

Supplementary Table 2. Sequence variants outside the HLA region associated with RA overall, in GWAS meta-analysis on study populations from six Northwestern-European countries (31,313 cases and 995,377 controls)^a

Chr	Position	rsID*	Close gene	Variant annotation	EA	OA	Sweden			Denmark			Iceland			Norway			UK		Finland			Combined			
							Freq EA (%)	OR	P	Freq EA (%)	OR	P	Freq EA (%)	OR	P	Freq EA (%)	OR	P	Freq EA (%)	OR	P	Freq EA (%)	OR	P	OR	P	P _{het}
chr1	2800059	rs897628*	TTG34	missense	T	C	30.22	0.92	1.18E-03	29.36	0.96	0.0296	29.65	0.93	0.0114	31.91	0.88	0.0253	33.62	0.96	0.063	35.00	0.91	4.82E-05	0.94	1.87E-10	0.302
chr1	113834946	rs2476601	PTPN22	missense	A	G	12.08	1.57	2.67E-49	10.56	1.43	1.94E-40	13.32	1.29	1.48E-11	11.03	1.50	2.56E-08	9.65	1.28	9.27E-18	14.88	1.45	7.47E-32	1.41	3.85E-144	0
chr2	191094763	rs4853458	STAT4, GLS	intron	A	G	23.83	1.10	1.44E-04	21.90	1.07	2.17E-03	20.64	1.12	6.97E-04	21.99	1.04	0.469	22.37	1.12	5.31E-07	23.14	1.14	7.25E-07	1.10	2.72E-19	0.424
chr2	203874196	rs3087243	CTLA4	downstream gene	A	G	39.35	0.89	1.07E-07	41.52	0.91	4.52E-07	40.04	0.95	0.0946	40.46	0.94	0.27	44.80	0.95	5.52E-03	32.99	0.89	8.30E-07	0.92	3.04E-19	0.0982
chr3	58197909	rs35677470	DNASE1L3	missense	A	G	6.86	1.21	7.69E-06	7.86	1.12	6.24E-04	7.59	1.07	0.174	6.44	1.05	0.651	7.79	1.07	0.0573	6.11	1.06	0.228	1.10	1.81E-08	0.21
chr4	26089240	rs932036	LINC02357	intergenic	T	A	27.90	1.13	1.69E-07	28.89	1.05	7.47E-03	25.99	1.11	9.98E-04	27.05	1.13	0.0282	29.95	1.10	6.80E-06	28.37	1.08	1.50E-03	1.09	6.65E-18	0.29
chr5	56148856	rs7731626	ANKRD55	intron	A	G	34.86	0.87	3.43E-09	35.34	0.88	7.22E-11	39.14	0.88	9.08E-06	36.44	0.82	1.47E-04	36.69	0.88	3.37E-10	27.83	0.88	5.61E-07	0.88	1.09E-39	0.827
chr6	137678425	rs35926684, rs397886367	.	regulatory region	G	GA	23.61	1.15	1.97E-08	22.63	1.07	1.60E-03	20.31	1.08	0.0244	24.18	1.12	0.0407	22.69	1.08	5.13E-04	20.86	1.05	0.0527	1.09	1.48E-14	0.19
chr6	167127770	rs3093017	CCR6	intron	C	G	45.47	1.10	5.70E-06	45.12	1.05	7.47E-03	46.27	1.07	0.0135	45.98	1.17	2.03E-03	43.37	1.04	0.07	44.77	1.13	1.22E-07	1.07	7.04E-15	0.0153
chr7	50313596	rs10261758*	IKZF1	intron	G	A	33.46	1.05	0.029	31.17	1.04	0.0555	31.04	1.05	0.104	31.02	1.15	0.0108	28.82	1.12	1.24E-08	38.40	1.07	0.00251	1.07	3.56E-12	0.0563
chr7	128938247	rs2004640*	IRF5	splice donor	G	T	46.83	0.93	5.32E-04	48.75	0.96	0.0142	47.26	0.92	1.20E-03	46.81	0.95	0.342	51.20	0.93	2.49E-04	47.89	0.93	5.36E-04	0.94	5.11E-13	0.752
chr8	11480078	rs2409780	.	regulatory region	C	T	26.29	1.08	1.09E-03	27.12	1.07	4.68E-04	21.76	1.09	7.07E-03	27.72	0.92	0.155	25.40	1.09	1.18E-04	25.85	1.09	7.34E-04	1.08	1.29E-12	0.153
chr8	100265412	rs1660322*	RNF19A	intron	C	T	29.41	1.04	0.11	29.86	1.07	4.56E-04	30.96	1.06	0.0478	29.74	1.17	2.97E-03	31.06	1.05	0.0164	30.25	1.10	8.22E-05	1.07	8.65E-11	0.24
chr9	120873843	rs10985070	PHF19, TRAF1	upstream gene	C	A	46.73	1.08	3.08E-04	46.03	1.07	2.85E-04	44.02	1.11	2.02E-04	45.73	1.06	0.261	43.64	1.01	0.556	48.59	1.05	0.0181	1.06	8.69E-10	0.0875
chr10	6060794	rs3118471	IL2RA	intron	G	A	34.47	1.06	0.0141	32.25	1.09	3.37E-06	34.12	1.02	0.532	33.48	1.09	0.108	29.67	1.06	4.79E-03	36.42	1.10	2.53E-05	1.07	1.72E-12	0.259
chr10	31122426	rs1538981	.	regulatory region	C	T	43.71	0.94	6.23E-03	45.56	0.94	7.51E-04	44.49	0.97	0.198	44.38	0.90	0.0413	48.96	0.94	7.64E-04	40.86	0.92	3.56E-04	0.94	9.37E-12	0.809
chr11	64340005	rs479777*	CCDC88B	upstream gene	C	T	33.47	0.92	2.07E-04	34.17	0.94	1.58E-03	32.87	0.95	0.0795	33.50	0.88	0.0144	33.41	0.96	0.0667	38.45	0.93	2.02E-03	0.94	1.38E-10	0.477
chr11	118870448	rs7117261	.	regulatory region	T	C	20.03	0.92	2.55E-03	20.08	0.90	8.01E-06	17.76	0.95	0.135	21.28	0.79	3.24E-04	19.34	0.94	0.0159	16.61	0.91	2.53E-03	0.92	7.63E-13	0.17
chr12	111446804	rs3184504	SH2B3	missense	T	C	46.74	1.08	5.65E-04	50.60	1.06	2.71E-03	37.86	1.07	0.0198	45.38	1.19	6.10E-04	46.35	1.08	4.67E-05	40.83	1.12	1.95E-07	1.08	1.10E-17	0.136
chr13	39771329	rs7320598	COG6	intron	T	C	33.63	0.93	1.27E-03	34.29	0.91	2.30E-07	31.89	0.95	0.106	34.12	0.89	3.27E-02	34.46	0.94	3.30E-03	35.69	0.93	1.80E-03	0.93	1.55E-14	0.599
chr14	92651884	rs117068593*	RIN3	missense	T	C	15.65	0.95	0.117	17.23	0.91	6.94E-05	15.57	0.84	1.98E-05	16.41	1.01	0.868	18.41	0.94	7.26E-03	14.22	0.95	0.141	0.93	1.93E-09	0.0795
chr15	69746861	rs2117234*	.	intergenic	T	C	46.69	1.12	4.99E-07	46.22	1.07	2.89E-04	49.83	1.09	2.83E-03	44.97	1.10	0.0574	47.08	1.05	5.26E-03	47.64	1.07	3.88E-03	1.08	2.71E-15	0.468
chr16	85977427	rs13333054	IRF8	intergenic	T	C	23.08	1.07	0.00561	22.49	1.10	1.58E-05	23.15	1.02	0.459	23.78	1.09	0.161	22.70	1.07	1.19E-03	19.25	1.07	0.0194	1.07	1.12E-10	0.671
chr19	10352442	rs34536443	TYK2	missense	C	G	3.64	0.71	2.94E-08	4.18	0.77	5.30E-08	4.38	0.79	8.11E-04	4.51	0.69	4.27E-03	4.39	0.78	9.52E-07	3.06	0.71	3.84E-07	0.75	2.54E-29	0.676
chr19	10359299	rs12720356*	TYK2	missense	C	A	8.60	0.92	0.0215	7.84	0.92	0.014	5.98	0.93	0.249	9.06	0.82	0.0296	9.31	0.89	4.52E-04	8.25	0.87	4.78E-04	0.90	4.31E-10	0.712

^aWe performed a meta-analysis using logistic regression assuming a multiplicative model, reporting odds ratios (OR) and two-sided *P*-values (Methods and Gudbjartsson et al, 2015). Variants were split into five classes based on their genome annotation, and significance threshold based on the number of variants in each class, thereby adjusting for all 60 million variants tested (Methods). The primary signal at each genomic locus was defined as the sequence variant with the lowest Bonferroni adjusted *P*-value using the adjusted significance thresholds. Conditional analysis was performed to identify lead signals and possible secondary signals within 500 kb from index variants (excluding the HLA locus). This applied to the following marker pair: chr19:10352442 and chr19:10359299.

*Sequence variants that are not correlated ($R^2 < 0.8$) with, and significant after adjustment for, previously reported sequence variants for RA (Supplementary Table 1).

Bold indicates sequence variants that are supported by functional variant annotation, where the variant or correlated variant, ($R^2 > 0.8$) are coding, associate with mRNA expression and/or plasma protein levels (summarized in Figure 2).

Abbreviations: EA: effect allele; OA: other allele; OR: odds ratio; *P*_{het}: a *P*-value for test of heterogeneity between the results in cohorts included in the meta-analysis.