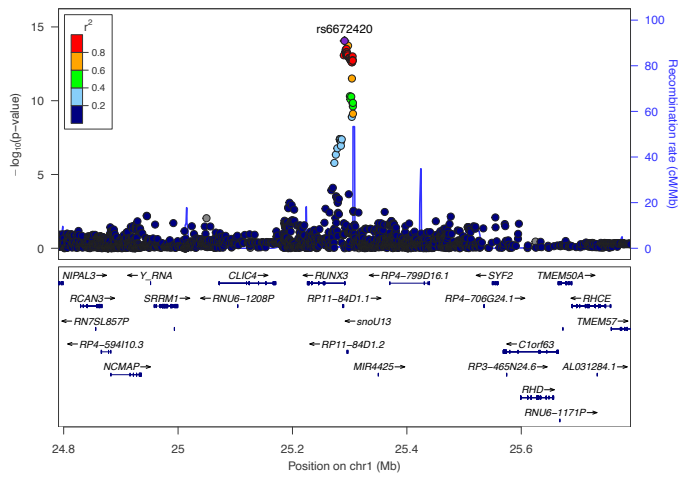
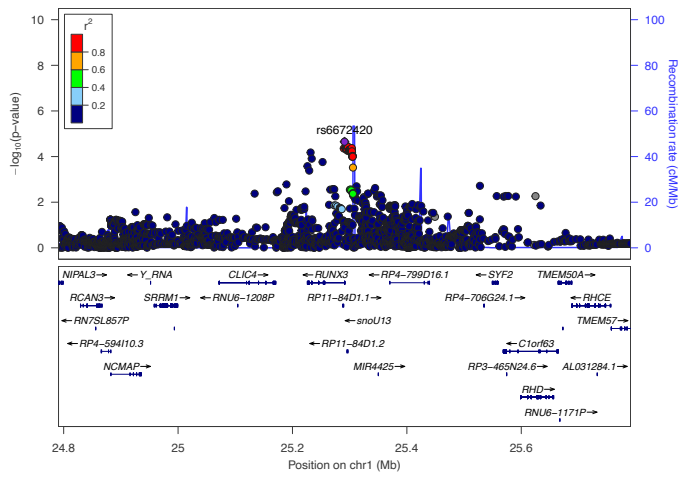


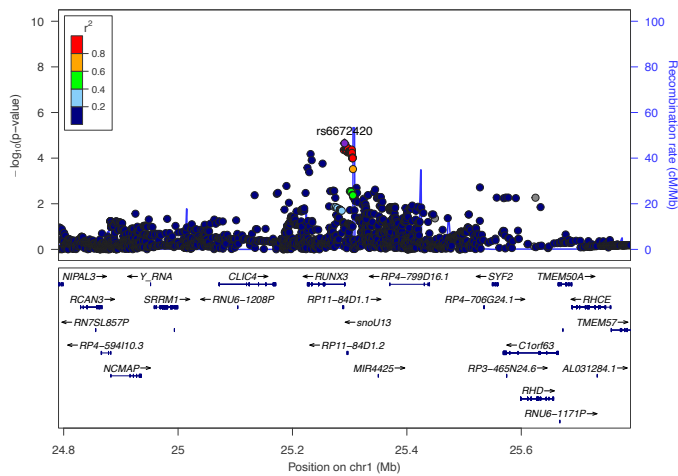
**Supplementary Figure 1: Equally weighted trans-disease meta-analysis (TDMA).** Circular diagram including the following: a) Manhattan plot of shared (same direction of effect) psoriasis/MS TDMA signals, showing markers more significant in TDMA than for either trait. b) Manhattan plot of opposing (opposite direction of effect) psoriasis/MS trans-disease meta-analysis (TDMA) signals, showing markers more significant in TDMA than for either trait. **Red** dashed lines indicate the genome-wide significance ( $p < 5 \times 10^{-8}$ ) threshold for shared and opposing signals, respectively. Loci which meet this threshold and are suggestively significant ( $p < 1 \times 10^{-4}$ ) for both traits are highlighted in **red** (if identified through our original TDMA approach) or **blue** (for additional loci identified using GCTA-COJO). c) Density of H3K27ac active enhancer marks for B-cell centroblasts (the most enriched cell type among the TDMA loci, compared to other established loci for psoriasis and MS). The darker the color, the higher the proportion of regulatory marks overlapping each 2Mbp region. Genes reported by previous psoriasis and MS GWAS<sup>1,4,96-99</sup> are labeled for each locus. d) Links between genes, according to co-expression in L1000 assay perturbation experiments from NIH's Library of Integrated Network-Based Cellular Signatures (LINCS). Each link has a random color, with transparency (alpha) values set proportional to the log-scaled number of experiments in which at least one gene from a locus is co-expressed with at least one gene from another locus, such that more opaque links represent pairs of loci with genes co-expressed in more experiments.



Psoriasis

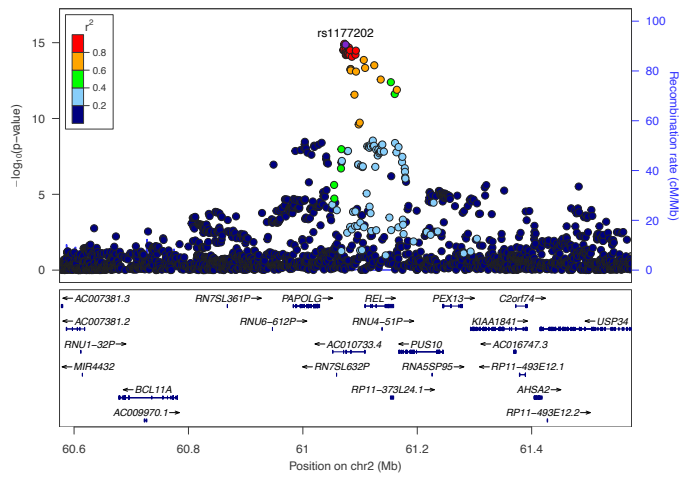


MS

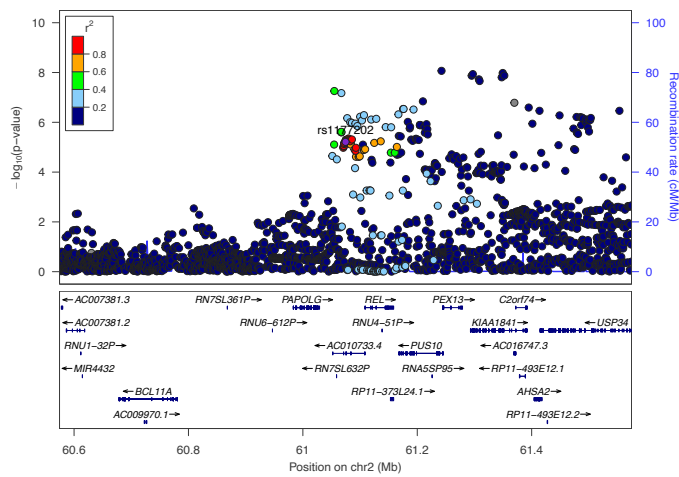


TDMA

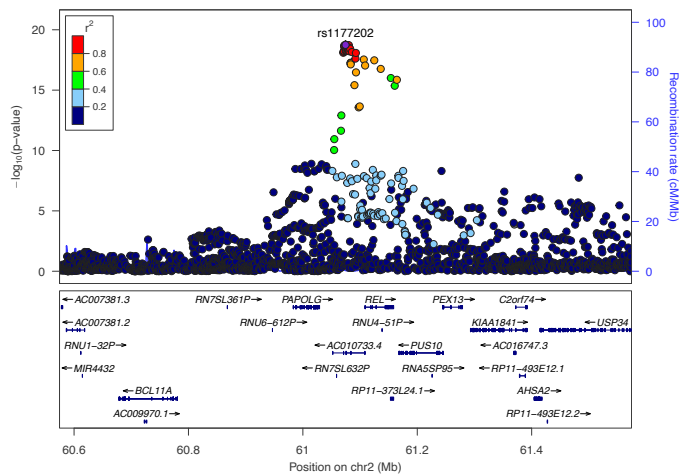
Supplementary Figure 2: Regional association plot (equally weighted TDMA) for opposing locus at 1p36.11



Psoriasis

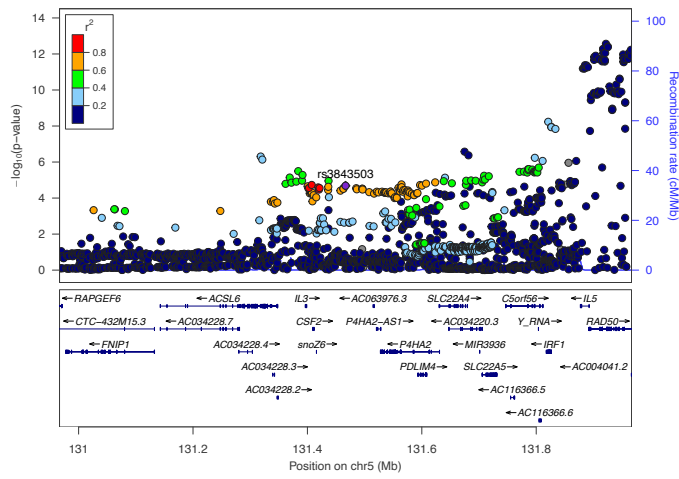


MS

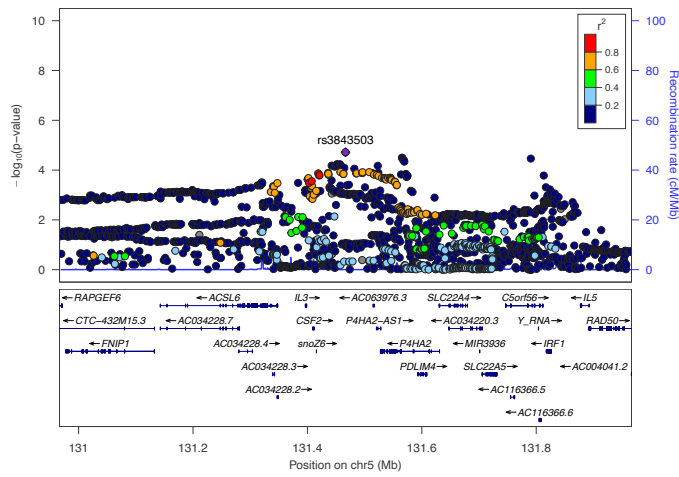


TDMA

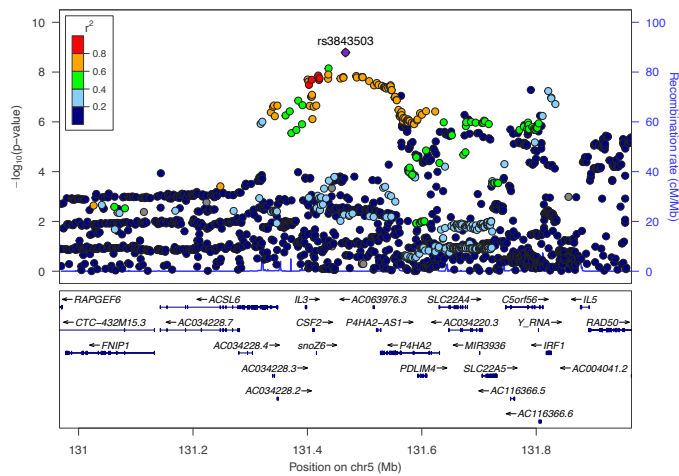
Supplementary Figure 3: Regional association plot (equally weighted TDMA) for opposing locus at 2p16.1



Psoriasis

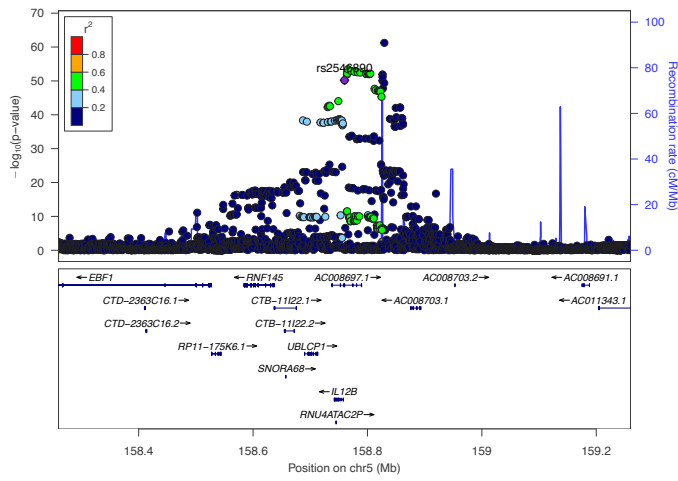


MS

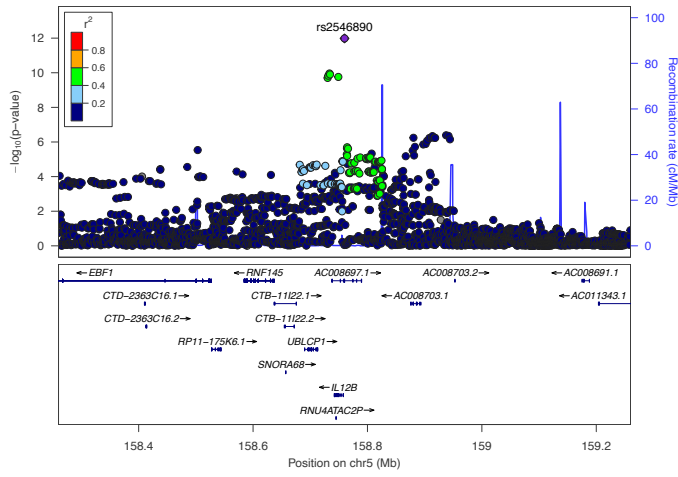


TDMA

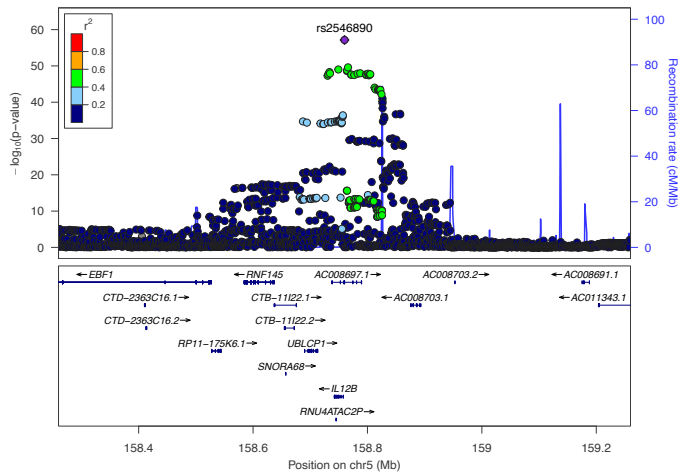
Supplementary Figure 4: Regional association plot (equally weighted TDMA) for opposing locus at 5q31.1



Psoriasis

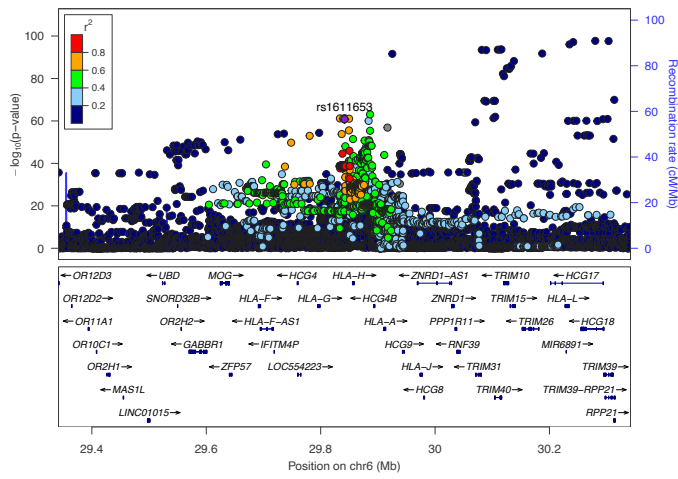


MS

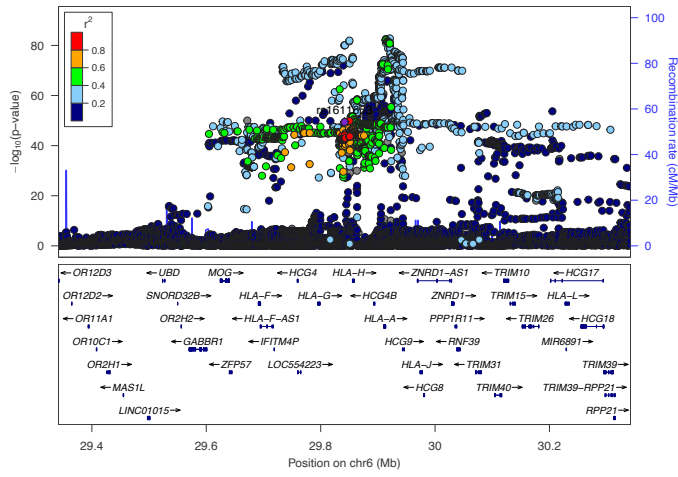


TDMA

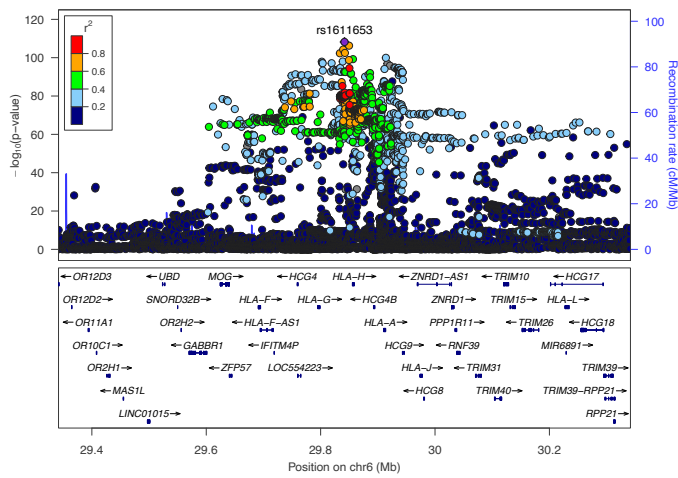
Supplementary Figure 5: Regional association plot (equally weighted TDMA) for shared locus at 5q33.3



Psoriasis

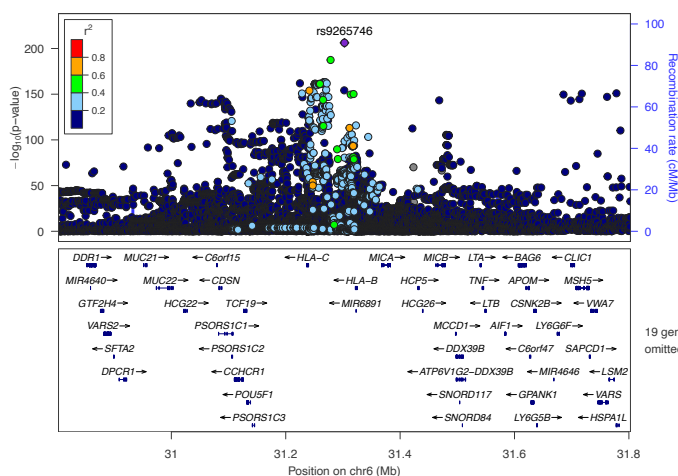
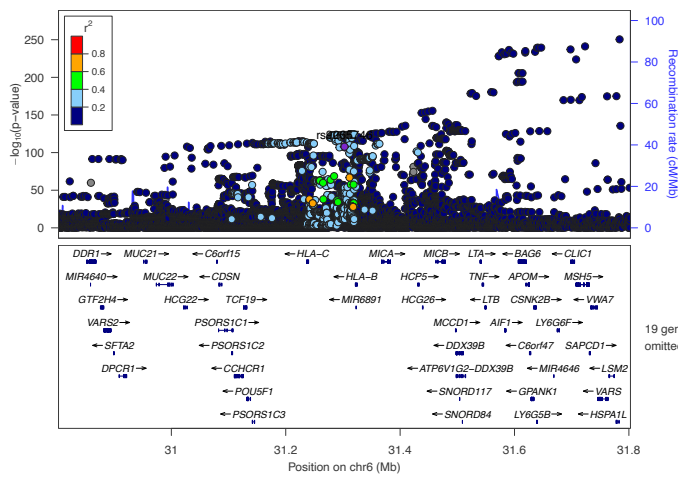
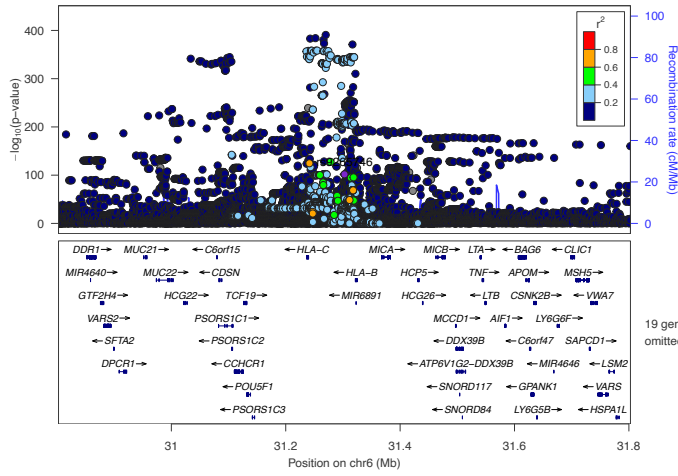


MS

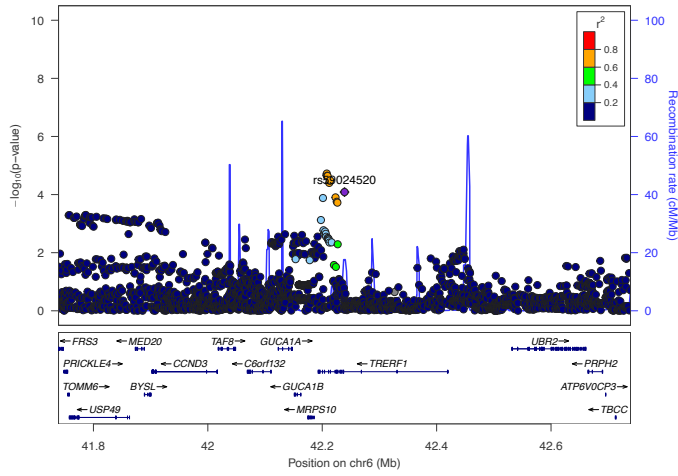


TDMA

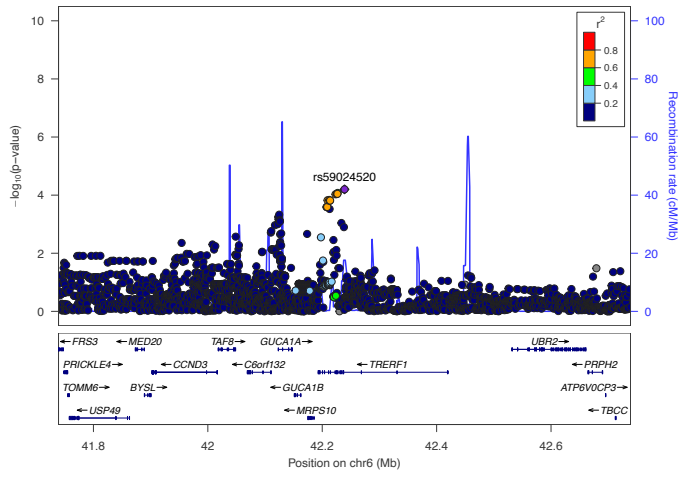
Supplementary Figure 6: Regional association plot (IVW TDMA) for opposing locus at 6q22.1



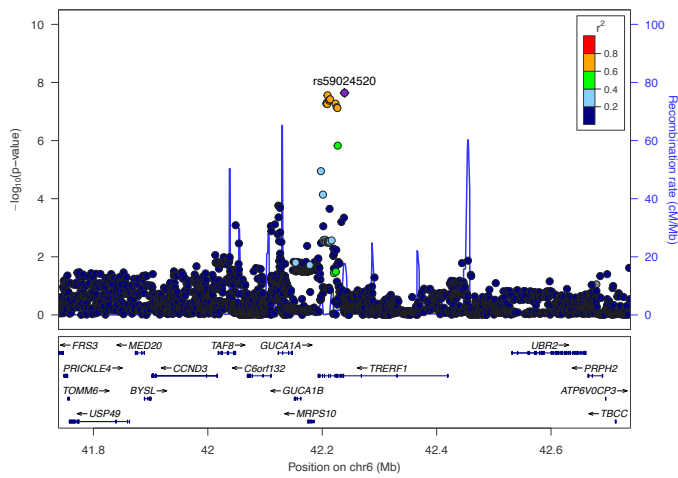
Supplementary Figure 7: Regional association plot (equally weighted TDMA) for shared locus at 6q21.33



Psoriasis



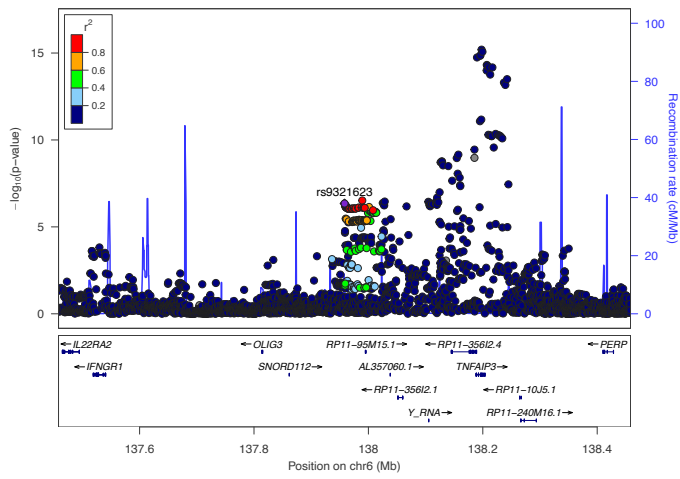
MS



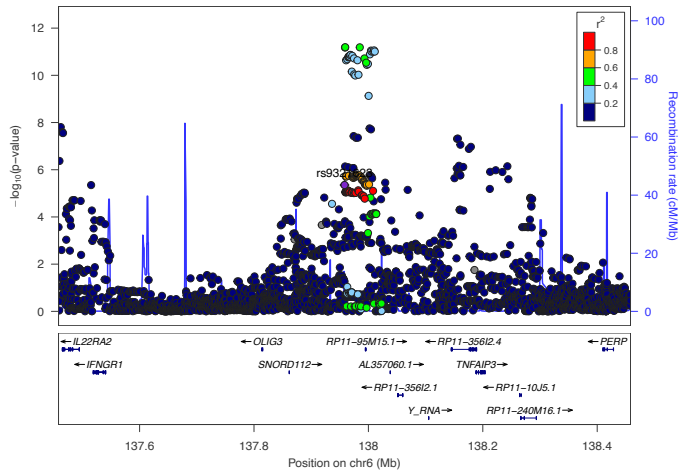
TDMA

Supplementary Figure 8: Regional association plot (IVW TDMA) for shared locus at 6p21.1

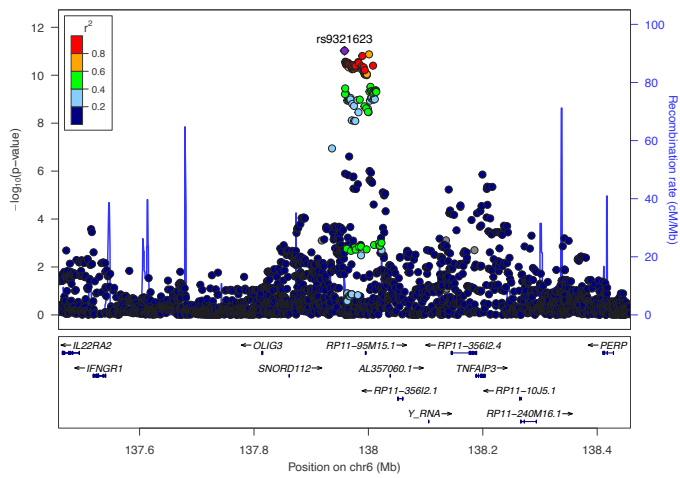




Psoriasis

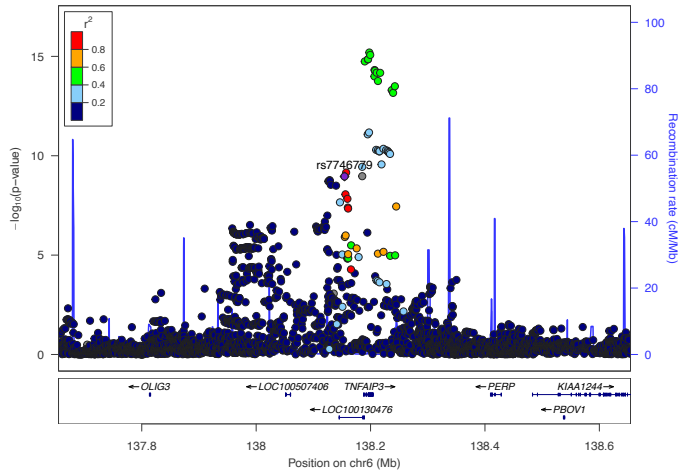


MS

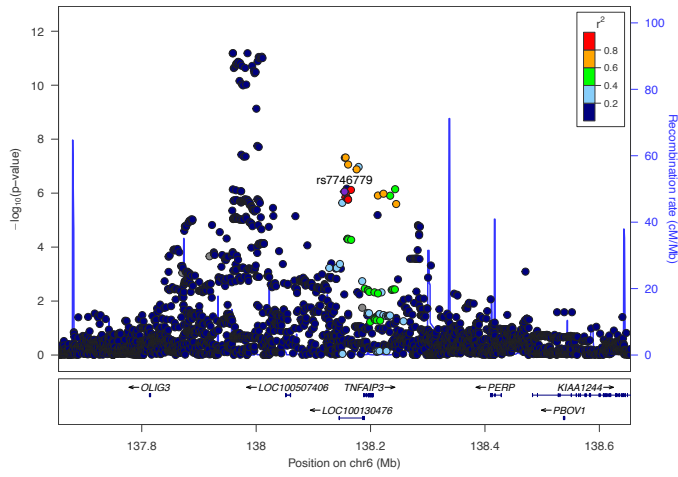


TDMA

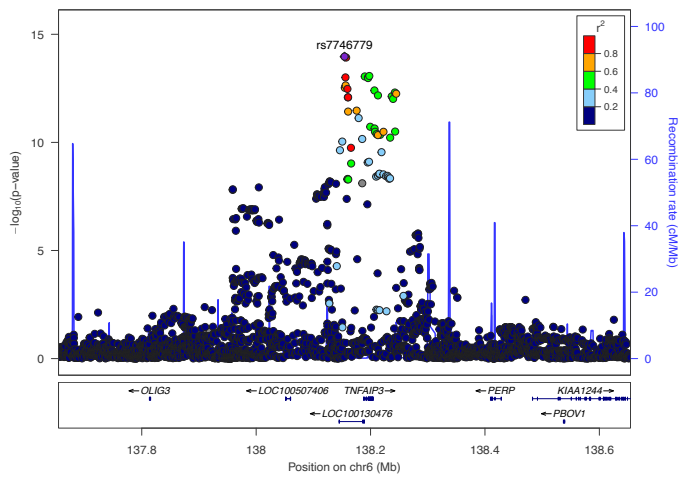
Supplementary Figure 9: Regional association plot (equally weighted TDMA) for shared locus at 6q23.3



Psoriasis

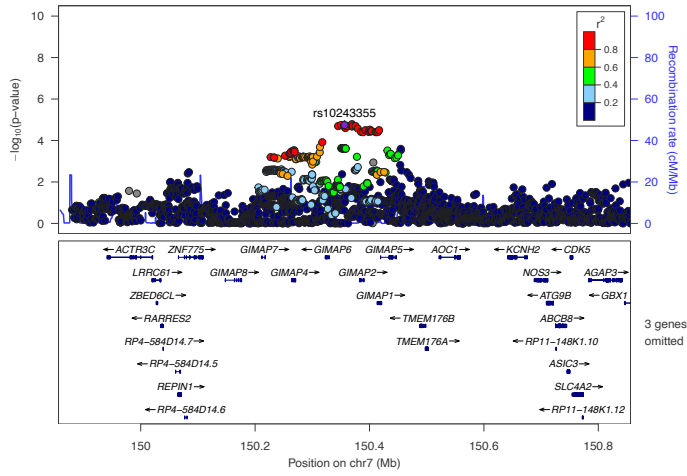


MS

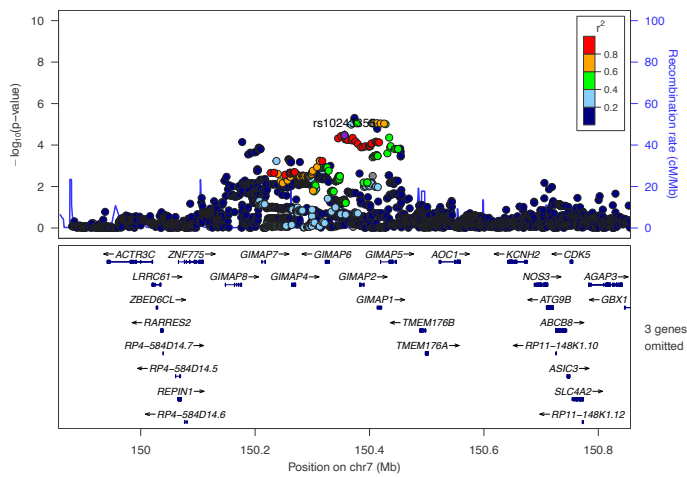


TDMA

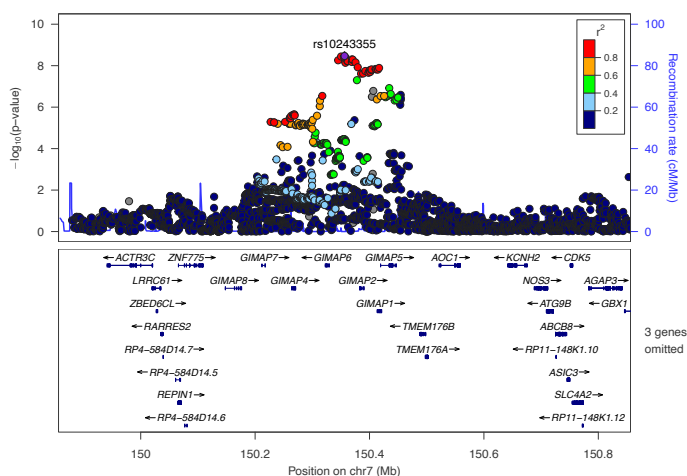
Supplementary Figure 10: Regional association plot (IVW TDMA) for opposing locus at 6q23.3



Psoriasis

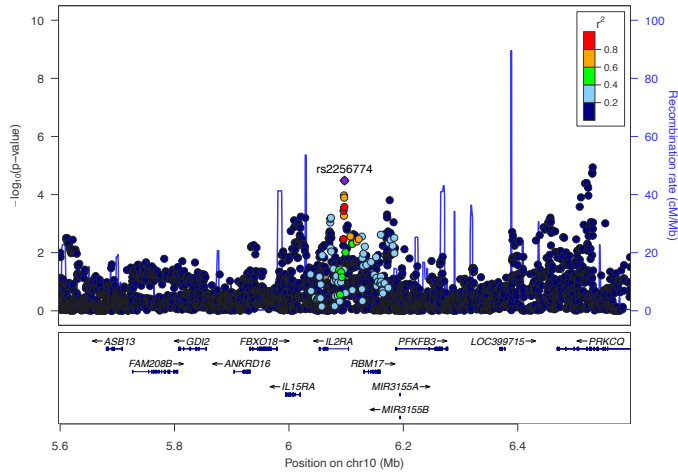


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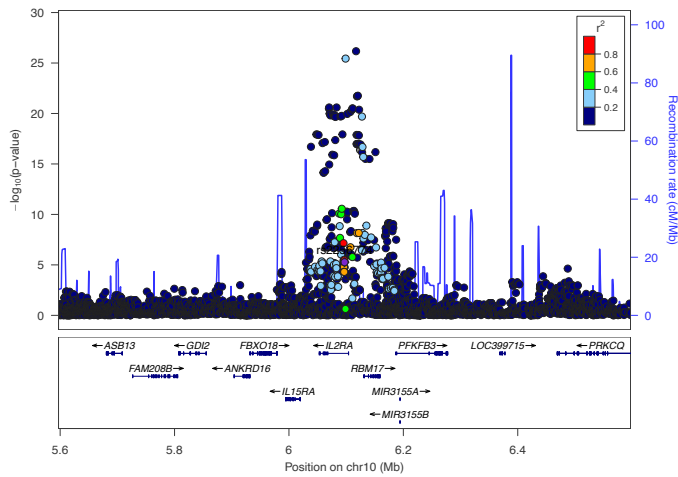


TDMA

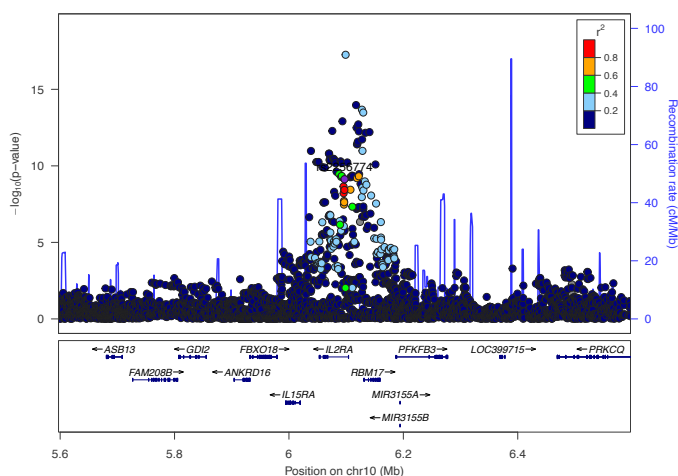
Supplementary Figure 11: Regional association plot (equally weighted TDMA) for opposing locus at 7q36.1



Psoriasis

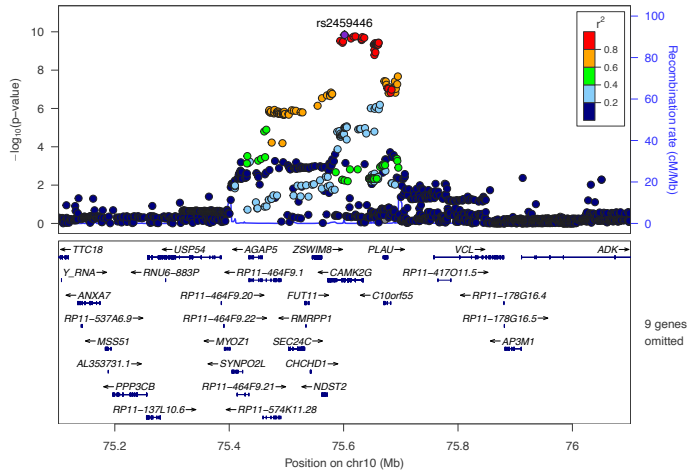


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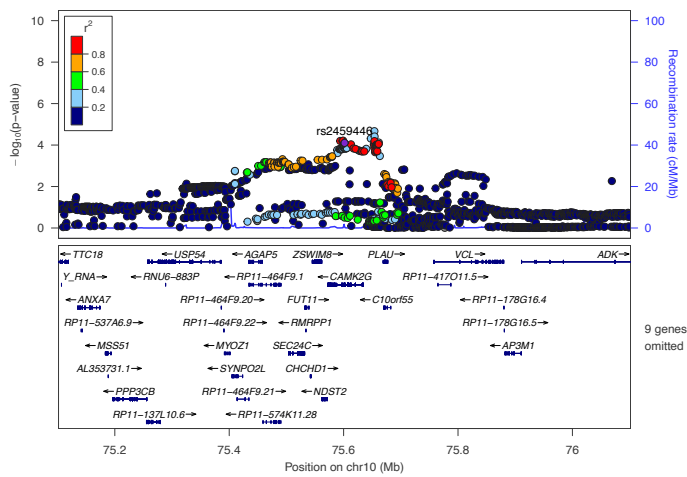


TDMA

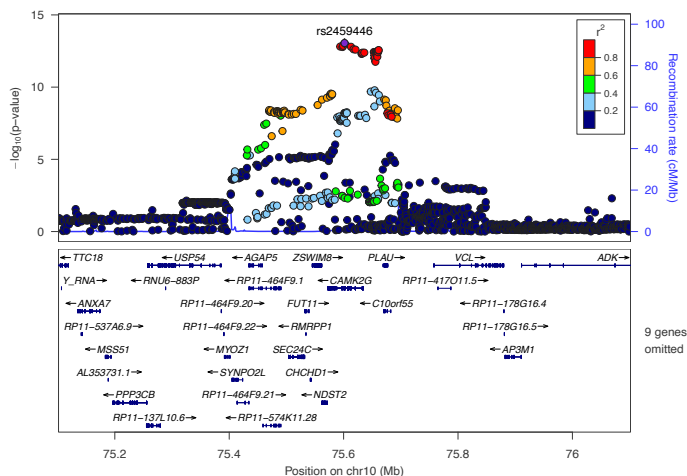
Supplementary Figure 12: Regional association plot (IVW TDMA) for opposing locus at 10q15.1



Psoriasis

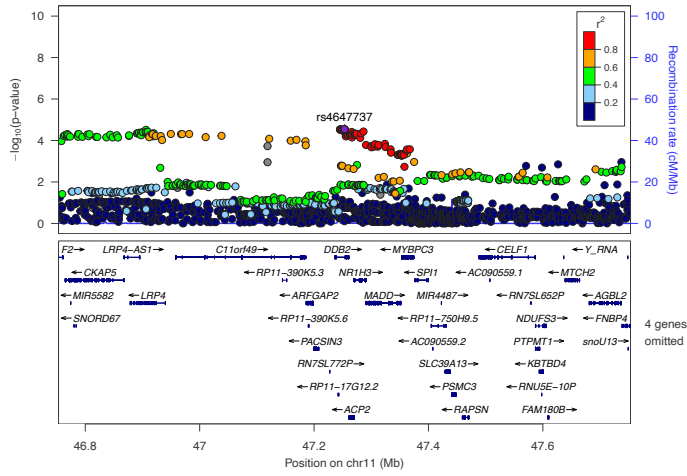


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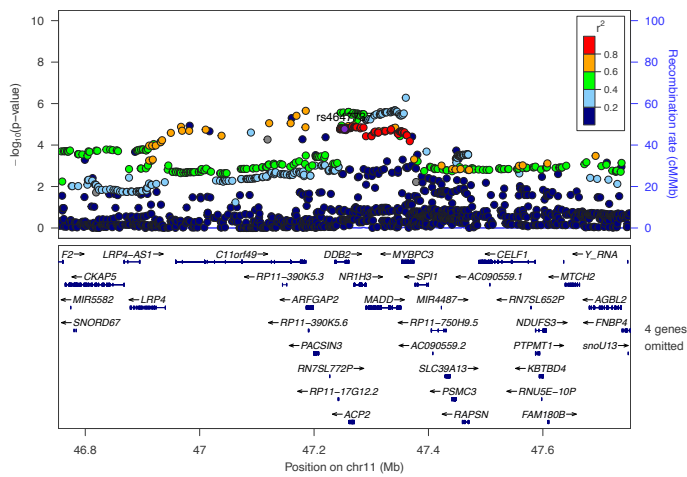


TDMA

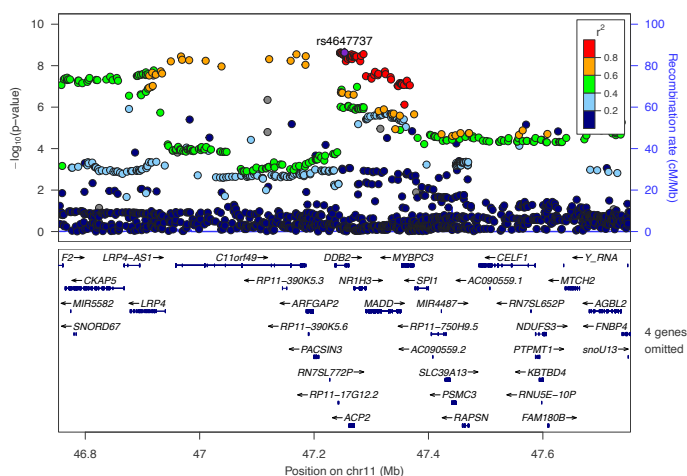
Supplementary Figure 13: Regional association plot (equally weighted TDMA) for shared locus at 10q22.2



Psoriasis

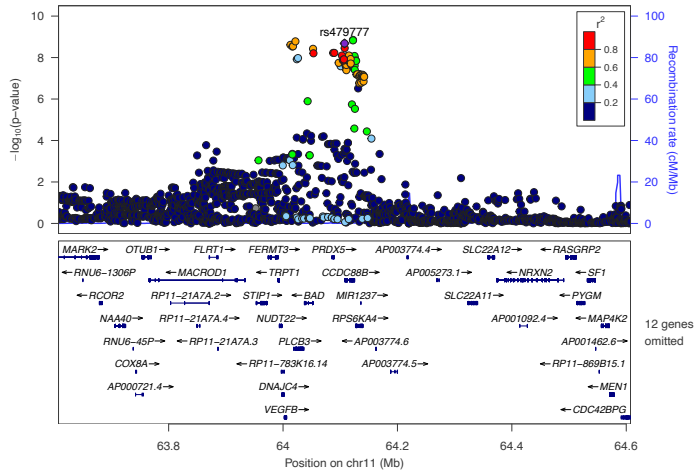


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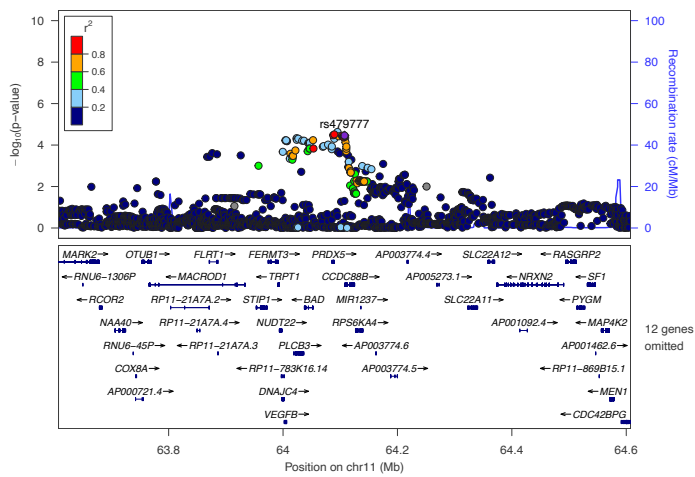


TDMA

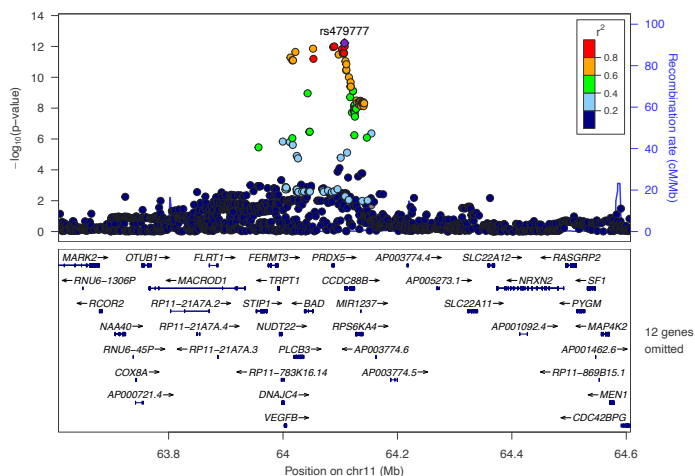
Supplementary Figure 14: Regional association plot (equally weighted TDMA) for opposing locus at 11p11.2



Psoriasis

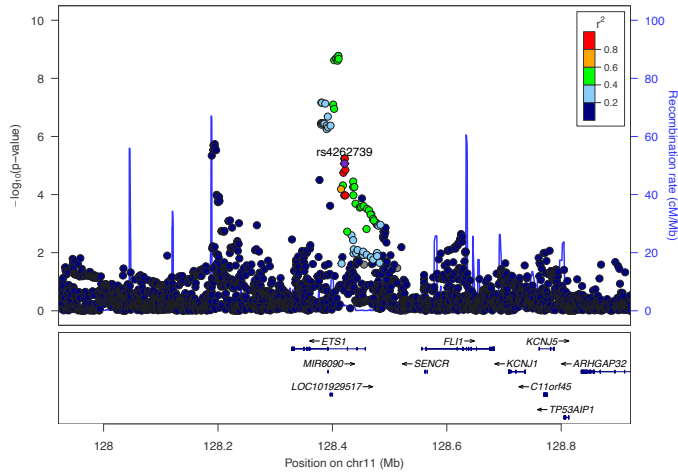


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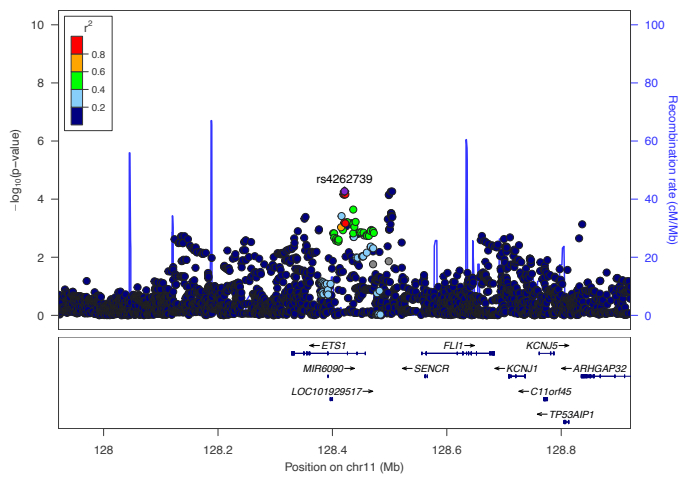


TDMA

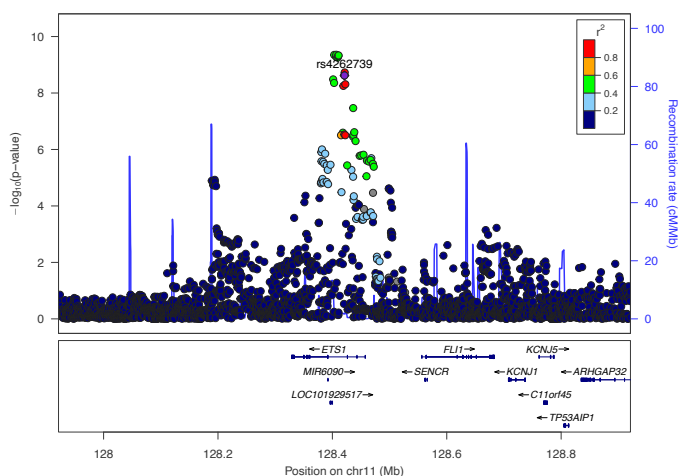
Supplementary Figure 15: Regional association plot (equally weighted TDMA) for shared locus at 11q13.1



Psoriasis



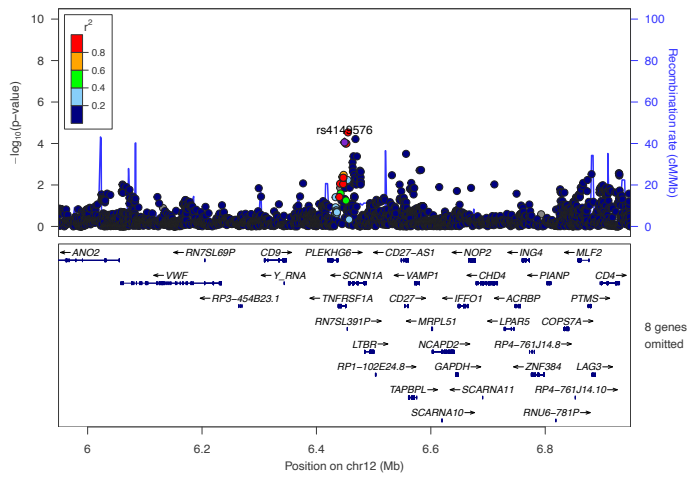
MS



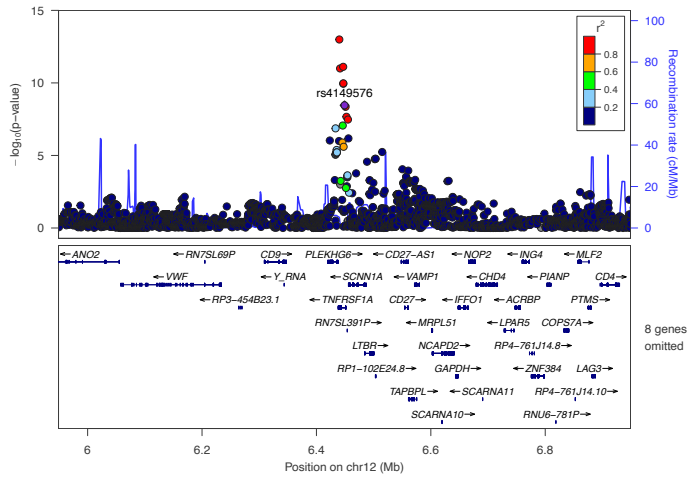
TDMA

Supplementary Figure 16: Regional association plot (IVW TDMA) for shared locus at 11q21.3

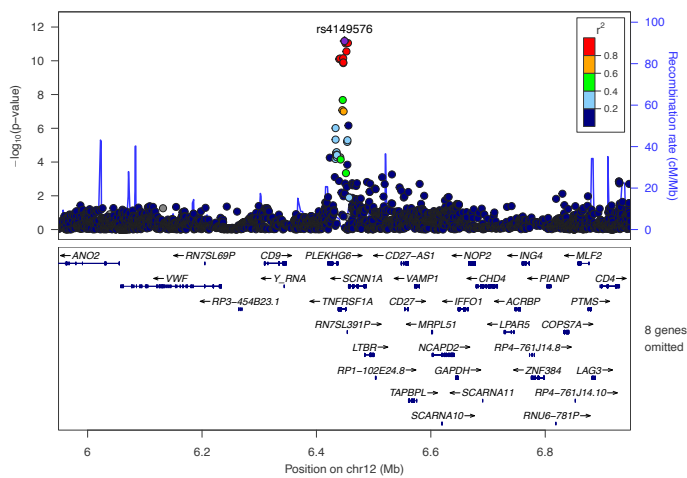




Psoriasis

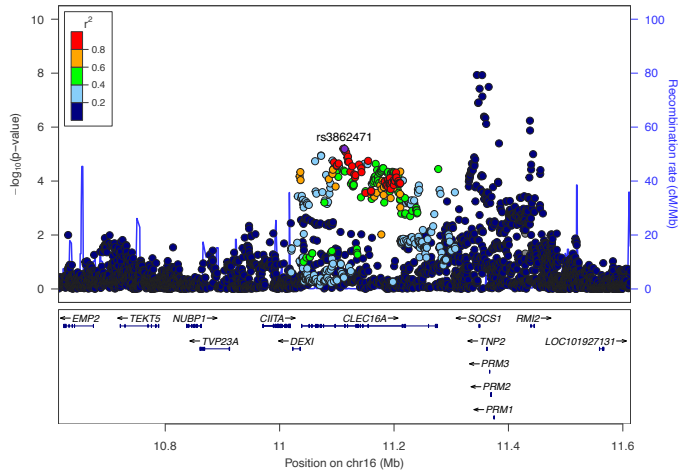


MS

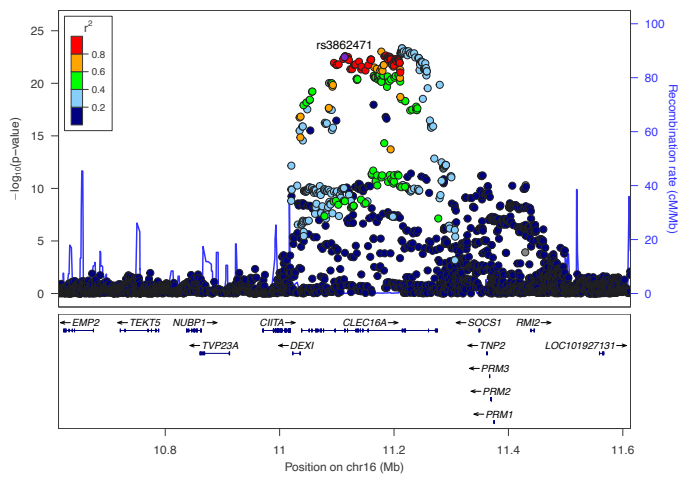


TDMA

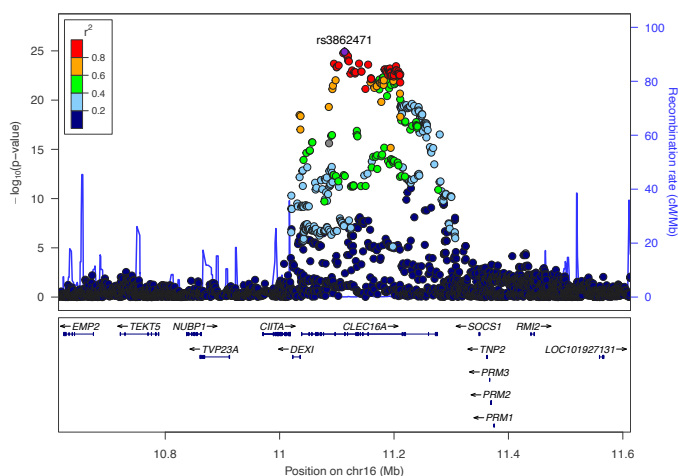
Supplementary Figure 17: Regional association plot (equally weighted TDMA) for shared locus at 12p13.31



Psoriasis

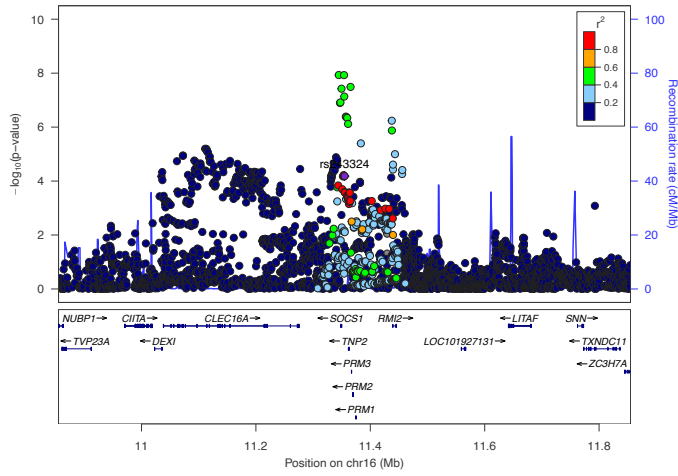


MS

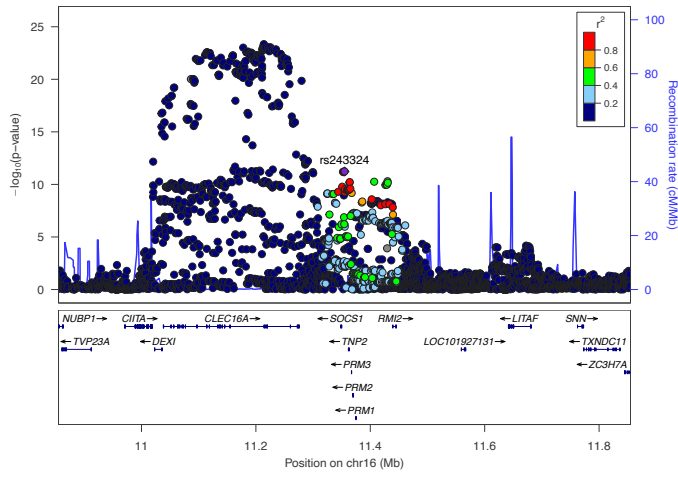


TDMA

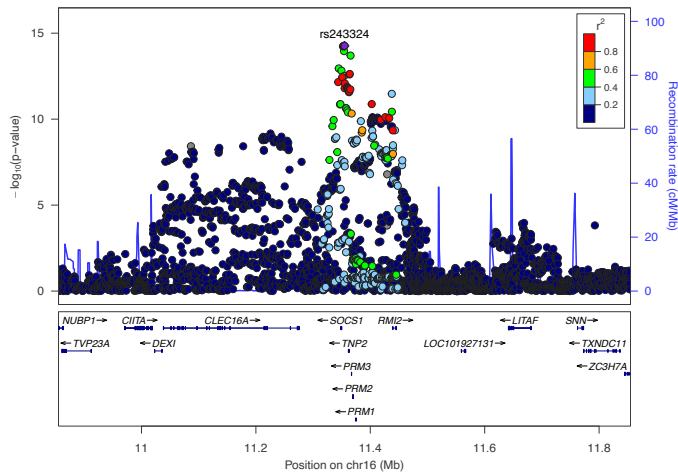
Supplementary Figure 18: Regional association plot (IVW TDMA) for opposing locus at 16p13.13



Psoriasis

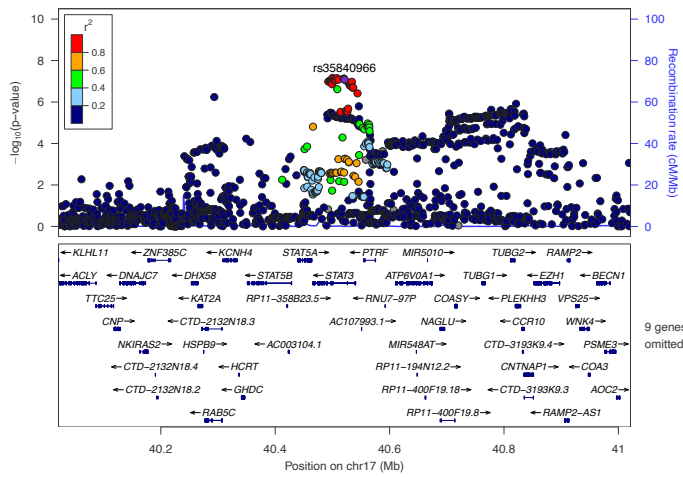


MS

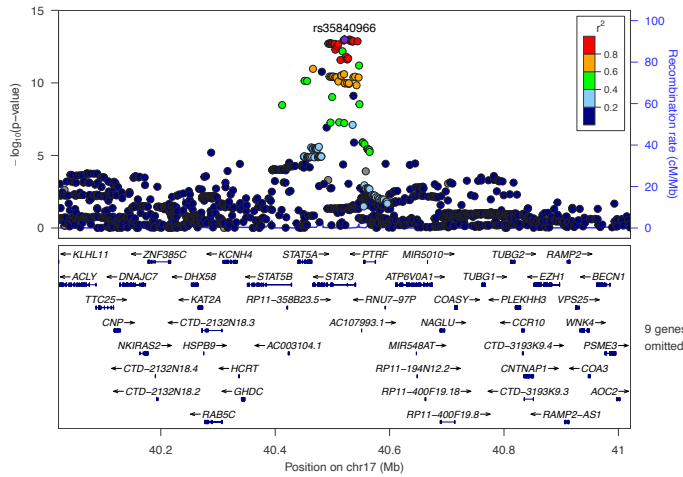


TDMA

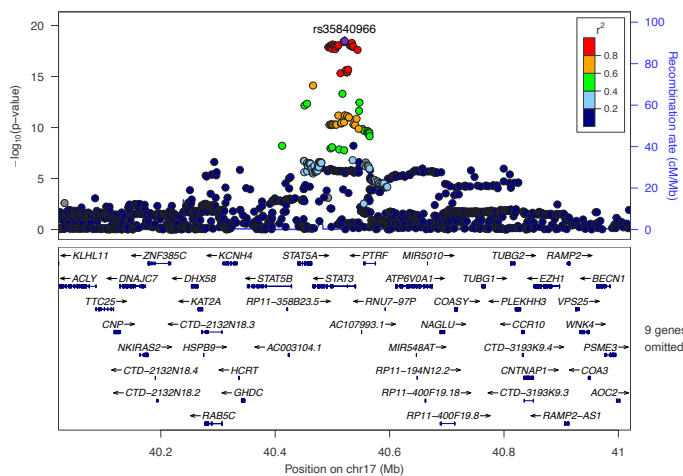
Supplementary Figure 19: Regional association plot (IVW TDMA) for shared locus at 16p13.13



Psoriasis

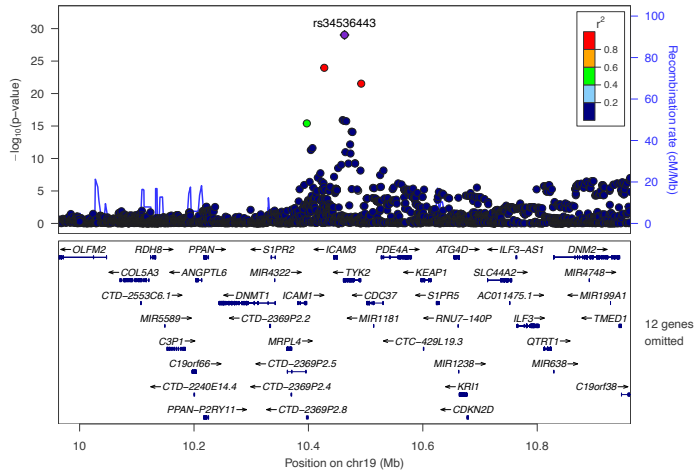


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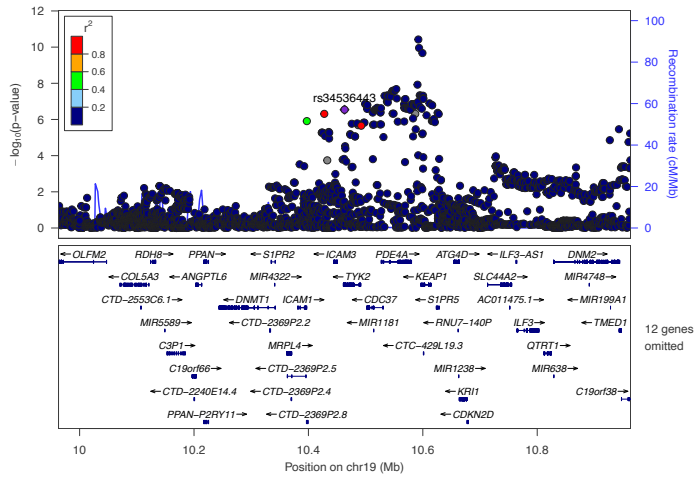


TDMA

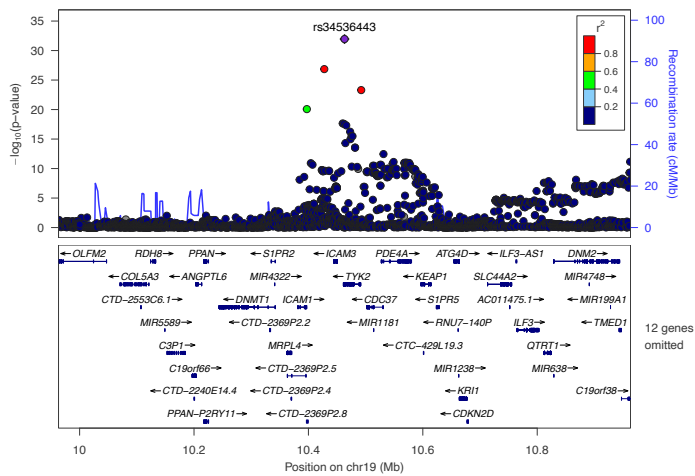
Supplementary Figure 20: Regional association plot (equally weighted TDMA) for shared locus at 17q21.2



Psoriasis

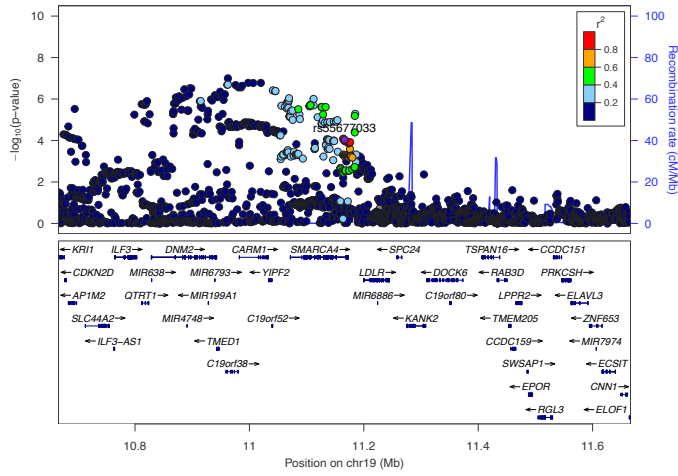


MS

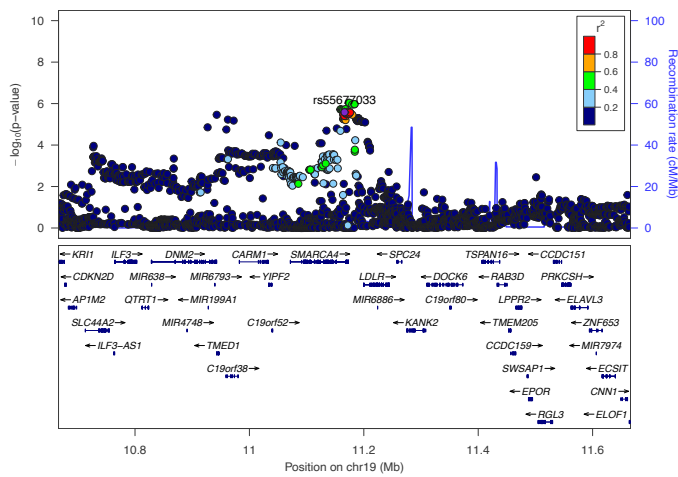


TDMA

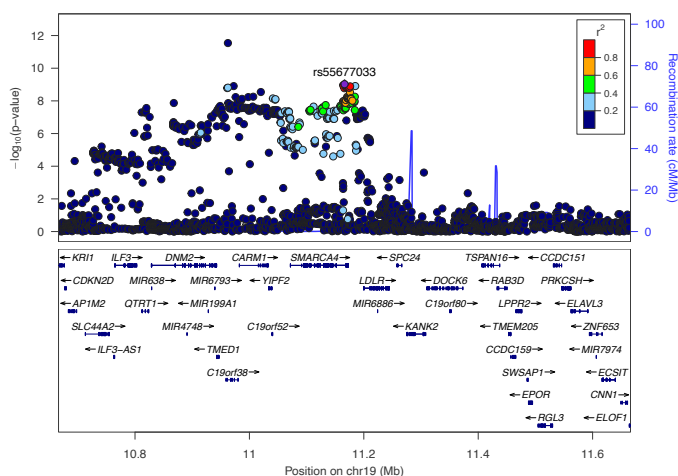
Supplementary Figure 21: Regional association plot (equally weighted TDMA) for shared locus at 19p13.2



Psoriasis

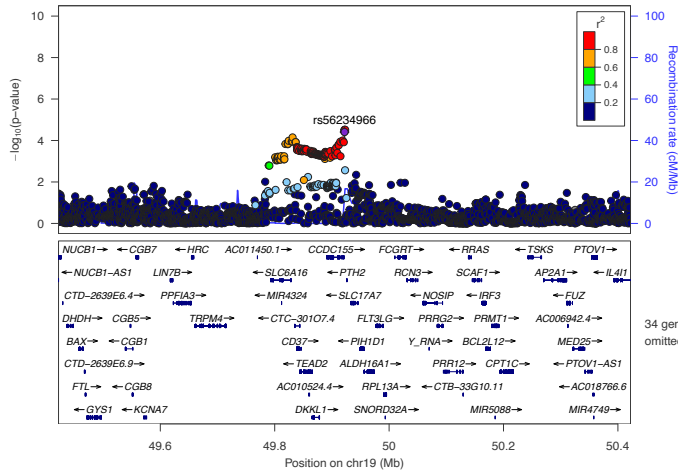


MS

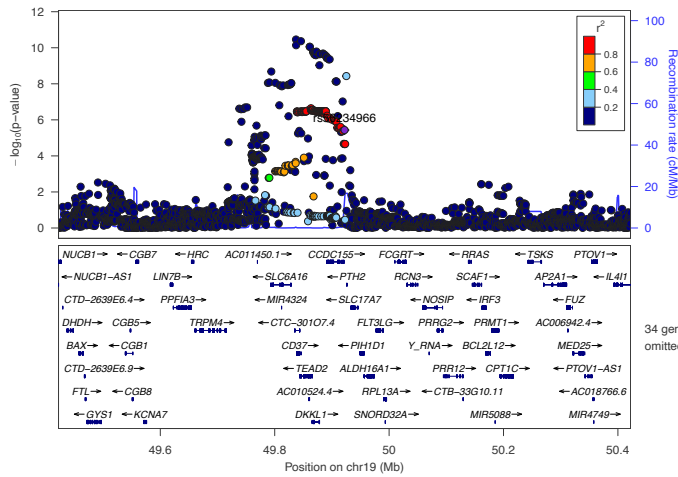


TDMA

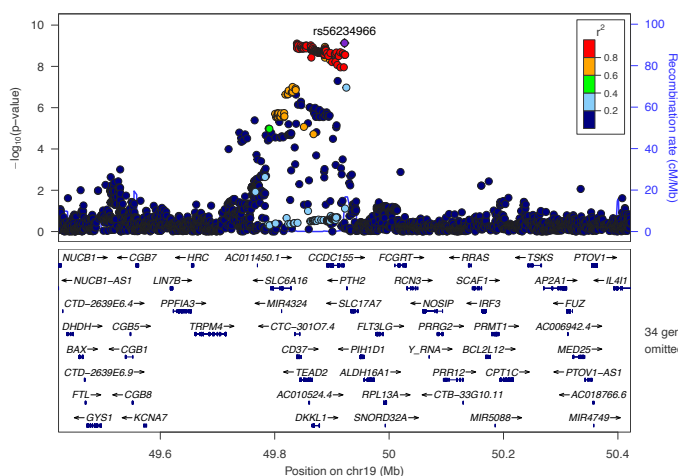
Supplementary Figure 22: Regional association plot (IVW TDMA) for shared locus at 19p13.2



Psoriasis

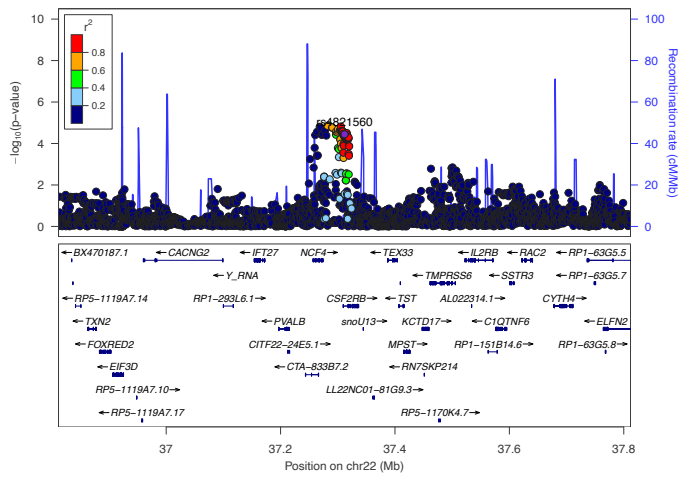


MS

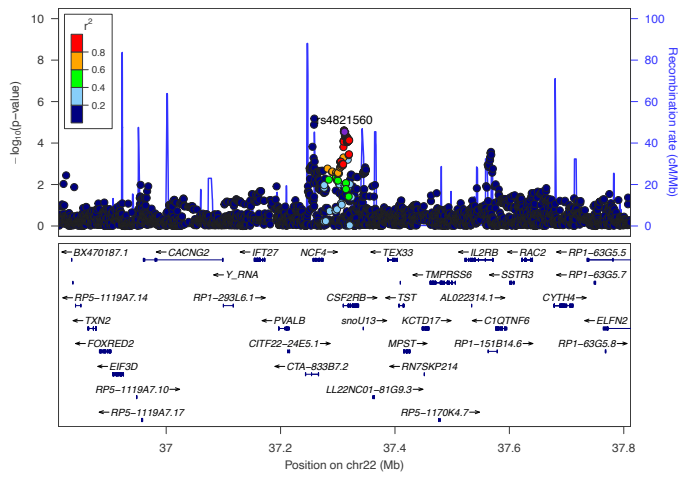


TDMA

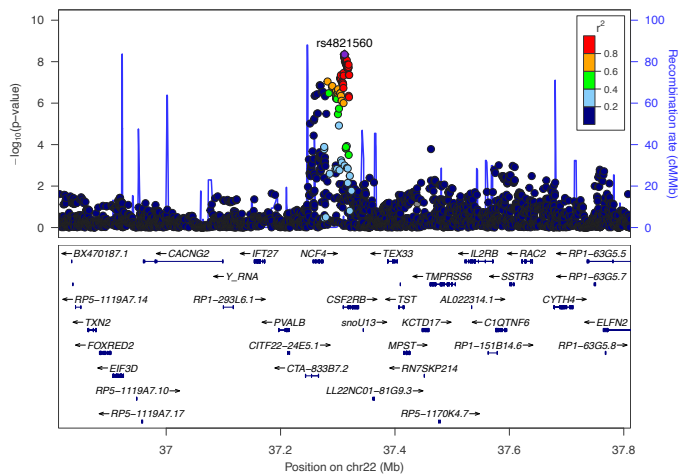
Supplementary Figure 23: Regional association plot (equally weighted TDMA) for shared locus at 19q13.33



Psoriasis



MS

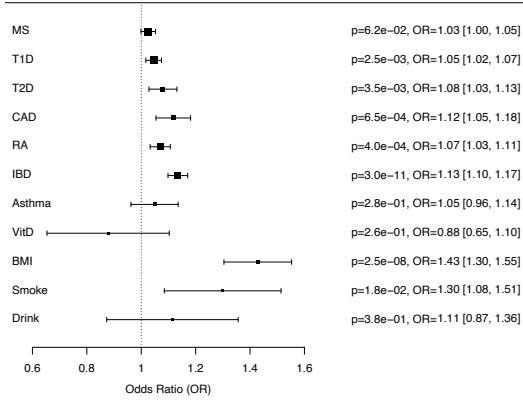


TDMA

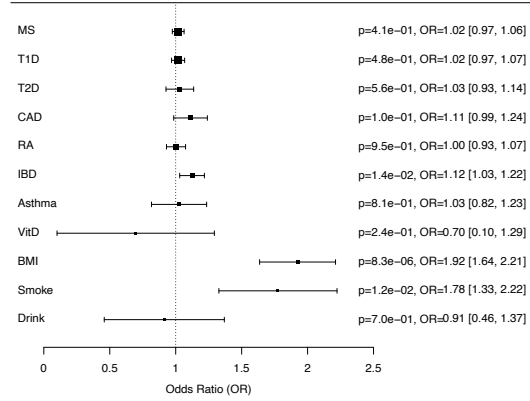
Supplementary Figure 24: Regional association plot (equally weighted TDMA) for opposing locus at 22q12.3



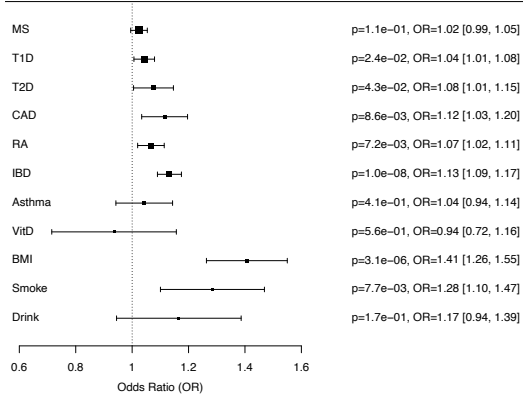
**a) MR-PRESSO**



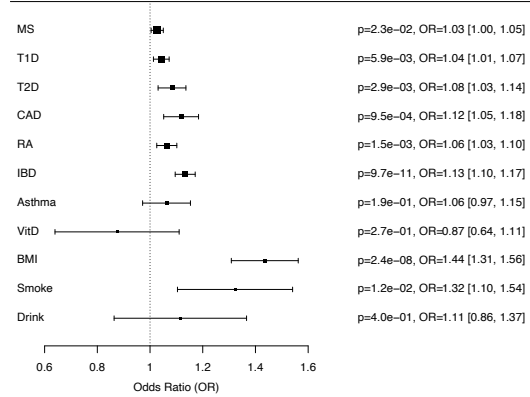
**b) MR-Egger**



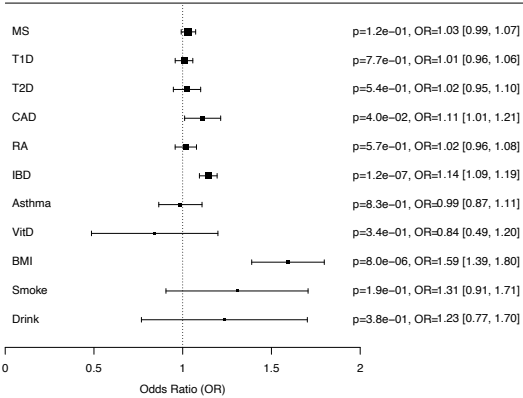
**c) MR-Robust**



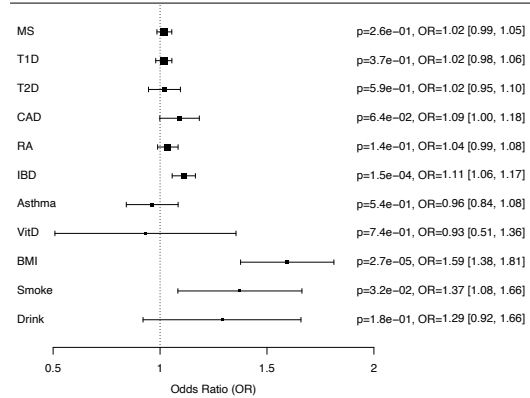
**d) MR-RAPS**



**e) MR-Median**



**f) MR-Mode**



**Supplementary Figure 25: Mendelian randomization (MR) results for the effects of multiple sclerosis (MS) and other comorbidities on psoriasis.** Forest plots generated from the results of six MR techniques (a-f). Abbreviations are as follows: T1D/T2D, type 1/2 diabetes; CAD, coronary artery disease; RA,

rheumatoid arthritis; IBD, inflammatory bowel disease; VitD, vitamin D (25OHD); BMI, body mass index; Smoke, cigarettes per day; Drink, drinks per week; p, p-value; OR, odds ratio.

**Supplementary Table 1: ICD-9/10 Codes for Traits/Diseases in our Epidemiological Study**

Trait/Disease	ICD-9*	ICD-10*
Psoriasis	696.0 696.1	L40
Multiple Sclerosis (MS)	340	G35
Type 1 Diabetes (T1D)	250.*(1 3)	E10
Type 2 Diabetes (T2D)	250.*(0 2)	E11
Coronary Artery Disease (CAD)	414	I25
Rheumatoid Arthritis (RA)	714	M0(5 6 8)
Inflammatory Bowel Disease (IBD)	55(5 6)	K5(0 1)
Asthma	493	J45
Vitamin D Deficiency	268	E55
Obesity – Obese	278.00 V85.3	E66.09 E66.9 Z68.3
Obesity – Morbidly Obese	278.01 V85.4	E66.01 E66.2 Z68.4
Smoking	305.1 V158.2	F17.21 Z878.91
Alcohol Use Disorder	291 303 305.0	F10

\*All sub-codes are also included

**Supplementary Table 2: Shared loci identified by equally weighted trans-disease meta-analysis (TDMA).** Susie # indicates the number of pairs of fine-mapped signals with evidence of colocalization (PP>0.7).

Cyt. Band	rsID	Position (hg19)	RA/NR	MS		Psoriasis		TDMA		Heterogeneity		Colocalization		Nearby Genes
				OR	P	OR	P	OR	P	Q	P	COLOC PP	SUSIE #	
5q33.3	rs2546890	158759900	A/G	1.12	1.0×10 <sup>-12</sup>	1.33	6.4×10 <sup>-51</sup>	1.22	7.1×10 <sup>-58</sup>	1.4×10 <sup>-2</sup>	0.91	4.4×10 <sup>-7</sup>	0	IL12B
	rs72804018**	158913657	G/A	1.10	4.6×10 <sup>-7</sup>	1.13	1.8×10 <sup>-7</sup>	1.12	4.6×10 <sup>-13</sup>	2.2×10 <sup>-4</sup>	0.99	7.8×10 <sup>-3</sup>	3	
6p21.33	rs9265746	31302724	A/G	1.73	1.5×10 <sup>-108</sup>	1.52	1.9×10 <sup>-102</sup>	1.62	6.0×10 <sup>-207</sup>	7.8×10 <sup>-3</sup>	0.93	-	-	HLA-B*/C, TNF
6q23.3	rs9321623	137958265	C/T	1.08	4.5×10 <sup>-6</sup>	1.10	4.5×10 <sup>-7</sup>	1.09	9.5×10 <sup>-12</sup>	1.7×10 <sup>-4</sup>	0.99	1.5×10 <sup>-3</sup>	1	TNFAIP3
7p14.1	rs17259252	37382520	G/A	1.08	8.4×10 <sup>-6</sup>	1.09	5.7×10 <sup>-6</sup>	1.08	2.1×10 <sup>-10</sup>	9.1×10 <sup>-5</sup>	0.99	0.80	3	ELMO1*
10q22.2	rs2459446	75601596	C/T	1.07	7.9×10 <sup>-5</sup>	1.13	1.5×10 <sup>-10</sup>	1.10	8.9×10 <sup>-14</sup>	1.8×10 <sup>-3</sup>	0.97	0.87	3	CAMK2G*
11q13.1	rs479777	64107477	T/C	1.08	3.5×10 <sup>-5</sup>	1.13	2.1×10 <sup>-9</sup>	1.11	6.0×10 <sup>-13</sup>	9.1×10 <sup>-4</sup>	0.98	0.87	0	PRDX5*, RPS6KA4*
12p13.31	rs4149576	6449115	T/C	1.11	3.5×10 <sup>-9</sup>	0.07	8.8×10 <sup>-5</sup>	1.09	6.8×10 <sup>-12</sup>	3.4×10 <sup>-4</sup>	0.99	0.07	6	CD27, TNFRSF1A*
13q14.2	rs9591325	50811220	T/C	1.24	4.2×10 <sup>-10</sup>	1.24	6.6×10 <sup>-9</sup>	1.24	2.0×10 <sup>-17</sup>	1.7×10 <sup>-5</sup>	1.00	0.99	2	DLEU1*
17q21.2	rs35840966	40521204	T/C	1.14	1.1×10 <sup>-13</sup>	0.11	8.2×10 <sup>-8</sup>	1.13	3.3×10 <sup>-19</sup>	3.1×10 <sup>-4</sup>	0.99	0.97	7	STAT3*, STAT5A*/B
19p13.2	rs34536443	10463118	G/C	1.30	2.9×10 <sup>-7</sup>	1.95	9.4×10 <sup>-30</sup>	1.59	1.1×10 <sup>-32</sup>	8.1×10 <sup>-2</sup>	0.78	0.91	2	TYK2*, CDG37
19p13.2	rs142213240	10972474	G/C	1.45	6.6×10 <sup>-6</sup>	1.28	2.2×10 <sup>-5</sup>	1.36	8.5×10 <sup>-10</sup>	7.4×10 <sup>-3</sup>	0.93	0.91	2	ILF3, CARM1
19q13.33	rs56234966	49922071	C/T	1.11	3.7×10 <sup>-6</sup>	1.10	3.9×10 <sup>-5</sup>	1.10	7.4×10 <sup>-10</sup>	7.4×10 <sup>-6</sup>	1.00	0.02	4	DKKL1*, SLC6A16*

\*eQTL evidence in eQTLGen or GTEx v8 \*\*Secondary signal identified through HESS

**Supplementary Table 3: Opposing loci identified by equally weighted trans-disease meta-analysis (TDMA). Susie # indicates the number of pairs of fine-mapped signals with evidence of colocalization (PP>0.7).**

Cyt. Band	rsID	Position (hg19)	RA/NR	MS		Psoriasis		TDMA		Heterogeneity		Colocalization Prob.		Nearby Genes
				OR	P	OR	P	OR	P	Q	P	COLOC PP	SusIE	
1p36.11	rs6672420	25291010	A/T	1.07	2.2×10 <sup>-5</sup>	0.86	8.8×10 <sup>-15</sup>	1.11	6.3×10 <sup>-18</sup>	1.4×10 <sup>-3</sup>	0.97	0.93	3	RUNX3
2p16.1	rs1177202	61074576	G/C	0.93	6.1×10 <sup>-6</sup>	1.17	1.3×10 <sup>-15</sup>	1.12	1.8×10 <sup>-19</sup>	1.6×10 <sup>-3</sup>	0.97	0.75	6	REL <sup>*</sup> , PUS10 <sup>*</sup>
5q31.1	rs3843503	131466629	T/A	1.08	1.9×10 <sup>-5</sup>	0.92	2.1×10 <sup>-5</sup>	1.08	1.6×10 <sup>-9</sup>	7.7×10 <sup>-7</sup>	1.00	0.68	3	CSF2, P4HA2 <sup>*</sup>
6q25.3	rs2451279	159515077	G/A	1.10	6.4×10 <sup>-8</sup>	0.91	3.6×10 <sup>-6</sup>	1.10	1.8×10 <sup>-12</sup>	2.1×10 <sup>-6</sup>	1.00	2.6×10 <sup>-3</sup>	2	TAGAP <sup>*</sup>
7q36.1	rs10243355	150356318	G/A	1.09	3.4×10 <sup>-5</sup>	0.89	1.8×10 <sup>-5</sup>	1.11	3.4×10 <sup>-9</sup>	3.1×10 <sup>-4</sup>	0.99	0.81	1	GIMAP2 <sup>*</sup> /6 <sup>*</sup>
10q22.3	rs1108618	81043743	G/A	1.11	5.5×10 <sup>-10</sup>	0.89	6.0×10 <sup>-10</sup>	1.12	2.1×10 <sup>-18</sup>	4.9×10 <sup>-5</sup>	0.99	0.83	2	ZMIZ1 <sup>*</sup>
11p11.2	rs4647737	47253244	G/T	1.10	1.7×10 <sup>-5</sup>	0.90	2.8×10 <sup>-5</sup>	1.11	2.3×10 <sup>-9</sup>	5.8×10 <sup>-5</sup>	0.99	0.72	0	MYBPC3 <sup>*</sup> , AGBL2 <sup>*</sup>
22q12.3	rs4821560	37311806	T/G	1.07	2.9×10 <sup>-5</sup>	0.92	3.6×10 <sup>-5</sup>	1.08	4.5×10 <sup>-9</sup>	3.1×10 <sup>-5</sup>	1.00	0.76	3	CSF2RB <sup>*</sup> , NCF4

\*eQTL evidence in eQTLGen or GTEx v8

**Supplementary Table 4: Shared loci identified using conditional analysis (GCTA-COJO).** The loci in red were identified by COJO but not unconditional IVW TDMA. The loci in bold were identified by COJO but not by the unconditional equally weighted TDMA.

Cyt. Band	rsID	Position (hg19)	RA/NR	MS			Psoriasis			TDMA IVW			TDMA (equally weighted)		
				OR	SE	P	OR	SE	P	OR	SE	P	OR	SE	P
6q23.3	rs9321623	137958265	C/T	1.08	0.02	4.5×10 <sup>-6</sup>	1.10	0.02	4.5×10 <sup>-7</sup>	1.09	0.01	1.2×10 <sup>-11</sup>	1.09	0.01	9.5×10 <sup>-12</sup>
7p14.1	rs17259252	37382520	G/A	1.08	0.02	8.4×10 <sup>-6</sup>	1.09	0.02	5.7×10 <sup>-6</sup>	1.08	0.01	2.3×10 <sup>-10</sup>	1.08	0.01	2.1×10 <sup>-10</sup>
10q22.2	rs2459446	75601596	C/T	1.07	0.02	7.9×10 <sup>-5</sup>	1.13	0.02	1.5×10 <sup>-10</sup>	1.09	0.01	7.9×10 <sup>-13</sup>	1.10	0.01	8.9×10 <sup>-14</sup>
<b>11q21.3</b>	<b>rs4262739</b>	<b>128421175</b>	<b>G/A</b>	<b>1.07</b>	<b>0.02</b>	<b>5.4×10<sup>-5</sup></b>	<b>1.09</b>	<b>0.02</b>	<b>8.6×10<sup>-6</sup></b>	<b>1.08</b>	<b>0.01</b>	<b>2.4×10<sup>-9</sup></b>	<b>1.08</b>	<b>0.01</b>	<b>1.9×10<sup>-9</sup></b>
12p13.31	rs11064145	6455098	G/T	1.11	0.02	3.4×10 <sup>-8</sup>	1.08	0.02	2.9×10 <sup>-5</sup>	1.09	0.01	6.0×10 <sup>-12</sup>	1.09	0.01	8.9×10 <sup>-12</sup>
13q14.2	rs9591325	50811220	T/C	1.24	0.03	4.2×10 <sup>-10</sup>	1.24	0.04	6.6×10 <sup>-9</sup>	1.24	0.03	1.5×10 <sup>-17</sup>	1.24	0.03	2.0×10 <sup>-17</sup>
<b>16p13.13</b>	<b>rs413024</b>	<b>11354091</b>	<b>A/G</b>	<b>1.10</b>	<b>0.02</b>	<b>1.3×10<sup>-7</sup></b>	<b>1.13</b>	<b>0.02</b>	<b>1.2×10<sup>-8</sup></b>	<b>1.11</b>	<b>0.01</b>	<b>1.1×10<sup>-14</sup></b>	<b>1.11</b>	<b>0.01</b>	<b>8.0×10<sup>-15</sup></b>
17q21.2	rs2306581	40500265	A/C	1.13	0.02	2.1×10 <sup>-13</sup>	1.11	0.02	6.9×10 <sup>-8</sup>	1.12	0.01	1.0×10 <sup>-19</sup>	1.12	0.01	7.3×10 <sup>-19</sup>
<b>19q13.33</b>	<b>rs73053942</b>	<b>49923166</b>	<b>T/G</b>	<b>1.10</b>	<b>0.02</b>	<b>2.2×10<sup>-5</sup></b>	<b>1.10</b>	<b>0.02</b>	<b>3.0×10<sup>-5</sup></b>	<b>1.10</b>	<b>0.02</b>	<b>2.7×10<sup>-9</sup></b>	<b>1.10</b>	<b>0.02</b>	<b>2.8×10<sup>-9</sup></b>

**Supplementary Table 5: Opposing loci identified using conditional analysis (GCTA-COJO).** The loci in red were identified by COJO but not unconditional IVW TDMA. The loci in bold were identified by COJO but not by the unconditional equally weighted TDMA.

Cyt. Band	rsID	Position (hg19)	RA/NR	MS			Psoriasis			TDMA IVW			TDMA (equally weighted)		
				OR	SE	P	OR	SE	P	OR	SE	P	OR	SE	P
1p36.11	rs6672420	25291010	A/T	1.07	0.02	2.2×10 <sup>-5</sup>	0.86	0.02	8.8×10 <sup>-15</sup>	1.11	0.01	6.3×10 <sup>-18</sup>	1.11	0.01	6.3×10 <sup>-18</sup>
2p16.1	rs35741374	61072567	C/T	1.08	0.02	6.7×10 <sup>-6</sup>	0.86	0.02	1.2×10 <sup>-15</sup>	1.11	0.01	6.1×10 <sup>-18</sup>	1.12	0.01	1.9×10 <sup>-19</sup>
<b>6q23.3</b>	<b>rs79570084</b>	<b>138160322</b>	<b>C/T</b>	<b>1.10</b>	<b>0.02</b>	<b>1.7×10<sup>-6</sup></b>	<b>0.87</b>	<b>0.03</b>	<b>4.1×10<sup>-8</sup></b>	<b>1.12</b>	<b>0.02</b>	<b>8.2×10<sup>-13</sup></b>	<b>1.13</b>	<b>0.02</b>	<b>3.6×10<sup>-13</sup></b>
7q36.1	rs10275417	150369447	C/T	1.08	0.02	5.6×10 <sup>-5</sup>	0.89	0.03	1.6×10 <sup>-5</sup>	1.10	0.02	7.2×10 <sup>-9</sup>	1.10	0.02	5.0×10 <sup>-9</sup>
<b>10p15.1</b>	<b>rs2256774</b>	<b>6097165</b>	<b>C/T</b>	<b>1.08</b>	<b>0.02</b>	<b>5.4×10<sup>-6</sup></b>	<b>0.92</b>	<b>0.02</b>	<b>3.3×10<sup>-5</sup></b>	<b>1.08</b>	<b>0.01</b>	<b>7.5×10<sup>-10</sup></b>	<b>1.08</b>	<b>0.01</b>	<b>9.4×10<sup>-10</sup></b>
10q22.3	rs1108617	81043573	G/A	1.11	0.02	3.6×10 <sup>-9</sup>	0.89	0.02	2.8×10 <sup>-10</sup>	1.12	0.01	8.9×10 <sup>-18</sup>	1.12	0.01	6.5×10 <sup>-18</sup>
16p13.13	rs7192287	11180537	A/T	1.18	0.02	1.9×10 <sup>-21</sup>	0.92	0.02	3.3×10 <sup>-5</sup>	1.14	0.01	5.1×10 <sup>-23</sup>	<i>Does not meet criteria</i>		

**Supplementary Table 6: Colocalization using approximate Bayes factors (COLOC).** The hypothesis with the largest posterior probability in each marker is in bold.

Lead Marker (RA/NR)	Direction	Approach	Num. SNPs	Posterior Probabilities (PP)*				
				H0	H1	H2	H3	H4
1:25291010 (A/T)	Opposing	EW/IVW TDMA	671	4.4×10 <sup>-11</sup>	7.0×10 <sup>-11</sup>	0.03	0.04	<b>0.93</b>
2:61074576 (G/C)	Opposing	EW TDMA	401	6.2×10 <sup>-13</sup>	4.2×10 <sup>-11</sup>	3.6×10 <sup>-3</sup>	0.24	<b>0.75</b>
2:61079090 (A/G)	Opposing	IVW TDMA	392	6.0×10 <sup>-13</sup>	4.5×10 <sup>-11</sup>	3.5×10 <sup>-3</sup>	0.26	<b>0.73</b>
5:131466629 (T/A)	Opposing	EW/IVW TDMA	383	0.03	0.04	0.11	0.14	<b>0.68</b>
5:158759900 (A/G)	Shared	EW/IVW TDMA	456	3.8×10 <sup>-60</sup>	2.9×10 <sup>-54</sup>	1.3×10 <sup>-6</sup>	<b>1.0</b>	4.4×10 <sup>-7</sup>
5:158913657 (G/A)	Shared	HESS	528	9.4×10 <sup>-56</sup>	2.8×10 <sup>-54</sup>	0.03	<b>0.96</b>	7.8×10 <sup>-3</sup>
6:42238973 (C/T)	Shared	IVW TDMA	603	0.07	0.02	0.06	0.02	<b>0.83</b>
6:137958265 (C/T)	Shared	EW/IVW TDMA	743	6.3×10 <sup>-9</sup>	0.01	5.8×10 <sup>-7</sup>	<b>0.99</b>	1.5×10 <sup>-3</sup>
6:138154501 (A/G)	Opposing	IVW TDMA	389	2.2×10 <sup>-12</sup>	2.5×10 <sup>-10</sup>	8.5×10 <sup>-3</sup>	<b>0.99</b>	3.2×10 <sup>-3</sup>
6:138160322 (C/T)	Opposing	COJO	398	2.2×10 <sup>-12</sup>	2.5×10 <sup>-10</sup>	8.5×10 <sup>-3</sup>	<b>0.99</b>	3.2×10 <sup>-3</sup>
6:159515077 (G/A)	Opposing	EW/IVW TDMA	710	7.1×10 <sup>-8</sup>	0.02	3.6×10 <sup>-6</sup>	<b>0.98</b>	2.6×10 <sup>-3</sup>
7:37382520 (G/A)	Shared	EW TDMA	750	4.6×10 <sup>-3</sup>	0.10	4.2×10 <sup>-3</sup>	0.09	<b>0.80</b>
7:37385365 (A/G)	Shared	IVW TDMA	758	4.6×10 <sup>-3</sup>	0.10	4.2×10 <sup>-3</sup>	0.09	<b>0.80</b>
7:150356318 (G/A)	Opposing	EW/IVW TDMA	842	0.01	0.04	0.03	0.10	<b>0.81</b>
10:6097165 (C/T)	Opposing	COJO	852	1.1×10 <sup>-20</sup>	<b>0.78</b>	2.9×10 <sup>-21</sup>	0.21	9.0×10 <sup>-3</sup>
10:75601596 (C/T)	Shared	EW/IVW TDMA	310	7.3×10 <sup>-7</sup>	8.0×10 <sup>-7</sup>	0.06	0.07	<b>0.87</b>
10:81043743 (G/A)	Opposing	EW TDMA	730	5.2×10 <sup>-11</sup>	1.3×10 <sup>-5</sup>	6.8×10 <sup>-7</sup>	0.17	<b>0.83</b>
10:81047015 (A/G)	Opposing	IVW TDMA	737	5.2×10 <sup>-11</sup>	1.3×10 <sup>-5</sup>	6.8×10 <sup>-7</sup>	0.17	<b>0.83</b>
11:47169228 (C/G)	Opposing	IVW TDMA	328	4.9×10 <sup>-3</sup>	0.04	7.3×10 <sup>-3</sup>	0.06	<b>0.88</b>
11:47253244 (G/T)	Opposing	EW TDMA	392	3.2×10 <sup>-3</sup>	0.09	6.1×10 <sup>-3</sup>	0.18	<b>0.72</b>
11:64107477 (T/C)	Shared	EW/IVW TDMA	348	8.4×10 <sup>-6</sup>	8.9×10 <sup>-6</sup>	0.07	0.07	<b>0.87</b>
11:128421175 (G/A)	Shared	COJO	469	1.3×10 <sup>-4</sup>	5.0×10 <sup>-5</sup>	<b>0.47</b>	0.19	0.35
12:6449115 (T/C)	Shared	EW/IVW TDMA	565	1.0×10 <sup>-7</sup>	<b>0.78</b>	2.1×10 <sup>-8</sup>	0.15	0.07
13:50811220 (T/C)	Shared	EW/IVW TDMA	502	1.0×10 <sup>-9</sup>	1.0×10 <sup>-5</sup>	6.6×10 <sup>-7</sup>	5.3×10 <sup>-3</sup>	<b>0.99</b>
16:11113463 (G/T)	Opposing	IVW TDMA	545	2.8×10 <sup>-20</sup>	0.02	1.6×10 <sup>-19</sup>	0.13	<b>0.85</b>
16:11354970 (A/G)	Shared	IVW TDMA	794	7.9×10 <sup>-19</sup>	3.0×10 <sup>-3</sup>	2.6×10 <sup>-16</sup>	<b>1.0</b>	3.1×10 <sup>-4</sup>
16:11354091 (A/G)	Shared	COJO	795	3.3×10 <sup>-19</sup>	3.0×10 <sup>-3</sup>	1.1×10 <sup>-16</sup>	<b>1.0</b>	2.6×10 <sup>-4</sup>
17:40519890 (A/G)	Shared	IVW TDMA	412	6.4×10 <sup>-13</sup>	8.4×10 <sup>-5</sup>	2.3×10 <sup>-10</sup>	0.03	<b>0.97</b>
17:40521204 (T/C)	Shared	EW TDMA	412	6.4×10 <sup>-13</sup>	8.4×10 <sup>-5</sup>	2.3×10 <sup>-10</sup>	0.03	<b>0.97</b>
19:10463118 (G/C)	Shared	EW TDMA	506	1.3×10 <sup>-25</sup>	6.9×10 <sup>-23</sup>	1.6×10 <sup>-4</sup>	0.09	<b>0.91</b>
19:10972474 (G/C)	Shared	EW TDMA	354	2.2×10 <sup>-4</sup>	4.4×10 <sup>-4</sup>	0.03	0.06	<b>0.91</b>
19:11166293 (T/C)	Shared	IVW TDMA	638	1.0×10 <sup>-3</sup>	0.04	0.02	<b>0.77</b>	0.17
19:49922071 (C/T)	Shared	EW TDMA	482	3.1×10 <sup>-6</sup>	0.47	3.4×10 <sup>-6</sup>	<b>0.52</b>	0.02
22:37310954 (A/G)	Opposing	IVW TDMA	812	0.02	0.03	0.07	0.12	<b>0.76</b>

22:37311806 (T/G)	Opposing	EW TDMA	817	0.02	0.03	0.07	0.12	<b>0.76</b>
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\***H0**: No association with either trait; **H1**: Association with MS, not with psoriasis; **H2**: Association with psoriasis, not with MS;  
**H3**: Association with both traits, two independent SNPs; **H4**: Association with both traits, one shared SNP.



**Supplementary Table 7: Colocalization using sum of single effects (SuSE)**

Lead Marker (RA/NR)	Colocalized Marker (RA/NR)	Posterior Probabilities (PP)				
		<i>H0</i>	<i>H1</i>	<i>H2</i>	<i>H3</i>	<i>H4</i>
5:158913657 (G/A)	5:158857072 (T/C)	0.00	0.00	0.00	$1.2 \times 10^{-13}$	<b>1.00</b>
	5:158857472 (C/T)	0.00	0.00	0.00	0.00	<b>1.00</b>
	5:158857873 (C/A)	0.00	0.00	0.00	0.00	<b>1.00</b>
6:137958265 (C/T)	6:137979971 (T/C)	0.00	0.00	0.00	$7.8 \times 10^{-4}$	<b>1.00</b>
6:159515077 (G/A)	6:159506600 (T/C)	0.00	0.00	0.00	0.00	<b>1.00</b>
	6:159507026 (T/C)	0.00	0.00	0.00	0.00	<b>1.00</b>
12:6449115 (T/C)	12:6441348 (G/C)	0.00	0.00	0.00	0.00	<b>1.00</b>
	12:6444963 (G/C)	0.00	0.00	0.00	0.00	<b>1.00</b>
	12:6445329 (C/G)	0.00	0.00	0.00	0.00	<b>1.00</b>
	12:6447437 (C/T)	0.00	0.00	0.00	0.00	<b>1.00</b>
	12:6447522 (A/G)	0.00	0.00	0.00	0.00	<b>1.00</b>
	12:6449115 (T/C)	0.00	0.00	0.00	0.00	<b>1.00</b>
19:49922071 (C/T)	19:49838891 (A/C)	0.00	0.00	0.00	0.00	<b>1.00</b>
	19:49839283 (A/G)	0.00	0.00	0.00	$2.0 \times 10^{-3}$	<b>1.00</b>
	19:49841054 (T/G)	0.00	0.00	0.00	0.00	<b>1.00</b>
	19:49845244 (A/T)	0.00	0.00	0.00	$7.7 \times 10^{-8}$	<b>1.00</b>

**Supplementary Table 8: Genetic associations with comorbidities of psoriasis and/or MS.** The odds ratios (OR) are with respect to the TDMA risk alleles. The Direction column indicates whether the risk allele of the TDMA shared signal would increase or decrease the comorbidity; for the opposing loci, it indicates whether the risk allele of the comorbidity would align with the risk allele of psoriasis or MS.  
<sup>1</sup>Restricting to European individuals

Study Details			Associations with TDMA Loci				
Trait	Sample Size	PubMed	Position (hg19)	rsID	P-value	OR	Direction
Body mass index	806,834 individuals	30239722	11:47253244	rs4647737	1.4×10 <sup>-7</sup>	1.01	Psoriasis
			13:50811220	rs9591325	9.8×10 <sup>-15</sup>	1.03	Increase
Coronary artery disease	122,733 cases 424,528 controls	29212778	19:10972474	rs142213240	3.0×10 <sup>-12</sup>	1.10	Increase
Inflammatory bowel disease	25,042 cases 34,915 controls	28067908	5:131466629	rs3843503	2.3×10 <sup>-16</sup>	1.11	Psoriasis
			10:75601596	rs2459446	3.6×10 <sup>-7</sup>	1.07	Increase
			10:81043743	rs1108618	4.2×10 <sup>-11</sup>	1.09	Psoriasis
			16:11354091	rs413024	2.7×10 <sup>-7</sup>	1.07	Increase
			17:40521204	rs35840966	1.9×10 <sup>-15</sup>	0.90	Decrease
Type 1 diabetes	18,942 cases 501,638 control	34012112	1:25291010	rs6672420	1.7×10 <sup>-7</sup>	1.08	Psoriasis
			6:138160322	rs79570084	6.1×10 <sup>-7</sup>	1.09	MS
			6:159515077	rs2451279	7.2×10 <sup>-6</sup>	1.07	MS
			10:6097165	rs2256774	8.5×10 <sup>-5</sup>	1.06	Psoriasis
			11:64107477	rs479777	4.7×10 <sup>-11</sup>	1.10	Increase
			16:11354091	rs413024	9.0×10 <sup>-7</sup>	1.08	Increase
			19:10463118	rs34536443	1.5×10 <sup>-23</sup>	1.47	Increase
Type 2 diabetes	74,124 cases 824,006 controls	30297969	No significant / suggestive significant associations				
Asthma	69,189 cases 702,199 controls	31959851	5:131466629	rs3843503	1.6×10 <sup>-11</sup>	1.04	MS
			10:6097165	rs2256774	8.2×10 <sup>-5</sup>	1.03	Psoriasis
			11:128421175	rs4262739	8.5×10 <sup>-5</sup>	1.03	Increase
Rheumatoid arthritis	22,350 cases 74,823 controls <sup>1</sup>	Preprint ( <a href="https://doi.org/10.1101/2021.12.01.21267132">https://doi.org/10.1101/2021.12.01.21267132</a> )	2:61074576	rs1177202	2.0×10 <sup>-8</sup>	1.07	Psoriasis
			6:159515077	rs2451279	8.5×10 <sup>-11</sup>	1.09	MS
			10:81043743	rs1108618	3.5×10 <sup>-5</sup>	1.04	MS
			11:64107477	rs479777	1.4×10 <sup>-11</sup>	1.08	Increase
			16:11354091	rs413024	7.6×10 <sup>-5</sup>	1.05	Increase
			19:10463118	rs34536443	5.5×10 <sup>-21</sup>	1.56	Increase
			22:37311806	rs4821560	4.4×10 <sup>-9</sup>	1.06	Psoriasis
Drinks per week	537,349 individuals	30643251	No significant / suggestive significant associations				
Cigarettes per day	263,954 individuals	30643251	No significant / suggestive significant associations				
Vitamin D (25OHD)	443,734 individuals	32059762	No significant / suggestive significant associations				

**Supplementary Table 9: Enrichment of H3K27ac marks for active enhancers.** Cell types with significant enrichment (adjusting for FDR) are colored in red. Abbreviations are as follows: N, number of loci overlapping active enhancer mark (out of 23 loci for equally weighted TDMA, 62 for MS TDMA-removed and 25 for psoriasis TDMA-removed, outside the MHC); Duodenum muc., Duodenum mucosa; Hippocampus m., Hippocampus middle; Inferior t. lobe, Inferior temporal lobe; Chondrogenic d., Chondrogenic diff.

TDMA Loci			MS Loci (TDMA Removed)			Psoriasis Loci (TDMA Removed)		
Cell type	N	P-value	Cell type	N	P-value	Cell type	N	P-value
B centroblast	12	7.7×10 <sup>-12</sup>	T (reg)	23	1.1×10 <sup>-14</sup>	Lymphoblastoid	6	4.4E-04
Lymphoblastoid	11	6.7×10 <sup>-9</sup>	Th0	21	6.8×10 <sup>-14</sup>	Colonic mucosa	6	1.3E-03
Th0	10	1.5×10 <sup>-8</sup>	Th1	20	2.5×10 <sup>-13</sup>	Monocytes	6	1.7E-03
Th17	10	2.1×10 <sup>-8</sup>	Th2	19	2.0×10 <sup>-12</sup>	Pancreatic islets	6	2.0E-03
Th2	9	1.2×10 <sup>-7</sup>	Th17	19	1.4×10 <sup>-11</sup>	B cell	5	2.2E-03
Th1	9	1.4×10 <sup>-7</sup>	Th (stim)	21	1.8×10 <sup>-11</sup>	HSMM	5	9.6E-03
B cell	9	6.4×10 <sup>-7</sup>	Lymphoblastoid	20	3.0×10 <sup>-11</sup>	Th17	4	0.011
T (naïve)	9	6.6×10 <sup>-7</sup>	T (mem)	18	8.1×10 <sup>-11</sup>	T (naïve)	4	0.014
Th (stim)	9	2.8×10 <sup>-6</sup>	CD8+ (mem)	17	2.5×10 <sup>-9</sup>	T (reg)	4	0.016
T (mem)	8	3.3×10 <sup>-6</sup>	Monocytes	20	2.9×10 <sup>-19</sup>	Duodenum muc.	4	0.022
T (reg)	8	9.9×10 <sup>-6</sup>	B cell	17	3.9×10 <sup>-9</sup>	Th (stim)	4	0.026
Monocytes	9	1.1×10 <sup>-5</sup>	T (naïve)	17	4.2×10 <sup>-9</sup>	Kidney	4	0.030
Liver	8	4.7×10 <sup>-5</sup>	B centroblast	13	4.6×10 <sup>-7</sup>	Liver	4	0.032
CD8+ (mem)	7	6.3×10 <sup>-5</sup>	CD8+ (naïve)	12	5.9×10 <sup>-7</sup>	B centroblast	3	0.038
Colonic mucosa	8	6.4×10 <sup>-5</sup>	Colonic mucosa	16	1.5×10 <sup>-6</sup>	Th2	3	0.043
CD8+ (naïve)	6	7.0×10 <sup>-5</sup>	Duodenum muc.	13	2.6×10 <sup>-5</sup>	Th1	3	0.045
Duodenum muc.	7	1.7×10 <sup>-4</sup>	Liver	12	3.8×10 <sup>-4</sup>	Th0	3	0.053
Mid-frontal lobe	8	1.9×10 <sup>-4</sup>	HepG2	10	8.0×10 <sup>-4</sup>	T (mem)	3	0.053
CD34+ (PB)	6	3.6×10 <sup>-4</sup>	NH osteoblast	12	1.1×10 <sup>-3</sup>	CD34+ (PB)	3	0.054
Hippocampus m.	7	1.0×10 <sup>-3</sup>	Adipose	12	1.1×10 <sup>-3</sup>	Inferior t. lobe	4	0.059
Inferior t. lobe	7	1.1×10 <sup>-3</sup>	Kidney	10	3.9×10 <sup>-3</sup>	Mid-frontal lobe	4	0.060
Adipose	6	4.2×10 <sup>-3</sup>	K562	8	7.8×10 <sup>-3</sup>	CD8+ (mem)	3	0.065
Angular gyrus	6	5.9×10 <sup>-3</sup>	Chondrogenic d.	9	0.021	CD8+ (naïve)	2	0.134
Anterior caudate	6	8.3×10 <sup>-3</sup>	Cingulate gyrus	9	0.037	Substantia nigra	3	0.143
Substantia nigra	5	0.016	Hippocampus m.	9	0.038	NH osteoblast	3	0.160
HSMM	5	0.018	Angular gyrus	9	0.041	Adipose	3	0.162
Cingulate gyrus	5	0.024	Inferior t. lobe	9	0.042	Hippocampus m.	3	0.181
HepG2	4	0.024	Mid-frontal lobe	9	0.044	Angular gyrus	3	0.187
Kidney	4	0.047	Substantia nigra	8	0.051	K562	2	0.237
NH osteoblast	4	0.073	Anterior caudate	9	0.060	Chondrogenic d.	2	0.387
Pancreatic islets	4	0.075	Pancreatic islets	8	0.069	Cingulate gyrus	2	0.439
K562	3	0.089	HSMM	7	0.128	Anterior caudate	2	0.487
Chondrogenic d.	3	0.1194	CD34+ (PB)	5	0.132	HepG2	1	0.632

**Supplementary Table 10: Clusters inferred from LINCS co-expression.** <sup>1</sup>Annotated in 'IL-17 signaling pathway' (KEGG), 'TNF signaling pathway' (KEGG) or 'TNF-alpha effects on cytokine activity, cell motility, and apoptosis' (BioPlanet). <sup>2</sup>Annotated in 'JAK-STAT signaling' (KEGG), 'JAK-STAT signaling pathway' (BioPlanet) or 'IL-6/JAK/STAT3 Signaling' (MSigDB).

Chr	rsID	Position (hg19)	Genes	Cluster	IL17/ TNFa <sup>1</sup>	JAK/ STAT <sup>2</sup>
1	rs6672420	25291010	<i>RUNX3</i>	1		
2	rs1177202	61074576	<i>REL, PUS10</i>	1		
5	rs3843503	131466629	<i>CSF2, P4HA2</i>	1	X	X
5	rs2546890	158759900	<i>IL12B</i>	2	X	X
6	rs2247179	31266952	<i>HLA-B/C, TNF, HLA-DRB1/5</i>	1	X	X
6	rs9321623	137958265	<i>TNFAIP3</i>	1	X	
6	rs2451279	159515077	<i>TAGAP</i>	N/A		
7	rs17259252	37382520	<i>ELMO1</i>	3		
7	rs10243355	150356318	<i>GIMAP2/6</i>	1		
10	rs2256774	6097165	<i>IL2RA</i>	2	X	X
10	rs2459446	75601596	<i>CAMK2G</i>	3		
10	rs1108618	81043743	<i>ZMIZ1</i>	1		
11	rs4647737	47253244	<i>MYBPC3, AGBL2</i>	2		
11	rs479777	64107477	<i>PRDX5, RPS6KA4</i>	2	X	
11	rs4262739	128421175	<i>ETS1</i>	1	X	
12	rs4149576	6449115	<i>CD27, LTBR, TNFRSF1A</i>	3	X	X
13	rs9591325	50811220	<i>DLEU1</i>	3		
16	rs413024	11354091	<i>PRM1/2, SOCS1, TNP2</i>	2		X
17	rs35840966	40521204	<i>STAT3, STAT5A/B</i>	3		X
19	rs34536443	10463118	<i>TYK2, CDC37, PDE4A</i>	2		X
19	rs142213240	10972474	<i>ILF3, CARM1, SLC44A2</i>	2		
19	rs56234966	49922071	<i>DKKL1, SLC6A16</i>	2		
22	rs4821560	37311806	<i>CSF2RB, NCF4</i>	1	X	X