

**DO GENETIC SUSCEPTIBILITY VARIANTS ASSOCIATE WITH DISEASE SEVERITY IN EARLY ACTIVE RHEUMATOID ARTHRITIS?**

**ONLINE SUPPLEMENTARY DATA**

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**Supplementary Table 1. Genotyping Quality Control Procedures**

<b>Individual-Level QC</b>		
<b>QC Stage</b>	<b>No. Individuals In Dataset</b>	<b>No. Individuals Removed</b>
Pre-QC	560	-
<95% SNP call rates	552	8
Anomalously high/low heterozygosity	550	2
Non-European ancestry <sup>a</sup>	530	20
Relatedness	530	0
Genotype-phenotype gender discordance	528	2
Duplicate samples	524	4
Post-QC	524	-
<b>Marker-Level QC</b>		
<b>QC Stage</b>	<b>No. SNPs In Dataset</b>	<b>No. SNPs Removed</b>
Pre-QC	196,524	-
Marker missingness >5%	193,054	3,470
Not in GRCh37 assembly/duplicate markers	191,306	1,748
HWE ( $P < 0.00001$ )	188,148	3,158
MAF < 0.01	138,873	49,275
Post-QC	138,873	-

a= Ethnic outliers identified by principal components analysis (PCA) plots of samples merged with HapMap3 data; QC = quality control; No. = number; GRCh37 = Genome Reference Consortium Human Build 37; MAF = minor allele frequency; HWE = Hardy-Weinberg equilibrium.

**Supplementary Table 2. Proxy SNPs Used In Analysis**

Meta-Analysis SNP				Proxy SNP			
SNP	Chr	BP Position	A1/ A2	SNP	BP Position	A1/ A2	r <sup>2</sup>
chr1:2523811	1	2523811	G/A	rs10752747	2524915	G/T	0.875
chr17:38031857	17	38031857	G/T	rs10852935	38031674	T/C	0.979
rs10790268	11	118729391	G/A	rs10892299	118726843	C/T	0.915
rs71508903	10	63779871	T/C	rs11593907	63786554	C/T	0.865
rs73194058	21	34764288	C/A	rs11702844	34759876	A/G	0.970
rs4452313	3	17047032	T/A	rs12108065	17074871	G/A	0.925
rs2105325	1	173349725	C/A	rs1557121	173353881	C/T	0.986
rs6715284	2	202154397	G/C	rs16837131	202173812	A/C	0.972
rs2736337	8	11341880	C/T	rs2061831	11339882	C/T	0.993
rs5987194	X	153301467	C/G	rs2075596	153297392	A/G	0.989
rs331463	11	36501787	T/A	rs2303439	36514290	C/T	0.944
rs28411352	1	38278579	T/C	rs2306627	38260503	T/C	0.844
chr21:35928240	21	35928240	C/T	rs2834512	35911599	G/A	0.979
rs8083786	18	12881361	G/A	rs34846641	12875975	G/A	1.000
chr7:128580042	7	128580042	G/A	rs3778754	128575552	G/C	0.948
rs3824660	10	8104722	C/T	rs3802604	8102272	G/A	0.926
rs508970	11	60906450	A/G	rs595158	60909581	C/A	0.929
rs10774624	12	111833788	G/A	rs653178	112007756	C/T	0.861
rs1516971	8	129542100	T/C	rs6651252	129567181	T/C	0.985
rs1633360	12	58108052	T/C	rs701006	58106836	G/A	0.979
rs773125	12	56394954	A/G	rs705700	56389293	T/C	0.967
rs706778	10	6098949	T/C	rs7073236	6106552	C/T	0.910
rs10175798	2	30449594	A/G	rs7579944	30445026	C/T	0.940
rs9603616	13	40368069	C/T	rs7993214	40350912	C/T	0.936
rs2234067	6	36355654	C/A	rs879036	36349890	C/T	0.964
rs12140275	1	38633879	A/T	rs883220	38616871	C/A	0.962
rs1950897	14	68760141	T/C	rs911263	68753593	T/C	0.994
rs9372120	6	106667535	G/T	rs9386514	106636902	C/T	0.992
rs72717009	1	161405053	T/C	rs9427372	161399920	C/T	0.966
rs9826828	3	136402060	A/G	rs9858105	136219264	C/T	1.000
rs8133843	21	36738242	A/G	rs9979383	36715761	T/C	0.894

Proxy SNPs obtained using 1,000 Genomes European population panels (CEU/TSI/GBR/FIN/IBS); BP position = base pair position based on GRCh37 assembly; Chr = chromosome; reference meta-analysis by Okada *et al* (1).

**Supplementary Table 3. Clinical Factors Associated With Larsen Scores in CARDERA**

<b>Variable</b>		<b>β (95% CI)</b>	<b>P-Value</b>
<i>Time</i>		1.20 (1.17-1.24)	<0.001
<i>Treatment*</i>	<i>MTX</i>	Reference	-
	<i>MTX/CIC</i>	1.22 (0.95-1.56)	0.115
	<i>MTX/Pred</i>	0.95 (0.74-1.23)	0.708
	<i>Triple Therapy</i>	0.85 (0.67-1.09)	0.200
	<i>Anakinra</i>	1.40 (1.01-1.95)	0.045
<i>Age</i>		1.04 (1.03-1.05)	<0.001
<i>Disease Duration</i>		1.04 (1.02-1.06)	<0.001
<i>RF</i>		1.35 (1.12-1.62)	0.002

Effect sizes and *P*-values from a linear mixed-effects model including time and clinical factors only as fixed-effects predictor variables; CI = confidence interval; MTX = methotrexate; CIC = ciclosporin; Pred = prednisolone; triple therapy = methotrexate, ciclosporin and prednisolone; \*although *P*-values are given for each treatment group, including treatment as a model covariate resulted in a significantly lower AIC (P=0.018).

**Supplementary Table 4. Association between 69 RA Susceptibility SNPs and Radiological Progression in CARDERA Using a Linear Mixed-Effects Model**

SNP	Chr	Gene	A1/A2	Allele Frequency		$\beta$	P-Value
				Meta-Analysis	CARDERA		
rs660895 <sup>A</sup>	6	<i>HLA-DRB1</i>	G/A	0.46	0.37	1.074	0.0003
rs7579944	2	<i>LBH</i>	C/T	0.65	0.66	1.057	0.0074
rs12108065	3	<i>PLCL2</i>	G/A	0.30	0.28	1.053	0.0194
rs10852935	17	<i>IKZF3-CSF3</i>	T/C	0.48	0.50	0.958	0.0253
rs653178	12	<i>SH2B3-PTPN11</i>	C/T	0.51	0.51	0.958	0.0338
rs3802604	10	<i>GATA3</i>	G/A	0.38	0.36	1.039	0.0615
rs11593907	10	<i>ARID5B</i>	C/T	0.24	0.20	0.959	0.0836
rs7752903	6	<i>TNFAIP3</i>	G/T	0.04	0.04	0.919	0.0950
rs624988	1	<i>CD2</i>	T/C	0.42	0.40	0.967	0.0971
rs678347	8	<i>GRHL2</i>	G/A	0.29	0.28	0.963	0.0981
rs2075596 <sup>B</sup>	X	<i>IRAK1</i>	A/G	0.15	0.15	1.048	0.1309
rs998731	8	<i>TPD52</i>	T/C	0.45	0.48	0.972	0.1324
rs11889341	2	<i>STAT4</i>	T/C	0.25	0.25	1.036	0.1398
rs4239702	20	<i>CD40</i>	C/T	0.75	0.74	1.031	0.1576
rs968567	11	<i>FADS1-FADS2-FADS3</i>	C/T	0.84	0.84	1.037	0.1657
rs34846641	18	<i>PTPN2</i>	G/A	0.17	0.17	0.965	0.1682
rs2561477	5	<i>C5orf30</i>	G/A	0.70	0.69	1.028	0.1849
rs73081554	3	<i>DNASE1L3-ABHD6-PXK</i>	T/C	0.08	0.09	0.957	0.1937
rs17264332	6	<i>TNFAIP3</i>	G/A	0.24	0.26	0.974	0.2239
rs11702844	21	<i>IFNGR2</i>	A/G	0.88	0.87	1.036	0.2250
rs2075596 <sup>C</sup>	X	<i>IRAK1</i>	A/G	0.15	0.15	0.956	0.2284
rs9386514	6	<i>ATG5</i>	C/T	0.21	0.21	0.973	0.2381
rs1858037	2	<i>SPRED2</i>	T/A	0.68	0.68	0.980	0.3253
rs10752747	1	<i>TNFRSF14-MMEL1</i>	G/T	0.70	0.67	1.020	0.3354
rs595158	11	<i>CD5</i>	C/A	0.51	0.54	0.983	0.4006
rs1893592	21	<i>UBASH3A</i>	A/C	0.73	0.73	0.983	0.4172
rs3087243	2	<i>CTLA4</i>	G/A	0.59	0.55	1.015	0.4240
rs45475795	4	<i>IL2-IL21</i>	G/A	0.08	0.08	0.975	0.4468
rs8026898	15	<i>LOC145837</i>	A/G	0.29	0.30	1.017	0.4492
rs1571878	6	<i>CCR6</i>	C/T	0.47	0.47	0.986	0.4688
rs10985070	9	<i>TRAF1-C5</i>	C/A	0.44	0.41	1.012	0.5212
rs9427372	1	<i>FCGR2A</i>	C/T	0.12	0.09	0.980	0.5564
rs879036	6	<i>ETV7</i>	C/T	0.88	0.88	0.983	0.5810
rs34695944	2	<i>REL</i>	C/T	0.39	0.39	1.010	0.6105
rs7993214	13	<i>COG6</i>	C/T	0.68	0.69	1.011	0.6180
rs11574914	9	<i>CCL19-CCL21</i>	A/G	0.36	0.37	1.010	0.6298
rs2301888	1	<i>PADI4</i>	G/A	0.67	0.66	0.991	0.6404
rs2306627	1	<i>MTF1-INPP5B</i>	T/C	0.31	0.30	1.009	0.6518

rs883220	1	<i>LOC339442</i>	C/A	0.77	0.76	0.990	0.6522
rs2451258	6	<i>TAGAP</i>	T/C	0.67	0.62	0.991	0.6575
rs2228145	1	<i>IL6R</i>	A/C	0.62	0.60	0.991	0.6624
rs13330176	16	<i>IRF8</i>	A/T	0.25	0.27	1.009	0.6717
rs909685	22	<i>SYNGR1</i>	A/T	0.32	0.32	1.008	0.6926
rs3218251	22	<i>IL2RB</i>	A/T	0.28	0.28	0.991	0.6931
rs17668708	1	<i>PTPRC</i>	C/T	0.91	0.90	1.012	0.7098
rs2303439	11	<i>TRAF6-RAG1/2</i>	C/T	0.86	0.87	1.011	0.7108
rs701006	12	<i>CDK4</i>	G/A	0.60	0.60	0.993	0.7338
rs947474	10	<i>PRKCQ</i>	A/G	0.83	0.83	0.992	0.7412
rs2834512	21	<i>RCANI</i>	G/A	0.89	0.89	1.010	0.7485
		<i>RUNX1-</i>					
rs9979383	21	<i>LOC100506403</i>	T/C	0.65	0.65	1.006	0.7567
rs10892299	11	<i>CXCR5</i>	C/T	0.83	0.83	0.993	0.7656
rs67250450	7	<i>JAZF1</i>	T/C	0.80	0.81	0.993	0.7791
rs705700	12	<i>CDK2</i>	T/C	0.61	0.62	1.005	0.7871
rs911263	14	<i>RAD51B</i>	T/C	0.73	0.73	0.994	0.7890
rs3806624	3	<i>EOMES</i>	G/A	0.47	0.44	0.995	0.7896
rs9858105	3	<i>IL20RB</i>	C/T	0.02	0.01	1.021	0.8146
rs9653442	2	<i>AFF3</i>	C/T	0.49	0.51	1.004	0.8189
rs7073236	10	<i>IL2RA</i>	C/T	0.44	0.43	0.996	0.8353
rs16837131	2	<i>CFLAR-CASP8</i>	A/C	0.10	0.11	1.005	0.8745
rs8032939	15	<i>RASGRP1</i>	C/T	0.28	0.26	1.003	0.8830
rs11933540	4	<i>C4orf52</i>	C/T	0.34	0.34	0.997	0.8872
rs4409785	11	<i>CEP57</i>	C/T	0.19	0.19	0.997	0.8912
rs2061831	8	<i>BLK</i>	C/T	0.27	0.25	0.997	0.8940
rs4272	7	<i>CDK6</i>	G/A	0.23	0.23	1.003	0.8946
rs1980422	2	<i>CD28</i>	C/T	0.25	0.22	1.002	0.9251
rs2476601	1	<i>PTPN22</i>	A/G	0.16	0.15	1.002	0.9284
rs1557121	1	<i>LOC100506023</i>	C/T	0.77	0.76	0.999	0.9664
rs3778754	7	<i>IRF5</i>	G/C	0.49	0.51	1.001	0.9688
rs34536443	19	<i>TYK2</i>	G/C	0.97	0.97	1.002	0.9716
rs6651252	8	<i>PVT1</i>	T/C	0.88	0.88	1.001	0.9723

Alleles ordered by significance (most significant listed first); A = SNP A1 frequency data from Raychaudhuri *et al* meta-analysis (2) (data unavailable in Eyre *et al* meta-analysis (3)); B = result in females; C = result in males; Chr = chromosome; unless otherwise stated reference meta-analysis is by Okada *et al* (1).

**Supplementary Table 5. Association between RA *HLA-DRB1* Susceptibility Alleles and Radiological Progression in CARDERA Using a Linear Mixed-Effects Model**

<i>HLA-DRB1</i> Allele	Allele Frequency		$\beta$	<i>P</i> - Value
	Meta- Analysis	CARDERA		
*04:01	0.31	0.22	1.10	0.0002
*04:08	0.02	0.01	1.36	0.0043
*13:02	0.01	0.02	0.88	0.0840
*15:01	0.09	0.10	0.95	0.0973
*03:01	0.08	0.11	0.95	0.1110
*13:01	0.02	0.02	0.92	0.2031
*07:01	0.06	0.09	0.97	0.3400
*10:01	0.02	0.01	0.92	0.3612
*14:01	0.01	0.01	1.08	0.4875
*01:01	0.13	0.13	1.02	0.5026
*04:04	0.09	0.09	0.98	0.6475
*11:04	0.01	0.02	0.97	0.6810
*11:01	0.03	0.04	1.02	0.7756
*04:05	0.01	0.01	1.01	0.8902
*08:01	0.01	0.02	1.00	0.9971

Alleles ordered by significance (most significant listed first); reference meta-analysis by Raychaudhuri *et al* (2).

**Supplementary Table 6. Relationship between HLA Amino Acid Polymorphisms and Radiological Progression in CARDERA Using a Linear Mixed-Effects Model**

HLA Amino Acid	Amino Acid Frequency		$\beta$	P-Value
	Meta-Analysis	CARDERA		
DR $\beta$ 1; position 13; Histidine	0.45	0.35	1.07	0.0005
DR $\beta$ 1; position 11; Valine	0.47	0.36	1.07	0.0012
DR $\beta$ 1; position 13; Serine	0.18	0.23	0.95	0.0278
DR $\beta$ 1; position 71; Lysine	0.40	0.34	1.05	0.0293
DR $\beta$ 1; position 71; Glutamic Acid	0.05	0.06	0.91	0.0308
DR $\beta$ 1; position 71; Alanine	0.09	0.11	0.94	0.0625
DR $\beta$ 1; position 11; Serine	0.21	0.27	0.96	0.0901
DR $\beta$ 1; position 74; Alanine	0.80	0.74	1.04	0.0929
DR $\beta$ 1; position 74; Arginine	0.08	0.11	0.95	0.1119
DR $\beta$ 1; position 13; Arginine	0.10	0.12	0.95	0.1133
DR $\beta$ 1; position 11; Proline	0.10	0.12	0.95	0.1135
DR $\beta$ 1; position 11; Aspartic Acid	0.01	0.01	0.90	0.2048
DR $\beta$ 1; position 13; Tyrosine	0.06	0.09	0.97	0.3379
DR $\beta$ 1; position 11; Glycine	0.06	0.09	0.97	0.3381
DR $\beta$ 1; position 74; Glutamine	0.06	0.09	0.97	0.3407
DP $\beta$ 1; position 9; Histidine	0.04	0.05	0.95	0.3863
DR $\beta$ 1; position 13; Glycine	0.03	0.04	1.04	0.4572
DR $\beta$ 1; position 74; Leucine	0.01	0.02	1.04	0.5478
DP $\beta$ 1; position 9; Phenylalanine	0.80	0.73	1.01	0.5764
B; position 9; Tyrosine	0.64	0.65	1.01	0.6844
DR $\beta$ 1; position 11; Leucine	0.15	0.15	1.01	0.6857
B; position 9; Histidine	0.23	0.22	0.99	0.7337
DR $\beta$ 1; position 13; Phenylalanine	0.18	0.18	0.99	0.7829
DR $\beta$ 1; position 71; Arginine	0.46	0.49	1.00	0.8221
DP $\beta$ 1; position 9; Tyrosine	0.17	0.22	0.99	0.8245
DR $\beta$ 1; position 74; Glutamic Acid	0.04	0.04	0.99	0.8754
B; position 9; Aspartic Acid	0.13	0.13	1.00	0.8912

Amino acids ordered by significance (most significant listed first); reference meta-analysis by Raychaudhuri *et al* (2).



**Supplementary Table 7. Weighted Genetic Risk Score Associations with Disease Outcomes in CARDERA**

wGRS Type	Larsen Progression		DAS28 Intercept		DAS28 Slope 1		DAS28 Slope 2		HAQ Intercept		HAQ Slope 1		HAQ Slope 2	
	$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>
Full	1.03	0.04	0.51	0.41	-0.12	0.11	0.02	0.78	0.01	0.72	-0.08	0.02	0.05	0.06
HLA	1.04	<0.01	0.09	0.04	-0.06	0.26	0.02	0.69	0.01	0.70	-0.05	0.03	0.03	0.08
Non-HLA	0.99	0.67	-0.07	0.41	-0.06	0.51	0.01	0.96	0.003	0.95	-0.05	0.23	0.02	0.53

The Larsen progression  $\beta$  and P-values are from the genotype\*time interaction term in the linear mixed-effects model.

**Supplementary Table 8. Genetic Variants Attaining Nominal Associations with DAS28**

SNPs									
SNP	Chr	Gene	A1	Intercept		Slope 1		Slope 2	
				$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>
rs10752747	1	<i>TNFRSF14-MMEL1</i>	G	0.113	0.1710	-0.141	0.1261	0.184	0.0434
rs1980422	2	<i>CD28</i>	C	0.200	0.0305	-0.141	0.1695	-0.080	0.4370
rs9858105	3	<i>IL20RB</i>	C	-0.125	0.7170	-1.046	0.0044	0.783	0.0339
rs9386514	6	<i>ATG5</i>	C	-0.239	0.0124	0.155	0.1493	-0.167	0.1148
rs660895	6	<i>HLA-DRB1</i>	G	0.179	0.0290	-0.151	0.0929	0.031	0.7256
rs3778754	7	<i>IRF5</i>	G	-0.128	0.1063	0.185	0.0350	-0.058	0.5094
rs11574914	9	<i>CCL19-CCL21</i>	A	-0.162	0.0473	0.064	0.4730	0.029	0.7478
rs653178	12	<i>SH2B3-PTPN11</i>	C	0.001	0.9953	0.119	0.1958	-0.252	0.0056
rs8026898	15	<i>LOC145837</i>	A	0.178	0.0415	-0.106	0.2711	-0.077	0.4191
rs3218251	22	<i>IL2RB</i>	A	0.252	0.0039	0.071	0.4600	-0.202	0.0327
HLA Alleles/Amino Acid									
Allele/Amino Acid	Chr	Gene	A1	Intercept		Slope 1		Slope 2	
				$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>
*15:01	6	<i>HLA-DRB1</i>	-	-0.398	0.0031	0.027	0.8592	0.211	0.1487
Aspartic acid at position 9 in HLA-B	6	<i>HLA-B</i>	-	-0.234	0.0444	0.114	0.3721	0.017	0.8930
Valine at position 11 in HLA-DR $\beta$ 1	6	<i>HLA-DRB1</i>	-	0.230	0.0054	-0.179	0.0505	-0.013	0.8842
Histidine at position 13 in HLA-DR $\beta$ 1	6	<i>HLA-DRB1</i>	-	0.213	0.0103	-0.181	0.0485	0.003	0.9756
Alanine at position 71 in HLA-DR $\beta$ 1	6	<i>HLA-DRB1</i>	-	-0.332	0.0108	-0.024	0.8671	0.182	0.1980

SNP = single nucleotide polymorphism; A1 = reference allele; Slope 1 = DAS28 at months 0-6; Slope 2 = DAS28 at months 6-24.

**Supplementary Table 9. Genetic Variants Attaining a Significant or Nominal Association with HAQ Scores**

SNPs									
SNP	Chr	Gene	A1	Intercept		Slope 1		Slope 2	
				$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>
rs11889341*	2	<i>STAT4</i>	T	-0.150	0.0038	-0.092	0.0433	0.142	0.0001
rs1980422	2	<i>CD28</i>	C	0.100	0.0443	-0.054	0.2149	0.045	0.1821
rs9858105	3	<i>IL20RB</i>	C	-0.367	0.0474	-0.100	0.5333	0.207	0.0937
rs660895	6	<i>HLA-DRB1</i>	G	0.021	0.6405	-0.088	0.0215	0.064	0.0342
rs7752903	6	<i>TNFAIP3</i>	G	-0.227	0.0428	0.051	0.5990	0.094	0.2170
rs3778754	7	<i>IRF5</i>	G	-0.040	0.3475	0.076	0.0421	-0.058	0.0462
rs998731	8	<i>TPD52</i>	T	-0.003	0.9339	0.079	0.0281	-0.062	0.0271
rs2061831	8	<i>BLK</i>	C	0.056	0.2268	-0.082	0.0422	-0.025	0.4362
rs7073236	10	<i>IL2RA</i>	C	0.007	0.8619	-0.078	0.0329	0.033	0.2440
rs4409785	11	<i>CEP57</i>	C	0.122	0.0265	-0.020	0.6829	0.041	0.2682
rs653178*	12	<i>SH2B3-PTPN11</i>	C	0.019	0.6695	0.048	0.2134	-0.109	0.0004
rs701006	12	<i>CDK4</i>	G	-0.089	0.0373	-0.002	0.9574	-0.009	0.7497
rs8026898	15	<i>LOC145837</i>	A	0.104	0.0278	0.013	0.7483	-0.064	0.0426
rs9979383	21	<i>RUNX1-LOC100506403</i>	T	0.029	0.5183	-0.005	0.9061	-0.068	0.0250
rs1893592	21	<i>UBASH3A</i>	A	0.037	0.4327	0.000	0.2542	-0.095	0.0348

  

HLA Alleles/Amino Acid									
Allele/Amino Acid	Chr	Gene	A1	Intercept		Slope 1		Slope 2	
				$\beta$	<i>P</i>	$\beta$	<i>P</i>	$\beta$	<i>P</i>
*04:01	6	<i>HLA-DRB1</i>	-	0.020	0.7122	-0.111	0.0194	0.044	0.2437
*04:04	6	<i>HLA-DRB1</i>	-	0.013	0.8747	-0.006	0.9348	0.117	0.0365
Valine at position 11 in HLA-DR $\beta$ 1	6	<i>HLA-DRB1</i>	-	0.041	0.3601	-0.099	0.0106	0.071	0.0192
Histidine at position 13 in HLA-DR $\beta$ 1	6	<i>HLA-DRB1</i>	-	0.035	0.4347	-0.097	0.0128	0.067	0.0288

\* = significant *P*-value for slope 2 after correction for multiple testing; SNP = single nucleotide polymorphism; A1 = reference allele; Slope 1 = HAQ scores at months 0-6; Slope 2 = HAQ scores at months 6-24.

## REFERENCES

1. Okada Y, Wu D, Trynka G, Raj T, Terao C, Ikari K, et al. Genetics of rheumatoid arthritis contributes to biology and drug discovery. *Nature* 2014;506:376-81.
2. Raychaudhuri S, Sandor C, Stahl EA, Freudenberg J, Lee H-S, Jia X, et al. Five amino acids in three HLA proteins explain most of the association between MHC and seropositive rheumatoid arthritis. *Nat Genet* 2012;44:291-6.
3. Eyre S, Bowes J, Diogo D, Lee A, Barton A, Martin P, et al. High-density genetic mapping identifies new susceptibility loci for rheumatoid arthritis. *Nat Genet* 2012;44:1336-40.