Common genetic variation in the *HLA* region is associated with late-onset sporadic Parkinson’s disease

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Supplementary Material

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Supplementary Table 1. Subjects

Group	Subjects genotyped		Subjects excluded		Subjects analyzed			
	N	Call rate Mean±s.d.	Enrolled twice	Related PI_HAT>.15	N	% Men	Onset age Mean±s.d.	Age Mean±s.d.
Parkinson	2014	99.92±0.08	1	13	2000	67.3	58.34±11.93	67.26±10.67
Controls	1999	99.92±0.08	3	10	1986	38.7	--	70.32±14.09
Total	4013	99.92±0.08	4	23	3986	100.0	58.34±11.93	68.78±12.58

Supplementary Table 2. Association of *HLA* rs3129882 across disease strata and population structure

Strata	N Case	N Control	MAF Case	MAF Control	HW	P-value	OR(95%CI)
NGRC all subjects	2000	1986	0.46	0.40	1.00	2.9x10^{-8}	1.31(1.19-1.44)
PD-associated strata							
Non-Familial	1565	1986	0.47	0.40	1.00	5.5x10^{-10}	1.38(1.25-1.52)
Familial	435	1986	0.42	0.40	1.00	0.15	1.12(0.96-1.31)
Late onset	1480	1986	0.46	0.40	1.00	2.4x10^{-8}	1.34(1.21-1.48)
Early onset	519	1986	0.45	0.40	1.00	3.1x10^{-3}	1.27(1.08-1.49)
Male	1346	769	0.46	0.38	0.25	1.1x10^{-7}	1.43(1.25-1.63)
Female	654	1217	0.45	0.41	0.37	1.7x10^{-2}	1.18(1.03-1.36)
Smokers	732	696	0.47	0.39	1.0	8.5x10^{-5}	1.38(1.18-1.62)
Non-smokers	866	810	0.45	0.40	0.61	6.5x10^{-3}	1.23(1.06-1.43)
Coffee-High	512	387	0.47	0.40	0.40	4.1x10^{-3}	1.34(1.10-1.63)
Coffee-Low	946	544	0.45	0.40	0.25	8.6x10^{-3}	1.24(1.06-1.46)
NSAIDs user	976	657	0.46	0.40	0.51	2.5x10^{-3}	1.26(1.09-1.47)
No-NSAIDs	594	326	0.46	0.40	0.82	6.9x10^{-3}	1.32(1.08-1.62)
Ashkenazi Jewish Ancestry							
Yes (genetically defined)*	89	40	0.45	0.38	1.00	0.41	1.28(0.71-2.28)
No (genetically defined core subsample)*	1214	1272	0.44	0.39	0.81	1.6x10^{-4}	1.26(1.12-1.42)
No/unknown by self report	1911	1946	0.46	0.40	1.00	1.5x10^{-8}	1.32(1.20-1.45)
Recruitment site in United States							
New York	412	300	0.52	0.46	0.35	0.022	1.30(1.04-1.63)
Oregon	504	898	0.43	0.40	0.15	0.114	1.14(0.97-1.35)
Georgia	231	113	0.47	0.37	1.00	0.012	1.57(1.10-2.23)
Washington	853	675	0.44	0.36	0.21	6.3x10^{-5}	1.39(1.18-1.63)
European country of paternal & maternal origin							
Great Britain	120	72	0.46	0.35	0.80	8x10^{-3}	1.93(1.19-3.14)
Germany/ Austria	101	54	0.48	0.35	1.00	0.08	1.57(0.95-2.60)
Ireland	44	26	0.42	0.40	0.44	0.79	1.11(0.52-2.36)
Scandinavia	65	34	0.49	0.37	0.29	0.21	1.45(0.81-2.61)
Eastern Europe	41	32	0.51	0.39	1.00	0.15	1.68(0.83-3.40)
Italy	56	36	0.63	0.46	0.50	0.05	2.10(0.99-4.44)
Russia	27	10	0.52	0.35	1.00	0.16	2.29(0.72-7.28)
European country of paternal or maternal origin							
Great Britain	537	356	0.44	0.37	0.73	2x10^{-3}	1.38(1.13-1.70)
Germany/ Austria	442	269	0.45	0.40	0.90	0.062	1.24(0.99-1.56)
Ireland	249	162	0.41	0.44	0.42	0.189	0.81(0.59-1.11)
Scandinavia	226	146	0.42	0.35	0.86	0.044	1.40(1.01-1.95)
Eastern Europe	92	78	0.48	0.43	0.49	0.244	1.32(0.83-2.09)
Italy	91	68	0.57	0.47	0.63	0.164	1.41(0.87-2.27)
France	82	68	0.44	0.44	0.15	0.646	1.13(0.66-1.93)
Russia	64	23	0.53	0.45	1.00	0.217	1.59(0.76-3.33)

Analyses were adjusted for PC1, PC2, sex and age. Tests of heterogeneity were performed within each strata; the differences were not significant unless noted below.

Family history: Patients who had at least one first or second degree relative with PD were classified as familial. All others were classified as non-familial (sporadic). MAF of the risk allele and OR were significantly higher in sporadic PD than familial PD (P=0.01 for MAF, P=0.02 for OR), however, the differences were not significant after adjusting for number of strata tests performed.

Age at onset: Late-onset defined as age >50 years, early onset as ≤50 years.

Smoker: >100 cigarettes in lifetime.

Coffee: Number of cups of caffeinated coffee drank per day multiplied by the number of years of consumption; high and low divided at the median in controls.

NSAIDs: Ever or never use of over the counter NSAIDs.

***Jewish/Non-Jewish clusters**: The core of the Jewish cluster was defined within $0.04 \leq PC1 \leq 0.055$ and $0.001 \leq PC2 \leq 0.013$. A core within non-Jewish Caucasian cluster was defined within $-0.0075 \leq PC1 \leq 0.0025$ & $-0.005 \leq PC2 \leq 0.003$.

Recruitment site: US states where subjects were recruited from. Test of heterogeneity across recruitment sites was significant for MAF (P=0.0007) but not for OR (P=0.16), indicating consistent evidence for association with PD despite varying allele frequency.

Paternal or maternal ancestry: Self reports of the countries from which ancestors immigrated to US. Since having only one lineage tracing back to a country was sufficient for this classification, an individual may fall in more than one group, and there could exist substructure within each group (for example, children of a couple of Irish and Italian origin). Test of heterogeneity across countries was marginal for MAF (P=0.08) but OR were consistently >1 ($P_{heterogeneity}$=0.16), indicating consistent evidence for association with PD despite varying allele frequency.

Paternal & maternal ancestry: Smaller group of subjects whose both paternal and maternal lineage were said to have originated from the same country.

Supplementary Table 3: In silico replication of SNPs that reached $P<10^{-5}$ in NGRC.

We used the individual-level "CIDR" dataset from dbGaP (Pankratz et al)[1] and Cochran-Mantel-Haenszel (CMH) test statistics for Meta-analysis. We imputed the SNPs that were not present in CIDR dataset using CEU-OMNI-HapMaP as reference panel. Heterogeneity between the two studies was tested using Breslow-Day (BD) test statistics.

				NGRC							CIDR from dbGaP[1]							Meta-Analysis							
				MAF		P					MAF		P					MAF		P	P				P
CHR	SNP	BP	A1	Case	Control	HWE	OR	L95	U95	P	Case	Control	HWE	OR	L95	U95	P	Case	Control	HWE	BD	OR	L95	U95	CMH
SNPs that were genotyped in both NGRC and CIDR datasets																									
1	rs1826316	101645453	C	0.17	0.21	0.84	0.75	0.66	0.84	1.5E-6	0.19	0.18	0.42	1.10	0.91	1.32	0.32	0.18	0.20	0.82	1.1E-3	0.84	0.76	0.92	3.4E-4
2	rs870575	45356764	T	0.20	0.25	0.21	0.75	0.68	0.84	5.9E-7	0.25	0.24	0.34	1.00	0.85	1.18	0.98	0.22	0.25	0.12	0.02	0.83	0.76	0.91	8.9E-5
3	rs4678550	36778998	C	0.16	0.20	0.32	0.76	0.67	0.85	6.4E-6	0.17	0.17	0.40	0.95	0.79	1.14	0.56	0.16	0.19	0.20	0.02	0.81	0.74	0.90	5.3E-5
4	rs2736990	90897564	C	0.51	0.45	0.22	1.30	1.18	1.42	5.0E-8	0.47	0.53	0.37	1.32	1.14	1.53	1.9E-4	0.52	0.46	0.60	0.85	1.28	1.19	1.38	1.7E-10
4	rs1350855	91413829	T	0.34	0.39	1.00	0.79	0.72	0.87	1.3E-6	0.37	0.39	1.00	0.89	0.77	1.03	0.12	0.35	0.39	0.97	0.31	0.83	0.77	0.90	3.5E-6
6	rs3117098	32466491	C	0.33	0.28	0.83	1.27	1.15	1.41	2.9E-6	0.32	0.29	0.50	1.18	1.01	1.38	0.04	0.33	0.29	0.85	0.30	1.25	1.15	1.36	1.8E-7
6	rs3129955	32473818	T	0.33	0.28	0.87	1.27	1.15	1.40	3.8E-6	0.32	0.29	0.50	1.18	1.01	1.38	0.04	0.33	0.29	0.82	0.27	1.25	1.15	1.35	2.1E-7
6	rs3129882	32517508	G	0.46	0.40	1.00	1.31	1.19	1.44	2.9E-8	0.45	0.41	0.57	1.21	1.04	1.39	0.01	0.46	0.40	0.72	0.24	1.28	1.19	1.39	2.8E-10
8	rs2046571	122424893	A	0.34	0.29	0.45	1.28	1.15	1.41	1.9E-6	0.33	0.30	0.06	1.15	0.98	1.33	0.08	0.33	0.29	0.09	0.69	1.24	1.14	1.34	3.6E-7
8	rs6981998	131622396	G	0.18	0.15	0.72	1.35	1.19	1.53	4.3E-6	0.18	0.16	0.80	1.06	0.88	1.28	0.52	0.18	0.15	0.94	0.32	1.27	1.15	1.41	5.3E-6
10	rs7096608	15239759	C	0.15	0.12	0.75	1.38	1.21	1.58	2.9E-6	0.14	0.14	0.89	1.02	0.82	1.25	0.89	0.15	0.13	0.73	0.03	1.23	1.11	1.38	1.8E-4
17	rs4790246	4912379	A	0.50	0.46	0.59	1.24	1.13	1.36	5.3E-6	0.47	0.49	0.84	0.92	0.79	1.06	0.23	0.49	0.47	0.76	4.2E-3	1.12	1.04	1.21	4.4E-3
17	rs12185268	41279463	G	0.18	0.23	0.03	0.76	0.68	0.86	6.7E-6	0.18	0.23	0.08	0.71	0.60	0.85	2.1E-4	0.18	0.23	0.39	0.27	0.75	0.69	0.83	4.2E-9
17	rs17660464	41533806	A	0.18	0.23	0.03	0.76	0.68	0.86	7.5E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.21	0.75	0.69	0.83	4.3E-9
17	rs199533	42184098	T	0.17	0.22	0.05	0.74	0.66	0.84	1.3E-6	0.16	0.21	0.05	0.73	0.61	0.88	8.4E-4	0.17	0.21	0.62	0.47	0.74	0.67	0.82	2.0E-9
SNPs that were genotyped in NGRC and imputed for CIDR																									
1	rs263912	101747739	T	0.14	0.18	0.82	0.73	0.64	0.83	2.2E-6	0.15	0.14	0.88	1.12	0.91	1.37	0.30	0.14	0.17	0.63	3.0E-3	0.83	0.75	0.92	5.1E-4
4	rs356220	90860363	T	0.44	0.36	0.38	1.38	1.25	1.52	3.4E-11	0.47	0.40	0.77	1.40	1.21	1.62	9.9E-6	0.45	0.37	0.55	0.72	1.37	1.27	1.48	2.9E-15
4	rs356168	90893454	G	0.52	0.45	0.28	1.30	1.18	1.42	4.6E-8	0.47	0.53	0.37	1.33	1.15	1.54	1.5E-4	0.52	0.46	0.68	0.80	1.29	1.19	1.39	1.0E-10
6	rs3117104	32456287	A	0.33	0.28	0.91	1.27	1.15	1.40	4.0E-6	0.32	0.29	0.50	1.19	1.01	1.39	0.03	0.33	0.28	0.78	0.30	1.25	1.15	1.36	1.8E-7
6	rs3117102	32458085	G	0.33	0.28	0.87	1.27	1.15	1.40	3.9E-6	0.32	0.29	0.50	1.19	1.01	1.39	0.03	0.33	0.28	0.82	0.29	1.25	1.15	1.36	1.9E-7
6	rs3129948	32462622	C	0.33	0.28	0.83	1.27	1.15	1.40	4.2E-6	0.32	0.29	0.50	1.19	1.01	1.39	0.03	0.33	0.28	0.85	0.31	1.25	1.15	1.35	2.1E-7
6	rs3129954	32473558	A	0.33	0.28	0.78	1.27	1.15	1.40	3.9E-6	0.32	0.29	0.50	1.19	1.01	1.39	0.03	0.33	0.28	0.89	0.31	1.25	1.15	1.36	1.9E-7
10	rs7915262	15238590	C	0.15	0.12	0.75	1.38	1.21	1.58	2.8E-6	0.14	0.13	0.46	1.05	0.85	1.30	0.66	0.15	0.12	0.49	0.05	1.25	1.12	1.40	6.8E-5
11	rs10741569	12173555	A	0.30	0.25	0.51	1.28	1.16	1.43	3.2E-6	0.30	0.29	0.93	1.02	0.87	1.19	0.82	0.30	0.26	0.59	0.09	1.19	1.09	1.29	8.2E-5
17	rs241041	41069708	C	0.18	0.23	0.03	0.76	0.68	0.86	5.8E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.42	0.29	0.75	0.68	0.83	3.6E-9
17	rs241039	41070456	A	0.18	0.23	0.03	0.76	0.68	0.86	6.3E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.42	0.28	0.75	0.68	0.83	3.9E-9
17	rs2942168	41070633	T	0.18	0.23	0.03	0.76	0.68	0.86	5.3E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.39	0.29	0.75	0.68	0.83	3.3E-9
17	rs2942167	41070801	G	0.18	0.23	0.03	0.76	0.68	0.86	5.8E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.42	0.29	0.75	0.68	0.83	3.6E-9
17	rs17334797	41181683	G	0.18	0.23	0.03	0.76	0.68	0.86	6.6E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.39	0.28	0.75	0.69	0.83	4.0E-9
17	rs17426064	41184469	T	0.18	0.23	0.02	0.76	0.68	0.86	5.7E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.39	0.28	0.75	0.68	0.83	3.2E-9
17	rs12150390	41252009	C	0.18	0.23	0.02	0.76	0.68	0.86	6.6E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.39	0.29	0.75	0.69	0.83	4.0E-9
17	rs1912151	41258725	A	0.18	0.23	0.03	0.76	0.68	0.86	7.3E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.39	0.31	0.75	0.69	0.83	4.4E-9
17	rs1396862	41258778	T	0.18	0.23	0.02	0.76	0.68	0.86	6.8E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.37	0.29	0.75	0.69	0.83	4.4E-9
17	rs17763086	41261262	G	0.18	0.23	0.02	0.76	0.68	0.86	7.2E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.39	0.29	0.75	0.69	0.83	4.4E-9
17	rs16940665	41263677	C	0.18	0.23	0.02	0.76	0.68	0.86	6.0E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.37	0.29	0.75	0.68	0.83	3.6E-9
17	rs1876828	41267306	A	0.18	0.23	0.05	0.76	0.68	0.86	7.6E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.52	0.31	0.75	0.68	0.83	3.9E-9
17	rs878886	41268271	G	0.18	0.23	0.03	0.76	0.68	0.86	7.6E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.42	0.27	0.75	0.69	0.83	4.6E-9
17	rs878887	41268363	T	0.18	0.23	0.03	0.76	0.68	0.86	6.9E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.39	0.29	0.75	0.69	0.83	4.3E-9
17	rs878888	41268416	G	0.18	0.23	0.02	0.76	0.68	0.86	7.1E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.39	0.28	0.75	0.69	0.83	4.4E-9

17	rs4525537	41268504	C	0.18	0.23	0.03	0.76	0.68	0.86	6.6E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.39	0.28	0.75	0.69	0.83	4.0E-9
17	rs4640231	41268567	C	0.18	0.23	0.02	0.76	0.68	0.86	6.4E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.39	0.29	0.75	0.68	0.83	3.8E-9
17	rs10445364	41272136	A	0.18	0.23	0.02	0.76	0.68	0.86	6.9E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.39	0.29	0.75	0.69	0.83	4.2E-9
17	rs17763596	41276990	T	0.18	0.23	0.03	0.76	0.68	0.86	7.4E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.39	0.28	0.75	0.69	0.83	4.5E-9
17	41279046	41279046	A	0.18	0.23	0.03	0.77	0.68	0.86	8.7E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.42	0.28	0.76	0.69	0.83	5.5E-9
17	rs12185233	41279434	C	0.18	0.23	0.03	0.76	0.68	0.86	7.0E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.45	0.29	0.75	0.68	0.83	3.7E-9
17	rs12185235	41279483	T	0.18	0.23	0.02	0.76	0.68	0.86	5.9E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.37	0.29	0.75	0.68	0.83	3.6E-9
17	rs12373123	41279853	C	0.18	0.23	0.02	0.76	0.68	0.86	5.6E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.39	0.30	0.75	0.68	0.83	3.4E-9
17	41279910	41279910	A	0.18	0.23	0.02	0.76	0.68	0.86	6.0E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.37	0.28	0.75	0.68	0.83	3.5E-9
17	rs12373142	41279980	G	0.18	0.23	0.02	0.76	0.68	0.86	5.5E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.37	0.29	0.75	0.68	0.83	3.5E-9
17	41306766	41306766	T	0.19	0.23	0.06	0.76	0.68	0.85	3.7E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.56	0.25	0.75	0.68	0.82	1.8E-9
17	rs17770343	41325948	C	0.18	0.23	0.03	0.77	0.68	0.86	8.8E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.39	0.27	0.75	0.69	0.83	4.7E-9
17	rs17691610	41326456	T	0.18	0.23	0.04	0.77	0.68	0.86	8.4E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.49	0.29	0.75	0.68	0.83	4.2E-9
17	41367654	41367654	C	0.18	0.23	0.04	0.76	0.68	0.86	7.0E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.46	0.25	0.75	0.68	0.83	3.6E-9
17	rs17650901	41395527	G	0.18	0.23	0.03	0.76	0.68	0.86	5.6E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.39	0.26	0.75	0.68	0.83	2.7E-9
17	rs1800547	41407682	G	0.18	0.23	0.03	0.76	0.68	0.86	6.8E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.24	0.75	0.68	0.83	3.4E-9
17	41416612	41416612	T	0.18	0.23	0.03	0.76	0.68	0.86	7.3E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.24	0.75	0.68	0.83	3.1E-9
17	rs17651549	41417115	T	0.18	0.23	0.03	0.76	0.68	0.86	4.8E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.39	0.23	0.75	0.68	0.82	2.2E-9
17	rs10445337	41423237	C	0.18	0.23	0.04	0.76	0.68	0.86	5.9E-6	0.18	0.23	0.08	0.72	0.60	0.86	2.4E-4	0.18	0.23	0.49	0.24	0.75	0.68	0.83	3.2E-9
17	rs10445338	41423519	A	0.18	0.23	0.03	0.76	0.68	0.86	6.8E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.24	0.75	0.68	0.83	3.4E-9
17	rs1052551	41424761	A	0.18	0.23	0.03	0.76	0.68	0.86	6.0E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.23	0.75	0.68	0.83	3.0E-9
17	rs17573175	41426926	G	0.18	0.23	0.03	0.76	0.68	0.86	6.6E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.25	0.75	0.68	0.83	3.3E-9
17	rs1052553	41429726	G	0.18	0.23	0.03	0.76	0.68	0.86	6.7E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.26	0.75	0.68	0.83	3.3E-9
17	rs17652121	41429810	C	0.18	0.23	0.03	0.76	0.68	0.86	6.8E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.24	0.75	0.68	0.83	3.4E-9
17	rs1078268	41431738	C	0.18	0.23	0.03	0.76	0.68	0.86	6.4E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.23	0.75	0.68	0.83	3.1E-9
17	rs17573509	41437061	A	0.18	0.23	0.03	0.76	0.68	0.86	6.0E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.23	0.75	0.68	0.83	3.0E-9
17	rs1052587	41458449	C	0.18	0.23	0.03	0.76	0.68	0.86	5.4E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.24	0.75	0.68	0.83	2.6E-9
17	rs17574040	41458711	C	0.18	0.23	0.03	0.76	0.68	0.86	7.0E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.23	0.75	0.68	0.83	3.5E-9
17	rs16940799	41458779	C	0.18	0.23	0.03	0.77	0.68	0.86	7.8E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.37	0.25	0.75	0.69	0.83	4.1E-9
17	rs2158257	41460189	G	0.18	0.23	0.03	0.76	0.68	0.86	6.8E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.24	0.75	0.68	0.83	3.4E-9
17	rs17574228	41460355	C	0.18	0.23	0.03	0.76	0.68	0.86	6.8E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.24	0.75	0.68	0.83	3.4E-9
17	rs7350928	41463947	T	0.18	0.23	0.03	0.76	0.68	0.86	7.3E-6	0.18	0.23	0.08	0.71	0.60	0.85	2.1E-4	0.18	0.23	0.42	0.23	0.75	0.69	0.83	4.0E-9
17	rs17574361	41464049	G	0.18	0.23	0.03	0.76	0.68	0.86	7.2E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.23	0.75	0.68	0.83	3.5E-9
17	1464753	41464753	G	0.18	0.23	0.03	0.76	0.68	0.86	7.1E-6	0.18	0.23	0.08	0.71	0.60	0.85	1.9E-4	0.18	0.23	0.42	0.23	0.75	0.68	0.83	3.5E-9
17	rs36076725	41466379	A	0.18	0.23	0.03	0.76	0.68	0.86	6.5E-6	0.18	0.23	0.08	0.71	0.60	0.85	2.1E-4	0.18	0.23	0.39	0.24	0.75	0.68	0.83	3.5E-9
17	rs35833914	41466388	A	0.18	0.23	0.03	0.77	0.68	0.86	7.7E-6	0.18	0.23	0.08	0.71	0.60	0.85	2.1E-4	0.18	0.23	0.42	0.23	0.75	0.69	0.83	4.1E-9
17	rs17574604	41467460	G	0.18	0.23	0.03	0.76	0.68	0.86	7.2E-6	0.18	0.23	0.08	0.71	0.60	0.85	2.1E-4	0.18	0.23	0.42	0.23	0.75	0.69	0.83	3.9E-9
17	41472966	41472966	G	0.18	0.23	0.03	0.76	0.68	0.86	6.8E-6	0.18	0.23	0.08	0.71	0.60	0.85	2.1E-4	0.18	0.23	0.42	0.24	0.75	0.68	0.83	3.6E-9
17	rs17576165	41515668	C	0.18	0.23	0.03	0.76	0.68	0.86	7.1E-6	0.18	0.23	0.08	0.71	0.60	0.85	2.1E-4	0.18	0.23	0.42	0.25	0.75	0.68	0.83	3.7E-9
17	rs2532274	41602941	C	0.19	0.23	0.02	0.77	0.68	0.86	6.9E-6	0.18	0.23	0.08	0.71	0.60	0.85	2.0E-4	0.19	0.23	0.37	0.19	0.76	0.69	0.83	5.6E-9
17	rs1881194	41604591	A	0.18	0.23	0.03	0.77	0.68	0.86	8.4E-6	0.18	0.23	0.08	0.71	0.60	0.85	2.2E-4	0.18	0.23	0.37	0.27	0.75	0.69	0.83	5.0E-9
17	rs2957316	41686991	G	0.18	0.23	0.03	0.77	0.68	0.86	9.7E-6	0.18	0.23	0.10	0.72	0.60	0.86	2.3E-4	0.18	0.23	0.39	0.23	0.76	0.69	0.83	6.4E-9
17	rs199454	42155294	G	0.20	0.25	0.44	0.77	0.69	0.87	8.0E-6	0.17	0.21	0.04	0.74	0.62	0.90	1.7E-3	0.19	0.24	0.64	0.56	0.77	0.70	0.85	4.0E-8
17	rs199528	42198305	T	0.17	0.22	0.05	0.74	0.66	0.84	1.4E-6	0.16	0.20	0.67	0.77	0.63	0.93	0.01	0.17	0.21	0.16	0.55	0.76	0.69	0.84	2.7E-8
17	rs415430	42214305	G	0.17	0.22	0.09	0.75	0.67	0.85	2.7E-6	0.16	0.20	0.67	0.77	0.63	0.93	0.01	0.17	0.21	0.22	0.46	0.77	0.69	0.84	6.3E-8

CHR-17 SNPs in the 41070 - 41605 KB region are in high LD ($R^2 \sim 1$) and have the same MAF in NGRC, in CIDR, as well as in CEU-HapMap data.

Supplementary Table 4. Replication of other GWAS

We imputed the SNPs that were not genotyped (shown in Italics). If imputed call rate was <95%, data were not used (blank cells).

(a) Pankratz et al.[1]

			Pankratz et al.				**NGRC**				**Individual-level Meta-analysis**				
			MAF				**MAF**				**MAF**				
CHR	**GENE**	**SNP**	**Case**	**Control**	**OR**	**P**	**Case**	**Control**	**OR**	**P**	**Case**	**Control**	**P BD**	**OR**	**P CMH**
4	*GAK/DGKQ*	rs1564282	0.13	0.09	1.70	6.0E-6	*0.12*	*0.09*	*1.32*	*4.1E-4*	0.12	0.09	0.39	1.45	8.3E-9
4		rs11248051	0.13	0.09	1.70	5.2E-6	0.12	0.09	1.32	3.1E-4	0.12	0.09	0.39	1.46	3.2E-9
4		rs11248060	0.15	0.10	1.69	3.4E-6	0.13	0.11	1.23	5.2E-3	0.14	0.10	0.19	1.36	2.9E-7
20	*COX6CP2/PTPN1*	rs4811072	0.29	0.24	1.40	6.5E-5	0.26	0.26	0.99	0.82	0.27	0.25	0.01	1.09	0.04
20		rs1997791	0.30	0.24	1.43	1.9E-5									
4	*LOC729075*	rs2654735	0.39	0.46	0.75	9.0E-5	0.44	0.43	1.04	0.46	0.43	0.44	6.3E-4	0.94	0.12
4		rs1806506	0.39	0.46	0.74	3.7E-5	0.43	0.42	1.04	0.38	0.42	0.43	2.5E-4	0.94	0.12
4		rs11729080	0.14	0.19	0.66	3.3E-5									
8	*LOC727725/ZMAT4*	rs4736788	0.22	0.28	0.70	4.9E-5	*0.23*	*0.23*	*0.96*	*0.49*	0.22	0.24	0.06	0.88	0.01
8		rs10094981	0.22	0.28	0.70	4.8E-5	*0.23*	*0.23*	*0.96*	*0.49*	0.22	0.25	0.07	0.88	0.01
17	*HRNBP3*	rs898528	0.30	0.37	0.74	4.9E-5	0.32	0.32	0.98	0.73	0.31	0.34	1.0E-4	0.90	0.01
13	*LAMP1*	rs12871648	0.38	0.32	1.36	5.0E-5	0.35	0.34	1.06	0.28	0.36	0.33	0.02	1.12	4.5E-3
2	LTBP1	rs4670322	0.32	0.26	1.38	5.1E-5	0.31	0.31	1.03	0.56	0.32	0.30	1.5E-3	1.10	0.02
10	Gene desert	rs11592212	0.09	0.05	1.80	5.2E-5	*0.05*	*0.06*	*0.86*	*0.14*	0.06	0.06	6.6E-4	1.12	0.18
4	SNCA/GPRIN3/MMRNI	rs4106153	0.17	0.22	0.70	9.2E-5									
4		rs1504489	0.36	0.42	0.75	8.4E-5	*0.41*	*0.40*	*1.04*	*0.48*	0.40	0.41	0.01	0.94	0.12
4		rs356229	0.44	0.37	1.35	5.5E-5									
4		rs356188	0.18	0.23	0.70	8.4E-5	*0.18*	*0.21*	*0.80*	*1.6E-4*	0.18	0.21	0.60	0.79	2.4E-6
4		rs3775478	0.10	0.07	1.69	6.1E-5	0.10	0.08	1.26	0.01	0.10	0.08	0.04	1.36	7.8E-6
6	PRDM13/MCHR2	rs4431442	0.32	0.26	1.39	5.6E-5	0.30	0.29	1.02	0.75	0.31	0.28	0.01	1.11	0.01
6		rs10937194	0.19	0.24	0.70	5.9E-5									
14	CGRRF1/SAMD4A	rs4901519	0.12	0.15	0.65	7.6E-5	*0.13*	*0.13*	*1.03*	*0.70*	0.13	0.14	0.02	0.91	0.11
17	C17orf69/PLEKHM1/MAPT	rs11012	0.14	0.20	0.68	8.8E-5	0.15	0.19	0.77	7.3E-5	0.15	0.19	0.25	0.75	3.0E-8
17		rs1724425	0.39	0.45	0.75	7.8E-5									
3	LEKR1	rs12638253	0.45	0.52	0.75	8.3E-5	*0.47*	*0.48*	*1.01*	*0.81*	0.47	0.49	3.3E-3	0.92	0.03
7	POU6F2	rs9655034	0.48	0.41	1.33	8.8E-5	0.47	0.47	1.00	0.96	0.47	0.45	3.3E-3	1.08	0.05
3	TMEM108	rs1197313	0.39	0.45	0.75	8.9E-5	0.41	0.42	0.98	0.74	0.41	0.43	0.04	0.92	0.04
12	LOC728328/PCTK2	rs7312607	0.49	0.43	1.33	9.3E-5	0.46	0.47	0.95	0.32	0.48	0.43	0.01	1.04	0.29
3	FGF12	rs9859577	0.13	0.17	0.67	9.9E-5	0.16	0.16	1.03	0.70	0.15	0.16	1.0E-3	0.90	0.04
12	LOC652429/TMEM132B	rs2108521	0.22	0.27	0.72	1.0E-4	*0.27*	*0.27*	*0.95*	*0.36*	0.25	0.27	0.03	0.88	0.01

(b) Satake et al.[2] and Simon-Sanchez et al.[3]

Three loci were reported by Satake et al as being PD risk factors in the Japanese, and were followed-up by Simon-Sanchez et al. in a Caucasian sample. We show Satake's results for "GWAS + Replication 1+2" and Simon-Sanchez's results for "Stage I+II". We used individual level data and the CMH method for Meta-analysis when combining Pankratz and NGRC data (all scenarios except *BST1* rs4698412). When combining Simon-Sanchez with NGRC, we used Aggregate Meta-analysis and Random Effects model (rs4698412). We used the same allele as Satake et al, which was at times not the minor allele in Caucasians, to keep risk allele consistent. We did not perform Meta-analysis with Satake data due to heterogeneity between Caucasians and Japanese. We did not combine Simon-Sanchez and Pankratz data because they used the same ~800 NINDS controls.

		Satake				**Simon-Sanchez**				**Pankratz**				**NGRC**				**Meta-Analysis**	
		MAF				**MAF**				**MAF**				**MAF**					
locus	**SNP**	**case**	**control**	**OR**	**P**	**case**	**control**	**OR**	**P**	**case**	**control**	**OR**	**P**	**case**	**control**	**OR**	**P**	**OR**	**P**
1q32	rs16856139	0.10-0.11	0.13-0.14	1.36	1.02E-7														
PARK16	rs823128	0.09-0.11	0.13-0.14	1.41	4.9E-9	0.03	0.04	0.66	7.3E-8	0.01	0.01	1.08	0.85	0.03	0.03	0.82	0.15	0.94	0.61
	rs823122	0.09-0.11	0.13-0.14	1.37	5.2E-8									0.05	0.06	0.83	0.08	0.97	0.72
	rs947211	0.42-0.43	0.48-0.50	1.30	1.5E-12					0.23	0.24	0.96	0.63	*0.23*	*0.24*	*0.88*	*0.03*	0.91	0.04
	rs823156	0.12-0.14	0.17-0.17	1.37	3.6E-9	0.16	0.18	0.89	7.6E-4					0.16	0.17	0.90	0.08		
	rs708730	0.12-0.15	0.17-0.18	1.33	2.4E-8					0.17	0.17	0.98	0.82	0.16	0.17	0.87	0.03	0.92	0.11
	rs11240572	0.12-0.13	0.16-0.17	1.33	1.1E-7	0.03	0.04	0.67	6.1E-7										
4p15	rs11931532	0.45-0.47	0.40-0.42	1.24	5.1E-9					0.98	0.98	0.94	0.81	0.97	0.97	1.03	0.84	1.02	0.89
BST1	rs12645693	0.45-0.47	0.40-0.42	1.24	8.7E-9					0.98	0.98	0.94	0.81	0.97	0.97	1.05	0.74	1.00	0.99
	rs4698412	0.38-0.40	0.33-0.35	1.24	1.8E-8	0.57	0.56	1.06	3.0E-2					0.58	0.55	1.13	0.01	1.08	1.5E-3
	rs4538475	0.41-0.43	0.36-0.38	1.24	3.9E-9					0.85	0.83	1.19	0.09	0.85	0.83	1.10	0.14	0.89	0.02
	rs12646913					0.07	0.08	0.92	3.0E-2	0.08	0.09	0.86	0.26	*0.07*	*0.08*	*0.78*	*0.01*	0.81	3.6E-3
	rs12502586					0.11	0.10	1.08	0.07										
12q12	rs1994090	0.10-0.12	0.08-0.08	1.39	2.7E-8					0.23	0.21	1.16	0.10	0.23	0.21	1.12	0.05	1.13	0.01
LRRK2	rs7304279	0.10-0.12	0.08-0.09	1.38	5.1E-8					0.17	0.15	1.22	0.05	*0.16*	*0.14*	*1.15*	*0.04*	1.17	4.6E-3
	rs4768212	0.10-0.12	0.07-0.08	1.37	1.1E-7					0.07	0.07	1.07	0.64	0.07	0.07	1.11	0.25	1.09	0.26
	rs2708453	0.10-0.13	0.08-0.08	1.38	9.7E-8					0.17	0.15	1.21	0.05	*0.17*	*0.15*	*1.15*	*0.03*	1.17	3.9E-3
	rs2046932	0.10-0.13	0.08-0.09	1.39	4.3E-8														
	rs11564162					0.19	0.21	0.87	9.5E-5										
	rs2896905					0.37	0.39	0.93	7.8E-3	*0.37*	*0.38*	*0.94*	*0.38*	0.38	0.39	0.97	0.57	0.96	0.26
	rs1491923					0.33	0.31	1.14	1.6E-5	*0.33*	*0.32*	*1.01*	*0.88*	0.33	0.33	1.02	0.69	1.02	0.67

Supplementary Table 5. *HLA*, PC1 and PD. (also see **Supplementary Figures 5 and 6**)

We used multiple logistic regression to study the independence of PD-associated SNP at *HLA-DRA* (rs3129882) with *HLA* SNPs that were associated with PC1 in three different ways (a-c).

(a) Tests of association of 50 most significant PC1-associated SNPs with PD adjusting for rs3129882 (columns 8 & 9) and of rs3129882 with PD adjusting for each of the top 50 PC1-SNPs (10 &11). The model was Dis ~ age + gender + PC1 + PC2 + rs3129882 + PC1-SNP. Association of rs3129882 with PD remained strong when adjusted for PC1 SNPs. However, association of PC1 SNPs with PD was not significant after adjusting for rs3129882. The *HLA* association with PD is therefore driven by rs3129882, not PC1-associated SNPs.

Ch 6 VARIANTS	**SNP**	**A1**	**Position**	**MAF Case**	**MAF Control**	**HWE**	**Assoc of PC1-SNPs with PD adj for rs3129882, sex, age, PC1,PC2**		**Assoc of rs3129882 with PD, adj for PC1-SNPs, sex, age, PC1,PC2**	
							OR	**P**	**OR**	**P**
HLA-DRA	rs3129882	G	32517508	0.46	0.40	1.00				
PC1 –associated variants in *HLA*	rs10456405	G	32320845	0.18	0.15	0.29	1.13	0.06	1.29	1.2E-7
	rs11751445	A	29575831	0.02	0.01	1.00	0.86	0.44	1.31	3.2E-8
	rs11753208	T	31113411	0.08	0.07	0.29	0.96	0.68	1.31	2.8E-8
	rs11756938	T	29564633	0.02	0.01	1.00	0.85	0.40	1.31	3.1E-8
	rs11758964	C	31554345	0.06	0.06	1.00	0.80	0.04	1.32	1.5E-8
	rs13194642	T	32319673	0.16	0.12	0.01	1.14	0.06	1.29	3.2E-7
	rs17200407	G	31497944	0.02	0.02	1.00	0.69	0.06	1.32	1.3E-8
	rs1724770	G	117708667	0.01	0.01	1.00	1.20	0.45	1.31	2.9E-8
	rs2244020	C	31455430	0.37	0.39	0.53	0.90	0.03	1.30	6.7E-8
	rs2517474	T	31154473	0.50	0.48	0.16	1.03	0.57	1.31	3.1E-8
	rs2517506	G	31139659	0.17	0.15	0.20	1.03	0.63	1.31	3.2E-8
	rs2517518	A	31136324	0.17	0.15	0.19	1.02	0.75	1.31	2.9E-8
	rs2523840	T	31138404	0.17	0.15	0.19	1.02	0.75	1.31	3.2E-8
	rs2523841	T	31138262	0.17	0.15	0.19	1.02	0.76	1.31	2.9E-8
	rs2523845	G	31135372	0.17	0.15	0.19	1.02	0.80	1.30	4.0E-8
	rs2523848	T	31133083	0.17	0.15	0.20	1.03	0.63	1.31	3.2E-8
	rs2523849	G	31133030	0.17	0.15	0.20	1.03	0.63	1.31	3.2E-8
	rs2523850	A	31132727	0.17	0.15	0.20	1.03	0.64	1.31	3.1E-8
	rs2523882	A	31150196	0.30	0.29	0.58	1.01	0.81	1.31	3.2E-8
	rs2849016	G	32317240	0.24	0.20	2.4E-4	1.11	0.08	1.27	1.6E-6
	rs371156	G	32317941	0.28	0.25	0.01	1.06	0.30	1.29	1.9E-7
	rs376549	G	32316675	0.40	0.37	0.47	1.09	0.07	1.32	1.5E-8
	rs377743	T	32319043	0.27	0.24	3.8E-3	1.04	0.47	1.30	1.1E-7
	rs380571	G	32317540	0.24	0.20	2.4E-4	1.11	0.09	1.28	1.4E-6
	rs382259	G	32317005	0.28	0.25	0.01	1.06	0.29	1.29	2.2E-7
	rs412657	C	32319063	0.43	0.40	1.00	1.07	0.16	1.30	4.5E-8
	rs41271257	A	35544173	0.03	0.02	0.09	1.10	0.52	1.31	3.0E-8
	rs416352	A	32315371	0.36	0.34	0.19	1.07	0.16	1.31	2.2E-8
	rs419132	C	32318777	0.29	0.26	0.03	1.04	0.44	1.30	2.0E-7
	rs427037	C	32320242	0.25	0.22	0.01	1.09	0.12	1.29	2.5E-7
	rs4713859	C	35514131	0.06	0.05	0.48	0.99	0.89	1.31	2.9E-8
	rs4959068	A	31451823	0.07	0.06	1.00	0.95	0.60	1.30	8.9E-8
	rs6457499	C	32306926	0.33	0.31	0.75	1.00	0.96	1.31	3.1E-8
	rs6910087	T	31485026	0.12	0.12	0.14	0.90	0.15	1.30	4.3E-8
	rs6911024	C	31476430	0.12	0.12	0.24	0.91	0.19	1.30	4.1E-8
	rs6915986	C	32791876	0.02	0.02	0.47	1.05	0.78	1.31	2.9E-8
	rs6932730	C	31462161	0.18	0.19	0.56	0.85	0.01	1.32	1.3E-8
	rs6936346	T	32308732	0.33	0.31	0.75	1.00	0.97	1.31	4.0E-8
	rs6936707	T	32792047	0.02	0.02	0.47	1.05	0.78	1.31	3.4E-8
	rs9263475	G	31158327	0.25	0.24	0.19	1.00	0.93	1.31	2.2E-8
	rs9267853	T	32303229	0.37	0.37	0.60	1.03	0.62	1.31	3.8E-8
	rs9268830	G	32535550	0.19	0.16	0.41	0.99	0.87	1.32	1.8E-7
	rs9296153	T	35488200	0.03	0.02	0.22	0.97	0.86	1.31	2.8E-8
	rs9296154	A	35495356	0.03	0.02	0.21	0.99	0.94	1.31	2.9E-8
	rs9357138	T	32327816	0.16	0.13	0.01	1.15	0.04	1.28	3.5E-7
	rs9454898	C	70576382	0.00	0.00	1.00	0.98	0.97	1.31	3.8E-8
	rs9462081	C	35483984	0.03	0.02	0.22	1.00	0.98	1.31	3.2E-8
	rs9463680	C	51251060	0.01	0.01	0.16	1.08	0.74	1.31	2.8E-8
	rs9470023	T	35506335	0.02	0.02	0.18	0.95	0.76	1.31	2.9E-8
	rs9496752	T	144078155	0.00	0.00	1.00	1.43	0.58	1.31	2.9E-8

(b) Association of *HLA-DRA* SNP with PD conditioned on SNPs that are associated with PC1 ($P < 10^{-20}$) and in LD ($r^2 > 0.05$) with rs3129882 adjusted for (i) sex and PC1-associated SNPs, and (ii) sex, age, PC1, PC2 and PC1-associated SNPs. Test begins with the top PC1-associated SNP and every iteration is cumulative including the prior PC1 SNP and adding the next significant one.

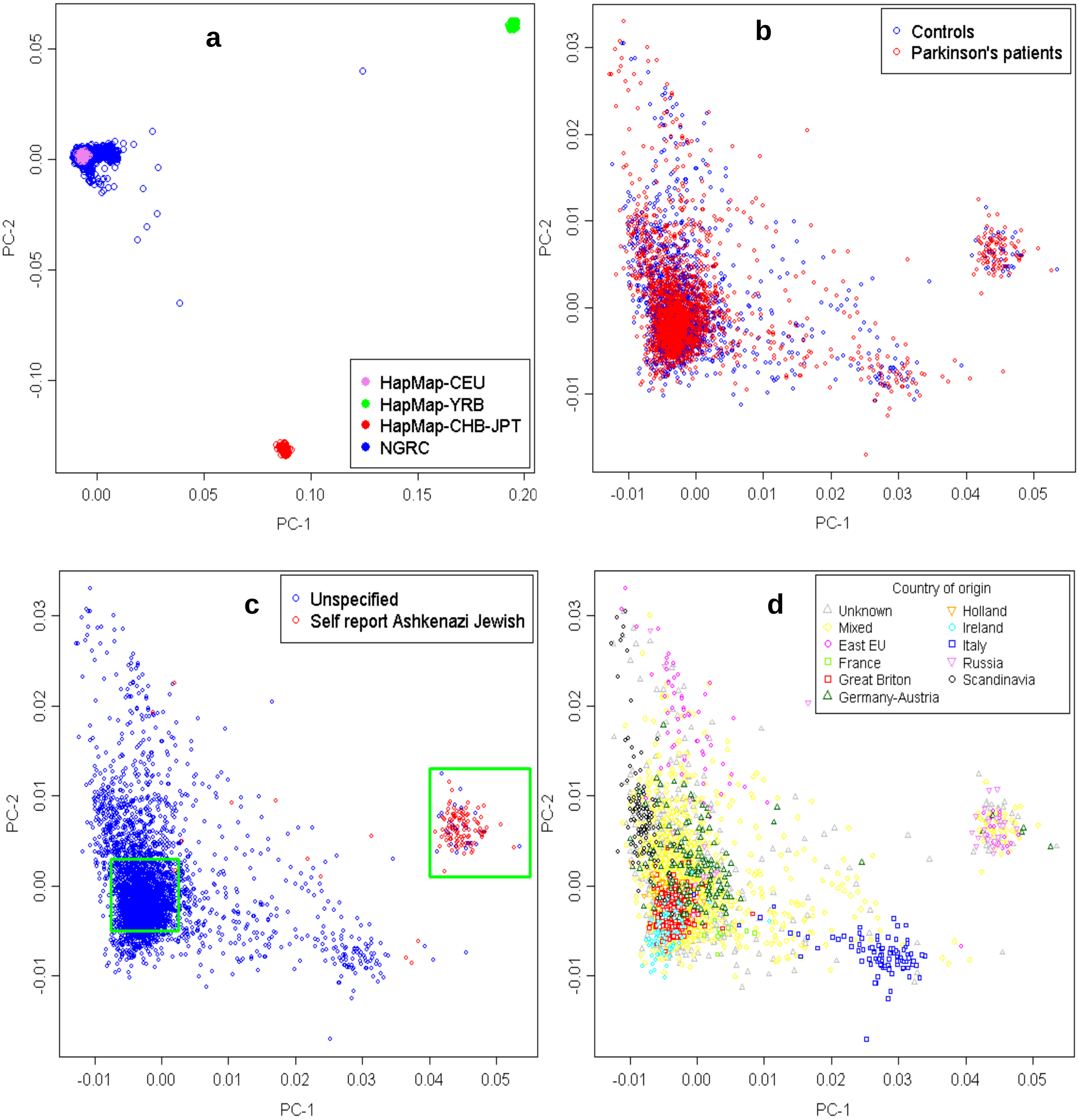
Number of PC1-SNPs adjusted for	**PC1-associated SNPs**	**BP**	**P for PC1-Association**	**r^2 with *HLA-DRA* rs3129882**	**(i) rs3129882 association with PD adjusted for sex & PC1-assoc SNPs**			**(ii) rs3129882 association with PD adjusted for sex, age, PC1, PC2 & PC1-assoc SNPs**		
					OR	**95% CI**	**P**	**OR**	**95% CI**	**P**
1	rs9268628	32513843	1.7E-28	0.26	1.26	1.13-1.41	2.6E-5	1.28	1.15-1.43	1.1E-5
2	rs9268628	32513843	1.7E-28	0.26	1.24	1.11-1.39	1.3E-4	1.28	1.14-1.43	2.2E-5
	rs3104404	32790152	1.3E-34	0.19						
3	rs9268628	32513843	1.7E-28	0.26	1.24	1.11-1.39	1.9E-4	1.27	1.14-1.43	3.2E-5
	rs3104404	32790152	1.3E-34	0.19						
	rs4424079	32710147	4.0E-28	0.15						
4	rs9268628	32513843	1.7E-28	0.26	1.25	1.12-1.40	1.2E-4	1.28	1.14-1.44	2.1E-5
	rs3104404	32790152	1.3E-34	0.19						
	rs4424079	32710147	4.0E-28	0.15						
	rs17577980	32467799	2.3E-33	0.14						
5	rs9268628	32513843	1.7E-28	0.26	1.25	1.11-1.40	1.2E-4	1.28	1.14-1.44	2.2E-5
	rs3104404	32790152	1.3E-34	0.19						
	rs4424079	32710147	4.0E-28	0.15						
	rs17577980	32467799	2.3E-33	0.14						
	rs17208811	32478440	1.3E-29	0.12						
6	rs9268628	32513843	1.7E-28	0.26	1.245	1.11-1.39	1.5E-4	1.28	1.14-1.44	2.3E-5
	rs3104404	32790152	1.3E-34	0.19						
	rs4424079	32710147	4.0E-28	0.15						
	rs17577980	32467799	2.3E-33	0.14						
	rs17208811	32478440	1.3E-29	0.12						
	rs8192564	32299800	4.8E-33	0.11						
7	rs9268628	32513843	1.7E-28	0.26	1.25	1.12-1.40	1.0E-4	1.28	1.15-1.44	2.0E-5
	rs3104404	32790152	1.3E-34	0.19						
	rs4424079	32710147	4.0E-28	0.15						
	rs17577980	32467799	2.3E-33	0.14						
	rs17208811	32478440	1.3E-29	0.12						
	rs8192564	32299800	4.8E-33	0.11						
	rs380571	32317540	1.6E-86	0.08						
8	rs9268628	32513843	1.7E-28	0.26	1.27	1.13-1.42	5.2E-5	1.30	1.16-1.46	1.0E-5
	rs3104404	32790152	1.3E-34	0.19						
	rs4424079	32710147	4.0E-28	0.15						
	rs17577980	32467799	2.3E-33	0.14						
	rs17208811	32478440	1.3E-29	0.12						
	rs8192564	32299800	4.8E-33	0.11						
	rs380571	32317540	1.6E-86	0.08						
	rs17581425	32788563	2.5E-29	0.06						

(c) Association of *HLA-DRA* SNP with PD conditioned on PC1-SNPs that are in LD (r^2≥0.30) with *HLA-DRA* SNP.

Number of PC1-SNPs adjusted for	PC1-asscoiated SNP	BP	P For PC1-Association	r^2 with *HLA-DRA* rs3129882	rs3129882 assoc with PD adj for sex & PC1 SNPs in column 1			rs3129882 assoc with PD adj for sex, age, PC1, PC2 & PC1 SNPs in column 1		
					OR	**95% CI**	**P**	**OR**	**95% CI**	**P**
1	rs3129883	32518115	1.4E-8	0.44	1.40	1.23-1.58	2.3E-7	1.34	1.18-1.52	9.0E-6
2	rs3129883	32518115	1.4E-8	0.44	1.36	1.17-1.58	6.3E-5	1.32	1.14-1.54	3.1E-4
	rs2076536	32447326	2.3E-15	0.35						
3	rs3129883	32518115	1.4E-8	0.44	1.38	1.16-1.63	1.8E-4	1.34	1.13-1.59	6.3E-4
	rs2076536	32447326	2.3E-15	0.35						
	rs3129859	32508917	2.8E-8	0.34						
4	rs3129883	32518115	1.4E-8	0.44	1.40	1.18-1.65	1.0E-4	1.35	1.14-1.60	5.0E-4
	rs2076536	32447326	2.3E-15	0.35						
	rs3129859	32508917	2.8E-8	0.34						
	rs2076534	32470394	3.8E-11	0.33						
5	rs3129883	32518115	1.4E-8	0.44	1.42	1.20-1.69	5.9E-5	1.38	1.16-1.64	3.1E-4
	rs2076536	32447326	2.3E-15	0.35						
	rs3129859	32508917	2.8E-8	0.34						
	rs2076534	32470394	3.8E-11	0.33						
	rs3135334	32510664	8.7E-10	0.32						
6	rs3129883	32518115	1.4E-8	0.44	1.50	1.26-1.80	9.3E-6	1.47	1.23-1.77	2.9E-5
	rs2076536	32447326	2.3E-15	0.35						
	rs3129859	32508917	2.8E-8	0.34						
	rs2076534	32470394	3.8E-11	0.33						
	rs3135334	32510664	8.7E-10	0.32						
	rs3129888	32519704	2.8E-13	0.32						
7	rs3129883	32518115	1.4E-8	0.44	1.50	1.26-1.80	9.6E-6	1.48	1.23-1.78	2.6E-5
	rs2076536	32447326	2.3E-15	0.35						
	rs3129859	32508917	2.8E-8	0.34						
	rs2076534	32470394	3.8E-11	0.33						
	rs3135334	32510664	8.7E-10	0.32						
	rs3129888	32519704	2.8E-13	0.32						
	rs3135343	32504291	4.0E-12	0.31						
8	rs3129883	32518115	1.4E-8	0.44	1.50	1.25-1.80	1.0E-5	1.48	1.23-1.78	2.8E-5
	rs2076536	32447326	2.3E-15	0.35						
	rs3129859	32508917	2.8E-8	0.34						
	rs2076534	32470394	3.8E-11	0.33						
	rs3135334	32510664	8.7E-10	0.32						
	rs3129888	32519704	2.8E-13	0.32						
	rs3135343	32504291	4.0E-12	0.31						
	rs3129877	32516575	1.2E-11	0.30						

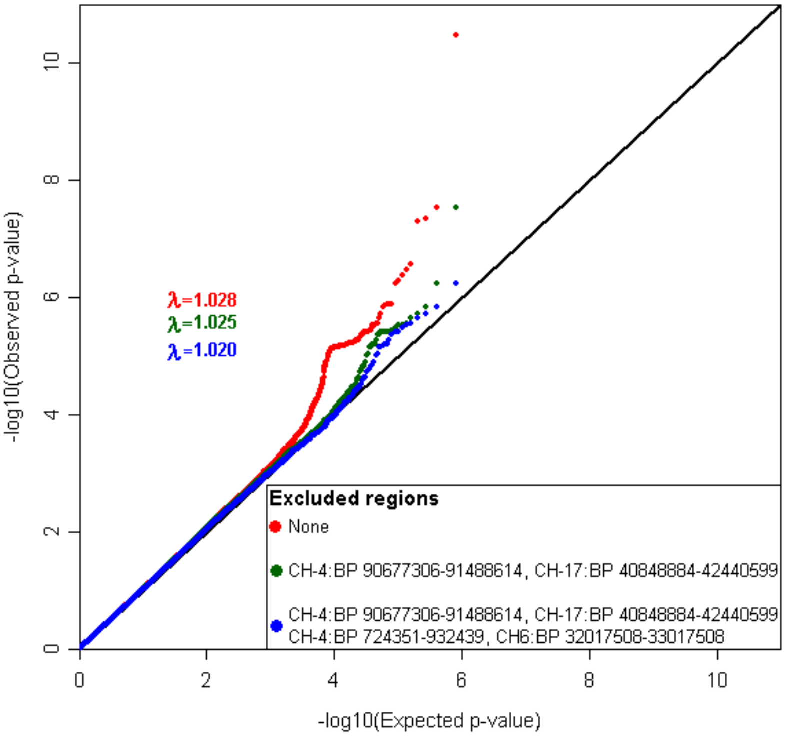
Supplementary Figure 1. Population substructure in Americans of European ancestry.

(a) PCA was used to plot NGRC samples (blue) against HapMap samples (Caucasian: purple, Chinese-Japanese: red, Yoruba African: green). **(b)** PCA was repeated without HapMap samples for an in-depth look at substructure within NGRC. PC1 and PC2 separate two clusters. **(c)** Subjects who reported as Ashkenazi Jewish are plotted in red and those who did not specify and therefore may or may not be Jewish are blue. The core of each cluster, used for population structure sub-analyses (**Suppl Table 2**), are marked. **(d)** Subjects whose paternal and maternal ancestors immigrated to the US from the same European country are designated by the same color. The resulting substructure follows the map of Europe, with Italians at the bottom (blue squares), moving clockwise to northwest into Germany (dark green triangles), France (light green squares) and Great Britain (red squares), then north to Scandinavia (black circles), and east to Eastern European countries (pink circle) and Russia (pink triangle). The cluster to the far right, which was shown above to be Ashkenazi Jews, immigrated from Russia, E. Europe and Germany, which is historically accurate.



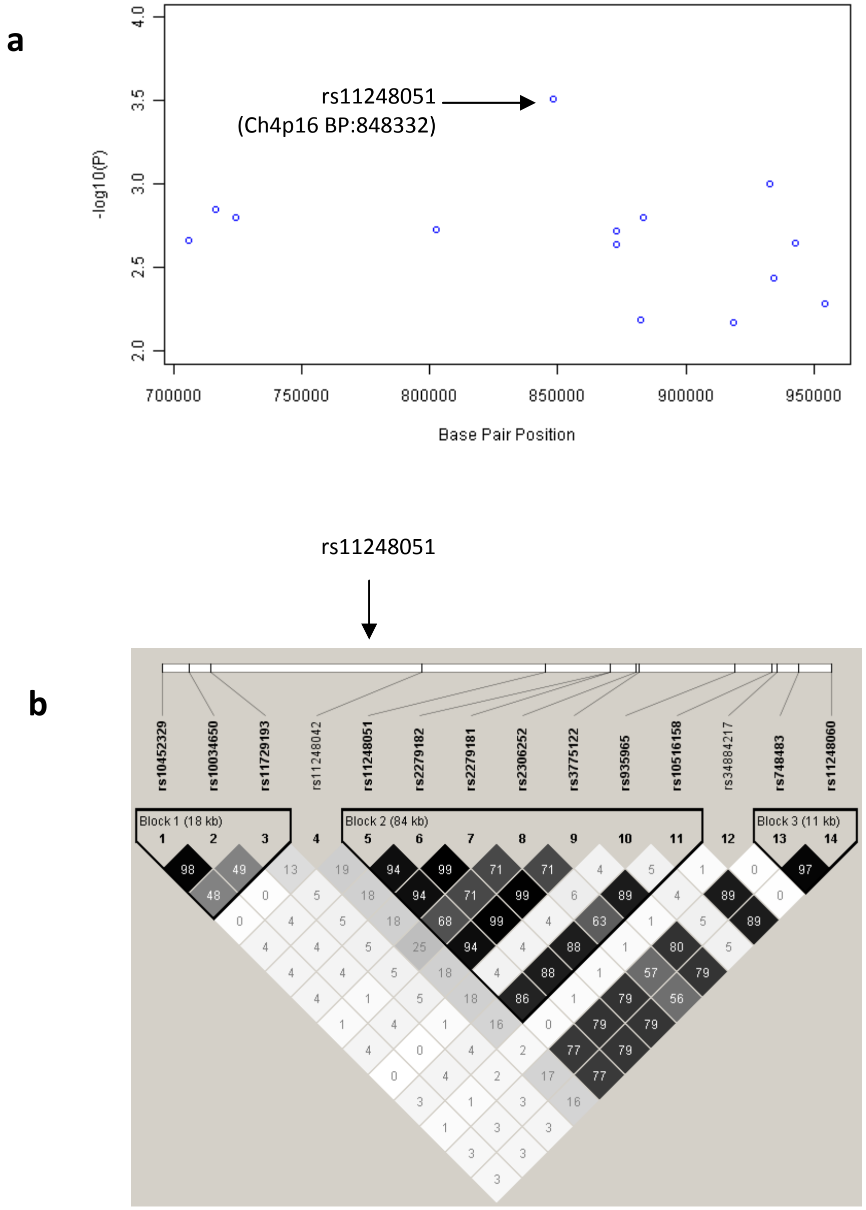
Supplementary Figure 2. Quantile-quantile plot

Distribution of expected P-values for no disease association (black line) vs. the observed P-values in NGRC dataset. The observed are plotted once for all 811,597 SNPs tested (red), once excluding *SNCA* and *MAPT* regions (green), and again excluding *SNCA*, *MAPT* and sub-region of *HLA* including PC1 and PD associated SNPs (blue). λ=Genomic inflation factor.



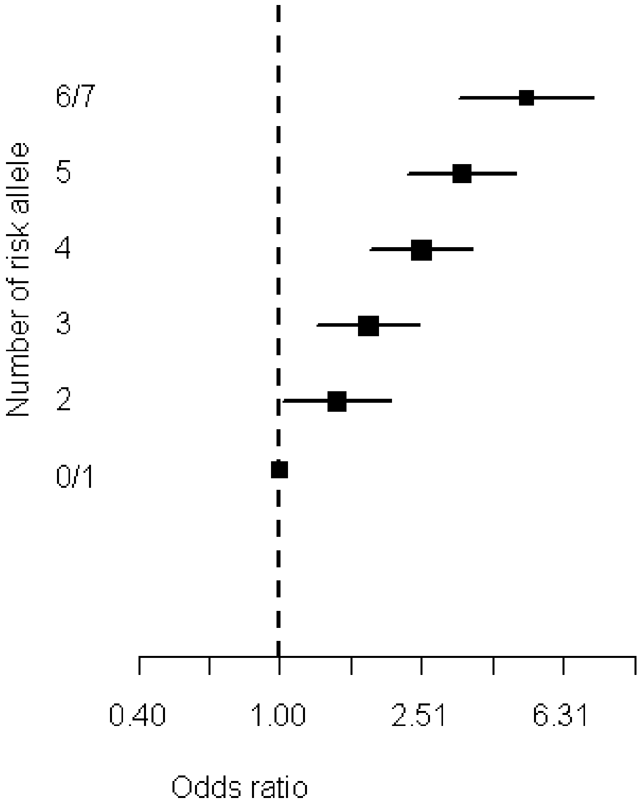
Supplementary Figure 3. *GAK* (*PARK17*)

(a) Manhattan plot of Ch4p16 (bp 700000-970000) surrounding PD-associated SNP (rs11248051) in *GAK* region.
(b) Haploview of all SNPs in the region with PD-association P<0.01.



Supplementary Figure 4. Odds ratios for the combination of *SNCA, MAPT, GAK* and *HLA*.

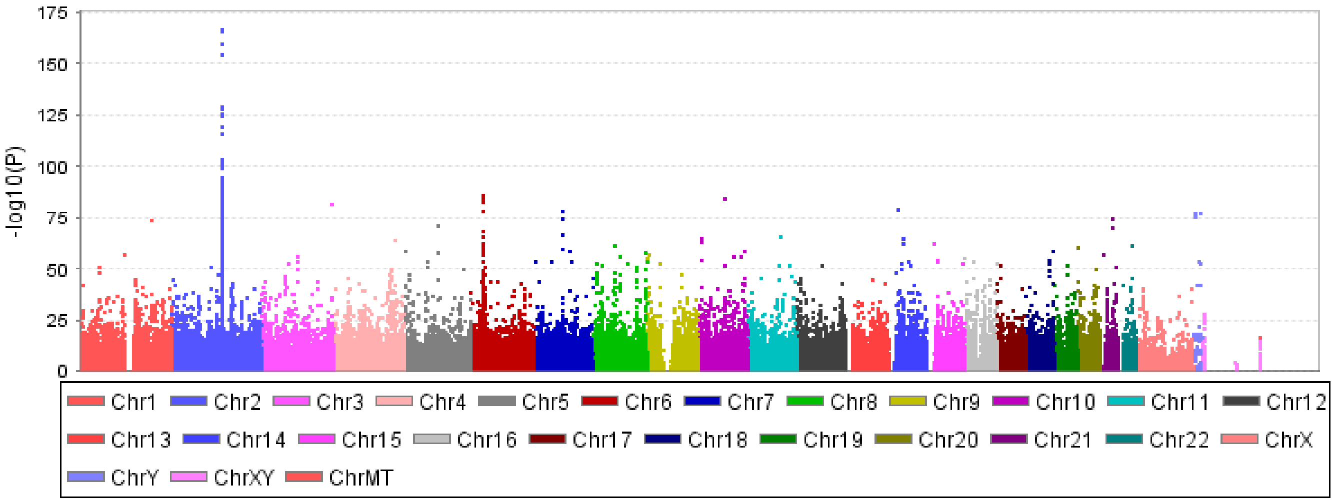
The individual ORs for each locus were similar; we therefore pooled them and assumed each risk allele increased risk by the same amount. The number of risk alleles (0 to 8 alleles) was regressed on disease status using logistic regression (OR and 95% CI are shown below). Due to small numbers, subjects who had 0 or 1 risk allele were combined as “low-risk” and used as reference. Similarly, genotypes with 6 or more risk alleles were rare and were therefore combined.



Carrier status (No of risk alleles)	OR (95% CI)	P	No of subjects	
			Case	Control
0	Ref.	Ref.	4	10
1			55	114
2	1.45 (1.03-2.05)	0.04	271	393
3	1.45 (1.03-2.05)	6.9×10^{-4}	548	650
4	2.49 (1.79-3.47)	6.5×10^{-8}	619	522
5	3.26 (2.29-4.62)	4.2×10^{-11}	364	235
6	4.95 (3.20-7.64)	5.5×10^{-13}	117	56
7			22	3
8			0	0

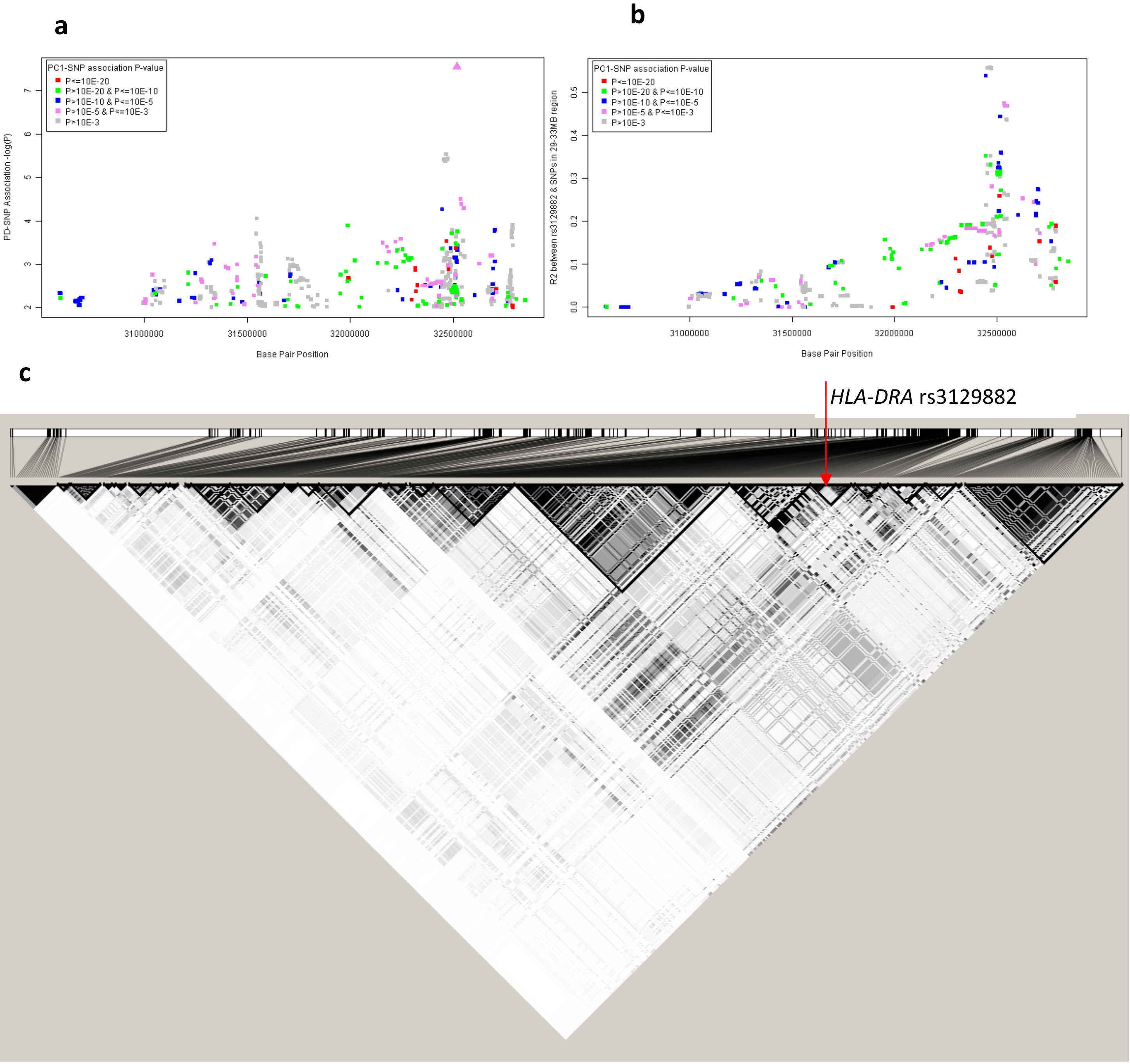
Supplementary Figure 5. Localization of genomic regions associated with principal component

To pinpoint the genomic regions that contribute most to PC1, linear regression was used to test association of SNPs with PC1 and the P-values were displayed in a Manhattan plot. As expected, several peaks were evident across the genome, most notably, a peak at the lactase (*LTC*) gene on chromosome 2 and one in *HLA* on chromosome 6. (Also see **Supplementary Figure 6**, and **Supplementary Table 5**).



Supplementary Figure 6. LD between PD-associated SNPs and PC1-associated SNPs within *HLA*

(a) Manhattan plot for the entire *HLA* complex (Chr6: 29MB-33Mb) indicating PD-associated SNPs with P<0.01. The association of each SNP with PC1 is indicated by color representing the P value. **(b)** Manhattan plot for the entire *HLA* complex (Chr6: 29MB-33Mb) indicating LD (r^2) between all SNPs associated with PD (P<0.01) and the *HLA-DRA* SNP. The association of each SNP with PC1 is indicated by color representing the P value. **(c)** The haploview diagram shows the level of LD (r^2) among PD-associated SNPs (P<0.01) in the Chr6: 29MB-33Mb region.



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