	11.805494 (2.534465-47.600259)
aa	0.679658 (0.433468-0.941995)	7.252292 (2.998925-18.119239)	8.663495 (1.407606-25.296296)

Odds ratio (95% confidence interval) of the SNP pair (rs2524057, rs5014418)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.766093 (0.622680-0.926022)	0.953875 (0.317430-2.107594)
Aa	0.848507 (0.731158-0.983871)	1.624995 (1.218614-2.086091)	8.645345 (1.691003-34.470171)
aa	0.683598 (0.458848-0.975772)	7.358683 (2.924812-17.624191)	8.594120 (1.115266-26.703089)

Odds ratio (95% confidence interval) of the SNP pair (rs2853934, rs9276448)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.803154 (0.653206-0.990836)	0.829751 (0.282509-1.741118)
Aa	0.824249 (0.712467-0.950776)	1.713919 (1.313821-2.180228)	11.260651 (2.225966-42.911094)
aa	0.795271 (0.491577-1.200085)	16.544499 (4.500612-79.974155)	8.896769 (1.413369-25.585720)

Odds ratio (95% confidence interval) of the SNP pair (rs2524115, rs9276448)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.799118 (0.648489-0.966980)	0.974614 (0.310351-2.133718)
Aa	0.831881 (0.715404-0.949712)	1.742896 (1.378488-2.207660)	10.044209 (1.972085-38.615174)
aa	0.784986 (0.477145-1.189450)	14.408144 (4.229527-66.857660)	8.624214 (1.155715-26.068527)

Odds ratio (95% confidence interval) of the SNP pair (rs3873385, rs9276448)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.701824 (0.569175-0.858580)	0.761205 (0.215802-1.820555)
Aa	0.792240 (0.681452-0.916233)	1.782476 (1.406795-2.275316)	7.163968 (1.726417-35.050812)
aa	0.753792 (0.482170-1.093480)	3.532791 (1.808364-6.789977)	10.338382 (1.431955-30.044416)

Odds ratio (95% confidence interval) of the SNP pair (rs3873385, rs5014418)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.703111 (0.563153-0.862652)	0.625254 (0.130193-1.486686)
Aa	0.791486 (0.678618-0.910262)	1.737873 (1.377238-2.153843)	7.039065 (1.691325-32.309307)
aa	0.748681 (0.473684-1.058481)	3.619657 (1.849901-7.636876)	10.032980 (1.462596-30.420561)

Odds ratio (95% confidence interval) of the SNP pair (rs3873385, rs6919798)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.705275 (0.559853-0.871188)	0.518320 (0.066014-1.181589)
Aa	0.817252 (0.712661-0.944343)	1.718165 (1.309495-2.177662)	5.001970 (1.456140-14.881499)
aa	0.809427 (0.532564-1.200045)	3.097251 (1.607091-5.928819)	16.155510 (4.311227-30.465748)

Odds ratio (95% confidence interval) of the SNP pair (rs396038, rs9276448)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.804466 (0.654949-0.979859)	0.940362 (0.310751-2.039541)
Aa	0.835198 (0.723344-0.955937)	1.720432 (1.337550-2.209702)	9.555448 (2.006199-37.939749)
aa	0.789622 (0.494006-1.193448)	15.797189 (4.794310-76.848935)	9.226793 (1.431434-28.671894)

Here we use “AA”, “Aa” and “aa” to denote the genotypes of the first SNP, where “A”, “a” stand for the major allele and the minor allele, respectively. We use “BB”, “Bb” and “bb” to denote the genotypes of the second SNP. The genotype combinations “Aa/Bb”, “Aa/bb”, “aa/Bb” and “aa/bb” have significantly higher disease risks than others

Table S4. Odds Ratios for the Interactions Given in Table S2

Odds ratio (95% confidence interval) of the SNP pair (rs2524095, rs9276815)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.642590 (0.500707-0.788818)	0.617596 (0.385972-0.892969)
Aa	0.830303 (0.669226-1.002420)	1.117218 (0.916431-1.332502)	0.656256 (0.490976-0.853231)
aa	0.530740 (0.386003-0.696604)	1.017748 (0.811893-1.258269)	1.848265 (1.279235-2.607252)

Odds ratio (95% confidence interval) of the SNP pair (rs2524095, rs9276825)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.801326 (0.640200-0.997137)	0.856674 (0.636023-1.127784)
Aa	0.781246 (0.614317-0.993044)	1.219126 (0.968191-1.503457)	1.013640 (0.789047-1.282054)
aa	0.454339 (0.309032-0.630959)	1.024010 (0.780013-1.311447)	2.205573 (1.570373-2.962693)

Odds ratio (95% confidence interval) of the SNP pair (rs2524095, rs9276832)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.618815 (0.493281-0.772356)	0.584853 (0.369357-0.849720)
Aa	0.825114 (0.681332-0.988475)	1.142797 (0.946765-1.389668)	0.655967 (0.489295-0.866161)
aa	0.523072 (0.388161-0.682963)	1.079508 (0.850498-1.342980)	1.859723 (1.270552-2.653359)

Odds ratio (95% confidence interval) of the SNP pair (rs2524089, rs9276815)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.638618 (0.509939-0.789681)	0.627544 (0.400878-0.895855)
Aa	0.829617 (0.679363-1.004452)	1.132458 (0.941323-1.355327)	0.651735 (0.475365-0.859302)
aa	0.526083 (0.380342-0.703060)	1.005187 (0.796840-1.249330)	1.898645 (1.306515-2.648811)

Odds ratio (95% confidence interval) of the SNP pair (rs2524089, rs9276825)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.800233 (0.630071-0.997722)	0.864079 (0.631823-1.141595)
Aa	0.803718 (0.620040-1.023794)	1.229757 (0.984252-1.497876)	1.015877 (0.789624-1.299686)
aa	0.446043 (0.303234-0.604510)	1.021996 (0.772193-1.298333)	2.249697 (1.612131-3.095434)

Odds ratio (95% confidence interval) of the SNP pair (rs2524089, rs9276832)

	BB	Bb	bb
AA	1.000000 (1.000000-1.000000)	0.617008 (0.492277-0.750980)	0.605171 (0.385295-0.868295)
Aa	0.834400 (0.692024-1.007078)	1.143351 (0.961350-1.365511)	0.661398 (0.479340-0.868185)
aa	0.513629 (0.382523-0.660724)	1.079555 (0.844477-1.340670)	1.894261 (1.277729-2.704239)

The notation is the same as in Table S3. The genotype combination "aa/bb" has a significantly higher disease risk than the rest.

Table S5. Simulation Models for Genetic Heterogeneity

	h^2=0.4	h^2=0.3	h^2=0.2	h^2=0.1	h^2=0.05	h^2=0.025	h^2=0.01
MAF=0.2	epi1	epi11	epi21	epi33	epi45	epi53	epi64
MAF=0.4	epi6	epi20	epi26	epi40	epi48	epi57	epi68

Table S6. These 91 Interactions Detected by BOOST in T1D Data Display Weak Main Effects

SNP 1				SNP 2				Interaction	
SNP	Chr	Position	Single-locus P-value	SNP	Chr	Position	Single-locus P-value	BOOST P-value	PLINK P-value
rs1633085	6	29823976	6.452e-001	rs753725	6	30998850	4.630e-004	1.068e-013	3.692e-011
rs1737031	6	29845460	1.219e-001	rs3130982	6	31192054	6.491e-002	4.863e-013	1.824e-012
rs1610677	6	29897150	2.793e-001	rs3869109	6	31292175	1.606e-001	1.676e-013	7.129e-012
rs1611699	6	29935732	8.261e-001	rs753725	6	30998850	4.630e-004	4.441e-016	5.529e-014
rs1611710	6	29936895	7.948e-001	rs753725	6	30998850	4.630e-004	4.441e-016	5.818e-014
rs1632879	6	30025682	7.275e-001	rs2523840	6	31138404	7.595e-001	3.719e-013	1.554e-015
rs3869070	6	30131847	5.581e-001	rs9266406	6	31444397	1.293e-006	4.241e-014	2.767e-013
rs3869070	6	30131847	5.581e-001	rs9266409	6	31444547	1.235e-006	2.764e-014	2.767e-013
rs3869070	6	30131847	5.581e-001	rs6910516	6	31451806	1.140e-006	6.695e-014	4.540e-013
rs1264703	6	30173395	5.085e-003	rs9267673	6	31991658	9.088e-006	3.030e-013	9.992e-016
rs1264702	6	30173554	3.111e-003	rs9267673	6	31991658	9.088e-006	2.696e-013	6.661e-016
rs2517592	6	30201116	1.237e-004	rs7452890	6	31285073	2.176e-004	6.743e-013	1.083e-005
rs2517592	6	30201116	1.237e-004	rs3130944	6	31304650	1.068e-006	5.840e-014	2.537e-006
rs2517592	6	30201116	1.237e-004	rs3130713	6	31313596	1.915e-006	1.182e-013	3.368e-006
rs2517592	6	30201116	1.237e-004	rs486416	6	31964049	2.425e-003	1.100e-016	2.717e-012
rs2523747	6	30336917	3.424e-001	rs2844615	6	31350938	1.413e-001	2.734e-013	7.438e-015
rs2523747	6	30336917	3.424e-001	rs2524057	6	31359874	4.807e-001	4.391e-013	3.664e-015
rs2523747	6	30336917	3.424e-001	rs2853934	6	31361907	8.336e-002	2.762e-013	8.327e-015
rs2523747	6	30336917	3.424e-001	rs2524051	6	31363479	9.983e-002	8.105e-014	3.331e-015
rs2523747	6	30336917	3.424e-001	rs2524132	6	31372891	8.827e-002	2.359e-013	7.327e-015
rs2523747	6	30336917	3.424e-001	rs2524115	6	31373533	1.215e-001	1.029e-013	3.331e-015
rs2523747	6	30336917	3.424e-001	rs396038	6	31380959	9.939e-002	1.961e-013	6.106e-015
rs1264616	6	30372286	2.572e-001	rs2524132	6	31372891	8.827e-002	8.626e-014	2.776e-015
rs1264616	6	30372286	2.572e-001	rs2524115	6	31373533	1.215e-001	5.873e-014	1.776e-015
rs1264616	6	30372286	2.572e-001	rs396038	6	31380959	9.939e-002	7.749e-014	2.220e-015
rs261948	6	30378588	2.673e-001	rs396038	6	31380959	9.939e-002	6.184e-014	1.887e-015
rs6905389	6	30427909	8.982e-001	rs2516486	6	31602181	4.689e-001	1.311e-013	2.087e-014
rs2516675	6	30538499	2.649e-005	rs486416	6	31964049	2.425e-003	1.511e-013	3.109e-015
rs3131043	6	30866445	6.152e-001	rs9267673	6	31991658	9.088e-006	2.220e-016	1.100e-016
rs6931717	6	30930392	8.263e-006	rs415929	6	32297010	9.819e-005	1.100e-016	1.100e-016
rs2532921	6	31030549	9.694e-002	rs9276832	6	32940378	1.064e-001	7.438e-013	2.655e-012
rs9262546	6	31101107	5.351e-001	rs427037	6	32320242	3.558e-002	1.108e-013	1.034e-012
rs9263715	6	31203780	6.220e-002	rs427037	6	32320242	3.558e-002	4.430e-014	3.371e-012
rs9263716	6	31203795	6.958e-002	rs427037	6	32320242	3.558e-002	5.018e-014	3.894e-012
rs9263794	6	31237998	5.678e-001	rs427037	6	32320242	3.558e-002	3.331e-015	1.554e-015
rs2894180	6	31280634	8.230e-003	rs427037	6	32320242	3.558e-002	1.100e-016	1.100e-016
rs2894180	6	31280634	8.230e-003	rs9276448	6	32823607	8.878e-003	1.100e-016	1.100e-016
rs2894180	6	31280634	8.230e-003	rs5014418	6	32827359	1.116e-002	1.100e-016	1.100e-016
rs2894180	6	31280634	8.230e-003	rs6919798	6	32840868	6.077e-002	1.110e-016	4.441e-016
rs2894180	6	31280634	8.230e-003	rs2621384	6	32867251	1.154e-004	1.810e-014	2.442e-015
rs7452890	6	31285073	2.176e-004	rs415929	6	32297010	9.819e-005	5.735e-013	8.505e-013
rs3869109	6	31292175	1.606e-001	rs9276832	6	32940378	1.064e-001	4.208e-014	9.824e-012
rs3130531	6	31314595	6.991e-003	rs427037	6	32320242	3.558e-002	1.110e-016	1.100e-016
rs3130531	6	31314595	6.991e-003	rs9268302	6	32432795	8.049e-002	1.100e-016	1.110e-016
rs3130531	6	31314595	6.991e-003	rs6907322	6	32432923	7.574e-003	1.100e-016	2.665e-015
rs3095250	6	31316319	1.230e-004	rs9268302	6	32432795	8.049e-002	2.591e-013	7.907e-012
rs3095250	6	31316319	1.230e-004	rs9276448	6	32823607	8.878e-003	1.554e-015	1.100e-016
rs3095250	6	31316319	1.230e-004	rs5014418	6	32827359	1.116e-002	6.661e-016	1.100e-016
rs3095250	6	31316319	1.230e-004	rs6919798	6	32840868	6.077e-002	3.220e-014	1.110e-016
rs6937967	6	31317024	2.804e-005	rs9268302	6	32432795	8.049e-002	5.851e-014	9.787e-012
rs6937967	6	31317024	2.804e-005	rs9276448	6	32823607	8.878e-003	3.275e-014	1.100e-016
rs6937967	6	31317024	2.804e-005	rs5014418	6	32827359	1.116e-002	2.176e-014	1.100e-016
rs6937967	6	31317024	2.804e-005	rs6919798	6	32840868	6.077e-002	6.474e-013	7.772e-016
rs2524057	6	31359874	4.807e-001	rs9276448	6	32823607	8.878e-003	5.362e-014	2.220e-016
rs2524057	6	31359874	4.807e-001	rs5014418	6	32827359	1.116e-002	2.738e-013	1.221e-015
rs2853934	6	31361907	8.336e-002	rs9276448	6	32823607	8.878e-003	2.507e-013	1.554e-015
rs2524115	6	31373533	1.215e-001	rs9276448	6	32823607	8.878e-003	6.456e-013	5.107e-015
rs2524095	6	31374096	2.254e-002	rs9276815	6	32933485	1.926e-001	1.443e-015	1.569e-011

SNP 1				SNP 2				Interaction	
SNP	Chr	Position	Single-locus P-value	SNP	Chr	Position	Single-locus P-value	BOOST P-value	PLINK P-value
rs2524095	6	31374096	2.254e-002	rs9276825	6	32937692	1.661e-005	9.259e-014	1.574e-011
rs2524095	6	31374096	2.254e-002	rs9276832	6	32940378	1.064e-001	1.100e-016	1.810e-013
rs2524089	6	31374501	1.796e-002	rs9276815	6	32933485	1.926e-001	4.441e-016	1.356e-011
rs2524089	6	31374501	1.796e-002	rs9276825	6	32937692	1.661e-005	3.364e-014	1.258e-011
rs2524089	6	31374501	1.796e-002	rs9276832	6	32940378	1.064e-001	1.100e-016	1.422e-013
rs3873385	6	31377287	3.368e-001	rs9276448	6	32823607	8.878e-003	3.186e-014	1.110e-016
rs3873385	6	31377287	3.368e-001	rs5014418	6	32827359	1.116e-002	3.841e-014	1.110e-016
rs3873385	6	31377287	3.368e-001	rs6919798	6	32840868	6.077e-002	4.257e-013	1.776e-015
rs396038	6	31380959	9.939e-002	rs9276448	6	32823607	8.878e-003	5.894e-013	4.663e-015
rs3016013	6	31459221	6.222e-001	rs9276448	6	32823607	8.878e-003	1.400e-013	6.328e-015
rs3016013	6	31459221	6.222e-001	rs1044043	6	32901959	8.631e-001	2.365e-014	3.234e-013
rs3099848	6	31459421	5.094e-001	rs1044043	6	32901959	8.631e-001	1.068e-013	3.692e-011
rs2516460	6	31526679	3.388e-004	rs9276448	6	32823607	8.878e-003	2.940e-013	2.220e-016
rs2516460	6	31526679	3.388e-004	rs5014418	6	32827359	1.116e-002	2.532e-013	4.441e-016
rs2523650	6	31557001	2.314e-005	rs9276227	6	32808662	5.975e-002	4.022e-013	2.220e-016
rs2523650	6	31557001	2.314e-005	rs9276299	6	32811086	9.175e-002	1.568e-013	1.110e-016
rs2523650	6	31557001	2.314e-005	rs9276448	6	32823607	8.878e-003	5.077e-013	4.441e-016
rs9267247	6	31563813	2.315e-003	rs9276448	6	32823607	8.878e-003	3.401e-013	1.532e-014
rs2516486	6	31602181	4.689e-001	rs9276227	6	32808662	5.975e-002	1.100e-016	1.100e-016
rs2516486	6	31602181	4.689e-001	rs9276299	6	32811086	9.175e-002	1.100e-016	1.100e-016
rs2516486	6	31602181	4.689e-001	rs9276448	6	32823607	8.878e-003	1.100e-016	1.100e-016
rs2516486	6	31602181	4.689e-001	rs5014418	6	32827359	1.116e-002	1.100e-016	1.100e-016
rs2516486	6	31602181	4.689e-001	rs6919798	6	32840868	6.077e-002	5.551e-016	1.100e-016
rs2516486	6	31602181	4.689e-001	rs2621384	6	32867251	1.154e-004	4.519e-014	1.665e-015
rs2516486	6	31602181	4.689e-001	rs7382347	6	32883664	7.856e-002	6.756e-013	3.764e-014
rs2516486	6	31602181	4.689e-001	rs2857129	6	32884601	8.365e-002	6.801e-013	3.908e-014
rs2516486	6	31602181	4.689e-001	rs241432	6	32910181	1.097e-005	4.508e-014	2.220e-016
rs2844463	6	31723146	4.337e-006	rs9276227	6	32808662	5.975e-002	2.665e-015	1.100e-016
rs2844463	6	31723146	4.337e-006	rs9276299	6	32811086	9.175e-002	3.775e-015	1.100e-016
rs2844463	6	31723146	4.337e-006	rs9276448	6	32823607	8.878e-003	7.772e-016	1.221e-015
rs2844463	6	31723146	4.337e-006	rs5014418	6	32827359	1.116e-002	1.110e-016	8.882e-016
rs2844463	6	31723146	4.337e-006	rs6919798	6	32840868	6.077e-002	5.551e-016	5.551e-016
rs707937	6	31838993	7.815e-002	rs6919798	6	32840868	6.077e-002	2.331e-015	1.654e-014

The P-values given in the table are unadjusted. Notice that the single-locus P-values of the SNPs listed here are not significant after the Bonferroni correction. The physical distance of the two interacting SNPs is at least 1Mb.

Table S7. Odds Tables for Four Epistasis Models

Model 1	BB	Bb	Bb
AA	α	α	α
Aa	α	$\alpha\ (1+\theta)$	$\alpha\ (1+\theta)^2$
aa	α	$\alpha\ (1+\theta)$	$\alpha\ (1+\theta)^4$

Model 2	BB	Bb	Bb
AA	α	$\alpha\ (1+\theta)$	$\alpha\ (1+\theta)$
Aa	$\alpha\ (1+\theta)$	α	α
aa	$\alpha\ (1+\theta)$	α	α

Model 3	BB	Bb	Bb
AA	α	α	$\alpha\ (1+\theta)$
Aa	α	$\alpha\ (1+\theta)$	α
aa	$\alpha\ (1+\theta)$	$\alpha\ (1+\theta)$	α

Model 4	BB	Bb	Bb
AA	α	$\alpha\ (1+\theta)$	α
Aa	$\alpha\ (1+\theta)$	α	$\alpha\ (1+\theta)$
aa	α	$\alpha\ (1+\theta)$	α

The parameters α and θ control the prevalence $p(D)$ and the heritability h^2 (see definitions in the main document).

Table S8. Penetrance Tables for Epistasis Models with h^2 = 0.4, MAF = 0.2, 0.4

h^2=0.4, MAF=0.2				h^2=0.4, MAF=0.4			
Model epi 1	AA	Aa	aa	Model epi1 6	AA	Aa	aa
BB	0.486	0.960	0.538	BB	0.077	0.656	0.880
Bb	0.947	0.004	0.811	Bb	0.892	0.235	0.312
bb	0.640	0.606	0.909	bb	0.174	0.842	0.106
h^2=0.4, MAF=0.2				h^2=0.4, MAF=0.4			
Model epi 2	AA	Aa	aa	Model epi1 7	AA	Aa	aa
BB	0.469	0.956	0.697	BB	0.895	0.323	0.161
Bb	0.945	0.019	0.585	Bb	0.068	0.728	0.806
bb	0.786	0.407	0.013	bb	0.925	0.233	0.362
h^2=0.4, MAF=0.2				h^2=0.4, MAF=0.4			
Model epi 3	AA	Aa	aa	Model epi1 8	AA	Aa	aa
BB	0.498	0.954	0.786	BB	0.805	0.251	0.085
Bb	0.978	0.038	0.428	Bb	0.002	0.668	0.638
bb	0.590	0.821	0.380	bb	0.830	0.079	0.542
h^2=0.4, MAF=0.2				h^2=0.4, MAF=0.4			
Model epi 4	AA	Aa	aa	Model epi1 9	AA	Aa	aa
BB	0.505	0.988	0.624	BB	0.307	0.682	0.958
Bb	0.945	0.085	0.807	Bb	0.997	0.390	0.281
bb	0.969	0.116	0.159	bb	0.012	0.990	0.698
h^2=0.4, MAF=0.2				h^2=0.4, MAF=0.4			
Model epi 5	AA	Aa	aa	Model epi1 10	AA	Aa	aa
BB	0.486	0.963	0.512	BB	0.083	0.891	0.037
Bb	0.941	0.006	0.899	Bb	0.619	0.271	0.691
bb	0.691	0.541	0.614	bb	0.853	0.079	0.742

Table S9. Penetrance Tables for Epistasis Models with h^2 = 0.3, MAF = 0.2, 0.4

h^2=0.3, MAF=0.2				h^2=0.3, MAF=0.4			
Model epi 11	AA	Aa	aa	Model epi1 16	AA	Aa	aa
BB	0.500	0.926	0.615	BB	0.891	0.362	0.480
Bb	0.895	0.131	0.647	Bb	0.213	0.829	0.601
bb	0.858	0.160	0.999	bb	0.925	0.267	0.685
h^2=0.3, MAF=0.2				h^2=0.3, MAF=0.4			
Model epi 12	AA	Aa	aa	Model epi1 17	AA	Aa	aa
BB	0.413	0.851	0.535	BB	0.077	0.689	0.417
Bb	0.831	0.008	0.580	Bb	0.763	0.150	0.491
bb	0.692	0.268	0.736	bb	0.196	0.657	0.247
h^2=0.3, MAF=0.2				h^2=0.3, MAF=0.4			
Model epi 13	AA	Aa	aa	Model epi1 18	AA	Aa	aa
BB	0.455	0.848	0.897	BB	0.132	0.793	0.274
Bb	0.890	0.088	0.016	Bb	0.799	0.213	0.514
bb	0.562	0.686	0.467	bb	0.255	0.528	0.793
h^2=0.3, MAF=0.2				h^2=0.3, MAF=0.4			
Model epi 14	AA	Aa	aa	Model epi1 19	AA	Aa	aa
BB	0.609	0.980	0.980	BB	0.611	0.104	0.759
Bb	0.993	0.300	0.275	Bb	0.180	0.674	0.019
bb	0.876	0.483	0.683	bb	0.532	0.189	0.681
h^2=0.3, MAF=0.2				h^2=0.3, MAF=0.4			
Model epi 15	AA	Aa	aa	Model epi1 20	AA	Aa	aa
BB	0.446	0.844	0.774	BB	0.091	0.827	0.863
Bb	0.879	0.044	0.233	Bb	0.869	0.393	0.415
bb	0.492	0.796	0.410	bb	0.738	0.508	0.363

Table S10. Penetrance Tables for Epistasis Models with h^2 = 0.2, MAF = 0.2, 0.4

h^2=0.2, MAF=0.2				h^2=0.2, MAF=0.4			
Model epi 21	AA	Aa	aa	Model epi1 26	AA	Aa	aa
BB	0.428	0.757	0.812	BB	0.356	0.891	0.809
Bb	0.788	0.132	0.044	Bb	0.955	0.508	0.611
bb	0.559	0.548	0.373	bb	0.617	0.755	0.630
h^2=0.2, MAF=0.2				h^2=0.2, MAF=0.4			
Model epi 22	AA	Aa	aa	Model epi1 27	AA	Aa	aa
BB	0.507	0.842	0.605	BB	0.086	0.536	0.641
Bb	0.845	0.162	0.629	Bb	0.677	0.275	0.096
bb	0.581	0.678	0.729	bb	0.219	0.413	0.712
h^2=0.2, MAF=0.2				h^2=0.2, MAF=0.4			
Model epi 23	AA	Aa	aa	Model epi1 28	AA	Aa	aa
BB	0.577	0.247	0.428	BB	0.855	0.339	0.772
Bb	0.227	0.928	0.578	Bb	0.513	0.651	0.607
bb	0.586	0.262	0.158	bb	0.250	0.999	0.154
h^2=0.2, MAF=0.2				h^2=0.2, MAF=0.4			
Model epi 24	AA	Aa	aa	Model epi1 29	AA	Aa	aa
BB	0.340	0.637	0.654	BB	0.506	0.838	0.024
Bb	0.689	0.017	0.041	Bb	0.603	0.454	0.957
bb	0.242	0.866	0.403	bb	0.729	0.427	0.753
h^2=0.2, MAF=0.2				h^2=0.2, MAF=0.4			
Model epi 25	AA	Aa	aa	Model epi1 30	AA	Aa	aa
BB	0.387	0.726	0.734	BB	0.393	0.764	0.664
Bb	0.749	0.090	0.034	Bb	0.850	0.398	0.733
bb	0.551	0.401	0.724	bb	0.406	0.927	0.147

Table S11. Penetrance Tables for Epistasis Models with h^2 = 0.1, MAF = 0.2, 0.4

h^2=0.1, MAF=0.2				h^2=0.1, MAF=0.4			
Model epi 31	AA	Aa	aa	Model epi1 36	AA	Aa	aa
BB	0.463	0.703	0.431	BB	0.137	0.484	0.187
Bb	0.653	0.277	0.806	Bb	0.482	0.166	0.365
bb	0.830	0.008	0.129	bb	0.193	0.361	0.430
h^2=0.1, MAF=0.2				h^2=0.1, MAF=0.4			
Model epi 32	AA	Aa	aa	Model epi1 37	AA	Aa	aa
BB	0.319	0.507	0.569	BB	0.469	0.198	0.754
Bb	0.553	0.105	0.045	Bb	0.337	0.502	0.141
bb	0.203	0.777	0.280	bb	0.339	0.453	0.285
h^2=0.1, MAF=0.2				h^2=0.1, MAF=0.4			
Model epi 33	AA	Aa	aa	Model epi1 38	AA	Aa	aa
BB	0.627	0.393	0.335	BB	0.478	0.311	0.864
Bb	0.396	0.779	0.953	Bb	0.387	0.579	0.263
bb	0.174	0.842	0.106	bb	0.634	0.436	0.138
h^2=0.1, MAF=0.2				h^2=0.1, MAF=0.4			
Model epi 34	AA	Aa	aa	Model epi1 39	AA	Aa	aa
BB	0.297	0.540	0.441	BB	0.068	0.299	0.017
Bb	0.541	0.072	0.278	Bb	0.289	0.044	0.285
bb	0.434	0.293	0.228	bb	0.048	0.262	0.174
h^2=0.1, MAF=0.2				h^2=0.1, MAF=0.4			
Model epi 35	AA	Aa	aa	Model epi1 40	AA	Aa	aa
BB	0.332	0.562	0.573	BB	0.539	0.120	0.258
Bb	0.583	0.112	0.147	Bb	0.165	0.378	0.325
bb	0.399	0.496	0.033	bb	0.123	0.426	0.276

Table S12. Penetrance Tables for Epistasis Models with h^2 = 0.05, MAF = 0.2, 0.4

h^2=0.05, MAF=0.2				h^2=0.05, MAF=0.4			
Model epi 41	AA	Aa	aa	Model epi1 46	AA	Aa	aa
BB	0.492	0.664	0.481	BB	0.002	0.155	0.214
Bb	0.642	0.330	0.746	Bb	0.199	0.071	0.022
bb	0.656	0.396	0.000	bb	0.081	0.122	0.135
h^2=0.05, MAF=0.2				h^2=0.05, MAF=0.4			
Model epi 42	AA	Aa	aa	Model epi1 47	AA	Aa	aa
BB	0.499	0.639	0.765	BB	0.188	0.020	0.171
Bb	0.666	0.389	0.083	Bb	0.032	0.174	0.059
bb	0.543	0.527	0.953	bb	0.134	0.087	0.092
h^2=0.05, MAF=0.2				h^2=0.05, MAF=0.4			
Model epi 43	AA	Aa	aa	Model epi1 48	AA	Aa	aa
BB	0.212	0.350	0.116	BB	0.005	0.179	0.251
Bb	0.336	0.054	0.495	Bb	0.211	0.100	0.026
bb	0.227	0.273	0.495	bb	0.156	0.098	0.156
h^2=0.05, MAF=0.2				h^2=0.05, MAF=0.4			
Model epi 44	AA	Aa	aa	Model epi1 49	AA	Aa	aa
BB	0.805	0.683	0.638	BB	0.174	0.321	0.154
Bb	0.657	0.936	0.989	Bb	0.223	0.254	0.245
bb	0.850	0.564	0.866	bb	0.448	0.025	0.424
h^2=0.05, MAF=0.2				h^2=0.05, MAF=0.4			
Model epi 45	AA	Aa	aa	Model epi1 50	AA	Aa	aa
BB	0.638	0.488	0.383	BB	0.098	0.219	0.302
Bb	0.464	0.765	0.957	Bb	0.302	0.126	0.121
bb	0.580	0.562	0.719	bb	0.053	0.308	0.136

Table S13. Penetrance Tables for Epistasis Models with h^2 = 0.025, MAF = 0.2, 0.4

h^2=0.025, MAF=0.2				h^2=0.025, MAF=0.4			
Model epi 51	AA	Aa	aa	Model epi1 56	AA	Aa	aa
BB	0.495	0.415	0.657	BB	0.166	0.165	0.128
Bb	0.429	0.616	0.121	Bb	0.114	0.199	0.143
bb	0.552	0.331	0.419	bb	0.281	0.028	0.281
h^2=0.025, MAF=0.2				h^2=0.025, MAF=0.4			
Model epi 52	AA	Aa	aa	Model epi1 57	AA	Aa	aa
BB	0.592	0.691	0.743	BB	0.108	0.006	0.080
Bb	0.712	0.493	0.419	Bb	0.026	0.079	0.046
bb	0.580	0.746	0.504	bb	0.021	0.090	0.025
h^2=0.025, MAF=0.2				h^2=0.025, MAF=0.4			
Model epi 53	AA	Aa	aa	Model epi1 68	AA	Aa	aa
BB	0.108	0.194	0.186	BB	0.006	0.094	0.008
Bb	0.196	0.037	0.045	Bb	0.079	0.016	0.076
bb	0.172	0.073	0.130	bb	0.052	0.043	0.057
h^2=0.025, MAF=0.2				h^2=0.025, MAF=0.4			
Model epi 54	AA	Aa	aa	Model epi1 59	AA	Aa	aa
BB	0.112	0.186	0.128	BB	0.199	0.072	0.168
Bb	0.193	0.024	0.138	Bb	0.086	0.187	0.076
bb	0.079	0.236	0.251	bb	0.125	0.108	0.226
h^2=0.025, MAF=0.2				h^2=0.025, MAF=0.4			
Model epi 55	AA	Aa	aa	Model epi1 60	AA	Aa	aa
BB	0.272	0.192	0.185	BB	0.165	0.096	0.262
Bb	0.172	0.367	0.390	Bb	0.166	0.151	0.091
bb	0.345	0.069	0.005	bb	0.050	0.250	0.056

Table S14. Penetrance Tables for Epistasis Models with h^2 = 0.01, MAF = 0.2, 0.4

h^2=0.01, MAF=0.2				h^2=0.01, MAF=0.4			
Model epi 61	AA	Aa	aa	Model epi1 66	AA	Aa	aa
BB	0.247	0.301	0.205	BB	0.103	0.063	0.124
Bb	0.300	0.173	0.378	Bb	0.098	0.086	0.069
bb	0.215	0.357	0.268	bb	0.021	0.147	0.059
h^2=0.01, MAF=0.2				h^2=0.01, MAF=0.4			
Model epi 62	AA	Aa	aa	Model epi1 67	AA	Aa	aa
BB	0.222	0.276	0.141	BB	0.185	0.291	0.234
Bb	0.259	0.169	0.401	Bb	0.286	0.201	0.277
bb	0.278	0.128	0.420	bb	0.249	0.266	0.166
h^2=0.01, MAF=0.2				h^2=0.01, MAF=0.4			
Model epi 63	AA	Aa	aa	Model epi1 68	AA	Aa	aa
BB	0.260	0.221	0.201	BB	0.073	0.042	0.015
Bb	0.204	0.315	0.348	Bb	0.024	0.064	0.059
bb	0.339	0.074	0.128	bb	0.068	0.019	0.095
h^2=0.01, MAF=0.2				h^2=0.01, MAF=0.4			
Model epi 64	AA	Aa	aa	Model epi1 69	AA	Aa	aa
BB	0.139	0.188	0.221	BB	0.046	0.127	0.069
Bb	0.190	0.111	0.020	Bb	0.115	0.067	0.097
bb	0.206	0.051	0.253	bb	0.107	0.069	0.108
h^2=0.01, MAF=0.2				h^2=0.01, MAF=0.4			
Model epi 65	AA	Aa	aa	Model epi1 70	AA	Aa	aa
BB	0.558	0.616	0.674	BB	0.095	0.122	0.127
Bb	0.632	0.499	0.418	Bb	0.097	0.129	0.010
bb	0.546	0.674	0.395	bb	0.201	0.044	0.122