Chinese-European SLE GWAS meta-analysis findings include ten new loci and a genetic basis for increased non-European prevalence

David L Morris[1,19] , Yujun Sheng[2,3,4,19], Yan Zhang[5,19], Yong–Fei Wang[5,], Zhengwei Zhu[2,3] Philip Tombleson[1,], Lingyan Chen[1], Deborah S Cunninghame Graham[1], James Bentham[6], Amy L Roberts[1], Ruoyan Chen[5], Xianbo Zuo[2,3], Tingyou Wang[5], Leilei Wen[2,3], Chao Yang[2,3], Lu Liu[2,3], Lulu Yang[2,3], Feng Li[2,3], Yuanbo Huang[2,3], Xianyong Yin[2,3], Sen Yang[2,3], Lars Rönnblom[7], Barbara G Fürnrohr[8–11], Reinhard E Voll[8,9,12,13], Georg Schett[8,9], Nathalie Costedoat–Chalumeau[14], Patrick M Gaffney[15], Yu Lung Lau[5,16], Xuejun Zhang[2,3,17], Wanling Yang[5,20], Yong Cui[2,3,4,20], Timothy J Vyse[1,19,20]

[19] These authors contributed equally to this work
[20] These authors jointly supervised the work

[1] Division of Genetics and Molecular Medicine, King's College London, UK.
[2] Department of Dermatology, NO. 1 Hospital, Anhui Medical University, Hefei, Anhui, China.
[3] Key Laboratory of Dermatology, Ministry of Education, Anhui Medical University, Hefei, Anhui, China.
[4] Department of Dermatology, China–Japan Friendship Hospital, Beijing, China.
[5] Department of Paediatrics and Adolescent Medicine, LKS Faculty of Medicine, The University of Hong Kong, Pokfulam, Hong Kong.
[6] Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, UK.
[7] Department of Medical Sciences, Science for Life Laboratory, Uppsala University, Uppsala, Sweden
[8] Department of Internal Medicine 3, Ulmenweg 18, University of Erlangen–Nuremberg, 91054 Erlangen, Germany
[9] Institute for Clinical Immunology, Ulmenweg 18, University of Erlangen–Nuremberg, 91054 Erlangen, Germany
[10] Division of Genetic Epidemiology, Innrain 80/IV, Medical University Innsbruck, 6020 Innsbruck, Austria
[11] Division of Biological Chemistry, Innrain 80/IV, Medical University Innsbruck, 6020 Innsbruck, Austria
[12] Department of Rheumatology, University Hospital Freiburg, Freiburg, Germany, Germany
[13] Clinical Immunology & Centre of Chronic Immunodeficiency, University Hospital Freiburg, Freiburg, Germany, Germany
[14] AP–HP, Hôpital Cochin, Centre de référence maladies auto–immunes et systémiques rares, Paris, France; Université Paris Descartes–Sorbonne Paris Cité, Paris, France.
[15] Arthritis and Clinical Immunology Program, Oklahoma Medical Research Foundation, Oklahoma City, OK 73104.
[16] The University of Hong Kong Shenzhen Hospital, ShenZhen, China.
[17] Department of Dermatology, Huashan Hospital of Fudan University, Shanghai, China.
[18] Division of Immunology, Infection and Inflammatory Disease, King's College London, UK.

Correspondence should be addressed to TJV (timothy.vyse@kcl.ac.uk), YC (wuhucuiyong@vip.163.com) and WY (yangwl@hku.hk).

Nature Genetics: doi:10.1038/ng.3603

Supplementary Material

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Supplementary Notes

1. An assessment of the robustness of the GRS

To assess the robustness of the GRS, we re–calculated the GRS in both Europeans and Asian samples using SNPs derived from the European GWAS data. We then re–calculated the GRS in both Europeans and Asian samples using SNPs derived from the Chinese GWAS data. In each case the SNPs were selected based on the following criteria:

1. SNPs passed QC and were located within 250Kbp of the reported SLE–associated SNPs (Supplementary Table 1a);

2. The SNPs have showed the best association *P* value in each known locus and did not have allele ambiguity (i.e., A/T or C/G);

3. The association *P* value was less than 1 x10^{-04}.

In both alternative GRS calculations (trained on the European GWAS and trained on the Chinese GWAS) the GRS for East Asians in the 1KG population were significantly greater than those in Europeans (Supplementary Fig. 8b, *t*–test *P*–value < 2.2 x 10^{-16} in both cases), supporting an increased SLE risk scores in Chinese compared with those of the Europeans. To address a potential bias caused by the genotyping Chip, we ran a simulation study by randomly selecting SNPs (equal in number to the number of SNPs used to generate Fig 4), and used the effect sizes estimated by the trans–ethnic meta–analysis to calculate the GRSs for each individual from both populations. We performed 1,000 simulations and plotted the median GRS from each simulation. The distribution of GRS medians in Europeans was slightly higher than those in EAS population, but the difference was not significant (Supplementary Fig. 8c, paired *t*–test *P*–value=0.65; *t*–test *P*–value=0.85), further suggesting that the difference in GRS between these two populations are unlikely to be caused by bias in the choice of SNPs. Also the ratio of the GRS between the two populations, EAS_median: EUR_median based on the reported SLE susceptibility markers and their

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effect sizes estimated from transancestral meta–analysis, was significantly greater than that from simulations (95% C.I. 0.913–1.097; *P*–value=0.001), further supporting real difference between Europeans and East Asians.

We also calculated the GRS in the five populations using the reported SNPs (Supplementary Table 1a) and using the same effect sizes across. We observed the same trend with the GRS increasing from west to east (Supplementary Fig. 8d), suggesting that the risk was mainly driven by increased risk allele frequency instead of effect size.

2. Prevalence of SLE

The estimates of SLE prevalence arise from many studies over a number of geographical locations and as these are not balanced with respect to the ethnicity we do not believe that absolute values of prevalence are currently available. However we can estimate relative prevalence by looking at studies that include multiple ethnicities within the same geographical location. From the studies displayed in table 2 in the paper cited here[1] we can see that within the USA the rank order of prevalence is: EUR (1) < AMR (2) < African–American (3), while in Canada the order is: EUR (1) < SAS (2) and in the UK the order is EUR (1) < SAS (2) < EAS (3) < Afro–Caribbean (4). We can assume therefore that over all locations that the African population has the highest prevalence and the European the lowest. The UK study demonstrated a higher prevalence in the EAS population than SAS. We have no study to directly compare AMR with Asians, however using the prevalence relative to the EUR population in the USA (18/7.4 = 2.43) we could estimate a prevalence of 20.5 * 2.43 = 49.86 for AMR in the UK, which is very similar to SAS. We therefore rank the ethnicities on prevalence as EUR (1) < AMR (2)/SAS (2) < EAS (3) < AFR (4). A linear model with rank of prevalence and the independent variable was used to test for correlation between predicted GRS and SLE prevalence.

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3. The limitations of using imputed data.

Our study suffers from a common limitation in fine mapping studies in that the results rely on imputed data. We set a high level for imputation quality to reduce the probability of false positives in the design for the replication study. The post imputation QC may remove potential causal variants due to poor quality in one population. In this case we are left with proxy SNPs that may not share the same risk allele across populations and we may therefore miss an association in the meta–analysis. This problem highlights the need for more population specific reference panels for imputation.

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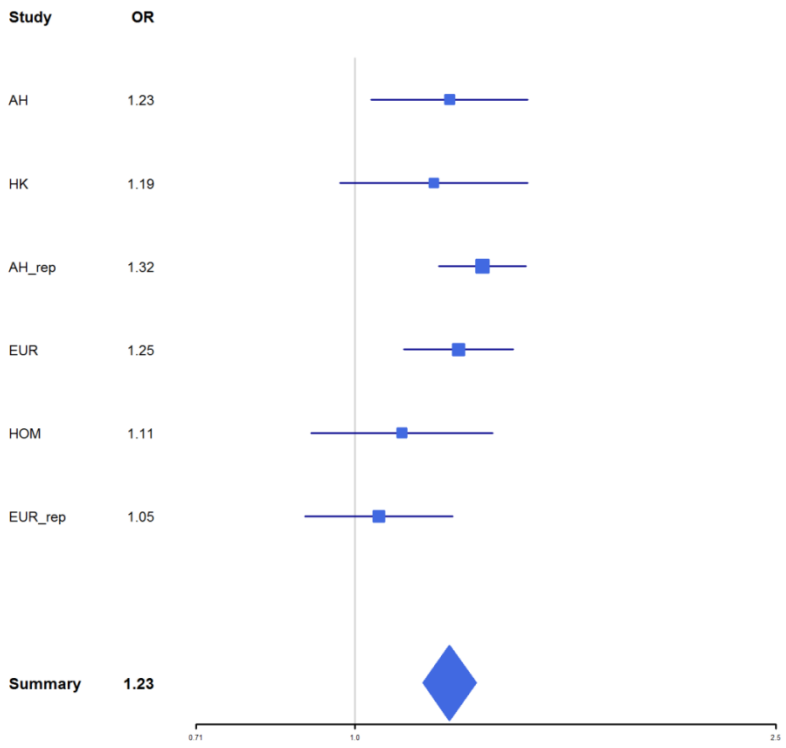
Supplementary Figures 1 a-l. Forest plots for all 11 associated SNPs reported in the paper. Each study is abbreviated as follows: AH Anhui GWAS; HK Hong Kong GWAS; AH_rep The Anhui Replication study; EUR The main European GWAS; HOM the additional European GWAS used for replication; EUR_rep The European replication study.

Supplementary Figure 1 a: rs34889541 (1q31.3)



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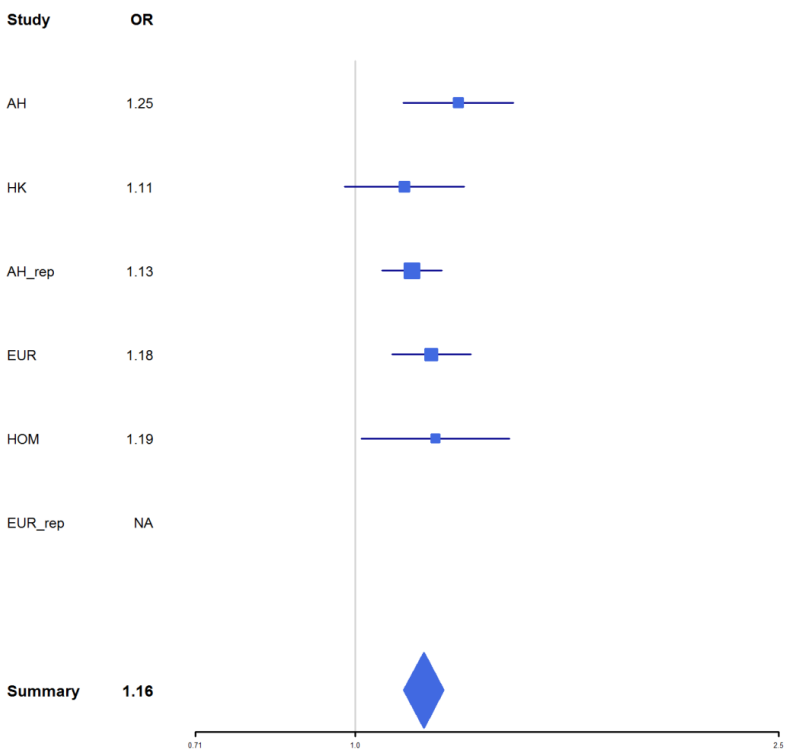
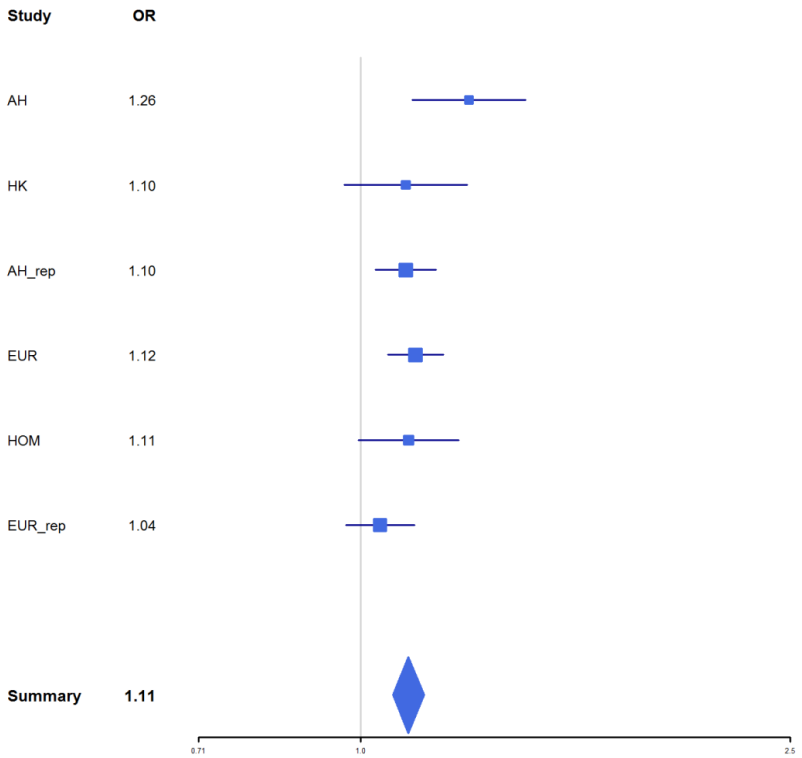
Supplementary Figure 1 b: rs2297550 (1q32.1)



Supplementary Figure 1 c: rs7579944 (2p23.1)



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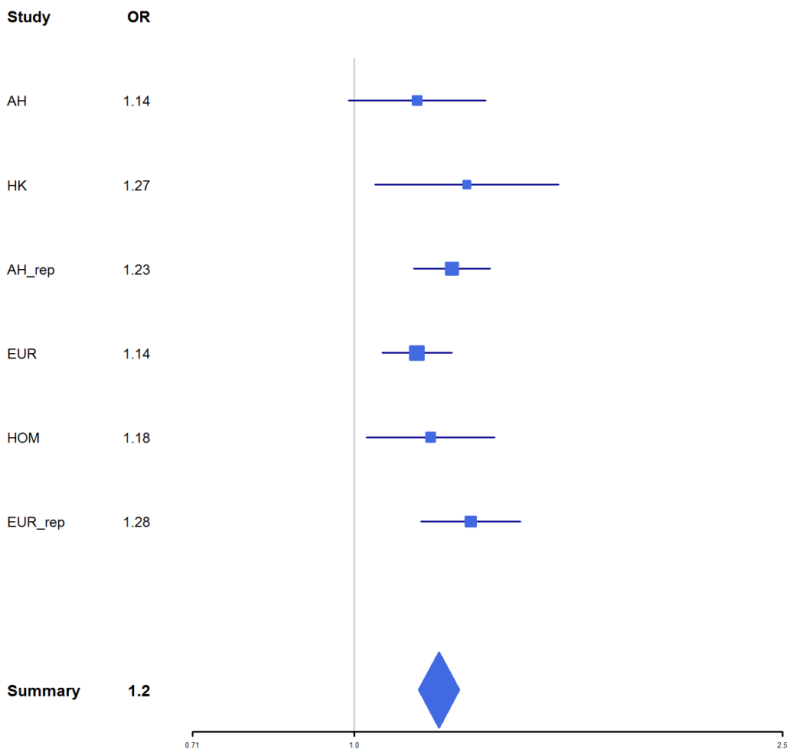
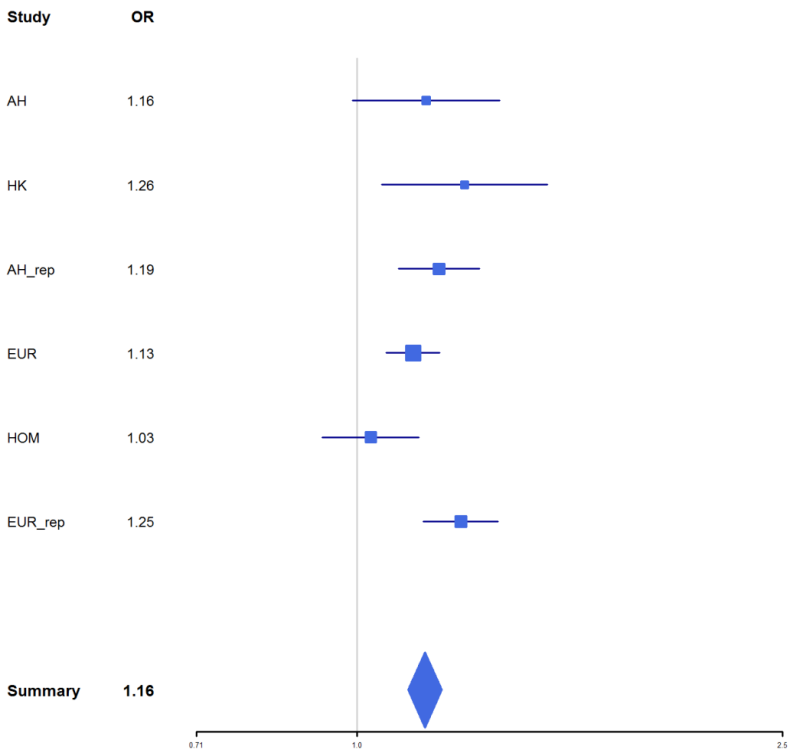
Supplementary Figure 1 d: rs17321999 (2p23.1)



Supplementary Figure 1 e: rs6762714 (3q28)



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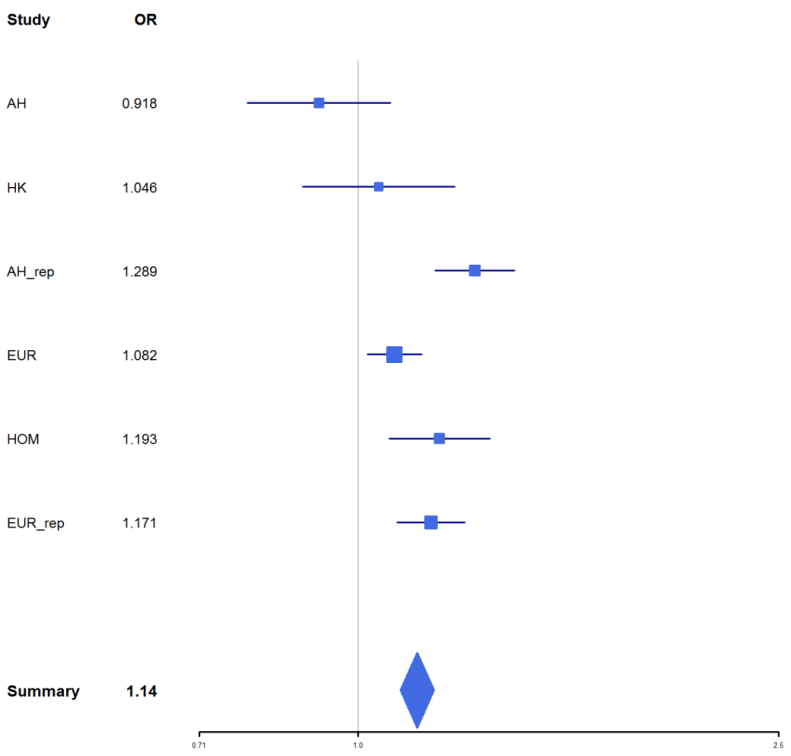
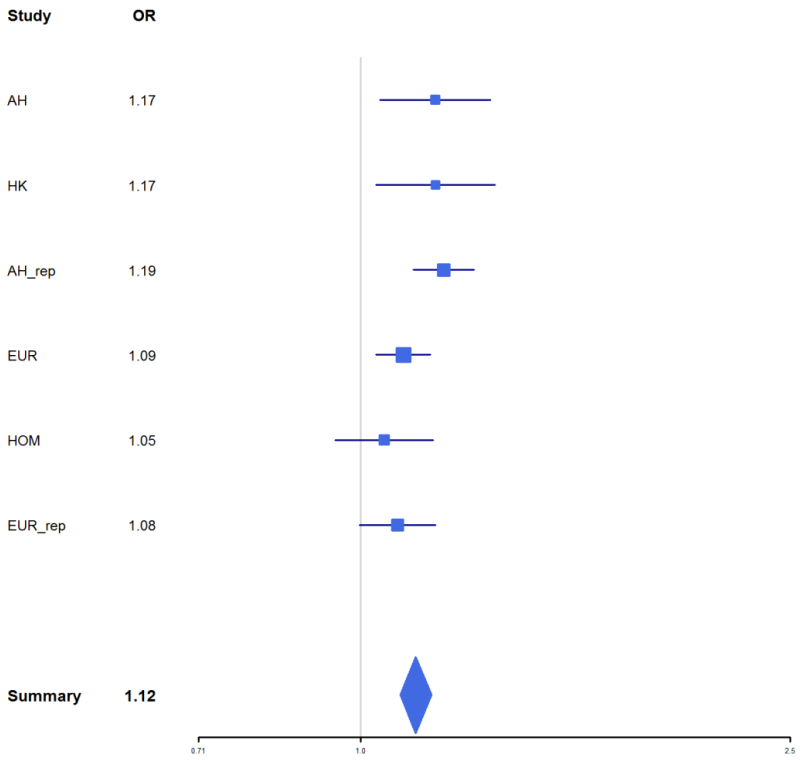
Supplementary Figure 1 f: rs17603856 (6p23)



Supplementary Figure 1 g: rs597325 (6q15)



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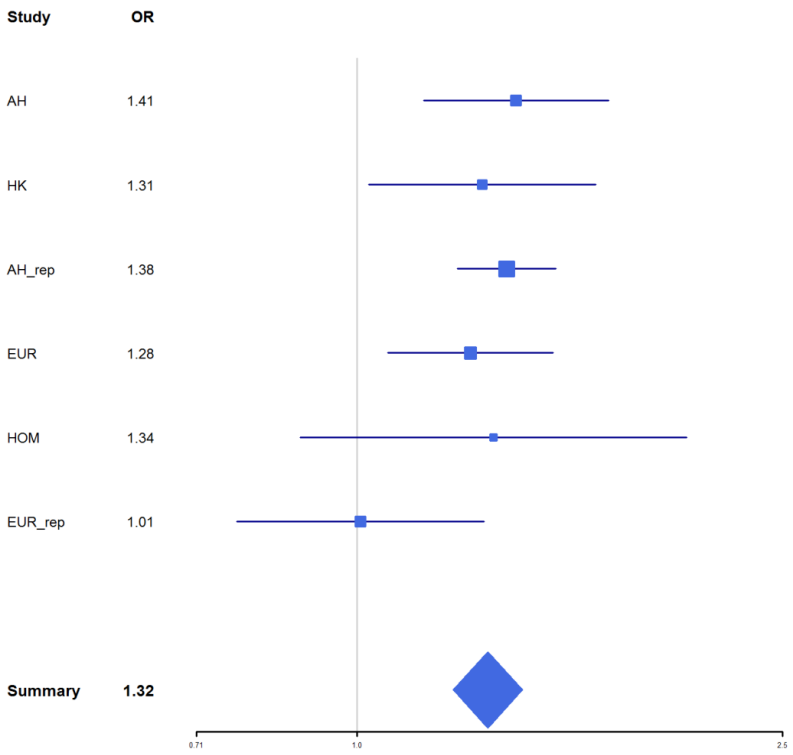
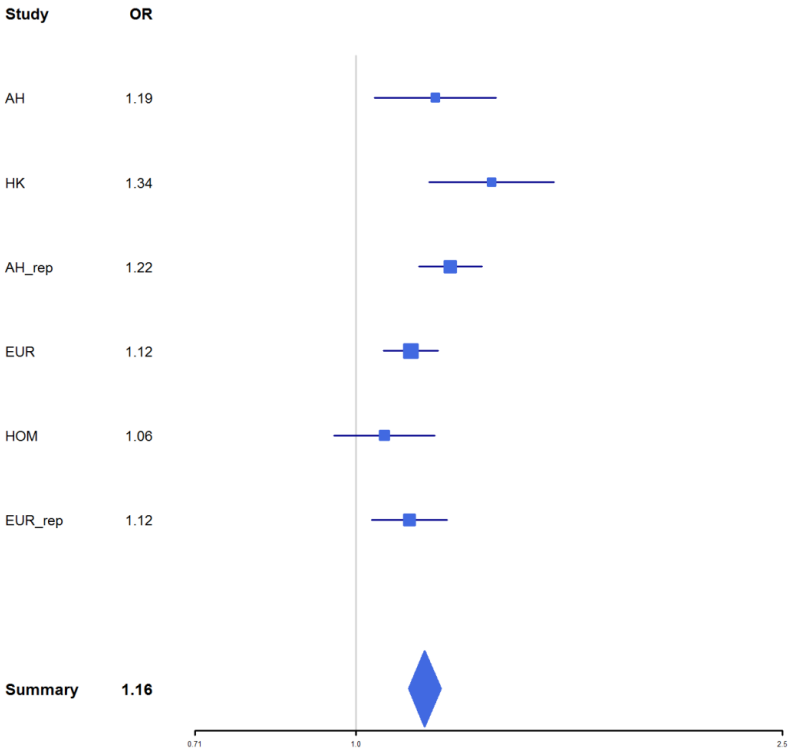
Supplementary Figure 1 h: rs73135369 (7q11.23)



Supplementary Figure 1 i: rs1887428 (9p24)



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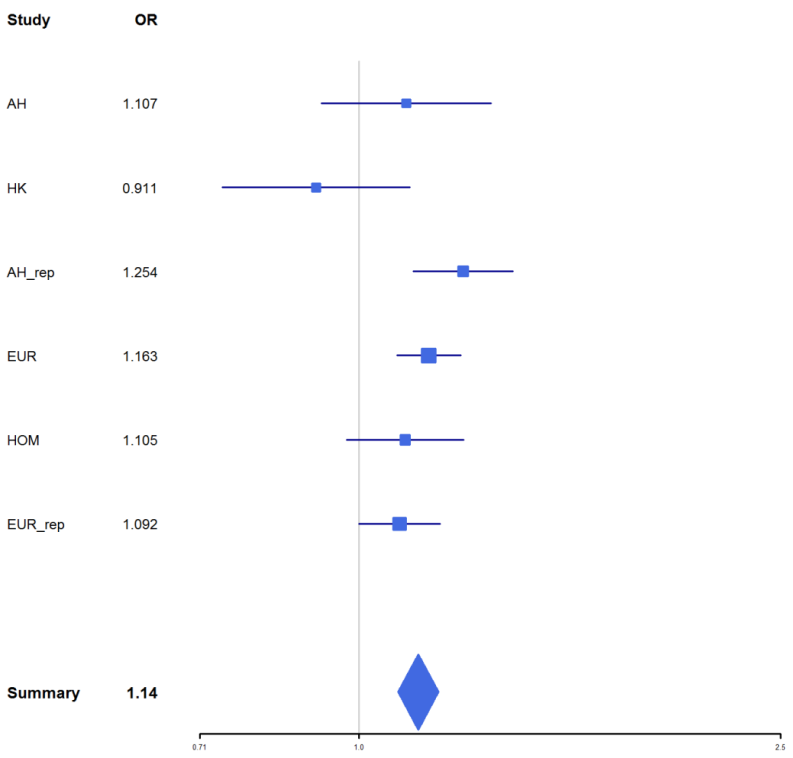
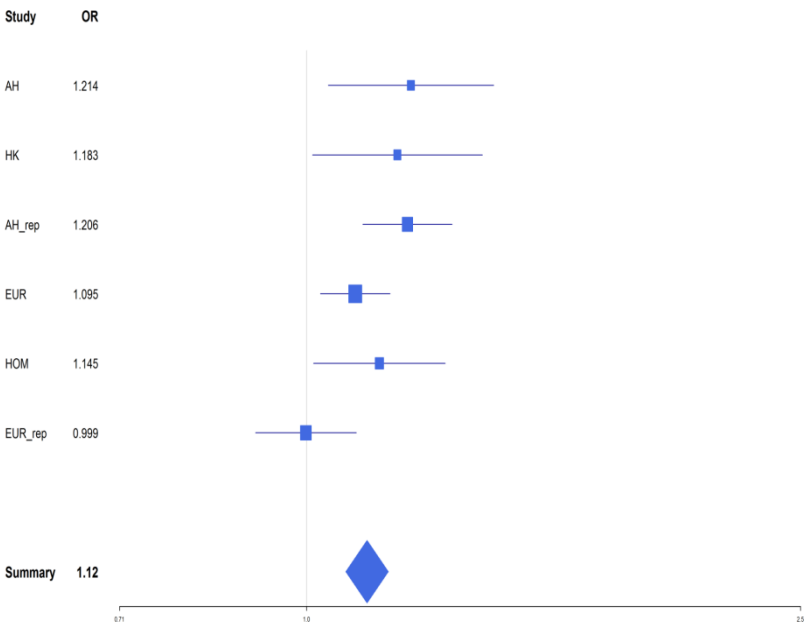
Supplementary Figure 1 j: rs494003 (11q13.1)



Supplementary Figure 1 k: rs1170426 (16q22.1)



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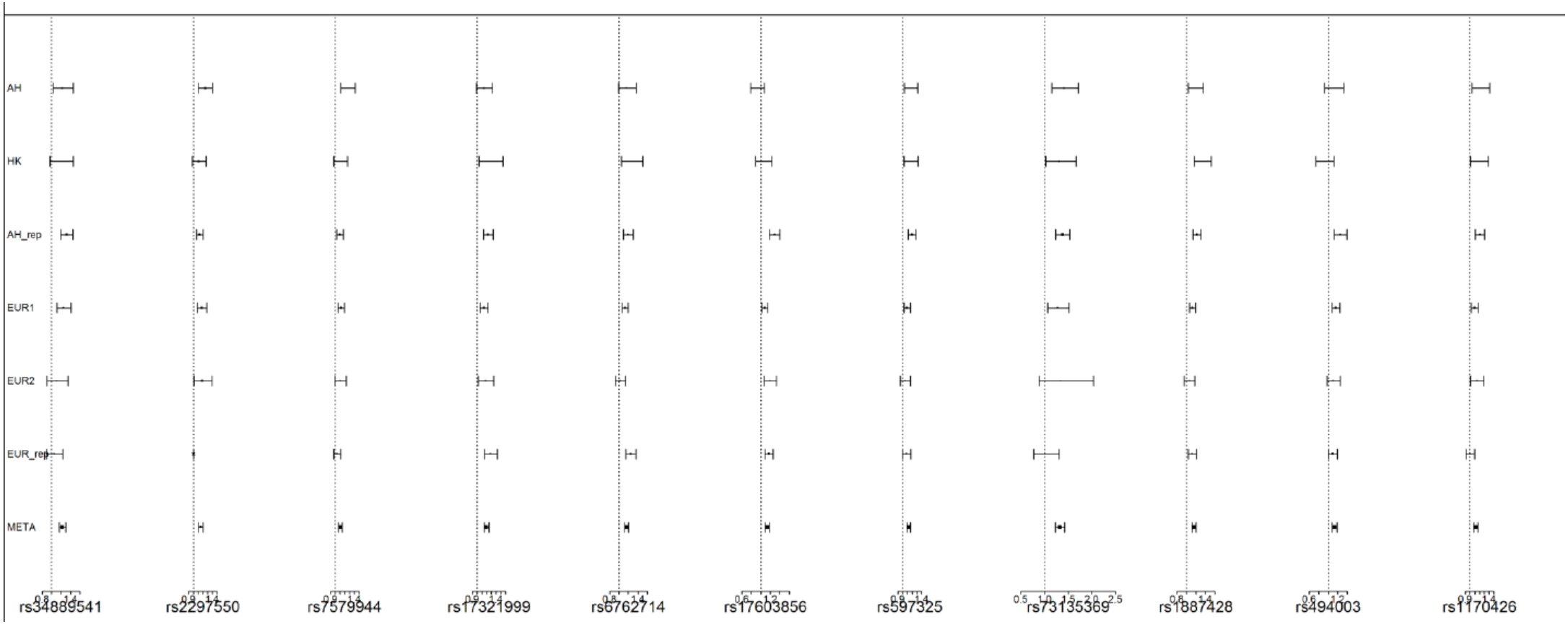
Supplementary Figure 1 l: all SNPs



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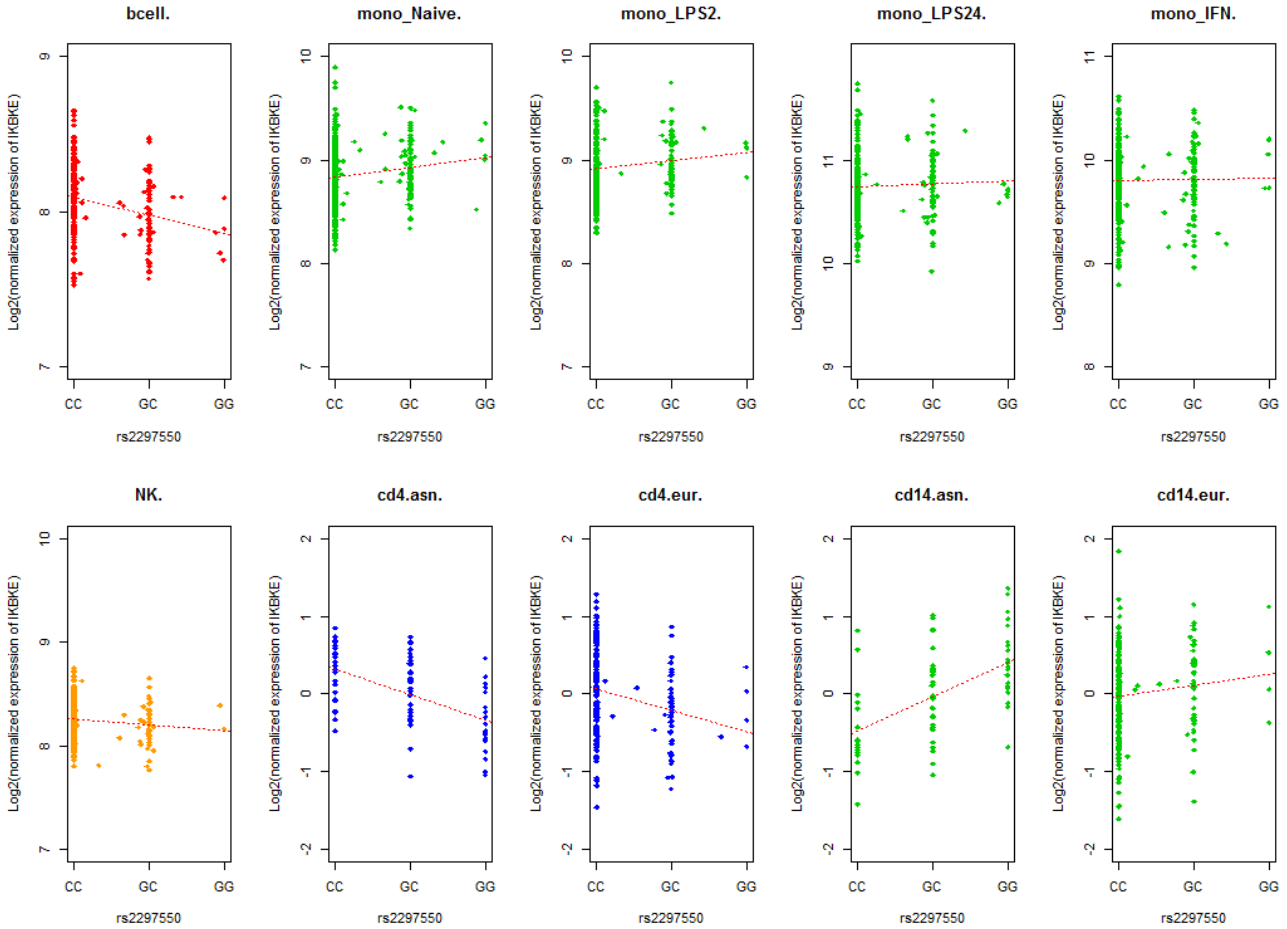
Supplementary Figure 2 a-g: Plots of the gene expression data for SNPs and genes reported in Supplementary Table 3. Expression levels for each individual are plotted on the y–axis against genotype on the x–axis.

Supplementary Figure 2 a: rs2297550 (1q32.1). *IKBKE*



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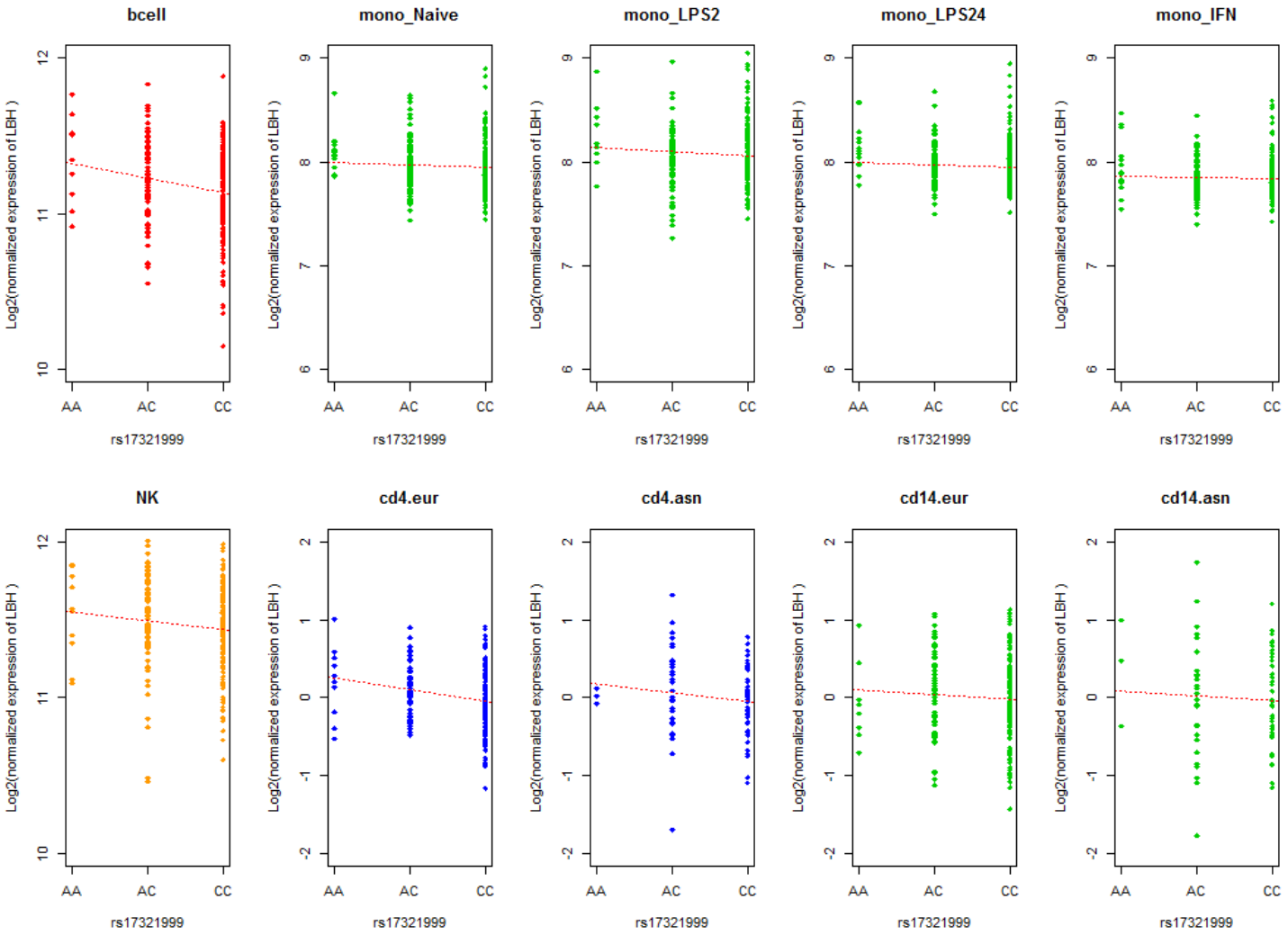
Supplementary Figure 2 b: rs17321999 (2p23.1). *LBH*



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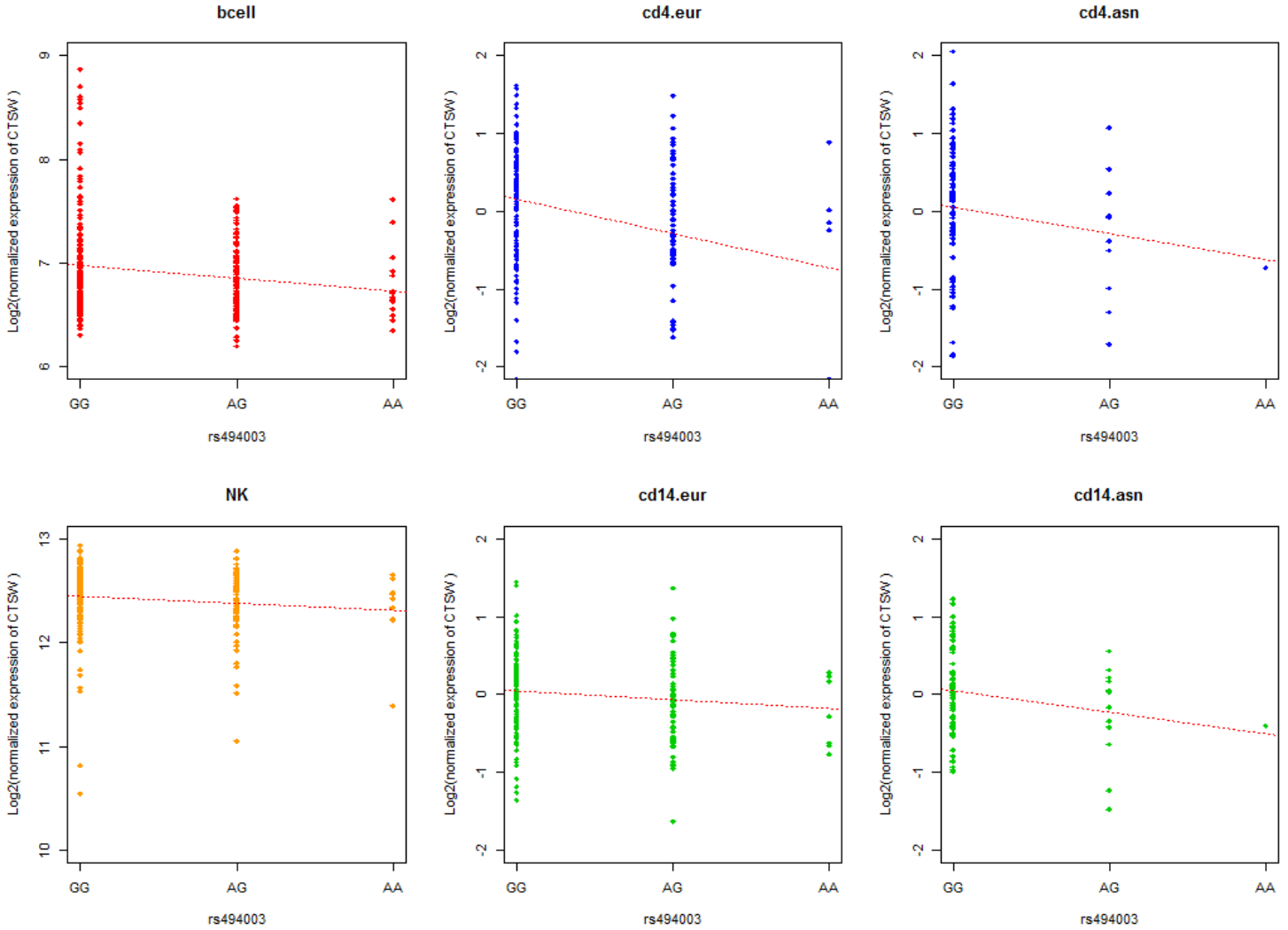
Supplementary Figure 2 c: rs494003 (11q13.1). *CTSW*



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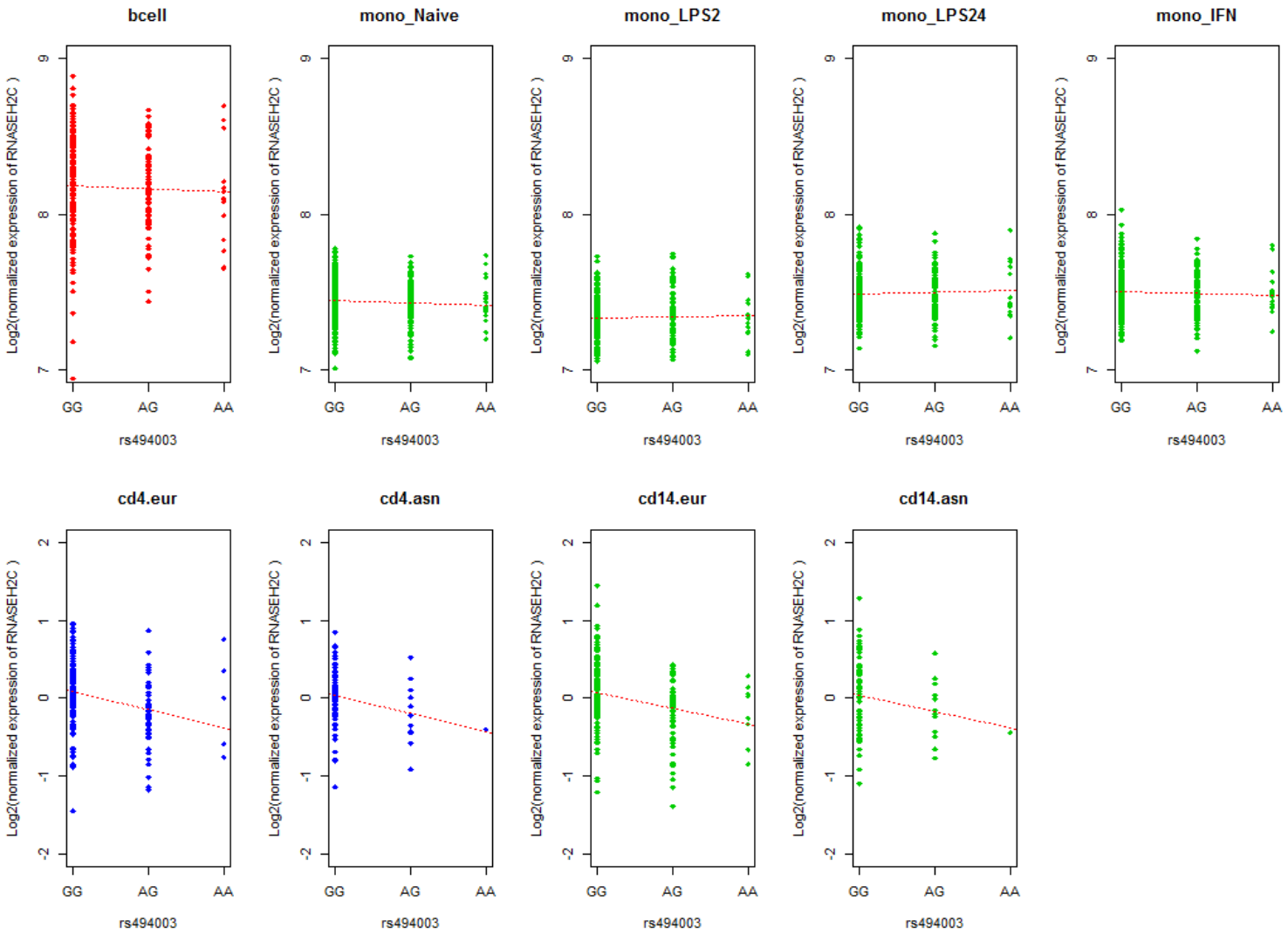
Supplementary Figure 2 d: rs494003 (11q13.1). *RNASEH2C*



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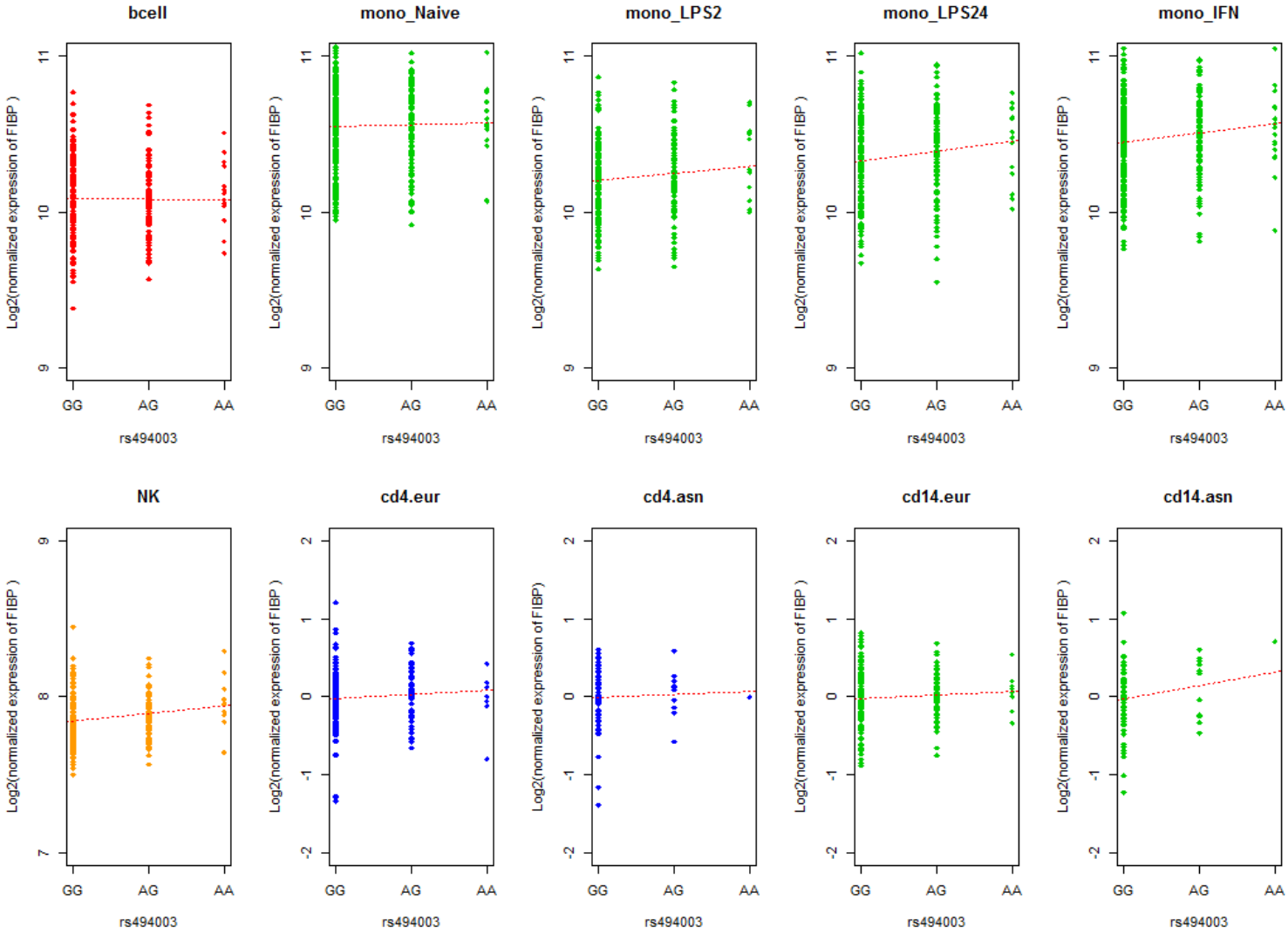
Supplementary Figure 2 e: rs494003 (11q13.1). *FIBP*



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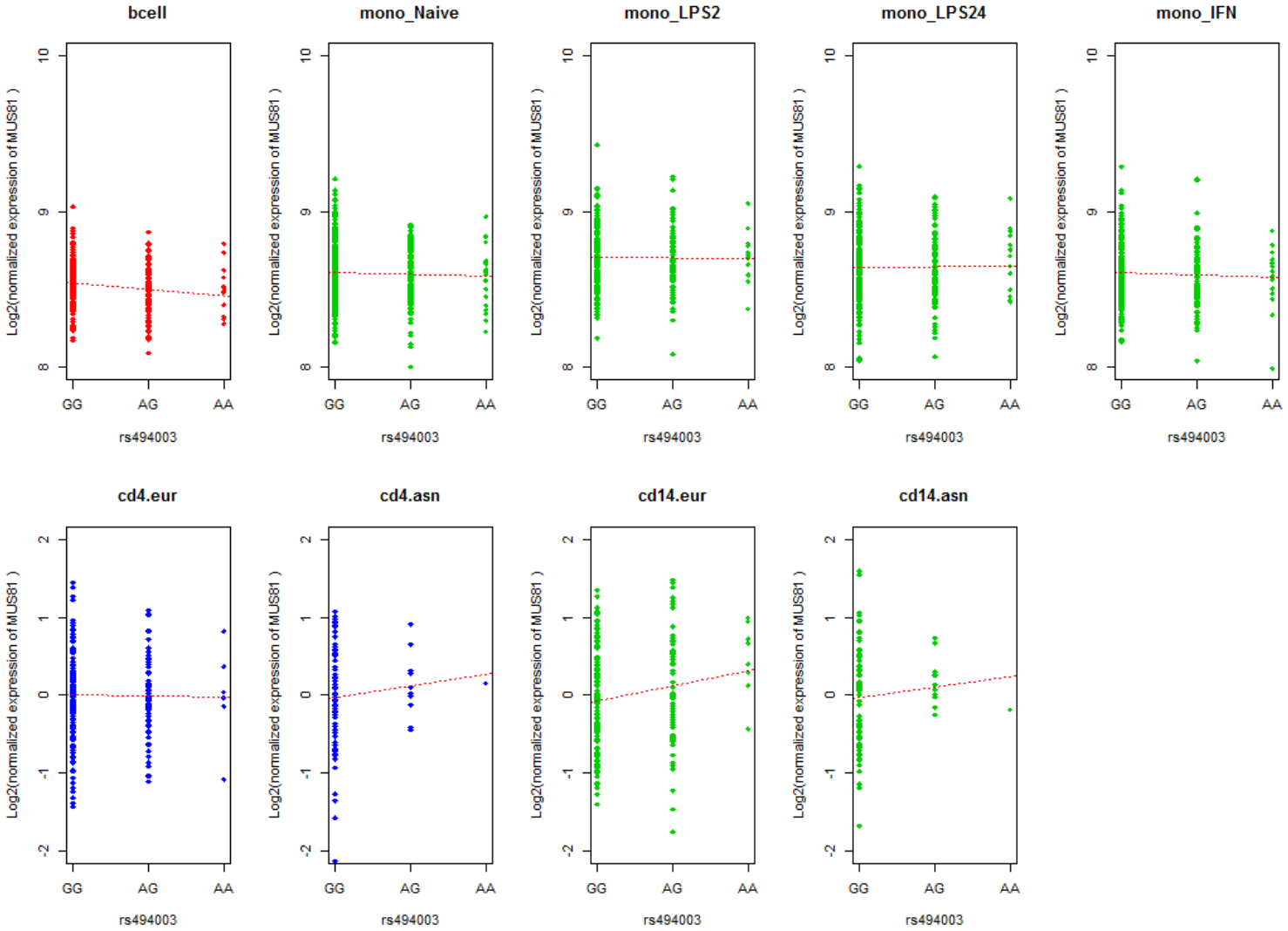
Supplementary Figure 2 f: rs494003 (11q13.1). *MUS81*



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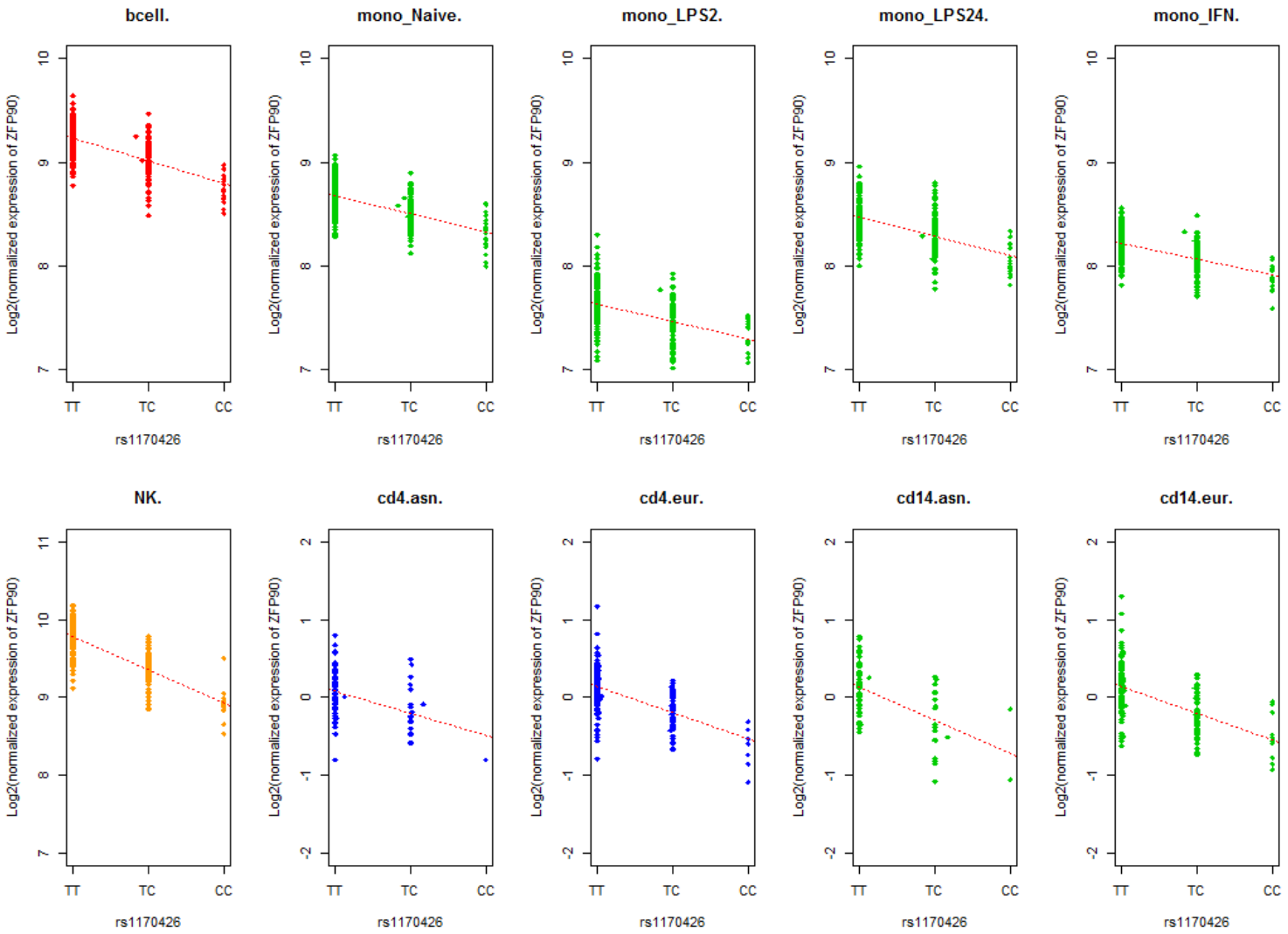
Supplementary Figure 2 g: rs1170426 (16q22.1). *ZFP90*



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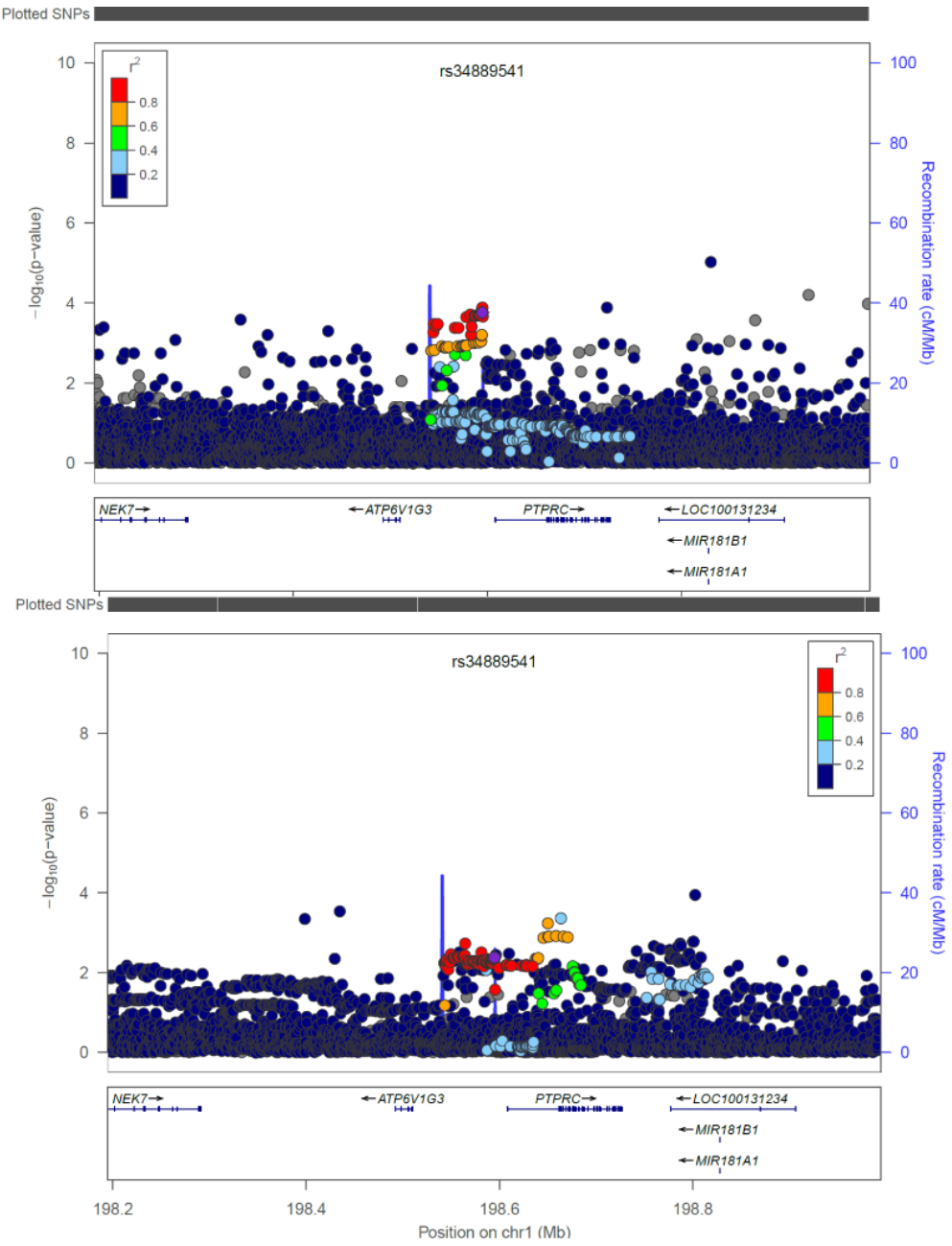
Supplementary Figure 3 LocusZoom[2] plots for each of the 10 loci reported as associated. Each page has two plots: association p–values for the European GWAS with the LD (R^2) taken from the European reference population used in LocusZoom; association p–values for the two Chinese GWAS combined (meta–analysis) with the LD (R^2) taken from the Asian reference population used in LocusZoom.

Supplementary Figure 3 a: rs34889541 (1q31.3)

European

Chinese



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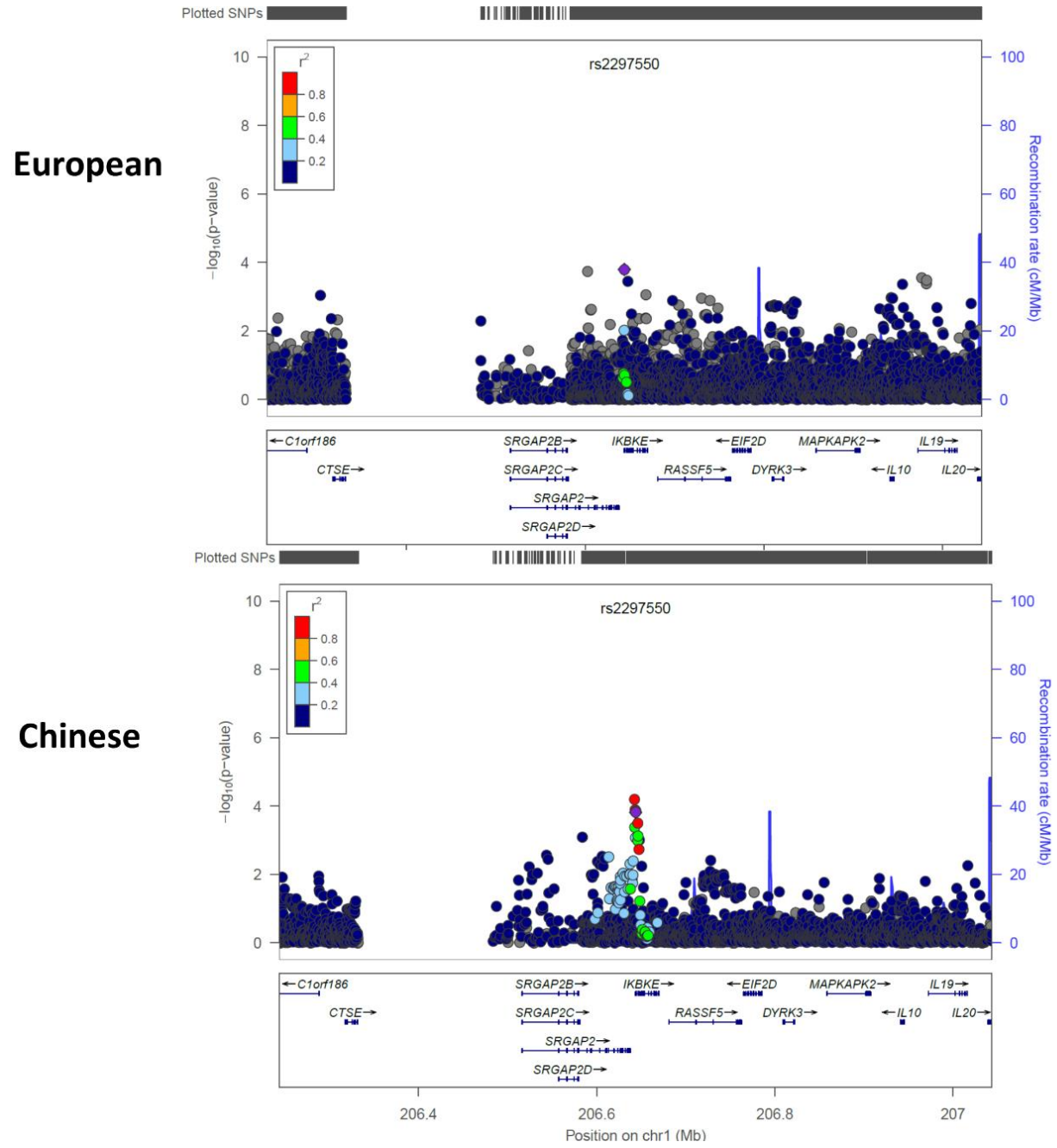
Supplementary Figure 3 b: rs2297550 (1q32.1)



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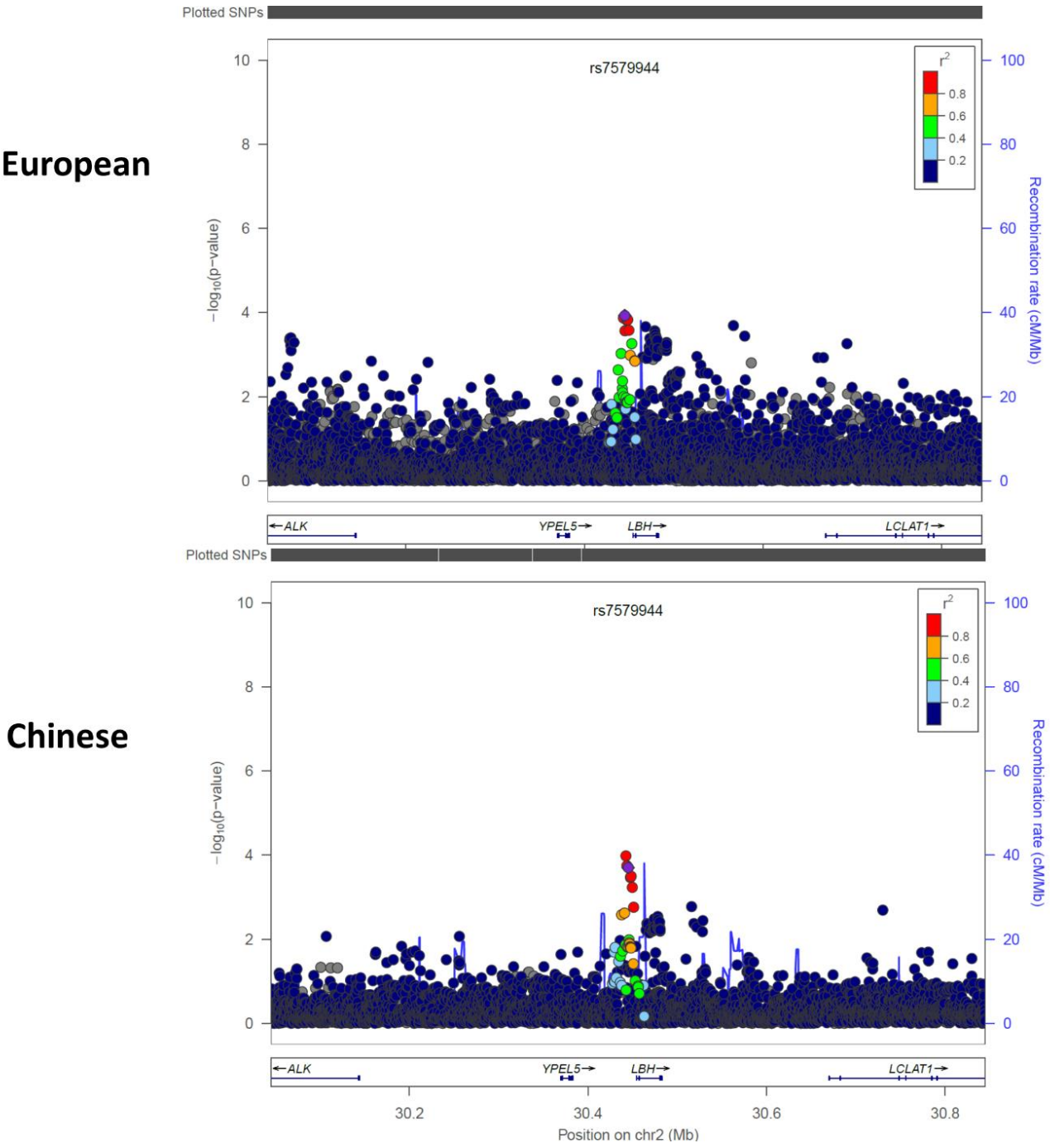
Supplementary Figure 3 c: rs7579944 (2p23.1)



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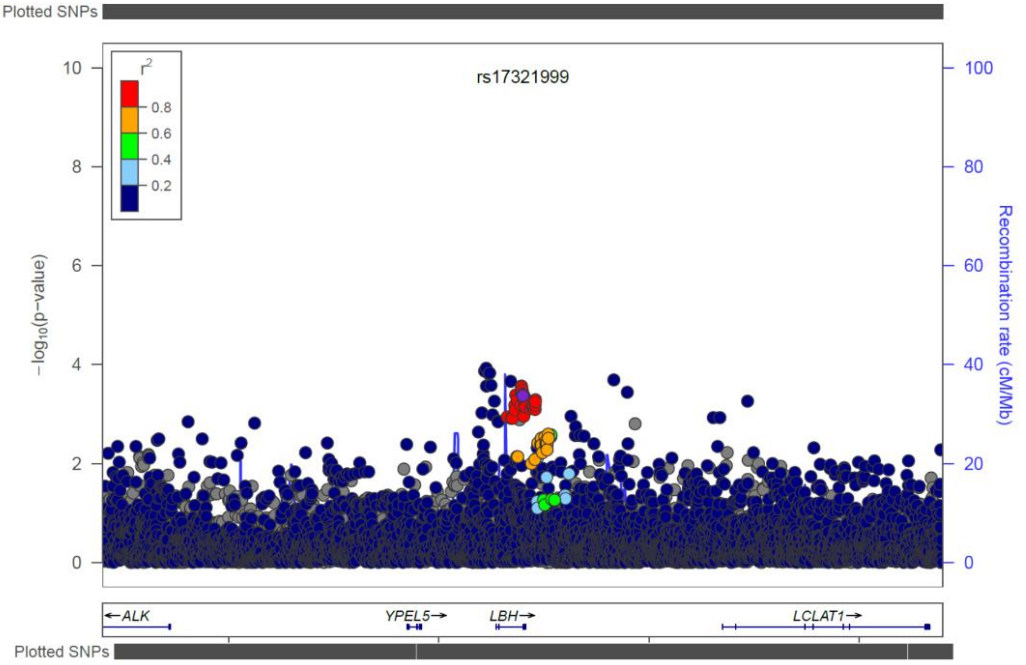
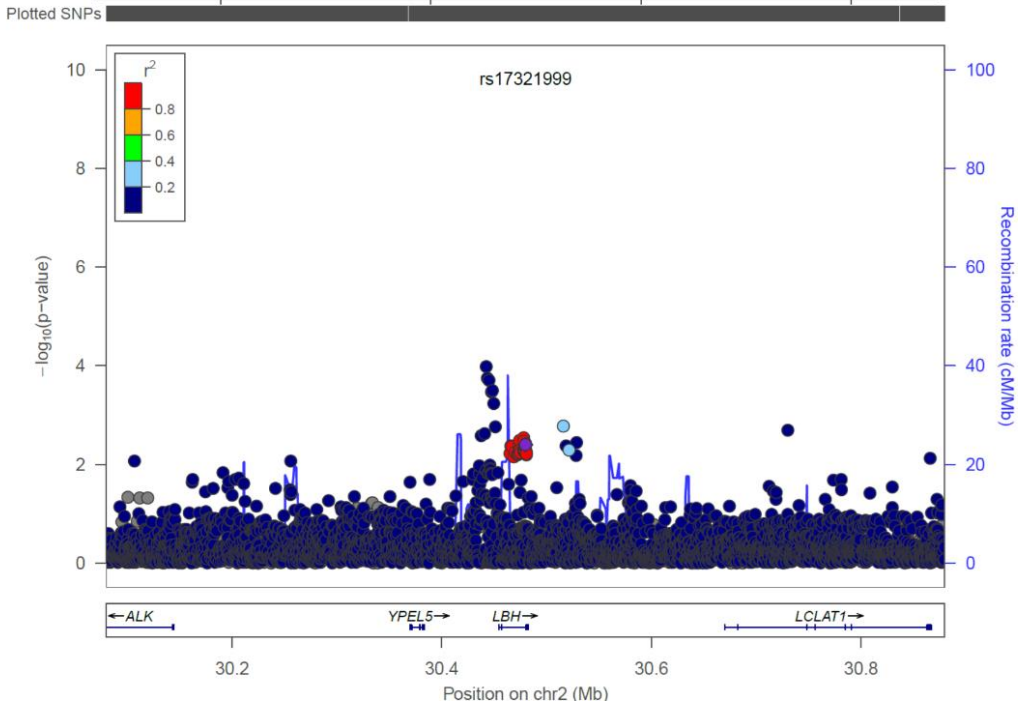
Supplementary Figure 3 d: rs17321999 (2p23.1)

European



Chinese



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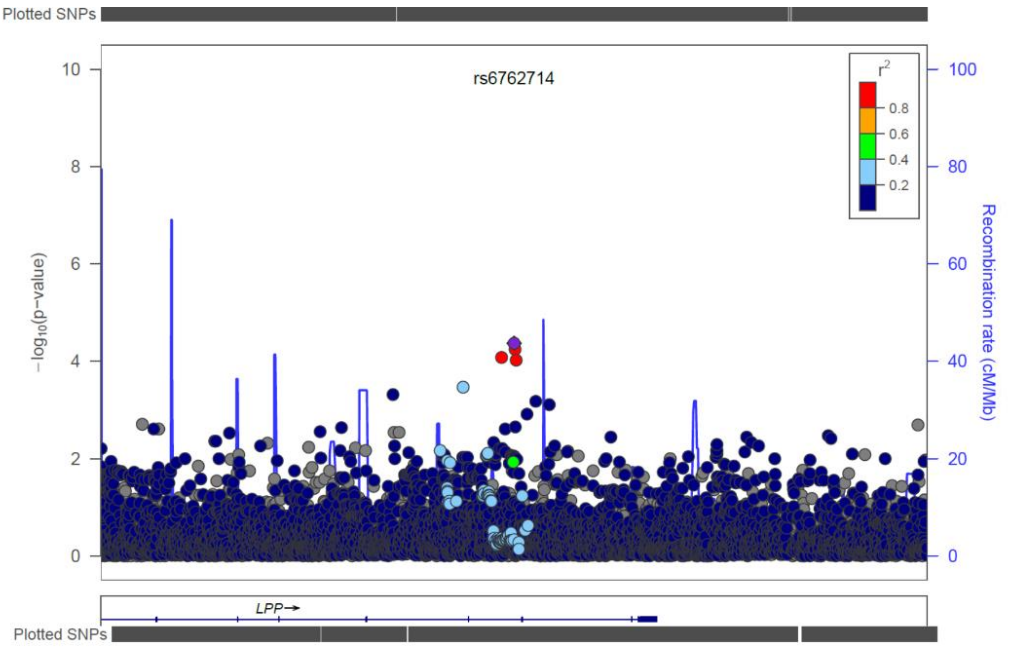
Supplementary Figure 3 e: rs6762714 (3q28)

European



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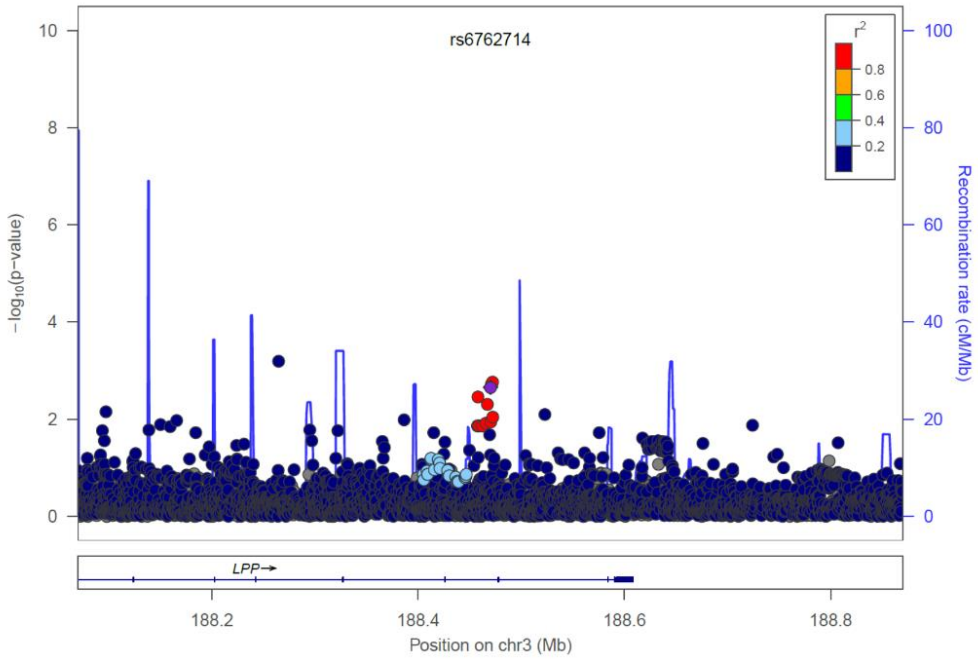

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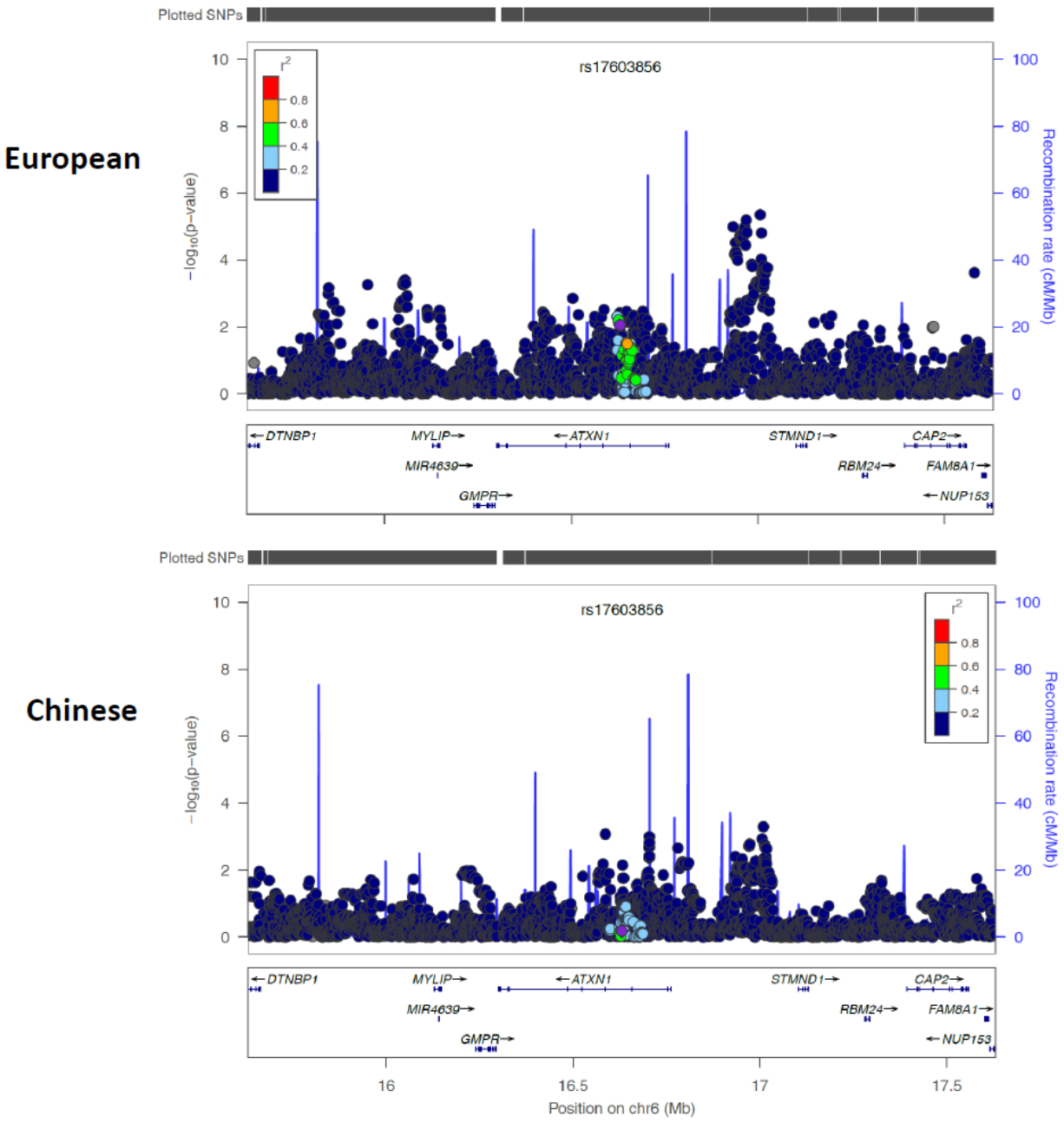
Supplementary Figure 3 f: rs17603856 (6p23)



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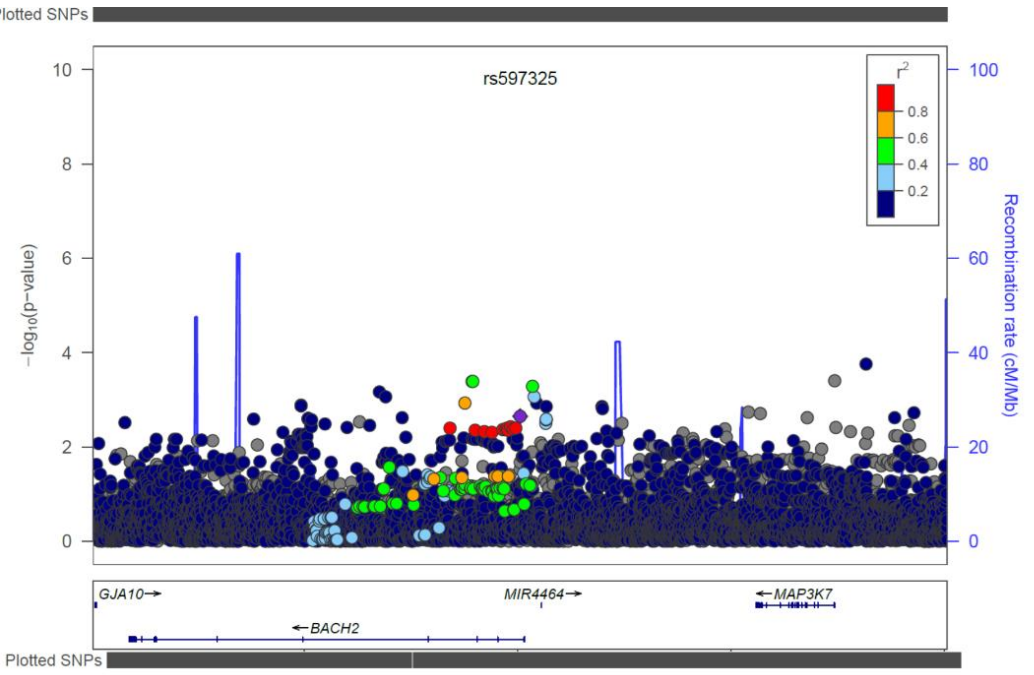
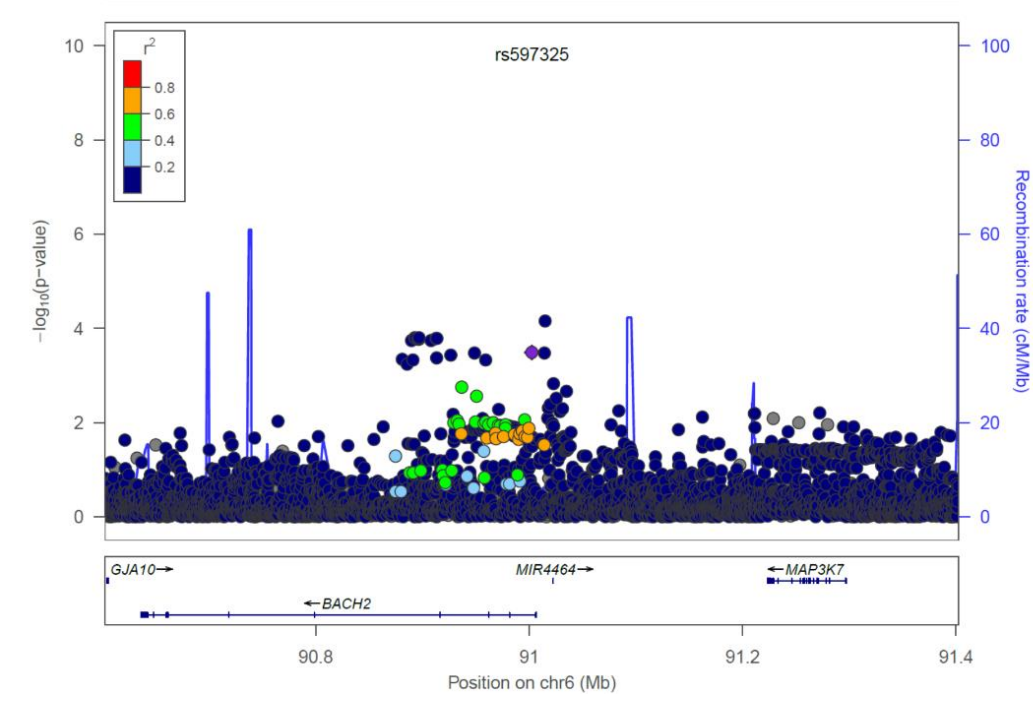
Supplementary Figure 3 g: rs597325 (6q15)

European



Chinese



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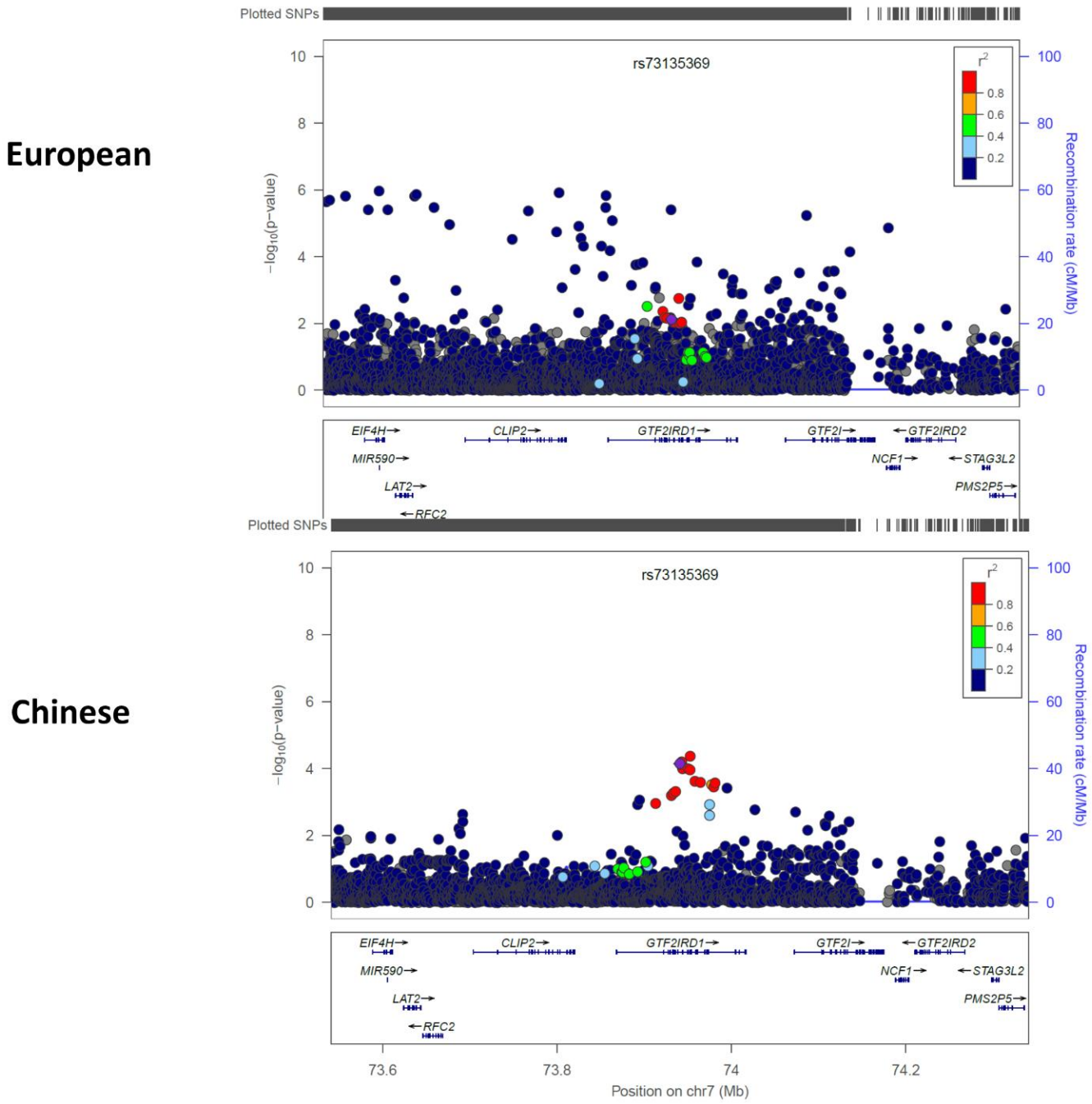
Supplementary Figure 3 h: rs73135369 (7q11.23)



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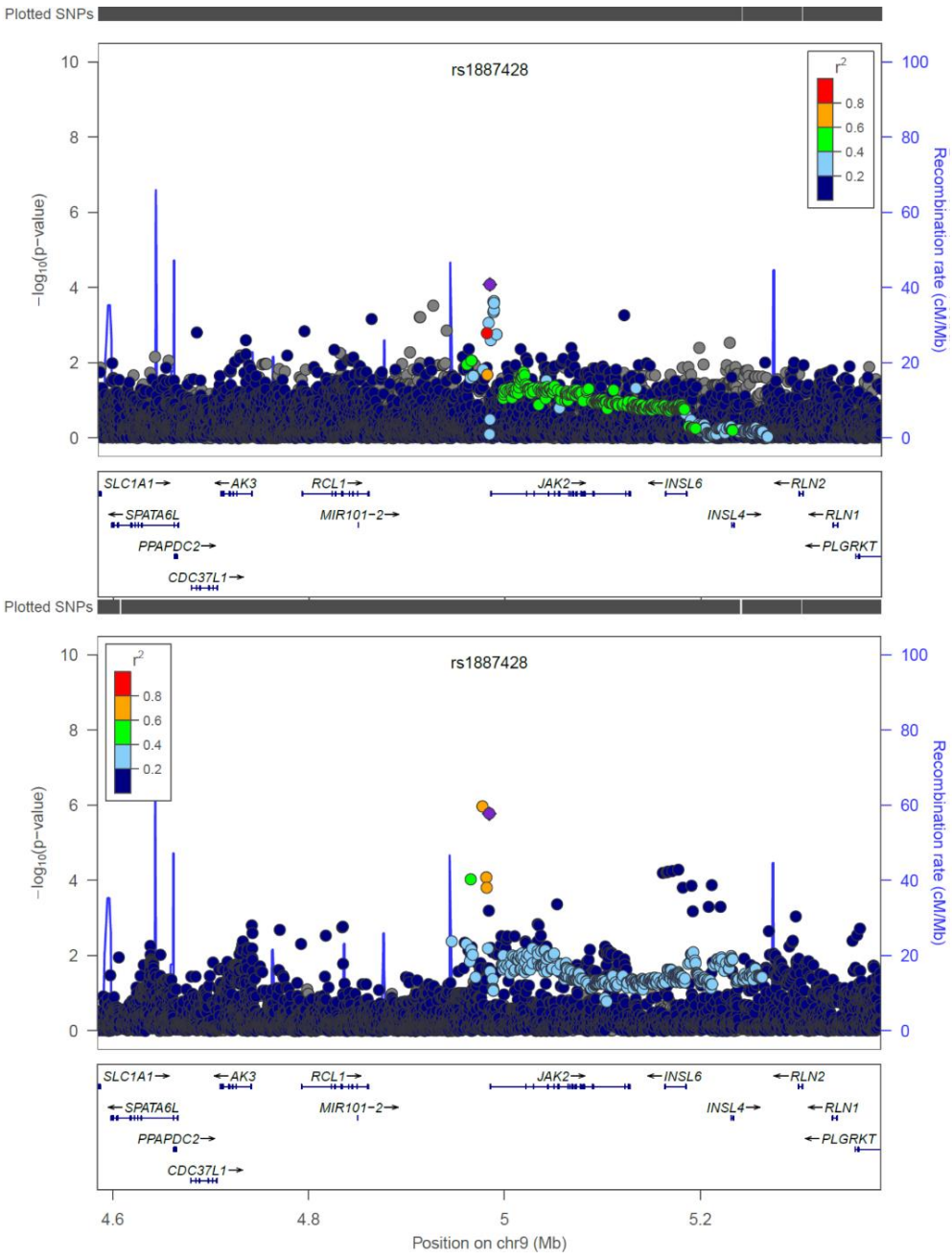
Supplementary Figure 3 i: rs1887428 (9p24)



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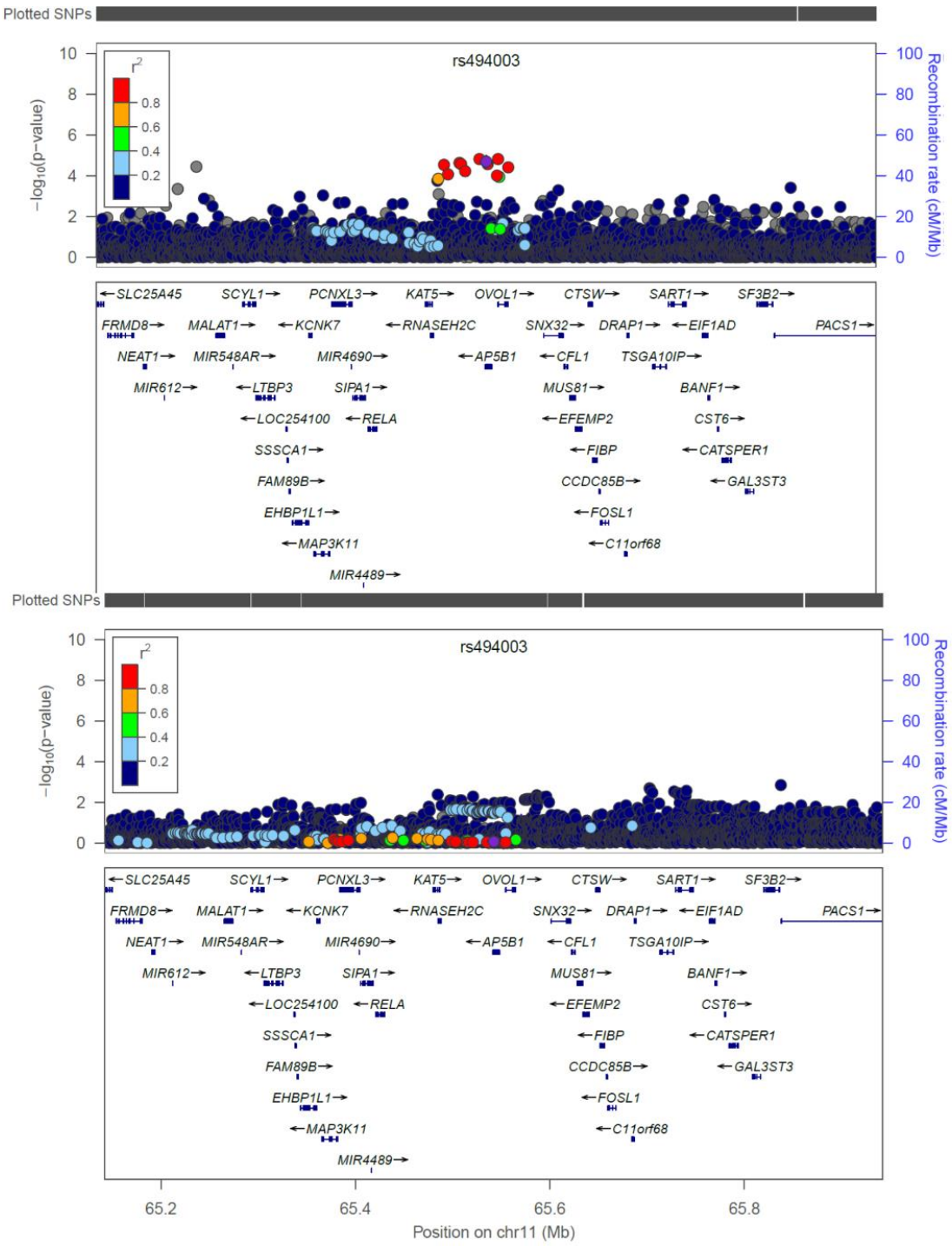
Supplementary Figure 3 j: rs494003 (11q13.1)

European

Chinese



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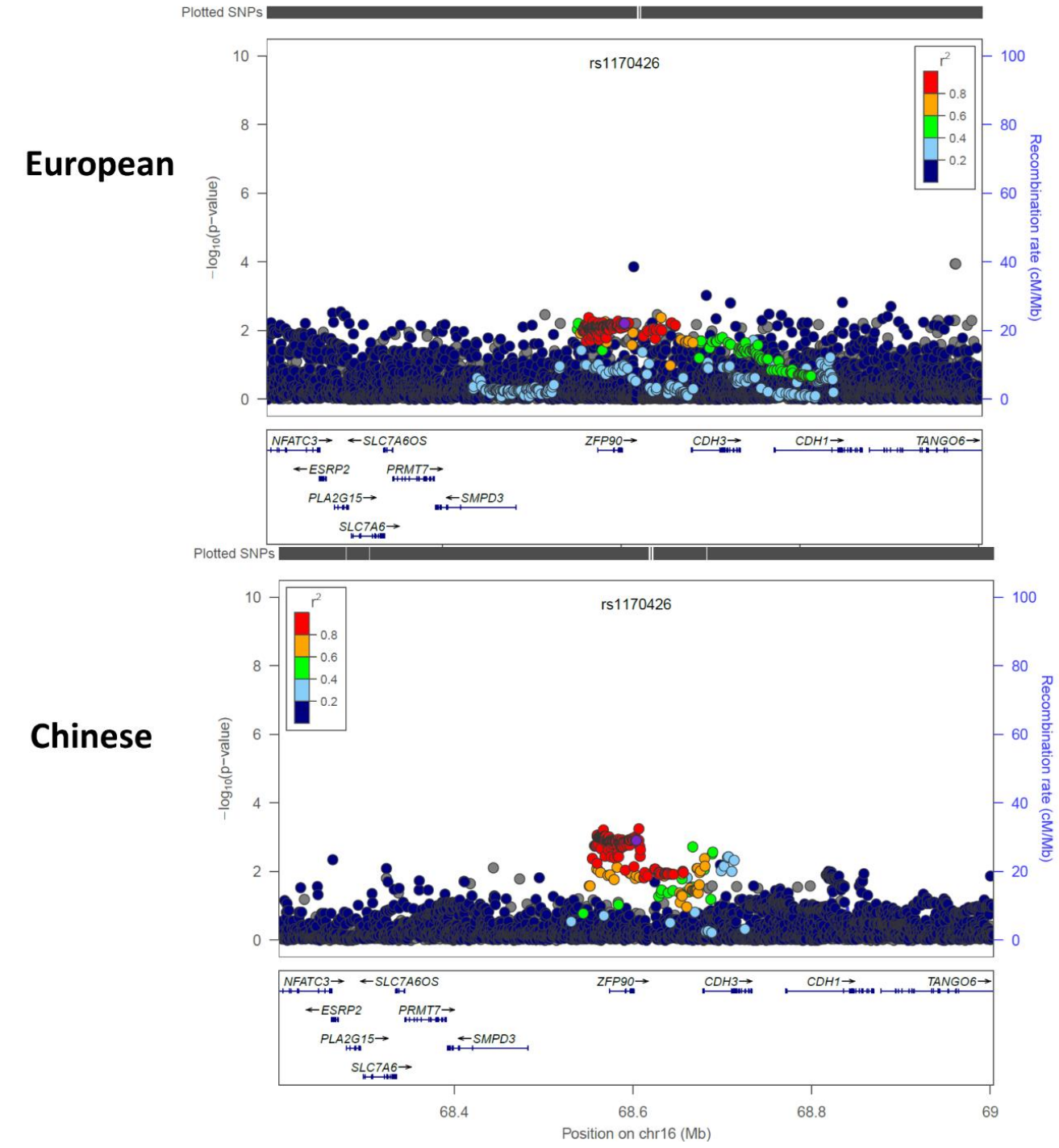
Supplementary Figure 3 k: rs1170426 (16q22.1)



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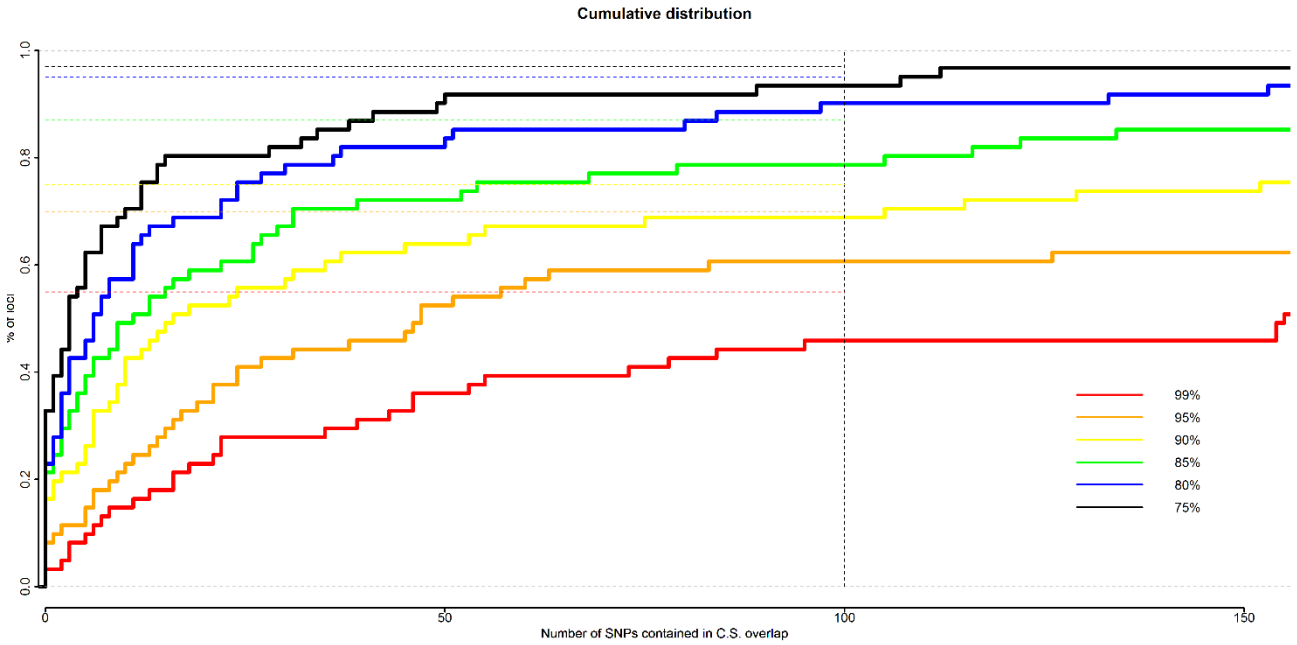
Supplementary Figure 4: Cumulative distribution for the number of SNPs in the intersection of the Bayesian Credibility Intervals



Supplementary Figure 4. Fine mapping results. (a) Cumulative distribution of the number of loci in relation to how many SNPs are included in the intersection of the credibility sets (C.S.) of the European and Chinese GWAS. The dotted lines are colour–coded to match the certainty of particular credibility sets. Each line shows the proportion of loci that generate a set of 100 or less SNPs within the set. For example, 45% of loci are mapped to less than 100 SNPs in a 99% credibility set (red), while 97% of loci are mapped to less than 100 SNPs in a 75% credibility set (black).

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Supplementary Figure 5: Fine-mapping for the novel loci.

Please see additional supplementary material.

Each figure has (1) Locuszoom* plots, (2) Venn diagrams for credibility sets (C.S.) and (3)stacked bar charts displaying the allele frequencies of SNPs in each credibility set and the intersection.

(1) The following three Locuszoom* plots are to the right of each figure:
Top plot: Association p-values for the Chinese GWASs (meta-analysis: Anhui + Hong Kong).
Middle plot: Association p-values for the European GWAS.
Bottom plot: Association p-values for the meta-analysis (European + Anhui + Hong Kong).
NOTE: **The locuszoom plots have circles for SNPs contained in each C.S. (Chinese, European and meta plots) and squares for SNPs not contained in the C.S.**

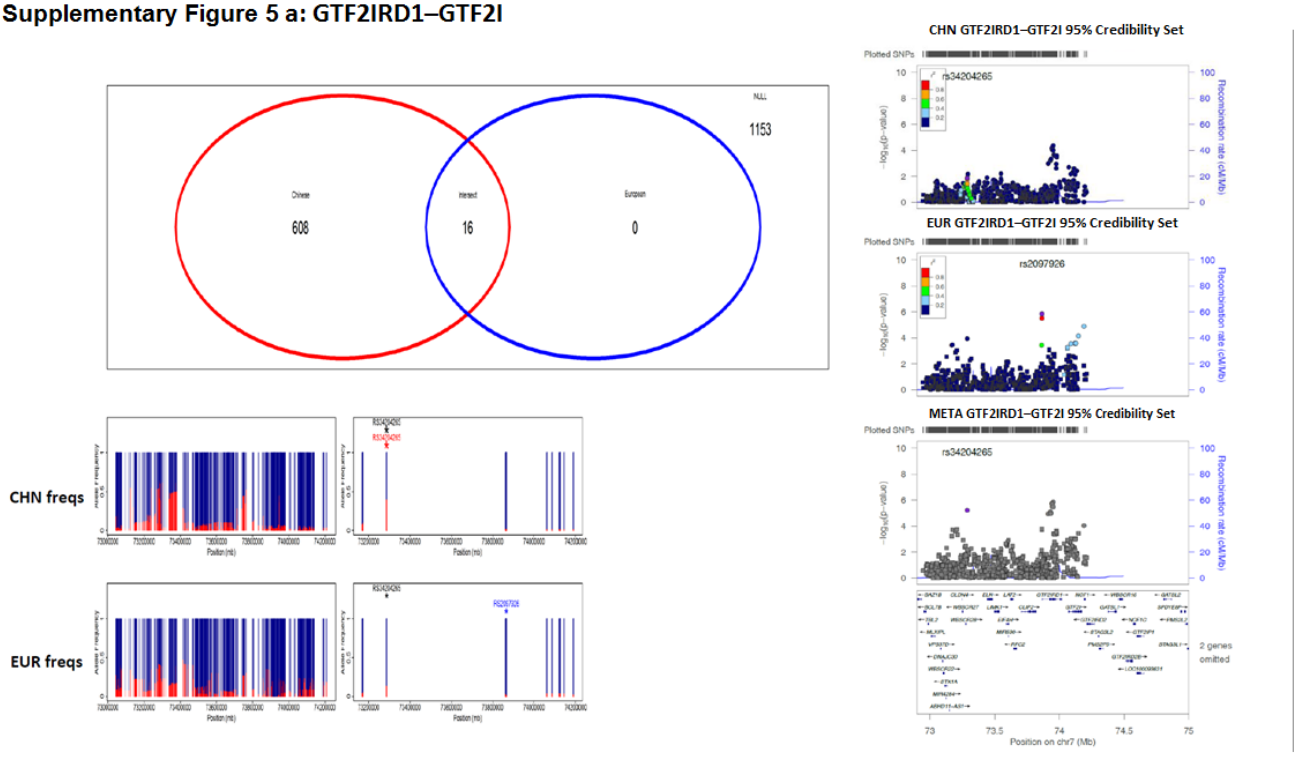
(2) The Venn diagrams display the number of SNPs in the credibility set calculated form the Chinese data, the credibility set calculated from the European data and the intersect of the two.

(3) The stacked bar charts display the allele frequency in Chinese (top) and European (bottom) for the SNPs in the Chinese C.S. the European C.S. and the intersect. The most associated SNP in the intersect of the credibility sets is also displayed. (**RED** for Chinese, **BLUE** for European and **BLACK** for meta-analysis)

The C.S.'s vary on their coverage (% level) so that the intersect contains at most 30 SNPs. We have separated the loci into groups where the level is at 95%, 90%, and 75%. Five loci had more than 30 SNPs in the intersect at any of the levels of coverage.

* http://locuszoom.sph.umich.edu/locuszoom/

Supplementary Figure 5 a: GTF2IRD1–GTF2I



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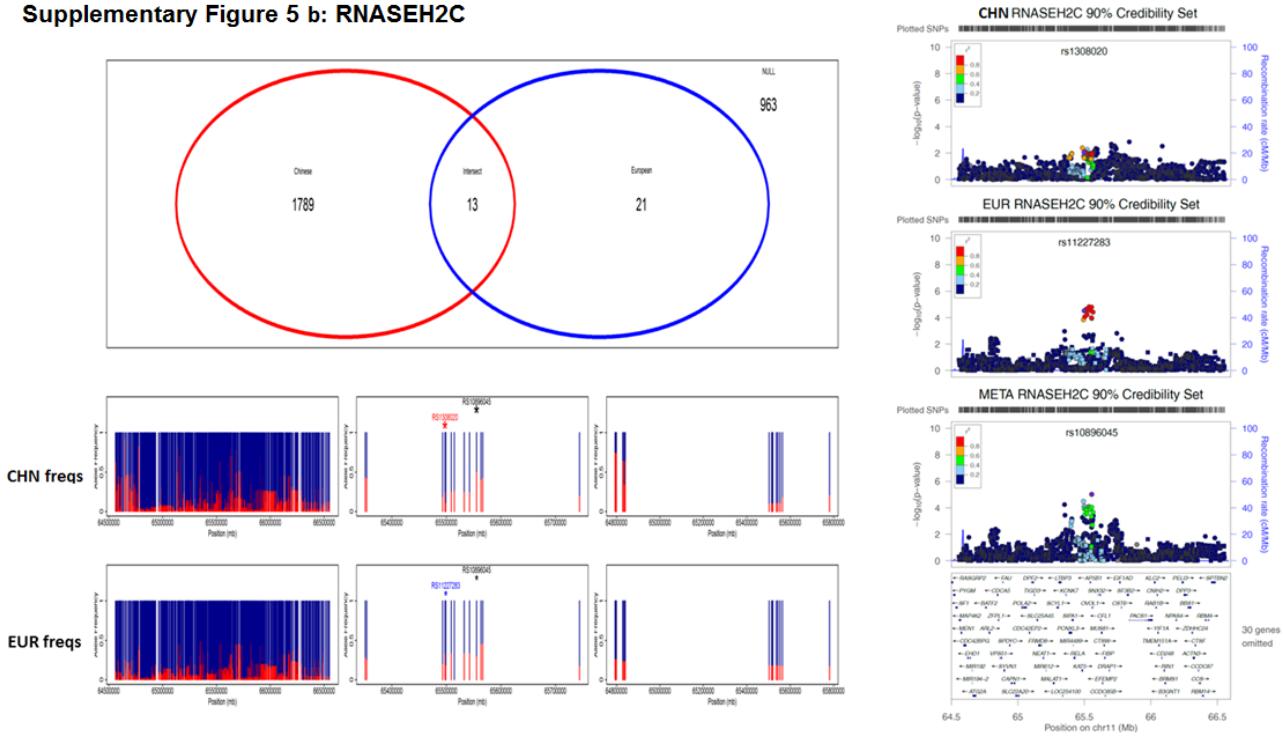
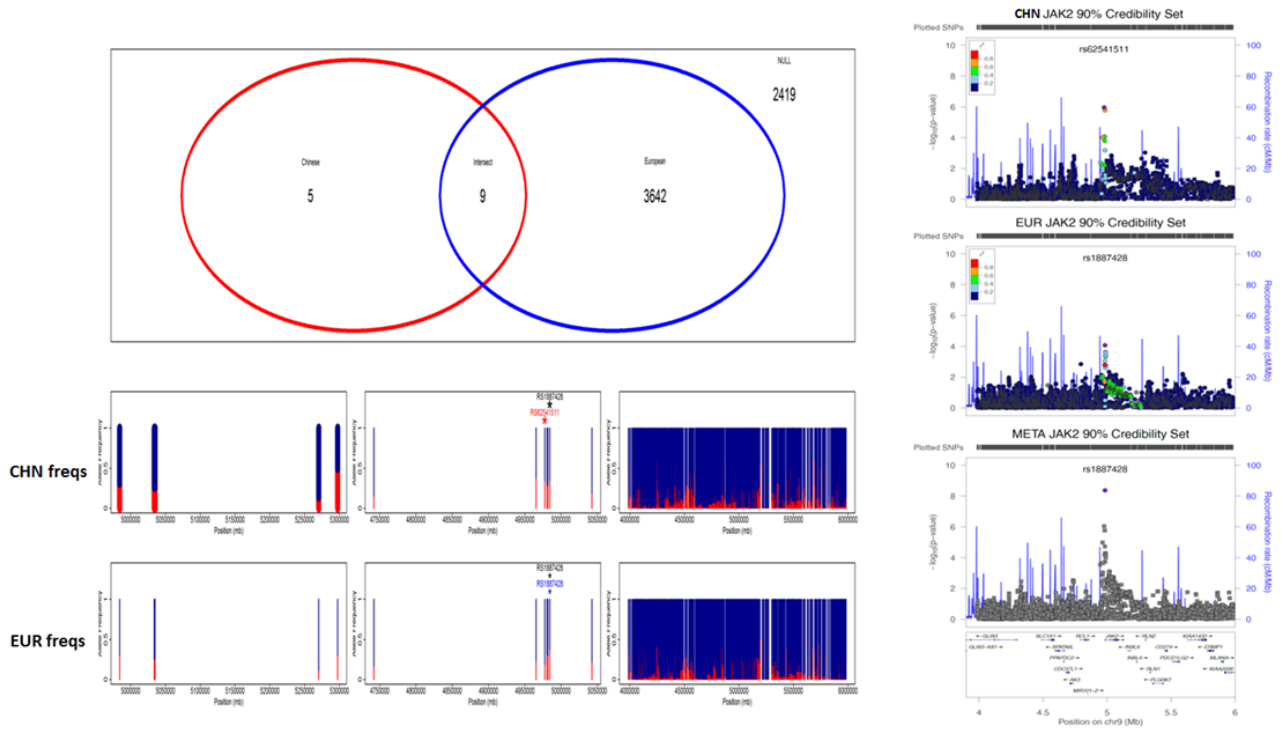
Supplementary Figure 5 b: RNASEH2C



Supplementary Figure 5 c: JAK2



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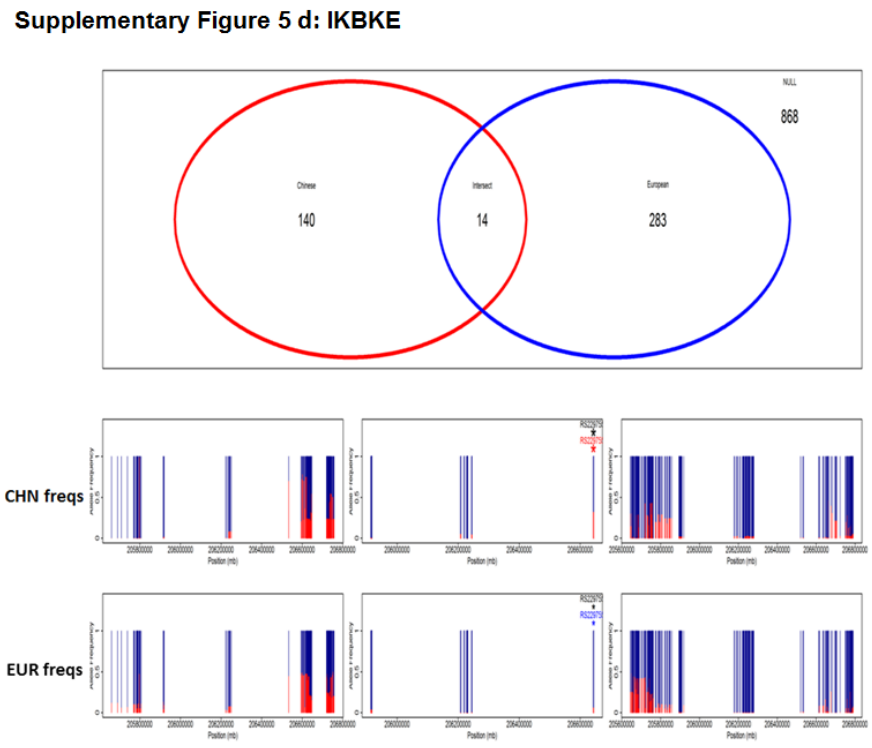
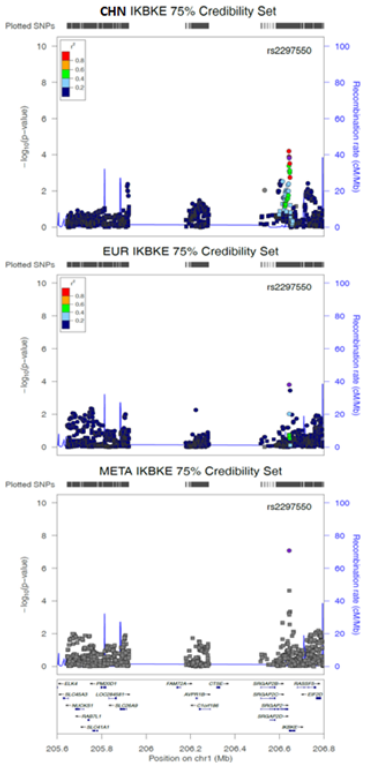
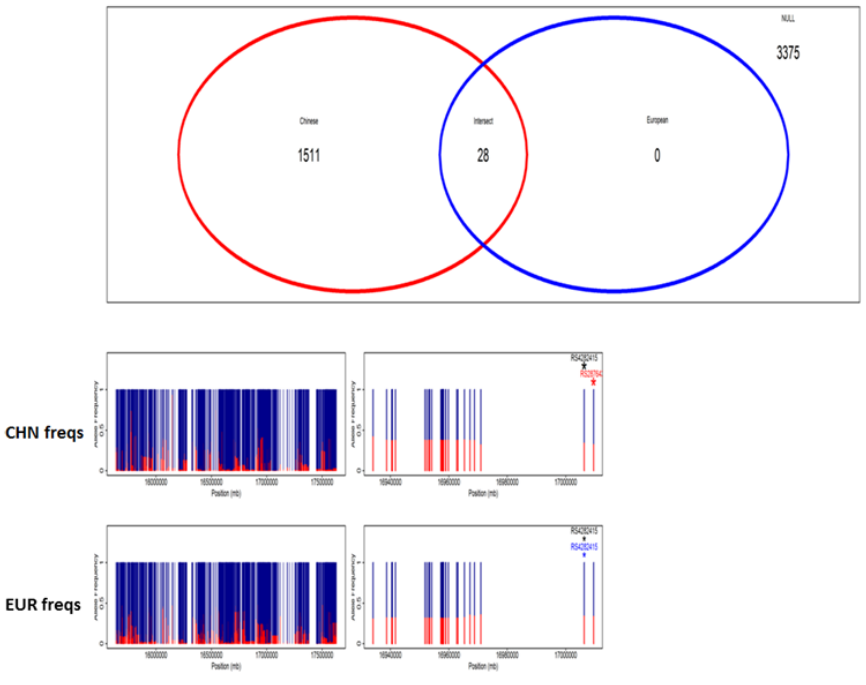
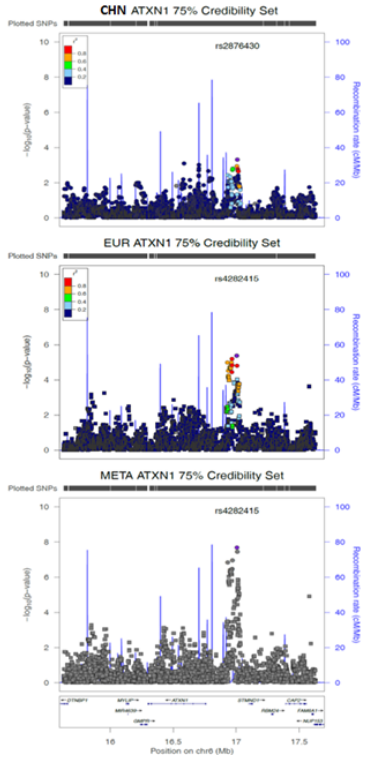
Supplementary Figure 5 d: IKBKE





Supplementary Figure 5e: ATXN1





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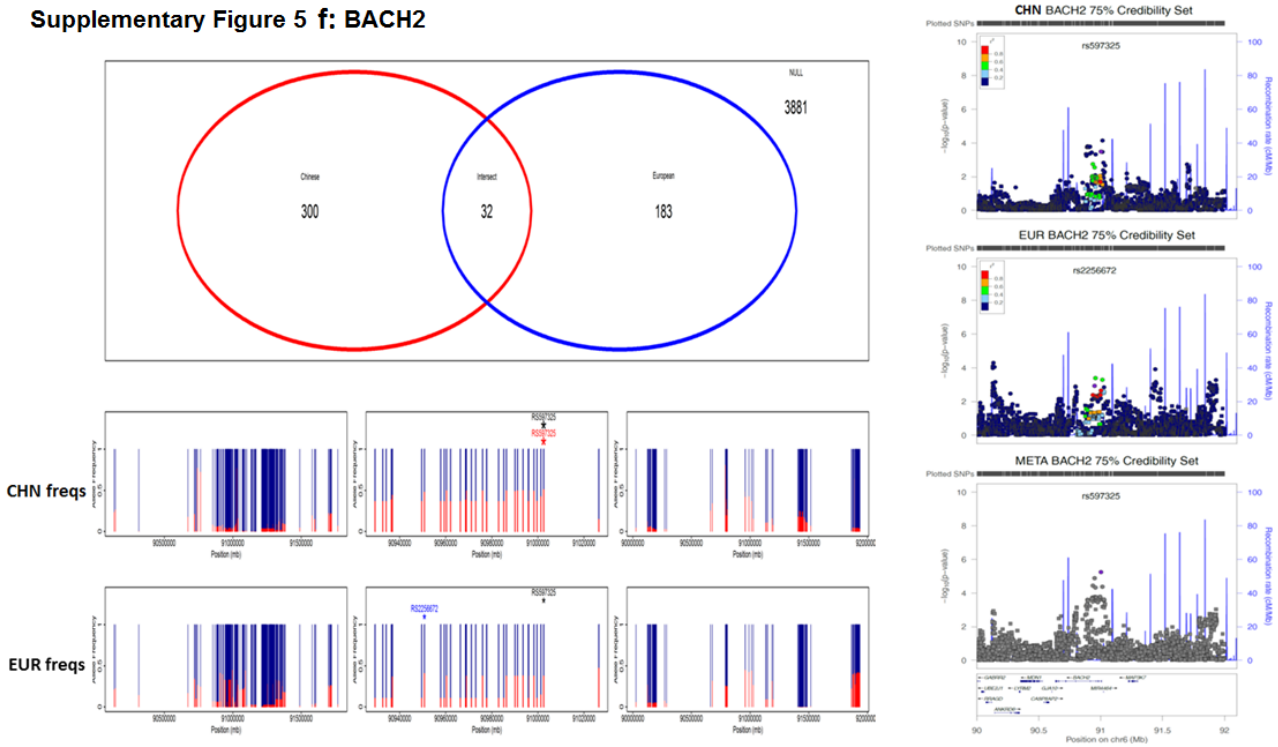
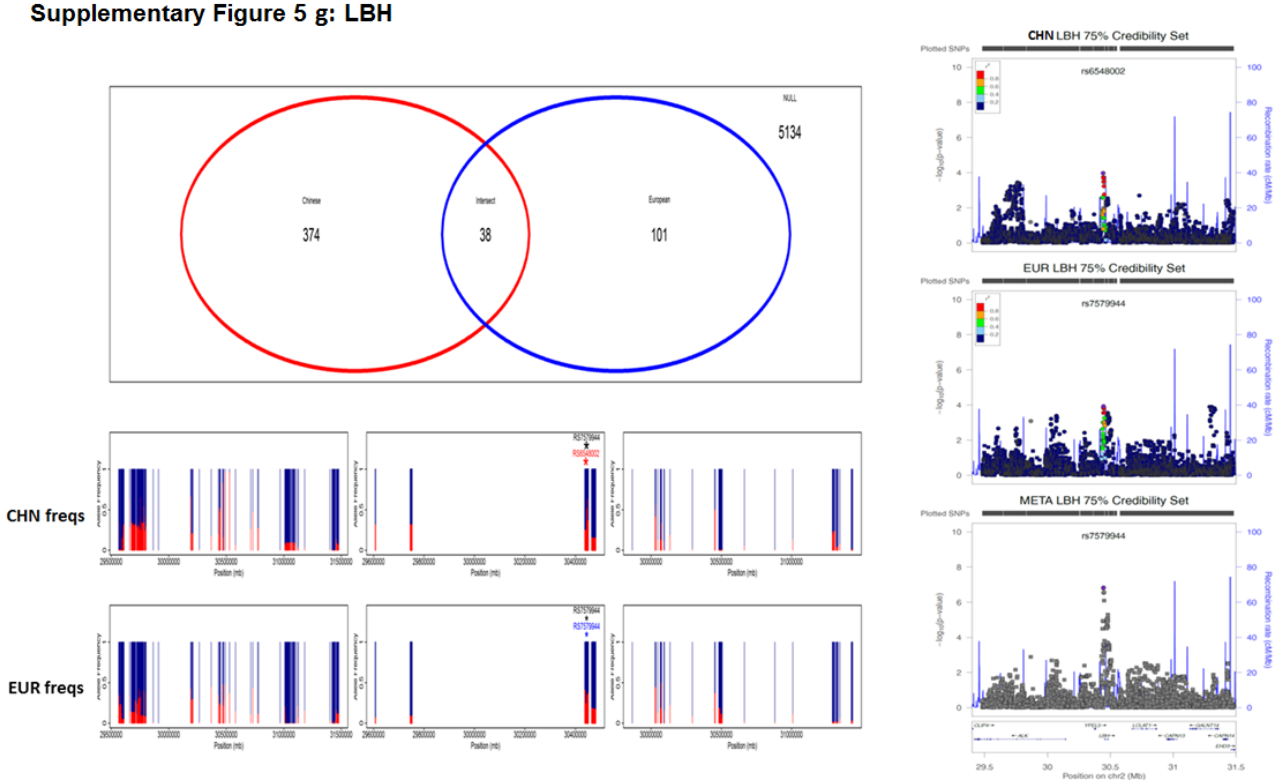
Supplementary Figure 5 f: BACH2

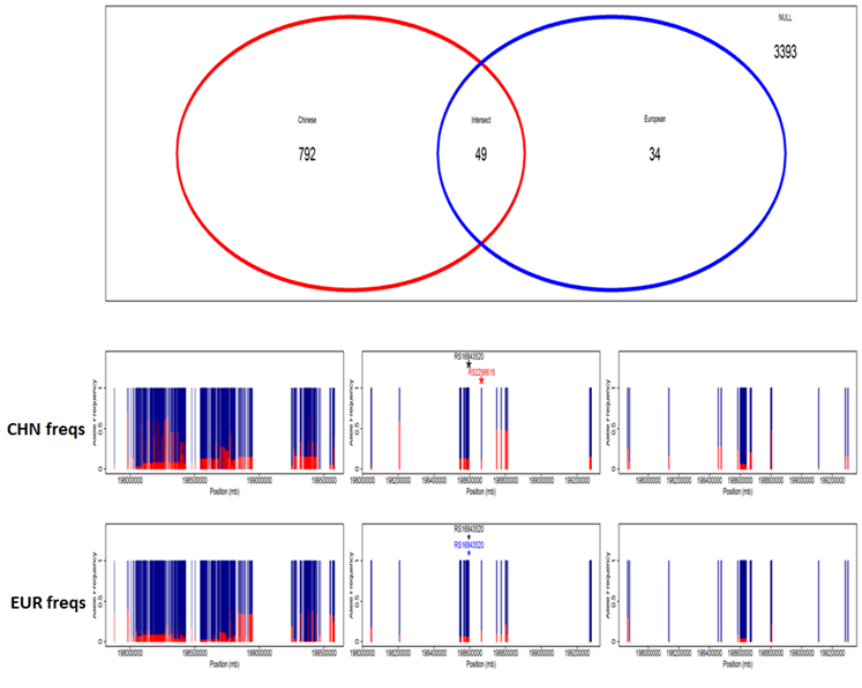


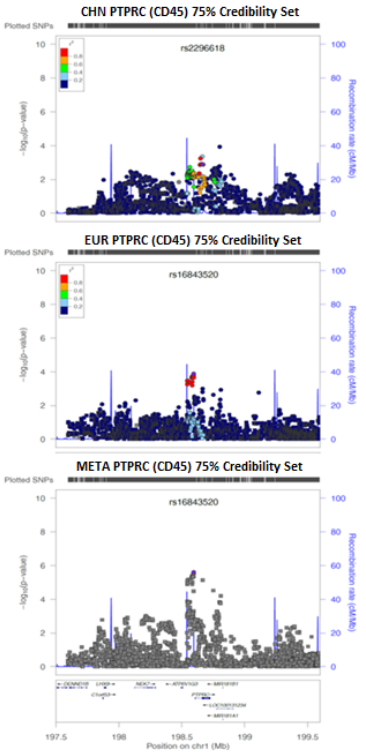
Supplementary Figure 5 g: LBH



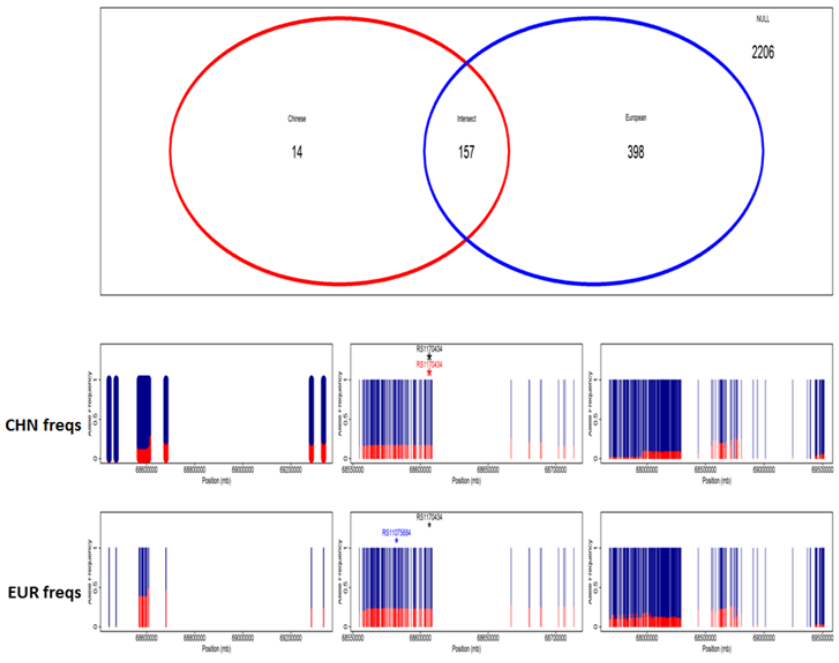
Nature Genetics: doi:10.1038/ng.3603

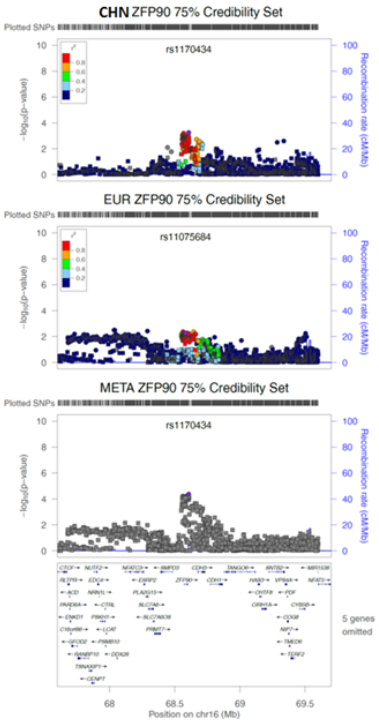
Supplementary Figure 5 i: PTPRC(CD45)





Supplementary Figure 5 i: ZFP90





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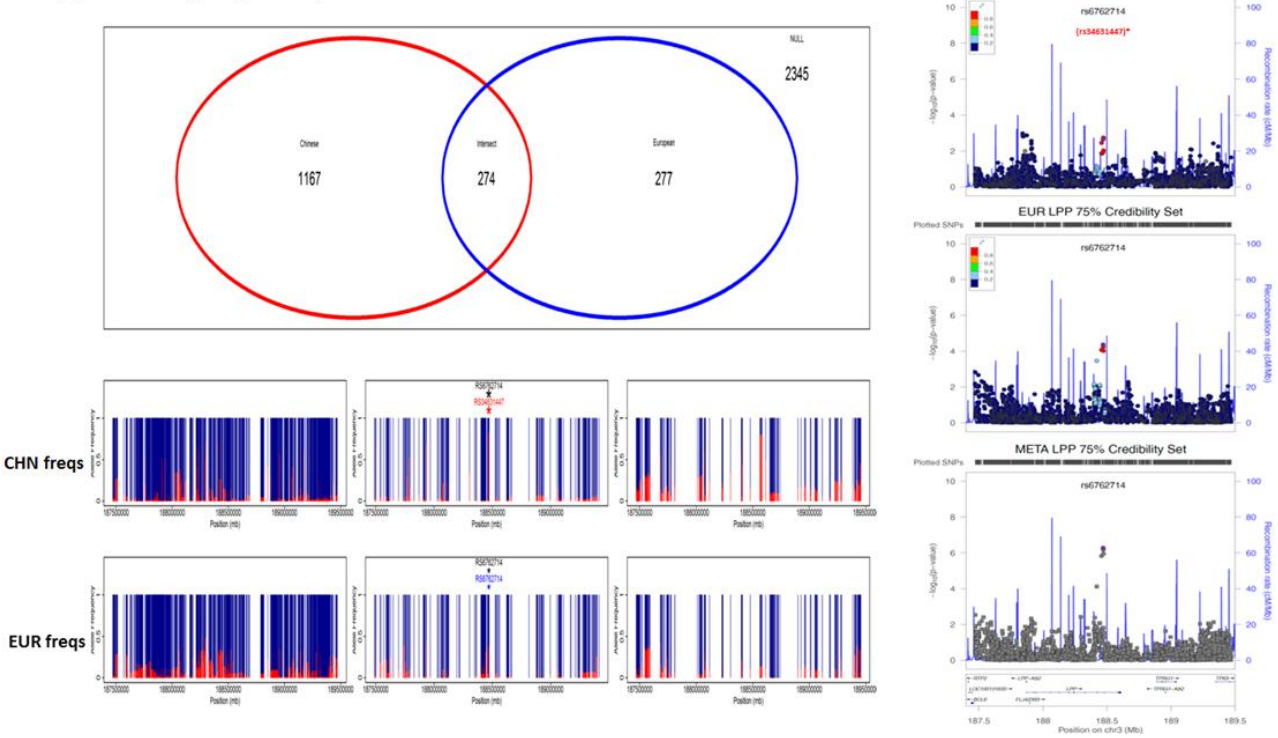
Supplementary Figure 5 j: LPP



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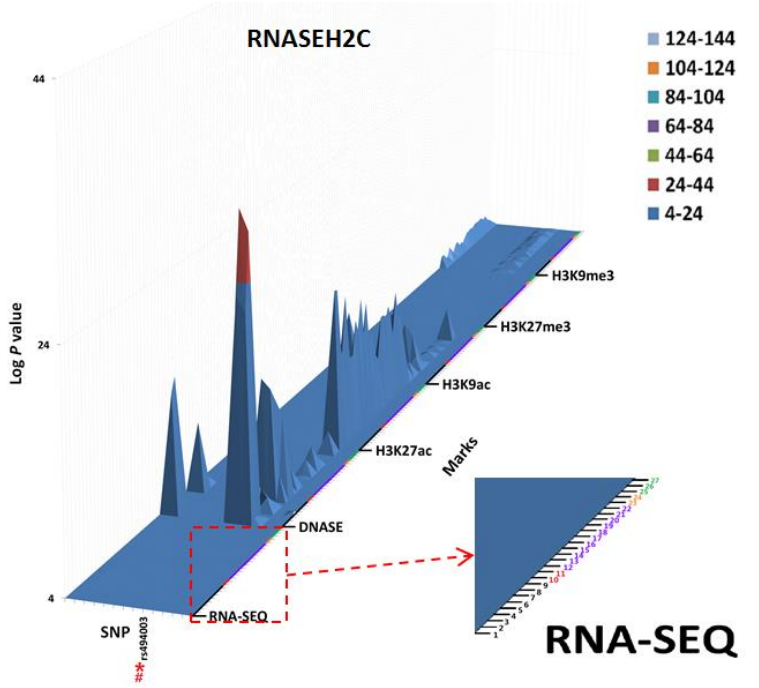
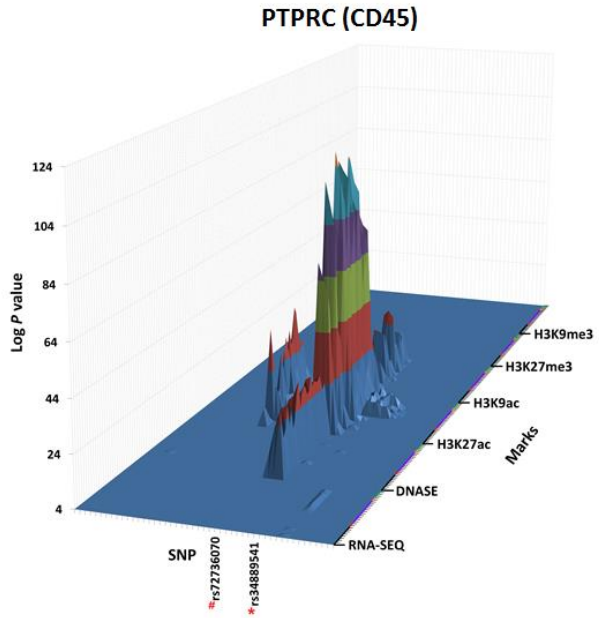
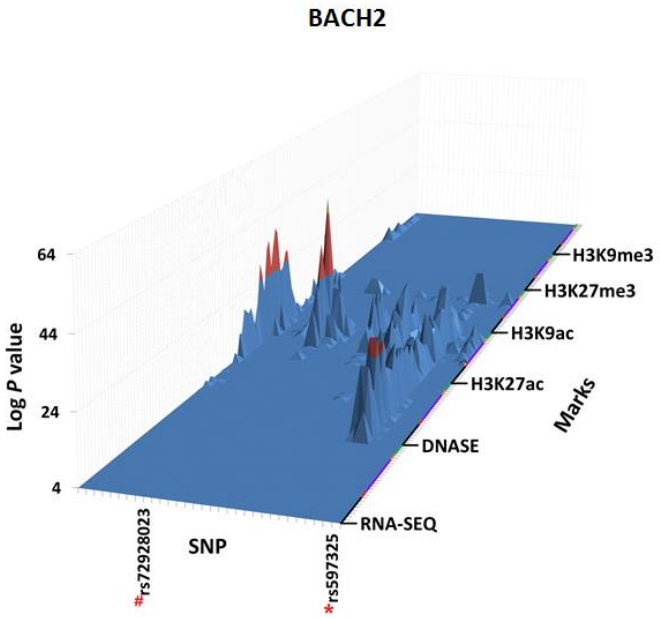
Supplementary Figure 6: 3D enrichment plots depict epigenetic modifications



*the identified SNP in this study.
#the most significant SNP in epigenetic marks annotation.

Cell line	Type	Description
1	Innate	Primary monocytes from peripheral blood
2	Innate	Primary neutrophils from peripheral blood
3	Innate	Primary hematopoietic stem cells
4	Innate	Primary hematopoietic stem cells short term culture
5	Innate	Primary Natural Killer cells from peripheral blood
6	Innate	Primary hematopoietic stem cells G-CSF-mobilized Female
7	Innate	Primary hematopoietic stem cells G-CSF-mobilized Male
8	Innate	Primary mononuclear cells from peripheral blood
9	Innate	Monocytes-CD14+ RO01746 Primary Cells
10	Adaptive	Primary B cells from cord blood
11	Adaptive	Primary B cells from peripheral blood
12	Adaptive	Primary T cells from cord blood
13	Adaptive	Primary T cells from peripheral blood
14	Adaptive	Primary T helper memory cells from peripheral blood
15	Adaptive	Primary T helper naive cells from peripheral blood
16	Adaptive	Primary T helper naive cells from peripheral blood
17	Adaptive	Primary T helper memory cells from peripheral blood
18	Adaptive	Primary T helper cells PMA-I stimulated
19	Adaptive	Primary T helper 17 cells PMA-I stimulated
20	Adaptive	Primary T helper cells from peripheral blood
21	Adaptive	Primary T regulatory cells from peripheral blood
22	Adaptive	Primary. T cells effector/memory enriched from peripheral blood
23	Adaptive	Primary T CD8+ naïve cells from peripheral blood
24	Adaptive	Primary T CD8+ memory cells from peripheral blood
25		Dnd41 T Cell Leukemia Cell Line
26		GM12878 Lymphoblastoid Cell Line
27		K562 Leukemia Cell Line





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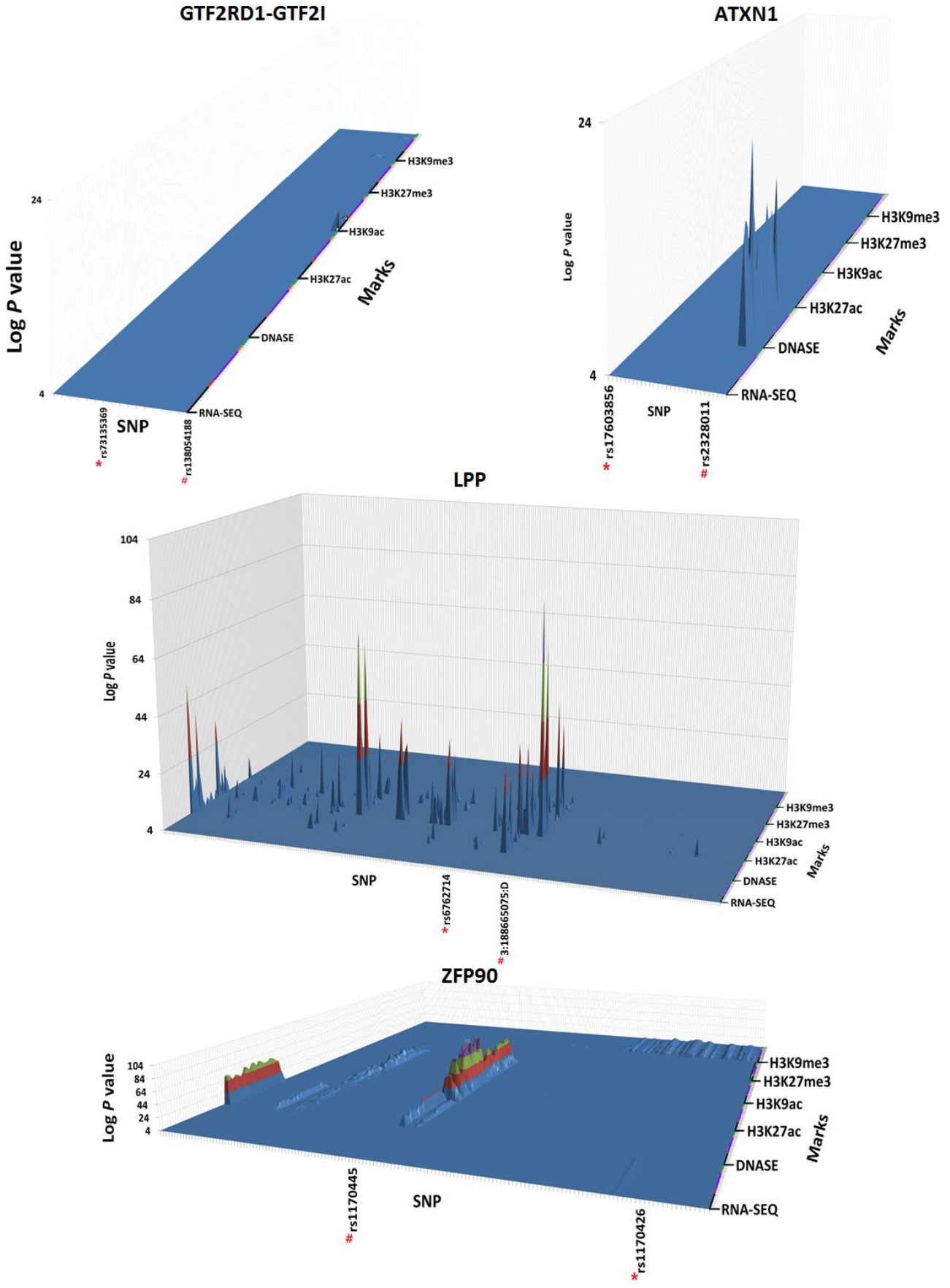

Supplementary Figure 6. 3D enrichment plots depict epigenetic modifications +/-50bp overlapping all SNPs in the Credibility Sets for the 11 novel associated SNPs. The SNPs are

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shown as individual tracks on the x-axis with the SNP used in the replication study marked (*) and the SNP that shows the best evidence for co-localisation with the most prominent epigenetic mark (#). Other SNP identities are listed in Supplementary Table 6. The z-axis represents $\log_{10}$ *P*–value against the null hypothesis that peak intensity arises from the control distribution. The z-axis is truncated at a lower level of ($P < 10^{-04}$). Each novel associated locus has a separate panel with results for RNA expression (RNA–seq), accessibility to DNAse, histone modification by acetylation (H3K27ac, H3K9ac) and histone modification by methylation (H3K27me3, H3K9me3) over 27 immune cells. The data from the blood cell types are consistently ordered on the y-axis according to the annotation to the right of the figure: Categories 1-9 innate response immune cells; Categories 10-24 Adaptive response immune cell types (Categories 10-11 B-cells; Categories 12-24 T-cells) and then Categories 25-27 cell lines.

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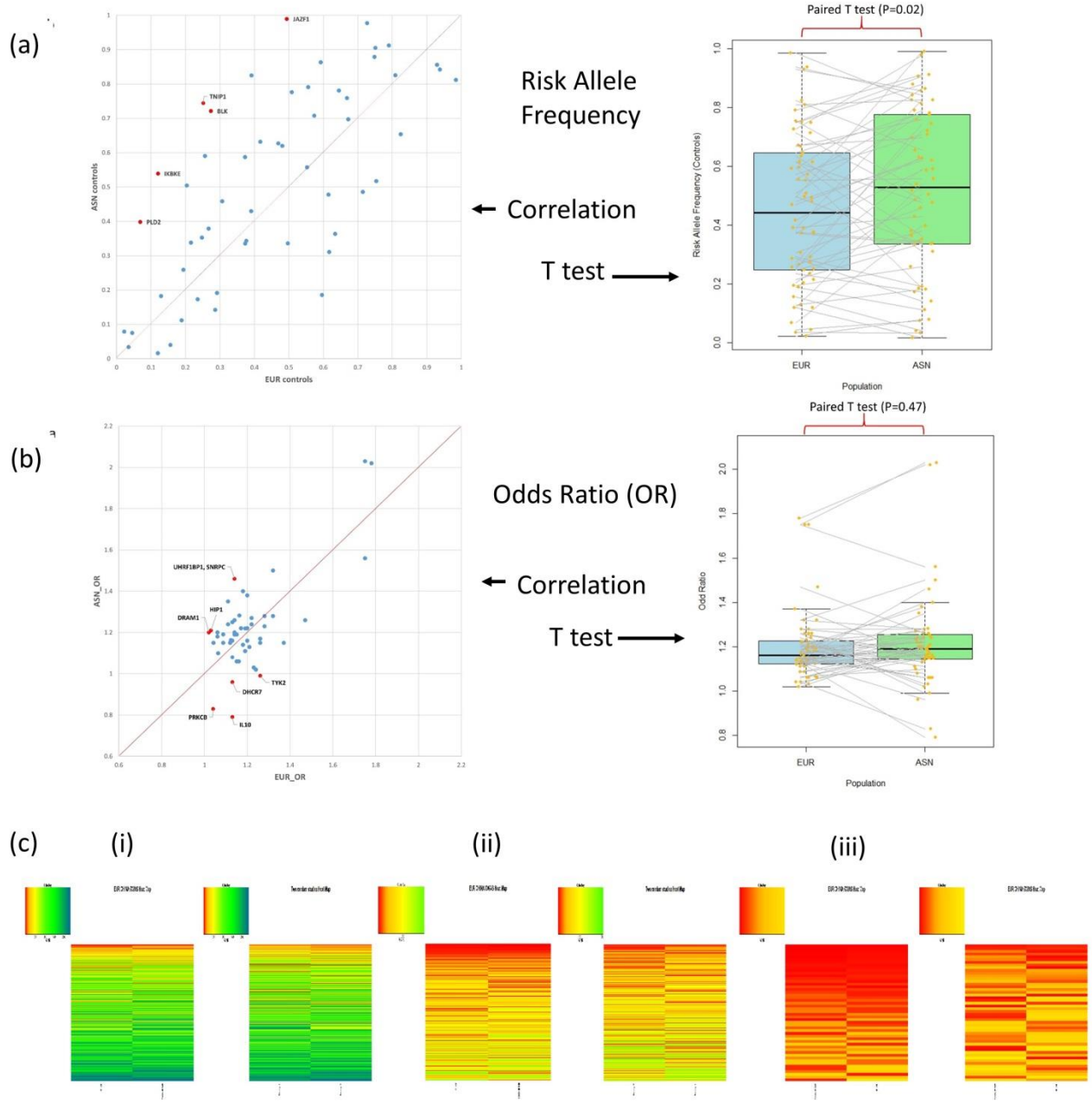
Supplementary Figure 7: Comparison of risk allele frequency and odds ratio between the Chinese and European populations. (a) Comparison of risk allele frequency; (b) Comparison of odds ratio; (c) Heat map of rank scores for each 1Mb region within each population, where the most associated region is ranked 1 and the least associated region is ranked highest. A heat map of two randomly ranked data is provided for comparison. The heat map is ordered (from top to bottom) by the sum of the ranks across the two populations. (ii) A subset of the heat map including only 250 regions (ranked by sum of the ranks). (iii) A subset of the including only 50 regions (ranked by sum of the ranks).



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Supplementary Figure 8a-d Comparison of GRS.

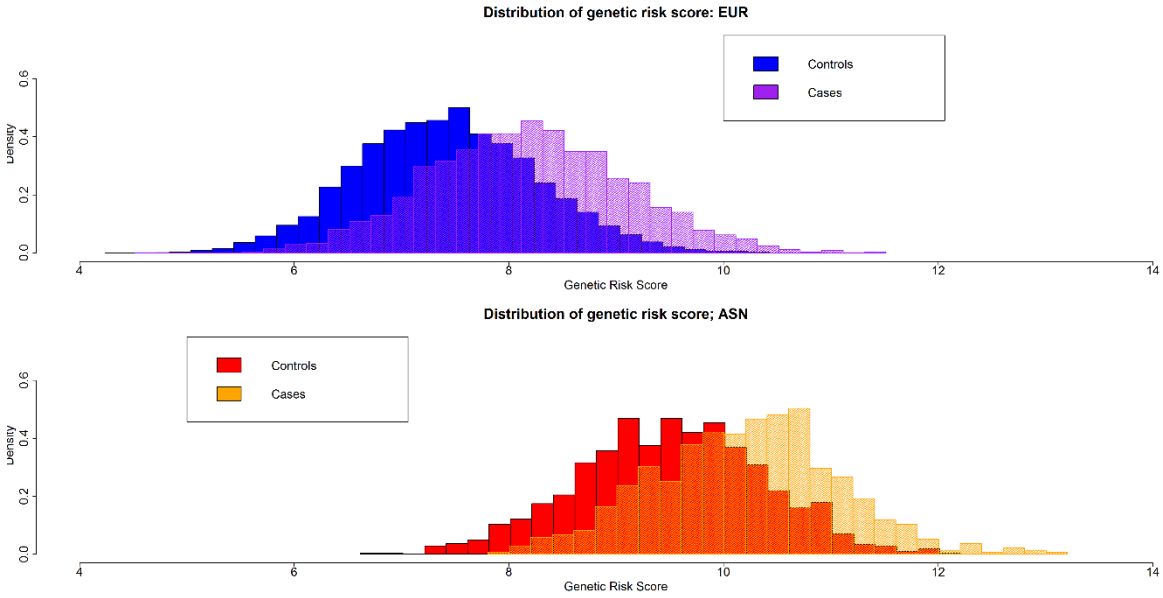

Fig. S8a. Histograms of genetic risk score (GRS) for a) European GWAS Cases versus Controls b) Chinese GWAS Cases versus Controls

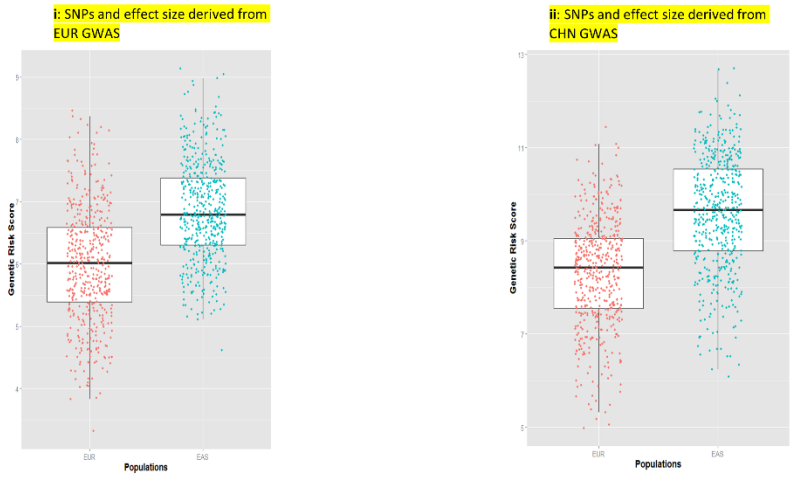

Fig S8b. Comparison of GRS between the European and Asian individuals based on susceptibility SNPs and their effect size chosen either based on EUR GWAS (i) or CHN GWAS data (i).

i) GRS calculated using the best SNPs in each locus based on data from EUR GWAS; ii) GRS calculated using the best SNPs in each associated locus based on the CHN GWAS data. In both situations, the GRS in East Asians are significantly greater than those in Europeans (t-test p-value < 2.2e-16 in both cases).

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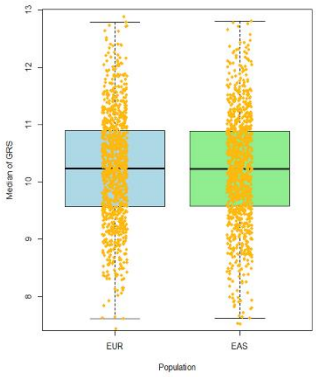
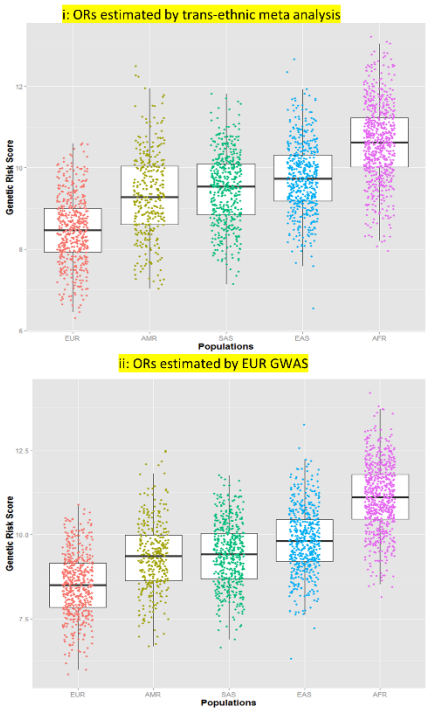


Fig S8c. Distribution of median GRS based on 1,000 simulation using randomly selected SNPs. The difference between the two populations is not significant (Paired t-test p-value=0.6536; t-test p-value=0.852).



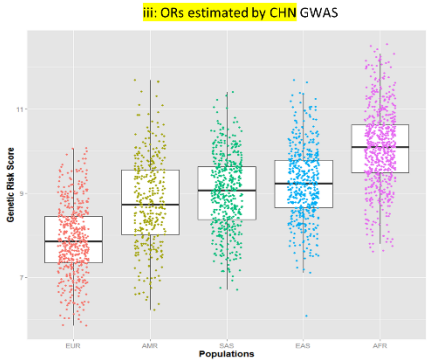


Fig S8d. Box plots of the genetic risk score (GRS) for five major populations. GRS calculations were based on reported SLE susceptibility SNPs and their corresponding effect size either estimated by trans-ethnic meta analysis (i), by EUR GWAS (ii) , or by CHN GWAS (iii). The differences in GRS among the populations are very consistent despite the different effect sizes used, indicating that it is the difference in SLE risk allele frequency rather than estimated effect size that explains the difference in GRS among the populations.

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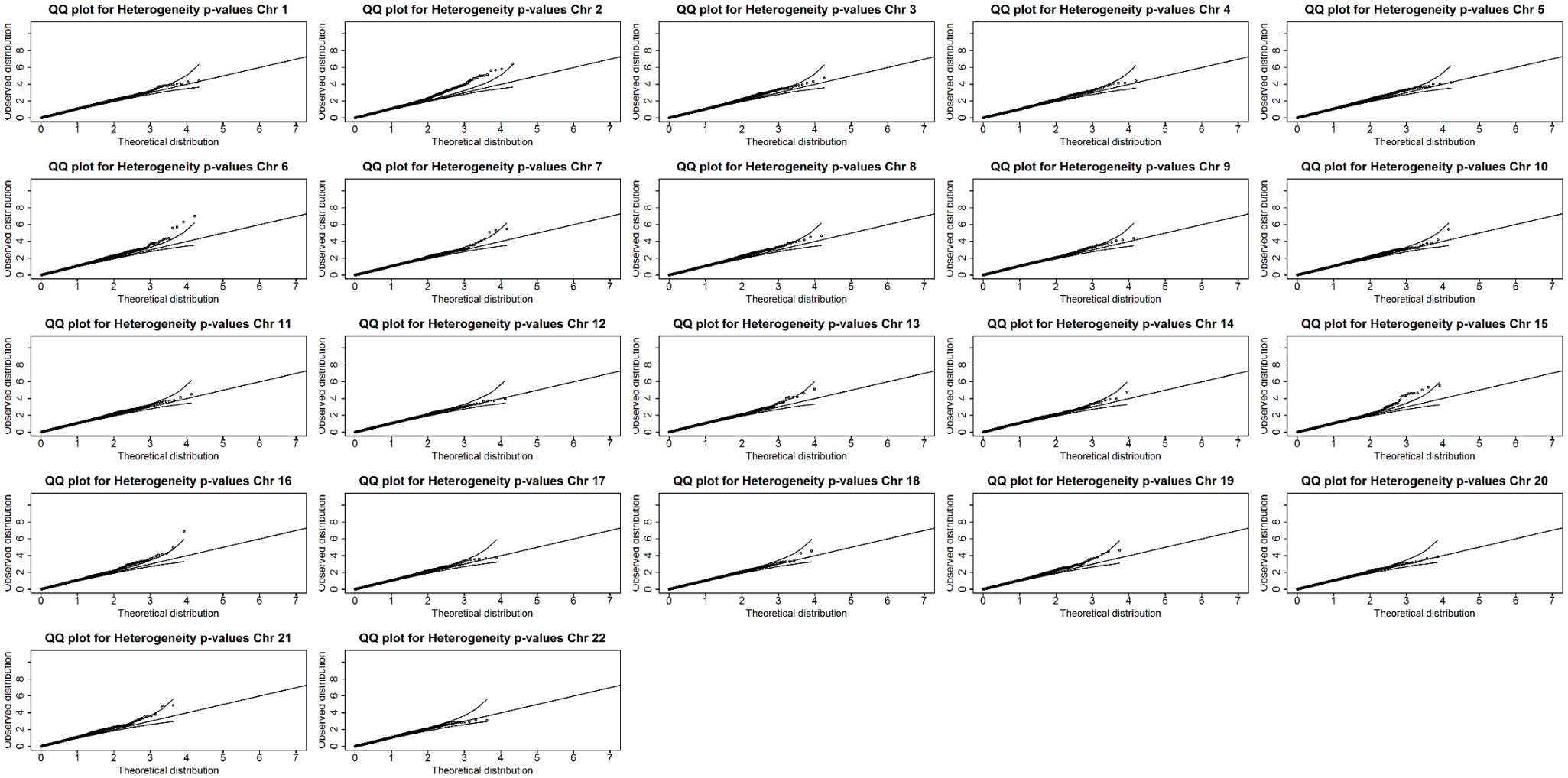
Supplementary Figure 9: QQ plots and Bland Altman plots comparing European and Chinese association results



Supplementary Figure 9a. QQ-plots for heterogeneity test p-values over each chromosome.

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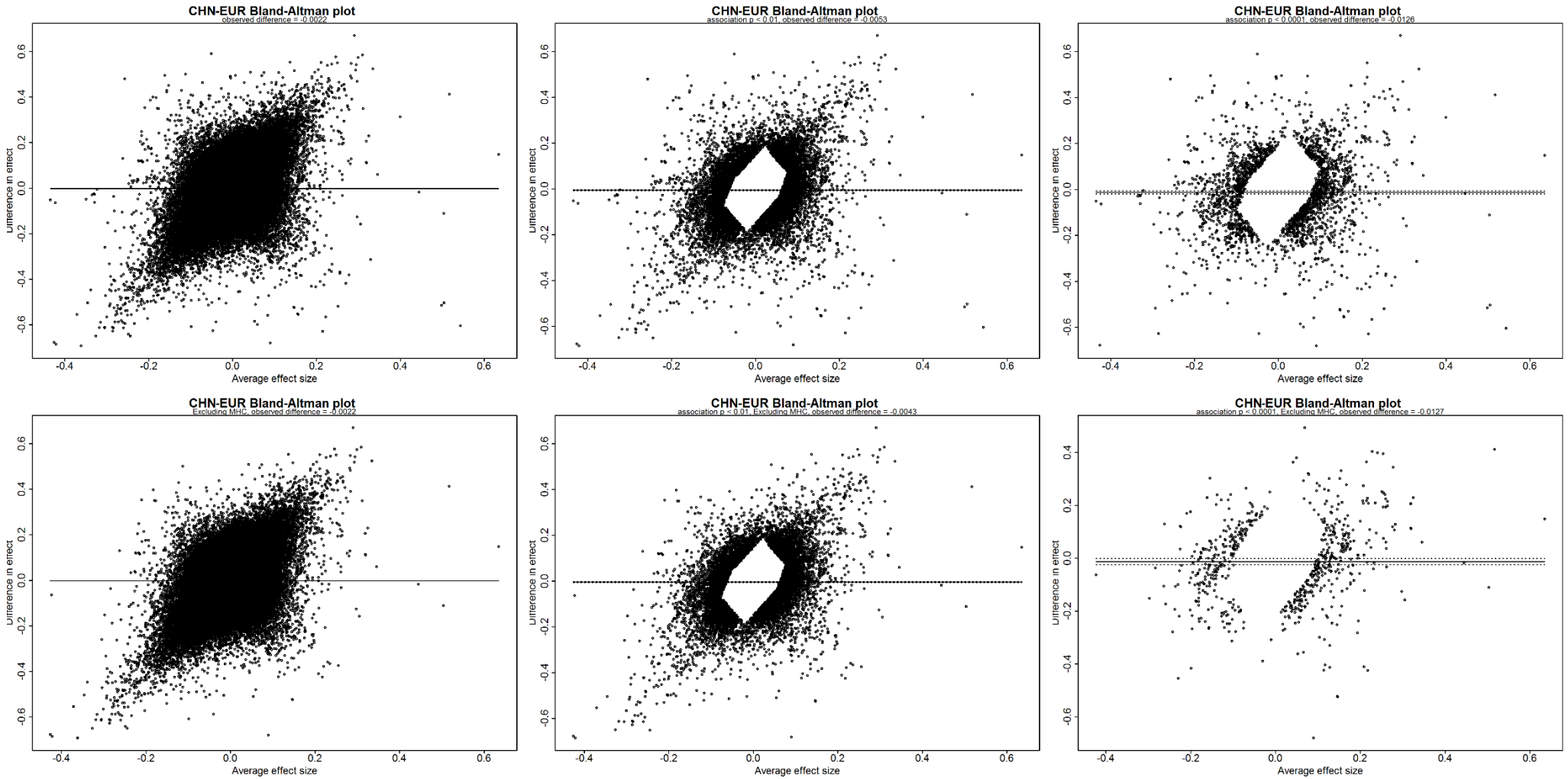

Supplementary Figure 9b. Bland Altman plots comparing European and Chinese association results.

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Supplementary table 1a: Comparison of genetic associations with SLE in European and/or Chinese studies.

SNP	Chr	Position (b37)	Locus	European GWAS		Chinese GWAS Meta[a]		Minor Allele Frequencies[b]		Summary of shared association		
				P–value	Odds Ratio	*P*–value	Odds Ratio	European	Chinese	Direction[c]	Het–*p*[d]	Shared (cumulative)[e]
Published in both Chinese and European GWAS												
rs1801274	1	161,479,745	*FCGR2A*	6.05E–11	1.21	7.36E–03	1.13	0.497	0.333	+++	0.56	1 (1)
rs10912578	1	173,251,856	*TNFSF4*	1.65E–15	1.28	1.98E–08	1.28	0.306	0.460	+++	0.69	1 (2)
rs11889341	2	191,943,742	*STAT4*	1.17E–65	1.75	3.73E–22	1.56	0.216	0.339	+++	0.18	1 (3)
rs6889239	5	150,457,771	*TNIP1*	2.19E–18	1.32	2.94E–06	1.28	0.251	0.743	+++	0.91	1 (4)
rs2431098	5	159,887,336	MIR146A	2.24E–15	1.26	5.69E–04	1.17	0.481	0.628	+++	0.65	1 (5)
rs1150757	6	32,029,205	MHC class III	2.08E–101	2.53	NA[f,k]	NA[f,k]	0.092	0.000	+??[f,k]	0.42	1 (6)
rs6568431	6	106,588,806	*PRDM1 ATG5*	4.33E–12	1.22	2.82E–06	1.24	0.376	0.347	+++	1.00	1 (7)
rs2230926	6	138,196,066	*TNFAIP3*	1.73E–16	1.75	1.11E–12	2.03	0.035	0.031	+++	0.06	1 (8)
rs4917014	7	50,305,863	*IKZF1*	4.10E–05	1.14	3.09E–06	1.26	0.328	0.299	+++	0.17	1 (9)
rs35000415	7	128,585,616	*IRF5*	1.86E–45	1.80	NA[g,k]	NA[g,k]	0.108	0.001	+??[g,k]	0.14	1 (10)
rs2736332	8	11,339,965	*BLK*	4.83E–18	1.32	2.50E–14	1.50	0.273	0.718	+++	0.22	1 (11)
rs7097397	10	50,025,396	*WDFY4*	8.60E–11	1.22	5.45E–07	1.27	0.383	0.694	+++	0.63	1 (12)
rs4948496	10	63,805,617	*ARID5B*	1.17E–06	1.15	1.76E–04	1.19	0.469	0.626	+++	0.50	1 (13)
rs387619	11	35,098,193	*CD44*	4.03E–11	1.22	1.87E–04	1.24	0.444	0.207	+++	0.98	1 (14)
rs7941765	11	128,499,000	*ETS1 FLI1*	9.82E–07	1.15	2.50E–01[h]	1.06	0.492	0.227	+++	0.52	1 (15)
rs1059312	12	129,278,864	*SLC15A4*	3.20E–06	1.14	5.21E–05	1.19	0.391	0.428	+++	0.66	1 (16)
rs9652601	16	11,174,365	*CIITA SOCS1*	3.86E–07	1.17	1.91E–04	1.22	0.332	0.237	+++	0.88	1 (17)
rs1143679	16	31,276,811	*ITGAM*	5.03E–48	1.78	4.31E–04	2.02	0.120	0.011	+++	0.77	1 (18)
rs13332649	16	85,966,683	*IRF8*	5.43E–17	1.37	9.75E–02[i]	1.15	0.210	0.088	+++	0.27	1 (19)
rs7444	22	21,976,934	*UBE2L3*	1.30E–13	1.28	2.40E–06	1.23	0.204	0.519	+++	0.34	1 (20)
Published in European GWAS only												
rs2476601	1	114,377,568	*PTPN22*	8.34E–13	1.39	NA[k]	NA[k]	0.091	0.006	+??[k]	0.98	0 (20)
rs17849501	1	183,542,323	*SMG7 NCF2*	1.63E–59	2.24	NA[k]	NA[k]	0.051	0.004	+??[k]	0.40	0 (20)
rs3024505	1	206,939,904	*IL10*	2.55E–03	1.13	4.30E–02	0.79	0.156	0.037	+—	0.03	0 (20)
rs9782955	1	236,039,877	*LYST*	5.58E–04	1.12	3.87E–02	1.15	0.252	0.122	+++	0.98	0 (20)

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rs268134	2	65,608,363	*SPRED2*	1.86E–07	1.19	1.70E–01	1.11	0.249	0.085	+++	0.75	1 (21)[j]
rs2111485	2	163,110,536	*IFIH1*	3.44E–06	1.15	2.59E–01	1.06	0.404	0.817	+–+	0.29	0 (21)
rs10048743	2	213,890,232	*IKZF2*	2.04E–08	1.26	1.14E–02	1.15	0.129	0.183	+++	0.51	1 (22)
rs9311676	3	58,470,351	*ABHD6 PXK*	5.37E–06	1.14	NA[k]	NA[k]	0.424	0.006	+??[k]	0.35	0 (22)
rs564799	3	159,728,987	*IL12A*	1.15E–06	1.16	3.94E–01	1.06	0.408	0.137	+++	0.62	0 (22)
4:102721293	4	102,721,293	*BANK1*	4.50E–10	1.20	2.92E–05	1.22	0.446	0.390	+++	0.35	1 (23)
rs4388254	5	133,428,601	*TCF7 SKP1*	3.71E–10	1.47	4.10E–03	1.26	0.045	0.079	+++	0.11	1 (24)
rs9462027	6	34,797,241	*UHRF1BP1*	1.80E–05	1.14	1.01E–10	1.46	0.286	0.142	+++	0.0016	1 (25)
rs849142	7	28,185,891	*JAZF1*	3.49E–05	1.13	3.40E–01	1.25	0.494	0.990	+++	0.82	0 (25)
rs1061502	11	614,318	*IRF7*	8.88E–11	1.23	8.25E–01	1.03	0.273	0.024	+–+	0.64	0 (25)
rs3794060	11	71,187,679	*DHCR7 NADSYN1*	1.13E–04	1.13	3.64E–01	0.96	0.256	0.603	++–	0.01	0 (25)
rs10774625	12	111,910,219	*SH2B3*	9.47E–08	1.17	NA[k]	NA[k]	0.499	0.014	+??[k]	0.44	0 (25)
rs4902562	14	68,731,458	*RAD51B*	4.85E–05	1.13	1.03E–01	1.08	0.417	0.643	+++	0.87	0 (25)
rs2289583	15	75,311,036	*CSK*	9.35E–09	1.20	7.80E–03	1.16	0.291	0.190	+++	0.85	1 (26)
rs2286672	17	4,712,617	*PLD2*	5.81E–05	1.24	5.90E–01	1.02	0.069	0.397	+++	0.11	0 (26)
rs2941509	17	37,921,194	*IKZF3*	4.32E–06	1.41	NA[k]	NA[k]	0.032	0.001	+??[k]	0.98	0 (26)
rs2304256	19	10,475,652	*TYK2*	2.34E–12	1.26	8.82E–01	0.99	0.286	0.528	++–	0.0003	0 (26)
Published in Chinese GWAS only												
rs4649203	1	24,519,920	*IL28RA*	7.82E–02	1.06	4.19E–02	1.10	0.267	0.386	+++	0.13	0 (26)
rs13385731	2	33,701,890	*RASGRP3*	9.17E–02	1.11	4.24E–06	1.35	0.062	0.160	+++	0.16	0 (26)
rs6705628	2	74,208,362	*TET3*	1.68E–01	1.18	3.23E–08	1.40	0.016	0.178	+++	0.22	0 (26)
rs12494314	3	119,122,820	*TMEM39A*	3.42E–03	1.12	3.23E–03	1.15	0.176	0.350	+++	0.79	1 (27)
rs1167796	7	75,173,180	rs1167796	3.63E–01	1.03	8.99E–05	1.21	0.427	0.295	+++	0.01	0 (27)
rs4639966	11	118,573,519	rs4639966	7.48E–02	1.06	5.46E–05	1.20	0.248	0.373	+++	0.04	0 (27)
rs34330	12	12,870,695	*CDKN1B*	8.89E–02	1.06	1.67E–04	1.18	0.247	0.486	+++	0.06	0 (27)
rs4622329	12	102,321,935	*DRAM1*	6.11E–01	1.02	6.60E–05	1.20	0.373	0.594	+++	0.02	0 (27)
rs7329174	13	41,558,110	*ELF1*	9.01E–01	1.03	3.02E–06	1.27	0.005	0.211	+++	0.13	0 (27)
rs8016947	14	35,832,666	*NFKBIA*	2.11E–01	1.04	1.23E–03	1.16	0.448	0.430	+++	0.10	0 (27)
rs16972959	16	23,901,376	*PRKCB*	3.19E–01	1.04	2.25E–04	0.83	0.194	0.255	+––	0.02	0 (27)

Nature Genetics: doi:10.1038/ng.3603

This table contains association results in the European GWAS and a meta–analysis of both Chinese GWAS for SNPs published as associated in European and Chinese studies. Association signals are declared as "shared" between the Chinese and European if the locus was published as associated in Chinese and European studies, if the locus was only published in European and the association *p*–values in the Chinese meta–analysis are significant (FDR < 0.01) plus the direction of effect in all 3 GWASs are the same, or if the locus was only published in Chinese study and the association *p*–values in the European GWAS are significant (FDR < 0.01) plus the direction of effect in all 3 GWASs are the same (see online methods).

[a] For loci published in both European and Chinese studies, we note the SNPs published in the European GWAS in this table. Only three SNPs did not pass a false discovery rate at 0.01 in the meta analysis of the Chinese GWAS and these are noted in points f,g and h. "NA" is placed where SNPs failed QC in the Chinese data due to IMPUTE INFO scores less than 0.7.

[b] The Minor allele refers to the minor allele in the European GWAS. In most cases, the Chinese and European data shared the same minor allele, while in some, rs10774625, *SH2B3* for example; the minor allele in the European is the major allele in the Chinese.

[c] The direction of effect (log odds ratio) across all three GWASs (European, Anhui, Hong Kong) is with respect to the GWAS risk allele, so +++ means that the direction is consistent across all three GWASs, while +–+ or ++– means that the Anhui study or Hong Kong study (respectively) has the opposite direction of effect to the European GWAS. Hence +—— means that both Chinese GWASs have the opposite effect to the European GWAS. A "?" is placed where SNPs failed QC in the Chinese data due to IMPUTE INFO scores less than 0.7.

[d] A test of heterogeneity (Cochran's Q statistic) was carried out, to test for heterogeneity of effect size over all three GWASs. "HET–*p*" displays the *p*–value from this test with only two SNPs (rs9462027 and rs2304256) showing evidence against the null (no heterogeneity). The direction of effect for rs9462027 is consistent; however, this locus is clearly associated in the Chinese.

[e] This column displays a "1" if the SNP is declared as associated in both the European and Chinese with a cumulative total in parentheses.

[f] A gene based test showed significant association: *HLA–DRB1* was significant [*P* = 2.81E–22 (GATES); *P* = 6.91E–27 (HYST)]

[g] A gene based test showed significant association: *IRF5* was significant [*P* = 6.39E–10 (GATES); *P* = 1.23E–41 (HYST)].

[h] A gene based test showed significant association: *ETS1* was significant [*P* = 5.89E–04 (GATES); *P* = 1.46E–03 (HYST)].

[i] The *IRF8* locus was replicated in a further set of Chinese samples[3] where the SNP rs2934498 had *P* = 4.97E–09 in meta–analysis (*P* = 4.29E–03 in the Chinese data we present here) .

[j] Some SNPs in this loci were included in the Anhui replication study and were statistically significant: rs268134 was not typed but three SNPs in this region were typed and were significant with the same direction of effect as in the European data (rs1876515, *P* = 6.62E–13; rs268131, *P* = 1.32E–12; rs6740462, *P* = 1.66E–04);

[k] These SNPs failed QC in the Chinese data due to IMPUTE INFO scores less than 0.7.

Nature Genetics: doi:10.1038/ng.3603

Supplementary table 1b: Comparison of genetic associations with SLE in European and/or Chinese studies post 1KG imputation analysis. Most associated SNP post meta–analysis

SNP	Chr	Position (b37)	Locus	European GWAS		Chinese GWAS Meta		Minor Allele Frequencies[a]		Summary of shared association		
				P–value	Odds Ratio	*P*–value	Odds Ratio	European	Chinese	Direction[b]	Het–*p*[c]	Shared (cumulative)[d]
Published in both Chinese and European GWAS												
rs7551957	1	161,470,042	*FCGR2A*	2.07E–11	1.21	3.27E–03	1.15	0.470	0.268	+++	3.58E–01	1 (1)
rs12039904	1	173,212,273	*TNFSF4*	7.20E–13	1.27	1.47E–12	1.41	0.240	0.259	+++	7.57E–02	1 (2)
rs4274624	2	191,958,656	*STAT4*	9.73E–66	1.75	1.19E–22	1.57	0.215	0.334	+++	5.46E–02	1 (3)
rs10036748	5	150,458,146	*TNIP1*	2.80E–18	1.32	2.24E–06	1.28	0.251	0.743	+++	5.92E–01	1 (4)
rs2431697	5	159,879,978	MIR146A	2.60E–14	1.25	3.44E–08	1.45	0.442	0.136	+++	3.99E–02	1 (5)
rs114883138	6	32,427,179	MHC class III	2.16E–78	1.78	1.02E–20	1.60	0.301	0.324	+++	6.33E–02	1 (6)
rs7768653	6	106,574,794	*PRDM1 ATG5*	3.11E–12	1.23	1.87E–06	1.25	0.385	0.301	+++	6.98E–01	1 (7)
rs77000060	6	138,237,989	*TNFAIP3*	8.34E–17	1.83	4.74E–13	2.08	0.031	0.031	+++	3.12E–01	1 (8)
rs11185603	7	50,306,810	*IKZF1*	2.81E–05	1.14	2.54E–06	1.26	0.328	0.299	+++	7.57E–02	1 (9)
rs3757387	7	128,576,086	*IRF5*	1.12E–38	1.45	2.55E–10	1.48	0.456	0.130	+++	8.09E–01	1 (10)
rs4840568	8	11,351,019	*BLK*	5.18E–18	1.31	1.45E–13	1.47	0.272	0.705	+++	6.33E–02	1 (11)
rs7097397	10	50,025,396	*WDFY4*	8.60E–11	1.21	5.45E–07	1.27	0.329	0.694	+++	4.40E–01	1 (12)
rs10761602	10	63,813,802	*ARID5B*	1.48E–07	1.17	1.25E–04	1.20	0.457	0.619	+++	6.10E–01	1 (13)
rs387619	11	35,098,193	*CD44*	4.03E–11	1.21	1.87E–04	1.24	0.444	0.207	+++	7.48E–01	1 (14)
rs61432431	11	128,322,622	*ETS1 FLI1*	4.60E–06	1.25	6.48E–09	1.30	0.092	0.346	+++	5.00E–01	1 (15)
12:129276658:I	12	129,276,658	*SLC15A4*	1.08E–07	1.27	3.00E–08	1.34	0.108	0.185	+++	4.05E–01	1 (16)
rs12917716	16	11,189,148	*CIITA SOCS1*	1.13E–06	1.15	2.68E–07	1.27	0.441	0.427	+++	8.04E–02	1 (17)
rs1143679	16	31,276,811	*ITGAM*	5.03E–48	1.78	4.31E–04	2.02	0.120	0.011	+++	5.40E–01	1 (18)
rs13332649	16	85,966,683	*IRF8*	5.43E–17	1.37	9.75E–02	1.15	0.210	0.088	+++	4.70E–02	1 (19)
rs2298428	22	21,982,892	*UBE2L3*	1.94E–12	1.28	2.70E–09	1.30	0.190	0.425	+++	7.71E–01	1 (20)
Published in European GWAS only												
rs11102701	1	114,449,829	*PTPN22*	8.16E–06	1.19	2.49E–01	1.06	0.156	0.487	++–	5.69E–02	0 (20)
1:183524640:I	1	183,524,640	*SMG7 NCF2*	4.21E–10	1.37	1.21E–02	1.21	0.108	0.104	+++	1.71E–01	0 (20)
rs3813977	1	206,643,534	*IL10*	9.69E–03	1.17	8.32E–04	1.19	0.070	0.329	+++	7.87E–01	0 (20)

Nature Genetics: doi:10.1038/ng.3603

1:235354571:D	1	235,354,571	*LYST*	1.71E–05	1.13	8.48E–02	1.09	0.453	0.261	+++	5.25E–01	0 (20)
rs268124	2	65,654,364	*SPRED2*	8.60E–09	1.21	5.92E–02	1.12	0.267	0.172	+++	2.37E–01	1 (21)
rs1990760	2	163,124,051	*IFIH1*	2.48E–06	1.15	1.65E–01	1.08	0.404	0.808	+++	2.99E–01	0 (21)
rs10048743	2	213,890,232	*IKZF2*	2.04E–08	1.26	1.14E–02	1.15	0.129	0.183	+++	1.79E–01	1 (22)
3:58416772:I	3	58,416,772	*ABHD6 PXK*	2.78E–08	1.19	7.26E–01	0.87	0.352	0.003	+—	4.34E–01	0 (22)
3:159732641:I	3	159,732,641	*IL12A*	2.70E–07	1.16	2.52E–01	1.06	0.414	0.213	+++	1.50E–01	0 (22)
rs6856202	4	102,716,709	*BANK1*	3.76E–09	1.19	2.52E–06	1.24	0.489	0.470	+++	4.56E–01	1 (23)
rs244687	5	133,423,616	*TCF7 SKP1*	1.31E–08	1.25	3.79E–05	1.21	0.162	0.381	+++	5.59E–01	1 (24)
6:34651199:I	6	34,651,199	*UHRF1BP1*	9.68E–09	1.29	4.69E–12	1.60	0.110	0.113	+++	7.70E–03	1 (25)
rs12531540	7	28,162,674	*JAZF1*	4.77E–06	1.14	3.14E–01	1.27	0.497	0.009	+++	6.53E–01	0 (25)
rs12418883	11	634,083	*IRF7*	3.51E–11	1.24	3.25E–01	1.14	0.297	0.040	+++	5.36E–01	0 (25)
rs7118246	11	71,231,124	*DHCR7 NADSYN1*	1.59E–04	1.14	4.00E–02	1.09	0.206	0.458	+++	4.76E–01	0 (25)
rs10850001	12	112,553,032	*SH2B3*	1.35E–06	1.16	1.02E–01	1.08	0.463	0.353	+++	2.21E–01	0 (25)
rs1275201	14	69,479,235	*RAD51B*	1.14E–04	1.12	5.18E–03	1.21	0.470	0.854	+++	2.78E–01	0 (25)
rs55655136	15	75,285,114	*CSK*	1.02E–05	1.15	1.92E–03	1.20	0.297	0.169	+++	5.34E–01	1 (26)
rs34548580	17	4,951,663	*PLD2*	1.05E–03	1.14	6.64E–02	1.09	0.157	0.467	+++	4.39E–01	0 (26)
rs12938617	17	37,993,352	*IKZF3*	5.12E–08	1.58	7.16E–01	1.30	0.025	0.001	+++	7.83E–01	0 (26)
rs11085725	19	10,462,513	*TYK2*	9.60E–13	1.27	5.58E–01	1.03	0.292	0.585	++–	3.13E–04	0 (26)
Published in Chinese GWAS only												
rs1538633	1	24,516,690	*IL28RA*	6.77E–04	1.11	3.91E–02	1.10	0.368	0.531	+++	9.01E–01	0 (26)
rs13385731	2	33,701,890	*RASGRP3*	9.17E–02	1.11	4.24E–06	1.35	0.062	0.160	+++	2.90E–02	0 (26)
rs28421442	2	74,219,615	*TET3*	6.21E–02	1.22	4.18E–09	1.44	0.021	0.179	+++	1.85E–01	0 (26)
rs2049502	3	119,254,385	*TMEM39A*	2.33E–03	1.13	1.17E–05	1.23	0.172	0.350	+++	1.49E–01	1 (27)
rs138054188	7	74,190,229	rs1167796	1.35E–05	1.46	9.50E–01	0.99	0.030	0.019	++–	7.52E–01	0 (27)
11:118740104:D	11	118,740,104	rs4639966	4.79E–04	1.14	1.76E–03	1.25	0.192	0.132	+++	2.70E–01	0 (27)
rs10845601	12	12,820,134	*CDKN1B*	3.71E–04	1.11	9.99E–07	1.31	0.395	0.238	+++	8.74E–03	0 (27)
rs9804869	12	101,825,294	*DRAM1*	1.25E–04	1.14	8.97E–03	1.14	0.197	0.510	+++	9.36E–01	0 (27)
rs17630801	13	41,539,817	*ELF1*	1.07E–01	1.40	1.27E–06	1.29	0.004	0.218	+++	1.09E–01	0 (27)
rs847521	14	36,459,347	*NFKBIA*	2.85E–01	1.06	2.43E–06	1.27	0.087	0.280	+++	1.00E–02	0 (27)
rs9935139	16	23,728,373	*PRKCB*	5.83E–03	1.12	2.74E–02	1.19	0.173	0.126	+++	5.48E–01	0 (27)

Nature Genetics: doi:10.1038/ng.3603

This table contains association results for the same loci as reported in supplementary table 1a but with the most associated SNPs from a meta–analysis of the European GWAS together with both the Chinese GWAS. Association signals are declared as “shared” between the Chinese and Europeans if the locus was published as associated in Chinese and European studies, if the locus was only published in Europeans and the association *p*–values in the Chinese meta–analysis are significant (post a Bonferroni adjusted for all test in each 2MB locus and FDR < 0.01 across all loci), or if the locus was only published in Chinese study AND the association *p*–values in the European GWAS are significant (post a Bonferroni adjusted for all test in each 2MB locus and FDR < 0.01 across all loci. See online methods. This analysis did not find any additional evidence of shared association (above that in Supplementary table 1a) however two of the associations ‘Published in Chinese GWAS only’ were marginally significant after a multiple testing adjustment within the loci tested (rs138054188 with adjusted *p*= 3E–03 and rs9804869 in the DRAM locus with adjusted *p* = 5E–02), however neither of these passed an FDR at 0.01 across all the loci tested.

[a] The Minor allele refers to the minor allele in the European GWAS. In most cases, the Chinese and European data shared the same minor allele, while in some, rs10774625, *SH2B3* for example; the minor allele in the Europeans is the major allele in the Chinese.

[b] The direction of effect (log odds ratio) across all three GWASs (European, Anhui, Hong Kong) is with respect to the GWAS risk allele, so +++ means that the direction is consistent across all three GWASs, while +–+ or ++– means that the Anhui study or Hong Kong study (respectively) has the opposite direction of effect to the European GWAS. Hence +—- means that both Chinese GWASs have the opposite effect to the European GWAS.

[c] A test of heterogeneity (Cochran’s Q statistic) was carried out, to test for heterogeneity of effect size over all three GWASs. “HET–*p*” displays the p–value from this test with only two SNP (rs9462027 and rs2304256) showing evidence against the null (no heterogeneity). The direction of effect for rs9462027 is consistent however and this locus is clearly associated in the Chinese.

[d] This column displays a “1” if the SNP is declared as associated in both the European and Chinese with a cumulative total in parentheses.

Nature Genetics: doi:10.1038/ng.3603

Supplementary Table 2a: Association results for all 18 SNPs that pass a FDR at 0.01 in the Chinese replication study.

			Chinese GWAS Meta[4,5] Cases = 1,659 Controls = 3,398		European GWAS[6] Cases = 4,036 Controls = 6,959		Chinese Replication Cases = 3,043 Controls = 5,074		European Replication Cases = 1,478 Controls = 6,925		European GWAS Replication[7] Cases = 1,165 Controls = 2,107		Meta all Cases = 11,381 Controls = 24,463		
SNP	**Chr**	**Pos**	**OR**	**p**	**OR**	**p**	**OR**	**p**	**OR**	**p**	**OR**	**p**	**OR**	**p**	**Gene**
rs34889541	1	198,594,769	0.83	4.14E–03	0.80	1.72E–04	0.76	7.45E–09	0.95	5.27E–01	0.90	3.12E–01	0.81	2.44E–12	*PTPRC (CD45)*
rs2297550	1	206,643,772	1.18	1.52E–04	1.18	1.59E–04	1.13	2.14E–04	NA	NA	1.19	3.52E–02	1.16	1.31E–11	*IKBKE*
rs7579944	2	30,445,026	0.84	2.00E–04	0.89	1.18E–04	0.91	3.56E–03	0.96	2.74E–01	0.90	6.13E–02	0.90	1.41E–09	*LBH*
rs17321999	2	30,479,857	0.84	4.03E–03	0.87	4.20E–04	0.81	4.86E–07	0.78	2.94E–06	0.85	1.91E–02	0.83	2.22E–16	*LBH*
rs6762714	3	188,470,238	1.20	2.21E–03	1.13	4.27E–05	1.19	6.63E–05	1.25	5.44E–08	1.03	5.90E–01	1.16	4.00E–15	*LPP/TPRG1–AS1*
rs17603856	6	16,630,898	1.02	6.73E–01	0.92	8.81E–03	0.78	6.17E–09	0.85	2.46E–05	0.84	1.52E–03	0.88	3.27E–12	*ATXN1*
rs597325	6	91,002,494	0.85	3.25E–04	0.91	2.23E–03	0.84	7.22E–08	0.93	5.80E–02	0.95	3.53E–01	0.89	4.03E–12	*BACH2*
rs73135369	7	73,940,978	1.37	7.13E–05	1.28	7.54E–03	1.38	2.72E–09	1.01	9.60E–01	1.34	1.71E–01	1.32	8.77E–14	*GTF2IRD1–GTF2I*
rs1887428	9	4,984,530	1.26	1.68E–06	1.12	8.29E–05	1.22	4.97E–09	1.12	6.00E–03	1.06	2.73E–01	1.16	2.19E–17	*JAK2*
rs494003	11	65,542,298	1.01	8.38E–01	1.16	2.13E–05	1.25	4.52E–05	1.09	5.34E–02	1.10	1.23E–01	1.14	5.81E–09	*RNASEH2C*
rs1170426	16	68,603,798	1.20	1.22E–03	1.09	6.31E–03	1.21	1.05E–05	1.00	9.78E–01	1.14	3.06E–02	1.12	2.24E–08	*ZFP90*
rs12753920	1	92,665,899	1.39	5.16E–03	1.14	9.35E–06	1.45	8.63E–05	0.98	5.52E–01	1.11	6.20E–02	1.11	5.76E–07	*KIAA1107 – C1orf146*
rs427221	3	28,075,985	1.18	2.00E–04	1.07	1.34E–02	1.10	2.73E–03	0.99	7.42E–01	1.06	2.64E–01	1.08	5.29E–06	*EOMES – CMC1*
rs9402743	6	136,001,034	0.94	1.67E–01	1.13	2.65E–05	1.10	2.30E–03	1.06	8.69E–02	1.08	1.50E–01	1.08	5.18E–06	*AHI1*
rs7090925	10	8,479,868	1.06	2.77E–01	0.85	3.79E–07	1.17	3.44E–04	0.95	1.81E–01	0.86	1.09E–02	0.95	1.04E–02	*LINC00708*
rs4082517	10	71,704,566	0.97	7.42E–01	0.82	2.16E–06	1.32	7.23E–04	NA	NA	1.00	9.54E–01	0.93	2.15E–02	*COL13A1*
rs11171683	12	39,693,347	0.82	4.92E–03	0.90	4.02E–04	0.84	7.00E–04	0.95	2.15E–01	0.97	6.14E–01	0.93	8.72E–05	*KIF21A*
rs7219	17	73,315,368	0.98	7.35E–01	0.86	5.34E–06	1.21	3.72E–04	0.88	1.00E–02	0.98	6.89E–02	0.94	3.95E–03	*MRPS7*

"Chinese GWAS" is the meta-analysis of the two Chinese GWAS[4,5]; "European GWAS" is data from the main European GWAS[6]; "Chinese replication" are data from the Anhui Replication study; "European Replication" are data from the European replication study; "European GWAS replication" are data the European GWAS[7] independent of the main European GWAS. All SNPs pass FDR at 1% in the Chinese replication study. The SNPs above the bold line pass genome wide significance ($p < 5 \times 10^{-08}$) after meta–analysis of all studies.

Nature Genetics: doi:10.1038/ng.3603

Supplementary Table 2b: Allele information

				Chinese MAF[b]		European MAF[b]		
SNP	**Chr**	**Pos**	**Risk allele[a]**	**Cases**	**Controls**	**Cases**	**Controls**	**Gene**
rs34889541	1	198,594,769	G	0.126	0.140	0.058	0.070	*PTPRC (CD45)*
rs2297550	1	206,643,772	G	0.577	0.546	0.140	0.120	*IKBKE*
rs7579944	2	30,445,026	C	0.590	0.641	0.338	0.366	*LBH*
rs17321999	2	30,479,857	C	0.160	0.164	0.161	0.191	*LBH*
rs6762714	3	188,470,238	T	0.848	0.825	0.421	0.392	*LPP/TPRG1–AS1*
rs17603856	6	16,630,898	T	0.221	0.222	0.325	0.355	*ATXN1*
rs597325	6	91,002,494	G	0.485	0.520	0.357	0.385	*BACH2*
rs73135369	7	73,940,978	C	0.107	0.076	0.028	0.022	*GTF2IRD1–GTF2I*
rs1887428	9	4,984,530	G	0.372	0.346	0.398	0.373	*JAK2*
rs494003	11	65,542,298	A	0.116	0.117	0.213	0.190	*RNASEH2C*
rs1170426	16	68,603,798	C	0.198	0.176	0.252	0.235	*ZFP90*
rs12753920	1	92,665,899	G	0.039	0.031	0.353	0.332	*KIAA1107 – C1orf146*
rs427221	3	28,075,985	C	0.457	0.447	0.499	0.479	*EOMES – CMC1*
rs9402743	6	136,001,034	G	0.463	0.482	0.387	0.358	*AHI1*
rs7090925	10	8,479,868	A	0.183	0.195	0.268	0.310	*LINC00708*
rs4082517	10	71,704,566	G	0.047	0.054	0.121	0.141	*COL13A1*
rs11171683	12	39,693,347	G	0.104	0.135	0.454	0.492	*KIF21A*
rs7219	17	73,315,368	T(E)/C(CH)[c]	0.120	0.150	0.252	0.270	*MRPS7*

[a] The risk allele refers to the effect in the overall meta–analysis

[b] MAF refers to the frequency of allele that is minor in Europeans.

[c] This marker has opposing risk alleles in each population (T is risk in Europeans while C is risk in Chinese)

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Supplementary Table 3: Significant eQTLs identified from analysis of all cis genes (within +/- 1MB of the SNP) across the 10 novel associated SNPs.

		CD4+ T cells (Naïve)		CD14+ Monocytes		Monocytes (Naïve)	Monocyte (LPS2)	Monocyte (LPS24)	Monocyte (IFN)	B cells	NK cells
SNP	Gene	EUR	Asian	EUR	Asian	EUR	EUR	EUR	EUR	EUR	EUR
rs2297550	*IKBKE*	4.07E-04 (0.915) ↓	3.07E-07 (0.998) ↓	9.20E-02 (0.949)↑	1.65E-07 (0.998) ↑	1.52E-08 (0.986) ↑	1.87E-07 (0.962) ↑	2.07E-04 (0.990) ↑	4.87E-03 (0.012) ↓	4.93E-04 (0.950) ↓	7.34E-03 (0.005) ↓
rs17321999	*LBH*	1.14E-03 (0.927) ↓	2.54E-01 (0.918) ↓	3.67E-01 (0.567) ↓	6.47E-01 (0.786) ↓	1.22E-01 (0.653) ↓	3.56E-01 (0.550) ↓	7.07E-01 (0.603) ↓	3.35E-01 (0.744) ↓	2.04E-11 (0.880) ↓	1.97E-04 (1.000) ↓
rs494003	*CTSW*	4.23E-06 (0.911) ↓	1.37E-01 (0.523) ↓	6.98E-02 (0.988) ↓	7.00E-02 (0.653) ↓	NA	NA	NA	NA	2.79E-02 (0.381) ↓	3.01E-03 (0.978) ↓
	RNASEH2C	1.64E-05 (0.924) ↓	2.69E-02 (0.984) ↓	6.05E-05 (0.983) ↓	1.09E-01 (0.977) ↓	2.47E-03 (0.870) ↓	7.75E-01 (0.099) ↑	6.53E-01 (0.014) ↑	5.61E-01 (0.633) ↓	6.70E-02 (0.546) ↓	NA
	FIBP	2.51E-01 (0.688) ↑	6.78E-01 (0.265) ↑	2.79E-01 (0.921) ↑	1.28E-01 (0.233) ↑	2.05E-03 (0.703) ↑	1.27E-02 (0.872) ↑	1.45E-08 (0.868) ↑	2.73E-07 (0.978) ↑	7.23E-02 (0.750) ↑	NA1.8E-04 (0.989) ↑
	MUS81	8.19E-01 (0.239) ↓	4.10E-01 (0.859) ↑	1.70E-02 (0.992) ↑	4.45E-01 (0.536) ↑	2.15E-01 (0.228) ↓	3.01E-01 (0.519) ↓	1.14E-01 (0.714) ↓	8.12E-02 (0.606) ↓	1.70E-05 (0.986) ↓	NA
rs1170426	*ZFP90*	7.23E-22 (0.901) ↓	9.31E-05 (0.889) ↓	3.39E-19 (0.958) ↓	2.53E-07 (0.756) ↓	4.09E-70 (0.743) ↓	8.66E-22 (0.717) ↓	7.15E-49 (0.665) ↓	1.34E-55 (0.796) ↓	4.64E-55 (0.721) ↓	1.00E-91 (0.677) ↓

P-values for SNP/gene-expression association are displayed along with RCT scores in brackets. The arrows depict the direction of effect of the GWAS associated allele (↓ indicates that the SLE risk allele correlates with reduced gene expression, while ↑ indicates that the SLE risk allele correlates with increased gene expression). We did find a significant eQTL for rs1887428 (9p24) with *JAK2* in monocytes (resting and stimulated) however the RTC score was < 0.4 in all cases.

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Supplementary Table 4: Likely Functional Role of Causal Genes in SLE

Chr	Likely Causal Gene	Gene Function and Potential Role in SLE
1	*PTPRC (CD45)*	*PTPRC* encodes a tyrosine phosphatase, CD45, a cell surface glycoprotein widely expressed on haematopoietic cells, well known as a marker of T cell exposure to antigen. CD45 has been directly implicated in the disease process as a factor down–regulating the activity of the T cell kinase, Lck, which is characteristic of cells from individuals with SLE[8]
1	*IKBKE*	Rs2297550 is located in the 5´–UTR of *IKBKE,* which encodes the IκB kinase epsilon (IKKε). This kinase acts in two disease relevant pathways. Firstly, it regulates NF–κB activation, which influences lymphocyte growth and differentiation; this pathway is up regulated in SLE, as highlighted by another autoimmunity susceptibility gene, *UBE2L3*[9]. Secondly, IKKε regulates the type I interferon response[10]. Increased activity of type I interferon is well described in many SLE patients.
2	*LBH*	Rs1732199 is in an intron within *LBH* (a transcriptional activator) and is one of two independent signals at this locus, the second (rs7579944, Chr 2: 30,455,026) being upstream of *LBH*. The locus has been associated with rheumatoid arthritis[11] but the causal gene has not been determined. *LBH* (Limb Bud and Heart Development) has, as the name implies, been studied primarily in embyogenesis and development. Of note, it is highly expressed in both B and T cells, although its function in lymphocytes has not been established.
3	*LPP, TPRG1–AS1*	*LPP* - LIM Domain Containing Preferred Translocation Partner In Lipoma *TPRG1-AS1* (Tumor Protein P63 Regulated 1) antisense RNA 1
6	*ATXN1*	The association at rs17603856 is in an intron of *ATXN1* (6p23), a chromatin–binding factor that represses Notch signalling. The *ATXN1* gene comprises a variable triplet repeat motif, the expansion of which is associated with spino-cerebellar ataxia type 1. It is not immediately apparent that *ATXN1* is relevant to SLE, although differential expression of this gene was associated with B cell malignancy[12]. Of note is our recent mapping of an SLE association at the *SH2B3–ATNX2* locus on chromosome 12[6]. At this locus, *SH2B3* is functionally the more likely causal gene, but the mapping of SLE risk alleles within two *ATXN* genes may indicate a hitherto unknown immune function of these genes or other functional similar effect based on homology.
6	*BACH2*	The transcriptional repressor, *BACH2* regulates both the commitment to the B cell lineage during lymphopoiesis, as well as the differentiation of B cells into Ig secreting plasma cells[13].
7	*GTF2IRD1–GTF2I*	*GTF2I* (General Transcription Factor IIi) is required for the formation of functional ARID3A DNA-binding complexes and for activation of immunoglobulin heavy-chain transcription upon B-lymphocyte activation. The protein encoded by *GTF2IRD1* contains five GTF2I-like repeats and each repeat possesses a potential helix-loop-helix (HLH) motif. It may have the ability to interact with other HLH-proteins and function as a transcription factor or as a positive transcriptional regulator under the control of Retinoblastoma protein. This gene plays a role in craniofacial and cognitive development and mutations have been associated with Williams-Beuren syndrome, a multisystem

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		developmental disorder caused by deletion of multiple genes at 7q11.23. Alternative splicing results in multiple transcript variants.
9	*JAK2*	*JAK2* belongs to the Janus Kinase gene family (as does another autoimmune associated gene, *TYK2*). These kinases act to control lymphocyte function and have been shown to critically affect differentiation of T cells into Th1 and Th17 functional subsets, which express pro–inflammatory mediators such as IFN–γ and IL–17, respectively.
11	*RNASEH2C*	Ribonuclease H2 (RNase H2) is the major nuclear enzyme that degrades RNA/DNA hybrids and removes ribonucleotides misincorporated in genomic DNA. Mutations, which impair activity, in each of the three RNase H2 subunits have been implicated in Aicardi–Goutières Syndrome (AGS), an auto–inflammatory disorder characterized by excessive activity of type I interferon[14]. Individuals who are heterozygous for rare coding AGS mutations in these genes exhibit an intermediate autoimmune phenotype[15]. The risk variant that we have identified at this locus correlates with reduced expression of *RNASEH2C* transcript. Thus both common variant association and rare variant association with a closely related phenotype support a role of *RNASEH2C* in SLE pathogenesis.
16	*ZFP90*	The association at rs1170426 is in an intron of the zinc finger protein, *ZFP90*. We find an extremely strong negative correlation between the carriage of the risk allele of rs1170426 and the expression of *ZFP90* in all cell types studied (see Supplementary Fig. 2). Interestingly, it has been shown that the gene product (also known as FIK) interacts with FOXP3, where it acts to maintain the suppressor function of T regulatory cells[16].

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Supplementary Table 5: Distinct association signals at established SLE susceptibility loci for which the 99% credible set contains no more than ten variants

									99% credible set	
Locus	SNP	Chr.	Position (Build 37)	Risk allele	Other allele	RAF (EUR/CHI)	*P* value	OR (95% CI)	SNPs	Interval length (bp)	Interval position (bp)
FCGR2A	rs7551957	1	161,470,042	C	T	0.470/0.268	4.27E-13	1.20 (1.14-1.26)	6	35376	161444369 - 161479745
TNFSF4	rs12039904	1	173,212,273	T	C	0.240/0.259	3.13E-23	1.31 (1.24-1.38)	5	23943	173212273 - 173236216
STAT4	rs4274624	2	191,958,656	C	T	0.215/0.334	8.48E-85	1.69 (1.60-1.78)	8	26378	191943742 - 191970120
TCF7-SKP1	rs4388254	5	133,423,616	T	C	0.045/0.079	1.50E-11	1.39 (1.26-1.53)	7	7030	133424804 - 133431834
TNIP1	rs10036748	5	150,458,146	T	C	0.251/0.743	3.79E-23	1.31 (1.24-1.38)	3	3278	150457771 - 150461049
MIR146A	rs2431697	5	159,879,978	T	C	0.558/0.864	5.69E-20	1.28 (1.21-1.35)	2	3239	159879978 - 159883217
TYK2	rs11085725	19	10,462,513	C	T	0.708/0.415	9.17E-10	1.18 (1.12-1.25)	3	6154	10459969 - 10466123

Association summary statistics and credible set construction are based on the meta-analysis of Chinese and European ancestry. In loci with multiple distinct signals of association, results are presented from unconditional analysis. Chr., chromosome; RAF, risk allele frequency; OR, odds ratio for the risk allele; CI, confidence interval.

Nature Genetics: doi:10.1038/ng.3603

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