

**Genome-wide association defines more than thirty distinct susceptibility loci for
Crohn's disease [Supplementary Information]**

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Supplementary Tables

Supplementary Table 1: 129 SNPs from 74 distinct loci followed up in replication

samples

Locus	SNP	Chr	Position	Scan	p values		Replication data?			
					Replication	Combined	N	U	B	F
1	rs11465804	1	67414547	5.05E-36	3.1E-29	3.33E-63	1	1	1	1
1	rs11209026	1	67417979	3.19E-34	1.5E-36	2.15E-68	1	1	1	1
1	rs11805303	1	67387537	1.35E-24	5.62E-17	1.82E-39	1	1		
2	rs2066844	16	49303427	NAN	NAN	NAN				
2	rs2066845	16	49314041	NAN	4.62E-08	4.62E-08	1	1		
2	rs2066847	16	49321280	NAN	1.49E-24	1.49E-24	1	1		
3	rs4613763	5	40428485	2.51E-22	2.79E-08	3.09E-27	1	1	1	1
3	rs17234657	5	40437266	2.26E-22	3.18E-08	3.41E-27	1	1	1	1
4	rs2241880	2	233965368	1.28E-21	3.66E-05	4.61E-25	1			
4	rs3828309	2	233962410	5.66E-21	7.67E-14	1.18E-32	1	1	1	1
5	rs10995271	10	64108492	9.51E-12	1.61E-10	2.23E-20		1	1	1
6	rs2542151	18	12769947	5.95E-12	2.41E-07	2.55E-17	1	1	1	1
6	rs1893217	18	12799340	3.27E-11	1.23E-06	7.05E-16	1	1	1	1
7	rs11190140	10	101281583	8.53E-11	1.69E-07	1.53E-16	1	1	1	
7	rs10883371	10	101282445	9.09E-11	3.1E-07	3.05E-16	1	1	1	
8	rs11747270	5	150239060	3.18E-11	2.57E-07	1.7E-16	1	1	1	1
8	rs13361189	5	150203580	4.09E-11	7.47E-07	7.33E-16	1	1	1	1
9	rs2188962	5	131798704	2.29E-09	3.52E-11	1.16E-18	1	1	1	1
9	rs1050152	5	131704219	NAN	1.54E-06	1.54E-06	1	1	1	
10	rs2024092	19	1075031	6.48E-09	0.021	1.18E-09		1		
10	rs4807569	19	1074378	5.8E-09	0.00347	1.06E-09	1	1	1	1
11	rs10045431	5	158747111	4.4E-09	3.66E-06	1.93E-13	1	1	1	1
12	rs3763313	6	32484449	7.23E-09	0.00602	2.6E-09	1	1	1	1
12	rs2858331	6	32789255	1.53E-08	0.00382	2.17E-09	1	1	1	1
13	rs3924462	3	49499240	2.42E-08	0.194	3.56E-08	1			
13	rs6784820	3	49425868	2.84E-08	0.107	1.2E-07	1	1		
13	rs3197999	3	49696536	1.08E-07	5.64E-07	5.76E-13	1	1	1	1
13	rs9858542	3	49676987	9.47E-08	2.24E-06	3.55E-12			1	1
14	rs3764147	13	43355925	8.04E-08	1.33E-07	1.04E-13	1	1	1	1
14	rs9562532	13	43497789	6.9E-07	0.00882	1.44E-07	1	1	1	1
15	rs11175593	12	38888207	6.64E-08	0.000165	1.54E-10	1	1	1	1
15	rs11564144	12	39104262	8.95E-08	6.55E-05	6.36E-11	1	1	1	1
16	rs6908425	6	20836710	1.26E-07	0.000278	4.48E-10	1	1	1	1
16	rs7748720	6	20797924	1.83E-07	0.0288	1.64E-07		1	1	1
17	rs7927894	11	75978964	7.16E-08	0.000732	6.6E-10		1	1	1
18	rs2301436	6	167408399	1.65E-07	3.26E-07	5.22E-13	1	1	1	1
18	rs7749278	6	167405736	1.65E-07	0.00121	1.58E-09	1	1		
19	rs9286879	1	169593891	2.01E-07	0.000321	7.66E-10	1	1	1	1
19	rs10489276	1	169594596	1.9E-07	0.026	9.01E-08	1		1	1
20	rs4263839	9	114645994	1.96E-07	6.58E-05	1.3E-10	1	1	1	1

20	rs6478109	9	114648320	1.31E-07	0.00422	3.67E-09	1			
21	rs2738758	20	61820069	2.04E-07	0.33	2.66E-06			1	1
21	rs2297441	20	61798026	7.6E-07	0.000138	1.3E-09		1		
22	rs11584383	1	197667523	3.41E-07	2.34E-06	7.17E-12	1	1	1	1
22	rs2297909	1	197691964	9.69E-07	0.0001	8.1E-10	1	1		
23	rs9545740	13	80973593	2.64E-07	0.0329	0.000554			1	1
23	rs6563216	13	80961793	1.61E-07	0.372	0.000223	1	1	1	1
24	rs2274910	1	157665119	1.75E-07	0.000481	7.3E-10		1	1	1
24	rs11265519	1	157691986	2.98E-07	0.0277	3.82E-07		1	1	1
25	rs2283790	22	20281207	8.65E-07	0.493	4.55E-05	1	1		
25	rs5754217	22	20264229	1.25E-06	0.325	6.26E-06		1		
26	rs12529198	6	5096246	3.54E-07	0.0192	3.48E-07	1	1	1	1
27	rs12604993	18	75866208	1.38E-06	0.256	0.00028	1	1		
27	rs12607007	18	75865061	2.11E-06	0.108	0.00692	1	1	1	1
28	rs6128541	20	57351084	1.73E-06	0.101	1.18E-05	1	1	1	1
29	rs12985909	19	18300383	5.43E-08	0.0526	7.54E-07	1	1	1	1
30	rs2872507	17	35294289	1.06E-06	0.000292	2.5E-09		1	1	1
30	rs2305480	17	35315722	3.41E-06	0.419	5.45E-05		1		
31	rs17309827	6	3378317	1.04E-06	0.0391	1.37E-06	1	1	1	1
31	rs4959830	6	3379241	1.15E-06	0.0582	2.83E-06	1	1	1	1
32	rs5974	4	187576360	1.35E-06	0.0865	7.81E-06	1	1	1	1
32	rs4253431	4	187585769	1.34E-06	0.107	1.33E-05	1	1	1	1
33	rs707472	1	7840274	1.47E-06	0.0541	3.63E-06	1	1	1	1
33	rs707458	1	7766478	1.45E-05	0.211	6.82E-05	1		1	1
34	rs10512670	5	37949301	1.74E-06	0.273	2.41E-05	1		1	1
34	rs11959616	5	37948752	1.06E-05	0.441	0.000478		1	1	1
35	rs921720	8	126603853	1.9E-06	0.000182	2.78E-09	1	1		
35	rs1551398	8	126609233	2.45E-06	0.000109	2.25E-09	1	1	1	1
36	rs744166	17	37767727	2.97E-06	9.15E-08	3.41E-12	1	1	1	1
36	rs12948909	17	37824128	7.42E-06	0.0074	7.1E-07	1	1	1	1
37	rs10753415	1	222692358	2.73E-06	0.393	5.08E-05	1	1		
38	rs991804	17	29611838	2.01E-06	0.0135	5.34E-07	1	1	1	1
38	rs8064381	17	29849794	1.25E-05	0.0961	1.01E-05			1	1
39	rs158865	18	54054001	5.56E-06	0.207	1.97E-05	1	1		
39	rs158862	18	54054701	9.4E-06	0.195	0.00528	1	1	1	1
40	rs17582416	10	35327656	4.24E-06	2.53E-05	8.93E-10		1	1	1
40	rs3936503	10	35589263	6.05E-06	0.000176	8.04E-09		1	1	1
41	rs7759649	6	21578398	4.97E-06	0.0678	5.02E-06	1		1	1
41	rs11758386	6	21565929	1.09E-05	0.123	3.4E-05	1	1	1	
42	rs7161377	14	75071147	4.71E-06	0.152	2.25E-05		1	1	1
42	rs175718	14	75056332	1.28E-05	0.331	0.000222	1		1	1
43	rs7758080	6	149618772	3.64E-06	0.044	4.39E-06	1	1	1	1
44	rs559928	11	63906946	4.74E-06	0.245	7.44E-06	1			
44	rs596308	11	63967228	1.6E-05	0.0882	3.45E-05	1	1	1	1
45	rs10863202	16	84545499	4.74E-06	0.226	1.4E-05			1	1
45	rs1915033	16	84542932	0.000344	0.278	0.00239	1			
46	rs1200610	1	181883035	1.04E-05	0.388	0.000932		1	1	1
47	rs4073149	15	72685472	5.81E-06	0.0771	0.0127	1	1	1	1
47	rs7497036	15	72660732	7.44E-06	0.273	0.00133		1	1	1

48	rs10758669	9	4971602	3.4E-07	0.00043	1.73E-09	1	1	1	
48	rs7849191	9	4978761	1.96E-06	0.00162	4.34E-08	1	1	1	
49	rs743479	21	44436378	5.21E-06	0.000361	1.43E-08	1	1		
49	rs762421	21	44439989	5.41E-06	1.59E-05	7.04E-10	1	1	1	1
50	rs13003464	2	61098480	3.82E-06	0.00565	1.57E-07	1	1		
50	rs10188217	2	61129193	3.07E-06	0.0028	6.36E-08	1	1		
51	rs7746082	6	106541962	1.85E-06	7.7E-06	1.22E-10	1	1	1	1
52	rs6743984	2	230934834	7.59E-06	0.0544	2.48E-06		1		
52	rs13397985	2	230916728	8.93E-06	0.0843	9.04E-06	1	1		
53	rs2836757	21	39215894	8.73E-06	0.263	0.000165	1	1	1	1
54	rs11931489	4	7649390	3.24E-06	0.352	5.27E-05	1	1		
55	rs2688610	10	75324937	1.12E-05	0.104	3.32E-05	1	1	1	1
55	rs2675671	10	75302766	1.23E-05	0.0314	3.03E-06	1	1		
56	rs12827915	12	13070503	8.89E-06	0.435	0.000327	1	1		
56	rs3825272	12	13046606	4.05E-05	0.455	0.000751	1	1		
57	rs1260326	2	27642591	3.44E-05	0.0108	2.3E-06	1	1		
57	rs780094	2	27652888	3.62E-05	0.00381	1.15E-06	1	1	1	1
58	rs6708413	2	102521887	1.02E-05	0.016	1.45E-06	1		1	1
58	rs917997	2	102529086	1.08E-05	0.0493	1.11E-05	1	1	1	1
59	rs7227145	18	59311578	1.01E-05	0.498	0.000948	1	1	1	1
60	rs1736020	21	15734423	1E-05	0.000444	3.36E-08	1	1		
60	rs1736135	21	15727091	1.03E-05	4.58E-05	3.7E-09	1	1	1	1
61	rs1040092	12	58052436	1.14E-05	0.289	0.00345	1	1	1	1
61	rs1996199	12	58059725	2.84E-05	0.149	3.97E-05			1	1
62	rs4543904	10	1453158	7.72E-06	0.29	0.000756	1	1		
63	rs9319943	18	55030807	1.75E-05	0.304	0.00106	1	1		
63	rs9961822	18	55028896	8.34E-06	0.356	0.0018	1	1	1	1
64	rs8098673	18	17927329	1.59E-05	0.0443	1.44E-05	1	1	1	1
65	rs1456896	7	50081722	1.58E-05	9.41E-06	1.39E-09	1	1	1	
65	rs1456893	7	50046933	2.46E-05	1.1E-05	2.3E-09	1	1	1	1
66	rs2944533	10	132842492	2.65E-05	0.441	0.000388	1	1		
67	rs10010325	4	106463957	6.25E-06	0.271	5.03E-05	1	1		
68	rs9829140	3	133674827	6.84E-06	0.161	6.21E-05	1	1	1	1
69	rs6679677	1	114015850	7.75E-06	8.25E-05	4.95E-09		1	1	1
69	rs2476601	1	114089610	9.05E-06	0.000101	7.3E-09	1	1	1	1
70	rs8111071	19	50999246	1.95E-05	0.46	0.00132	1	1	1	
71	rs17814449	7	130385443	1.24E-05	0.381	0.000964	1	1	1	1
72	rs6987445	8	83235127	1.32E-05	0.223	0.000128		1	1	1
73	rs3011410	10	122495603	2.08E-05	0.363	0.000198	1	1		
74	rs1784493	8	107743073	2.59E-05	0.143	0.0136	1	1	1	1
74	rs1580428	8	107779719	2.92E-05	0.314	0.00278		1	1	1

Final four columns show success of replication experiments: **N** - North American family samples, **U** - UK unrelated case/control samples, **B** - Belgian unrelated case/control samples, **F** - French family samples.

Supplementary Table 2: Nominally significant SNP-SNP interactions

SNP1	SNP2	P
rs11265519	rs4613763	0.0496
rs11265519	rs2188962	0.001713
rs11265519	rs3764147	0.007312
rs9286879	rs13003464	0.0368
rs9286879	rs1456893	0.04274
rs9286879	rs7849191	0.006887
rs11584383	rs6743984	0.01683
rs11584383	rs11747270	0.0243
rs780094	rs917997	0.03249
rs780094	rs6784820	0.02849
rs780094	rs7746082	0.04362
rs780094	rs1456893	0.00265
rs780094	rs7849191	0.04246
rs780094	rs10995271	0.02404
rs780094	rs744166	0.02902
rs780094	rs2542151	0.00169
rs780094	rs4807569	0.02133
rs13003464	rs2301436	0.02274
rs13003464	rs10995271	0.04577
rs13003464	rs2542151	0.01959
rs917997	rs6784820	0.02225
rs917997	rs4613763	0.03703
rs917997	rs7758080	0.02673
rs917997	rs17582416	0.02064
rs917997	rs8098673	0.01276
rs6743984	rs17582416	0.03731
rs3828309	rs2301436	0.03148
rs3828309	rs1736135	0.02527
rs6784820	rs7758080	0.0327
rs6784820	rs2301436	0.04931
rs6784820	rs10995271	0.03066
rs6784820	rs3764147	0.008501
rs4613763	rs7758080	0.0006182
rs2188962	rs7758080	0.02726
rs2188962	rs2872507	8.17E-05
rs11747270	rs2301436	0.03407
rs11747270	rs2872507	0.03232
rs11747270	rs1736135	0.04903
rs17309827	rs6908425	0.02921
rs17309827	rs2542151	0.01143
rs17309827	rs1736135	0.04143
rs12529198	rs17582416	0.04465
rs12529198	rs2066847	0.02834
rs6908425	rs1456893	0.04442
rs6908425	rs762421	0.002305
rs11758386	rs1456893	0.03435

rs7746082	rs7849191	0.001362
rs7746082	rs4263839	0.02635
rs7746082	rs10995271	0.01366
rs7746082	rs8098673	0.03668
rs7758080	rs3764147	0.03878
rs7849191	rs17582416	0.0345
rs7849191	rs2542151	0.008799
rs17582416	rs11190140	0.025
rs10995271	rs6128541	0.02217
rs11190140	rs2542151	0.0007632
rs2066847	rs991804	0.04447
rs2066847	rs2872507	0.001565
rs991804	rs8098673	0.002871
rs2872507	rs6128541	0.04778
rs744166	rs2542151	0.02249
rs2542151	rs8098673	0.04003
rs8098673	rs762421	0.01574

Supplementary Table 3: Crohn's risk loci containing a highly correlated non-synonymous SNP.

Chr	Position (Mb)	Gene(s)	nsSNP(s)
1	67.4	<i>IL23R</i>	rs11209026
1	113.79 - 114.17	<i>PTPN22, DCLRE1B</i>	rs2476601, rs12022378
2	230.9	<i>ATG16L1</i>	rs2241880
3	48.73 - 49.87	<i>MST1</i>	rs3197999
5	131.44 - 131.90	<i>SLC22A4</i>	rs2631367
12	38.61 - 39.31	<i>MUC19</i>	rs4768252, rs4768253, rs2114566, rs17467164, rs11564170, rs10506156, rs11564125
13	43.13 - 43.54	<i>C13orf31</i>	rs3764147
16	49.3	<i>NOD2</i>	rs2066844, rs2066845, rs2066847
17	34.63 - 35.34	<i>GSDML</i>	rs2305480, rs2305479

Supplementary Table 4: cis-eQTL effects for CD associated SNPs

SNP	Chr	Gene	LOD score	Distance SNP-gene
rs2188962	5	SLC22A5	2.9	39,502
rs2858331	6	HLA-DRB4	4.2	
rs17582416	10	CREM	4.3	128,151
rs3764147	13	C13orf31	4.2	0
rs2872507	17	GSDML	2.6	122,801
		ORMDL3	20.3	139,249

Supplementary Table 5. Allele frequencies in all control groups for 40 loci showing at least nominal replication

SNP	CHR	POS	UK	B/F	NA/J	NA/NJ
rs11465804	1	67414547	0.0625	0.0848	0.1035	0.0648
rs2476601	1	114089610	0.1081	0.0826	0.0541	0.0973
rs2274910	1	157665119	0.3327	0.3146	0.3022	0.3241
rs9286879	1	169593891	0.2369	0.2511	0.2565	0.2713
rs11584383	1	197667523	0.3163	0.2691	0.2536	0.3048
rs780094	2	27652888	0.3831	0.4798	0.5334	0.3954
rs13003464	2	61098480	0.372	0.3884	0.4757	0.3894
rs917997	2	102529086	0.2186	0.2423	0.2247	0.213
rs3828309	2	233962410	0.4802	0.4497	0.3968	0.4938
rs3197999	3	49696536	0.2578	0.2872	0.4281	0.2976
rs4613763	5	40428485	0.1246	0.1204	0.0812	0.1226
rs2188962	5	131798704	0.4309	0.4469	0.4248	0.4153
rs11747270	5	150239060	0.0679	0.0886	0.1418	0.0852
rs10045431	5	158747111	0.2979	0.2943	0.3675	0.3051
rs17309827	6	3378317	0.3749	0.3643	0.3875	0.383
rs12529198	6	5096246	0.0527	0.064	0.0738	0.0591
rs6908425	6	20836710	0.2299	0.2051	0.2053	0.2168
rs3763313	6	32484449	0.1875	0.1767	0.1734	0.1907
rs7746082	6	106541962	0.2885	0.2746	0.3039	0.3158
rs7758080	6	149618772	0.2718	0.2555	0.3847	0.2812
rs2301436	6	167408399	0.4728	0.4595	0.4318	0.462
rs1456893	7	50046933	0.3205	0.2992	0.2652	0.2946
rs7800941	7	114534019	0.156	0.1685	0.1978	0.1768
rs1551398	8	126609233	0.3917	0.4015	0.4083	0.4112
rs10758669	9	4971602	0.3359	0.343	0.3791	0.3442
rs4263839	9	114645994	0.3282	0.3282	0.2241	0.3058
rs17582416	10	35327656	0.3279	0.3528	0.3887	0.3404
rs10995271	10	64108492	0.387	0.3846	0.4102	0.4218
rs11190140	10	101281583	0.4768	0.5126	0.5283	0.5066
rs7927894	11	75978964	0.3957	0.3632	0.3896	0.3856
rs11175593	12	38888207	0.0147	0.0191	0.0444	0.0208

rs3764147	13	43355925	0.2085	0.2385	0.3694	0.2361
rs17361350	16	61784340	0.3177	0.2752	0.3154	0.2851
rs991804	17	29611838	0.2742	0.2648	0.2947	0.3083
rs2872507	17	35294289	0.4799	0.4354	0.4301	0.4416
rs744166	17	37767727	0.4387	0.4223	0.3782	0.4091
rs2542151	18	12769947	0.163	0.1433	0.1062	0.1732
rs8098673	18	17927329	0.3196	0.3397	0.3446	0.3301
rs4807569	19	1074378	0.2015	0.2123	0.1839	0.214
rs1736135	21	15727091	0.4241	0.4458	0.3394	0.4307
rs762421	21	44439989	0.3925	0.3895	0.3902	0.3705

UK: WTCCC samples from the UK, B/F: Belgian/French, NA/J: North American of

Jewish descent, NA/NJ: North American of non-Jewish descent.

Supplementary Table 6: TDT p-values for 32 replicated Crohn's loci

SNP	TDT p
rs11465804	1.67E-13
rs2066847	4.02E-11
rs4613763	0.000687
rs3828309	4.11E-07
rs10995271	4.71E-06
rs2542151	0.0392
rs11190140	0.000687
rs11747270	0.000664
rs2188962	1.17E-05
rs3197999	0.000874
rs4263839	0.147
rs10045431	1.92E-06
rs3764147	0.00219
rs11175593	0.011
rs6908425	0.0901
rs7927894	0.192
rs2301436	0.0057
rs9286879	0.111
rs11584383	0.00118
rs2274910	0.00233
rs2872507	0.00587
rs1551398	4.07E-05
rs744166	9.20E-05
rs17582416	0.00379
rs10758669	0.0057
rs762421	0.000501
rs7746082	0.00199
rs1736135	0.0548
rs1456893	0.0183
rs2476601	0.063
rs4807569	0.000104
rs3763313	0.472

Supplementary Note

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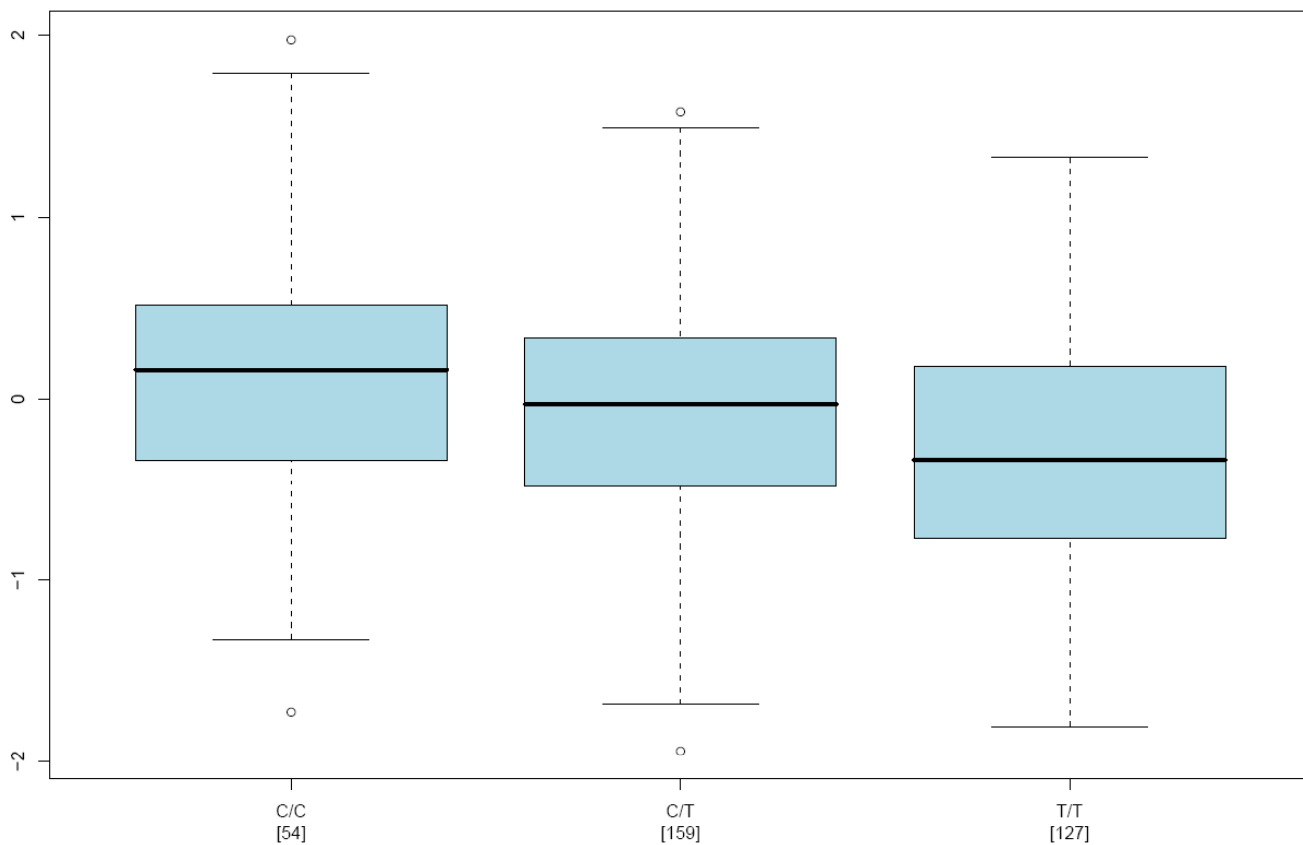
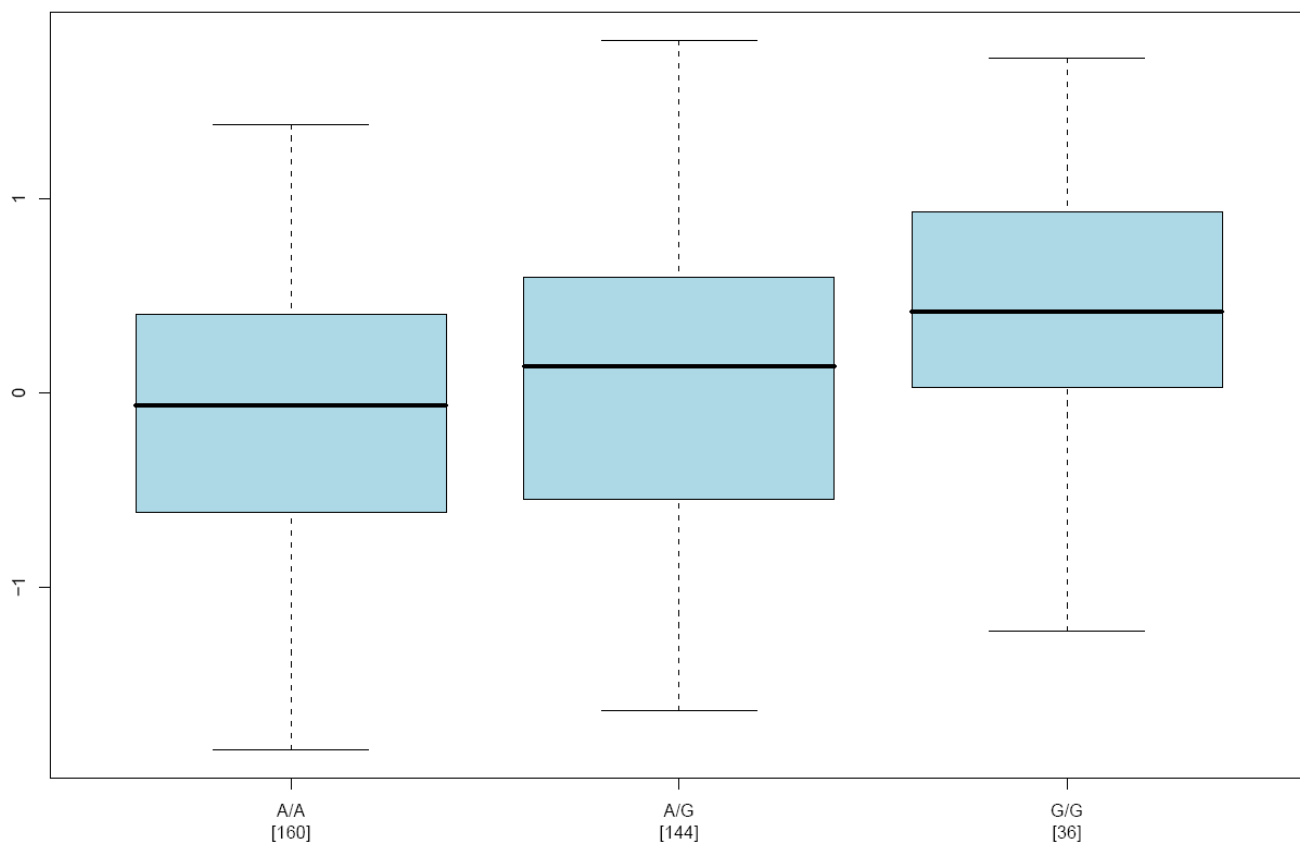
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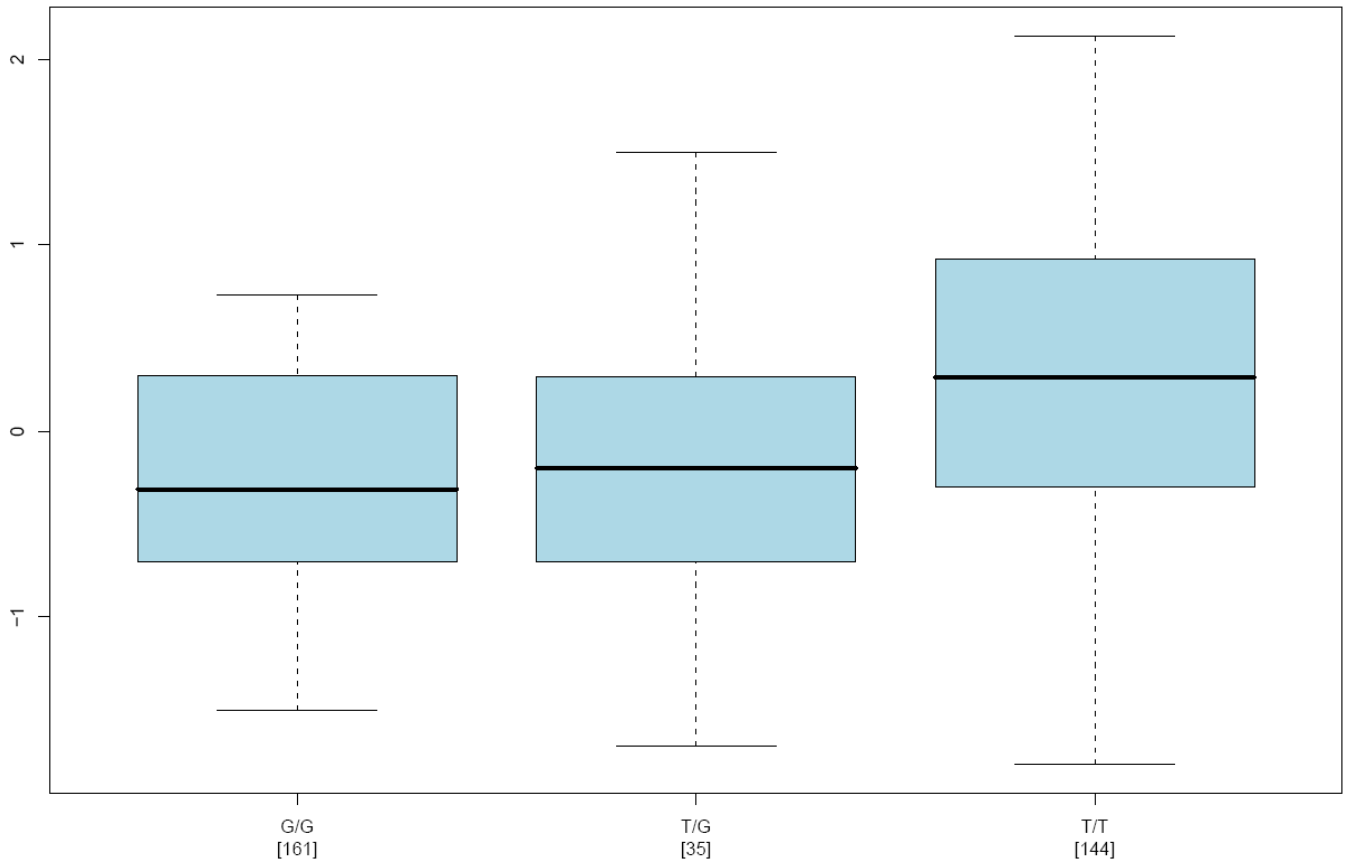
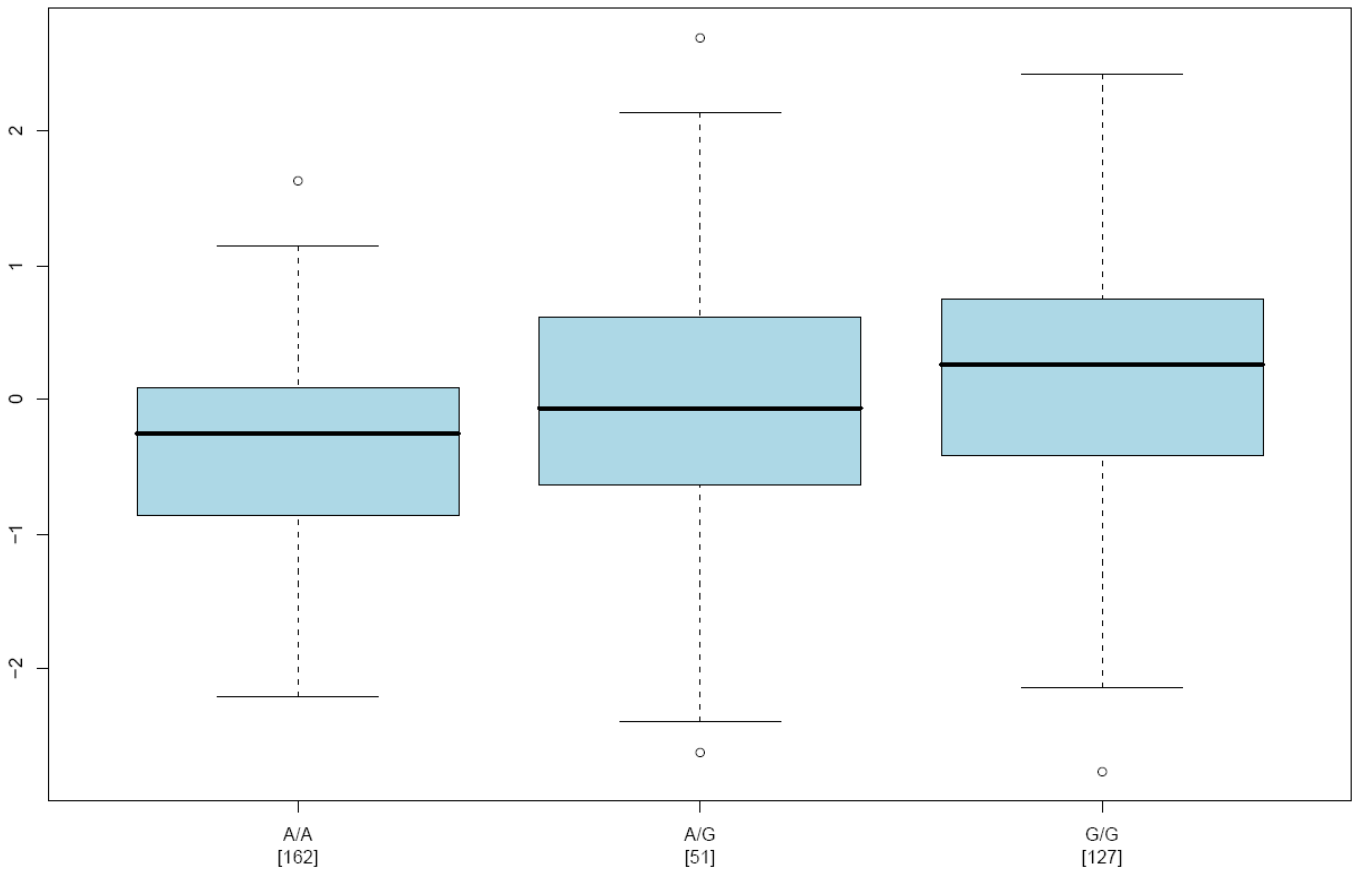
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Supplemental Figure 1: (A-E) Boxplots of gene (probe average) expression levels by genotype for the eQTL effects reported in Table 4. Respective gene and SNP identifiers are given for each graph. Numbers of individuals of a given genotype are given in parentheses. Data are from Dixon et al. (2007).

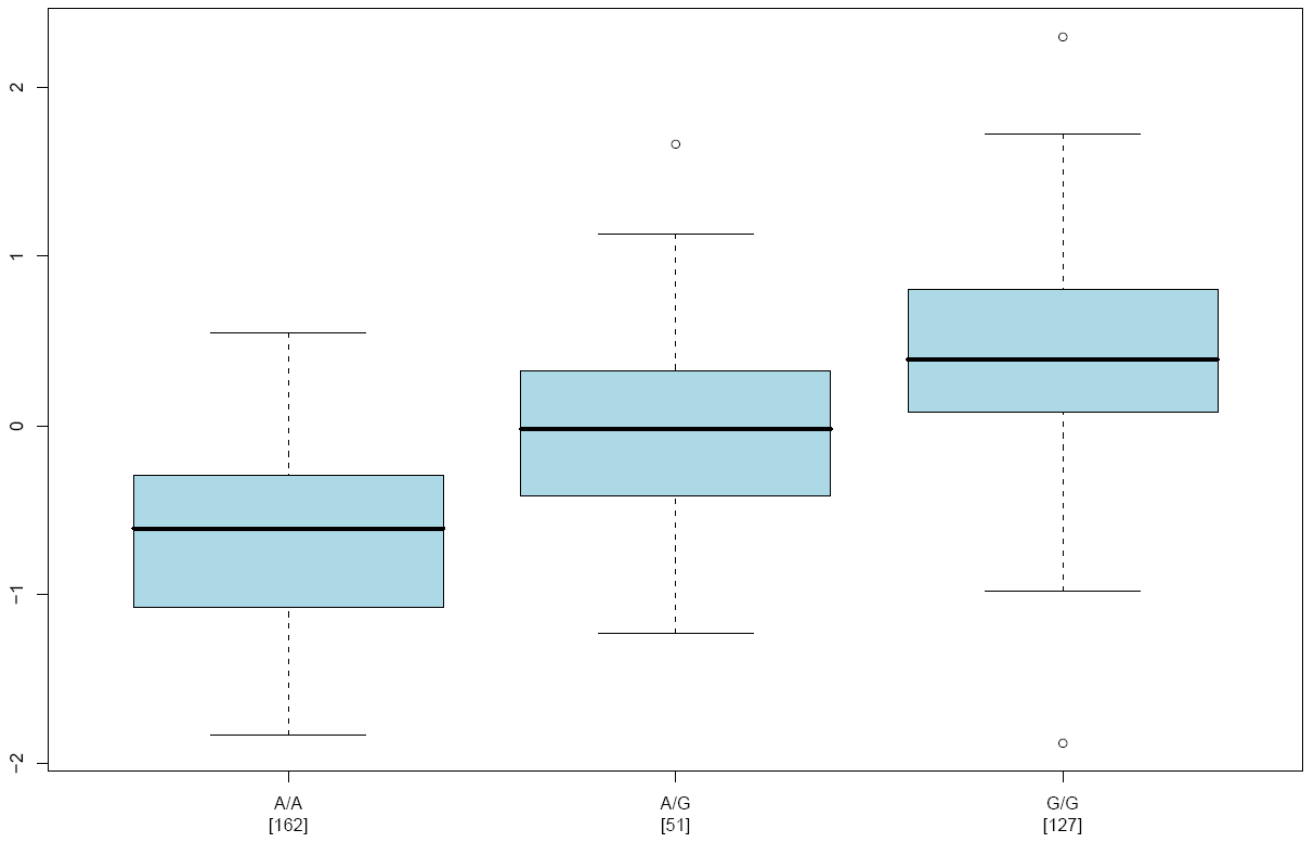
(F-G) Blue bar graphs: Frequency distribution of number of genes with lod scores > 2 (**F**), and sum of lod scores > 2 (**G**) for 1,000 sets of 39 SNPs matching the true SNP set in terms of allelic frequency and gene context. Red bar graphs: cfr. blue bar graph, except that associated intergenic SNPs were replaced by intronic SNPs in the simulations to increase their proximity to genes. Red arrows: corresponding values obtained with the 39 CD associated SNPs.

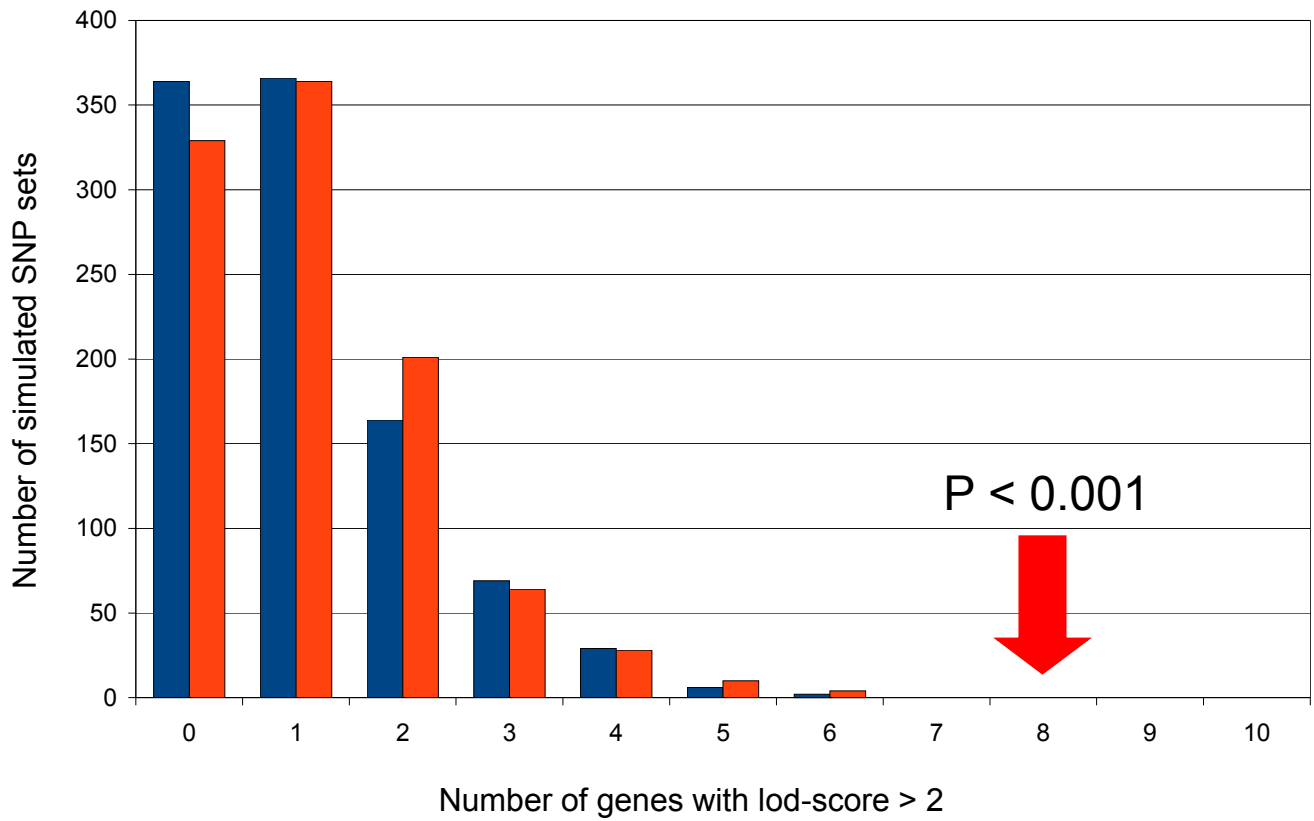
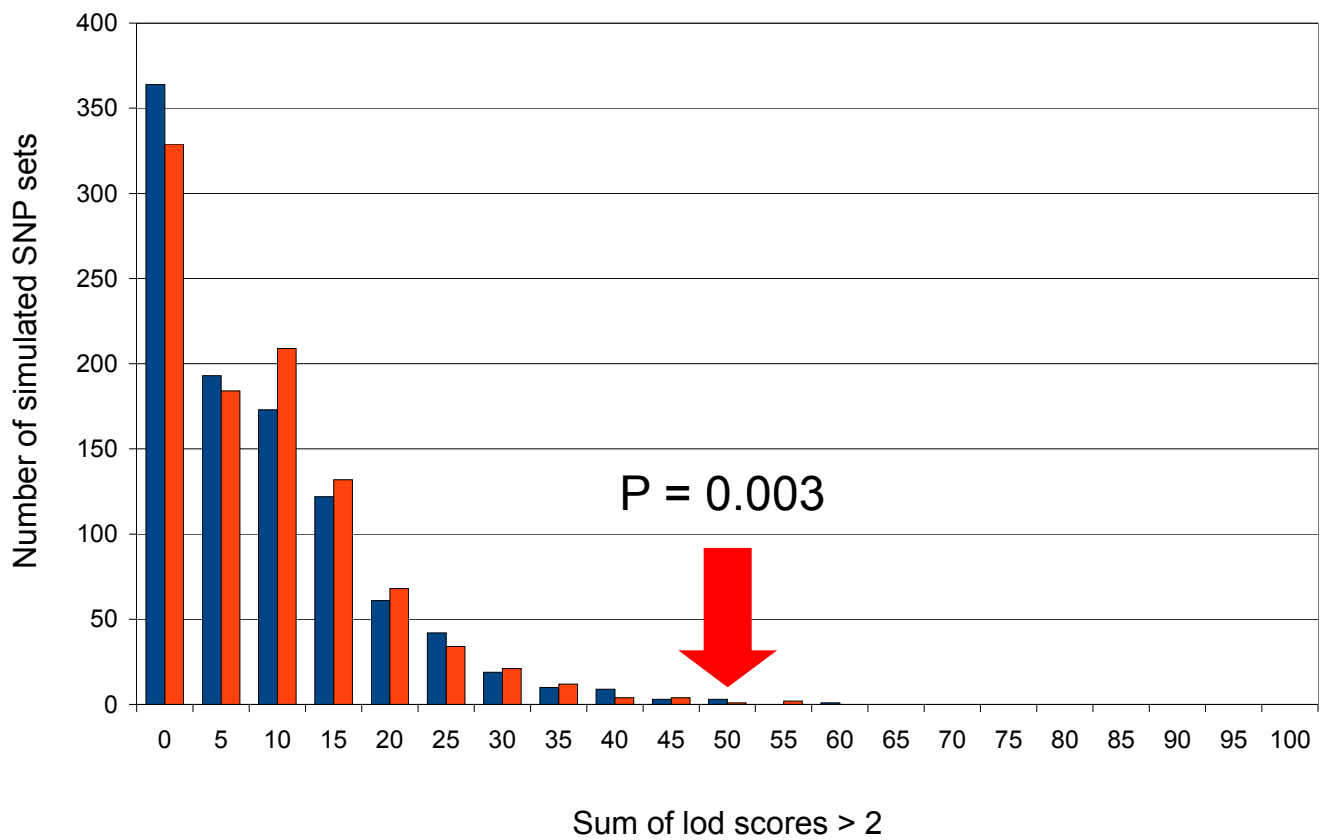
A**SLC22A5 / rs2188962****B****HLA-DRB4 / rs2858331**

C**CREM / rs17582416****D****GSDML / rs2872507**

E

ORMDL3 / rs2872507



F**G**

Supplementary Figure 2: Ideogram showing chromosomal location of significant loci for Crohn's disease identified in genome wide association scan meta-analysis, and major regions of linkage for inflammatory bowel disease detected by whole genome linkage scans. *Arrows* indicate significant loci identified from present genome wide association meta-analysis and replication, *numbered* as ordered per Table 2. *Red bars* indicate regions significant linkage and *blue bars* suggestive linkage. *MHC*, major histocompatibility complex. Regions where association and linkage findings coincide are chromosomes 1p, 3p, 5q, 6p, 10p, 12q, and 16q. Figure is modified and linkage data is compiled from review by CG Mathew and CM Lewis, Genetics of inflammatory bowel disease: progress and prospects Hum. Mol. Genet., 2004; 13: R161 - R168, with inclusion of inflammatory bowel disease linkage data from three more recent linkage studies (Barmada M.M. et al., A Genome Scan in 260 Inflammatory Bowel Disease-Affected Relative Pairs. Inflamm Bowel Dis, **10**, 15-22 (2004); Vermeire S. et al. Genome wide scan in a Flemish inflammatory bowel disease population: support for the IBD4 locus, population heterogeneity, and epistasis. Gut **53**, 980–986, (2004); and Shugart Y.Y. et al An SNP linkage scan identifies significant Crohn's disease loci on chromosomes 13q13.3 and, in Jewish families, on 1p35.2 and 3q29. Genes and Immunity, In Press).

Comparison of Association Loci with Published Linkage Loci

