SUPPLEMENTARY INFORMATION

Methods

Details HLA sequencing

Long range PCR was used to amplify the entire gene from each of the *HLA* class I loci (>200 bp 5'UTR to 3'UTR ~200-400 bp), *HLA-DQA1* (~200 bp of the 5'UTR to ~200 bp of the 3'UTR), and DQB1 (~70bp of the 5'UTR to ~100 bp of the 3'UTR). For the remaining class II loci specific key regions of the gene were amplified. For *HLA-DPA1*, this coverage was from exon 1 through to exon 4 and for HLA-DPB1 from exon 2 to exon 4. All *HLA-DRB1/3/4/5* genes were co-amplified in two separate reactions. The coverage for HLA-DRB1/3/4 loci included ~300-500 bp of the 5'UTR to the first ~270 bp of intron-1 and the end of intron-1 (~250 bp) to exon-6. For the *HLA-DRB5* gene exons 2 to exon 6 were amplified. Each PCR amplification contained 100 ng genomic DNA and a solution of PCR master mix consisting of a cocktail of enzymes, buffers and primers specific for each *HLA* locus. The thermal cycling parameters for all genes were as follows; initial denaturation 94^0C/30 sec, followed by 15 cycles at 94^0C/1 min 15 sec, 60^0C/30 sec, 66^0C/7 min 30 sec, followed by 20 cycles at 94^0C/30 sec, 60^0C/30 sec, 66^0C/7 min 30 sec, ending with a final extension step at 66^0C for 10 min. PCR's were performed using Veriti Thermal Cyclers (Applied Biosystems/Thermo Fisher Scientific, Waltham, MA, USA). PCR products were quantified using a PicoGreen assay (Invitrogen/Thermo Fisher Scientific, Waltham, MA, USA) using a Victor X plate reader (Perkin Elmer, Waltham, MA, USA). Amplicons for all genes were pooled in optimal molar amounts, and purified using Agencourt AMPure XP beads (Beckman Coulter, Fullerton, CA). Barcoded sample libraries were prepared as follows: enzymatic cleavage into 300 - 500 bp fragments, followed by enzymatic end repair to remove dNTPs overhangs and incorporation of deoxynucleotide dAMP to blunt ended 3' ends, purification using Agencourt AMPure beads, followed by ligation of a unique adaptor indices to each pooled sample. All adaptor ligated samples were pooled into a single tube, purified using

Agencourt AMPure XP beads and DNA fragments were size selected for 400 - 500 bp fragments using the Blue Pippin system (Sage Science, Inc., Beverly, MA, USA). The eluted sample was enriched by a short PCR cycle using Illumina primers that contain adaptor sequences required for binding to the surface of the Illumina flow cell, purified using Agencourt AMPure XP beads and quality checked using the Agilent 2200 TapeStation instrument (Agilent Technologies, Inc., Santa Clara, CA, USA). The library was quantified using the Qubit™ dsDNA BR Assay Kit (ThermoFisher Scientific, Waltham, MA, USA) with the Qubit Fluorometer. The sample was denatured with sodium hydroxide and sequenced at a final concentration of 1.3 pM spiked with 0.2 % phi X on the Illumina NextSeq 500 or MiniSeq instruments using 150 cycle paired-end kits (Illumina, Inc., San Diego, CA, USA).

HLA NGS reads were analyzed using the MIA FORA NGS FLEX v3.0 software which employs two complementary strategies: competitive mapping of paired-end NGS reads and *de novo* assembly to construct phased consensus sequences to analyze data and generate genotype calls. Paired-end reads and phased consensus sequences were compared to three sources of *HLA* reference sequences: IPD-IMGT/HLA database v3.24.0 (http://www.ebi.ac.uk/imgt/hla/) and internal references generated by cloning and sequencing experiments as well as computationally filled *in silico HLA* sequences to find the closest fit. Final genotyping calls were made after manual review.

Supplementary Table 1. Frequency of HLA alleles in PD cases and controls in the discovery dataset.

Locus	Allele	Control	PD
A	01:01:01:01	0.15722	0.16218
A	01:01:13	0	0.00031
A	01:02	0.00062	0
A	01:03	0	0.00063
A	01:06	0.00031	0
A	01:25	0.00031	0
A	02:01:01:01	0.26152	0.26299
A	02:01:01:03	0	0.00031
A	02:01:01:05	0.00062	0.00188
A	02:01:02	0	0.00031
A	02:01:04	0.00062	0
A	02:01:05	0.00031	0.00031
A	02:01:14Q	0.00031	0
A	02:02:01:01	0.00062	0.00031
A	02:02:01:02	0.00031	0
A	02:05:01	0.01214	0.01127
A	02:06:01:01	0.00187	0.00188
A	02:07:01	0.00031	0
A	02:08	0.00031	0
A	02:09	0	0.00031
A	02:17:02	0	0.00094
A	02:20:01	0	0.00063
A	02:24:01	0.00031	0.00031
A	02:30	0.00031	0.00031
A	02:34	0.00031	0
A	02:36	0	0.00031
A	03:01	0	0.00031
A	03:01:01:01	0.1373	0.14089
A	03:01:01:03	0.00125	0.00438
A	03:01:01:05	0.00529	0.00376
A	03:02:01	0.00342	0.00219
A	11:01:01:01	0.07192	0.05949
A	23:01:01	0.01868	0.01972
A	23:17	0	0.00031
A	24:02:01:01	0.07877	0.06794
A	24:02:01:02L	0.00093	0
A	24:02:01:04	0.00311	0.0025
A	24:02:01:05	0.0028	0.00407
A	24:03:01	0.00187	0.00157
A	24:226:01	0.00031	0
A	24:314	0	0.00031

A	24:58:00	0.00031	0
A	24:72	0	0.00031
A	25:01:01	0.0193	0.02223
A	25:03:00	0	0.00031
A	26:01:01:01	0.03767	0.03632
A	26:01:01:02	0	0.00063
A	26:08:00	0.00187	0.00094
A	26:17:00	0	0.00031
A	26:26:00	0.00031	0
A	29:01:01:01	0.00342	0.00689
A	29:02:01:01	0.03113	0.02849
A	29:02:01:02	0.00249	0.0025
A	30:01:01	0.01152	0.01378
A	30:02:01:01	0.00965	0.01033
A	30:02:01:02	0.00031	0.00063
A	30:02:01:03	0	0.00063
A	30:04:01	0.00093	0.00344
A	31:01:02:01	0.02335	0.02693
A	32:01:01	0.0411	0.03882
A	33:01:01	0.00965	0.00845
A	33:03:01	0.00374	0.00407
A	34:02:01	0.00093	0.00157
A	36:01:00	0	0.00031
A	66:01:01	0.00405	0.00188
A	68:01:01:02	0.00841	0.0072
A	68:01:02:01	0.00218	0.0025
A	68:01:02:02	0.01339	0.01659
A	68:01:02:03	0.00031	0.00031
A	68:02:01:01	0.00716	0.00877
A	68:02:01:03	0	0.00031
A	68:03:01	0	0.00031
A	68:13:01	0	0.00031
A	69:01:00	0.00249	0.00094
A	74:01:01	0.00031	0.00031
B	07:02:01	0.13325	0.1268
B	07:04	0.00031	0
B	07:05:01	0.00342	0.00407
B	07:06	0.00062	0.00157
B	07:09	0.00031	0
B	08:01:01	0.10243	0.11616
B	13:02:01	0.02397	0.02379
B	14:01:01	0.00996	0.00626
B	14:02:01:01	0.02833	0.02974
B	14:02:01:02	0.00031	0.00031
B	15:01:01:01	0.05573	0.05009

B	15:01:01:04	0.00311	0.00438
B	15:03:01:02	0	0.00094
B	15:07:01	0.00187	0.00063
B	15:08:01	0	0.00031
B	15:09	0.00062	0
B	15:10:01	0	0.00063
B	15:16:01	0.00093	0.00063
B	15:17:01:01	0.00498	0.0047
B	15:18:01	0.0028	0.00282
B	15:220	0.00031	0.00063
B	15:228	0.00031	0
B	15:29	0.00031	0
B	15:34	0.00031	0
B	15:35	0.00031	0
B	15:39:01	0	0.00063
B	15:50	0.00031	0
B	18:01:01:01	0.01276	0.01378
B	18:01:01:02	0.03425	0.03068
B	18:03	0.00062	0.00094
B	18:05	0.00031	0
B	18 :78	0.00031	0
B	27:02:01	0.00467	0.00344
B	27:05:02	0.03238	0.04352
B	27:05:03	0.00093	0.00063
B	27:05:04	0.00031	0.00031
B	27:05:07	0	0.00031
B	27:07:01	0.00062	0.00031
B	27:09:00	0	0.00031
B	27:13:00	0.00031	0
B	35:01:01:02	0.05853	0.05886
B	35:01:07	0.00031	0
B	35:02:01	0.0109	0.01127
B	35:03:01	0.02024	0.01972
B	35:08:01	0.0056	0.00532
B	35:41:00	0.00031	0.00094
B	35:42:01	0	0.00031
B	37:01:01	0.01245	0.01691
B	38:01:01	0.02615	0.02818
B	38:09:00	0	0.00031
B	39:01:01:03	0.00903	0.01033
B	39:05:01	0	0.00031
B	39:06:02	0.00685	0.00407
B	39:10:01	0	0.00031
B	39:24:01	0.00031	0.00157
B	39:35:00	0.00031	0

B	40:01:02	0.04981	0.04822
B	40:02:01	0.01401	0.01002
B	40:06:01:02	0.00031	0
B	40:32:00	0	0.00031
B	41:01:01	0.00498	0.00595
B	41:02:01	0.00498	0.00125
B	42:01:01	0	0.00031
B	42:02:01:02	0.00031	0.00031
B	44:02:01:01	0.06445	0.0717
B	44:02:01:03	0.00996	0.01002
B	44:03:01:01	0.04359	0.04665
B	44:03:01:02	0.00093	0
B	44:03:02	0.00062	0.00031
B	44:03:03	0	0.00031
B	44:04:00	0.00125	0
B	44:05:01	0.00529	0.00344
B	44:23N	0	0.00031
B	44:27:01	0.00249	0.00125
B	44:29:00	0	0.00031
B	45:01:01	0.00592	0.00564
B	47:01:01:03	0.00311	0.00282
B	47:02:00	0.00031	0
B	48:01:01	0.0028	0.00031
B	49:01:01	0.01868	0.01816
B	50:01:01	0.0109	0.01221
B	50:02:00	0	0.00031
B	51:01:01:01	0.05106	0.04258
B	51:01:07	0	0.00031
B	51:05:00	0.00062	0.00031
B	51:07:01	0.00062	0.00031
B	51:08:01	0.00218	0.00125
B	51:09:01	0.00062	0
B	51:22:00	0.00031	0
B	52:01:01:01	0	0.00031
B	52:01:01:02	0.01152	0.00971
B	52:01:01:03	0	0.00031
B	53:01:01	0.00374	0.00376
B	55:01:01	0.02179	0.01659
B	55:01:03	0.00031	0.00094
B	56:01:01:02	0.00187	0.0025
B	56:01:01:03	0.00529	0.00438
B	57:01:01	0.033	0.03851
B	57:02:01	0	0.00063
B	57:03:01	0.00093	0.00125
B	57:79N	0.00031	0

B	58:01:01:01	0.00747	0.0072
B	58:02:00	0	0.00031
B	58:02:01	0.00031	0
B	73:01:00	0	0.00094
C	01:02:01	0.03269	0.03726
C	02:02:02:01	0.04421	0.04383
C	02:02:02:02	0.00218	0.00094
C	02:10	0	0.00094
C	03:02:02:01	0.0028	0.00188
C	03:02:02:02	0.00031	0
C	03:03:01	0.05666	0.05479
C	03:03:02	0	0.00031
C	03:04:01:01	0.06196	0.05479
C	03:04:01:02	0.00872	0.00814
C	03:04:02	0	0.00031
C	03:08	0.00031	0
C	03:44	0	0.00031
C	04:01:01:01	0.06849	0.07451
C	04:01:01:05	0.0165	0.01158
C	04:01:01:06	0.02802	0.02599
C	04:09N	0.00156	0.00063
C	05:01:01:01	0.01276	0.01284
C	05:01:01:02	0.06476	0.07107
C	05:01:05	0.00031	0.00031
C	05:09:01	0.00031	0.00031
C	06:02:01:01	0.07192	0.08422
C	06:02:01:02	0.00965	0.01158
C	06:02:01:03	0.0056	0.00501
C	06:06	0.00031	0
C	07:01:01:01	0.13979	0.15216
C	07:01:02	0.00529	0.00532
C	07:02:01:01	0.0137	0.01221
C	07:02:01:03	0.13014	0.12367
C	07:04:01	0.01681	0.01565
C	07:06	0.00062	0.00031
C	07:18	0.00498	0.00564
C	07:38:01	0	0.00031
C	07 :419	0	0.00031
C	07:46	0.00031	0
C	07:57	0.00062	0
C	08:01:01	0.00125	0
C	08:02:01:01	0.02677	0.02974
C	08:02:01:02	0.01152	0.00626
C	08:03:01	0.00125	0.00031
C	08:22	0.00031	0

C	12:02:02	0.01152	0.01033
C	12:03:01:01	0.05573	0.05448
C	12:05	0.00031	0
C	14:02:01	0.0137	0.00877
C	14:03	0	0.00031
C	15:02:01:01	0.02117	0.01534
C	15:02:01:02	0.00031	0.00094
C	15:04:01	0.00031	0.00031
C	15:05:01	0	0.00094
C	15:05:02	0.00436	0.00689
C	15:09	0.00031	0.00031
C	15:13	0.00156	0
C	16:01:01:01	0.02802	0.0335
C	16:02:01	0.0056	0.0047
C	16:04:01	0.00218	0.00125
C	16:85	0.00062	0
C	17:01:01:02	0.00031	0.00063
C	17:01:01:05	0.00467	0.00532
C	17:03	0.00529	0.00125
C	18:02	0	0.00094
DPA1	01:03:01:01	0.13169	0.1268
DPA1	01:03:01:02	0.29421	0.28272
DPA1	01:03:01:03	0.099	0.09205
DPA1	01:03:01:04	0.18182	0.18096
DPA1	01:03:01:05	0.11115	0.12993
DPA1	01:03:04	0.00031	0
DPA1	01:03:05	0.00031	0.00157
DPA1	01:04	0.00716	0.00532
DPA1	01:05	0.00062	0.00031
DPA1	02:01:01	0.099	0.09768
DPA1	02:01:02	0.03798	0.04508
DPA1	02:01:04	0.00093	0.00407
DPA1	02:01:07	0.00031	0.00031
DPA1	02:01:08	0.00031	0.00031
DPA1	02:02:02	0.01743	0.01315
DPA1	02:02:05	0.00031	0
DPA1	02:06	0.00685	0.00845
DPA1	02:07	0.00841	0.00845
DPA1	03:01	0.00187	0.00282
DPA1	04:01	0.00031	0
DPB1	01:01:01	0.04639	0.05229
DPB1	01:01:02	0.00093	0.00094
DPB1	02:01:02	0.13605	0.13118
DPB1	02:01:04	0.00062	0.00125
DPB1	02:02	0.00654	0.00751

DPB1	03:01:01	0.08219	0.07796
DPB1	04:01:01:01	0.43244	0.43049
DPB1	04:01:01:02	0.00156	0.00031
DPB1	04:01:03	0.00031	0
DPB1	04:01:06	0	0.00031
DPB1	04:02:01:01	0.02304	0.03569
DPB1	04:02:01:02	0.08686	0.09267
DPB1	05:01:01	0.02055	0.01785
DPB1	06:01	0.01432	0.01127
DPB1	09:01:01	0.00716	0.00626
DPB1	10:01:01	0.0165	0.01346
DPB1	104:01:00	0.01681	0.01503
DPB1	105:01:00	0.00311	0.0047
DPB1	11:01:01	0.01961	0.01847
DPB1	124:01:00	0.00093	0.00125
DPB1	126:01:00	0	0.00063
DPB1	13:01:01	0.01526	0.02254
DPB1	131:01:00	0.00031	0
DPB1	132:01:00	0	0.00031
DPB1	138:01:00	0.00062	0.00063
DPB1	14:01:01	0.01993	0.01534
DPB1	15:01:01	0.00747	0.00751
DPB1	16:01:01	0.00685	0.00564
DPB1	17:01	0.00996	0.0119
DPB1	18:01	0	0.00031
DPB1	19:01	0.00654	0.00501
DPB1	20:01:01	0.00374	0.00376
DPB1	23:01:01	0.00809	0.00438
DPB1	26:01:02	0.00031	0
DPB1	33:01:00	0.00031	0
DPB1	34:01:00	0.00156	0.00063
DPB1	35:01:01	0.00031	0
DPB1	350:01:00	0.00125	0.00094
DPB1	416:01:00	0	0.00031
DPB1	417:01:00	0	0.00031
DPB1	45:01:00	0.00093	0
DPB1	46:01:01	0	0.00063
DPB1	52:01:00	0.00031	0
DPB1	63:01:00	0	0.00031
DPB1	81:01:00	0.00031	0
DQA1	01:01:01	0.09029	0.11083
DQA1	01:01:02	0.01432	0.01565
DQA1	01:01:03	0	0.00031
DQA1	01:02:01	0.13636	0.12774
DQA1	01:02:01:04	0.04701	0.04571

DQA1	01:02:02	0.02148	0.01503
DQA1	01:02:04	0.00031	0
DQA1	01:03:01:01	0.0109	0.00783
DQA1	01:03:01:02	0.05791	0.05729
DQA1	01:03:01:06	0.00031	0
DQA1	01:04:01	0.02397	0.02254
DQA1	01:04:02	0.00125	0.00063
DQA1	01:05:01	0.00841	0.00877
DQA1	01:05:02	0.00031	0.00063
DQA1	01:07Q	0.00031	0
DQA1	01:10	0.00031	0.00188
DQA1	02:01	0.12516	0.13056
DQA1	03:01:01	0.09527	0.0789
DQA1	03:02	0.00934	0.00877
DQA1	03:03:01	0.07908	0.06763
DQA1	04:01:01	0.01899	0.02192
DQA1	04:01:02:01	0.00187	0
DQA1	04:02	0.00093	0.00188
DQA1	05:01:01:01	0.01494	0.01785
DQA1	05:01:01:02	0.09994	0.11897
DQA1	05:01:02	0	0.00031
DQA1	05:02	0	0.00031
DQA1	05:03	0.00156	0.00094
DQA1	05:05:01	0.13138	0.12837
DQA1	05:05:01:03	0.00093	0.0025
DQA1	05:08	0.00031	0
DQA1	05:09	0.00374	0.00219
DQA1	06:01:01	0.00311	0.00407
DQB1	02:01:01	0.11457	0.13682
DQB1	02:02:01:01	0.09247	0.09299
DQB1	02:05	0	0.00031
DQB1	03:01:01:01	0.08126	0.07796
DQB1	03:01:01:02	0.01183	0.01002
DQB1	03:01:01:03	0.10648	0.09987
DQB1	03:01:04	0	0.00063
DQB1	03:02:01	0.10492	0.08579
DQB1	03:02:02	0.00062	0
DQB1	03:03:02	0.01526	0.01534
DQB1	03:03:02:01	0.0274	0.03193
DQB1	03:04:01	0.00187	0.00219
DQB1	03:05:01	0.00125	0.00125
DQB1	03:09	0	0.00031
DQB1	03:12	0.00031	0
DQB1	03:19	0.00249	0.00344
DQB1	03:22	0.00031	0.00031

DQB1	04:02:01	0.02397	0.02599
DQB1	05:01:01:01	0.01463	0.01534
DQB1	05:01:01:02	0.00903	0.00939
DQB1	05:01:01:03	0.0906	0.11209
DQB1	05:02:01	0.02366	0.01503
DQB1	05:02:07	0	0.00031
DQB1	05:03:01	0.02584	0.02286
DQB1	05:04	0.00187	0.00219
DQB1	05:51	0	0.00031
DQB1	06:01:01	0.01059	0.00783
DQB1	06:01:03	0.00031	0
DQB1	06:02:01	0.12671	0.12492
DQB1	06:03:01	0.06258	0.0598
DQB1	06:04:01	0.03456	0.03413
DQB1	06:07:01	0.00031	0
DQB1	06:09:01	0.0137	0.01002
DQB1	06:09:05	0	0.00031
DQB1	06:11:02	0	0.00031
DQB1	06:16	0.00031	0
DQB1	06:39	0.00031	0
DRB1	01:01:01	0.08095	0.10175
DRB1	01:01:04	0.00031	0
DRB1	01:02:01	0.01432	0.01597
DRB1	01:03	0.01245	0.01252
DRB1	03:01:01	0.11613	0.13807
DRB1	03:02:01	0	0.00031
DRB1	03:04:01	0.00031	0
DRB1	04:01:01	0.0906	0.07765
DRB1	04:02:01	0.01526	0.01221
DRB1	04:03:01	0.00778	0.00845
DRB1	04:04:01	0.03394	0.02849
DRB1	04:05:01	0.00592	0.00344
DRB1	04:06:02	0	0.00063
DRB1	04:07:01	0.00965	0.01033
DRB1	04:08:01	0.00685	0.00407
DRB1	04:10:01	0.00031	0
DRB1	04:11:01	0.00031	0
DRB1	04:51	0.00031	0
DRB1	07:01:01	0.1264	0.1315
DRB1	08:01:01	0.00093	0
DRB1	08:01:03	0.0193	0.02223
DRB1	08:02:01	0.00031	0.00094
DRB1	08:03:02	0.0028	0.00407
DRB1	08:04:01	0.00187	0.00094
DRB1	08:06	0	0.00063

DRB1	08:10	0.00031	0
DRB1	09:01:02	0.00934	0.00845
DRB1	10:01:01	0.00841	0.00845
DRB1	11:01:01	0.05729	0.05448
DRB1	11:01:02	0.00062	0.00063
DRB1	11:01:13	0	0.00031
DRB1	11:02:01	0.00218	0.00313
DRB1	11:03:01	0.00654	0.00532
DRB1	11:04:01	0.03954	0.0335
DRB1	11:12:01	0	0.00031
DRB1	11:13:02	0.00031	0
DRB1	11:14:01	0	0.00031
DRB1	11:36	0.00031	0
DRB1	11:43	0.00031	0
DRB1	12:01:01	0.01712	0.02098
DRB1	13:01:01	0.05635	0.05636
DRB1	13:02:01	0.04981	0.04634
DRB1	13:03:01	0.01027	0.01002
DRB1	13:05:01	0.0028	0.0047
DRB1	13:10	0.00031	0.00031
DRB1	13:14:01	0	0.00031
DRB1	14:01:01	0.0028	0.00219
DRB1	14:03:01	0.00031	0
DRB1	14:04:01	0.00187	0.00063
DRB1	14:07:01	0.00031	0
DRB1	14:54:01	0.02055	0.0216
DRB1	15:01:01	0.13294	0.12586
DRB1	15:01:08	0	0.00031
DRB1	15:02:01	0.0109	0.00751
DRB1	15:02:02	0.00031	0
DRB1	15:03:01:01	0.00031	0.00063
DRB1	15:14	0.00031	0
DRB1	16:01:01	0.01868	0.01096
DRB1	16:02:01	0.00187	0.00219

Supplementary Table 2. Results of the DRB1 amino acid association analysis.

Locus	Position	Residue	OR	CI.lower	CI.upper	p.value
DRB1	Position.9	W	1.03	0.89	1.19	0.65707
DRB1	Position.9	E	0.97	0.84	1.13	0.71337
DRB1	Position.9	K	0.86	0.38	1.99	0.68662
DRB1	Position.10	Q	0.86	0.75	1	0.044068
DRB1	Position.10	Y	1.17	1.02	1.36	0.02711
DRB1	Position.10	E	0.69	0.31	1.54	0.31194
DRB1	Position.11	L	1.26	1.01	1.57	0.036154
DRB1	Position.11	S	1.17	1.02	1.36	0.02711
DRB1	**Position.11**	**V**	**0.73**	**0.6**	**0.88**	**0.00064185**
DRB1	Position.11	G	1.1	0.88	1.37	0.38772
DRB1	Position.11	D	0.86	0.38	1.99	0.68662
DRB1	Position.11	P	0.81	0.67	0.99	0.035353
DRB1	Position.12	K	0.85	0.74	0.98	0.02711
DRB1	Position.12	T	1.17	1.02	1.36	0.02711
DRB1	Position.13	F	1.18	0.96	1.46	0.1076
DRB1	Position.13	S	1.16	1	1.34	0.04604
DRB1	**Position.13**	**H**	**0.73**	**0.6**	**0.89**	**0.0012386**
DRB1	Position.13	Y	1.1	0.88	1.37	0.38772
DRB1	Position.13	G	1.11	0.78	1.58	0.55033
DRB1	Position.13	R	0.81	0.67	0.99	0.035353
DRB1	Position.14	E	0.91	0.73	1.13	0.38772
DRB1	Position.14	K	1.1	0.88	1.37	0.38772
DRB1	Position.16	H	0.9	0.63	1.28	0.55033
DRB1	Position.16	Y	1.11	0.78	1.58	0.55033
DRB1	Position.25	R	0.91	0.73	1.13	0.38772
DRB1	Position.25	Q	1.1	0.88	1.37	0.38772
DRB1	Position.26	L	1.22	1	1.49	0.050809
DRB1	Position.26	Y	1.17	0.95	1.45	0.12278
DRB1	**Position.26**	**F**	**0.81**	**0.69**	**0.94**	**0.006488**
DRB1	Position.28	E	1.19	1.02	1.4	0.028617

DRB1	Position.28	D	0.85	0.72	0.99	0.036914
DRB1	Position.28	H	0.86	0.38	1.99	0.68662
DRB1	Position.30	C	1.26	1.01	1.57	0.036154
DRB1	Position.30	Y	0.85	0.72	0.99	0.035274
DRB1	Position.30	L	1.1	0.88	1.37	0.38772
DRB1	Position.30	G	0.86	0.38	1.99	0.68662
DRB1	Position.30	R	0.69	0.31	1.54	0.31194
DRB1	Position.30	H	1.23	0.7	2.21	0.44534
DRB1	Position.31	I	1.23	0.99	1.52	0.053699
DRB1	Position.31	F	0.85	0.69	1.04	0.1076
DRB1	Position.31	V	0.69	0.31	1.54	0.31194
DRB1	Position.32	Y	0.83	0.71	0.97	0.01906
DRB1	Position.32	H	1.2	1.03	1.41	0.01906
DRB1	Position.33	N	1.36	1.12	1.65	0.0012386
DRB1	**Position.33**	**H**	**0.73**	**0.6**	**0.89**	**0.0012386**
DRB1	Position.37	S	0.99	0.85	1.16	0.90793
DRB1	Position.37	N	1.18	1	1.4	0.043824
DRB1	**Position.37**	**Y**	**0.8**	**0.68**	**0.93**	**0.003297**
DRB1	Position.37	F	1.13	0.92	1.39	0.22206
DRB1	Position.37	L	1.23	0.7	2.21	0.44534
DRB1	Position.38	V	0.99	0.62	1.55	0.95872
DRB1	Position.38	A	0.69	0.31	1.54	0.31194
DRB1	Position.38	L	1.23	0.7	2.21	0.44534
DRB1	Position.40	F	1.46	0.65	3.25	0.31194
DRB1	Position.40	Y	0.69	0.31	1.54	0.31194
DRB1	Position.47	Y	0.93	0.81	1.07	0.30036
DRB1	Position.47	F	1.08	0.93	1.24	0.30036
DRB1	Position.57	D	0.91	0.76	1.08	0.26286
DRB1	Position.57	S	0.97	0.68	1.39	0.85911
DRB1	Position.57	V	1.1	0.9	1.35	0.32766
DRB1	Position.57	A	1.27	0.77	2.13	0.32725
DRB1	Position.58	A	1.03	0.8	1.3	0.83338
DRB1	Position.58	E	0.98	0.77	1.24	0.83338

DRB1	Position.60	Y	0.88	0.73	1.07	0.18883
DRB1	Position.60	S	1.1	0.9	1.35	0.32766
DRB1	Position.60	H	1.27	0.77	2.13	0.32725
DRB1	Position.67	L	1.04	0.9	1.2	0.61839
DRB1	Position.67	I	0.99	0.85	1.14	0.84823
DRB1	Position.67	F	0.96	0.78	1.17	0.66663
DRB1	Position.70	Q	0.97	0.84	1.12	0.64672
DRB1	Position.70	D	1.03	0.89	1.19	0.66814
DRB1	Position.70	R	1.02	0.7	1.48	0.93332
DRB1	Position.71	R	1.12	0.97	1.29	0.11587
DRB1	Position.71	E	1	0.81	1.23	0.99203
DRB1	Position.71	K	0.94	0.79	1.11	0.42852
DRB1	Position.71	A	0.87	0.71	1.08	0.19064
DRB1	Position.73	A	0.85	0.72	1	0.045738
DRB1	Position.73	G	1.18	1	1.39	0.045738
DRB1	Position.74	A	0.84	0.73	0.98	0.026734
DRB1	Position.74	R	1.2	0.97	1.49	0.083138
DRB1	Position.74	E	1.12	0.8	1.58	0.48977
DRB1	Position.74	Q	1.1	0.88	1.37	0.38772
DRB1	Position.74	L	1.03	0.66	1.63	0.89123
DRB1	Position.77	T	0.83	0.67	1.03	0.083138
DRB1	Position.77	N	1.2	0.97	1.49	0.083138
DRB1	Position.78	Y	0.93	0.75	1.14	0.46538
DRB1	Position.78	V	1.08	0.87	1.34	0.46538
DRB1	Position.85	V	0.92	0.61	1.37	0.66026
DRB1	Position.85	A	1.09	0.73	1.65	0.66026
DRB1	Position.86	G	0.88	0.77	1.02	0.081663
DRB1	Position.86	V	1.13	0.98	1.31	0.081663

OR: Odds Ratio; CI:

Supplementary Table 3. Frequency of shared epitope alleles in individuals with and without available data for smoking history, in Parkinson's disease cases and controls.

Cases	Smoking data+	Smoking data+
SE-	0.74	0.78
SE+V11-	0.13	0.11
SE+V11+	0.13	0.11
Control		
SE-	0.76	0.76
SE+V11-	0.10	0.09
SE_V11+	0.13	0.15

Supplementary Table 4. Interaction of HLA and smoking history in Parkinson's disease cases and controls.

HLA Shared Epitope (Copy Number)	**Smoking History**	**Case (N=837)**	**Control (N=918)**	**p value**	**Odds Ratio (95% Confidence Interval)**
+11V					
1/2	negative	116	143	*NS*	
	positive	59	118	0.0001	0.51 (0.36-0.72)
0	negative	384	377	0.04	1.2 (1.01-1.47)
	positive	278	280	*NS*	
-11V					
1/2	negative	115	88	0.01	1.51 (1.08-2.12)
	positive	60	65	*NS*	
0	negative	385	429	*NS*	
	positive	277	333	*NS*	

Supplementary Table 5. Predicted binding affinity (nM) for alpha-synuclein derived peptides.

Peptide	**DRB1_ 0101**	**DRB1_ 0102**	**DRB1_ 0103**	**DRB1_ 0401**	**DRB1_ 0402**	**DRB1_ 0404**	**DRB1_ 0405**
MDVFMKGLSK AKEGV	62	189	1314	844	460	353	1064
DVFMKGLSKA KEGVV	90	248	1759	1143	602	489	1415
VFMKGLSKAK EGVVA	122	277	1963	1388	697	586	1650
FMKGLSKAKE GVVAA	201	492	3255	2294	1185	959	2598

MKGLSKAKEGVVAAA	271	1305	4463	3387	2553	1967	4551
KGLSKAKEGVVAAAE	361	2116	5588	3762	4018	2941	5656
GLSKAKEGVVAAAEK	564	2804	7400	3989	4993	3283	6082
LSKAKEGVVAAAEKT	841	3432	9255	4188	6578	3888	6419
SKAKEGVVAAAEKTK	1021	4077	11420	4524	7756	4601	6872
KAKEGVVAAAEKTKQ	855	3625	10958	4228	6330	4058	6527
AKEGVVAAAEKTKQG	948	3728	11861	4480	6254	4192	7213
KEGVVAAAEKTKQGV	929	3143	11582	3922	5275	3419	6761
EGVVAAAEKTKQGVA	1344	3645	12858	4308	5336	3332	7361
GVVAAAEKTKQGVAE	1759	4141	14073	4793	5586	3542	7858
VVAAAEKTKQGVAEA	2884	5856	16813	6261	7262	4775	9359
VAAAEKTKQGVAEAA	3527	8239	17759	8545	10955	7682	11786
AAAEKTKQGVAEAAG	3577	9237	18534	10700	14090	10653	14197
AAEKTKQGVAEAAGK	2909	8098	17110	9603	13553	9951	13759
AEKTKQGVAEAAGKT	2473	7441	15681	8940	13374	9955	13541
EKTKQGVAEAAGKTK	2119	6331	14566	8581	12530	9529	13789
KTKQGVAEAAGKTKE	2230	6285	14864	9139	12544	9983	14574
TKQGVAEAAGKTKEG	3064	7485	16890	11289	13978	12174	17063
KQGVAEAAGKTKEGV	3187	7616	17046	11735	13498	12031	17072
QGVAEAAGKTKEGVL	4445	8836	18815	13992	14358	13321	17647
GVAEAAGKTKEGVLY	4966	8698	17852	14719	13836	13326	16941
VAEAAGKTKEGVLYV	3403	7254	15144	9943	11742	9886	11475
AEAAGKTKEGVLYVG	2707	6592	15091	8599	11911	8429	10017

EAAGKTKEGVLYVGS	2163	5652	14046	7330	10816	6881	8386
AAGKTKEGVLYVGSK	1758	4636	12965	6304	8893	5498	6933
AGKTKEGVLYVGSKT	1136	3476	9781	4981	6064	3933	4913
GKTKEGVLYVGSKTK	623	1905	6117	3107	2611	1956	3102
KTKEGVLYVGSKTKE	526	1555	5552	2542	2095	1546	2649
TKEGVLYVGSKTKEG	476	1447	5560	1937	1983	1457	2532
KEGVLYVGSKTKEGV	335	1220	4493	1062	1617	1147	1848
EGVLYVGSKTKEGVV	301	1426	5069	785	1812	1229	1641
GVLYVGSKTKEGVVH	307	1567	5445	765	2006	1361	1734
VLYVGSKTKEGVVHG	436	2592	7962	1044	3261	2115	2343
LYVGSKTKEGVVHGV	898	4272	11161	1933	6440	3812	4263
YVGSKTKEGVVHGVA	2181	5483	13569	6109	9064	6338	9770
VGSKTKEGVVHGVAT	2662	5960	14223	8819	10261	7314	11561
GSKTKEGVVHGVATV	1424	4978	10680	6979	8535	5775	9362
SKTKEGVVHGVATVA	282	2613	5968	3174	4470	2250	5017
KTKEGVVHGVATVAE	154	1911	4775	1934	3247	1227	3101
TKEGVVHGVATVAEK	98	1417	3653	1333	2233	735	2114
KEGVVHGVATVAEKT	87	1290	3401	1192	2012	632	1850
EGVVHGVATVAEKTK	133	1644	4617	1497	2627	828	2153
GVVHGVATVAEKTKE	179	1940	5548	1855	3038	991	2504
VVHGVATVAEKTKEQ	546	3310	9900	3139	5228	1850	3735
VHGVATVAEKTKEQV	2138	5832	15272	5612	8584	4977	7131
HGVATVAEKTKEQVT	3309	7369	17348	7159	9999	6727	9715

GVATVAEKTKEQVTN	4815	8680	19555	8500	11107	7558	11009
VATVAEKTKEQVTNV	5654	10177	20485	8489	12204	8384	10748
ATVAEKTKEQVTNVG	6246	11719	21138	8408	13320	9383	11465
TVAEKTKEQVTNVGG	6423	12433	21569	8157	13149	8887	11572
VAEKTKEQVTNVGGA	5260	11767	19878	6609	12163	6909	10238
AEKTKEQVTNVGGAV	2443	9175	11735	5019	9542	5169	8262
EKTKEQVTNVGGAVV	587	4775	5851	3581	6153	3447	5996
KTKEQVTNVGGAVVT	277	3099	4288	3092	4859	2653	5023
TKEQVTNVGGAVVTG	253	2923	4356	3711	5269	3085	5820
KEQVTNVGGAVVTGV	202	2528	3905	3833	5100	2776	5872
EQVTNVGGAVVTGVT	334	3303	5464	4986	6697	3702	7561
QVTNVGGAVVTGVTA	431	3534	6764	5259	7688	3677	7826
VTNVGGAVVTGVTAV	638	4335	9102	4646	8290	3421	6454
TNVGGAVVTGVTAVA	427	3494	7984	2465	4888	1672	3939
NVGGAVVTGVTAVAQ	235	2274	6701	1315	2926	730	2438
VGGAVVTGVTAVAQK	151	1596	5529	874	1846	401	1709
GGAVVTGVTAVAQKT	140	1490	5284	825	1662	353	1628
GAVVTGVTAVAQKTV	149	1514	5516	944	1670	362	1673
AVVTGVTAVAQKTVE	216	1830	6770	1364	2163	504	2093
VVTGVTAVAQKTVEG	441	2559	8947	2293	3235	946	3133
VTGVTAVAQKTVEGA	757	3436	11518	3043	5105	1927	4699
TGVTAVAQKTVEGAG	1098	4277	13591	3598	6345	2503	6101
GVTAVAQKTVEGAGS	1346	4637	14805	3575	6325	2305	6144

VTAVAQKTVEGAGSI	1383	4906	14949	3790	7030	2402	6288
TAVAQKTVEGAGSIA	1209	5149	13351	4533	8121	3270	7470
AVAQKTVEGAGSIAA	565	3812	9095	3278	7056	3100	6117
VAQKTVEGAGSIAAA	253	2874	6576	1995	5554	1995	4389
AQKTVEGAGSIAAAT	194	2648	6069	1633	5098	1582	3875
QKTVEGAGSIAAATG	204	2719	6489	1789	5201	1642	4355
KTVEGAGSIAAATGF	260	3138	7251	2193	5943	2002	5117
TVEGAGSIAAATGFV	412	3525	8068	3122	7247	2955	5884
VEGAGSIAAATGFVK	152	1287	3539	1734	2452	1106	2597
EGAGSIAAATGFVKK	76	694	2149	1110	1371	603	1685
GAGSIAAATGFVKKD	86	763	2541	1143	1553	636	1761
AGSIAAATGFVKKDQ	83	718	2585	1126	1458	605	1722
GSIAAATGFVKKDQL	104	825	3211	1359	1696	743	2013
SIAAATGFVKKDQLG	181	1206	4597	2138	2362	1174	2864
IAAATGFVKKDQLGK	684	2464	7477	3968	3609	2795	5000
AAATGFVKKDQLGKN	2170	4183	11590	4942	5109	4528	6104
AATGFVKKDQLGKNE	2236	4477	12398	4506	5361	4430	5988
ATGFVKKDQLGKNEE	2410	4887	13262	4517	5994	4664	6164
TGFVKKDQLGKNEEG	2745	5522	14352	4870	6872	5272	6731
GFVKKDQLGKNEEGA	3442	6568	16140	5655	8245	6446	8043
FVKKDQLGKNEEGAP	6260	9768	20189	8353	11962	9565	11250
VKKDQLGKNEEGAPQ	11525	16709	26660	14299	20767	16292	17801
KKDQLGKNEEGAPQE	13684	19495	28663	17350	23460	19964	21294

KDQLGKNEEGAPQEG	15545	21119	29905	19296	24841	22025	23405
DQLGKNEEGAPQEGI	15418	21101	30035	19701	25686	23709	23836
QLGKNEEGAPQEGIL	12693	18902	27937	18162	24826	22434	22134
LGKNEEGAPQEGILE	12391	18499	27863	18307	25988	22896	21283
GKNEEGAPQEGILED	13408	19863	29259	19697	27309	24381	21570
KNEEGAPQEGILEDM	11615	17935	27597	17514	25339	21259	17858
NEEGAPQEGILEDMP	12780	18796	28586	18158	25806	21113	17930
EEGAPQEGILEDMPV	8608	14819	25606	12705	21142	13695	11439
EGAPQEGILEDMPVD	7681	13570	24221	10575	19725	11594	9717
GAPQEGILEDMPVDP	6395	11466	21206	6711	14892	8606	7271
APQEGILEDMPVDPD	6212	10849	20732	5543	12817	7128	6029
PQEGILEDMPVDPDN	5901	10385	20426	4813	11757	6064	5288
QEGILEDMPVDPDNE	5986	10570	20669	4752	11657	5965	5243
EGILEDMPVDPDNEA	6790	11396	21467	5001	12048	6305	5448
GILEDMPVDPDNEAY	7797	12806	22416	5319	12440	6717	6053
ILEDMPVDPDNEAYE	10766	15303	24848	7819	15563	9455	8371
LEDMPVDPDNEAYEM	14159	18818	26586	9247	18839	12837	11373
EDMPVDPDNEAYEMP	16494	21753	27899	11411	21697	16458	14367
DMPVDPDNEAYEMPS	16539	22237	28104	11855	22335	17286	15071
MPVDPDNEAYEMPSE	16874	22244	28503	12534	22803	18527	15306
PVDPDNEAYEMPSEE	18523	23185	29769	15998	25707	22584	16226
VDPDNEAYEMPSEEG	14176	21490	29900	13562	25286	19379	14140
DPDNEAYEMPSEEGY	8208	18303	27075	8827	22458	15424	10071

PDNEAYEMPSEEGYQ	6711	16702	25668	7312	20825	13523	8592
DNEAYEMPSEEGYQD	7727	17638	26240	7700	21319	14275	9050
NEAYEMPSEEGYQDY	6571	16680	25240	6875	20406	12904	7984
EAYEMPSEEGYQDYE	7697	18381	26820	8195	22188	14462	9382
AYEMPSEEGYQDYEP	9909	20663	28550	10751	24681	16940	11619
YEMPSEEGYQDYEPE	15992	24332	31415	16224	27562	21692	16014
EMPSEEGYQDYEPEA	20360	25836	32680	19012	27762	23729	18181

Supplementary Table 6. Predicted binding affinity (nM) for modified alpha-synuclein derived peptides.

Peptide	DRB1_0101	DRB1_0102	DRB1_0103	DRB1_0401	DRB1_0402	DRB1_0404	DRB1_0405
MDVFMXGLSXAXEGV	41	604	2853	505	1526	426	564
DVFMXGLSXAXEGVV	57	890	3775	684	2326	634	780
VFMXGLSXAXEGVVA	76	1103	4532	913	3027	880	1031
FMXGLSXAXEGVVAA	206	2071	7502	1982	5481	1862	2114
MXGLSXAXEGVVAAA	553	4194	9861	3309	8455	3649	4527
XGLSXAXEGVVAAAE	665	4826	11014	3438	9709	4444	5595
GLSXAXEGVVAAAEX	755	5139	11730	3477	10187	4662	5650
LSXAXEGVVAAAEXT	1000	5787	13420	3802	11705	5321	6077
SXAXEGVVAAAEXTX	1862	7134	16596	5181	14015	6942	7763
XAXEGVVAAAEXTXQ	1958	6907	17343	4911	12305	5423	6941
AXEGVVAAAEXTXQG	1935	6705	18160	4309	11874	4451	6514
XEGVVAAAEXTXQGV	1447	5723	17493	3035	10290	3101	5130

EGVVAAAEXTXQGVA	1444	5693	17441	2619	9701	2766	4666
GVVAAAEXTXQGVAE	1743	6510	18409	2873	10261	3027	5066
VVAAAEXTXQGVAEA	2893	8994	20314	4039	12610	4509	6422
VAAAEXTXQGVAEAA	3733	10597	21120	6523	15667	8080	9513
AAAEXTXQGVAEAAG	4090	11202	21892	9437	17613	10953	12268
AAEXTXQGVAEAAGX	4121	10729	21900	10158	18349	11662	13258
AEXTXQGVAEAAGXT	4087	10609	21429	10682	18735	12668	14523
EXTXQGVAEAAGXTX	3993	10395	20770	10906	18974	13317	16166
XTXQGVAEAAGXTXE	3782	10498	21140	10932	19248	13103	16365
TXQGVAEAAGXTXEG	4111	11344	22349	12020	20271	13954	17713
XQGVAEAAGXTXEGV	3523	10976	22004	10935	19676	12720	15807
QGVAEAAGXTXEGVL	3639	11243	21940	10471	19269	12283	14334
GVAEAAGXTXEGVLY	4079	11469	21749	10585	18672	12596	13016
VAEAAGXTXEGVLYV	3098	9682	18658	7451	16044	9835	8747
AEAAGXTXEGVLYVG	2559	8761	18562	6778	15342	8789	8052
EAAGXTXEGVLYVGS	2073	7684	17679	6122	14100	7385	7009
AAGXTXEGVLYVGSX	1917	7261	17720	6032	13712	6782	6757
AGXTXEGVLYVGSXT	1546	6301	15130	5418	10683	5245	5590
GXTXEGVLYVGSXTX	569	3822	11263	2381	5586	1695	2355
XTXEGVLYVGSXTXE	332	2876	10006	1432	3960	934	1453
TXEGVLYVGSXTXEG	278	2550	9441	869	3490	779	1161
XEGVLYVGSXTXEGV	179	2072	7663	444	2667	580	704
EGVLYVGSXTXEGVV	158	1983	7249	311	2588	559	551

GVLYVGSXTXEGVVH	172	2176	7688	300	2847	660	587
VLYVGSXTXEGVVHG	293	3471	10452	392	4732	1220	821
LYVGSXTXEGVVHGV	740	5881	14272	793	9023	2916	1782
YVGSXTXEGVVHGVA	1622	6971	16433	2974	11522	5225	5444
VGSXTXEGVVHGVAT	2221	7227	17665	6310	12997	6776	9353
GSXTXEGVVHGVATV	1810	6213	13723	6356	11034	6334	9366
SXTXEGVVHGVATVA	428	3487	7700	3786	5902	2948	5976
XTXEGVVHGVATVAE	236	2553	6168	2638	4317	1747	3927
TXEGVVHGVATVAEX	189	2249	5635	2172	3700	1321	3076
XEGVVHGVATVAEXT	166	2112	5345	1936	3419	1122	2699
EGVVHGVATVAEXTX	185	2256	5745	2023	3627	1187	2783
GVVHGVATVAEXTXE	258	2690	6977	2516	4340	1443	3255
VVHGVATVAEXTXEQ	890	4813	12920	4079	7967	2785	4732
VHGVATVAEXTXEQV	3926	9103	20048	5878	13751	6084	6697
HGVATVAEXTXEQVT	4587	10524	21539	5912	14999	6455	6664
GVATVAEXTXEQVTN	5197	11782	23188	5990	15638	6686	6702
VATVAEXTXEQVTNV	4663	12866	22594	5800	15631	6853	6321
ATVAEXTXEQVTNVG	5288	13979	23231	6532	16896	8393	7630
TVAEXTXEQVTNVGG	5822	14636	23220	6767	16921	9271	8752
VAEXTXEQVTNVGGA	5310	13863	21857	5838	15821	8326	9381
AEXTXEQVTNVGGAV	2856	11151	13496	4791	12029	6443	8123
EXTXEQVTNVGGAVV	839	6133	7257	3632	7936	4301	6125
XTXEQVTNVGGAVVT	421	4075	5520	3398	6314	3394	5492

TXEQVTNVGGAVVTG	378	3677	5506	3913	6370	3629	6181
XEQVTNVGGAVVTGV	302	3185	4965	4515	6225	3580	6889
EQVTNVGGAVVTGVT	334	3303	5464	4986	6697	3702	7561
QVTNVGGAVVTGVTA	431	3534	6764	5259	7688	3677	7826
VTNVGGAVVTGVTAV	638	4335	9102	4646	8290	3421	6454
TNVGGAVVTGVTAVA	427	3494	7984	2465	4888	1672	3939
NVGGAVVTGVTAVAQ	235	2274	6701	1315	2926	730	2438
VGGAVVTGVTAVAQX	200	1978	6481	1106	2379	533	2019
GGAVVTGVTAVAQXT	188	1897	6371	1052	2200	476	1946
GAVVTGVTAVAQXTV	209	2035	6857	1202	2263	500	1975
AVVTGVTAVAQXTVE	313	2480	8453	1671	2875	696	2436
VVTGVTAVAQXTVEG	627	3404	11017	2579	4321	1276	3387
VTGVTAVAQXTVEGA	1001	4458	13831	2857	6569	2147	3949
TGVTAVAQXTVEGAG	1313	5240	15888	2894	7729	2209	4186
GVTAVAQXTVEGAGS	1462	5461	16907	2664	7542	1899	3893
VTAVAQXTVEGAGSI	1366	5379	16201	2661	7870	1859	3803
TAVAQXTVEGAGSIA	1269	5639	13969	3218	9214	2529	4796
AVAQXTVEGAGSIAA	717	4539	10024	3140	8450	2919	5327
VAQXTVEGAGSIAAA	342	3590	7553	2539	6984	2592	5216
AQXTVEGAGSIAAAT	275	3331	7162	2216	6482	2271	5010
QXTVEGAGSIAAATG	300	3460	7566	2441	6577	2342	5618
XTVEGAGSIAAATGF	379	3829	8344	2949	7285	2784	6411
TVEGAGSIAAATGFV	412	3525	8068	3122	7247	2955	5884

VEGAGSIAAATGFVX	140	1609	4683	1752	3439	1131	2410
EGAGSIAAATGFVXX	76	1054	3563	1209	2322	675	1595
GAGSIAAATGFVXXD	84	1140	4152	1217	2565	688	1625
AGSIAAATGFVXXDQ	78	1068	4156	1150	2392	625	1503
GSIAAATGFVXXDQL	98	1266	5065	1382	2777	761	1690
SIAAATGFVXXDQLG	168	1844	7059	1961	3830	1188	2119
IAAATGFVXXDQLGX	528	3609	10894	2395	6142	2391	2241
AAATGFVXXDQLGXN	942	5195	13515	1870	7641	2641	1889
AATGFVXXDQLGXNE	898	5224	13804	1709	7573	2495	1814
ATGFVXXDQLGXNEE	938	5554	14363	1729	7958	2588	1881
TGFVXXDQLGXNEEG	1114	6149	15265	1991	8820	3012	2219
GFVXXDQLGXNEEGA	1590	7396	17318	2686	10462	4094	3082
FVXXDQLGXNEEGAP	4166	12094	22361	5836	16001	8588	6772
VXXDQLGXNEEGAPQ	13462	20906	29583	16313	25180	19845	18660
XXDQLGXNEEGAPQE	15674	22840	31079	19655	27198	23564	22154
XDQLGXNEEGAPQEG	17159	23221	31528	20443	27751	24682	23549
DQLGXNEEGAPQEGI	16119	21957	30888	20197	27348	25343	23630
QLGXNEEGAPQEGIL	13719	20044	29014	18868	26547	24420	22391
LGXNEEGAPQEGILE	13307	19502	28821	18873	27090	24492	21734
GXNEEGAPQEGILED	14243	20478	29929	20155	28039	25138	21935
XNEEGAPQEGILEDM	12373	18429	28174	17973	25842	21787	18230
NEEGAPQEGILEDMP	12780	18796	28586	18158	25806	21113	17930
EEGAPQEGILEDMPV	8608	14819	25606	12705	21142	13695	11439

EGAPQEGILEDMPVD	7681	13570	24221	10575	19725	11594	9717
GAPQEGILEDMPVDP	6395	11466	21206	6711	14892	8606	7271
APQEGILEDMPVDPD	6212	10849	20732	5543	12817	7128	6029
PQEGILEDMPVDPDN	5901	10385	20426	4813	11757	6064	5288
QEGILEDMPVDPDNE	5986	10570	20669	4752	11657	5965	5243
EGILEDMPVDPDNEA	6790	11396	21467	5001	12048	6305	5448
GILEDMPVDPDNEAY	7797	12806	22416	5319	12440	6717	6053
ILEDMPVDPDNEAYE	10766	15303	24848	7819	15563	9455	8371
LEDMPVDPDNEAYEM	14159	18818	26586	9247	18839	12837	11373
EDMPVDPDNEAYEMP	16494	21753	27899	11411	21697	16458	14367
DMPVDPDNEAYEMPS	16539	22237	28104	11855	22335	17286	15071
MPVDPDNEAYEMPSE	16874	22244	28503	12534	22803	18527	15306
PVDPDNEAYEMPSEE	18523	23185	29769	15998	25707	22584	16226
VDPDNEAYEMPSEEG	14176	21490	29900	13562	25286	19379	14140
DPDNEAYEMPSEEGY	8208	18303	27075	8827	22458	15424	10071
PDNEAYEMPSEEGYQ	6711	16702	25668	7312	20825	13523	8592
DNEAYEMPSEEGYQD	7727	17638	26240	7700	21319	14275	9050
NEAYEMPSEEGYQDY	6571	16680	25240	6875	20406	12904	7984
EAYEMPSEEGYQDYE	7697	18381	26820	8195	22188	14462	9382
AYEMPSEEGYQDYEP	9909	20663	28550	10751	24681	16940	11619
YEMPSEEGYQDYEPE	15992	24332	31415	16224	27562	21692	16014
EMPSEEGYQDYEPEA	20360	25836	32680	19012	27762	23729	18181

Supplementary Table 7. Samples Quality Control – Discovery cohort.

Quality control step	NIH-GWAS		NIH-NeuroX		UCSF-GeneMSA
	Cases	Controls	Cases	Controls	Controls
Pre-QC dataset	**779**	**675**	**842**	**634**	**331**
HLA sequencing rate (< 100%)	-0	-0	-0	-0	-0
SNP data unavailable	-0	-0	-0	-0	-0
Non-White (Self-identification)	-13	-4	-6	-17	-6
SNP Genotyping Rate (< 90%)	-0	-0	-0	-0	-0
Genetic outliers	-5	-4	-0	-1	-2
Post-QC dataset	**761**	**667**	**836**	**616**	**323**

Pre-QC dataset consists of sequenced sample data that were received back from the Stanford Genome Technology Center: Genetic outliers are PC-based genetic outliers using the NIH/UCSF population only (removing all population specific outliers at greater than 6 standard deviations from the mean for any of the first 10 principal components).

Supplementary Table 8. Samples Quality Control – Replication cohort.

Quality control step	MJFF - BioFIND		MJFF - DATATOP	UCSF1
	Cases	Controls	Cases	Controls
Pre-QC dataset	**120**	**93**	**451**	**386**
HLA sequencing rate (< 100%)	-2	-0	-16	-0
Non-White (Self-identification)	-9	-14	-8	-3
Post-QC dataset	**109**	**79**	**427**	**383**

Pre-QC dataset consists of sequenced sample data that were received back from the Stanford Genome Technology Center

Supplementary Table 9. Demographics of the datasets used in the study.

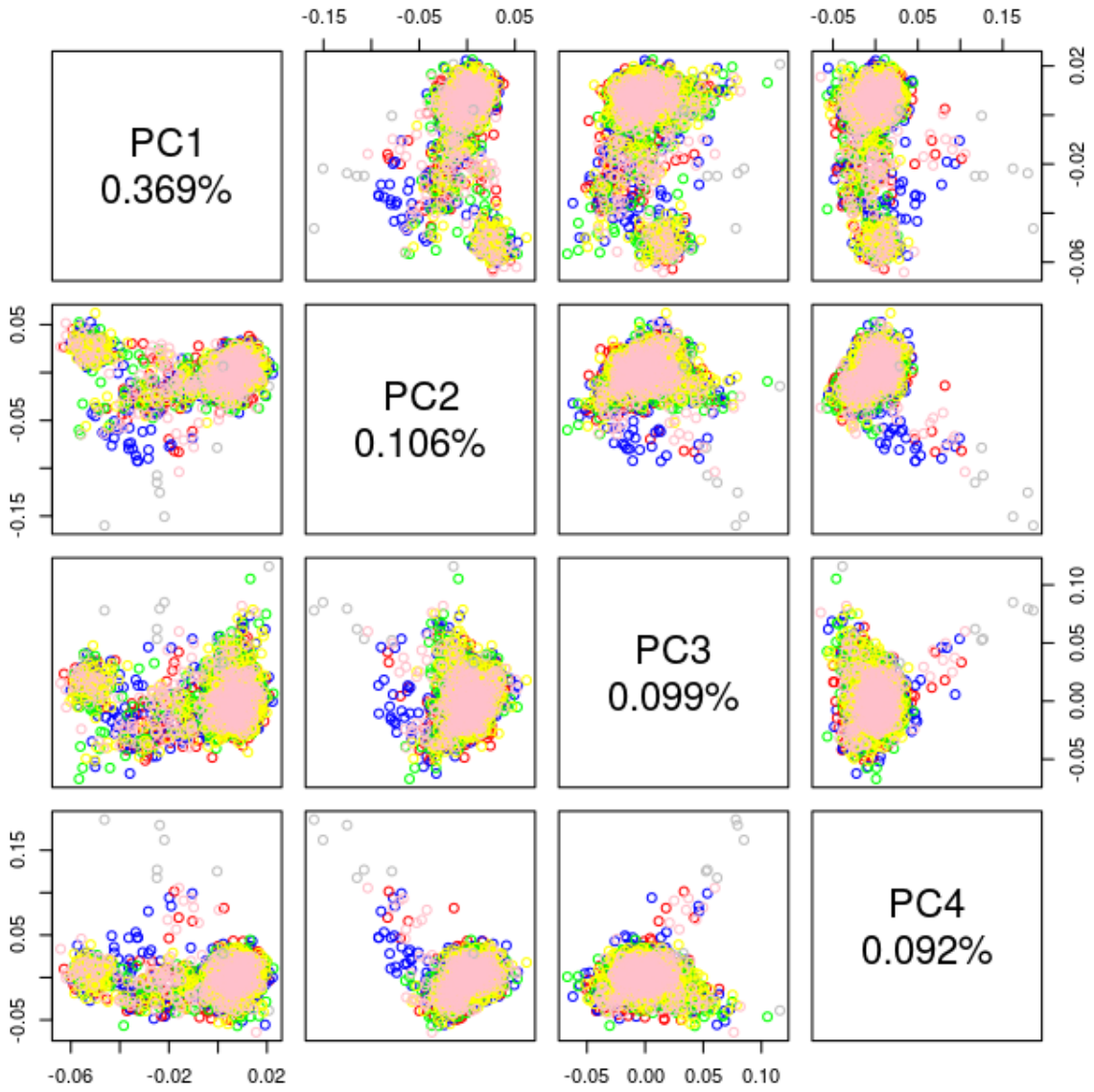
	Discovery datasets					Replication datasets			
	NIH-GWAS		NIH-NeuroX		UCSF-GeneMSA	MJFF-BioFind		MJFF-DATATOP	UCSF1
	Cases	Controls	Cases	Controls	Controls	Cases	Controls	Cases	Controls
Number of individuals	761	667	836	616	323	109	79	427	383
Gender (Male/Female)	454/307	280/387	550/286	247/369	119/204	71/38	39/40	284/143	220/163
Age at Sample Mean (SD)	-	58.5 (16.4)	-	52.0 (17.2)	42.4 (11.0)	-	65.9 (7.2)	-	45.6 (13.5)
Age at Onset Mean (SD)	58.9 (13.0)	-	58.9 (10.4)	-	-	68.2 (6.5)	-	58.8 (9.1)	-

Supplementary Table 10. SNP Quality Control.

Quality control step	NIH-GWAS	NIH-NeuroX	UCSF-GeneMSA
Pre-QC dataset	**453,723**	**267,607**	**553,139**
Remove duplicated variants	0	-1,280	0
HWE (p < 0:001)	-306	-610	-853
Call Rate (< 95%)	-107	-12,711	-1,818
Post-QC dataset	**453,310**	**253,381**[a]	**550,486**[b]

HWE: Hardy-Weinberg Equilibrium
[a] 375 SNPs were removed because of quality controls on both HWE and call-rate
[b] 18 SNPs were removed because of quality controls on both HWE and call-rate

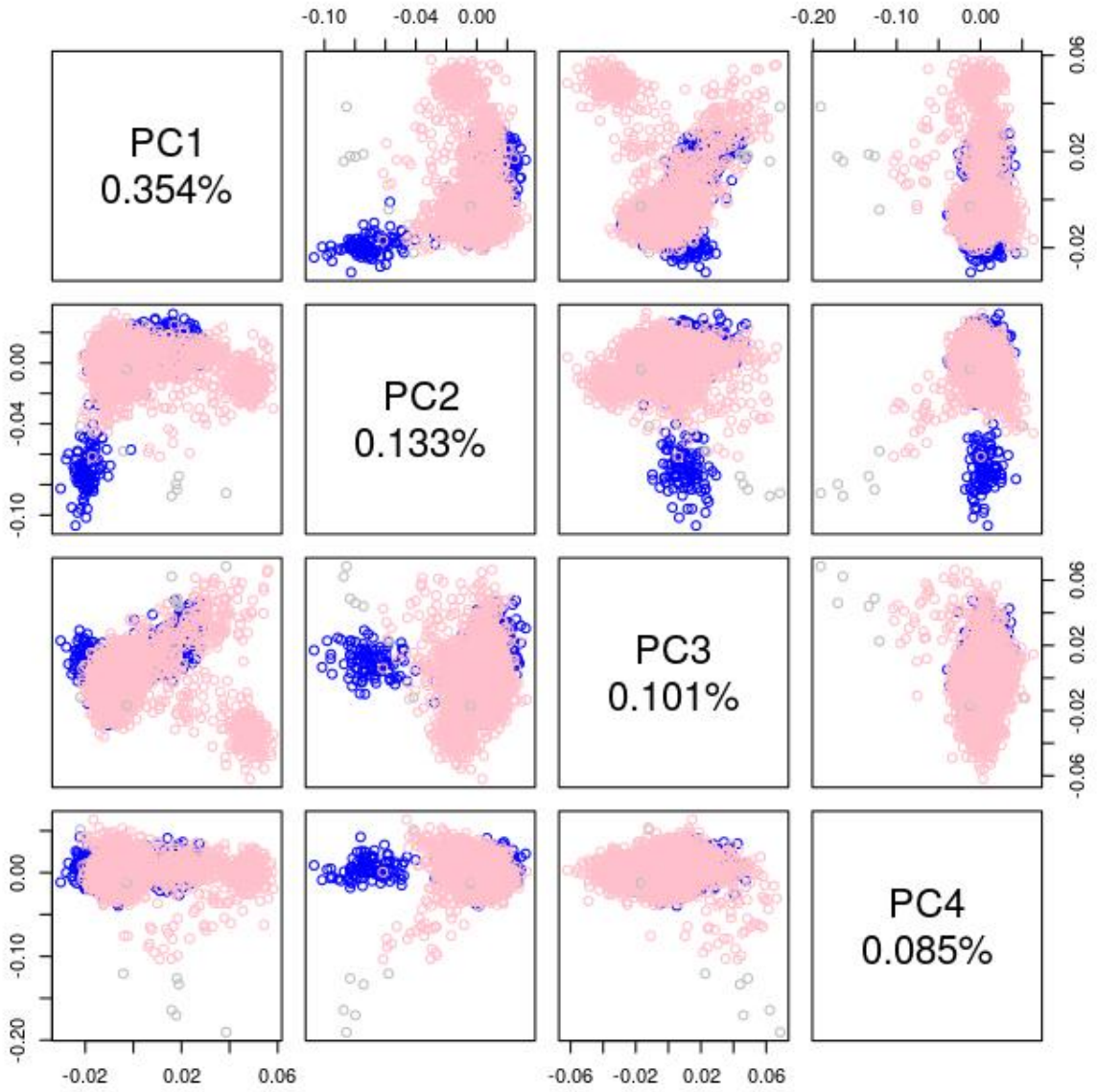
Supplementary Figure 1. Population stratification analysis on NIH/UCSF samples.



Principal components were computed using a core set of 8,004 SNPs in NIH-GWAS, NIH-NeuroX and UCSF-GeneMSA datasets.
Controls samples from NIH-GWAS dataset are colored in red.
Cases samples from NIH-GWAS dataset are colored in blue.
Controls samples from NIH-NeuroX dataset are colored in green.

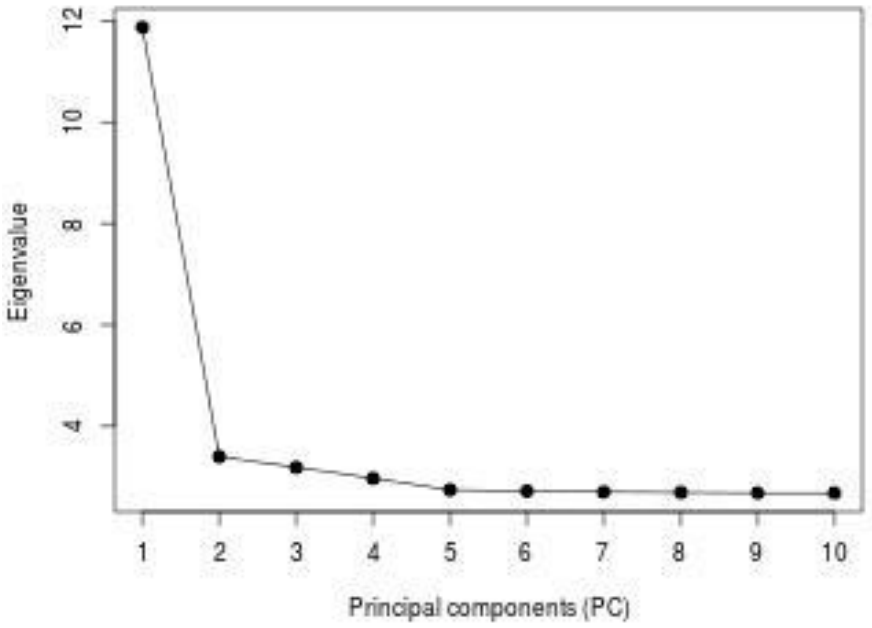
Cases samples from NIH-NeuroX dataset are colored in yellow.
Controls samples from UCSF-GeneMSA dataset are colored in pink.
Outliers are colored in grey.

Supplementary Figure 2. Population stratification analysis on NIH/UCSF samples and White 1000 Genomes samples.



Principal components were computed using a core set of 7,918 SNPs in the NIH-GWAS, NIH-NeuroX and UCSF-GeneMSA datasets and White 1000 Genomes samples.
NIH/UCSF samples are colored in pink.
White 1000 genomes samples are colored in blue.
Outliers are colored in grey.

Supplementary Figure 3. Population stratification analysis on NIH/UCSF samples.



Scree plot of the first ten components of principal component analysis within the NIH/UCSF samples. There was a gap between principal components 4 (PC4) and 5 (PC5).