Supplementary Table 4. Coding variants at loci associated with RA or its subsets and their functional prediction[±]

Lead variant (chr:pos)	Coding variant	R^2	EA	OA	*Gene*	Coding effect	Available in dbNSFP v4.1	Damaging	Tolerated	Neutral	MPC (rankscore)	SIFT	SIFT4G	LRT	Mutation Taster	Mutation Assessor	FATHMM	PROVEAN	MetaSVM	MetaLR	MxCAP	PrimateAI	DEOGEN2	BayesDel addAF	BayesDel noAF	LIST-S2	Aloft	fathmmxMKL coding	fathmmxXF coding
chr1:2800059	chr1:2595307	0.89	G	A	*MMEL1*	missense	x	1	9	5	0.22	T	T	N	P	N	D	N	T	T	.	T	T	T	T	T	.	N	N
chr1:2800059	chr1:2596694	0.96	C	T	*MMEL1*	splice region	-																							
chr1:2800059	chr1:2609830	0.92	G	A	*MMEL1*	splice region	-																							
chr1:2800059	chr1:2800059	1.00	C	T	*TTC34*	missense	x	0	2	2	.	.	.	.	P	.	.	.	.	.	.	.	.	.	.	T	.	N	.
chr1:113834946	chr1:113834946	1.00	G	A	*PTPN22*	missense	x	0	10	4	0.15	T	T	N	P	.	T	N	T	T	.	T	T	T	T	T	.	N	N
chr1:161506414*	chr1:161506414	1.00	T	C	*FCGR2A*	stop gained	x	0	3	3	.	.	.	N	P	.	.	.	.	.	.	.	.	T	T	.	T	N	N
chr1:161506414*	chr1:161506415	1.00	G	A	*FCGR2A*	missense	x	0	10	4	0.26	T	T	N	P	M	T	N	T	T	.	T	T	T	T	T	.	N	N
chr2:191073180*	chr2:191073180***	1.00	A	T	*STAT4*	missense	x	10	5	1	0.67	T	T	D	D	L	D	N	D	D	D	T	T	T	D	D	.	D	D
chr3:58197909**	chr3:58197909	1.00	A	G	*DNASE1L3*	missense	x	10	4	0	.	D	D	D	P	H	D	D	T	T	.	T	D	T	D	D	.	D	D
chr6:137678425*[#]	chr6:137874929	<0.2	T	G	*TNFAIP3*	missense	x	2	10	2	0.47	T	T	N	P	L	T	D	T	T	.	T	T	T	T	T	.	D	N
chr7:128938247	chr7:128938247	1.00	G	T	*IRF5*	splice donor	-																							
chr12:111446804	chr12:111446804	1.00	C	T	*SH2B3*	missense	x	0	10	5	0.12	T	T	N	P	N	T	N	T	T	.	T	T	T	T	T	.	N	N
chr13:39771329**	chr13:39724484	0.95	CTT	TTT	*COG6*	splice region	-																							
chr13:39788092*	chr13:39724484	0.95	CTT	TTT	*COG6*	splice region	-																							
chr14:92651884**	chr14:92651884	1.00	T	C	*RIN3*	missense	x	4	8	2	0.37	D	D	N	P	M	T	D	T	T	.	T	T	T	T	T	.	D	N
chr17:39908216*	chr17:39905943	1.00	A	G	*GSDMB*	missense	x	1	9	3	0.23	T	T	N	P	.	T	D	T	T	.	T	.	T	T	T	.	N	N
chr17:39908216*	chr17:39905964	0.80	T	C	*GSDMB*	missense	x	2	8	3	0.57	T	D	N	P	.	T	D	T	T	.	T	.	T	T	T	.	N	N
chr17:39908216*	chr17:39908216	1.00	C	T	*GSDMB*	splice acceptor	x	0	2	2	.	.	.	.	P	.	.	.	.	.	.	.	.	T	T	.	.	N	N
chr19:10352442	chr19:10352442	1.00	C	G	*TYK2*	missense	x	7	7	1	0.66	D	D	N	D	L	T	D	T	T	.	T	T	T	T	D	.	D	D
chr19:10359299	chr19:10359299***	1.00	C	A	*TYK2*	missense	x	7	6	1	0.77	D	D	N	P	M	T	D	T	T	.	T	T	T	D	D	.	D	D
chr19:10354167*	chr19:10354167***	1.00	A	G	*TYK2*	missense	x	28	4	0	0.72	D	D	D	D	L	D	D	D	D	D	T	T	D	D	D	.	D	D
[#]	chr19:10467167	<0.2	C	A	*PDE4A*	missense	x	1	9	4	.	D	T	.	P	N	T	N	T	T	.	T	T	T	T	T	.	N	N
chr21:44236891*	chr21:44236891	1.00	C	T	*ICOSLG*	missense	x	0	10	4	0.71	T	T	N	P	M	T	N	T	T	.	T	T	T	T	T	.	N	N

Lead variants that are only GWAS significant in seropositive RA (*) or in RA overall (**), other variants are significant in both. Coding variants that are independent secondary signals after adjustment for lead variants are marked with (***), see Supplementary Tables 2,3 and 8.

[#]Association with seropositive RA of missense variant in *TNFAIP3* (chr6:137874929, OR=1.25, P=7.7x10^{-11}) is not GWAS significant after adjustment for lead signal at the locus (chr6:137678425, adjusted OR=1.18, adjusted *P* =3.2x10^{-7}), despite the fact that they are not correlated (R^2<0.2). Similarly, missense variant in *PDE4A* (chr19:10467167, OR=0.90, P=6.3x10^{-10})

±Functional prediction was performed using the dbNSFP (version 4.1) database (https://sites.google.com/site/ jpopgen/dbNSFP).

dbNSFP results are presented as a summarized score, rankscore or as D, damaging; T, tolerated; N, neutral, indicating predicted functional effect of the sequence variant.

Sources of prediction tools used in the dbNSFP v4.1 database:

MVP 1.0, https://github.com/ShenLab/missense **MPC** release1, ftp://ftp.broadinstitute.org/pub/ExAC_release/release1/regional_missense_constraint/

SIFT ensembl 86, released Jan, 2016 http://provean.jcvi.org/index.php

SIFT4G 2.4, released Nov. 1, 2016 http://sift.bii.a-star.edu.sg/sift4g/public//Homo_sapiens/

LRT, released November, 2009 http://www.genetics.wustl.edu/jflab/lrt_query.html

Mutation Taster 2, data retrieved in 2015 http://www.mutationtaster.org/

MutationAssessor release 3, http://mutationassessor.org /

PROVEAN 1.1 ensembl 86, released Jan, 2015 http://provean.jcvi.org/index.php

FATHMM v2.3, http://fathmm.biocompute.org.uk

fathmm-MKL, http://fathmm.biocompute.org.uk/fathmmMKL.htm

fathmm-XF, http://fathmm.biocompute.org.uk/fathmm-xf/

MetaSVM and **MetaLR**, doi: 10.1093/hmg/ddu733

PrimateAI, https://github.com/Illumina/PrimateAI

DEOGEN2, https://deogen2.mutatrame.com/

ALoFT 1.0, http://aloft.gersteinlab.org/

BayesDel v1, http://fengbj-laboratory.org/BayesDel/BayesDel.html

LIST-S2 Release: 2019_10, https://precomputed.list-s2.msl.ubc.ca/