Supplementary Materials

Title: Discovering Genetic Factors for psoriasis through exhaustively searching for significant second order SNP-SNP interactions

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	phs000019.v1.p1	phs000982.v1.p1
Missing rate	>0.01	>0.05
Minor allele frequency (MAF)	<0.01	
Hardy–Weinberg equilibrium (HWE)	p-value<0.00001	
Missing rate deviation between cases and controls	p-value<0.00001	

Supplementary Table S1: This table shows the data cleansing parameters for filtering low-quality SNPs. SNPs satisfying any one of the following conditions listed in this table are filtered.

	phs000019.v1.p1	phs000982.v1.p1
Missing rate	>0.05	>0.005
Gender	Inconsistency between reported gender and gender predicted with X chromosome	
Heterozygosity rate	-	<0.2775 or >0.2875

Supplementary Table S2: This table shows the data cleansing parameters for filtering low-quality samples. Samples satisfying any one of the following conditions listed in this table are filtered.

SNP1	SNP2	Pattern	SNP1 p-value	SNP2 p-value	2nd Order p-value	Improvement Metric Value	Odds Ratio	2nd Order p-value (phs000982)
rs12191877	rs2534666	4	6.89×10^{-23}	2.08×10^{-6}	6.93×10^{-30}	9.95×10^{6}	3.9339	1.28×10^{-14}
rs3130573	rs12191877	4	6.76×10^{-8}	6.89×10^{-23}	6.98×10^{-29}	9.87×10^{5}	3.7570	8.04×10^{-17}
rs9262492	rs12191877	4	4.39×10^{-6}	6.89×10^{-23}	3.28×10^{-28}	2.10×10^{5}	3.5653	2.75×10^{-26}
rs2894176	rs12191877	4	1.93×10^{-6}	6.89×10^{-23}	3.64×10^{-28}	1.89×10^{5}	3.5434	1.40×10^{-25}
rs3130517	rs12191877	4	3.57×10^{-17}	6.89×10^{-23}	4.45×10^{-28}	1.55×10^{5}	3.5369	1.51×10^{-18}
rs9262498	rs12191877	4	3.90×10^{-6}	6.89×10^{-23}	5.01×10^{-28}	1.38×10^{5}	3.5473	3.65×10^{-26}
rs1265078	rs12191877	4	2.40×10^{-11}	6.89×10^{-23}	6.80×10^{-28}	1.01×10^{5}	3.5547	1.81×10^{-18}
rs12191877	rs2516417	3	6.89×10^{-23}	6.72×10^{-4}	8.30×10^{-28}	8.31×10^{4}	3.3355	1.34×10^{-20}
rs12191877	rs2844502	3	6.89×10^{-23}	9.32×10^{-3}	1.35×10^{-27}	5.12×10^{4}	3.3261	8.76×10^{-20}
rs3130467	rs12191877	4	2.81×10^{-16}	6.89×10^{-23}	1.57×10^{-27}	4.40×10^{4}	3.4868	1.66×10^{-18}
rs12191877	rs2516510	3	6.89×10^{-23}	1.04×10^{-2}	1.90×10^{-27}	3.62×10^{4}	3.3109	1.54×10^{-20}
rs3130517	rs2894207	4	3.57×10^{-17}	1.28×10^{-15}	2.14×10^{-27}	1.67×10^{10}	3.4250	5.65×10^{-18}
rs3094205	rs12191877	4	2.29×10^{-9}	6.89×10^{-23}	3.97×10^{-27}	1.74×10^{4}	3.4440	6.78×10^{-16}
rs2244027	rs12191877	2	4.46×10^{-2}	6.89×10^{-23}	4.28×10^{-27}	1.61×10^{4}	3.2691	3.23×10^{-20}
rs12191877	rs10848821	3	6.89×10^{-23}	2.27×10^{-2}	6.76×10^{-27}	1.02×10^{4}	3.3101	3.26×10^{-20}
rs3130467	rs2894207	4	2.81×10^{-16}	1.28×10^{-15}	7.28×10^{-27}	3.86×10^{10}	3.3781	6.15×10^{-18}
rs12191877	rs2523708	3	6.89×10^{-23}	1.60×10^{-2}	8.76×10^{-27}	7.87×10^{3}	3.2564	2.13×10^{-20}
rs12191877	rs10483336	3	6.89×10^{-23}	2.40×10^{-4}	9.21×10^{-27}	7.49×10^{3}	3.2045	9.55×10^{-23}
rs12191877	rs6075938	3	6.89×10^{-23}	7.79×10^{-3}	1.15×10^{-26}	5.98×10^{3}	3.2515	1.58×10^{-20}
rs1265078	rs2894207	4	2.40×10^{-11}	1.28×10^{-15}	1.43×10^{-26}	8.94×10^{10}	3.3389	6.79×10^{-18}

Supplementary Table S3: This table shows the top 20 statistically significant 2nd order SNP-SNP interactions in terms of p-value from psoriasis dataset phs000019.v1.p1.

SNP1	SNP2	Pattern	SNP1 p-value	SNP2 p-value	2nd Order p-value	Improvement Metric Value	Odds Ratio	2nd Order p-value (phs000019)
rs13203895	rs4349859	5	6.79×10^{-26}	7.20×10^{-9}	1.18×10^{-34}	5.77×10^{8}	2.6638	3.14×10^{-21}
rs13191519	rs4349859	5	4.07×10^{-26}	7.20×10^{-9}	1.26×10^{-34}	3.23×10^{8}	2.6829	8.25×10^{-21}
rs13203895	rs4418214	5	6.79×10^{-26}	2.02×10^{-19}	1.67×10^{-34}	4.06×10^{8}	2.6480	1.79×10^{-19}
rs13191519	rs4418214	5	4.07×10^{-26}	2.02×10^{-19}	1.86×10^{-34}	2.18×10^{8}	2.6651	6.38×10^{-19}
rs10484554	rs4349859	5	9.96×10^{-26}	7.20×10^{-9}	4.17×10^{-34}	2.39×10^{8}	2.6451	7.11×10^{-21}
rs10484554	rs4418214	5	9.96×10^{-26}	2.02×10^{-19}	5.89×10^{-34}	1.69×10^{8}	2.6294	5.56×10^{-19}
rs13203895	rs45533135	5	6.79×10^{-26}	1.20×10^{-8}	7.72×10^{-34}	8.80×10^{7}	2.6206	8.50×10^{-20}
rs13191519	rs45533135	5	4.07×10^{-26}	1.20×10^{-8}	8.72×10^{-34}	4.67×10^{7}	2.6371	1.76×10^{-19}
rs75851973	rs13203895	5	8.19×10^{-10}	6.79×10^{-26}	2.05×10^{-33}	3.31×10^{7}	2.6087	1.13×10^{-21}
rs76956521	rs13203895	5	8.19×10^{-10}	6.79×10^{-26}	2.05×10^{-33}	3.31×10^{7}	2.6087	1.13×10^{-21}
rs17728338	rs13203895	5	1.59×10^{-9}	6.79×10^{-26}	2.14×10^{-33}	3.17×10^{7}	2.6073	6.55×10^{-22}
rs75851973	rs13191519	5	8.19×10^{-10}	4.07×10^{-26}	2.26×10^{-33}	1.80×10^{7}	2.6260	1.85×10^{-20}
rs76956521	rs13191519	5	8.19×10^{-10}	4.07×10^{-26}	2.26×10^{-33}	1.80×10^{7}	2.6260	1.85×10^{-20}
rs17728338	rs13191519	5	1.59×10^{-9}	4.07×10^{-26}	2.37×10^{-33}	1.72×10^{7}	2.6244	1.07×10^{-20}
snp5-150450166	rs13203895	5	1.25×10^{-9}	6.79×10^{-26}	2.47×10^{-33}	2.75×10^{7}	2.6058	—
rs10484554	rs45533135	5	9.96×10^{-26}	1.20×10^{-8}	2.69×10^{-33}	3.70×10^{7}	2.6021	1.53×10^{-19}
snp5-150450166	rs13191519	5	1.25×10^{-9}	4.07×10^{-26}	2.72×10^{-33}	1.50×10^{7}	2.6231	—
rs75851973	rs10484554	5	8.19×10^{-10}	9.96×10^{-26}	4.74×10^{-33}	2.10×10^{7}	2.5966	9.32×10^{-21}
rs76956521	rs10484554	5	8.19×10^{-10}	9.96×10^{-26}	4.74×10^{-33}	2.10×10^{7}	2.5966	9.32×10^{-21}
rs17728338	rs10484554	5	1.59×10^{-9}	9.96×10^{-26}	4.95×10^{-33}	2.01×10^{7}	2.5952	5.40×10^{-21}

Supplementary Table S4: This table shows the top 20 statistically significant 2nd order SNP-SNP interactions in terms of p-value from psoriasis dataset phs000982.v1.p1.

SNP1	SNP2	Pattern	SNP1 p-value	SNP2 p-value	2nd Order p-value	Improvement Metric Value	Odds Ratio	2nd Order p-value (phs000982)
rs1265078	rs7773175	4	2.40×10^{-11}	3.04×10^{-13}	4.69×10^{-25}	6.48×10^{11}	3.0436	6.50×10^{-16}
rs1265078	rs2894207	4	2.40×10^{-11}	1.28×10^{-15}	1.43×10^{-26}	8.94×10^{10}	3.3389	6.79×10^{-18}
rs3130573	rs7773175	4	6.76×10^{-8}	3.04×10^{-13}	5.68×10^{-24}	5.35×10^{10}	3.0176	1.79×10^{-13}
rs9380237	rs2534666	4	5.59×10^{-10}	2.08×10^{-6}	1.11×10^{-20}	5.02×10^{10}	2.7506	1.12×10^{-9}
rs3130467	rs2894207	4	2.81×10^{-16}	1.28×10^{-15}	7.28×10^{-27}	3.86×10^{10}	3.3781	6.15×10^{-18}
rs7756521	rs1265078	4	4.65×10^{-9}	2.40×10^{-11}	7.98×10^{-22}	3.00×10^{10}	3.1234	1.22×10^{-11}
rs1265078	rs9380237	4	2.40×10^{-11}	5.59×10^{-10}	9.45×10^{-22}	2.53×10^{10}	2.8208	2.75×10^{-18}
rs3130517	rs2894207	4	3.57×10^{-17}	1.28×10^{-15}	2.14×10^{-27}	1.67×10^{10}	3.4250	5.65×10^{-18}
rs2894207	rs2534666	4	1.28×10^{-15}	2.08×10^{-6}	1.09×10^{-25}	1.17×10^{10}	3.3436	4.22×10^{-12}
rs3130517	rs7773175	4	3.57×10^{-17}	3.04×10^{-13}	1.45×10^{-26}	2.46×10^{9}	3.1788	2.10×10^{-15}
rs2853950	rs3130573	4	3.93×10^{-6}	6.76×10^{-8}	2.93×10^{-17}	2.30×10^{9}	2.4168	4.15×10^{-8}
rs3094205	rs1265078	4	2.29×10^{-9}	2.40×10^{-11}	1.37×10^{-20}	1.75×10^{9}	2.6799	6.27×10^{-13}
rs7756521	rs8365	4	4.65×10^{-9}	1.29×10^{-8}	3.36×10^{-18}	1.38×10^{9}	3.3442	3.03×10^{-6}
rs3130467	rs7773175	4	2.81×10^{-16}	3.04×10^{-13}	2.08×10^{-25}	1.35×10^{9}	3.0823	3.11×10^{-15}
rs2894176	rs3130467	4	1.93×10^{-6}	2.81×10^{-16}	2.61×10^{-25}	1.08×10^{9}	3.0994	4.16×10^{-13}
rs7756521	rs3130573	4	4.65×10^{-9}	6.76×10^{-8}	5.13×10^{-18}	9.07×10^{8}	2.7101	1.04×10^{-8}
rs2894176	rs3130517	4	1.93×10^{-6}	3.57×10^{-17}	5.38×10^{-26}	6.64×10^{8}	3.1598	2.12×10^{-13}
rs9262498	rs1265078	4	3.90×10^{-6}	2.40×10^{-11}	3.71×10^{-20}	6.46×10^{8}	2.6695	4.27×10^{-11}
rs2844645	rs3094205	2	2.56×10^{-9}	2.29×10^{-9}	3.72×10^{-18}	6.14×10^{8}	2.4554	1.42×10^{-7}
rs3130573	rs2894207	4	6.76×10^{-8}	1.28×10^{-15}	2.26×10^{-24}	5.66×10^{8}	3.1827	1.81×10^{-15}

Supplementary Table S5: This table shows the top 20 statistically significant 2nd order SNP-SNP interactions in terms of improvement metric value from psoriasis dataset phs000019.v1.p1.

SNP1	SNP2	Pattern	SNP1 p-value	SNP2 p-value	2nd Order p-value	Improvement Metric Value	Odds Ratio	2nd Order p-value (phs000019)
rs2517985	rs4358666	5	5.02×10^{-8}	2.62×10^{-9}	1.07×10^{-21}	2.45×10^{12}	2.3225	6.84×10^{-11}
rs2517985	rs34100370	5	5.02×10^{-8}	2.62×10^{-9}	1.07×10^{-21}	2.45×10^{12}	2.3225	4.55×10^{-11}
rs2517985	rs2395491	5	5.02×10^{-8}	5.01×10^{-8}	3.46×10^{-20}	1.45×10^{12}	2.2707	3.04×10^{-9}
rs2517985	rs4624908	5	5.02×10^{-8}	7.03×10^{-8}	3.83×10^{-20}	1.31×10^{12}	2.268 69	3.04×10^{-9}
rs2517985	rs7754026	5	5.02×10^{-8}	6.74×10^{-8}	4.41×10^{-20}	1.14×10^{12}	2.2664	3.04×10^{-9}
rs2517985	rs13194571	5	5.02×10^{-8}	4.98×10^{-8}	4.95×10^{-20}	1.00×10^{12}	2.2637	3.04×10^{-9}
rs2517985	rs7775117	5	5.02×10^{-8}	6.27×10^{-8}	5.03×10^{-20}	9.99×10^{11}	2.2632	3.04×10^{-9}
rs1265079	rs4358666	5	7.09×10^{-8}	2.62×10^{-9}	3.16×10^{-21}	8.30×10^{11}	2.3042	4.77×10^{-11}
rs1265079	rs34100370	5	7.09×10^{-8}	2.62×10^{-9}	3.16×10^{-21}	8.30×10^{11}	2.3042	3.33×10^{-11}
rs1265079	rs4624908	5	7.09×10^{-8}	7.03×10^{-8}	1.11×10^{-19}	6.33×10^{11}	2.2501	2.17×10^{-9}
rs746647	rs4358666	5	9.60×10^{-8}	2.62×10^{-9}	4.62×10^{-21}	5.67×10^{11}	2.2955	4.77×10^{-11}
rs746647	rs34100370	5	9.60×10^{-8}	2.62×10^{-9}	4.62×10^{-21}	5.67×10^{11}	2.2955	3.33×10^{-11}
rs1576	rs4358666	5	9.60×10^{-8}	2.62×10^{-9}	4.62×10^{-21}	5.67×10^{11}	2.2955	7.19×10^{-11}
rs1576	rs34100370	5	9.60×10^{-8}	2.62×10^{-9}	4.62×10^{-21}	5.67×10^{11}	2.2955	4.93×10^{-11}
rs1265114	rs4358666	5	9.60×10^{-8}	2.62×10^{-9}	4.62×10^{-21}	5.67×10^{11}	2.2955	6.84×10^{-11}
rs1265114	rs34100370	5	9.60×10^{-8}	2.62×10^{-9}	4.62×10^{-21}	5.67×10^{11}	2.2955	4.55×10^{-11}
rs1265079	rs7754026	5	7.09×10^{-8}	6.74×10^{-8}	1.28×10^{-19}	5.27×10^{11}	2.2477	2.17×10^{-9}
rs1265112	rs4358666	5	8.43×10^{-8}	2.62×10^{-9}	5.14×10^{-21}	5.10×10^{11}	2.2934	6.84×10^{-11}
rs1265112	rs34100370	5	8.43×10^{-8}	2.62×10^{-9}	5.14×10^{-21}	5.10×10^{11}	2.2934	4.55×10^{-11}
rs1265067	rs4358666	5	1.05×10^{-7}	2.62×10^{-9}	5.14×10^{-21}	5.10×10^{11}	2.2934	6.84×10^{-11}

Supplementary Table S6: This table shows the top 20 statistically significant 2nd order SNP-SNP interactions in terms of improvement metric value from psoriasis dataset phs000982.v1.p1.

SNP	Chr	Position	Annotation	Consequence	GeneName	GeneType
rs10483336	14	28837590	Transcript	INTRONIC	CTD-2591A6.2	lincRNA
rs10484554	6	31274555	Intergenic	DOWNSTREAM	XXbac-BPG248L24.10	pseudogene
rs10848821	12	3298031	Transcript	INTRONIC	TSPAN9	protein coding
rs12191877	6	31252925	Intergenic	DOWNSTREAM	RPL3P2	pseudogene
rs1265067	6	31116142	Transcript	INTRONIC	CCHCR1	protein coding
rs1265078	6	31112602	Intergenic	DOWNSTREAM	PSORS1C1	protein coding
rs1265079	6	31112108	Intergenic	UPSTREAM	PSORS1C2	protein coding
rs1265112	6	31118019	Transcript	INTRONIC	CCHCR1	protein coding
rs1265114	6	31117188	Transcript	INTRONIC	CCHCR1	protein coding
rs13191519	6	31265752	Transcript	INTRONIC	XXbac-BPG248L24.13	lincRNA
rs13194571	6	31342960	Intergenic	DOWNSTREAM	RNU6-283P	snRNA
rs13203895	6	31244082	Non-Coding Transcript	NONCODING_CHANGE	USP8P1	pseudogene
rs1576	6	31110391	Regulatory Feature	NON_SYNONYMOUS	CCHCR1	protein coding
rs17728338	5	150478318	Intergenic	DOWNSTREAM	ANXA6	protein coding
rs2244027	6	31347566	Intergenic	UPSTREAM	ZDHHC20P2	pseudogene
rs2395491	6	31342420	Intergenic	DOWNSTREAM	RNU6-283P	snRNA
rs2516417	6	31459636	Regulatory Feature	REGULATORY	-	-
rs2516510	6	31449914	Intergenic	DOWNSTREAM	HCP5	sense overlapping
rs2517985	6	31118942	Transcript	INTRONIC	CCHCR1	protein coding
rs2523708	6	31451279	Intergenic	INTERGENIC	-	-
rs2534666	6	31468546	Intergenic	UPSTREAM	Y_RNA	misc RNA
rs2844502	6	31445216	Non-Coding Transcript	NONCODING_CHANGE	HCP5	sense overlapping
rs2844645	6	31015182	Intergenic	INTERGENIC	-	-
rs2853950	6	31236175	Intergenic	DOWNSTREAM	HLA-C	protein coding
rs2894176	6	30986038	Transcript	INTRONIC	MUC22	protein coding
rs2894207	6	31263751	Transcript	INTRONIC	XXbac-BPG248L24.13	lincRNA
rs3094205	6	31091862	Intergenic	UPSTREAM	CDSN	protein coding
rs3130467	6	31187075	Intergenic	UPSTREAM	XXbac-BPG299F13.15	pseudogene
rs3130517	6	31190303	Intergenic	UPSTREAM	XXbac-BPG299F13.15	pseudogene
rs3130573	6	31106268	Intergenic	DOWNSTREAM	CCHCR1	protein coding
rs34100370	6	31339937	Intergenic	DOWNSTREAM	RNU6-283P	snRNA
rs4349859	6	31365787	Regulatory Feature	REGULATORY	-	-
rs4358666	6	31340477	Intergenic	DOWNSTREAM	RNU6-283P	snRNA
rs4418214	6	31391401	Transcript	INTRONIC	HCP5	sense overlapping
rs45533135	6	31430951	Non-Coding Transcript	NONCODING_CHANGE	HCP5	sense overlapping
rs4624908	6	31342827	Intergenic	DOWNSTREAM	RNU6-283P	snRNA
rs6075938	20	22689686	Intergenic	INTERGENIC	-	-
rs746647	6	31114182	Transcript	INTRONIC	CCHCR1	protein coding
rs7754026	6	31345064	Intergenic	UPSTREAM	ZDHHC20P2	pseudogene
rs7756521	6	30848253	Intergenic	UPSTREAM	DDR1	protein coding
rs7773175	6	31240959	Intergenic	UPSTREAM	HLA-C	protein coding
rs7775117	6	31345486	Coding Transcript	NONCODING_CHANGE	FGFR3P1	pseudogene
rs8365	6	32148403	Intergenic	DOWNSTREAM	PBX2	protein coding
rs9262492	6	30986015	Transcript	INTRONIC	MUC22	protein coding
rs9262498	6	30986835	Transcript	INTRONIC	MUC22	protein coding
rs9380237	6	31264392	Transcript	INTRONIC	XXbac-BPG248L24.13	lincRNA

Supplementary Table S7: This table shows the genomic position and the nearest gene of every SNP in the top 20 SNP-SNP interactions in terms of p-value or improvement metric value from both datasets.

| Gene1	Gene2	phs000019.v1.p1				phs000982.v1.p1			
		SNP1,SNP2,Pattern	Pairwise Pval	Improvement Metric Value	Odds Ratio	SNP1,SNP2,Pattern	Pairwise Pval	Improvement Metric Value	Odds Ratio
HLA-C	PSORS1C1	rs1265078,rs7773175,4	4.69×10^{-25}	6.48×10^{11}	3.0436	rs6911408,rs2853953,4	3.51×10^{-28}	1.30×10^{9}	2.5349
PSORS1C1	XXbac-BPG248L24.13	rs1265078,rs2894207,4	1.43×10^{-26}	8.94×10^{10}	3.3389	rs6911408,rs9468932,4	2.00×10^{-28}	4.77×10^{10}	2.5974
CCHCR1	HLA-C	rs3130573,rs7773175,4	5.68×10^{-24}	5.35×10^{10}	3.0176	rs3130453,rs2249742,2	7.09×10^{-18}	1.11×10^{9}	1.9954
XXbac-BPG248L24.13	Y_RNA	rs9380237,rs2534666,4	1.11×10^{-20}	5.02×10^{10}	2.7506	rs9380237,rs2596542,4	6.23×10^{-20}	6.53×10^{6}	2.1035
XXbac-BPG248L24.13	XXbac-BPG299F13.15	rs3130467,rs2894207,4	7.28×10^{-27}	3.86×10^{10}	3.3781	rs1639110,rs9380238,4	6.25×10^{-19}	3.34×10^{7}	2.2810
HLA-C	XXbac-BPG299F13.15	rs3130517,rs7773175,4	1.45×10^{-26}	2.46×10^{9}	3.1788	rs6933647,rs2524096,5	5.16×10^{-18}	5.07×10^{6}	2.5830
MUC22	PSORS1C1	rs9262498,rs1265078,4	3.71×10^{-20}	6.46×10^{8}	2.6695	rs7776233,rs9263717,4	1.99×10^{-22}	6.19×10^{6}	2.2224
CCHCR1	XXbac-BPG248L24.13	rs3130573,rs2894207,4	2.26×10^{-24}	5.66×10^{8}	3.1827	rs130076,rs9380238,4	4.02×10^{-18}	1.40×10^{7}	2.2358
PSORS1C1	RNU6-283P	rs2844580,rs1265078,2	6.06×10^{-14}	394.984	2.1622	rs1265078,rs4624908,5	1.43×10^{-19}	4.90×10^{11}	2.2451
CDSN	XXbac-BPG248L24.13	rs3094205,rs9380237,4	2.96×10^{-18}	1.89×10^{8}	2.5056	rs3130982,rs9366778,5	5.54×10^{-16}	3.63×10^{6}	3.1811
MICA	RNU6-283P	rs9266490,rs6933779,4	6.74×10^{-15}	8.79×10^{7}	2.9467	rs4358666,rs9468992,5	4.52×10^{-19}	4.74×10^{6}	2.0073
CCHCR1	CDSN	rs3094205,rs3130573,4	2.89×10^{-17}	7.90×10^{7}	2.4316	rs6913137,rs130069,5	3.62×10^{-22}	1.82×10^{6}	2.2245
CCHCR1	MUC22	rs9262498,rs3130573,4	9.46×10^{-16}	7.15×10^{7}	2.3177	rs13210132,rs130069,5	1.27×10^{-19}	2.27×10^{6}	2.2636
MUC22	XXbac-BPG248L24.13	rs9262492,rs2894207,4	2.86×10^{-23}	4.47×10^{7}	3.0012	rs7776233,rs1960278,4	4.34×10^{-15}	6.28×10^{8}	1.8616
HLA-C	XXbac-BPG248L24.13	rs3132486,rs9380237,2	1.89×10^{-17}	2.96×10^{7}	2.4126	rs2853952,rs9468932,4	6.31×10^{-28}	6.98×10^{8}	2.5409
CDSN	MUC22	rs9394031,rs3094205,4	1.01×10^{-16}	5.85×10^{6}	2.9664	rs7776233,rs2233959,4	1.54×10^{-15}	1.33×10^{6}	1.8673
HCG27	HCP5	rs7762933,rs9501106,2	4.19×10^{-15}	4.85×10^{6}	2.5424	rs3132506,rs45533135,5	5.56×10^{-20}	5.90×10^{7}	2.0667
HCP5	XXbac-BPG248L24.13	rs2894207,rs2844502,3	1.16×10^{-21}	1.10×10^{6}	2.7467	rs1960278,rs4947314,4	2.87×10^{-18}	2.09×10^{9}	2.1659
CDSN	HLA-C	rs3094205,rs7773175,4	1.23×10^{-19}	2.48×10^{6}	2.6222	rs3094222,rs2524096,5	2.83×10^{-18}	9.25×10^{6}	2.5940
HCP5	RNU6-283P	rs9266490,rs9501106,4	1.12×10^{-14}	1.81×10^{6}	2.9946	rs4358666,rs10223568,5	2.52×10^{-19}	4.53×10^{6}	2.0154
HCP5	MUC22	rs9394031,rs9501106,4	4.48×10^{-16}	1.31×10^{6}	3.4966	rs13210132,rs45533135,5	5.05×10^{-20}	5.71×10^{6}	2.2482
HLA-B	PSORS1C1	rs1265078,rs2156875,3	2.17×10^{-16}	110 613	2.3419	rs6911408,rs2523619,4	2.29×10^{-25}	7.73×10^{9}	2.3932
RNU6-283P	XXbac-BPG299F13.15	rs2844580,rs3130467,2	7.02×10^{-20}	4000.37	2.5763	rs1639110,rs4358666,5	1.31×10^{-21}	1.60×10^{10}	2.2792
HCG20	PSORS1C1	rs12526186,rs1265078,4	2.64×10^{-16}	90 558.8	2.7948	rs28894086,rs1265078,4	2.99×10^{-17}	4.10×10^{9}	2.0505
PSORS1C1	RPL3P2	rs1265078,rs12191877,4	6.80×10^{-28}	101 408	3.5547	rs6931633,rs2853935,4	7.53×10^{-25}	2.18×10^{9}	2.3316
HCP5	HLA-C	rs7773175,rs2516510,3	1.06×10^{-16}	2864.29	2.3592	rs2853952,rs45533135,5	7.64×10^{-29}	5.76×10^{9}	2.4587
CDSN	HCG22	rs2523857,rs3094205,2	1.23×10^{-14}	185 829	2.2090	rs16898629,rs6913137,5	2.40×10^{-22}	2.74×10^{6}	2.2284
CDSN	HCP5	rs3094205,rs9295991,4	1.31×10^{-14}	174 387	2.3617	rs6913137,rs45533135,5	1.60×10^{-22}	4.11×10^{6}	2.2155
HCP5	RPL3P2	rs12191877,rs2844502,3	1.35×10^{-27}	51 197.2	3.3261	rs2524052,rs4947314,4	4.16×10^{-18}	1.44×10^{9}	2.1490
USP8P1	XXbac-BPG248L24.13	rs3132485,rs9380237,2	3.64×10^{-15}	153 429	2.2475	rs2844603,rs9468932,4	7.15×10^{-24}	1.34×10^{6}	2.3445
HLA-C	LINC01149	rs7773175,rs2516460,4	8.99×10^{-18}	33 819.1	2.4525	rs2524096,rs28575156,4	1.51×10^{-20}	4.55×10^{7}	2.3562
HLA-C	USP8P1	rs3132485,rs7773175,2	7.92×10^{-18}	38 353.5	2.4264	rs9264602,rs9468914,5	5.92×10^{-15}	1.81×10^{6}	2.3210
PSORS1C1	WASF5P	rs1265078,rs9468926,3	1.36×10^{-14}	1759.12	2.2168	rs6931633,rs2524163,4	1.18×10^{-24}	1.39×10^{9}	2.3224
RNU6-283P	XXbac-BPG154L12.4	rs9266490,rs6916062,4	4.25×10^{-16}	27 453.4	4.3360	rs4358666,rs6916062,5	2.92×10^{-15}	898 239	1.8483
PSORS1C3	XXbac-BPG248L24.13	rs887464,rs9380237,2	2.97×10^{-14}	18 803.2	2.1875	rs887468,rs9468932,4	7.80×10^{-28}	1.29×10^{7}	2.5444
RPL3P2	ZDHHC20P2	rs2244027,rs12191877,2	4.28×10^{-27}	16 113.6	3.2691	rs12191877,rs13202464,5	3.90×10^{-30}	3.10×10^{6}	2.4911
HLA-C	ZDHHC20P2	rs2244027,rs7773175,2	2.35×10^{-15}	129.232	2.2599	rs2853952,rs13202464,5	1.52×10^{-28}	2.91×10^{9}	2.4497
CCHCR1	PSORS1C1	rs1265078,rs3130453,3	3.30×10^{-15}	7258.28	2.2521	rs6929464,rs1265112,4	5.22×10^{-16}	8.38×10^{7}	2.0687
HLA-B	HLA-C	rs7773175,rs2156875,3	7.53×10^{-17}	4038.26	2.3627	rs2844624,rs2523619,4	3.00×10^{-21}	2.16×10^{7}	2.1636
POU5F1	XXbac-BPG248L24.13	rs3094188,rs2894207,2	8.07×10^{-19}	1585.26	2.5253	rs6929434,rs9380238,5	1.55×10^{-17}	1.55×10^{7}	1.9712
HCP5	XXbac-BPG299F13.15	rs3130467,rs9501106,4	4.43×10^{-19}	634.442	3.3513	rs1639110,rs45533135,5	1.28×10^{-19}	1.64×10^{8}	2.0320
XXbac-BPG248L24.13	ZDHHC20P2	rs2244027,rs2894207,2	2.64×10^{-18}	484.266	2.4920	rs9380237,rs6927154,4	7.49×10^{-24}	2.42×10^{8}	2.3400
HLA-C	TCF19	rs2073717,rs7773175,2	3.25×10^{-16}	936.341	2.3163	rs7750641,rs2524096,5	3.95×10^{-18}	6.62×10^{6}	2.5844
HCG20	HLA-C	rs3131039,rs7773175,2	9.48×10^{-15}	32.0711	2.2230	rs12527188,rs2853961,4	5.51×10^{-19}	7.34×10^{8}	2.3412
XXbac-BPG299F13.15	ZDHHC20P2	rs2244027,rs3130517,2	5.40×10^{-19}	66.149	2.5096	rs1639110,rs7754026,5	3.78×10^{-20}	5.53×10^{8}	2.2293
LINC01149	PSORS1C1	rs1265078,rs2516460,4	7.68×10^{-14}	311.706	2.1767	rs6931633,rs28575156,4	4.52×10^{-23}	3.63×10^{7}	2.6075
DHFRP2	XXbac-BPG248L24.13	rs2894207,rs9266329,3	5.93×10^{-18}	215.656	2.4661	rs9366778,rs4959062,6	1.21×10^{-16}	1.66×10^{7}	4.1400
HLA-C	MICB	rs3131636,rs7773175,4	1.46×10^{-15}	208.315	2.6027	rs2524096,rs3130612,5	1.79×10^{-17}	1.46×10^{7}	2.4908
HLA-C	RNU6-283P	rs2844580,rs7773175,2	5.32×10^{-15}	57.1072	2.2327	rs2853952,rs2523535,3	4.78×10^{-27}	9.20×10^{7}	2.3439
C2	CCHCR1	rs3130573,rs9267673,4	1.79×10^{-20}	119.671	3.3632	rs130069,rs9267673,5	3.31×10^{-17}	688 988	2.0498
MICA	XXbac-BPG299F13.15	rs3130467,rs9266844,4	2.69×10^{-18}	104.609	2.8307	rs1639110,rs17206680,5	8.36×10^{-18}	2.50×10^{6}	1.9661
HLA-C	PSORS1C3	rs4713438,rs7773175,2	9.56×10^{-15}	31.7954	2.2270	rs3130506,rs2249742,2	2.35×10^{-16}	3.35×10^{7}	1.9880
C2	ZDHHC20P2	rs2442749,rs9267673,2	4.05×10^{-20}	52.8453	3.0754	rs13202464,rs9267677,5	4.84×10^{-18}	4.99×10^{6}	2.0148
PSORS1C1	XXbac-BPG299F13.15	rs1265078,rs3130467,4	1.02×10^{-17}	27.5987	2.4224	rs6929464,rs1639110,4	8.13×10^{-19}	2.57×10^{7}	2.2778
LINC00243	XXbac-BPG248L24.13	rs1264344,rs2894207,2	3.54×10^{-17}	36.1766	2.4510	rs4248149,rs9380237,4	2.92×10^{-20}	1.39×10^{7}	2.4030
PPIAP9	RNU6-283P	rs2253907,rs9267464,4	2.38×10^{-17}	50.5393	3.6310	rs4358666,rs9267464,5	1.22×10^{-15}	2.15×10^{6}	1.8643
HCG22	HLA-C	rs2523857,rs7773175,2	8.42×10^{-15}	36.079	2.2320	rs3131788,rs2524096,5	2.66×10^{-18}	9.85×10^{6}	2.5957
HCG20	XXbac-BPG299F13.15	rs3129980,rs3130517,2	1.01×10^{-18}	35.4352	2.5010	rs28894086,rs3130517,4	5.44×10^{-18}	5.53×10^{6}	2.1174
LINC00243	RPL3P2	rs886423,rs12191877,2	2.61×10^{-24}	26.4495	2.9820	rs12660883,rs2524052,4	4.03×10^{-16}	1.22×10^{6}	2.1390
HCP5	PPIAP9	rs9501106,rs9267464,4	5.23×10^{-17}	22.9963	3.9233	rs45533135,rs9267464,5	5.90×10^{-15}	2.04×10^{6}	1.9821

**Supplementary Table S8:** This table shows the common gene-gene interactions predicted from the SNP-SNP interactions with top 10000th improvement metric value from datasets phs000019.v1.p1 and phs000982.v1.p1

Gene	Chr	Start Pos	End Pos	Type
LINC00243	6	30,766,431	30,798,436	Known processed transcript
MUC22	6	30,978,251	31,003,179	Known protein coding
HCG22	6	31,021,227	31,027,667	Known lincRNA
PSORS1C1	6	31,082,527	31,107,869	Known protein coding
CDSN	6	31,082,867	31,088,223	Known protein coding
CCHCR1	6	31,110,216	31,126,015	Known protein coding
TCF19	6	31,126,319	31,134,936	Known protein coding
POU5F1	6	31,132,119	31,148,508	Known protein coding
PSORS1C3	6	31,141,512	31,145,676	Known sense intronic
HCG27	6	31,165,537	31,171,745	Known protein coding
XXbac-BPG299F13.15	6	31,190,690	31,190,870	Known pseudogene
HLA-C	6	31,236,526	31,239,907	Known protein coding
USP8P1	6	31,243,349	31,246,531	Known pseudogene
RPL3P2	6	31,248,094	31,249,296	Known pseudogene
WASF5P	6	31,255,287	31,256,741	Known pseudogene
XXbac-BPG248L24.13	6	31,261,685	31,269,419	Novel lincRNA
HLA-B	6	31,321,649	31,324,965	Known protein coding
DHFRP2	6	31,334,129	31,334,675	Known pseudogene
RNU6-283P	6	31,337,911	31,338,017	Known snRNA
ZDHHC20P2	6	31,348,188	31,348,616	Known pseudogene
HCP5	6	31,368,479	31,445,283	Known sense overlapping
Y_RNA	6	31,369,929	31,370,027	Novel misc RNA
MICA	6	31,371,356	31,383,092	Known protein coding
LINC01149	6	31,409,444	31,414,750	Novel lincRNA
MICB	6	31,462,658	31,478,901	Known protein coding
PPIAP9	6	31,487,257	31,488,068	Known pseudogene
C2	6	31,865,562	31,913,449	Known protein coding
XXbac-BPG154L12.4	6	32,223,488	32,233,615	Novel antisense
HCG20	6	30,760,027	30,760,027	Known lincRNA

Supplementary Table S9: This table shows the genes found among the 60 common gene-gene interactions predicted from the SNP-SNP interactions with top 10000 improvement metric value from datasets phs000019.v1.p1 and phs000982.v1.p1

No. of SNP	Mode	Heritability			
		0.1	0.2	0.3	0.4
1000	Without Look-up Table	54.81s	54.93s	54.82s	54.97s
	With Look-up Table	6.155s	6.303s	6.280s	6.292s
	Speed-Up	8.906x	8.715x	8.729x	8.737x
5000	Without Look-up Table	1470s	1467s	1465s	1469s
	With Look-up Table	138.2s	138.3s	138.366s	138.5s
	Speed-Up	10.63x	10.61x	10.59x	10.60x
10000	Without Look-up Table	5777s	5784s	5783s	5833s
	With Look-up Table	550s	551s	551s	551s
	Speed-Up	10.50x	10.50x	10.50x	10.59x

Supplementary Table S10: This table shows the runtime of the program with or without the pre-computed look-up table under different datasets.
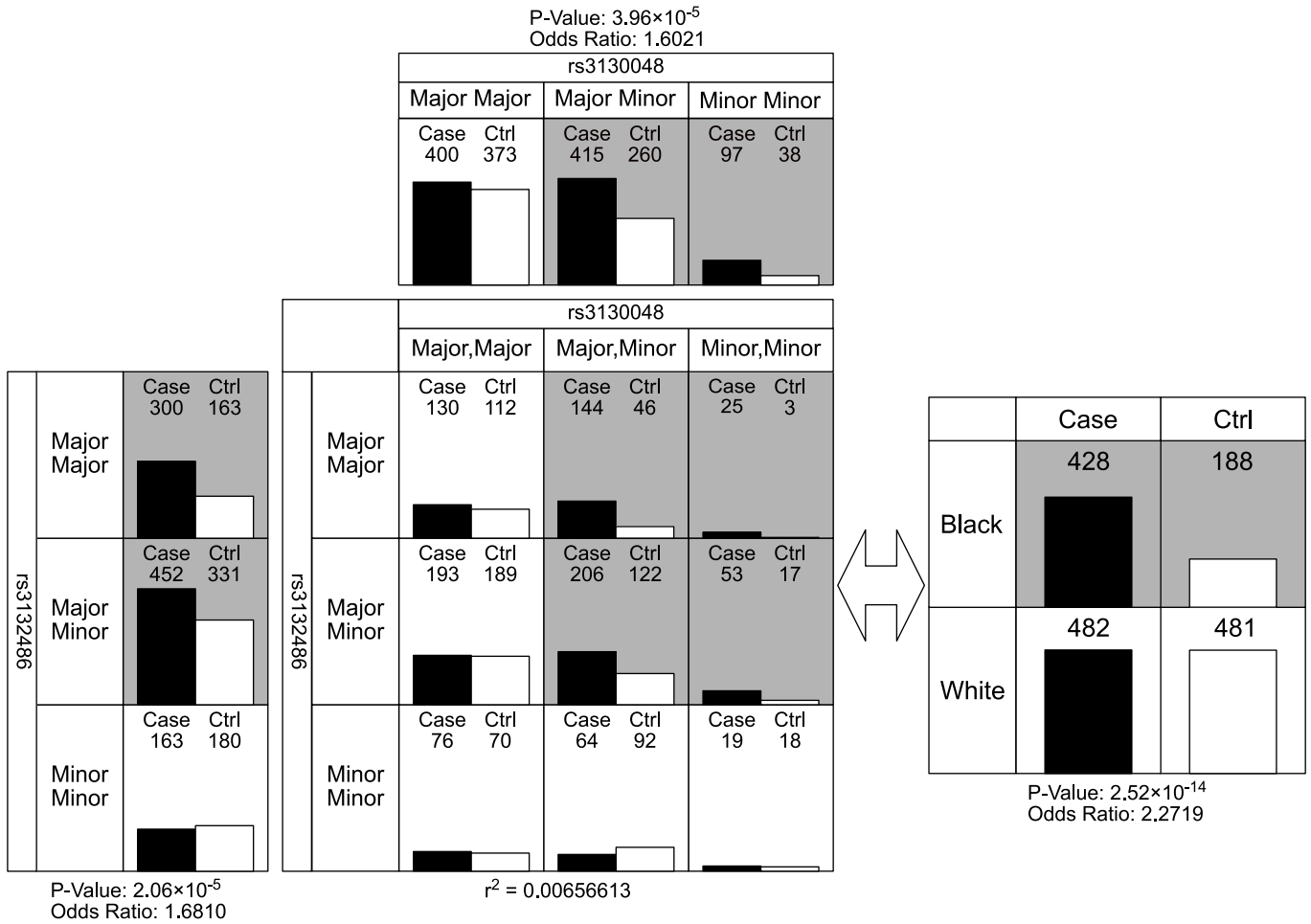
Supplementary Figure S1: This figure shows the interaction between SNPs rs3132486 and rs3130048 found from dataset phs000019.v1.p1 which is an example of an potential non-linear SNP-SNP interaction.
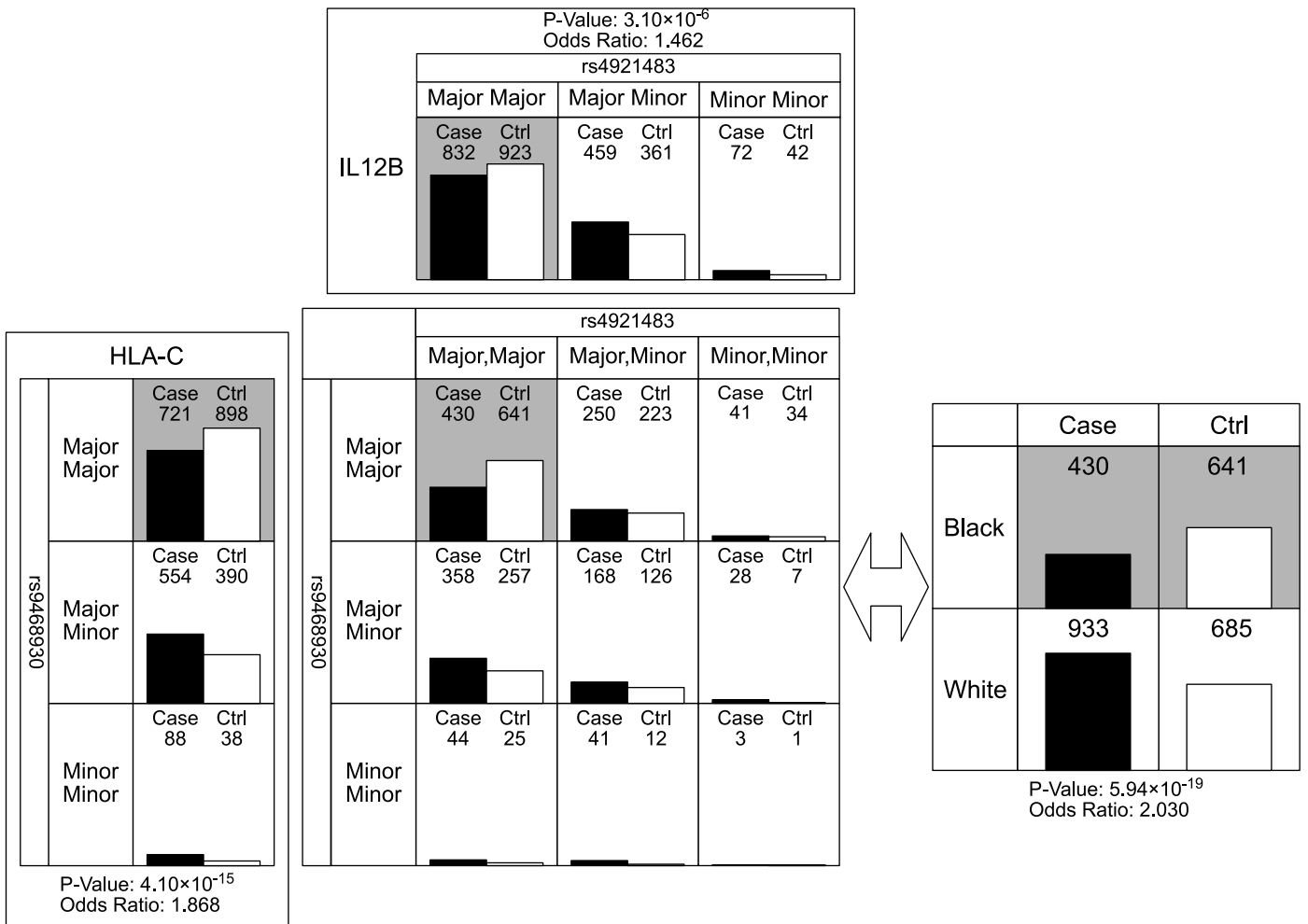
Supplementary Figure S2: This figure shows the interaction between two SNPs rs9468930 and rs4921483 imputed from dataset phs000982.v1.p1. which is an example of a SNP-SNP interaction between two psoriasis associated genes *HLA-C* and *IL12B*.
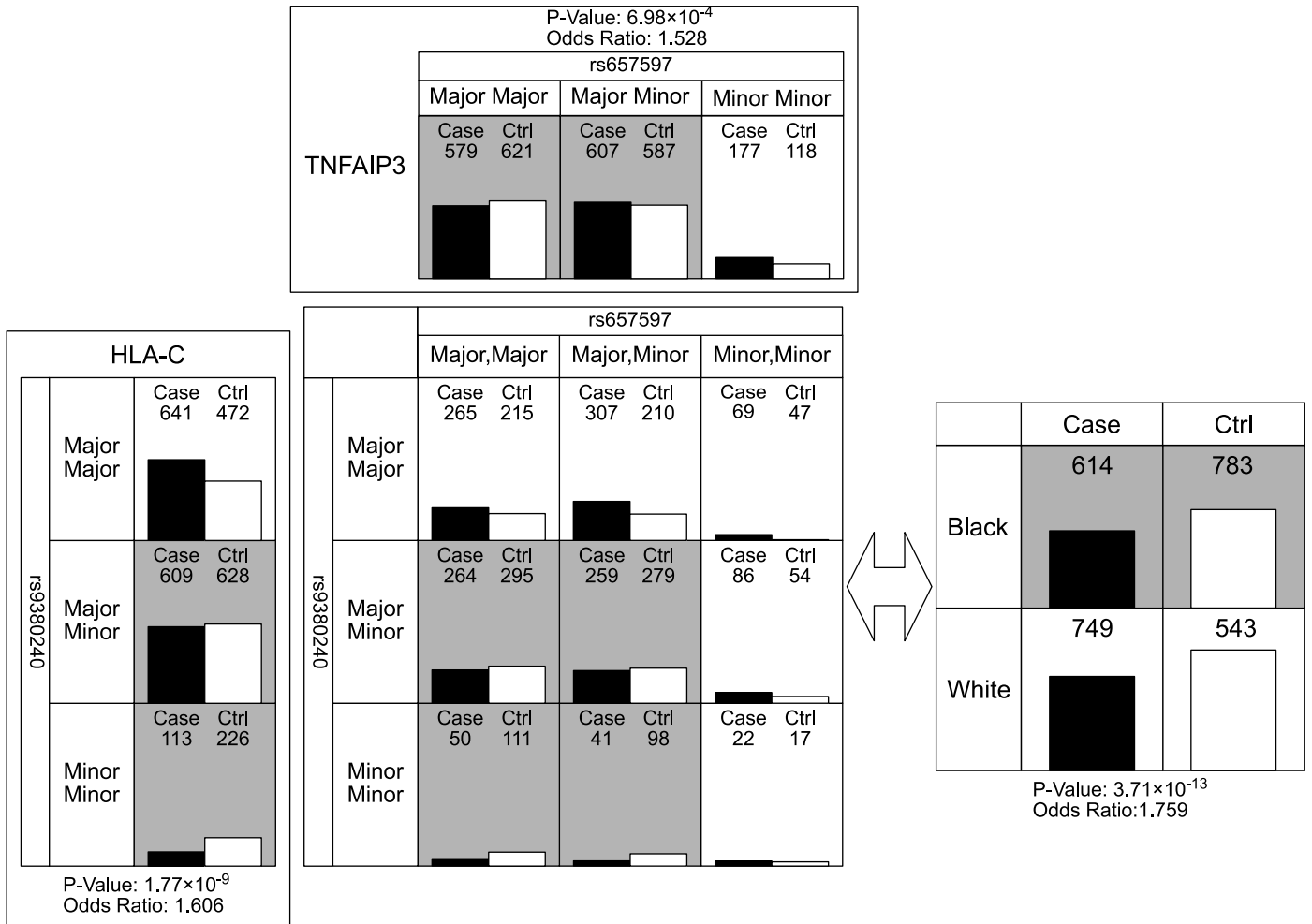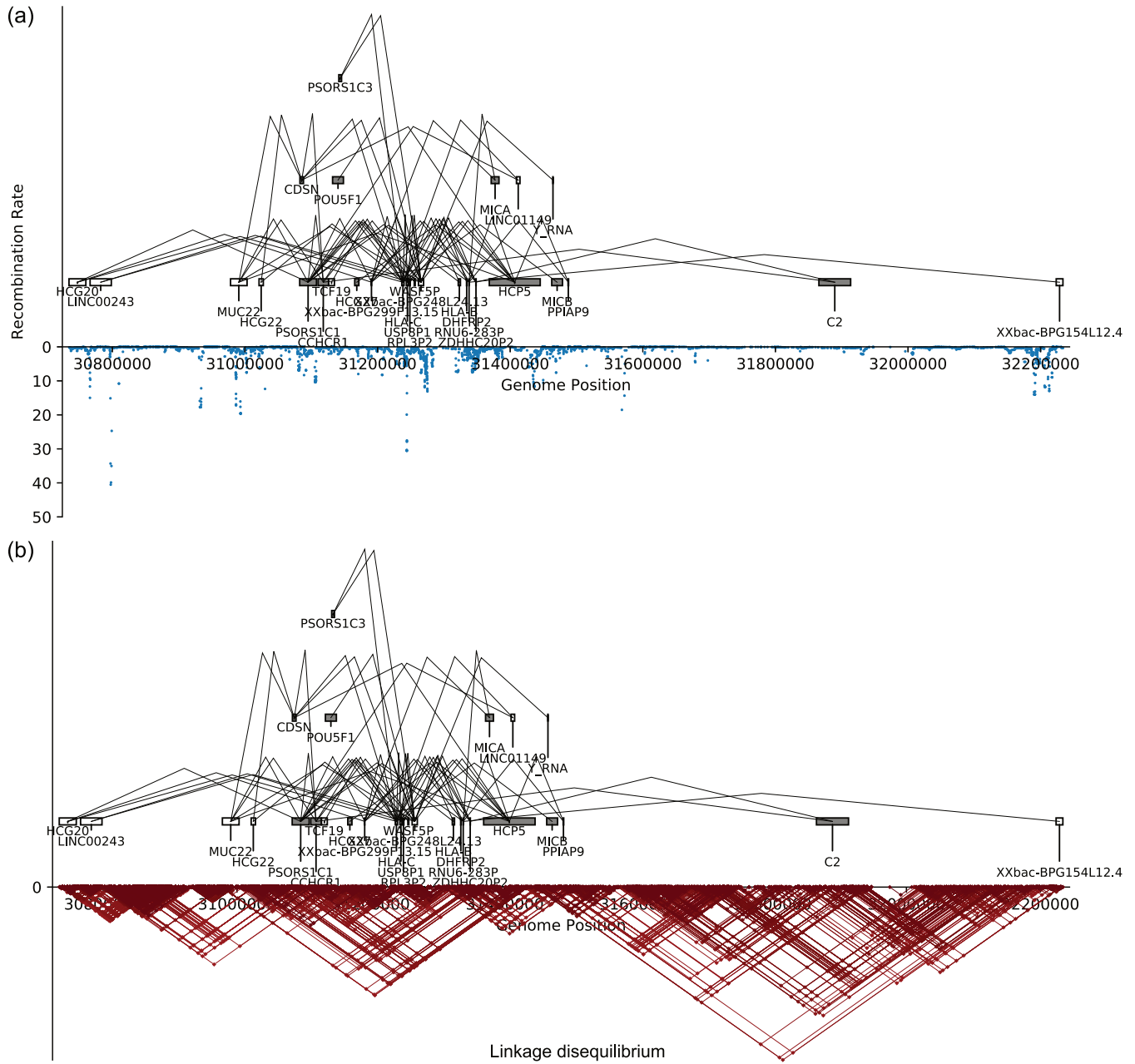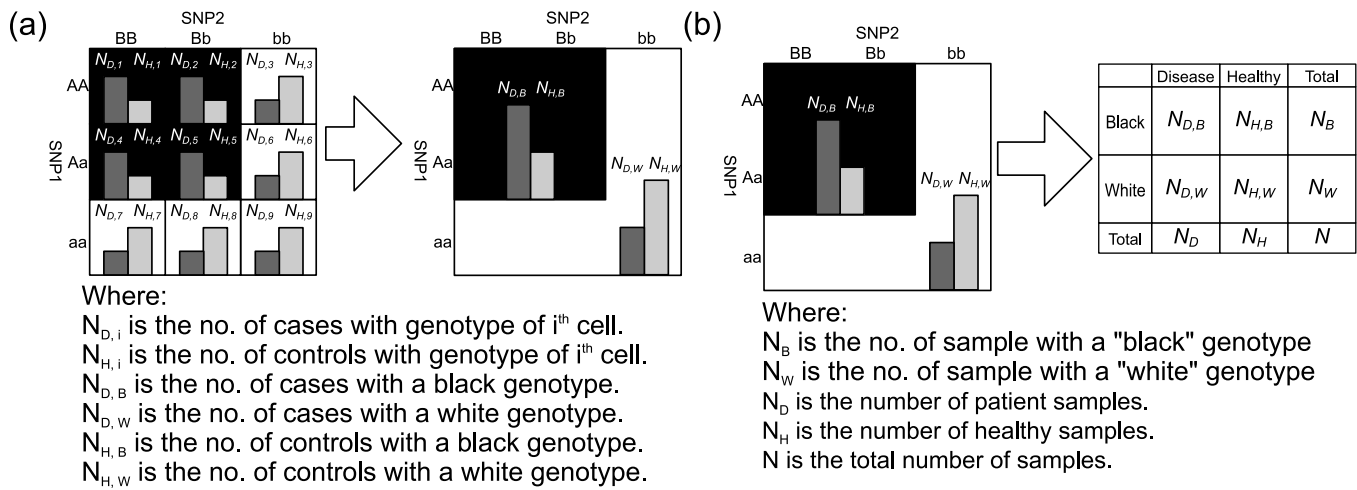
Supplementary Figure S3: This figure shows the interaction between two SNPs rs9380240 and rs657597 imputed from dataset phs000982.v1.p1 which is an example of a SNP-SNP interaction between two psoriasis associated genes *HLA-C* and *TNFAIP3*.

Venn diagram on gene pairs between phs000019 and phs000982

3439   62   368

phs000019   phs000982
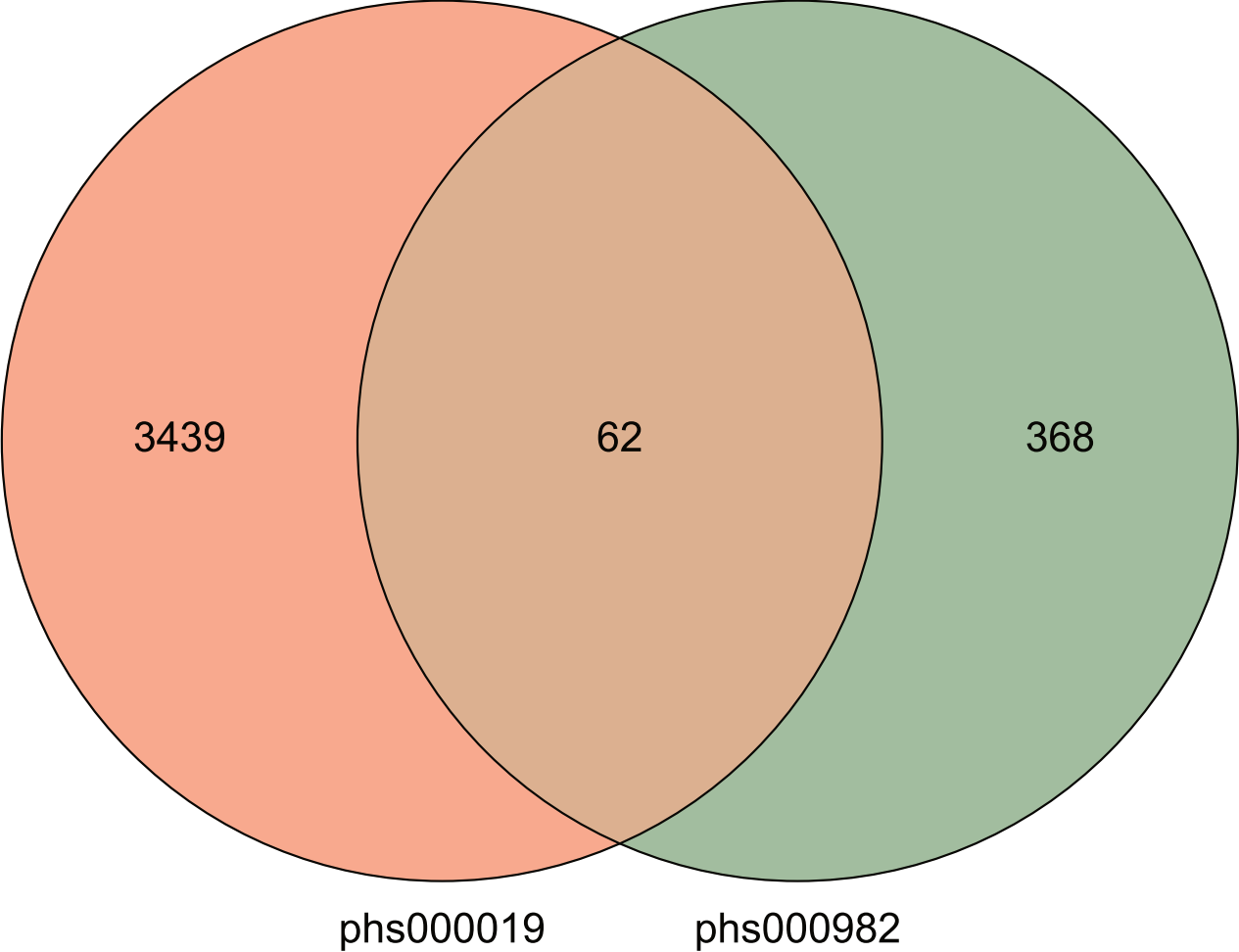
Supplementary Figure S4: This figure shows the number of gene-gene interactions predicted from the top 10000 SNP-SNP interactions in terms of improvement metric value found from datasets phs000019.v1.p1 and phs000982.v1.p1.

Supplementary Figure S5: In this figure, both parts (a) and (b) show the gene network constructed from 60 common gene-gene interactions predicted from the top 10000 SNP-SNP interactions in terms of improvement metric value found from datasets phs000019.v1.p1 and phs000982.v1.p1 with a linear layout, where the genes are laid down according to their genomic position in Chromosome 6. The genomic combination rate and the SNP pairs with a significant linkage disequilibrium score (r larger than 0.9) along Chromosome 6 from position 30734602 to 32233615 are plotted in parts (a) and (b) respectively.

Supplementary Figure S6: In this figure, part (a) shows the process of aggregating the number of cases and controls with black and white genotypes in the 3x3 genotype table of SNP_1 and SNP_2, where the genotypes are coloured according to the pattern 1 in Fig. 5b. Meanwhile, part (b) shows the process of arranging the total numbers of cases and controls calculated in part (a) into a 2x2 contingency table. Major alleles are represented by upper-case letters (i.e. A, B) and minor alleles are represented by lower-case letters (i.e. a, b).