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Supplemental Data

Rare and Common Variants in *CARD14*, Encoding an Epidermal Regulator of NF-kappaB, in Psoriasis

Catherine T. Jordan, Li Cao, Elisha D.O. Roberson, Shenghui Duan, Cynthia A. Helms, Rajan P. Nair, Kristina Callis Duffin, Philip E. Stuart, David Goldgar, Genki Hayashi, Emily H. Olfson, Bing-Jian Feng, Clive R. Pullinger, John P. Kane, Carol Wise, Raphaela Goldbach-Mansky, Michelle A. Lowes, Lynette Peddle, Vinod Chandran, Wilson Liao, Proton Rahman, Gerald G. Krueger, Dafna Gladman, James T. Elder, Alan Menter, and Anne M. Bowcock

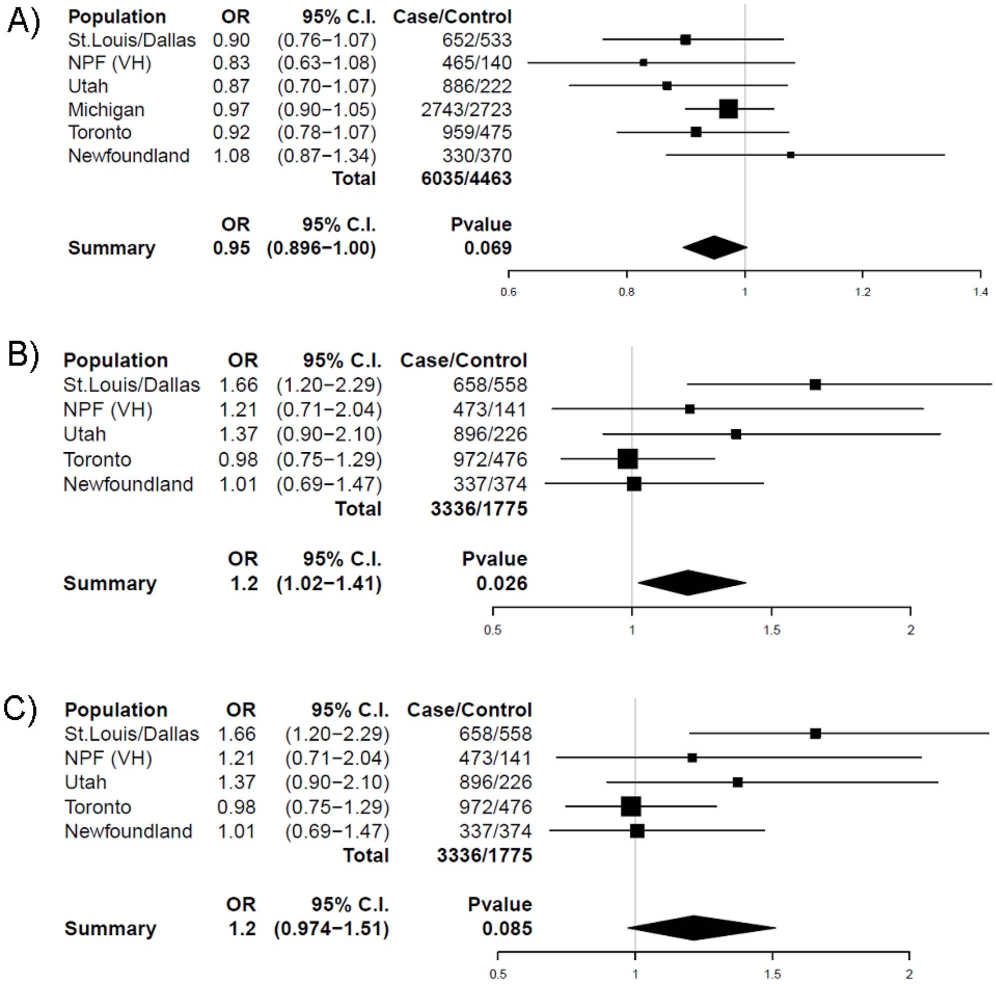
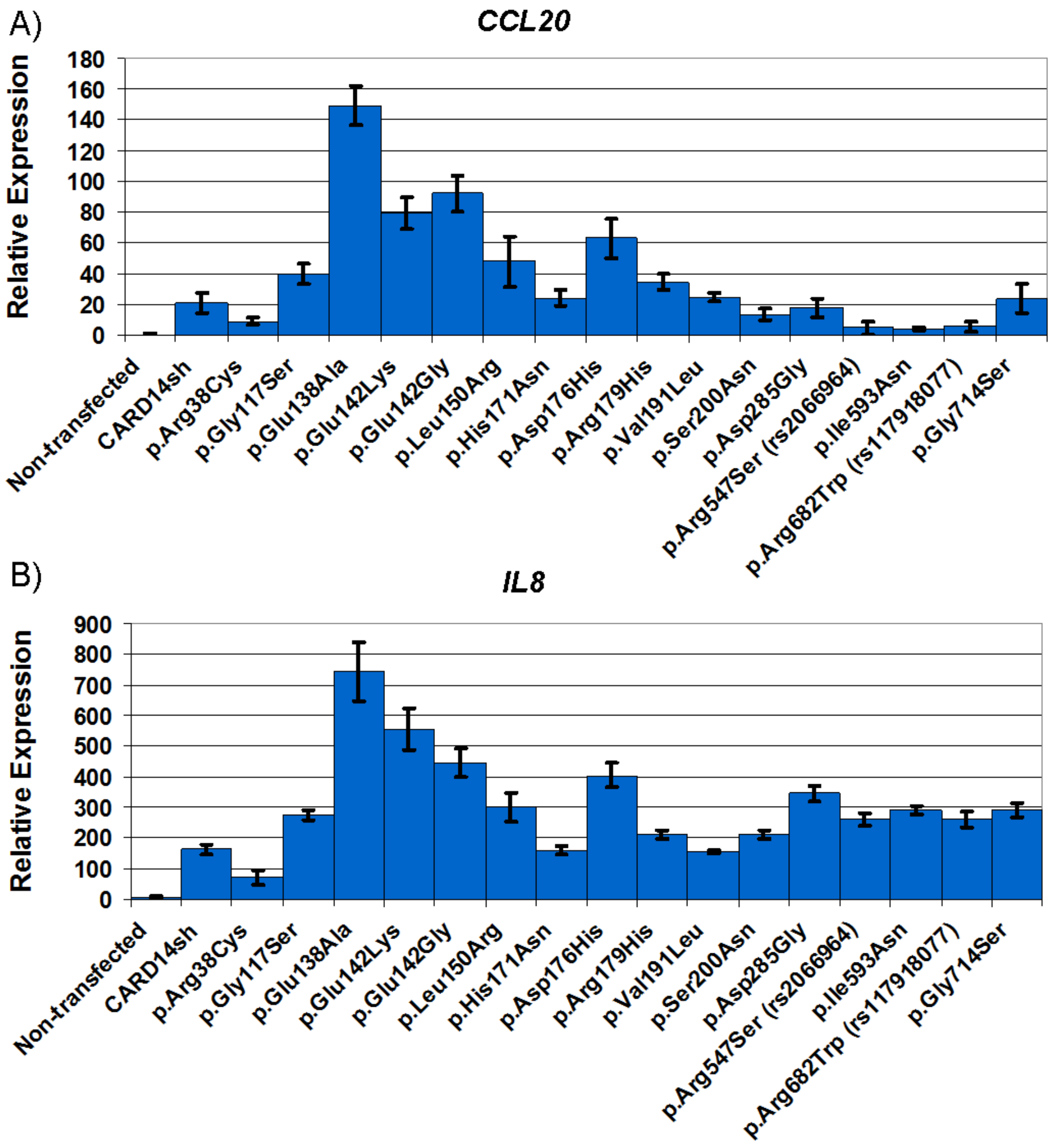


Figure S1. Test for Association of Psoriasis with rs2066964 and rs34367357 across 6 Case/Control Cohorts of European Ancestry

The results of meta-analysis in the six cohorts of European ancestry based on the fixed- and random-effects models are shown.

(A) fixed-effects meta-analysis for rs2066964, (B) fixed-effects meta-analysis for rs34367357, and (C) random-effects meta-analysis for rs34367357. Results of random-effects meta-analysis for rs2066964 were identical to those for fixed-effects and are thus not presented.


A)
CCL20
Relative Expression
0
20
40
60
80
100
120
140
160
180
Non-transfected
CARD14sh
p.Arg38Cys
p.Gly117Ser
p.Glu138Ala
p.Glu142Lys
p.Glu142Gly
p.Leu150Arg
p.His171Asn
p.Asp176His
p.Arg179His
p.Val191Leu
p.Ser200Asn
p.Asp285Gly
p.Arg547Ser (rs2066964)
p.Ile593Asn
p.Arg682Trp (rs117918077)
p.Gly714Ser
B)
IL8
Relative Expression
0
100
200
300
400
500
600
700
800
900
Non-transfected
CARD14sh
p.Arg38Cys
p.Gly117Ser
p.Glu138Ala
p.Glu142Lys
p.Glu142Gly
p.Leu150Arg
p.His171Asn
p.Asp176His
p.Arg179His
p.Val191Leu
p.Ser200Asn
p.Asp285Gly
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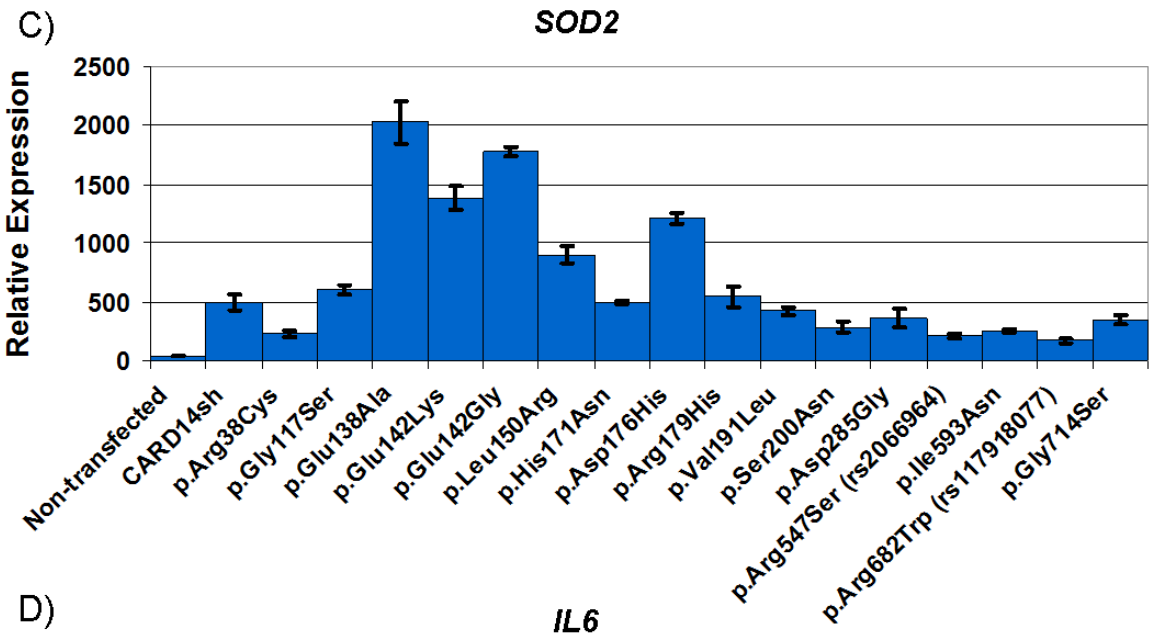
p.Ile593Asn
p.Arg682Trp (rs117918077)
p.Gly714Ser

C)


SOD2
Relative Expression
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500
1000
1500
2000
2500
Non-transfected
CARD14sh
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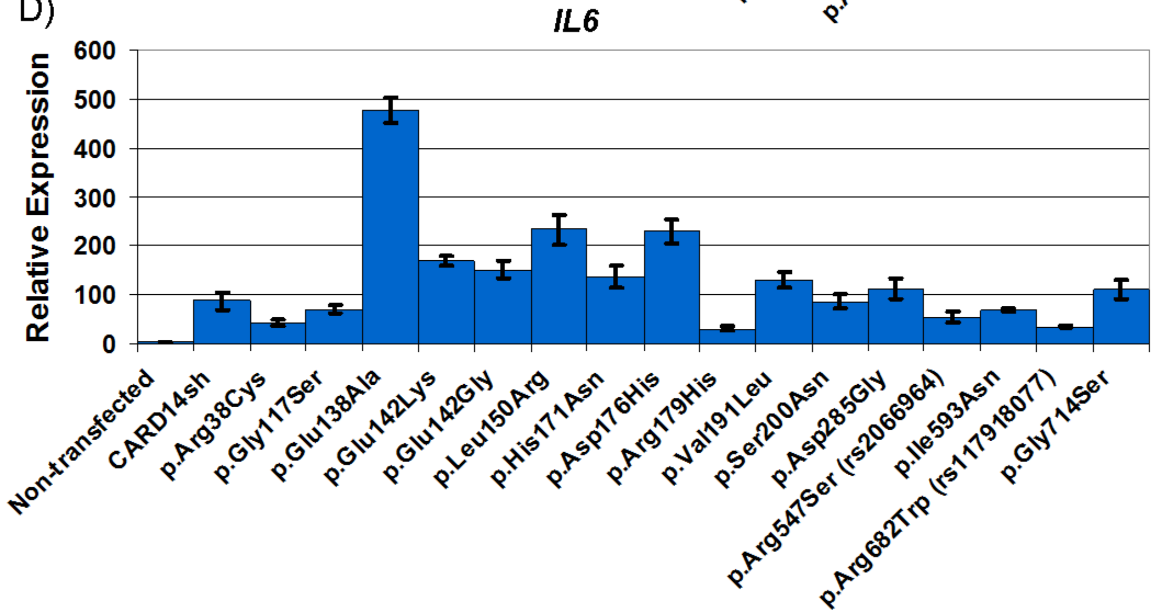
p.Gly117Ser
p.Glu138Ala
p.Glu142Lys
p.Glu142Gly
p.Leu150Arg
p.His171Asn
p.Asp176His
p.Arg179His
p.Val191Leu
p.Ser200Asn
p.Asp285Gly
p.Arg547Ser (rs2066964)
p.Ile593Asn
p.Arg682Trp (rs117918077)
p.Gly714Ser

D)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Relative Expression
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100
200
300
400
500
600
Non-transfected
CARD14sh
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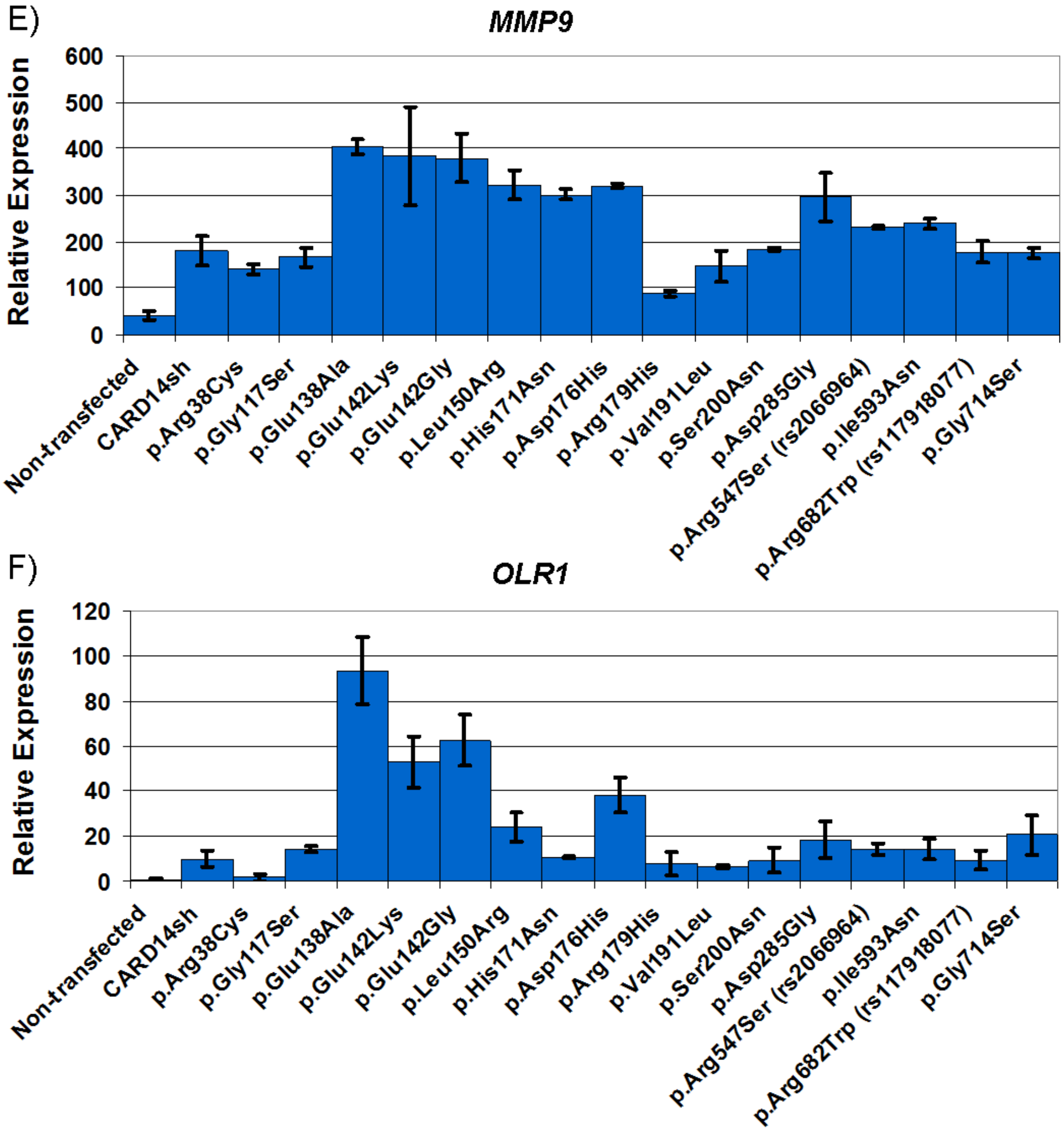
p.Glu142Lys
p.Glu142Gly
p.Leu150Arg
p.His171Asn
p.Asp176His
p.Arg179His
p.Val191Leu
p.Ser200Asn
p.Asp285Gly
p.Arg547Ser (rs2066964)
p.Ile593Asn
p.Arg682Trp (rs117918077)
p.Gly714Ser


E)
MMP9
Relative Expression
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100
200
300
400
500
600
Non-transfected
CARD14sh
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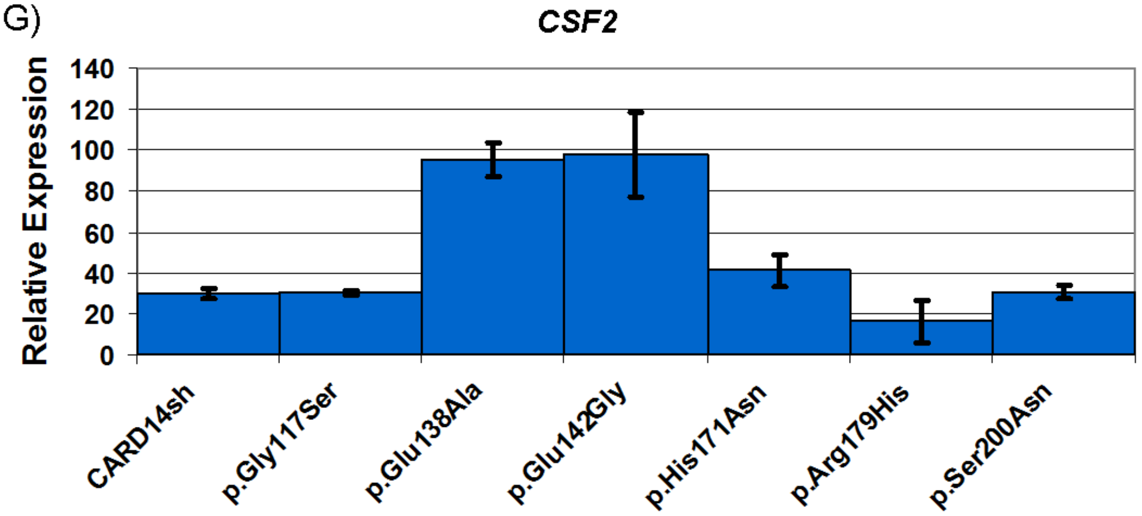
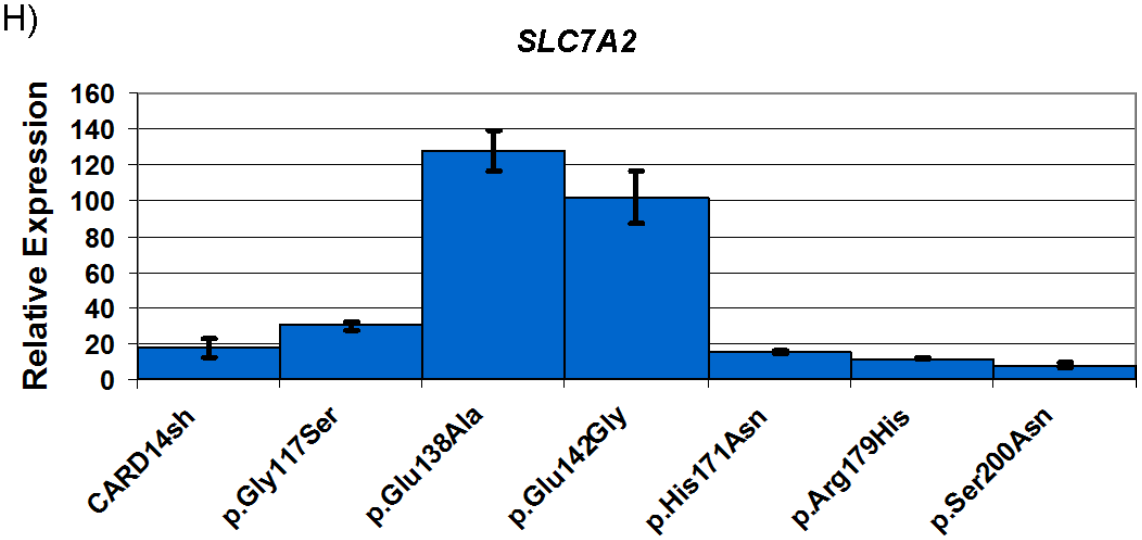
p.Gly117Ser
p.Glu138Ala
p.Glu142Lys
p.Glu142Gly
p.Leu150Arg
p.His171Asn
p.Asp176His
p.Arg179His
p.Val191Leu
p.Ser200Asn
p.Asp285Gly
p.Arg547Ser (rs2066964)
p.Ile593Asn
p.Arg682Trp (rs117918077)
p.Gly714Ser
F)
OLR1
Relative Expression
0
20
40
60
80
100
120
Non-transfected
CARD14sh
p.Arg38Cys
p.Gly117Ser
p.Glu138Ala
p.Glu142Lys
p.Glu142Gly
p.Leu150Arg
p.His171Asn
p.Asp176His
p.Arg179His
p.Val191Leu
p.Ser200Asn
p.Asp285Gly
p.Arg547Ser (rs2066964)
p.Ile593Asn
p.Arg682Trp (rs117918077)
p.Gly714Ser

G)


CSF2
Relative Expression
140
120
100
80
60
40
20
0
CARD14sh
p.Gly117Ser
p.Glu138Ala
p.Glu142Gly
p.His171Asn
p.Arg179His
p.Ser200Asn

H)


SLC7A2
Relative Expression
160
140
120
100
80
60
40
20
0
CARD14sh
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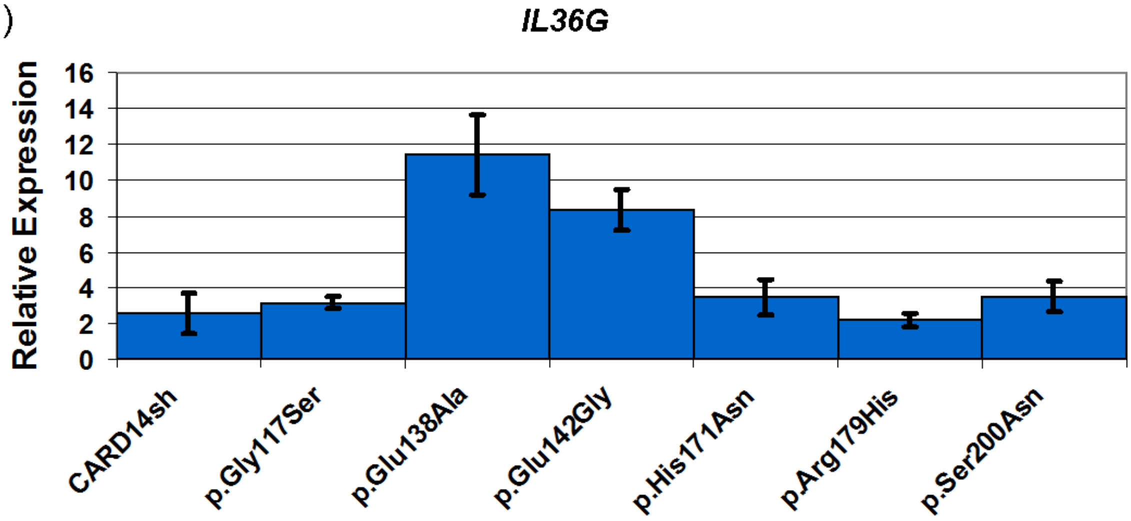
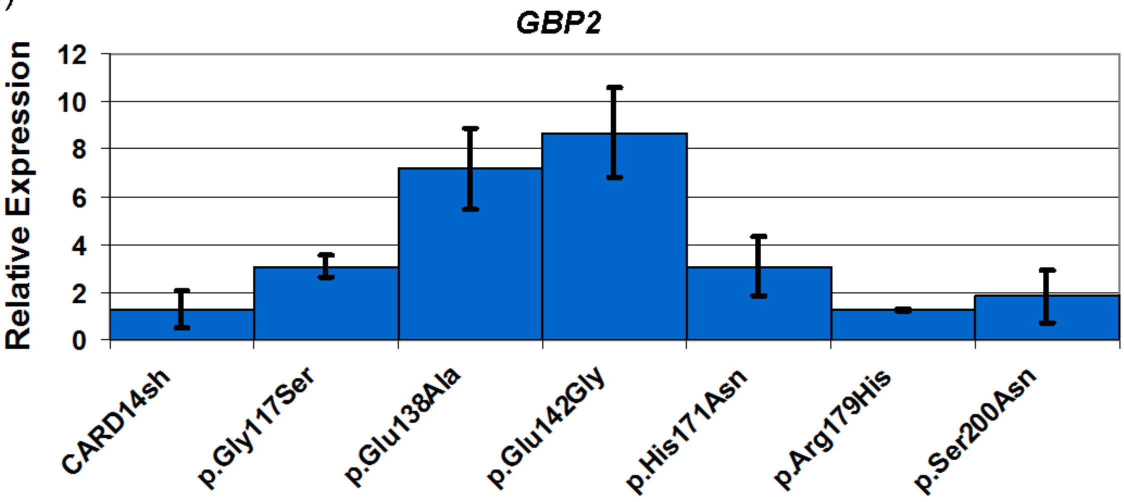
p.Glu138Ala
p.Glu142Gly
p.His171Asn
p.Arg179His
p.Ser200Asn

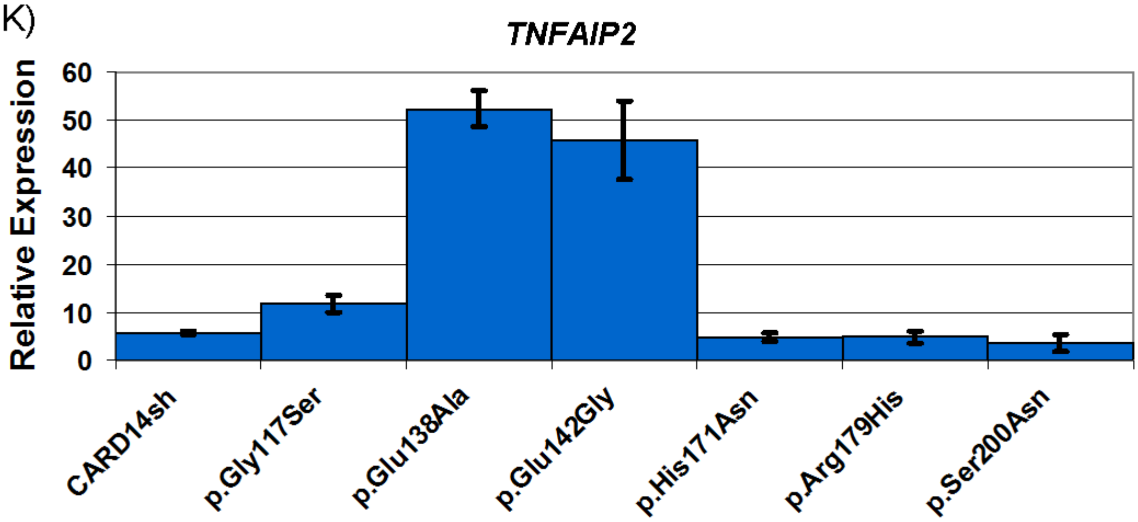
I)


IL36G

J)

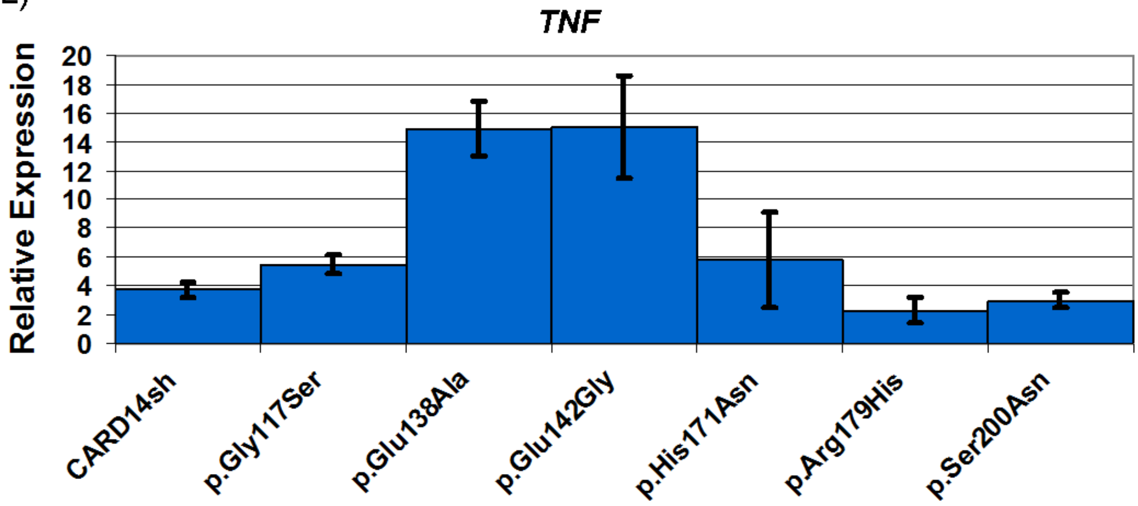

GBP2

K)



TNFAIP2
Relative Expression
0
10
20
30
40
50
60
CARD14sh
p.Gly117Ser
p.Glu138Ala
p.Glu142Gly
p.His171Asn
p.Arg179His
p.Ser200Asn

L)



TNF
Relative Expression
0
2
4
6
8
10
12
14
16
18
20
CARD14sh
p.Gly117Ser
p.Glu138Ala
p.Glu142Gly
p.His171Asn
p.Arg179His
p.Ser200Asn

M)

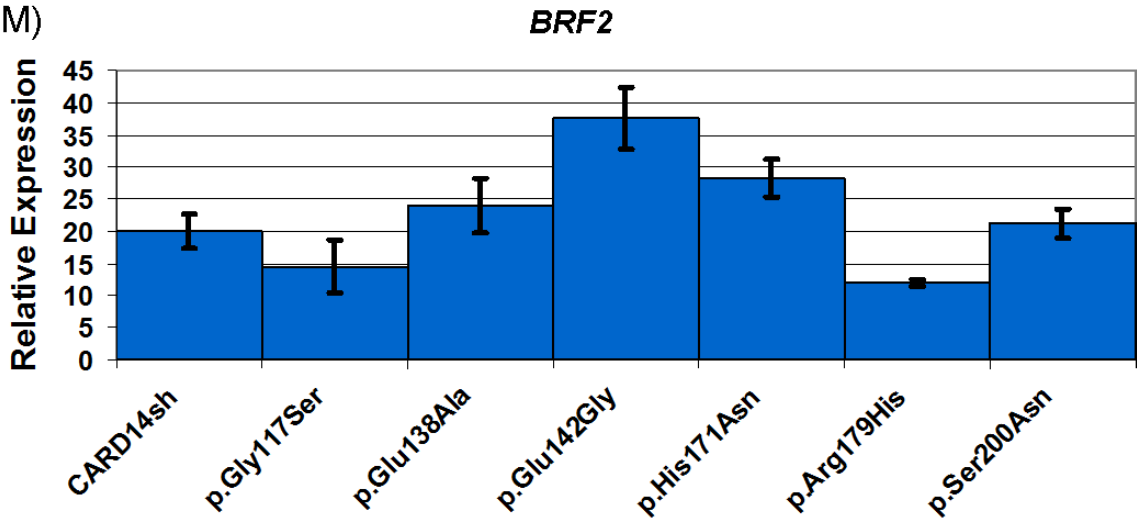


Figure S2. qRT-PCR Confirmation of Effects of Wild-Type and Variant CARD14 on Transcriptional Activation of a Select Set of Psoriasis-Associated Transcripts

HEK 001 cells were transfected with wildtype or altered CARD14sh and qRT-PCR was performed to confirm the effects of constructs on expression of *CCL20* (A), *IL8* (B), *SOD2* (C), *IL6* (D), *MMP9* (E), *OLR1* (F), *CSF2* (G), *SLC7A2* (H), *IL36G* (I), *GBP2* (J), *TNFAIP2* (K), *TNF* (L), and *BRF2* (M) identified with global expression profiling. For all qRT-PCR, expression levels were normalized to 18S by the 2-ΔΔCt method. Expression levels in transfected cells were also normalized to levels of FLAG to correct for differences in transfection efficiency. To transform expression levels to non-decimal integers, all expression levels were multiplied by 100,000 before plotting on graphs. Error bars represent the standard deviation of replicates.

Table S1. Rare Variants Detected in *CARD14*, Their Predicted Functional Effects, and Number of Observations of Each Variant in Unrelated Cases and Controls from European and Asian Cohorts

CARD14 **Exon**	**hg19 Position (chr17)**	**cDNA Change**	**Protein Change**	**SIFT[a] Predicted Effect**	**# Eur. Cases (Total # Screened)**	**# Eur. Controls (Total # Screened)**	**# Asian Cases (Total # Screened)**	**# Asian Controls (Total # Screened)**
2	78155349	c.112C>T	p.Arg38Cys	Affect protein function	1 (2691)	0 (1271)	0 (79)	0 (190)
2	78155422	c.185G>A	p.Arg62Gln (rs115582620)	Tolerated	8 (3284)	2 (1797)	0 (79)	0 (190)
3	78156589	c.349G>A	p.Gly117Ser	Affect protein function	3[b] (6630)	0[c] (4731)	0 (194)	0 (191)
3	78156594	c.349+5G>A	None	NA	0[b] (2871)	0 (1339)	1[b] (78)	0 (183)
4	78157775	c.413A>C	p.Glu138Ala	Affect protein function	1[b] (3488)	0 (1902)	0 (189)	0 (193)
4	78157786	c.424G>A	p.Glu142Lys	Affect protein function	1 (4107)	0 (1874)	0 (187)	0 (21)
4	78157787	c.425A>G	p.Glu142Gly	Affect protein function	1 (2848)	0 (1451)	0 (79)	0 (189)
4	78157811	c.449T>G	p.Leu150Arg[#]	Affect protein function	30 (6140)	16 (4614)	0 (183)	0 (192)
4	78157873	c.511C>A	p.His171Asn	Tolerated	2 (4077)	0 (1858)	0 (183)	0 (21)
4	78157888	c.526G>C	p.Asp176His	Affect	4 (3575)	2 (1609)	1 (85)	0 (18)

				protein function				
4	78157898	c.536G>A	p.Arg179His	Tolerated	2 (4061)	1 (1848)	0 (177)	0 (20)
4	78157933	c.571G>T	p.Val191Leu	Tolerated	1 (3575)	0 (1613)	0 (86)	0 (18)
4	78157740	c.599G>A	p.Ser200Asn	Tolerated	134 (6163)	75 (4624)	2 (190)	0 (190)
6	78163562	c.854A>G	p.Asp285Gly	Affect Protein Function	1 (2673)	0 (1467)	0 (79)	0 (190)
13	78172317	c.1778T>A	p.Ile593Asn	Affect protein function	1 (2049)	1 (1039)	0 (128)	0 (176)
15	78176044	c.2044C>T	p.Arg682Trp (rs117918077)	Affect protein function	58 (2169)	25 (1042)	0 (116)	0 (173)
15	78176140	c.2140G>A	p.Gly714Ser	Tolerated	9 (2105)	3 (1038)	0 (132)	0 (176)
21	78182048	c.2919C>G	p.Asp973Glu	Tolerated	25 (5177)	12 (4099)	0 (72)	0 (164)

All coding exons of *CARD14* (full-length, *CARD14fl*) were re-sequenced in 192 psoriasis cases and 96 controls. Exons in which rare, missense mutations were identified were resequenced in an additional 95 controls. Exon 3 of *CARD14* was sequenced in an additional 194 controls of European ancestry, 145 Asian controls, and 384 psoriasis cases. Exon 4 of CARD14 was resequenced in another 1856 cases and 882 controls of European ancestry. Numbering of *CARD14* exons is based on isoform 1 (full-length CARD14, RefSeq NM_024110.3). These variants were then successfully genotyped in the numbers of cases and controls indicated. [a] SIFT.[1] [b]These numbers include the familial cases and *de novo* sporadic pustular case described in the text. [c]One control from the National Psoriasis Foundation Victor Henschel Tissue Repository (NPF) cohort, had the p.Gly117Ser mutation, but the ancestry of that individual was unknown. Eur = of Northern European ancestry.

Table S2. Results after PLINK[2] Analysis for All Rare Variants Genotyped in *CARD14* in Individual Cohorts

A) Saint Louis/Dallas/UCSF

Variant	hg19 Position (chr17)	A1	F_A	F_U	A2	P	OR (95% CI)	Cases HWE P	Controls HWE P
rs2289539	78152119	T	0.313	0.359	C	0.0195	0.811 (0.681, 0.967)	0.848	0.926
rs6565643	78154501	T	0.313	0.355	A	0.0362	0.828 (0.694, 0.988)	0.847	1
p.Arg38Cys	78155349	T	0	0	C	NA	NA	NA	NA
rs115582620/ p.Arg62Gln	78155422	A	0.00492	0.00177	G	0.312	2.021 (0.516, 7.912)	0.0123	0.000887
rs9909462	78156291	A	0.336	0.318	G	0.362	1.088 (0.908, 1.303)	0.130	0.922
p.Gly117Ser	78156589	A	0	0	G	NA	NA	NA	NA
c.349+5G>A	78156594	A	0	0	G	NA	NA	NA	NA
rs9902358	78156762	T	0.416	0.437	G	0.290	0.913 (0.771, 1.081)	0.932	0.168
p.Glu138Ala	78157775	C	0	0	A	NA	NA	NA	NA
p.Glu142Lys	78157786	A	0	0	G	NA	NA	NA	NA
p.Glu142Gly	78157787	G	0	0	A	NA	NA	NA	NA
p.Leu150Arg	78157811	G	0.0569	0	T	0.998	$1.49x10^{-9}$ (0, inf)	1	1
p.His171Asn	78157873	A	0	0	C	NA	NA	NA	NA
p.Asp176His	78157888	C	0.000856	0.000901	G	0.971	0.950 (0.0593, 15.23)	1	1
p.Arg179His	78157898	A	0	0.000893	G	0.999	$6.20x10^{-10}$ (0, inf)	1	1
p.Val191Leu	78157933	T	0	0	G	NA	NA	NA	NA
p.Ser200Asn	78157961	A	0.0159	0.00712	G	0.0508	2.269 (0.997, 5.163)	1	1
rs114688446/ p.Ser200Ile	78157961	T	0	0	G	NA	NA	NA	NA
rs4889990	78158995	A	0.372	0.371	G	0.985	1.002 (0.840, 1.194)	0.642	0.461
rs3829612	78161402	T	0.354	0.345	C	0.662	1.040 (0.871, 1.243)	0.312	0.508

rs117360605/ p.Arg275His	78162324	A	0	0	G	NA	NA	NA	NA
rs8065364	78162959	C	0.310	0.290	T	0.3029	1.099 (0.919, 1.314)	0.288	0.409
p.Asp285Gly	78163562	G	0	0	A	NA	NA	NA	NA
rs8068433	78165456	C	0.357	0.323	T	0.495	1.148 (0.773, 1.703)	0.0919	1
rs61751629/ p.Glu422Lys	78166326	A	0.0397	0.0266	G	0.0925	1.452 (0.940, 2.241)	0.0162	0.0536
rs61751630/ p.Pro506Leu	78169374	T	0.0110	0.0165	C	0.276	0.676 (0.334, 1.368)	1	0.1179
rs750541	78169636	A	0.329	0.332	G	0.879	0.987 (0.829, 1.174)	0.925	0.848
rs2018229	78169899	G	0.365	0.377	A	0.680	0.965 (0.813, 1.145)	1	0.647
rs2066964/ p.Arg547Ser	78171944	C	0.361	0.386	G	0.220	0.900 (0.761, 1.065)	0.498	0.202
rs34367357/ p.Val585Ile	78172292	A	0.0897	0.0574	G	0.00219	1.657 (1.199, 2.288)	0.0507	0.700
p.Ile593Asn	78172317	A	0	0.000890	T	0.999	5.50 $\times 10^{-10}$ (0, inf)	1	1
rs73429414/ p.Arg597Trp	78172328	T	0	0	C	NA	NA	NA	NA
rs2304856	78175483	T	0.513	0.434	C	0.000161	1.388 (1.171, 1.646)	0.403	0.727
rs3813063	78175854	A	0.437	0.527	C	1.85×10^{-5}	0.694 (0.588, 0.821)	1	0.671
rs117918077/ p.Arg682Trp	78176044	T	0.0135	0.0106	C	0.518	1.276 (0.609, 2.672)	1	1
p.Gly714Ser	78176140	A	0.00226	0.000899	G	0.424	2.523 (0.262, 24.32)	1	1
rs34822755/ p.Cys756Tyr	78177668	A	0	0.000890	G	0.999	5.21 $\times 10^{-10}$ (0, inf)	1	1
rs4889997	78178189	A	0.444	0.525	G	0.000154	0.720 (0.607, 0.853)	1	0.932
rs11653893	78178830	G	0.419	0.517	A	2.75×10^{-6}	0.665 (0.560, 0.788)	0.667	0.496
rs11652075/ p.Arg820Trp	78178893	T	0.381	0.482	C	1.28×10^{-6}	0.663 (0.562, 0.783)	0.306	0.797
rs2289541/	78179408	A	0	0	G	NA	NA	NA	NA

p.Arg883His									
p.Asp973Glu	78182048	G	0	0	C	NA	NA	NA	NA

B) National Psoriasis Foundation

Variant	hg19 Position (chr17)	A1	F_A	F_U	A2	P	OR (95% CI)	Cases HWE P	Controls HWE P
rs2289539	78152119	T	0.309	0.328	C	0.522	0.911 (0.684, 1.212)	0.0332	1
rs6565643	78154501	T	0.305	0.324	A	0.521	0.910 (0.682, 1.214)	0.0306	1
p.Arg38Cys	78155349	T	0	0	C	NA	NA	NA	NA
rs115582620/ p.Arg62Gln	78155422	A	0.00111	0.00345	G	0.423	0.321 (0.0200, 5.172)	1	1
rs9909462	78156291	A	0.363	0.320	G	0.235	1.227 (0.876, 1.720)	0.173	0.526
p.Gly117Ser	78156589	A	0.00105	0	G	0.999	5.17x10^{8} (0, inf)	1	1
c.349+5G>A	78156594	A	0	0	G	NA	NA	NA	NA
rs9902358	78156762	T	0.450	0.389	G	0.0660	1.290 (0.983, 1.692)	0.781	1
p.Glu138Ala	78157775	C	0	0	A	NA	NA	NA	NA
p.Glu142Lys	78157786	A	0	0	G	NA	NA	NA	NA
p.Glu142Gly	78157787	G	0	0	A	NA	NA	NA	NA
p.Leu150Arg	78157811	G	0.00226	0	T	0.999	5.14 x10^{8} (0, inf)	1	1
p.His171Asn	78157873	A	0	0	C	NA	NA	NA	NA
p.Asp176His	78157888	C	0.001538	0	G	0.999	6.18x10^{8} (0, inf)	1	1
p.Arg179His	78157898	A	0	0	G	NA	NA	NA	NA
p.Val191Leu	78157933	T	0	0	G	NA	NA	NA	NA
p.Ser200Asn	78157961	A	0.0116	0.0132	G	0.822	0.875 (0.275, 2.79)	1	1
rs114688446/ p.Ser200Ile	78157961	T	0	0	G	NA	NA	NA	NA
rs4889990	78158995	A	0.323	0.376	G	0.165	0.799 (0.583, 1.097)	0.280	0.841

rs3829612	78161402	T	0.377	0.339	C	0.305	1.181 (0.860, 1.621)	0.904	1
rs117360605/ p.Arg275His	78162324	A	0	0	G	NA	NA	NA	NA
rs8065364	78162959	C	0.324	0.296	T	0.354	1.138 (0.866, 1.497)	0.756	0.0822
p.Asp285Gly	78163562	G	0	0	A	NA	NA	NA	NA
rs8068433	78165456	C	0.328	0.324	T	0.924	1.021 (0.668, 1.559)	0.741	0.404
rs61751629/ p.Glu422Lys	78166326	A	0.0388	0.0362	G	0.837	1.074 (0.542, 2.131)	0.516	1
rs61751630/ p.Pro506Leu	78169374	T	0.0133	0.0109	C	0.749	1.233 (0.343, 4.433)	1	1
rs750541	78169636	A	0.363	0.292	G	0.0232	1.386 (1.046, 1.838)	0.555	0.701
rs2018229	78169899	G	0.416	0.345	A	0.0306	1.342 (1.028, 1.751)	0.575	0.723
rs2066964/ p.Arg547Ser	78171944	C	0.375	0.421	G	0.171	0.829 (0.633, 1.084)	0.622	0.729
rs34367357/ p.Val585Ile	78172292	A	0.0835	0.0709	G	0.481	1.208 (0.714, 2.043)	0.235	1
p.Ile593Asn	78172317	A	0	0	T	NA	NA	NA	NA
rs73429414/ p.Arg597Trp	78172328	T	0	0	C	NA	NA	NA	NA
rs2304856	78175483	T	0.461	0.487	C	0.485	0.896 (0.657, 1.220)	1	0.0420
rs3813063	78175854	A	0.499	0.458	C	0.200	1.188 (0.913, 1.545)	0.785	0.196
rs117918077/ p.Arg682Trp	78176044	T	0.0126	0.0197	C	0.358	0.627 (0.231, 1.699)	1	1
p.Gly714Ser	78176140	A	0.00105	0.00662	G	0.131	0.157 (0.0141, 1.738)	1	1
rs34822755/ p.Cys756Tyr	78177668	A	0	0	G	NA	NA	NA	NA
rs4889997	78178189	A	0.497	0.458	G	0.223	1.177 (0.906, 1.531)	0.856	0.254
rs11653893	78178830	G	0.495	0.451	A	0.177	1.198 (0.922, 1.558)	0.785	0.330
rs11652075/ p.Arg820Trp	78178893	T	0.464	0.443	C	0.524	1.089 (0.837, 1.418)	1	0.741

rs2289541/ p.Arg883His	78179408	A	0.00105	0.00329	G	0.418	0.317 (0.0197, 5.102)	1	1
p.Asp973Glu	78182048	G	0	0	C	NA	NA	NA	NA

B) Utah

Variant	**hg19 Position (chr17)**	**A1**	**F_A**	**F_U**	**A2**	**P**	**OR (95% CI)**	**Cases HWE P**	**Controls HWE P**
rs2289539	78152119	T	0.419	0.298	C	4.70x10^{-9}	2.529 (1.854, 3.449)	3.59x10^{-55}	0.000192
rs6565643	78154501	T	0.154	0.197	A	0.0677	0.758 (0.564, 1.020)	0.00169	0.138
p.Arg38Cys	78155349	T	0	0	C	NA	NA	NA	NA
rs115582620/ p.Arg62Gln	78155422	A	0.000544	0	G	0.999	4.15x10^{8} (0, inf)	1	1
rs9909462	78156291	A	0.321	NA	G	1	1 (0, inf)	1.65x10^{-9}	NA
p.Gly117Ser	78156589	A	0.000543	0	G	0.999	4.04x10^{-8} (0, inf)	1	1
c.349+5G>A	78156594	A	0	0	G	NA	NA	NA	NA
rs9902358	78156762	T	0.426	0.500	G	0.00282	0.654 (0.495, 0.864)	1.02x10^{-13}	9.50x10^{-6}
p.Glu138Ala	78157775	C	0	0	A	NA	NA	NA	NA
p.Glu142Lys	78157786	A	0	0	G	NA	NA	NA	NA
p.Glu142Gly	78157787	G	0	0	A	NA	NA	NA	NA
p.Leu150Arg	78157811	G	0.00110	0	T	0.999	4.14x10^{8} (0, inf)	1	1
p.His171Asn	78157873	A	0	0	C	NA	NA	NA	NA
p.Asp176His	78157888	C	0.000786	0	G	1	1 (0, inf)	1	NA
p.Arg179His	78157898	A	0	0	G	NA	NA	NA	NA
p.Val191Leu	78157933	T	0	0	G	NA	NA	NA	NA
p.Ser200Asn	78157961	A	0.00926	0.002183	G	0.157	4.302 (0.570, 32.49)	1	1
rs114688446/ p.Ser200Ile	78157961	T	0	0.002137	G	0.999	1.68x10^{-10} (0, inf)	1	1
rs4889990	78158995	A	0.345	NA	G	1	1 (0, inf)	0.000970	NA

rs3829612	78161402	T	0.329	NA	C	1	1 (0, inf)	5.75x10^{-8}	NA
rs117360605/ p.Arg275His	78162324	A	0	0	G	NA	NA	NA	NA
rs8065364	78162959	C	0.299	0.308	T	0.694	0.945 (0.713, 1.252)	2.00x10^{-12}	3.14x10^{-5}
p.Asp285Gly	78163562	G	0	0	A	NA	NA	NA	NA
rs8068433	78165456	C	0.355	NA	T	1	1 (0, inf)	0.438	NA
rs61751629/ p.Glu422Lys	78166326	A	0.0267	0.0393	G	0.1598	0.678 (0.395, 1.165)	0.482	0.294
rs61751630/ p.Pro506Leu	78169374	T	0.020	0.0313	C	0.2766	0.645 (0.292, 1.422)	1	0.107
rs750541	78169636	A	0.368	0.359	G	0.674	1.059 (0.810, 1.385)	1.09x10^{-18}	0.000238
rs2018229	78169899	G	0.401	0.382	A	0.401	1.139 (0.841, 1.541)	2.32x10^{-29}	5.93x10^{-9}
rs2066964/ p.Arg547Ser	78171944	C	0.371	0.405	G	0.190	0.868 (0.703, 1.072)	0.429	0.781
rs34367357/ p.Val585Ile	78172292	A	0.0781	0.0575	G	0.1437	1.374 (0.897, 2.104)	0.242	0.534
p.Ile593Asn	78172317	A	0	0	T	NA	NA	NA	NA
rs73429414/ p.Arg597Trp	78172328	T	0	0	C	NA	NA	NA	NA
rs2304856	78175483	T	0.439	NA	C	1	1 (0, inf)	0.00019	NA
rs3813063	78175854	C	0.498	0.457	A	0.0681	1.287 (0.982, 1.687)	6.87x10^{-27}	0.000598
rs117918077/ p.Arg682Trp	78176044	T	0.0131	0.0108	C	0.697	1.213 (0.458, 3.215)	1	1
p.Gly714Ser	78176140	A	0.00217	0	G	0.999	4.04x10^{-8} (0, inf)	1	1
rs34822755/ p.Cys756Tyr	78177668	A	0	0	G	NA	NA	NA	NA
rs4889997	78178189	A	0.472	0.517	G	0.0824	0.795 (0.613, 1.030)	3.44x10^{-13}	0.179
rs11653893	78178830	G	0.484	0.470	A	0.470	1.127 (0.814, 1.561)	7.02x10^{-60}	1.61x10^{-06}
rs11652075/ p.Arg820Trp	78178893	T	0.453	0.515	C	0.0166	0.778 (0.633, 0.955)	0.342	0.361

rs2289541/ p.Arg883His	78179408	A	0.00109	0	G	0.999	4.04x10^{-8} (0, inf)	1	1
p.Asp973Glu	78182048	G	0.00443	0.00219	C	0.514	2.027 (0.243, 16.93)	1	1

C) Michigan

Variant	hg19 Position (chr17)	A1	F_A	F_U	A2	P	OR (95% CI)	Cases HWE P	Controls HWE P
p.Gly117Ser	78156589	A	0	0	G	NA	NA	NA	NA
p.Leu150Arg	78157811	G	0.00235	0.00238	T	0.976	0.988 (0.457, 2.135)	1	1
p.Ser200Asn	78157961	A	0.0114	0.00968	G	0.370	1.184 (0.818, 1.713)	1	1
rs2066964	78171944	C	0.377	0.384	G	0.469	0.972 (0.909, 1.049)	0.155	0.257
rs11652075	78178893	T	0.470	0.492	C	0.0233	0.917 (0.851,0.988)	0.565	1
p.Asp973Glu	78182048	G	0.00235	0.00164	C	0.406	1.434 (0.612, 3.361)	1	1

D) Newfoundland

Variant	hg19 Position (chr17)	A1	F_A	F_U	A2	P	OR (95% CI)	Cases HWE P	Controls HWE P
rs2289539	78152119	T	0.328	0.349	C	0.370	0.901 (0.718, 1.131)	0.0545	0.172
rs6565643	78154501	T	0.327	0.333	A	0.796	0.970 (0.769, 1.223)	0.0892	0.152
p.Arg38Cys	78155349	T	0	0	C	NA	NA	NA	NA
rs115582620/ p.Arg62Gln	78155422	A	0	0	G	NA	NA	NA	NA
rs9909462	78156291	A	0.331	0.317	G	0.560	1.068 (0.113, 0.856)	0.336	0.806
p.Gly117Ser	78156589	A	0	0	G	NA	NA	NA	NA
c.349+5G>A	78156594	G	0	0	A	NA	NA	NA	NA
rs9902358	78156762	T	0.413	0.389	G	0.343	1.112 (0.893, 1.384)	1	0.317

p.Glu138Ala	78157775	C	0	0	A	NA	NA	NA	NA
p.Glu142Lys	78157786	A	0	0	G	NA	NA	NA	NA
p.Glu142Gly	78157787	G	0	0	A	NA	NA	NA	NA
p.Leu150Arg	78157811	G	0.00274	0.00134	T	0.557	2.055 (0.186, 22.76)	1	1
p.His171Asn	78157873	A	0.00408	0	C	0.999	4.19x10^{8} (0, inf)	0.00408	1
p.Asp176His	78157888	C	0	0	G	NA	NA	NA	NA
p.Arg179His	78157898	A	0	0	G	NA	NA	NA	NA
p.Val191Leu	78157933	T	0	0	G	NA	NA	NA	NA
p.Ser200Asn	78157961	A	0.0110	0.00401	G	0.132	2.787 (0.734, 10.59)	1	1
rs114688446/ p.Ser200Ile	78157961	T	0	0	G	NA	NA	NA	NA
rs4889990	78158995	A	0.339	0.376	G	0.144	0.852 (0.686, 1.056)	0.0972	0.368
rs3829612	78161402	T	0.356	0.336	C	0.431	1.089 (0.881, 1.347)	0.168	0.636
rs117360605/ p.Arg275His	78162324	A	0	0	G	NA	NA	NA	NA
rs8065364	78162959	C	0.333	0.293	T	0.101	1.204 (0.965, 1.504)	1	0.802
p.Asp285Gly	78163562	G	0	0	A	NA	NA	NA	NA
rs8068433	78165456	C	0.380	0.332	T	0.190	1.234 (0.901, 1.692)	0.1037	0.0414
rs61751629/ p.Glu422Lys	78166326	A	0.0415	0.0430	G	0.890	0.9641 (0.573, 1.623)	0.443	1
rs750541	78169636	A	0.357	0.319	G	0.124	1.190 (0.954, 1.484)	0.909	0.337
rs2018229	78169899	G	0.411	0.352	A	0.0189	1.306 (1.045, 1.631)	0.580	0.201
rs2066964/ p.Arg547Ser	78171944	C	0.376	0.358	G	0.497	1.078 (0.868, 1.339)	0.481	0.214
rs34367357/ p.Val585Ile	78172292	A	0.0861	0.0856	G	0.973	1.007 (0.689, 1.471)	0.491	1
rs2304856	78175483	T	0.469	0.460	C	0.745	1.035 (0.843, 1.271)	0.396	0.593
rs3813063	78175854	A	0.493	0.487	C	0.803	1.027 (0.835, 1.263)	0.597	1
rs4889997	78178189	A	0.496	0.489	G	0.800	1.027 (0.836, 1.263)	0.672	0.676

rs11653893	78178830	G	0.484	0.484	A	0.992	1.001 (0.814, 1.232)	0.668	0.756
rs11652075/ p.Arg820Trp	78178893	T	0.503	0.487	C	0.546	1.065 (0.868, 1.306)	0.744	0.254
p.Asp973Glu	78182048	G	0.00141	0.00151	C	0.962	0.935 (0.0583, 15.01)	1	1

E) Toronto

Variant	hg19 Position (chr17)	A1	F_A	F_U	A2	P	OR (95% CI)	Cases HWE P	Controls HWE P
rs2289539	78152119	T	0.337	0.341	C	0.840	0.983 (0.832, 1.161)	0.345	0.919
rs6565643	78154501	T	0.336	0.336	A	0.996	1 (0.845, 1.184)	0.423	0.917
p.Arg38Cys	78155349	T	0	0	C	NA	NA	NA	NA
rs115582620/ p.Arg62Gln	78155422	A	0	0	G	NA	NA	NA	NA
rs9909462	78156291	A	0.330	0.341	G	0.539	0.949 (0.804, 1.121)	0.941	0.176
p.Gly117Ser	78156589	A	0	0	G	NA	NA	NA	NA
c.349+5G>A	78156594	A	0	0	G	NA	NA	NA	NA
rs9902358	78156762	T	0.450	0.451	G	0.956	0.996 (0.852, 1.163)	0.598	0.401
p.Glu138Ala	78157775	C	0	0	A	NA	NA	NA	NA
p.Glu142Lys	78157786	A	0	0	G	NA	NA	NA	NA
p.Glu142Gly	78157787	G	0	0	A	NA	NA	NA	NA
p.Leu150Arg	78157811	G	0.00155	0.00210	T	0.740	0.738 (0.123, 4.434)	1	1
p.His171Asn	78157873	A	0	0	C	NA	NA	NA	NA
p.Asp176His	78157888	C	0.000529	0.00105	G	0.626	0.502 (0.0313, 8.045)	1	1
p.Arg179His	78157898	A	0.00105	0	G	0.999	7.76x10^8 (0, inf)	1	1
p.Val191Leu	78157933	T	0.000540	0	G	0.999	8.26x10^8 (0, inf)	1	1

p.Ser200Asn	78157961	A	0.00722	0.00632	G	0.783	1.145 (0.437, 2.998)	1	1
rs114688446/ p.Ser200Ile	78157961	T	0	0	G	NA	NA	NA	NA
rs4889990	78158995	A	0.371	0.353	G	0.364	1.078 (0.917, 1.268)	0.290	0.542
rs3829612	78161402	T	0.355	0.359	C	0.849	0.984 (0.836, 1.159)	1	0.158
rs117360605/ p.Arg275His	78162324	A	0	0.00213	G	0.999	1.73x10^{-5} (0, inf)	1	0.00107
rs8065364	78162959	C	0.312	0.303	T	0.653	1.039 (0.879, 1.228)	0.707	0.517
p.Asp285Gly	78163562	G	0	0	A	NA	NA	NA	NA
rs8068433	78165456	C	0.339	0.328	T	0.664	1.051 (0.838, 1.319)	0.291	0.766
rs61751629/ p.Glu422Lys	78166326	A	0.0377	0.0398	G	0.788	0.947 (0.640, 1.404)	0.642	0.164
rs750541	78169636	A	0.353	0.341	G	0.557	1.049 (0.894, 1.231)	0.260	0.102
rs2018229	78169899	G	0.380	0.376	A	0.838	1.017 (0.865, 1.197)	0.945	0.842
rs2066964/ p.Arg547Ser	78171944	C	0.369	0.390	G	0.285	0.918 (0.784, 1.074)	0.0151	0.209
rs34367357/ p.Val585Ile	78172292	A	0.0859	0.0872	G	0.909	0.984 (0.748, 1.294)	0.683	0.772
rs2304856	78175483	T	0.507	0.460	C	0.0222	1.202 (1.027, 1.406)	0.551	0.398
rs3813063	78175854	A	0.459	0.524	C	0.00116	0.772 (0.660, 0.902)	0.697	0.356
rs4889997	78178189	A	0.456	0.522	G	0.00131	0.771 (0.658, 0.904)	0.741	0.303
rs11653893	78178830	G	0.443	0.476	A	0.104	0.874 (0.742, 1.028)	0.289	0.924
rs11652075/ p.Arg820Trp	78178893	T	0.459	0.517	C	0.00364	0.795 (0.681, 0.9279)	0.846	0.233
p.Asp973Glu	78182048	G	0.00160	0.00111	C	0.975	0.962 (0.0870, 10.63)	1	1

G) Asians

Variant	**hg19 Position (chr17)**	**A1**	**F_A**	**F_U**	**A2**	**P**	**OR (95% CI)**	**Cases HWE P**	**Controls HWE P**

rs2289539	78152119	T	0.392	0.400	C	0.918	0.965 (0.493, 1.892)	0.877	0.385
rs6565643	78154501	T	0.376	0.375	A	0.994	1.003 (0.486, 2.072)	0.202	0.319
p.Arg38Cys	78155349	T	0	0	C	NA	NA	NA	NA
rs115582620/ p.Arg62Gln	78155422	A	0	0.00260	G	0.999	6.29x10^{-10} (0, inf)	1	1
rs9909462	78156291	A	0.244	0.294	G	0.513	0.744 (0.307, 1.804)	0.374	1
p.Gly117Ser	78156589	A	0	0	G	NA	NA	NA	NA
c.349+5G>A	78156594	A	0.0128	0	G	NA	NA	NA	NA
rs9902358	78156762	T	0.347	0.375	G	0.718	0.882 (0.445, 1.748)	0.617	0.339
p.Glu138Ala	78157775	C	0	0	A	NA	NA	NA	NA
p.Glu142Lys	78157786	A	0	0	G	NA	NA	NA	NA
p.Glu142Gly	78157787	G	0	0	A	NA	NA	NA	NA
p.Leu150Arg	78157811	G	0	0	T	NA	NA	NA	NA
p.His171Asn	78157873	A	0	0	C	NA	NA	NA	NA
p.Asp176His	78157888	C	0.005814	0	G	0.999	3.42x10^{8} (0, inf)	1	1
p.Arg179His	78157898	A	0	0	G	NA	NA	NA	NA
p.Val191Leu	78157933	T	0	0	G	NA	NA	NA	NA
p.Ser200Asn	78157961	A	0.00521	0	G	0.999	1.62x10^{9} (0, inf)	1	1
rs114688446/ p.Ser200Ile	78157961	T	0	0	G	NA	NA	NA	NA
rs4889990	78158995	A	0.383	0.265	G	0.225	1.633 (0.739, 3.609)	0.469	0.525
rs3829612	78161402	T	0.259	0.324	C	0.439	0.7266 (0.324, 1.631)	1	1
rs117360605/ p.Arg275His	78162324	A	0	0	G	NA	NA	NA	NA
rs8065364	78162959	C	0.213	0.262	T	0.472	0.765 (0.369, 1.587)	1	0.578
p.Asp285Gly	78163562	G	0	0	A	NA	NA	NA	NA
rs8068433	78165456	C	0.436	0.250	T	0.244	2.283 (0.570, 9.145)	0.748	1
rs61751629/ p.Glu422Lys	78166326	A	0.00262	0.00262	G	1	1 (0.06209, 16.1)	1	1
rs61751630/	78169374	T	0.00417	0	C	0.999	2.17x10^{9} (0, inf)	1	1

p.Pro506Leu									
rs750541	78169636	A	0.361	0.262	G	0.167	1.729 (0.795, 3.758)	0.0371	1
rs2018229	78169899	G	0.361	0.350	A	0.886	1.055 (0.509, 2.187)	0.141	1
rs2066964/ p.Arg547Ser	78171944	C	0.356	0.437	G	0.0252	0.707 (0.522, 0.958)	0.523	0.357
rs34367357/ p.Val585Ile	78172292	A	0.0812	0.0767	G	0.820	1.064 (0.625, 1.809)	1	1
p.Ile593Asn	78172317	A	0	0	T	NA	NA	NA	NA
rs73429414/ p.Arg597Trp	78172328	T	0	0	C	NA	NA	NA	NA
rs2304856	78175483	T	0.355	0.472	C	0.192	0.610 (0.290, 1.281)	1	1
rs3813063	78175854	C	0.354	0.333	A	0.788	1.099 (0.552, 2.191)	0.745	1
rs117918077/ p.Arg682Trp	78176044	T	0	0	C	NA	NA	NA	NA
p.Gly714Ser	78176140	A	0	0	G	NA	NA	NA	NA
rs34822755/ p.Cys756Tyr	78177668	A	0	0	G	NA	NA	NA	NA
rs4889997	78178189	A	0.361	0.368	G	0.931	0.969 (0.474, 1.981)	0.618	1
rs11653893	78178830	G	0.368	0.310	A	0.440	1.327 (0.648, 2.717)	0.429	0.611
rs11652075/ p.Arg820Trp	78178893	T	0.322	0.431	C	0.00287	0.639 (0.476, 0.858)	0.739	0.138
rs2289541/ p.Arg883His	78179408	A	0.0644	0.0739	G	0.644	0.860 (0.327, 0.453)	1	1
p.Asp973Glu	78182048	G	0	0	C	NA	NA	NA	NA

Cases and controls were genotyped by Sequenom MassARRAY or TaqMan (Michigan cohort only). Results are shown for seven sets of case-control logistic regression analyses of genotypes (unless otherwise specified, cohorts were of European ancestry): A) Saint Louis/Dallas/UCSF (676 cases, 570 controls), B) National Psoriasis Foundation (486 cases, 154 controls), C) Utah (931 cases, 236 controls), D) Michigan (2768 cases, 2749 controls), E) Newfoundland (340 cases, 379 controls), F) Toronto (981 cases, 483 controls), G) Asian (194 cases, 193 controls). A1 – minor/mutant allele, A2 –major/wildtype allele, F_A – frequency of allele 1 (A1) among affected individuals, F_U – frequency of A1 among unaffected individuals, P – p-value, OR – odds ratio, CI – confidence interval, inf – infinity, d – deletion, HWE – Hardy-Weinberg equilibrium.

Table S3. Results of Association Tests with *CARD14* Missense Variants Conditioned on PSORS1

		Logistic Regression No Covariate		**Logistic Regression Cw6 Genotype as Covariate**	
Cohort	**Variant**	**OR (95%CI)**	**P**	**OR (95%CI)**	**P**
St. Louis/Dallas	p.Ser200Asn	2.27 (1, 5.16)	0.051	1 (0, inf)	1
	rs2066964	0.9 (0.76, 1.07)	0.22	1 (0, inf)	1
	rs34367357	1.66 (1.20, 2.29)	0.0022	1 (0, inf)	1
	rs11652075	0.66 (0.56, 0.78)	1.28×10^{-6}	1 (0, inf)	1
	rs13191343	8.90 (0.43, 183.60)	0.16	NA	NA
NPF (European ancestry)	p.Ser200Asn	0.88 (0.27, 2.79)	0.82	0.68 (0.17, 2.68)	0.58
	rs2066964	0.83 (0.63, 1.08)	0.17	0.86 (0.62, 1.20)	0.38
	rs34367357	1.21 (0.71, 2.04)	0.48	1.18 (0.63, 2.21)	0.61
	rs11652075	1.09 (0.84, 1.42)	0.52	1.04 (0.76, 1.42)	0.81
	rs13191343	2.03 (1.38, 2.99)	0.00035	NA	NA
Utah	p.Ser200Asn	4.3 (0.57, 32.49)	0.16	3.98 (0.51, 30.86)	0.19
	rs2066964	0.87 (0.70, 1.07)	0.19	0.86 (0.69, 1.07)	0.18
	rs34367357	1.37 (0.90, 2.10)	0.14	1.49 (0.97, 2.30)	0.071
	rs11652075	0.78 (0.63, 0.96)	0.017	0.75 (0.60, 0.93)	0.0086
	rs13191343	2.03 (1.53, 2.70)	1.07×10^{-6}	NA	NA
Michigan	p.Ser200Asn	1.18 (0.82, 1.71)	0.37	1.08 (0.73, 1.59)	0.71
	rs2066964	0.97 (0.90, 1.05)	0.47	0.96 (0.88, 1.04)	0.28
	rs11652075	0.92 (0.85, 0.99)	0.023	0.88 (0.81, 0.95)	0.0021
	HLA-Cw6	3.39 (2.99, 3.83)	8.47×10^{-3}	NA	NA
Newfoundland	p.Ser200Asn	2.63 (0.67, 10.26)	0.16	2.42 (0.61, 9.58)	0.21
	rs2066964	1.08 (0.87, 1.34)	0.50	1.09 (0.87, 1.36)	0.44
	rs34367357	1.01 (0.69, 1.47)	0.97	1.02 (0.69, 1.50)	0.93
	rs11652075	1.07 (0.87, 1.31)	0.55	1.022 (0.83, 1.26)	0.84

	rs13191343	1.76 (1.29, 2.40)	0.00037	NA	NA
Toronto	p.Ser200Asn	1.15 (0.44, 3.00)	0.78	1.07 (0.39, 2.92)	0.89
	rs2066964	0.92 (0.78, 1.07)	0.29	0.91 (0.77, 1.07)	0.25
	rs34367357	0.98 (0.75, 1.29)	0.91	1.01 (0.76, 1.34)	0.93
	rs11652075	0.78 (0.67, 0.90)	0.00099	0.78 (0.67, 0.92)	0.0033
	rs13191343	2.17 (1.76, 2.69)	$7.30\text{x}10^{-13}$	NA	NA
Asians	p.Ser200Asn	$1.62\text{x}10^{9}$ (0, inf)	1	$1.41\text{x}10^{9}$ (0, inf)	1
	rs2066964	0.71 (0.52, 0.96)	0.025	0.78 (0.51, 1.19)	0.25
	rs34367357	1.06 (0.63, 1.81)	0.82	1.53 (0.77, 3.04)	0.23
	rs11652075	0.64 (0.48, 0.86)	0.0029	0.57 (0.37, 0.89)	0.013
	rs13191343	4.03 (2.50, 6.52)	$1.27\text{x}10^{-8}$	NA	NA

Logistic regression tests were performed to determine the association of p.Ser200Asn, rs2066964, rs34367357, and rs11652075 when conditioned on the PSORS1 HLA-Cw6 risk allele. In the Michigan cohort, HLA-Cw6 status was determined by genotyping several proxy markers seven coding SNPs in exon 2 and 3 of the HLA-C gene. Two of those seven distinguish HLA-Cw6 from all other HLA-C alleles when phasing is unambiguous; the other five allow discrimination of HLA-Cw6 even when haplotype phasing contains uncertainty. For all other cohorts, genotype at a single proxy SNP, rs13191343, was used. HLA-Cw6 status was coded as a dominant trait. Values are also shown in each population for the logistic regression test of Cw6 or rs13191343. In the Utah and Michigan cohorts, stratifying on the presence of the PSORS1 HLA-Cw6 risk allele increased evidence of association for rs11652075, supporting a genetic connection between rs11652075 and PSORS1.

Table S4. Pathway Analysis of the "CARD14 Pathologic Keratinocyte" Signature

Ingenuity Canonical Pathways	Analysis	-log[P]	Ratio	Molecules
Glucocorticoid Receptor Signaling	CARD14 pathologic keratinocyte signature	5.44E00	5.82E-02	IL8, ICAM1, JAK1, SGK1, NFATC3, HSPA6, BGLAP, IL6, CCL5, ERCC2, IL1R2, AKT1, IL1RN, POLR2E, PLAU, CSF2, TNF
Role of Hypercytokinemia/hyperchemokinemia in the Pathogenesis of Influenza	CARD14 pathologic keratinocyte signature	5.18E00	1.71E-01	CXCL10, IL8, IL36G, IL1RN, CCL5, IL6, TNF
Role of Hypercytokinemia/hyperchemokinemia in the Pathogenesis of Influenza	Published psoriasis transcriptome	1.72E00	2.2E-01	CXCL10, IL8, IL36G, CCL4, CCL2, IL1RN, IL36RN, IL1B, IL37
Hepatic Fibrosis / Hepatic Stellate Cell Activation	CARD14 pathologic keratinocyte signature	4.5E00	7.64E-02	IL1R2, IL8, ICAM1, FN1, EDN1, CCL5, IL6, IFNAR2, TNF, MMP9, SERPINB2
Hepatic Fibrosis / Hepatic Stellate Cell Activation	Published psoriasis transcriptome	3.51E00	2.01E-01	CTGF, LEP, LEPR, FGF2, PDGFA, ACTA2, MYH11, PDGFC, BCL2, IGF1, CCL2, CYP2E1, IGF1R, STAT1, MMP1 (includes EG:300339), TIMP2 (includes EG:21858), EGFR, IL8, IL4R, CXCL9, FGFR1, BAMBI, IGFBP5, MET, MYL9, TGFA, IL1B, AGTR1, MMP9
Role of Cytokines in Mediating Communication between Immune Cells	CARD14 pathologic keratinocyte signature	4.47E00	1.35E-01	IL8, IL36G, IL1RN, IL6, CSF2, IL24, TNF
Role of Cytokines in Mediating Communication between	Published psoriasis transcriptome	4.07E-01	1.15E-01	IL8, IL36G, IL1RN, IL36RN, IL1B, IL37

Immune Cells				
IL-17A Signaling in Gastric Cells	CARD14 pathologic keratinocyte signature	4.18E00	2E-01	CXCL10, IL8, CCL20, CCL5, TNF
IL-17A Signaling in Gastric Cells	Published psoriasis transcriptome	1.39E00	2.4E-01	CXCL10, IL8, MAPK14, CXCL1, CCL20, EGFR
Communication between Innate and Adaptive Immune Cells	CARD14 pathologic keratinocyte signature	4.01E00	8.08E-02	CXCL10, IL8, IL36G, IL1RN, CCL5, IL6, CSF2, TNF
Communication between Innate and Adaptive Immune Cells	Published psoriasis transcriptome	3.58E-01	8.08E-02	CXCL10, IL8, IL36G, CCL4, IL1RN, IL36RN, IL1B, IL37
Acute Phase Response Signaling	CARD14 pathologic keratinocyte signature	3.73E00	6.18E-02	SOCS3, IL36G, SOD2, FN1, AKT1, IL1RN, OSMR, SERPINA1, IL6, TNF, HNRNPK
Acute Phase Response Signaling	Published psoriasis transcriptome	5.38E-01	1.12E-01	PIK3R1, SOCS2, CP, SERPINA3, IL37, STAT3, HMOX2, SHC1 (includes EG:20416), HMOX1, IL36G, MAPK14, SOD2, IL1RN, CRABP2, IL36RN, AKT3 (includes EG:10000), IL1B, SERPINA1, OSMR, RBP4
IL-10 Signaling	CARD14 pathologic keratinocyte signature	3.72E00	8.97E-02	IL1R2, SOCS3, IL36G, JAK1, IL1RN, IL6, TNF
IL-10 Signaling	Published psoriasis transcriptome	7.7E-01	1.28E-01	HMOX1, IL36G, IL4R, MAPK14, IL1RN, IL36RN, IL1B, ARG2 (includes EG:11847), STAT3, IL37
Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	CARD14 pathologic keratinocyte signature	3.69E00	4.69E-02	IL8, SOCS3, ICAM1, FN1, NFATC3, DVL1, GNAQ, IL6, CCL5, IL1R2, IL36G, AKT1, IL1RN, CSF2, TNF
Role of Macrophages, Fibroblasts and Endothelial Cells in Rheumatoid Arthritis	Published psoriasis transcriptome	2.01E00	1.29E-01	FRZB, PDGFA, FGF2, PIK3R1, PRSS2, CSNK1A1, LTB, FZD1, CCND1, PDGFC, IL36G, PRSS1/PRSS3, NFAT5, WIF1, CCL2, AKT3 (includes EG:10000), DKK2, PLCB1, TRAF5, MMP1 (includes

				EG:300339), PRKCA, IL8, SELE (includes EG:20339), PIK3C2G, NFATC1, TCF7L1, STAT3, IL37, PLCB4, MAPK14, FZD4, IL1RN, IL36RN, IL1B, FZD5, SFRP1, PDGFD, TCF7L2, WNT5A, FZD7, PRKCB
Differential Regulation of Cytokine Production in Macrophages and T Helper Cells by IL-17A and IL-17F	CARD14 pathologic keratinocyte signature	3.62E00	2.22E-01	CCL5, IL6, CSF2, TNF
Differential Regulation of Cytokine Production in Macrophages and T Helper Cells by IL-17A and IL-17F	Published psoriasis transcriptome	9.69E-01	2.22E-01	CCL4, CCL2, CXCL1, IL1B
TREM1 Signaling	CARD14 pathologic keratinocyte signature	3.58E00	9.68E-02	IL8, ICAM1, AKT1, IL6, CSF2, TNF
TREM1 Signaling	Published psoriasis transcriptome	7.88E-01	1.29E-01	IL8, NOD2, CCL2, CASP1, ITGA5, AKT3 (includes EG:10000), IL1B, STAT3
Airway Pathology in Chronic Obstructive Pulmonary Disease	CARD14 pathologic keratinocyte signature	3.54E00	3.33E-01	IL8, TNF, MMP9
Airway Pathology in Chronic Obstructive Pulmonary Disease	Published psoriasis transcriptome	1.32E00	3.33E-01	IL8, MMP9, MMP1 (includes EG:300339)
Role of Tissue Factor in Cancer	CARD14 pathologic keratinocyte signature	3.24E00	7.21E-02	IL8, AKT1, CDC42, GNAQ, RPS6KA1 (includes EG:20111), ITGA3, CSF2, ITGB5
Role of Tissue Factor in Cancer	Published psoriasis transcriptome	2.87E00	1.98E-01	IL8, FYN, CTGF, PIK3R1, GNA11, PIK3C2G, CXCL1, HBEGF, PLAUR, F3, EIF4E, F10, LCK, MAPK14, LYN, PLCB1, AKT3 (includes EG:10000), IL1B, ITGB5, MMP1 (includes EG:300339), EGFR, PRKCA
Role of IL-17F in Allergic	CARD14 pathologic	3.18E00	1.16E-01	CXCL10, IL8, IL6, RPS6KA1 (includes

Inflammatory Airway Diseases	keratinocyte signature			EG:20111), CSF2
Role of IL-17F in Allergic Inflammatory Airway Diseases	Published psoriasis transcriptome	9.36E-01	1.63E-01	CXCL10, IL8, CCL4, IGF1, CCL2, CXCL1, IL1B
Role of JAK family kinases in IL-6-type Cytokine Signaling	CARD14 pathologic keratinocyte signature	3.05E00	1.48E-01	SOCS3, JAK1, OSMR, IL6
Role of JAK family kinases in IL-6-type Cytokine Signaling	Published psoriasis transcriptome	5.76E-01	1.48E-01	MAPK14, OSMR, STAT3, STAT1
Atherosclerosis Signaling	CARD14 pathologic keratinocyte signature	2.98E00	6.2E-02	IL8, IL36G, ICAM1, IL1RN, SERPINA1, IL6, TNF, MMP9
Atherosclerosis Signaling	Published psoriasis transcriptome	3.23E00	1.89E-01	IL8, ALOX12B, SELE (includes EG:20339), PDGFA, CXCR4, CD36, PLA2G3, IL37, PDGFC, F3, IL36G, PLA2G2F, CCL2, IL1RN, LPL, IL36RN, IL1B, PDGFD, MMP9, MMP1 (includes EG:300339)
IL-6 Signaling	CARD14 pathologic keratinocyte signature	2.86E00	7E-02	IL1R2, IL8, IL36G, IL1RN, IL6, TNFAIP6, TNF
IL-6 Signaling	Published psoriasis transcriptome	3.84E-01	1.1E-01	IL8, SHC1 (includes EG:20416), IL36G, MAPK14, IL1RN, IL36RN, CSNK2A1, IL1B, HSPB7, STAT3, IL37
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	CARD14 pathologic keratinocyte signature	2.78E00	4.64E-02	IL1R2, IL36G, AKT1, NFATC3, IL1RN, DVL1, BGLAP, IL6, ITGA3, CSF2, TNF
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis	Published psoriasis transcriptome	1.97E00	1.39E-01	FRZB, PIK3R1, BMP2, CSNK1A1, FZD1, BCL2, IL36G, WIF1, NFAT5, IGF1, AKT3 (includes EG:10000), DKK2, TRAF5, ADAMTS5, MMP1 (includes EG:300339), ACP5, PIK3C2G, ITGA5, NFATC1, IL37, TCF7L1, FZD4, MAPK14, FOXO1 (includes EG:2308), IL1RN, IL36RN, IL1B, BMP7, FZD5, SFRP1, TCF7L2, FZD7,

				WNT5A
VDR/RXR Activation	CARD14 pathologic keratinocyte signature	2.6E00	7.41E-02	CXCL10, SERPINB1, CCNC, BGLAP, CCL5, CSF2
VDR/RXR Activation	Published psoriasis transcriptome	2.08E00	1.98E-01	DEFB4A/DEFB4B, IGFBP6, SERPINB1, PPARD, PDGFA, KLK6, IGFBP5, CXCL10, FOXO1 (includes EG:2308), MXD1, HOXA10, CSNK2A1, CST6 (includes EG:1474), HSD17B2, PRKCA, PRKCB
Oncostatin M Signaling	CARD14 pathologic keratinocyte signature	2.54E00	1.14E-01	EPAS1, JAK1, OSMR, PLAU
Oncostatin M Signaling	Published psoriasis transcriptome	1.14E00	2E-01	SHC1 (includes EG:20416), TIMP3, OSMR, STAT3, PLAU, STAT1, MMP1 (includes EG:300339)
Interferon Signaling	CARD14 pathologic keratinocyte signature	2.54E00	1.11E-01	IFIT3, JAK1, IFNAR2, BAK1
Interferon Signaling	Published psoriasis transcriptome	2.79E00	2.78E-01	IFIT3, IFIT1, OAS1, PIAS1, MX1, IFI35, STAT2, STAT1, IRF1 (includes EG:16362), BCL2
LXR/RXR Activation	CARD14 pathologic keratinocyte signature	2.35E00	5.34E-02	IL1R2, IL36G, IL1RN, SERPINA1, IL6, TNF, MMP9
LXR/RXR Activation	Published psoriasis transcriptome	1.37E00	1.4E-01	APOE, CD36, ABCG1, ARG2 (includes EG:11847), IL37, IL36G, LDLR, CCL2, IL1RN, LPL, IL36RN, IL1B, MMP9
Huntington's Disease Signaling	CARD14 pathologic keratinocyte signature	2.32E00	4.27E-02	AKT1, POLR2E, SGK1, CASP2, CAPN1, HDAC7, HSPA6, GNAQ, STX1A, GNG12
Huntington's Disease Signaling	Published psoriasis transcriptome	5.05E-01	1.03E-01	YKT6, SGK1, PIK3R1, GLS, GNA11, PIK3C2G, UBE2S, NAPG, HSPA2, CDK5R1, DNM1, HSPA4, SHC1 (includes EG:20416), PLCB4, IGF1, CASP1, IGF1R,

				PLCB1, AKT3 (includes EG:10000), SNCA, EGFR, PRKCA, CAPN3, PRKCB
Graft-versus-Host Disease Signaling	CARD14 pathologic keratinocyte signature	2.13E00	8.33E-02	IL36G, IL1RN, IL6, TNF
Graft-versus-Host Disease Signaling	Published psoriasis transcriptome	6.69E-01	1.25E-01	IL36G, IL1RN, IL36RN, IL1B, IL37, GZMB
Differential Regulation of Cytokine Production in Intestinal Epithelial Cells by IL-17A and IL-17F	CARD14 pathologic keratinocyte signature	2.13E00	1.3E-01	CCL5, CSF2, TNF
Differential Regulation of Cytokine Production in Intestinal Epithelial Cells by IL-17A and IL-17F	Published psoriasis transcriptome	1.77E00	2.73E-01	DEFB4A/DEFB4B, CCL4, CCL2, LCN2, CXCL1, IL1B
IL-22 Signaling	CARD14 pathologic keratinocyte signature	2.08E00	1.2E-01	SOCS3, JAK1, AKT1
IL-22 Signaling	Published psoriasis transcriptome	6.66E-01	1.6E-01	MAPK14, AKT3 (includes EG:10000), STAT3, STAT1
IL-17 Signaling	CARD14 pathologic keratinocyte signature	2.05E00	6.76E-02	CXCL10, IL8, JAK1, AKT1, IL6
IL-17 Signaling	Published psoriasis transcriptome	6.57E-01	1.35E-01	DEFB4A/DEFB4B, CXCL10, IL8, IL19, MAPK14, CCL2, PIK3R1, CXCL1, PIK3C2G, AKT3 (includes EG:10000)
TNFR1 Signaling	CARD14 pathologic keratinocyte signature	2.03E00	7.69E-02	CDC42, CASP2, TNFAIP3, TNF
Pathogenesis of Multiple Sclerosis	CARD14 pathologic keratinocyte signature	1.99E00	2.22E-01	CXCL10, CCL5
Pathogenesis of Multiple Sclerosis	Published psoriasis transcriptome	1.18E00	3.33E-01	CXCL10, CXCL9, CCL4
mTOR Signaling	CARD14 pathologic	1.87E00	4.1E-02	EIF3G, AKT1, EIF4G2, STK11, RPS15,

	keratinocyte signature			RPTOR, HIF1A, RPS6KA1 (includes EG:20111)
Sphingolipid Metabolism	CARD14 pathologic keratinocyte signature	1.85E00	4.55E-02	ARSK, SPTLC1, SPHK2, SGPP1, ARSA
Sphingolipid Metabolism	Published psoriasis transcriptome	7.14E-01	8.11E-02	CERS6, VNN1, SPTLC2, PPAP2B, ARSF, UGCG, SMPD3, VNN3, SPTSSA
Altered T Cell and B Cell Signaling in Rheumatoid Arthritis	CARD14 pathologic keratinocyte signature	1.85E00	5.75E-02	IL36G, IL1RN, IL6, CSF2, TNF
Hereditary Breast Cancer Signaling	CARD14 pathologic keratinocyte signature	1.82E00	4.84E-02	AKT1, MSH2, POLR2E, WEE1, HDAC7, SLC19A1
Role of IL-17A in Arthritis	CARD14 pathologic keratinocyte signature	1.82E00	6.35E-02	IL8, CCL20, CCL5, RPS6KA1 (includes EG:20111)
Role of IL-17A in Arthritis	Published psoriasis transcriptome	6.88E-01	1.27E-01	IL8, MAPK14, CCL2, PIK3R1, CXCL1, PIK3C2G, CCL20, MMP1 (includes EG:300339)
Cleavage and Polyadenylation of Pre-mRNA	CARD14 pathologic keratinocyte signature	1.74E00	1.67E-01	CPSF1, CSTF3
Dendritic Cell Maturation	CARD14 pathologic keratinocyte signature	1.74E00	3.91E-02	IL36G, ICAM1, AKT1, IL1RN, IL6, CSF2, TNF
Dendritic Cell Maturation	Published psoriasis transcriptome	5.1E-01	9.5E-02	FCGR3B, LEP, LEPR, PIK3R1, PIK3C2G, LTB, IL37, IL36G, MAPK14, CD1A, IL1RN, IL36RN, AKT3 (includes EG:10000), IL1B, STAT2, IRF8, STAT1
Systemic Lupus Erythematosus Signaling	CARD14 pathologic keratinocyte signature	1.73E00	3.74E-02	SNRPN, IL36G, AKT1, NFATC3, IL1RN, ZMAT5, IL6, TNF
Apoptosis Signaling	CARD14 pathologic keratinocyte signature	1.7E00	5.32E-02	CASP2, CAPN1, RPS6KA1 (includes EG:20111), TNF, BAK1
Role of IL-17A in Psoriasis	CARD14 pathologic keratinocyte signature	1.67E00	1.54E-01	IL8, CCL20

Role of IL-17A in Psoriasis	Published psoriasis transcriptome	3.75E00	5.38E-01	DEFB4A/DEFB4B, S100A7, IL8, S100A9, CXCL1, CCL20, S100A8
IL-9 Signaling	CARD14 pathologic keratinocyte signature	1.66E00	7.5E-02	SOCS3, JAK1, TNF
IL-9 Signaling	Published psoriasis transcriptome	1.2E00	1.75E-01	IRS1, PIK3R1, SOCS2, PIK3C2G, IRS2, STAT3, STAT1
ERK5 Signaling	CARD14 pathologic keratinocyte signature	1.65E00	6.35E-02	AKT1, SGK1, GNAQ, RPS6KA1 (includes EG:20111)
HMGB1 Signaling	CARD14 pathologic keratinocyte signature	1.61E00	5.05E-02	IL8, ICAM1, AKT1, CDC42, TNF
PXR/RXR Activation	CARD14 pathologic keratinocyte signature	1.6E00	4.82E-02	AKT1, CES2, IL6, TNF
PXR/RXR Activation	Published psoriasis transcriptome	9E-01	1.2E-01	GSTM1, GSTM2, PRKAR2B, FOXO1 (includes EG:2308), ALDH3A2, AKT3 (includes EG:10000), INSR, HMGCS2, CYP3A5, PPARGC1A
Role of MAPK Signaling in the Pathogenesis of Influenza	CARD14 pathologic keratinocyte signature	1.6E00	6.06E-02	CXCL10, AKT1, CCL5, TNF
Role of MAPK Signaling in the Pathogenesis of Influenza	Published psoriasis transcriptome	6E-01	1.21E-01	CXCL10, MAPK14, PLA2G2F, CCL2, PLA2G3, AKT3 (includes EG:10000), PRKCA, BCL2
IL-17A Signaling in Airway Cells	CARD14 pathologic keratinocyte signature	1.6E00	5.56E-02	JAK1, AKT1, CCL20, IL6
IL-17A Signaling in Airway Cells	Published psoriasis transcriptome	6.56E-01	1.25E-01	DEFB4A/DEFB4B, IL19, MAPK14, PIK3R1, CXCL1, PIK3C2G, AKT3 (includes EG:10000), CCL20, STAT3
Notch Signaling	CARD14 pathologic keratinocyte signature	1.57E00	7.32E-02	MAML1, FURIN, JAG2
Hypoxia Signaling in the Cardiovascular System	CARD14 pathologic keratinocyte signature	1.56E00	6.06E-02	AKT1, EDN1, HIF1A, UBE2J2

Hypoxia Signaling in the Cardiovascular System	Published psoriasis transcriptome	3.8E-01	1.06E-01	UBE2H, UBE2G1, UBE2N, UBE2S, UBE2L6, UBE2C, UBE2I
Mitochondrial Dysfunction	CARD14 pathologic keratinocyte signature	1.53E00	3.49E-02	FURIN, SOD2, NDUFA10, APP, TXNRD2, NDUFA13
Mismatch Repair in Eukaryotes	CARD14 pathologic keratinocyte signature	1.5E00	8.33E-02	MSH2, SLC19A1
Neuroprotective Role of THOP1 in Alzheimer's Disease	CARD14 pathologic keratinocyte signature	1.48E00	5.56E-02	THOP1, APP, MMP9
Neuroprotective Role of THOP1 in Alzheimer's Disease	Published psoriasis transcriptome	3.47E-01	9.26E-02	PRKAR2B, SERPINA3, MAPT, IDE, MMP9
HIF1α Signaling	CARD14 pathologic keratinocyte signature	1.48E00	4.72E-02	AKT1, EDN1, HIF1A, NAA10, MMP9
HIF1α Signaling	Published psoriasis transcriptome	4.44E-01	1.13E-01	MMP7, MAPK14, MMP28, PIK3R1, PIK3C2G, AKT3 (includes EG:10000), MMP12, PDGFC, MMP9, SLC2A3, MMP1 (includes EG:300339), P4HTM
Hepatic Cholestasis	CARD14 pathologic keratinocyte signature	1.47E00	3.49E-02	IL1R2, IL8, IL36G, IL1RN, IL6, TNF
Hepatic Cholestasis	Published psoriasis transcriptome	4.03E-01	8.72E-02	IL8, ADCY2, CYP7B1, IL37, IL36G, PRKAR2B, SLCO3A1, IL1RN, ABCC1, IL36RN, IL1B, INSR, GNAL, PRKCB, PRKCA
Androgen and Estrogen Metabolism	CARD14 pathologic keratinocyte signature	1.42E00	3.23E-02	ARSK, AKR1C1/AKR1C2, ARSA, AKR1C4
Androgen and Estrogen Metabolism	Published psoriasis transcriptome	1.13E00	8.13E-02	CYP7B1, SRD5A3, DHRS9, CYP2E1, ARSF, SULT1E1, STS, HSD17B1, HSD11B1, HSD17B2
ILK Signaling	CARD14 pathologic keratinocyte signature	1.41E00	3.76E-02	FN1, AKT1, CDC42, HIF1A, TNF, ITGB5, MMP9
ILK Signaling	Published psoriasis	9.11E-01	1.24E-01	MUC1, BMP2, PIK3R1, ACTA2, FERMT2,

	transcriptome			PIK3C2G, MYH11, PDGFC, CCND1, MYL9, TGFB1I1, RHOB, KRT18, IRS1, PPAP2B, AKT3 (includes EG:10000), PPP1R12A, IRS2, ACTG2, MMP9, ITGB5, ACTA1, TESK1
C21-Steroid Hormone Metabolism	CARD14 pathologic keratinocyte signature	1.4E00	3.08E-02	AKR1C1/AKR1C2, AKR1C4
C21-Steroid Hormone Metabolism	Published psoriasis transcriptome	2.7E-01	3.08E-02	HSD11B1, HSD17B2
HER-2 Signaling in Breast Cancer	CARD14 pathologic keratinocyte signature	1.36E00	5.06E-02	AKT1, CDC42, PARD6B, ITGB5
HER-2 Signaling in Breast Cancer	Published psoriasis transcriptome	1.28E00	1.65E-01	CCNE2, PIK3R1, PIK3C2G, CCND1, AREG/AREGB, CCNE1, FOXO1 (includes EG:2308), AKT3 (includes EG:10000), PARD3, ITGB5, PRKCA, EGFR, PRKCB
Axonal Guidance Signaling	CARD14 pathologic keratinocyte signature	1.36E00	2.79E-02	AKT1, SDCBP, GLI3, CDC42, NFATC3, ADAM19, GNAQ, PLXNB2, ITGA3, ADAM9, GNG12, FARP2
Axonal Guidance Signaling	Published psoriasis transcriptome	2.12E00	1.23E-01	SLIT3, RAC2, ITSN1, EPHB2, PIK3R1, GNA15, ABLIM3, PLCB1, SRGAP2, ACTR2, PTCH1, ITGA5, MYL9, FZD5, PDGFD, EPHA2, GNAL, FYN, MMP7, PDGFA, BMP2, ARHGEF7, GNA11, EPHA4, FZD1, PLXNA2, PDGFC, EIF4E, EPHB6, SHC1 (includes EG:20416), EFNB2, WASL, NFAT5, IGF1, SDC2, EFNA5, AKT3 (includes EG:10000), PRKCA, SEMA3G, CXCR4, PFN2, PIK3C2G, NFATC1, SLIT2, PLCB4, FZD4, NTRK2, PRKAR2B, ADAM10, BMP7, PRKCB, FZD7, WNT5A

CNTF Signaling	CARD14 pathologic keratinocyte signature	1.26E00	5.77E-02	JAK1, AKT1, RPS6KA1 (includes EG:20111)
Colorectal Cancer Metastasis Signaling	CARD14 pathologic keratinocyte signature	1.25E00	3.16E-02	JAK1, AKT1, MSH2, DVL1, IL6, TNF, MMP9, GNG12
Colorectal Cancer Metastasis Signaling	Published psoriasis transcriptome	5.82E-01	1.07E-01	MMP7, PTGER3, PIK3R1, FZD1, CCND1, PDGFC, BIRC5, RHOB, AKT3 (includes EG:10000), STAT1, MMP12, MMP1 (includes EG:300339), EGFR, ADCY2, MMP28, PIK3C2G, STAT3, TCF7L1, CDH1, PRKAR2B, FZD4, FZD5, MMP9, GNAL, TCF7L2, FZD7, WNT5A
Amyloid Processing	CARD14 pathologic keratinocyte signature	1.24E00	5.56E-02	AKT1, CAPN1, APP
Amyloid Processing	Published psoriasis transcriptome	8.25E-01	1.48E-01	MAPK14, PRKAR2B, CSNK2A1, CSNK1A1, AKT3 (includes EG:10000), MAPT, CDK5R1, CAPN3
FXR/RXR Activation	CARD14 pathologic keratinocyte signature	1.21E00	4.04E-02	IL36G, AKT1, IL1RN, TNF
FXR/RXR Activation	Published psoriasis transcriptome	3.57E-01	9.09E-02	APOE, IL36G, FOXO1 (includes EG:2308), IL1RN, IL36RN, AKT3 (includes EG:10000), IL1B, IL37, PPARGC1A
FAK Signaling	CARD14 pathologic keratinocyte signature	1.18E00	3.96E-02	AKT1, CSK, CAPN1, ITGA3
FAK Signaling	Published psoriasis transcriptome	9.29E-01	1.29E-01	FYN, ARHGEF7, HMMR, PIK3R1, ACTA2, PIK3C2G, ITGA5, AKT3 (includes EG:10000), ACTG2, TNS1, ACTA1, EGFR, CAPN3
Tumoricidal Function of Hepatic Natural Killer Cells	CARD14 pathologic keratinocyte signature	1.18E00	8.33E-02	ICAM1, SRGN
Tumoricidal Function of	Published psoriasis	5.76E-01	1.67E-01	SERPINB9, SRGN, LYVE1, GZMB

Hepatic Natural Killer Cells	transcriptome			
Role of JAK1, JAK2 and TYK2 in Interferon Signaling	CARD14 pathologic keratinocyte signature	1.18E00	7.41E-02	JAK1, IFNAR2
Role of JAK1, JAK2 and TYK2 in Interferon Signaling	Published psoriasis transcriptome	3.02E-01	1.11E-01	STAT2, STAT3, STAT1
Insulin Receptor Signaling	CARD14 pathologic keratinocyte signature	1.17E00	3.76E-02	SOCS3, JAK1, AKT1, SGK1, RPTOR
Insulin Receptor Signaling	Published psoriasis transcriptome	5.41E-01	1.13E-01	FYN, SGK1, PPP1R3C, PIK3R1, PIK3C2G, EIF4E, EIF4EBP1, SHC1 (includes EG:20416), PRKAR2B, FOXO1 (includes EG:2308), IRS1, PPP1R12A, AKT3 (includes EG:10000), IRS2, INSR
Airway Inflammation in Asthma	CARD14 pathologic keratinocyte signature	1.16E00	1.67E-01	TNF
NF-κB Signaling	CARD14 pathologic keratinocyte signature	1.16E00	3.51E-02	IL1R2, IL36G, AKT1, IL1RN, TNFAIP3, TNF
NF-κB Signaling	Published psoriasis transcriptome	1.5E00	1.4E-01	BMP2, UBE2N, TGFBR3, FGFR1, PIK3R1, PIK3C2G, IL37, MALT1, TANK, LCK, IL36G, GHR, NTRK2, IL1RN, IL36RN, TGFA, CSNK2A1, IGF1R, AKT3 (includes EG:10000), IL1B, TRAF5, INSR, EGFR, PRKCB
N-Glycan Degradation	CARD14 pathologic keratinocyte signature	1.15E00	8E-02	MANEA, MAN2B1
N-Glycan Degradation	Published psoriasis transcriptome	1.47E00	2.4E-01	MAN1C1, GM2A, MAN1A1, MAN1A2, MAN2A2, ENGASE
G Beta Gamma Signaling	CARD14 pathologic keratinocyte signature	1.14E00	3.54E-02	AKT1, CDC42, GNAQ, GNG12
G Beta Gamma Signaling	Published psoriasis transcriptome	4.67E-01	9.73E-02	SHC1 (includes EG:20416), ADCY2, PRKAR2B, GNA15, GNA11, AKT3

				(includes EG:10000), HBEGF, GNAL, PRKCA, EGFR, PRKCB
Methionine Metabolism	CARD14 pathologic keratinocyte signature	1.12E00	2.67E-02	MAT2B, AMD1
PPAR Signaling	CARD14 pathologic keratinocyte signature	1.11E00	3.92E-02	IL1R2, IL36G, IL1RN, TNF
PPAR Signaling	Published psoriasis transcriptome	6.17E-01	1.18E-01	SHC1 (includes EG:20416), IL36G, PPARD, PDGFA, IL1RN, IL36RN, IL1B, INSR, IL37, PDGFD, PDGFC, PPARGC1A
Glioma Invasiveness Signaling	CARD14 pathologic keratinocyte signature	1.1E00	5E-02	PLAU, ITGB5, MMP9
Glioma Invasiveness Signaling	Published psoriasis transcriptome	1.97E00	2E-01	TIMP3, TIMP4, F2R, RHOB, HMMR, PIK3R1, PIK3C2G, PLAUR, PLAU, ITGB5, MMP9, TIMP2 (includes EG:21858)
IL-15 Production	CARD14 pathologic keratinocyte signature	1.09E00	6.45E-02	JAK1, IL6
IL-15 Production	Published psoriasis transcriptome	4.65E-01	1.29E-01	TWF1 (includes EG:19230), MST1R, STAT1, IRF1 (includes EG:16362)
Ephrin Receptor Signaling	CARD14 pathologic keratinocyte signature	1.08E00	3.03E-02	AKT1, SDCBP, CDC42, GNAQ, ITGA3, GNG12
Ephrin Receptor Signaling	Published psoriasis transcriptome	1.9E00	1.36E-01	RAC2, FYN, ITSN1, EPHB2, PDGFA, GNA11, EPHA4, PDGFC, EPHB6, EFNB2, SHC1 (includes EG:20416), WASL, GNA15, SDC2, SORBS1, EFNA5, AKT3 (includes EG:10000), ACTR2, ANGPT1, CXCR4, PIK3C2G, ITGA5, STAT3, ADAM10, PDGFD, EPHA2, GNAL
TNFR2 Signaling	CARD14 pathologic keratinocyte signature	1.06E00	6.06E-02	TNFAIP3, TNF
Pyruvate Metabolism	CARD14 pathologic	1.05E00	2.33E-02	ME2, ACOT9, HAGH

	keratinocyte signature			
Pyruvate Metabolism	Published psoriasis transcriptome	4.66E-01	5.38E-02	ACSL3, ACACB, ALDH1A3, ALDH3A2, DLAT, PCK1 (includes EG:18534), ME1
IL-15 Signaling	CARD14 pathologic keratinocyte signature	1.03E00	4.48E-02	JAK1, AKT1, CSF2
IL-15 Signaling	Published psoriasis transcriptome	9.72E-01	1.49E-01	SHC1 (includes EG:20416), LCK, MAPK14, SYK, PIK3R1, PIK3C2G, AKT3 (includes EG:10000), STAT3, AXL, BCL2
Role of JAK1 and JAK3 in γc Cytokine Signaling	CARD14 pathologic keratinocyte signature	1.03E00	4.55E-02	IL7R, SOCS3, JAK1
Role of JAK1 and JAK3 in γc Cytokine Signaling	Published psoriasis transcriptome	1.01E00	1.52E-01	BLNK, SHC1 (includes EG:20416), IL4R, IRS1, SYK, PIK3R1, PIK3C2G, IRS2, STAT3, STAT1
JAK/Stat Signaling	CARD14 pathologic keratinocyte signature	1.03E00	4.69E-02	SOCS3, JAK1, AKT1
JAK/Stat Signaling	Published psoriasis transcriptome	7.14E-01	1.41E-01	SHC1 (includes EG:20416), PIK3R1, PIAS1, SOCS2, PIK3C2G, AKT3 (includes EG:10000), STAT2, STAT3, STAT1
Nicotinate and Nicotinamide Metabolism	CARD14 pathologic keratinocyte signature	1.02E00	2.99E-02	NAPRT1, SGK1, NAMPT, PKN1
Nicotinate and Nicotinamide Metabolism	Published psoriasis transcriptome	3.4E-01	7.52E-02	MAP3K9, NEK2, VNN1, SGK1, PNP, CSNK1A1, NAMPT, TTK, VNN3, CDK1
Paxillin Signaling	CARD14 pathologic keratinocyte signature	1.01E00	3.64E-02	CDC42, CSK, ITGA3, ITGB5
G Protein Signaling Mediated by Tubby	CARD14 pathologic keratinocyte signature	9.86E-01	5.13E-02	GNAQ, GNG12
G Protein Signaling Mediated by Tubby	Published psoriasis transcriptome	4.04E-01	1.03E-01	LCK, PLCB4, PLCB1, INSR
Cholecystokinin/Gastrin-mediated Signaling	CARD14 pathologic keratinocyte signature	9.85E-01	3.77E-02	IL36G, IL1RN, GNAQ, TNF

Cholecystokinin/Gastrin-mediated Signaling	Published psoriasis transcriptome	1.63E00	1.6E-01	ITPR2, EPHA4, IL37, SHC1 (includes EG:20416), PLCB4, IL36G, MAPK14, RHOB, IL1RN, ITPR3, IL36RN, IL1B, PLCB1, MEF2C, PRKCB, EGFR, PRKCA
Regulation of eIF4 and p70S6K Signaling	CARD14 pathologic keratinocyte signature	9.71E-01	2.98E-02	EIF3G, AKT1, EIF4G2, RPS15, ITGA3
Inhibition of Angiogenesis by TSP1	CARD14 pathologic keratinocyte signature	9.4E-01	5.26E-02	AKT1, MMP9
Inhibition of Angiogenesis by TSP1	Published psoriasis transcriptome	1.26E00	1.84E-01	FYN, CD47, MAPK14, SDC2, CD36, AKT3 (includes EG:10000), MMP9
Role of JAK2 in Hormone-like Cytokine Signaling	CARD14 pathologic keratinocyte signature	9.4E-01	5.71E-02	SOCS3, JAK1
Role of JAK2 in Hormone-like Cytokine Signaling	Published psoriasis transcriptome	1.33E00	2E-01	SHC1 (includes EG:20416), GHR, IRS1, SOCS2, IRS2, STAT3, STAT1
Agrin Interactions at Neuromuscular Junction	CARD14 pathologic keratinocyte signature	9.4E-01	4.41E-02	CDC42, DVL1, ITGA3
Agrin Interactions at Neuromuscular Junction	Published psoriasis transcriptome	3.94E-01	1.18E-01	RAC2, ARHGEF7, ACTA2, LAMA2, ITGA5, ACTG2, ACTA1, EGFR
IL-4 Signaling	CARD14 pathologic keratinocyte signature	9.4E-01	4.17E-02	JAK1, AKT1, NFATC3
IL-4 Signaling	Published psoriasis transcriptome	8.66E-01	1.39E-01	SHC1 (includes EG:20416), IL4R, NFAT5, IL13RA1, IRS1, PIK3R1, PIK3C2G, AKT3 (includes EG:10000), NFATC1, NR3C2 (includes EG:110784)
Pancreatic Adenocarcinoma Signaling	CARD14 pathologic keratinocyte signature	9.39E-01	3.39E-02	JAK1, AKT1, CDC42, MMP9
Pancreatic Adenocarcinoma Signaling	Published psoriasis transcriptome	1.14E00	1.36E-01	PIK3R1, PIK3C2G, HBEGF, STAT3, PDGFC, CCND1, BIRC5, BCL2, HMOX1, CCNE1, CYP2E1, TGFA, AKT3 (includes EG:10000), STAT1, MMP9, EGFR

p38 MAPK Signaling	CARD14 pathologic keratinocyte signature	9.28E-01	3.77E-02	IL1R2, IL36G, IL1RN, TNF
p38 MAPK Signaling	Published psoriasis transcriptome	7.13E-01	1.23E-01	MAPKAPK3, PLA2G3, H3F3A/H3F3B, IL37, IL36G, MAPK14, PLA2G2F, IL1RN, IL36RN, IL1B, HSPB7, MEF2C, STAT1
Neurotrophin/TRK Signaling	CARD14 pathologic keratinocyte signature	9.26E-01	3.95E-02	AKT1, CDC42, RPS6KA1 (includes EG:20111)
Renal Cell Carcinoma Signaling	CARD14 pathologic keratinocyte signature	9.12E-01	4.11E-02	AKT1, CDC42, HIF1A
Coagulation System	CARD14 pathologic keratinocyte signature	8.98E-01	5.26E-02	SERPINA1, PLAU
Coagulation System	Published psoriasis transcriptome	1.95E00	2.37E-01	F10, F12, F2R, PLAUR, SERPINA1, PLAU, TFPI, F3, PLAT
Nucleotide Excision Repair Pathway	CARD14 pathologic keratinocyte signature	8.98E-01	5.71E-02	POLR2E, ERCC2
Selenoamino Acid Metabolism	CARD14 pathologic keratinocyte signature	8.98E-01	2.74E-02	GGT2, MAT2B
Tight Junction Signaling	CARD14 pathologic keratinocyte signature	8.8E-01	3.12E-02	AKT1, CDC42, CPSF1, TNF, CSTF3
Tight Junction Signaling	Published psoriasis transcriptome	4.95E-01	1.06E-01	CLDN10, OCLN, TJP1 (includes EG:21872), ACTA2, MYH11, CASK, MYL9, MYLK, MPDZ, PRKAR2B, CLDN8, JAM3, AKT3 (includes EG:10000), ACTG2, SPTAN1, MAGI2, ACTA1
Androgen Signaling	CARD14 pathologic keratinocyte signature	8.75E-01	2.88E-02	POLR2E, GNAQ, ERCC2, GNG12
Role of Pattern Recognition Receptors in Recognition of Bacteria and Viruses	CARD14 pathologic keratinocyte signature	8.59E-01	3.66E-02	CCL5, IL6, TNF
Role of Pattern Recognition	Published psoriasis	1.45E00	1.59E-01	OAS1, OAS2, PIK3R1, PIK3C2G, OAS3,

Receptors in Recognition of Bacteria and Viruses	transcriptome			IFIH1, CLEC7A, IRF7, NOD2, SYK, DDX58, CASP1, IL1B
NF-κB Activation by Viruses	CARD14 pathologic keratinocyte signature	8.59E-01	3.66E-02	AKT1, ITGA3, ITGB5
NF-κB Activation by Viruses	Published psoriasis transcriptome	2.68E-01	9.76E-02	LCK, PIK3R1, PIK3C2G, ITGA5, AKT3 (includes EG:10000), ITGB5, PRKCA, PRKCB
CD28 Signaling in T Helper Cells	CARD14 pathologic keratinocyte signature	8.55E-01	3.1E-02	AKT1, CDC42, NFATC3, CSK
CD28 Signaling in T Helper Cells	Published psoriasis transcriptome	6.49E-01	1.09E-01	FYN, ACTR2, ITPR2, PIK3R1, PIK3C2G, NFATC1, MALT1, PTPRC, LCK, NFAT5, SYK, ITPR3, AKT3 (includes EG:10000), LCP2

A list of the top 200 upregulated and top 200 downregulated genes that differentiate the global transcriptome of overtly pathogenic and non-pathogenic CARD14 variants was generated as described in Methods. Pathway analysis was performed with Ingenuity Pathway Analysis (IPA), and a comparison was made with the results of a published psoriasis transcriptome.[3] The top 100 pathways (by –log[P]) from the CARD14 pathway analysis were selected and compared to the published transcriptome.[3] This table presents the results of that comparison. Each pathway in this table has results reported from the CARD14 pathologic keratinocyte signature. Most, but not all, of the pathways have a second listing with results from the psoriasis transcriptome. Pathways with a listing only for the CARD14 transfectants were not identified by IPA in the general psoriasis transcriptome. In the table, "Analysis" refers to the expression data used for the pathway analysis, e.g. CARD14 pathologic keratinocyte signature or published psoriasis transcriptome.[3] –log[P] – the negative logarithm of the p-value, Ratio – the ratio of the number of molecules in the indicated expression signature to the total number of genes in that pathway according to IPA.

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