Supplementary Figures

A) Cross-validation of admixture analysis

C) Origin of immunogroups

Figure S1: Cross-validation scores for each value of K.
The arrow points to the selected value of 30.

B) Immunoancestries
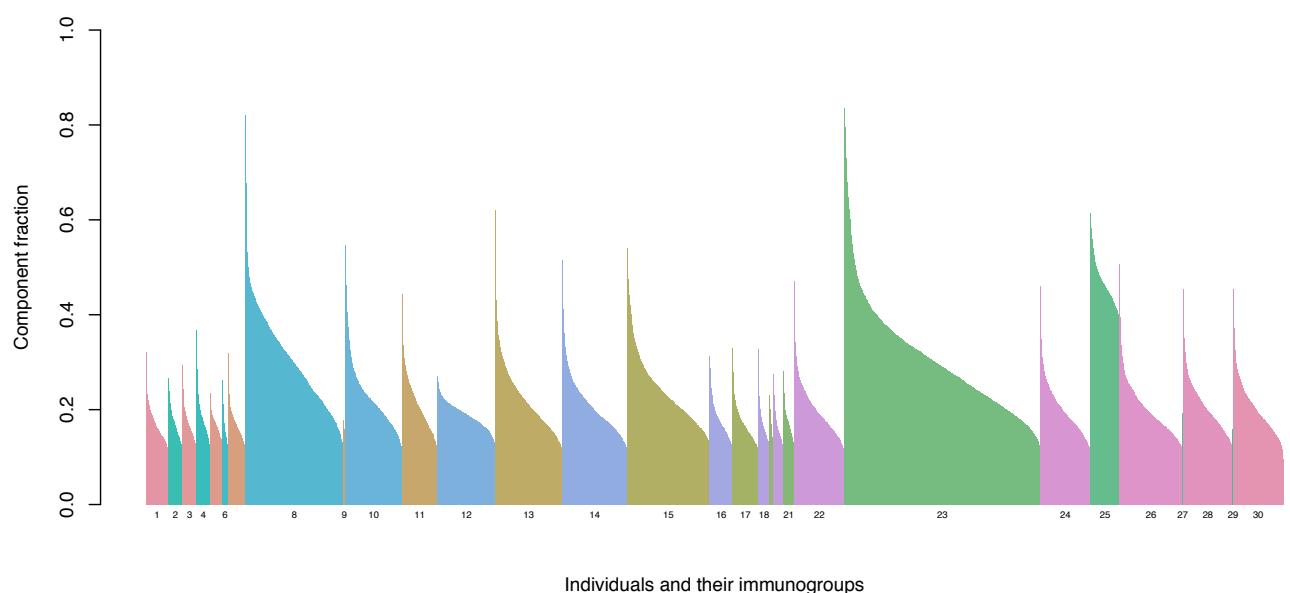
Figure S2: Assignation of each individual to an immunogroup.
Based upon his/her predominant immunoancestry when K=30.

Individuals and their immunogroups
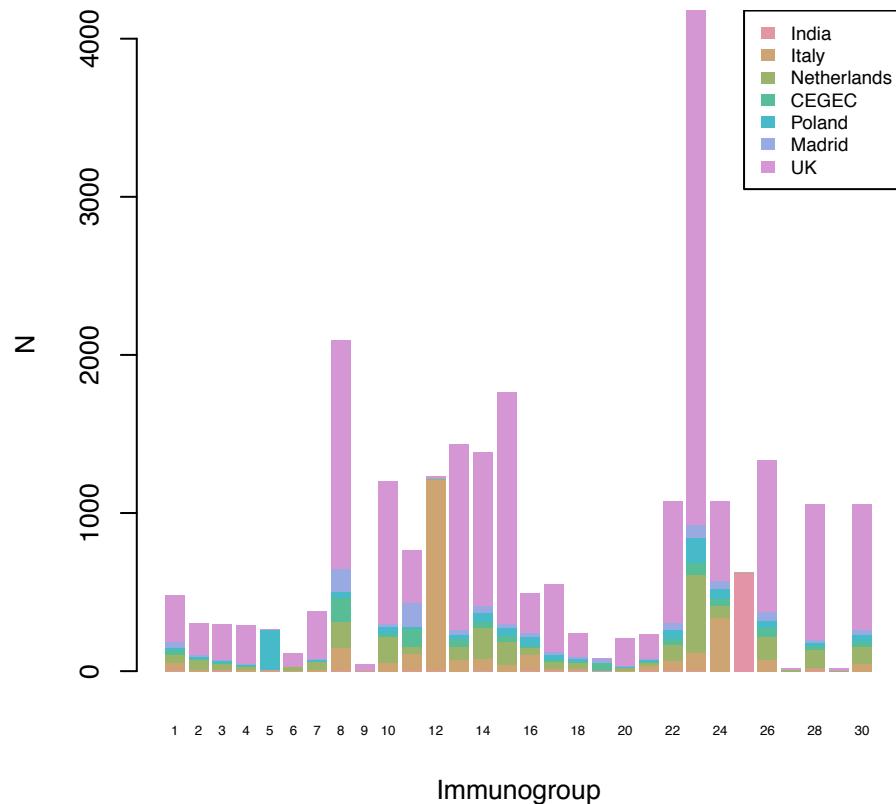
Figure S3: Distribution of the geographical origins of samples in each immunogroup.

Individuals and their immunogroups
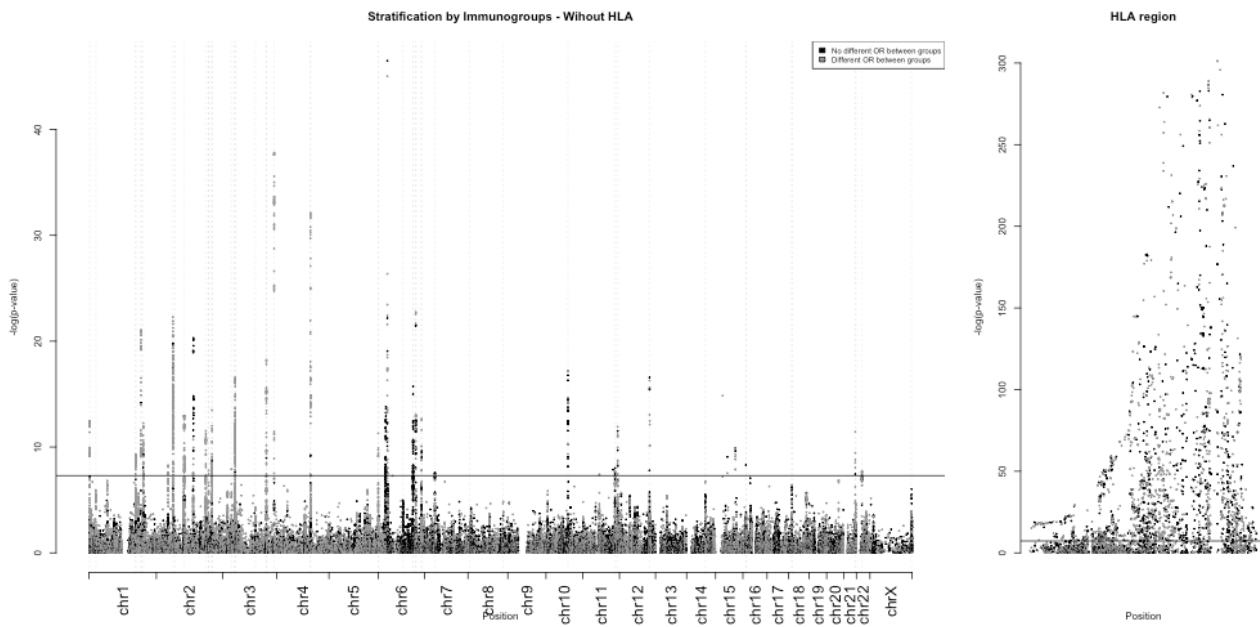
Figure S4: Manhattan-plot of association-analysis corrected by stratification of immunogroups. Vertical black line, significance cut-off used in our study; gray horizontal lines, previously described regions.
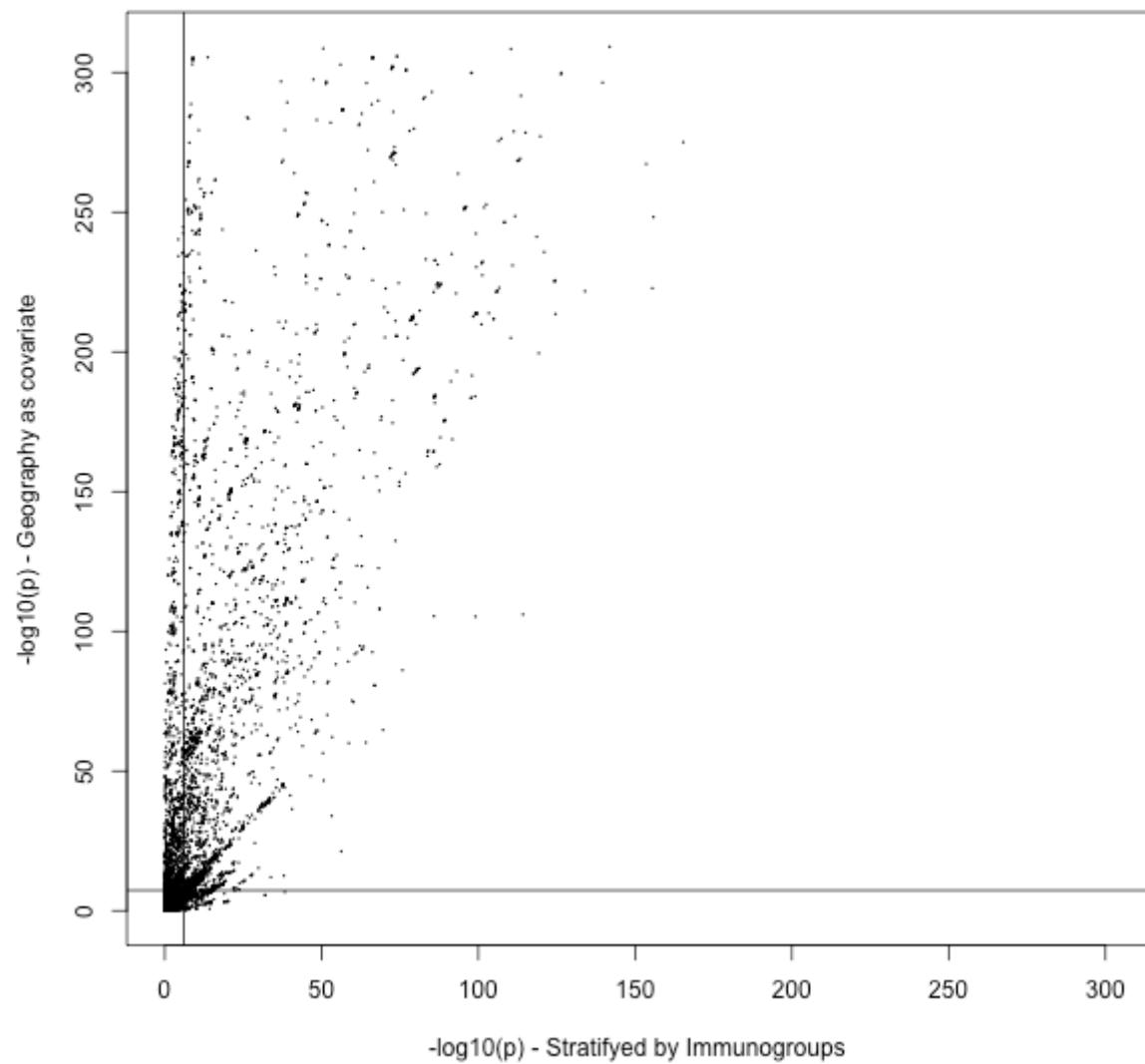
Figure S5: Comparison of results from original analysis of the Immunochip and the present study. Horizontal line, significance cut-off used in the original Immunochip analysis. Vertical line, significance cut-off used in our study.
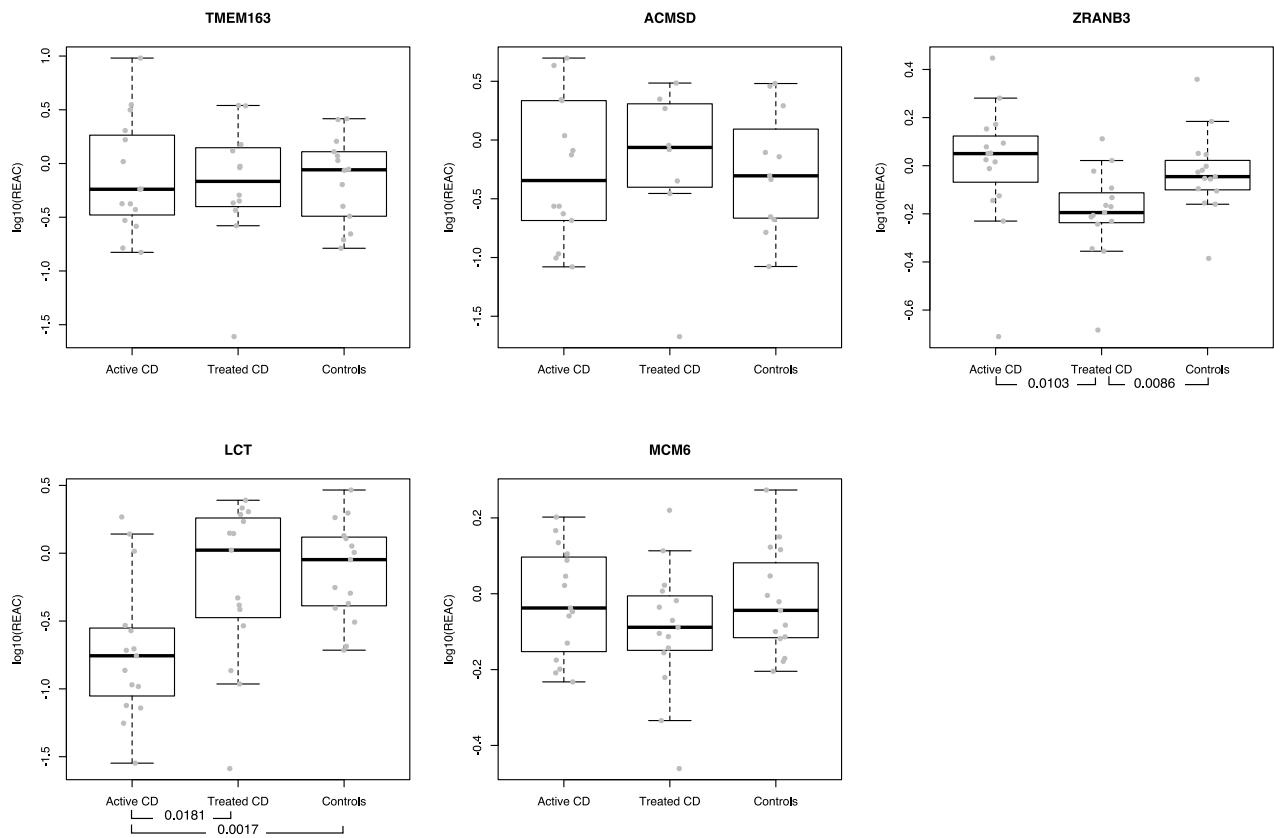
Figure S6: Expression analysis of the rest of genes from the region chr2:134533564-136169524. REAC, relative expression to average of controls; below each gene the significance of Mann-Whitney test for each comparison.
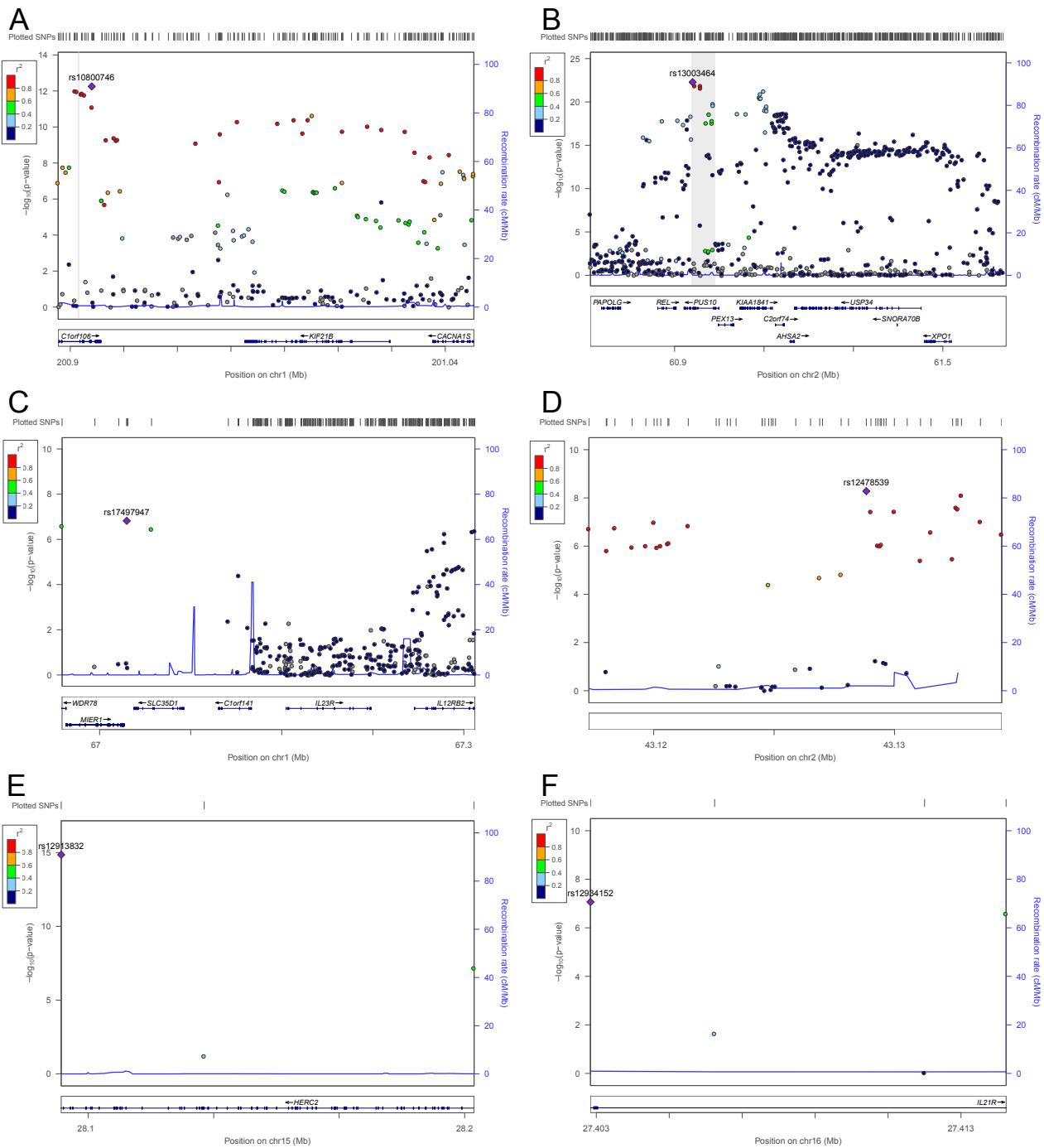
Figure S7: Representation of the rest relevant regions using Locuszoom. In gray previously described regions.
A, chr1:200899734-201054931; B, chr2:60731152-61660852; C, chr1:66920521-67373890; D, chr2:43116667-43133808; E, chr15:28120472-28285036; F, chr16:27403018-27414415.
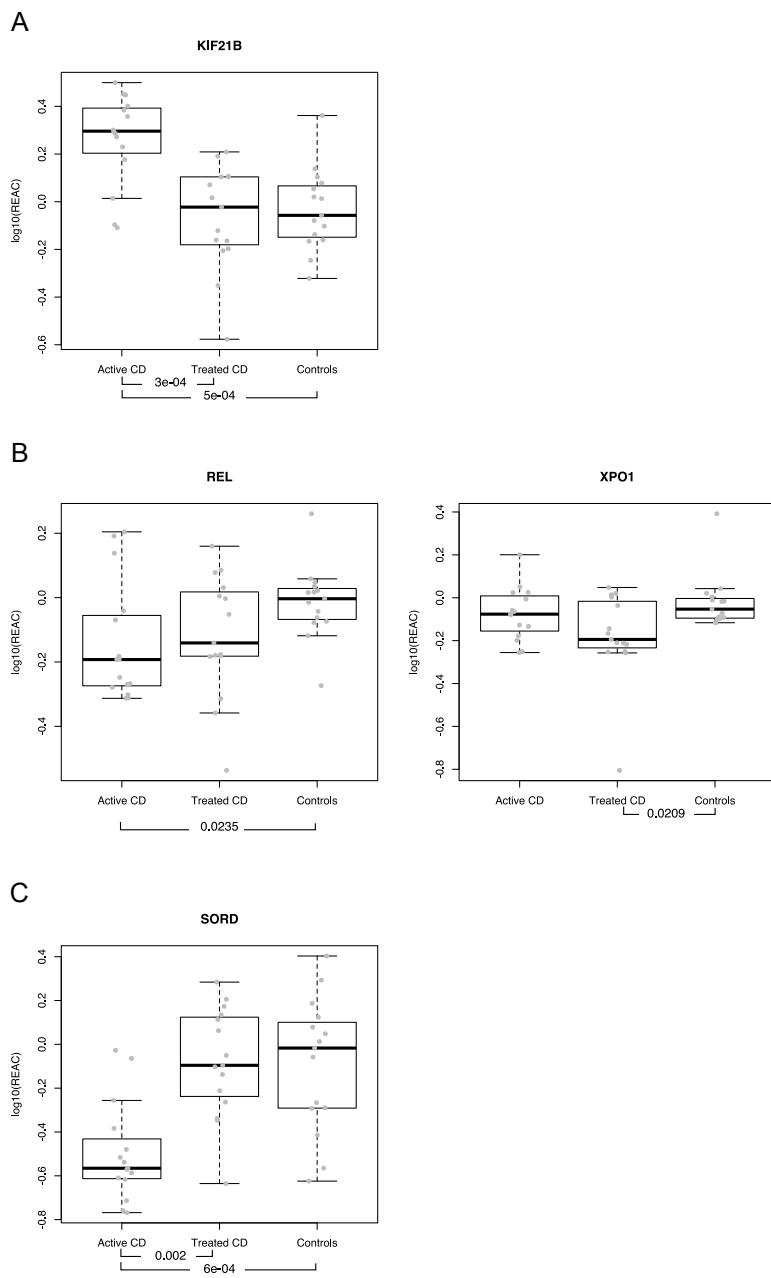
Figure S8: Expression analysis of the rest of analyzed genes.
REAC, relative expression to average of controls; below each gene the significance of Mann-Whitney test for each comparison. A, analyzed gene from chr1:200899734-201054931; B, analyzed genes from chr2:60731152-61660852; C, analyzed gene with a solitary SNP.

Table S1: Number of individuals in each immunogroup.

IG	Total	Cases	Controls
1	480	125	355
2	302	85	217
3	299	109	190
4	290	58	232
5	263	82	181
6	115	29	86
7	377	99	278
8	2091	1230	861
9	43	9	34
10	1203	885	318
11	763	478	285
12	1231	587	644
13	1431	329	1102
14	1383	434	949
15	1764	1256	508
16	489	151	338
17	548	181	367
18	242	174	68
19	81	51	30
20	207	46	161
21	236	76	160
22	1075	217	858
23	4178	3031	1147
24	1074	425	649
25	621	230	391
26	1335	1003	332
27	19	14	5
28	1054	329	725
29	19	16	3
30	1056	302	754

Table S2: Summary of significant SNPs located outside relevant regions.
[a]In the case of solitary SNPs, SNPs located 100 kilobases around.

Region (hg38)	previously reported region (hg38)	Number of significant new SNPs	Number of SNPs in the region	Top SNP (p-value; odds-ratio)	Novel candidate genes
chr1:1199862	-	1	14[a]	rs9729550:A>C; hg38 chr1:g.1199862A>C (5.714e-07; 0.8922)	-
chr1:2553995-2642288	chr1:24963243-24978061	9	113	rs4310388:G>T; hg38 chr1:g.2575976G>T (6.015e-08; 0.8934)	*TNFRSF14, LOC115110*
chr1:12173697	-	1	4[a]	rs976881:A>G; hg38 chr1:g.12173697T>C (1.934e-07; 0.8945)	*TNFRSF1B*
chr1:167451188	-	1	7[a]	rs2056626:G>T; hg38 chr1:g.167451188T>G (2.321e-07; 0.9004)	*CD247*
chr1:172718118-172890052	chr1:172704443-172895512	24	185	rs2639624:A>G; hg38 chr1:g.172792701G>A (6.033e-10; 1.14)	-
chr2:62254323-62309536	-	9	124	rs3924500:C>T; hg38 chr2:g.62305910G>A (4.3e-09; 1.2)	-
chr2:100240555	-	1	595[a]	rs12474386:A>G; hg38 chr2:g.100240555G>A (4.418e-07; 1.107)	*LINC01104*
chr2:102308763-102489875	chr2: 102291655-102476622	79	514	rs4851011:C>T; hg38 chr2:g.102473219C>T (5.07e-09; 0.8777)	-
chr2:181256403	chr2:183472533-183567488	1	359[a]	rs1371617:C>T; hg38 chr2:g.181256403A>G (3.185e-07; 0.8979)	-
chr2:191073874	chr2:191048308-191070307	1	272[a]	rs7594501:A>G; hg38 chr2:g.191073874G>A (4.674e-07; 0.8289)	-
chr2:203750149-203937382	chr2:203545673-203995238	11	359	rs73055463:G>T; hg38 chr2:g.203848084T>G (1.792e-07; 1.246)	-
chr3:32977882	-	1	113[a]	rs6764245:A>G; hg38 chr3:g.32977882G>A (2.986e-07; 1.116)	-

Region (hg38)	previously reported region (hg38)	Number of significant new SNPs	Number of SNPs in the region	Top SNP (p-value; odds-ratio)	Novel candidate genes
chr3:45902103-46604535	chr3:46442139-46463825	20	1304	rs7623238:A>G; hg38 chr3:g.46418860G>A (3.457e-08; 1.169)	-
chr3:69203748	-	1	5[a]	rs6806528:C>T; hg38 chr3:g.69203748C>T (3.84e-07; 1.184)	FRMD4B
chr3:159907756-159911578	chr3:159849517-160049519	2	10	rs9873580:C>T; hg38 chr3:g.159911578C>T (5.6e-08; 0.8412)	-
chr3:188415798	-	1	144[a]	rs116392971:C>T; hg38 chr3:g.188415798T>C (2.357e-07; 0.7522)	-
chr4:26909378	-	1	2[a]	rs12642608:C>T; hg38 chr4:g.26909378T>C (4.767e-07; 0.9032)	STIM2
chr4:122053452	-	1	52[a]	rs10516615:A>G; hg38 chr4:g.122053452A>G (6.326e-07; 0.8627)	-
chr4:122600025-122602201	chr4:122128437-122629959	7	14	rs6820791:C>T; hg38 chr4:g.122600628C>T (4.163e-08; 0.8945)	-
chr6:382559-421281	chr6:375000-455000	4	91	rs7773324:A>G; hg38 chr4:g.382559G>A (1.989e-10; 1.139)	-
chr7:37360866-37362887	chr7:37360866-37398274	2	4	rs111796602:C>T; hg38 chr7:g.37362887T>C (8.868e-08; 1.184)	-
chr7:74615423	-	1	62	rs6460086:G>T; hg38 chr7:g.74615423T>G (1.857e-07; 1.186)	-
chr10:79941767	-	1	5	rs911887:A>G; hg38 chr10:g.79941767T>C (1.915e-07; 0.9)	SFTPD
chr10:102135182	-	1	1[a]	rs4919611:A>C; hg38 chr10:g.102135182C>A (5.523e-07; 1.161)	PPRC1
chr11: 61057137-61057550	-	2	3	rs175112:A>T; hg38 chr11:g.61057550A>T (3.907e-08; 1.123)	-

Region (hg38)	previously reported region (hg38)	Number of significant new SNPs	Number of SNPs in the region	Top SNP (p-value; odds-ratio)	Novel candidate genes
chr11:128507585-128549329	-	4	75	rs4396302:A>G; hg38 chr11:g.128549329G>A (3.67e-07; 0.902)	-
chr15:46772530	-	1	2[a]	rs11637803:C>T; hg38 chr15:g.44852020T>C (2.94e-08; 1.492)	-
chr15:46946227	-	1	2[a]	rs11636774:A>C; hg38 chr15:g.45025717A>C (8.634e-10; 1.416)	*SORD*
chr15: 74770056-74833304	chr15:74318390-75191270	6	11	rs1378942:G>T; hg38 chr15:g.74785026C>A (1.244e-10; 1.144)	-
chr17:8144851	-	1	5[a]	rs2253820:A>G NC; hg38 chr17:g.8144851T>C (5.254e-07; 1.144)	-
chr21:42446949-42455624	chr21:42389975-42467035	6	26	rs9680344:A>G; hg38 chr21:g.42454314A>G (3.54e-10; 0.8796)	-

Table S3: relative expression values of analyzed genes. GFD: CD patient on gluten-free diet

Sample ID	disease status	ACMSD	CCNT2	DARS	KIF21B	LCT	MAP3K19	MCM6	R3HDM1	RAB3GAP1	REL	SORD	TMEM163	XPO1	ZRANB3
23017	Active	0.0991	0.5652	0.8222	3.1598	0.0754	0.0000	0.5856	0.5271	0.4724	0.5648	0.1706	0.4215	0.5609	0.9727
23014	Active	0.2732	0.5972	0.5678	2.2777	0.1041	0.0000	0.6327	0.5444	0.5261	0.4880	0.1742	0.2953	0.6331	0.5886
24051	Active	0.2734	0.7145	0.6968	2.5174	1.8507	0.0000	0.8737	0.7061	0.9003	0.8521	0.8622	0.3729	0.7348	0.7168
26047	Active	1.0893	0.5633	0.7791	2.4231	0.2934	0.0000	1.0516	0.6531	0.7800	0.5404	0.2897	1.0426	0.8728	1.0372
25016	Active	0.8148	1.0581	1.2466	2.8033	1.3848	0.0000	1.3639	0.9724	1.4051	1.5538	0.5545	3.1556	0.8330	1.4842
25022	Active	0.0000	0.8043	1.1126	2.8295	1.0345	0.0000	1.5927	0.5977	1.8580	1.6010	0.9385	0.1490	1.0561	2.8016
23040	Active	0.1073	0.4429	0.6419	1.6985	0.1975	0.0000	0.6184	0.6323	0.5604	0.6419	0.3047	1.6641	0.6653	0.7497
23057	Active	0.2358	0.6303	0.7679	1.9356	0.0723	0.0000	0.7408	0.8117	0.6392	0.9094	0.2590	0.2603	1.5869	1.1281
23068	Active	0.0833	0.6224	0.6431	1.9773	0.1754	0.0000	0.6684	0.6265	0.5928	0.4992	0.2419	0.1635	0.8385	1.0591
27050	Active	0.2065	0.5094	0.7625	0.8013	0.1072	0.0000	0.8968	0.5927	0.5777	0.4864	0.2719	0.5759	0.7463	1.4217
27056	Active	2.1643	0.6576	0.9096	1.0328	0.1924	0.0000	1.2252	0.6160	0.6938	0.5375	0.2456	3.5159	0.8627	1.1228
28049	Active	4.9842	0.9305	1.2373	1.8705	0.1368	0.0000	1.1124	0.8932	0.8061	0.6434	0.2687	9.5762	0.9853	1.2417
25061	Active	2.2063	0.7533	1.0773	1.9974	0.2686	0.0000	1.4673	0.7862	1.1979	0.6571	0.4135	2.0246	1.1243	1.1977
25037	Active	0.7477	0.4672	0.9152	0.7787	0.0558	0.0000	0.9171	0.5854	0.5296	0.5265	0.1934	0.4224	0.5551	0.1948
24052	Active	4.3109	0.7921	1.3068	1.5030	0.0283	0.0000	1.2743	0.6505	1.7905	1.3744	0.3313	0.5797	1.0602	1.9095
25052	GFD	0.0000	0.5295	0.5957	1.2715	1.4060	0.0000	0.7859	0.5002	0.6829	0.4851	1.1549	0.0245	0.5621	0.7374
25040	GFD	0.9015	1.0661	0.9770	1.2790	2.1547	0.0000	1.6599	0.9302	1.3543	1.2165	0.8021	0.4477	0.9203	1.2940
27031	GFD	0.4481	0.1574	0.1438	0.9494	0.0259	0.0000	0.6014	0.5385	0.2783	0.2905	0.4589	1.3112	0.1566	0.6844
28050	GFD	2.2294	0.6907	0.7024	1.0389	0.4143	0.0000	0.6990	0.5154	0.6532	0.7231	0.2315	3.4396	1.1166	0.4411

Sample ID	disease status	ACMSD	CCNT2	DARS	KIF21B	LCT	MAP3K19	MCM6	R3HDM1	RAB3GAP1	REL	SORD	TMEM163	XPO1	ZRANB3
27005	GFD	0.0000	0.5737	0.7573	1.6180	2.4582	0.0000	0.8157	0.6770	1.0006	0.8867	1.9230	0.4293	0.7181	0.6385
27023	GFD	0.0000	0.3449	0.7234	0.6233	0.1364	0.0000	0.3460	0.3076	0.4205	0.4381	0.7290	0.0000	0.6062	0.5875
25080	GFD	0.0000	0.3582	0.6434	0.6856	0.4684	0.0000	0.8506	0.5799	0.7059	0.6618	0.5450	0.3675	0.5582	0.6220
25085	GFD	0.0000	0.8782	1.1916	1.5529	1.7141	0.0000	1.0531	0.7110	1.4145	1.4444	1.6049	0.0000	1.0334	0.2074
25087	GFD	0.0000	0.9967	0.9367	1.2715	1.9299	0.0000	1.2979	0.8247	1.5733	1.0736	1.2985	0.5077	1.0489	0.9491
29091	GFD	0.3509	0.9313	0.9037	0.6351	1.0539	0.0000	1.0161	1.0343	0.9774	0.9928	1.4899	0.9155	1.0070	1.0508
29109	GFD	0.0212	0.5587	0.7156	0.2650	1.3962	0.0000	0.9217	0.5886	0.6723	0.6595	1.3628	0.0000	0.6816	0.6128
210051	GFD	3.0543	1.0005	0.9696	0.7566	2.0244	0.0000	0.9589	0.6534	0.9547	1.1966	0.7896	3.4672	0.6145	0.4519
27057	GFD	0.8297	0.8041	0.7121	0.4454	0.3850	0.0000	0.7193	0.4923	0.5959	0.6558	0.8901	1.4997	0.6390	0.8074
27035	GFD	0.0000	0.5147	0.7963	1.1776	0.2917	0.0000	0.4630	0.6258	0.6722	0.6651	0.6139	0.9432	0.5530	0.5718
26060	GFD	1.8542	0.6418	0.8445	0.6907	0.1087	0.0000	0.7710	0.7077	0.9012	1.0105	0.4491	0.2636	0.6164	0.6757
24012	Control	2.8736	0.8746	0.9601	0.5678	0.5587	0.0000	0.6752	0.8696	0.8146	0.8365	0.5099	0.3996	0.7981	0.8860
21013	Control	0.0000	2.3894	2.0341	2.2992	2.9244	0.0000	1.8773	2.6514	2.8176	1.8221	1.1179	0.0000	2.4646	2.2849
29129	Control	0.7211	0.9323	0.9418	0.4767	1.2821	0.0000	1.3069	0.7715	1.0189	0.8667	0.5419	1.1758	0.9636	1.5278
210006	Control	0.0000	1.0217	1.1313	0.8768	0.3105	0.0000	1.1140	1.0160	0.8594	1.0828	0.2724	0.3231	0.8849	0.8020
210007	Control	0.4959	0.7272	0.7967	1.3738	1.0132	0.0000	0.9898	0.6151	0.5588	0.5329	0.2375	1.2875	0.7921	0.4118
210008	Control	0.7840	0.9172	1.0092	1.1328	1.3483	0.0000	1.4125	0.7386	0.9965	0.8441	1.0304	1.0667	0.9600	0.9397
211073	Control	0.0000	0.8917	0.7743	0.7899	1.9779	0.0000	1.3270	0.8895	0.7582	1.0375	1.3283	0.1953	0.7648	0.6993
211074	Control	3.0264	0.7758	1.0813	1.0472	0.3936	0.0000	0.7700	0.9813	0.8684	1.1145	0.8744	2.6105	0.9755	1.1250
211075	Control	0.0000	0.8303	0.9458	1.2704	0.1928	0.0000	0.6244	1.0201	0.7813	1.0524	1.1961	1.6100	1.0492	0.6916

Sample ID	disease status	ACMSD	CCNT2	DARS	KIF21B	LCT	MAP3K19	MCM6	R3HDM1	RAB3GAP1	REL	SORD	TMEM163	XPO1	ZRANB3
211078	Control	0.2106	0.9720	0.8886	0.6824	0.8971	0.0000	0.9530	1.0210	0.9057	0.9668	0.5132	0.2212	0.8141	0.9579
211084	Control	0.0838	0.8855	0.8687	0.8329	0.5072	0.0000	0.6632	0.8315	1.1664	0.7611	2.5304	0.1626	0.7658	1.1129
211090	Control	0.1637	0.8619	0.7906	0.7285	1.8327	0.0000	0.7948	0.8928	0.8925	0.9059	0.9616	0.8636	0.8084	0.8802
211091	Control	0.2221	1.1078	1.0998	1.0307	0.2060	0.0000	0.7616	1.0960	1.0841	1.1438	1.9629	0.8843	1.1032	0.9007
211096	Control	0.4612	0.7939	0.6803	1.1993	1.1296	0.0000	0.8265	0.6846	0.6497	1.0408	1.5376	0.6369	1.0094	0.9947
211101	Control	1.9575	1.0187	0.9973	0.6915	0.4260	0.0000	0.9040	0.9210	0.8281	0.9920	0.3855	2.5627	0.8462	0.7855