Supplementary File

Single nucleus RNA sequencing profile analysis to reveal cell type specific common molecular drivers of Parkinsons disease and therapeutic agents

Md. Al Amin Pappu[a], Md. Alamin[b*], Most. Humaira Sultana[b], A K M Azad[c,d], Md. Rabiul Auwul[e], Sabkat Mahmud [a], Alvira Ajadee [a], Arnob Sarker [a], Salem A. Alyami[c,d], and Md. Nurul Haque Mollah[a*]

[a]Bioinformatics Lab (Dry), Department of Statistics, University of Rajshahi, Rajshahi-6205, Bangladesh.

[b]Department of Mathematics and Physics, School of Engineering & Physical Sciences, North South University Dhaka-1229, Bangladesh.

[c]Department of Mathematics and Statistics, College of Science, Imam Muhammad Ibn Saud Islamic University, Riyadh 11432, Saudi Arabia.

[d]King Salman Center for Disability Research, Riyadh 11614, Saudi Arabia

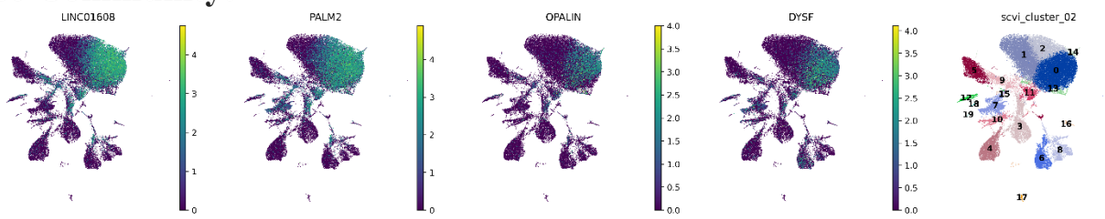
[e]Department of Statistics, Gazipur Agricultural University, Gazipur, Dhaka, Bangladesh

***Corresponding Authors:** Md. Alamin (Email: md.alamin06@northsouth.edu) and Md. Nurul Haque Mollah (Email: mollah.stat.bio@ru.ac.bd)

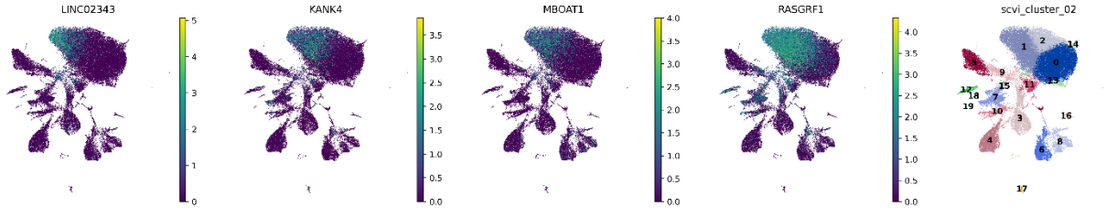
Supplementary Figure

Oligodendrocytes: [c0, c1, c2]

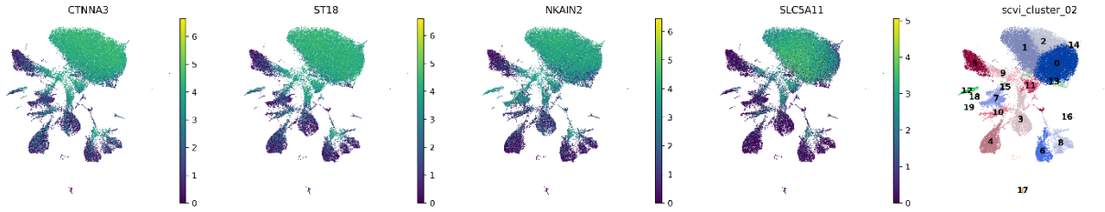
c0 Community:



c1 Community:

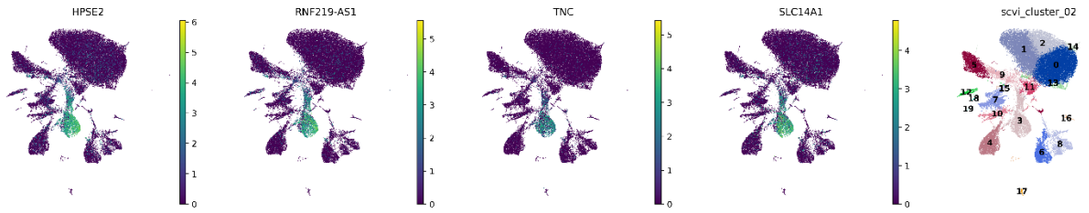


c2 Community:



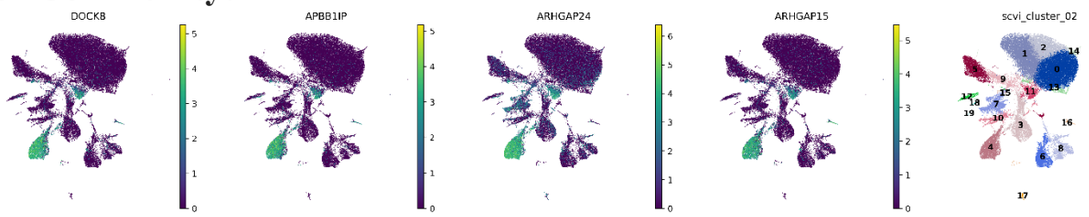
Astrocytes: [c3]

c3 Community:

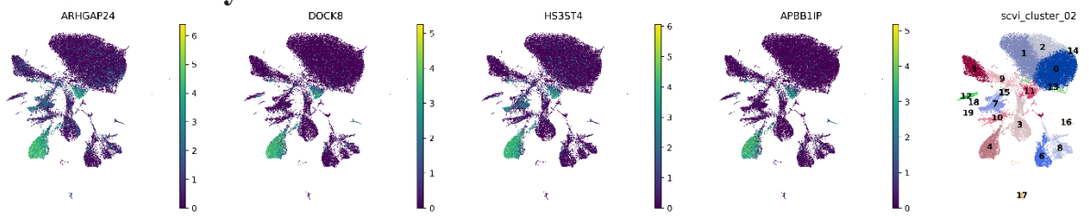


Microglia: [c4, c11]

c4 Community:

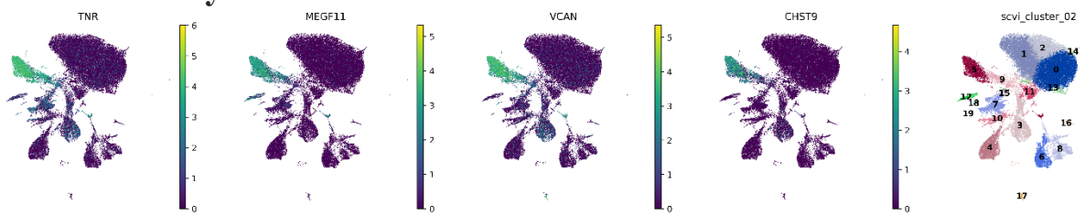


c11 Community:

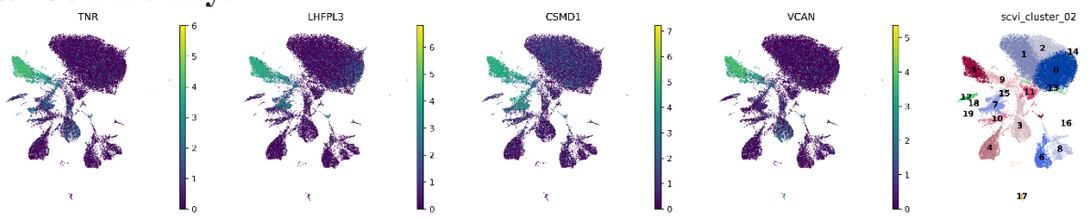


Oligodendrocyte precursor cells (OPC): [c5, c9]

c5 Community:

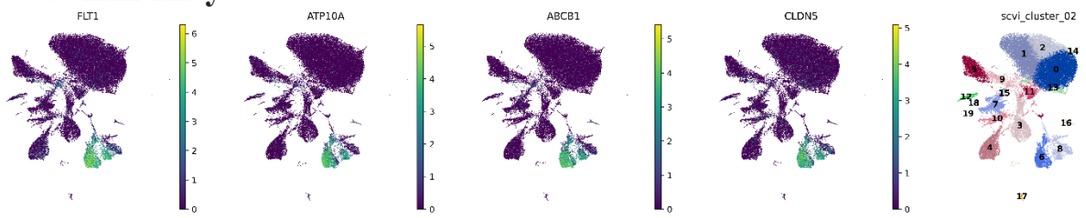


c9 Community:



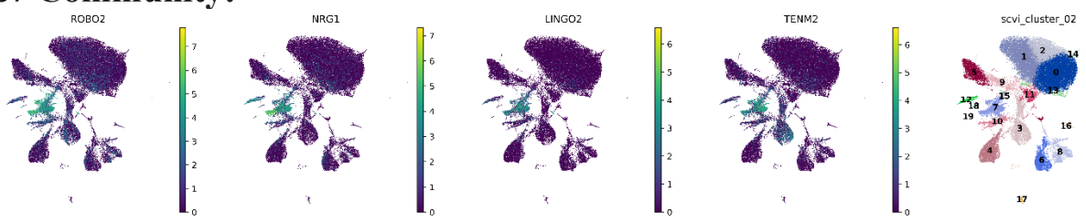
Endothelial: [c6]

c6 Community:

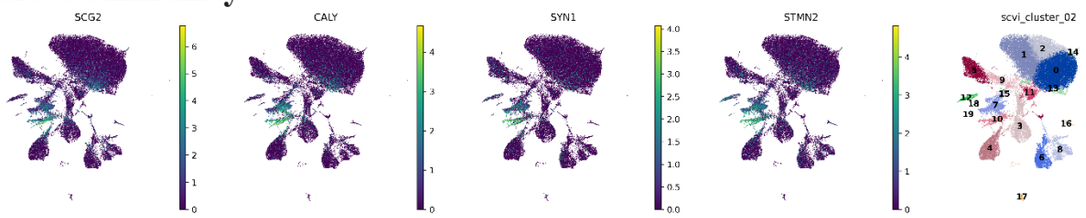


Neurons: [c7, c10, c12, c13, c14, c15, c18, c19]

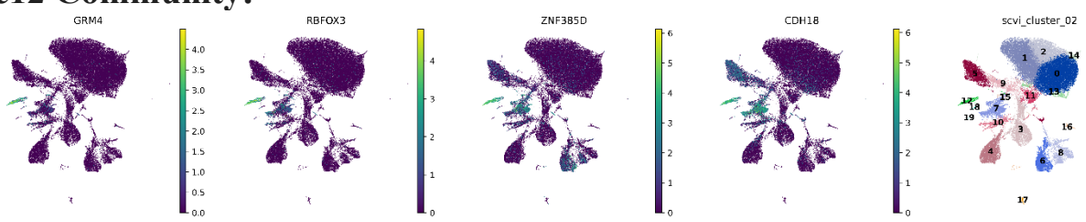
c7 Community:



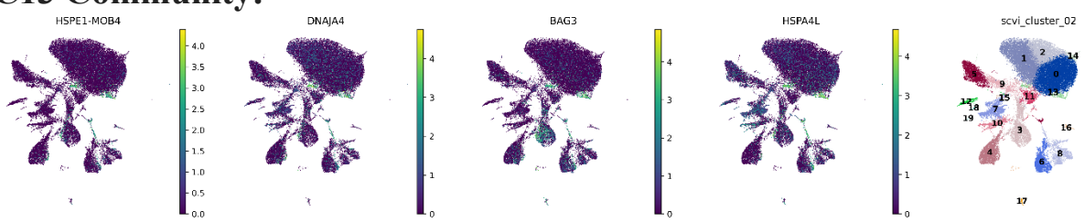
c10 Community:



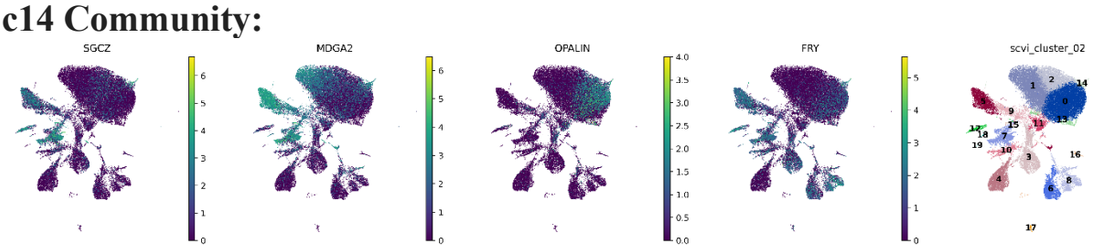
c12 Community:



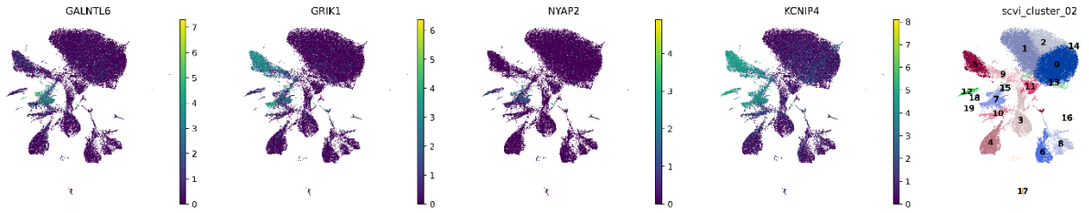
C13 Community:



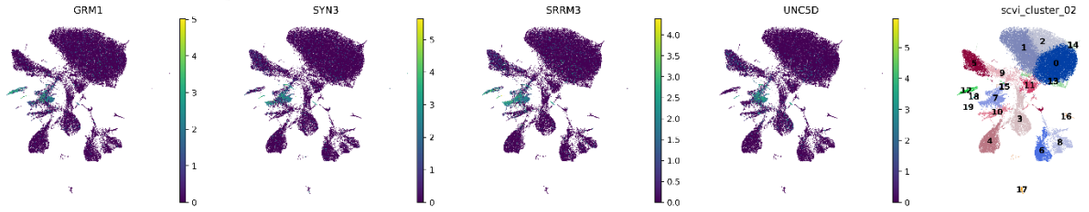
c14 Community:



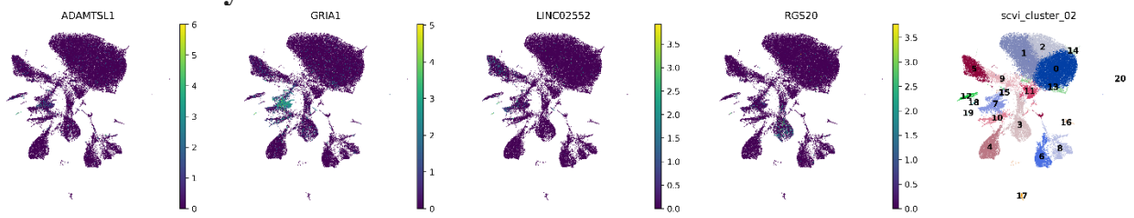
c15 Community:



c18 Community:

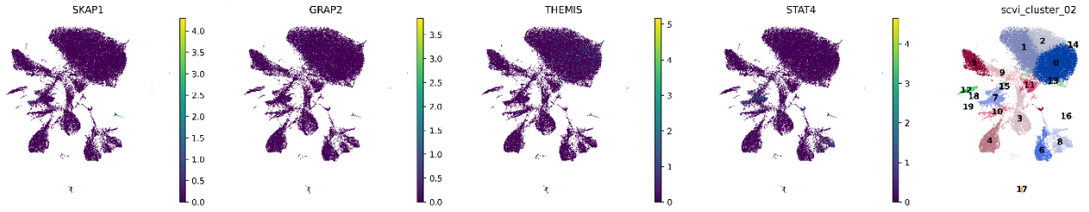


c19 Community:



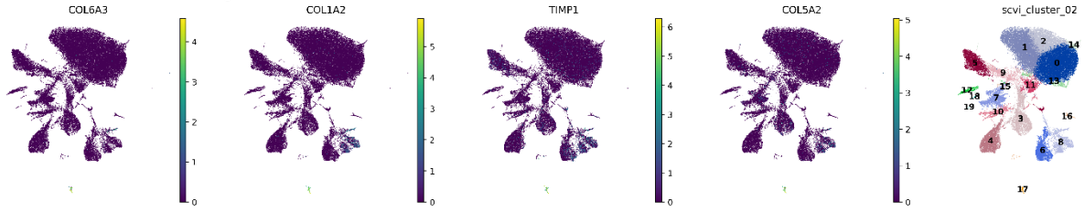
T cells: [c16]

c16 Community:



Fibroblast: [c17]

c17 Community:



Pericytes: [c8]

c8 Community:

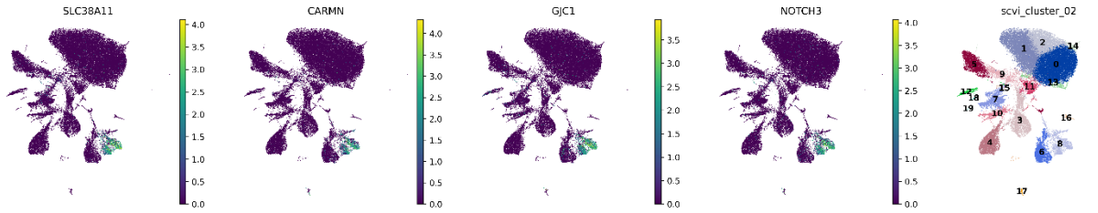


Figure S1. Four marker genes per community.

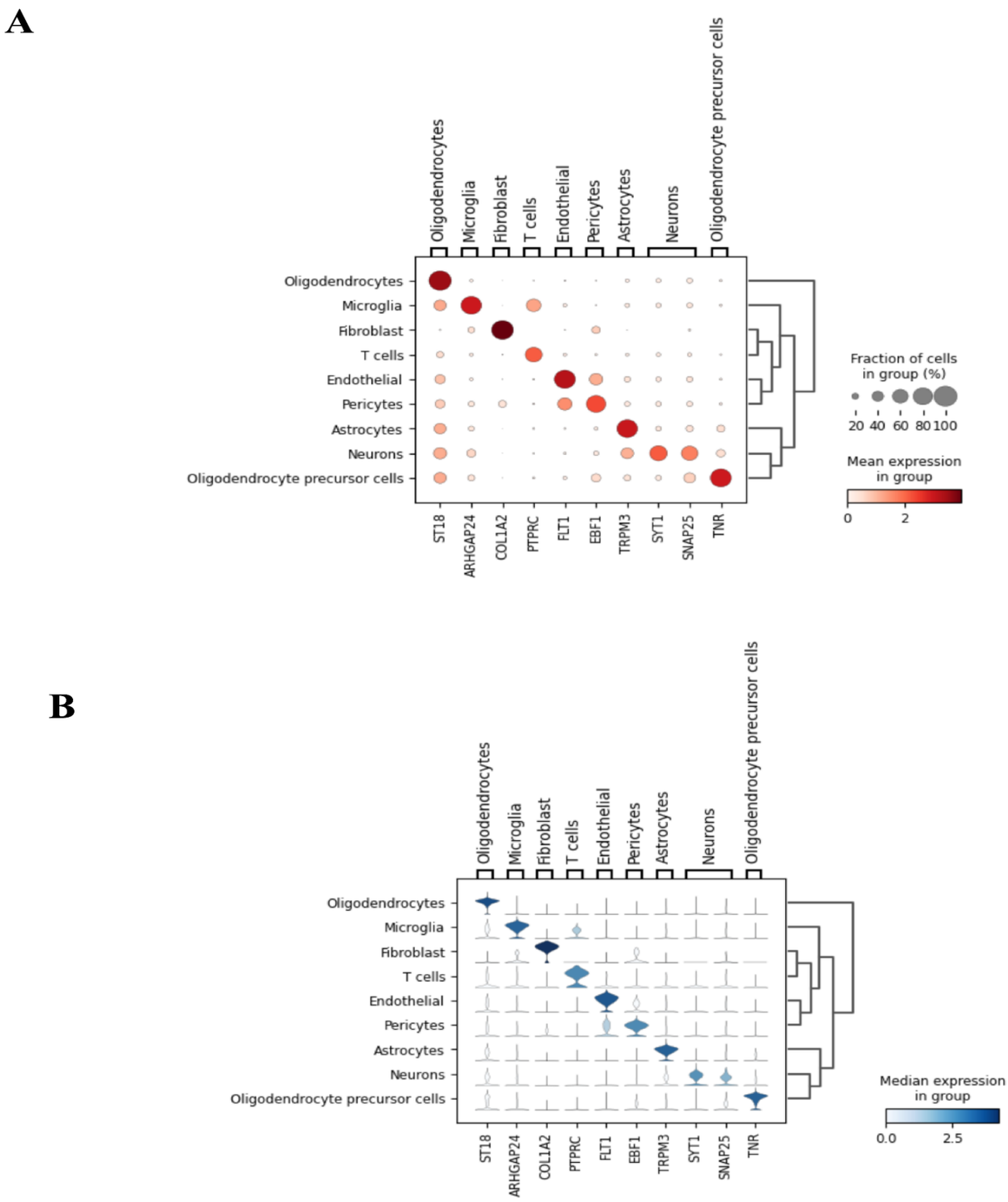


Figure S2. Annotate the marker gene based on the **(A)** dot plot using the mean gene expression and **(B)** stacked violin graph using the median gene expression.

Supplementary Tables

Table S1. A total of 32 samples include characteristics of the population. Before and after quality control, the number of genes is listed as the total number of genes found from all nuclei.

Accession No.	Sample	Disease state	Age	Sex	Number of nuclei without preprocessing	Number of genes without preprocessing	Number of nuclei with preprocessing	Number of genes with preprocessing
GSE184950	GSM5602315	Control	84	Male	11055	33538	5208	23437
	GSM5602316	Parkinson	74	Male	2165	33538	233	16467
	GSM5602317	Parkinson	90	Male	11760	33538	4612	23682
	GSM5602318	Control	71	Female	17752	33538	6283	23935
	GSM5602319	Parkinson	82	Male	18139	33538	3860	23938
	GSM5602320	Parkinson	83	Female	27603	33538	10092	25870
	GSM5602321	Parkinson	91	Female	18841	33538	4391	25045
	GSM5602322	Parkinson	79	Male	22577	33538	3964	23642
	GSM5602323	Parkinson	71	Female	5017	33538	193	18359
	GSM5602324	Parkinson	79	Female	7421	33538	1280	21020
	GSM5602325	Parkinson	71	Male	3608	33538	1599	18695
	GSM5602326	Parkinson	69	Female	18811	33538	5695	23090
	GSM5602327	Control	82	Female	6356	33538	96	17874
	GSM5602328	Control	89	Male	6193	33538	132	19503
	GSM5602329	Control	77	Male	7489	33538	776	18956
	GSM5602330	Parkinson	73	Male	7804	33538	4395	22665
	GSM5602331	Parkinson	81	Female	10243	33538	7170	21189
	GSM5602332	Parkinson	91	Male	9683	33538	7620	21970
	GSM5602333	Parkinson	77	Male	19620	33538	1332	22067
	GSM5602335	Control	93	Female	21450	33538	8538	24021
	GSM5602336	Parkinson	78	Male	12615	33538	9073	22023
	GSM5602337	Parkinson	91	Male	4782	33538	1402	18749
	GSM5602338	Parkinson	73	Male	19450	33538	61	20772
	GSM5602339	Parkinson	87	Male	34060	33538	5	20907
	GSM5602340	Control	74	Male	14933	33538	12766	24745
	GSM5602341	Parkinson	84	Male	15832	33538	9517	24023
	GSM5602342	Control	91	Female	19263	33538	9560	24860
	GSM5602343	Parkinson	69	Male	13202	33538	525	20432
	GSM5602345	Control	93	Female	14068	33538	6600	23991
	GSM5602347	Parkinson	78	Male	10794	33538	11	20115
	GSM6042297	Parkinson	66	Male	7792	33538	46	17733
	GSM6042298	Parkinson	76	Male	6508	33538	2438	21232

Table S2. Twenty communities with log fold change values ranging from C0 to C19, where C0 represents community 0, C1 corresponds to community 1, and so forth.

c0 community	c0_logfc		c1 community	c1_logfc		c2 community	c2_logfc		c3 community
LINC00463	3.103642		LINC02343	3.829883		LINC00609	2.61036		HPSE2
LINC01608	2.933715		GGT2	3.201758		CTNNA3	2.526349		AC073941.1
PALM2	2.489904		MIR4527HG	3.04425		AC090502.1	2.453005		RNF219-AS1
LINC01792	2.470299		RBFOX1	3.03687		ATP6V0D2	2.381376		TNC
LINC01010	2.465276		PPEF1	3.020253		AC025810.1	2.319528		RYR3
OPALIN	2.38542		ADAMTS12	2.938447		ST18	2.314387		RFX4
DYSF	2.365383		KANK4	2.904003		NKAIN2	2.297657		LINC01088
AL034405.1	2.331141		CPA2	2.898922		LINC01877	2.189593		TRPM3
ANO4	2.321764		MBOAT1	2.825864		LINC02511	2.17274		SERPINI2
CDH1	2.25034		AL353604.1	2.689122		AC026316.5	2.154313		FRMPD2
KIRREL3	2.214642		RASGRF1	2.680995		SLC5A11	2.139376		SLC14A1
ADA	2.184856		MPPED1	2.667997		CNTNAP4	2.12865		MRVI1
GREM1	2.170602		EMILIN2	2.661891		AC100801.1	2.125402		PAMR1
PDE1C	2.137184		KCNK12	2.654379		LINC01992	2.080895		LAMA1
AL354809.1	2.129609		LUCAT1	2.647561		SLC24A2	2.023159		FAM189A2

Table S3. Cell-type specificity scores and logFC values to assess the exclusivity of a marker gene in identifying a specific cell type.

Neurons						Astrocyte				
Gene ID	**Scores**	**logFC**	**pvals**	**pvals_adj**		**Gene ID**	**Scores**	**logFC**	**pvals**	**pvals_adj**
SYT1	124.759	4.726952	0	0		TRPM3	156.3509	5.730299	0	0
ROBO2	95.00155	4.18023	0	0		NRG3	148.0549	5.048868	0	0
SNAP25	94.74099	3.465574	0	0		HPSE2	137.1517	6.498016	0	0
NRG1	90.63195	4.749167	0	0		LINC01088	124.4254	5.748676	0	0
RIMS2	90.27653	3.775462	0	0		RYR3	119.6572	5.894115	0	0
CELF4	82.95389	4.21169	0	0		RNF219-AS1	108.302	6.216844	0	0
KCNIP4	82.85629	3.426161	0	0		SORBS1	107.2191	3.862542	0	0
FGF14	82.54153	3.247062	0	0		ADCY2	104.6923	4.912457	0	0
CADPS	82.53909	3.530591	0	0		PITPNC1	102.1218	3.964344	0	0
FAM155A	81.28446	3.059624	0	0		GLIS3	99.63332	4.628837	0	0
ATP8A2	81.00098	3.64354	0	0		RFX4	95.66502	5.788445	0	0
GRIK2	79.29987	3.031014	0	0		GPC5	94.23904	3.978223	0	0
MYT1L	78.8815	3.953688	0	0		FMN2	94.03922	4.109834	0	0
CDH18	78.7949	4.056036	0	0		SLC14A1	92.89619	5.572173	0	0
FGF12	74.19513	2.986077	0	0		GPM6A	87.78948	3.446067	0	0
RAB3C	74.15955	3.387868	0	0		RORA	87.59466	3.17389	0	0
CNTN1	74.07328	2.507624	0	0		DTNA	87.48186	2.697035	0	0
GRIN1	73.94498	3.422539	0	0		NEBL	86.90349	3.397049	0	0

Table S4. List of upregulated and downregulated DEGs between PD and control samples based on cell-type specific snRNA-seq dataset with accession GSE184950.

Cell-types	Upregulated DEGs	Downregulated DEGs
Astrocyte	RMRP,HSPE1-MOB4,NR4A3,ABCC3, LUCAT1,BBOX1-AS1,SERPINH1, HSPA1B,MRPL18,MAFF,NR4A1,DNAJ B1,ANXA1,ZFAND2A,DNAJA4,CGAS, ATF3,HSPH1,SEPT4-AS1,FOS,RGS2, NMB, PARD6G-AS1,HIF1A-AS2, RAB39A, AL355075.4,HSPA1A,HSPB1,GPNMB, BAG3,CHORDC1,AKR1C1,NQO1,SESN 2,HMOX1,HSPA4L,ADCY7,HSPD1,KC NE4,BACE2,COL24A1,PGF,KLHL25,FO SL2,CDKN1A,SOCS3,BAMBI,TGES3,P LOD1,GBP2,PPP1R15A,SH3BGR,NFIL3,	SEMA4A,RHBDD2,EGFL7,CPS1,PCBP3,SCAMP5,G AP43,CRMP1,CD200,GUCY1A2,TSPAN7,GNG2,GP RASP1,SRSF12,WIPF3,ADAMTS10,SLIT1,GPX3,NE FL,MIR137HG,NPFFR1,CXCL14,CAMK4, CACNA1E,BEX2,MCF2,VSX1,AL591518.1,GRIK1,C DH12,DNAH14,SUMO3,NEFH,B4GALT6,TMEM59L ,PCSK1N,LRRC34,FRRS1L,SNTG1,SLC9A7,ZDHHC 22,GRM7,GRIK2,OPCML,CNTNAP5,PNMA2,NCDN, SLC2A13,NXPH1,CHD3,HEYL, STX1B,GABBR2,GFRA1,BASP1,ZNF730,GUCY1B1, AL033504.1,TUSC3,ADGRL2,ANKRD30BL,CHRNA 4,CDKN2D,SAMD5,CEP170B,RUNDC3B,AL359091. 1,KCNJ6,MAP7D2,AC074286.1,CNTN4, PAK3,TENM1,CDK5R1,TSPYL1,AC005237.1,DOK6, NRSN1,RPH3A,NRG1,NAP1L2,PRKAR1B,LPCAT4, ADD2,RAB3A,CACNA2D2,REEP1,KCNIP4,EPHA6, GAD1,SV2A,CA10,SYN2,KCNH7,ARHGDIG, NEFM,CNTN5,CAMK2A,PNMA3,ACHE,CLSTN3,U CHL1,ELAVL4,NAP1L3,TAGLN3,NAP1L5,ZNF385D ,LY6E,CHD5,CELF4,SEZ6,VAT1L,SMIM10L2B,CNT N6,PCDH15,KCNQ2,SEZ6L2, SNCB,RIMS2,GNG3,PEG10,SNCG,PCDH11X,ATP8 A2,ELAVL2,VWC2L,FGF13,STMN2,PJA1,FBLL1,SY T1,SCN2A,GRIN2B,THY1,SLC12A5,CPLX2,DNM1,E EF1A2,RAB3C,VSNL1,SCN9A,MEG8,SLC4A10,KLH L1,NSG2,AC022639.1,NRIP3,BEX1,UNC13C,GPRAS P2,GABRB2,INA,GABRA1,NSG1,TMEM35A,RIMS3, CAMK2N2,MYT1L,SYNGR3,GRIN1,RAB3B,SYT4,A C092957.1,GALNTL6,SLC6A3,SLC17A6,AC105402.3 ,SCN3A,GAD2,CDH18,CRHBP,SYN1,SCG2,GABRG 2,PIANP,HTR2C,SULT4A1,LY6H,LINGO2,CALY,PT PRN,CALB2,TMEM130,TAC1, F11-AS1
Microglia	NR4A3,HSPE1-MOB4,HSPA1B,BAG3, NR4A1,SERPINH1,DNAJB1,HSPA1A,N R4A2,TSNAX-DISC1,LONRF3,HSPH1, PPP1R15A,CLIC2, FOSL2,HIF1A-AS2,ATF3,EMP2,DUSP1, SMIM35,DNAJA4,KLHL25,HSPB1,RGS 2, PLAUR,LINC02343,ARG2,CD83,P4HA1, MIR4300HG,HMOX1,VEGFA,LINC0151 5,CHORDC1,LGALS3,MYO5B,HSPD1, LUCAT1, FOS	CLVS2,RIMS1,AC009226.1,RAP1GAP,ATP2B2,KCN T2,MLLT11,SLC24A3,DYNLT3,CLSTN2,LINC01322 ,BRINP3,TSPYL1,GNAL,RNF208,SHISA9,AC008591. 1,ANXA6,GRIP1,TUB,SV2B,RHBDD2,SCAMP5,KL HL1,MGAT4C,LONRF2,RHBDL3,DACH1,PCP4,TSP AN7,FXYD7,KIF5A,AKAP12,AMPH,SLC35F1,GAB RB1,PGM2L1,DKK3,CNKSR2,CD200,KCNIP4,CRM P1,ENO2,LINC02008,LRFN5,GUCY1B1,AGBL4,SYN 3,RUSC1,KCNJ6,SEZ6L,TRO,BEX2,KCND2,CNTNA P5,SCN9A,NXPH1,ACOT7,ZNF385D,GRM8,ARHGA P44,PYGO1,SNPH,CNTN3,EPHA7,KNDC1,B4GALT 6,ADCYAP1R1,GALNTL6,NOL4,PCDH7,C1QL1,GR M1,MTUS2,SEZ6L2,NRIP3,PJA1,FGF14,CA10,NTNG

		1,NPTXR,SV2C,SPOCK2,DENND6B,TEX41,DZIP1,PDZD4,SLC9A3R2,SNTG1,GABRB3,KCNJ3,NEFL,NPFFR1,ID4,ANK1,NDRG4,RUNDC3B,UNC13C,CHRNA4,KSR2,CEP170B,KCNA2,PAK3,CDKN2D,SLC4A3,LY6E,GLRB,DIRAS1,GULP1,CADPS,CDK5R1,CPLX2,ELMOD1,NAP1L2,ZNF804B,ANKRD30BL,DOK6,HS6ST3,TUBB2A,ARHGDIG,PACSIN1,PHYHIP,FGF12,ATP8A2,CACNB2,NRSN1,MYT1L,UNC80,EFNA5,FNDC10,PRKG1,RAB6B,NCDN,CELF4,SYBU,NR2F2,FGF13,VWC2,SNCB,GRIK1,PLCB4,FRRS1L,GPX3,CNTN5,SMIM10L2B,CPLX1,REEP1,RFK,PEG10,OPCML,CHST1,FAM155A,EGFL7,FBLL1,XKR4,CEND1,PPFIA3,FRMPD4,GAP43,GRIN2B,HECW1,VAT1L,NEFM,MAP7D2,COL25A1,GRIA1,NRSN2,PSD,CACNA1E,GALNT17,UCHL1,GABRG2,AC105402.3,SLC4A10,CAP2,SV2A,SNAP25,PRKAR1B,PLAC8,GRM7,CHRM3,TENM2,CNTN4,CRHBP,NEFH,PCDH15,RPH3A,SYNGR3,CADM3,STX1B,SYT16,STXBP5L,CAMK2N2,GPRASP2,DMTN,MIR137HG,GRIK2,NAP1L3,PLPPR3,TMEM59L,PNMA2,SCN3A,TAGLN3,DNM1,REEP2,ADD2,NAP1L5,KCNB2,CLSTN3,ROBO2,RIMS2,NSG2,GRM5,RALYL,CDK5R2,ATCAY,PNMA3,GABRB2,SCN1A,EEF1A2,NSG1,ELAVL2,SLC44A5,RAVER2,OLFM3,BEX1,SRRM3,PTPRT,SYT1,SLC12A5,CAMK2B,RIMS3,NELL2,UNC5D,CREG2,RAB3C,TUBA4A,STMN2,CHD5,INA,LINGO2,RAB3A,GABRA1,LINC02240,THY1,TMEM130,VSNL1,IGLON5,MEG8,SNCG,SCN2A,KCNH7,ACHE,EPHA6,TMEM35A,HTR2C,CHGB,PIANP,SLC17A6,SULT4A1,KCNC2,SYT4,NRG1,SYN1,SEZ6,SYN2,GNG3,KCNQ2,MAST1,CDH18,RAB3B,GRIN1,GAD2,CALY,PTPRN,LY6H,SCG2,BAIAP3,CALB2,TAC1

Neurons	HSPE1-MOB4,SERPINH1,BAG3, CGAS,CCDC81,AL136115.2,SEPT4-AS1, RMRP,CHRNA5,HSPA1A,KLHL25, DIRC3-AS1,ZSCAN31, BACE2,HSPA1B,DNAJB1,AL592295.3, MRPL18,PARD6G-AS1, AC022075.1,ZFAND2A,NLRC5,HIF1A-AS2,NGFR,AC018797.2,LUCAT1,EBF2, CHORDC1,AC073342.1,MORC4,TMEM140,ATF3,MBOAT1,CYP39A1,AC004949.1,ABHD3,LINC00877,PTGES3,SNAP23,IL17RB,PAX5,TUBA1C,DNAJA4,SP110,SH3BGR,TRIM16L,CASZ1,OSMR-AS1, AL132780.1,PLOD1,HSPD1,HEY2,TBC1D10A,ADGRF3,ABTB2,AL355075.4,SALL3,AC243829.1,USPL1,AC092115.3,RAB39A,ERAP2,MATN2,PIEZO2,ADCY7, EYA4,FBXO32,ABCA1,MAFF,DUSP10, PTPN13,HUNK,FOS,AP001978.1,AC004690.2,SLC16A4,P4HA2,CAV1,CD9,HSPH1,BBOX1-AS1,CD36,HMOX1,HGF,SNX31, HSPB1,AC017074.1,NQO1,IGFL4,RASGRP3,P4HA1,DNAH12,LINC01515,EN2,SPATS2L,PARP9,PROX1,MCTP2,OPALIN,MET,CPB1,METTL21A,STK40,PPEF1,KLK6,AP002373.1,ELOVL5,MYO5B,NDUFV2-AS1,C17orf67,PYGL,LINC01099, LINC01792,LINC02197,AC063944.1,LYPD6,AP000282.1,AL139383.1,HBEGF,CPEB1-AS1,LINC01588,PRIMA1,IL12A-AS1,CCDC59,AC036108.3,CRYAB,HIST2H2BF,ACP7,MRPS6,ECT2L,EEPD1,HSPA4L,CPEB1,CTNNAL1,HMGB1,TBX19,AL138720.1,LINC02240,PARP12,KIRREL1,C5AR1,LINC00639,STAT3,PRKD1, NUP210L,PKDCC,AC007785.1,TSHR,ELL2,PACRG-AS3,PPP1R1C,AC096564.1, AC091167.6,LATS2,MCUB,PAX8,ST3GAL6-AS1,KCNMB4,OSBPL1A,CASS4, TMEM246-AS1, CMYA5,CCDC62, SMAD1,PLEKHH2,KLRD1,ATP10B,ITGB3BP,CACNG3	CYP26B1,CRHBP,KCNF1,EFHD2,SLC17A7,LINC02381,ZIC2,CBLN1,FAM43A,STUM,SLC17A6,HOPX,CALB2,TAC1,TPBG,CLDN5,RASGRP1,NEFH,KCNA1,STAC2,SPON2,IGSF1,SCN4B,CITED2,RNF182,PCSK1,DOC2A,CSF1R,CHGB,NEFM,CARMIL2,CSPG4, TMEM156,RNF212,CDKN2D,LST1,NEU4,PAX6,IGFBP6,CAMK2N2,SLC25A22,NEFL,FAM43B,HAPLN4, TLR2,VWF,FNDC10,KCNC3,TMEM158,KLF2,EEF1A2,CCK,IGLON5,CD83,ID1,ISYNA1,LY6E,PHF24,DIRAS1,VAMP1,SYT2,IFITM2,C1RL,DYNLT3,COL5A3,GPX3,MME,PRSS23,SNCG,ATXN7L3,NUDT11,JCAD,IRX2,KCNC4,CDHR1,STX1B,WNT7B,LRMP,TUBB2A,PNMA6A,ANO3,SYN1,SCG2,ARHGDIG,THY1,AL359091.1,IKZF1,CDK5R2,CREG2,SYNPO,OTUB1,CYBA,PTMS,ZIC1,STOML1,GNG3,SMIM10L2B,TMEM35A,ALDH1L1,SCN1B,SLC2A5,CALY,C15orf53,SNCB,SYNGR3,HLA-DRA, CREB3L1,KCNMB2,PLPPR3,ITIH5,EGFL7,NECAB2,NDUFA4L2,FBLL1,RNF208,CCDC68,PDE8B,C22orf34,WDR54,FRMPD2,CDK5R1,REEP2,PHYHIP,PNMA8C,COTL1,OGFRL1,SUMO3,AC114316.2,LINC02334,PNMA2,TSPYL1,LAMB2,C1QA,KCNA2,SULT4A1,TSPAN7,LIMS2,EIF5A2,S100A10,LIMK1,IL4R,SNPH,KCNK3,YWHAH,GTPBP3,TCEAL2,FRZB,INHBB,TUBA4A,FAM57B,MLLT11
Oligodendrocytes	LINC01515,HSPA1B,HSPE1-MOB4, TPH2,MYRFL,AC104041.1,SLC8A3,NR4A3,SERPINH1,HSPA1A,JPH1,DNAJB1,	TAC1,CALB2,CBLN1,PCSK1,CCK,RTP5,SCG2,CAMKV,C11orf87,BAIAP3,ACTL6B,SLC6A7,NUDT11,CDH9,CHRM2,SYT4,CLSTN3,KCNT1,HRH3,CELF3,TMEM35A,CALY,RIMS3,GABRA4,KCNK3,ZIC2,CH

	BAG3,LINC02343,CFAP161,FOS,TRPM1,LINC01983,EN2,SNX31,TDRD9,DIRAS2	GB,SYN1,SCN3B,PTPRN,GABRA5,TMEM130,CDH18,OPRM1,SLC12A5,IGF1,SLC17A6,SLC6A17,GRIN1,IGLON5,VSNL1,FAM43B,SRRM4,SCN7A,LY6H,KCNC2,CDK5R2,AC105402.3,SYT5,CACNB3,GAD2,CACNA1G,GRIP2,ST8SIA3,NECAB2,PLPPR3,SULT4A1,SLC6A3,GALNTL6,INA,VSTM2A,SHISAL1,PNMA2,KCNH5,SYT13,QPCT,FGF13,LINC00599,GABRG3,SYNPR,VWC2,PTPN5,SYT1,EPHA6,GRM4,LINGO2,NRG1,PNMA3,CDH7,TMEM196,GRIK1,RERGL,DOC2A,,STMN2,MAL2,SYN2,SYT7,SLC4A10,RAB3B,RAB27B,MEIS3,GABRB2,KCNQ2,SYNGR3,CAMSAP3,THY1,DNM1,MAST1,GFRA2,PNMA6A,EPHA5,AL033504.1,CHRNB2,PHF24,ENC1,CHD5,HOOK1,BTBD11,GALNT9,RGS4,GPR149,PRR16,ELAVL2,CAMK2B,CACNA2D2,CARMIL2,HTR2C,PRR36,LRFN5,CYP4F26P,B4GALNT1,CAMK2N2,NEFH,KIAA1549L,CITED2,TMEM158,TTC9,SLC9A7,TUSC3,ADD2,RNF212,AC016717.2,NYAP2,GNG3,GABRG2,CYP26B1,GAD1,CAMK1G,NSG2,NDST4,LY6E,SLC17A7,TLL1,SLC25A22,RIMS2,KCNQ5,KIAA1211L,CNTN4,AL445623.2,SEZ6L,ANO3,ZNF804A,RERG,HAPLN4,SAMD5,CDHR1,IL34,SYT12,ITGA3,PAM,UBE2QL1,PDE1B,SPHKAP,PACSIN1,PIANP,GREM2,MYT1L,CPLX2,SNCB,GABBR2,TBC1D9,NSG1,RAB3C,KCNA1,BASP1,SNCG,KCNF1,ADAMTS10,MEG8,TENM2,GRIN2B,SVOP,GLRA3,ANKRD34C-AS1,EPS8L2,GRIA1,KSR2,ARHGEF17,CNTN5,ZDHHC22,ELAVL4,KLHL1,SNAP25,SH2D3C,NTSR1,DMTN,HS6ST3,PDLIM7,GPX3,SCN1A,C2orf80,SLC4A3,FRAS1,SYNDIG1L,LBH,RUNDC3B,C4orf50,CELF5,ACHE,SNPH,SLC35F4,ELMOD1,AL442647.1,SYBU,MAP7D2,CADM3,WNT7B,PRKCG,RIT2,WNK2,GRIN3A,CNR1,FGF9,GRID2,PNPLA3,ATP2B3,SMIM10L2B,CX3CL1,EFNA5,FAM155A,KLHDC8A,ATP2A3,MGAT4C,NPAS1,UNC13C,GAP43,TRMT9B,LRRC3B,GRIN2D,MYT1,ANKRD30B,CNKSR2,KCNB2,KCNJ3,PLCXD1,PCDH15,DOC2B,FAM57B,GNG2,ADGRL2,KCNC4,FBLL1,ROBO2,FBXO41,NEFM,SNTG1,NEFL,PTGER3,RGS7BP,TSPOAP1,TRHDE,KCNJ6,PLCXD2,UNC5D,NELL2,DOK6,IQSEC3,CYB561,PTPRO,GFRA1,GUCY1A1,KNDC1,CPNE5,PHYHIP,PARM1,RELL2,HPCAL4,TMEM200C,ENTPD3,REEP2,DLGAP3,BEX1,CHD3,GABRA1,RALYL,TAGLN3,VSTM2L,CACNA1E,SYK,ATP2B2,NRSN1,ATP8A2,ZNF385D,ZNF804B,ATRNL1,CSF3R,RNF175,UNC80,ZIC1,RBFOX3,KCNH7,TRIM67,GPRASP2,AC092535.3,FRMPD4,CA12,PLPPR4,CAP2,OGDHL,PAK3,PDE4A,AC005537.1,PRKG1,TMEM59L,PGM2L1,PTPRR,GPR162,HECW1,CLEC2L,CABP1,EPSTI1,ELFN2,LHX1,SLC8A1,AC109466.1,MGAT5B,SV2C,HTR2A,GRIN2A,CACNA1I,

		RAP1GAP2,PRICKLE1,MRAP2,ANKRD55,PSD,SYT16,GNG4,KCND2,PLCXD3,UNC13A,NR2F2-AS1,GDAP1L1,RNF182,CACNG8,NTN4,MIAT,STUM,TOX2,KCNIP4,KCNC1,PCDH7,STAC2,GALNT17,STAT4,SCN2A,AGAP2,KIF21B,HPCA,COL12A1,PCDH11X,PPARGC1B,TSPAN11,NELL1,CD84,AC092813.1,PRKAR1B,CA10,SLC45A4,TUBA4A,ATCAY,AC022639.1,TVP23A,CUX2,NOL4,AKAP12,EEF1A2,EGFR,PTPRT,AL449403.2,HCN1,GALNT16,GPR161,RAB3A,AL365361.1,SLC16A6,NPM2,CGREF1,TM6SF1,CREG2,JPH4,OPCML,ARL4C,SPTB,UNC5A,DTX1,STX1B,HS6ST2,PTMS,NTRK3,PLPPR5,TSPAN13,TRPM2,CDH10,BRINP3,CNNM1,LRRN2,RIMS4,FAR2,AC005165.1,TCERG1L,DACH2,SPOCK2,CDKN2D,WNT5A,FNDC5,ASS1,AC096719.1,KIRREL1,GABRB3,ISYNA1,SLC25A48,SYT2,SRRM3,LINC02223,CELF4,PTK7,JAG2,CPNE4,SCRT1,ZNF385B,FGF12,NR2F2,CDS1,FES,HES4,ERICH3,KCNA2,SMIM10L2A,CRMP1,JAK3,LINC00351,CAMK4,BASP1-AS1,SLC44A5,TOX,CASKIN1,RPH3A,COL11A1,SCN3A,ST3GAL6,EMB,GABRA3,EPHA4,CACNG2,PBX4,LAMB1,HS3ST2,PCP4L1,IMPDH1,ADAM11,IGFBP3,CPLX1
OPCs	NR4A3,EGR1,TRPM1,HSPE1-MOB4,BAG3,FOS,HSPA1A,HSPA1B,SERPINH1,NGFR,ATF3,HSPH1,EMP1,OLR1,DNAJB1,MIR4527HG,LINC02343,JUNB,SNX31,ZFAND2A,NR4A1,LINC01515,AC017074.1,KLK6,IER2,CDKN1A,HSPB1,BTG2,DNAJA4,HSPD1,AC004949.1,DEPDC1B,EMILIN2,CHORDC1,PPP1R15A,JUN,FOSL2,MAFF,MRPL18,MXD1,HSPA8,LINC00323,SGMS2,USH1C,MYRFL,LINC01099,EYA4,FNTB,GADD45B,ZSCAN31,MET,CP,TM4SF1,HSPA4L,GPD1,TSNAX-DISC1,HIST1H2BD,PTGES3,HIST2H2BF,PPIF,LINC01315,CHST2,KCNE4,ADAMTS4,UAP1,LCP1,CD44,P4HA1,AKR1C3,PPEF1,CAV1,FNTA,ADARB2-AS1,SIAH2,FABP5,TNFAIP6,NPB,NABP1,TSPAN8,KIAA0040,CPA6,RGS2,NR4A2	TAC1,CHRM5,CDK5R2,CALB2,AC100801.1,SLC12A5,AC092535.3,SLC17A6,GRIN1,NEFH,PTPRN,DMTN,SYNGR3,UNC13C,RIMS3,SYT2,NEFM,GPX3,CRHBP,BAIAP3,SLC18A2,AC005697.1,CALY,SNCB,ATP10A,CHD5,SEZ6,AC092957.1,MTRNR2L1,SYN1,AC025810.1,ELAVL2,CPLX2,SYT13,PACSIN1,SV2B,SYT1,DISP2,CREG2,OR2L2,STMN2,NEFL,RERG
Pericytes	AL136115.2, TRIB1, MYOM2, NEK10, BAG3, NABP1, ITGB1-DT, HSPA1B, DNAJA4, SNX31, CCDC81, SOD2, MRPL18, PLSCR2, ST8SIA5, ZFAND2A, HMOX1, LY96, HSPA1A, CHORDC1, ABHD3, EGR1, SERPINE1, NOCT, SOCS3, PLAUR, SHISA3, LUCAT1, DIRAS2, HSPH1, AL138828.1, CA13,	SLC17A6, TAC1, SYN2, ADD2, LY6H, THY1, SNCB, TMEM35A, DNM1, GRIN1, CALY, SCG2, STX1B, CAMK2N2, KCNQ5, HTR2C, PNMA2, TMEM59L, NRG1, SYN1, SYT4, GNG3, NEFH, VSNL1, KLHL1, ELAVL4, CAMK2B, SNAP25, MYT1L, INA, SLC4A10, BAIAP3, EPHA6, SLC44A5, CDK5R1, PTPRN, EEF1A2, REEP2, CPLX2, SV2B, SULT4A1, RSAD2, CDH18, RAB3A, CNTN5, NAP1L3, RAB3C,

	CYTOR, AL132780.1, HSPA4L, BIRC3, DNAJB1, PARD6G-AS1, ZSCAN31, GNLY, KLHL6, AF127577.4, AC068234.1, ADAM32, CLIC2, ICAM1, HSPD1, RBKS, SOCS2, TRIM5, TCAF2, CD93, FAM167B, SNAP23, SEMA3E, C4orf47, SEPT4-AS1, IL32, MLKL, CLEC2B, MCTP1, CCDC15, BACE2, GNA14, CGAS, TRIM25, PVT1, IGF2BP2, KLHL25, ADM, LONRF3, PTGES3, ARRDC3, TNFAIP3, TNFRSF10D	ATP8A2, BEX1, LINGO2, NCDN, SCAMP5, SYT1, IPO9-AS1, SCN1A, TAGLN3, STMN2, LMTK3, AL512625.3, UCHL1, VAMP1, ATP2B2, KCNQ2, SMIM10L2A, AC105402.3, PRKAR1B, AL359232.1, SEZ6L2, MAP7D2, ENC1, STXBP5L, NSG2, UNC13C, SLC2A6, GRIN2B, CLSTN3, ARHGDIG, GALNTL6, AL359091.1, NELL2, NPTXR, ROBO2, FRMPD4, TUBB2A, PEG10, RNF208, B3GALNT1, AC016708.1, ELAVL2, UNC80, CEND1, FGF14, SCN2A, PKIB, CHRM5, LPCAT4, PTGIS, STMN3, NCAN, AL035530.2, FRRS1L, SV2A, KSR2, HECW1, RIMS3, IQSEC2, SCN8A
Endothelial	NEK10, LUCAT1, SNX31, CCDC15, EGR1, SOD2, CA3, AP001831.1, NABP1, HSPE1-MOB4, KLHL6, PGF, SERPINE1, OVCH1-AS1, TRIB1, BAG3, HSPA1B, PLSCR2, CLIC2, P4HA2, AF127577.4, AC027288.3, ADAM32, ANXA1, AC092115.3, MPZL3, HSPA1A, NFIL3, CHORDC1, PLAUR, DNAJA4, SBF2-AS1, NUDT4, HSPA4L, ABHD3, ITGA8, FAM210A, RBKS, BIRC3, SNAP23, TRIM5, ATF3, HSPH1, CA13, LY96, AL078459.1, DCDC1, CGAS, CHST2, CMTM7, MRPL18, BACE2, KLRD1, NR4A2, EFCAB13, AC018797.2, CYP1B1-AS1, ACKR1, TMEM70, SOCS3, CCDC18, TNFAIP3, TSPYL2, IL3RA, FAM167B, NRIP1, CD93, HSPD1, KITLG, PARD6G-AS1, ANGPTL4, ADM, AC069277.1, CYTOR, DNAJB1, TRIM25, OSBPL3, SCUBE2, PLOD2, PPP1R3B, LGI2, SNTG2	COL26A1, TENM2, NSG2, CADPS, LY6H, RAB3C, GALNTL6, PTPRN, ATP8A2, PHYHIP, GNG3, CEND1, CNTN5, REEP2, MAP7D2, KCND2, SNCG, SEZ6L2, UNC13C, ATP2B2, ATRNL1, PRKAR1B, CNTNAP5, NAP1L2, PCDH15, UNC80, GRIK2

Table S5. List of upregulated and downregulated common DEGs (cDEGs) between PD and control samples based on five distinct cell types.

Upregulated cDEGs	**Downregulated cDEGs**

HSPA1B, DNAJB1, SERPINH1, FOS, BAG3, HSPA1A,HSPE1-MOB4	GPX3, NEFL, NEFH, NEFM, SNCB, SYNGR3, SLC17A6, SYN1, CALY, CALB2, TAC1

Table S6: List of GO and KEGG based on cDEGs

Biological Process:

GO Terms	GO ID	P-value	Adjusted P-value	Genes
Intermediate Filament Bundle Assembly	GO:0045110	2.14E-08	3.60E-06	NEFL;NEFM;NEFH
Cellular Response To Heat	GO:0034605	4.11E-08	3.60E-06	DNAJB1;BAG3;HSPA1B;HSPA1A
Negative Regulation Of Inclusion Body Assembly	GO:0090084	7.32E-08	3.60E-06	DNAJB1;HSPA1B;HSPA1A
Regulation Of Inclusion Body Assembly	GO:0090083	7.32E-08	3.60E-06	DNAJB1;HSPA1B;HSPA1A
Chaperone Cofactor-Dependent Protein Refolding	GO:0051085	1.77E-06	6.96E-05	DNAJB1;HSPA1B;HSPA1A
De Novo' Post-Translational Protein Folding	GO:0051084	2.99E-06	9.81E-05	DNAJB1;HSPA1B;HSPA1A
Cellular Heat Acclimation	GO:0070370	7.64E-06	1.73E-04	HSPA1B;HSPA1A
Heat Acclimation	GO:0010286	7.64E-06	1.73E-04	HSPA1B;HSPA1A
Response To Unfolded Protein	GO:0006986	7.92E-06	1.73E-04	DNAJB1;SERPINH1;HSPA1A
Regulation Of Nucleotide-Binding Oligomerization Domain Containing 2 Signaling Pathway	GO:0070432	1.15E-05	2.26E-04	HSPA1B;HSPA1A
Positive Regulation Of Microtubule Nucleation	GO:0090063	1.60E-05	2.87E-04	HSPA1B;HSPA1A
Positive Regulation Of Tumor Necrosis Factor-Mediated Signaling Pathway	GO:1903265	2.14E-05	3.51E-04	HSPA1B;HSPA1A
Regulation Of Microtubule Nucleation	GO:0010968	3.43E-05	5.19E-04	HSPA1B;HSPA1A
Negative Regulation Of Cellular Component Organization	GO:0051129	4.64E-05	6.53E-04	DNAJB1;HSPA1B;HSPA1A
Cellular Response To Unfolded Protein	GO:0034620	1.03E-04	0.001356	BAG3;HSPA1A
Regulation Of Mitotic Spindle Assembly	GO:1901673	1.44E-04	0.001722	HSPA1B;HSPA1A
Cellular Response To Oxidative Stress	GO:0034599	1.49E-04	0.001722	FOS;HSPA1B;HSPA1A
Negative Regulation Of Extrinsic Apoptotic Signaling Pathway In Absence Of Ligand	GO:2001240	1.75E-04	0.001722	HSPA1B;HSPA1A
Cellular Response To Topologically Incorrect Protein	GO:0035967	1.75E-04	0.001722	BAG3;HSPA1A
Negative Regulation Of Signal Transduction In Absence Of Ligand	GO:1901099	1.75E-04	0.001722	HSPA1B;HSPA1A
Cellular Response To Steroid Hormone Stimulus	GO:0071383	2.27E-04	0.002127	HSPA1B;HSPA1A
Positive Regulation Of Erythrocyte Differentiation	GO:0045648	2.45E-04	0.002198	HSPA1B;HSPA1A
Regulation Of Extrinsic Apoptotic Signaling Pathway In Absence Of Ligand	GO:2001239	2.65E-04	0.002234	HSPA1B;HSPA1A
Regulation Of Protein Modification By Small Protein Conjugation Or Removal	GO:1903320	3.06E-04	0.002234	HSPA1B;HSPA1A
Regulation Of Spindle Assembly	GO:0090169	3.06E-04	0.002234	HSPA1B;HSPA1A
Positive Regulation Of Microtubule Polymerization	GO:0031116	3.06E-04	0.002234	HSPA1B;HSPA1A
Response To Steroid Hormone	GO:0048545	3.06E-04	0.002234	HSPA1B;HSPA1A
Purine Ribonucleoside Triphosphate Metabolic Process	GO:0009205	3.73E-04	0.002627	HSPA1B;HSPA1A
ATP Metabolic Process	GO:0046034	4.22E-04	0.002866	HSPA1B;HSPA1A
Regulation Of Erythrocyte Differentiation	GO:0045646	4.73E-04	0.003008	HSPA1B;HSPA1A
Positive Regulation Of Myeloid Cell Differentiation	GO:0045639	4.73E-04	0.003008	HSPA1B;HSPA1A
Regulation Of Mitotic Spindle Organization	GO:0060236	5.56E-04	0.003422	HSPA1B;HSPA1A
mRNA Catabolic Process	GO:0006402	6.76E-04	0.004035	HSPA1B;HSPA1A
Positive Regulation Of Cytokine-Mediated Signaling Pathway	GO:0001961	7.08E-04	0.0041	HSPA1B;HSPA1A

Protein Stabilization	GO:0050821	8.06E-04	0.004538	BAG3;HSPA1B;HSPA1A
Regulation Of Tumor Necrosis Factor-Mediated Signaling Pathway	GO:0010803	8.42E-04	0.004608	HSPA1B;HSPA1A
Positive Regulation Of Transport	GO:0051050	9.13E-04	0.004864	CALY;SYNGR3
Neurotransmitter Transport	GO:0006836	9.88E-04	0.005121	SLC17A6;SYN1
Negative Regulation Of Protein Modification By Small Protein Conjugation Or Removal	GO:1903321	0.001065	0.005244	HSPA1B;HSPA1A
Negative Regulation Of Protein Ubiquitination	GO:0031397	0.001065	0.005244	HSPA1B;HSPA1A
RNA Catabolic Process	GO:0006401	0.001186	0.005697	HSPA1B;HSPA1A
Regulation Of Cell Death	GO:0010941	0.00127	0.005956	SNCB;HSPA1B
Positive Regulation Of Interleukin-8 Production	GO:0032757	0.001357	0.006215	HSPA1B;HSPA1A
Chemical Synaptic Transmission	GO:0007268	0.001763	0.0078	SLC17A6;SNCB;SYN1
Negative Regulation Of Extrinsic Apoptotic Signaling Pathway	GO:2001237	0.001782	0.0078	HSPA1B;HSPA1A
Regulation Of Interleukin-8 Production	GO:0032677	0.002376	0.010178	HSPA1B;HSPA1A
Positive Regulation Of Proteasomal Ubiquitin-Dependent Protein Catabolic Process	GO:0032436	0.002493	0.010233	HSPA1B;HSPA1A
Positive Regulation Of Ubiquitin-Dependent Protein Catabolic Process	GO:2000060	0.002493	0.010233	HSPA1B;HSPA1A
Purine Ribonucleotide Metabolic Process	GO:0009150	0.002553	0.010264	HSPA1B;HSPA1A
mRNA Metabolic Process	GO:0016071	0.002613	0.010295	HSPA1B;HSPA1A
Cellular Response To Chemical Stress	GO:0062197	0.00286	0.011048	HSPA1B;HSPA1A
Positive Regulation Of Proteasomal Protein Catabolic Process	GO:1901800	0.002924	0.011076	HSPA1B;HSPA1A
Cellular Response To Hormone Stimulus	GO:0032870	0.003184	0.011835	HSPA1B;HSPA1A
Regulation Of Proteasomal Ubiquitin-Dependent Protein Catabolic Process	GO:0032434	0.004253	0.015517	HSPA1B;HSPA1A
Negative Regulation Of Programmed Cell Death	GO:0043069	0.004525	0.016053	BAG3;HSPA1B;HSPA1A
Regulation Of Protein Ubiquitination	GO:0031396	0.004563	0.016053	HSPA1B;HSPA1A
Negative Regulation Of Growth	GO:0045926	0.005467	0.018861	HSPA1B;HSPA1A
Negative Regulation Of Cell Growth	GO:0030308	0.005553	0.018861	HSPA1B;HSPA1A
Response To Hydroperoxide	GO:0033194	0.006284	0.020632	GPX3
Sodium-Dependent Phosphate Transport	GO:0044341	0.006284	0.020632	SLC17A6
Negative Regulation Of Muscle Cell Apoptotic Process	GO:0010656	0.008072	0.025346	BAG3
Cellular Response To Organic Cyclic Compound	GO:0071407	0.008106	0.025346	HSPA1B;HSPA1A
Positive Regulation Of NF-kappaB Transcription Factor Activity	GO:0051092	0.008106	0.025346	HSPA1B;HSPA1A

Molecular Function:

GO Terms	GO ID	P-value	Adjusted P-value	Genes
C3HC4-type RING Finger Domain Binding	GO:0055131	7.64E-06	3.74E-04	HSPA1B;HSPA1A
ATP Binding	GO:0005524	0.001876	0.033637	SYN1;HSPA1B;HSPA1A
Adenyl Ribonucleotide Binding	GO:0032559	0.002509	0.033637	SYN1;HSPA1B;HSPA1A
Cadherin Binding	GO:0045296	0.002746	0.033637	DNAJB1;BAG3;HSPA1A
Histone Deacetylase Binding	GO:0042826	0.003524	0.034537	HSPA1B;HSPA1A
G Protein-Coupled Receptor Binding	GO:0001664	0.006916	0.041049	HSPA1B;HSPA1A
Cuprous Ion Binding	GO:1903136	0.007179	0.041049	SNCB
Lipase Inhibitor Activity	GO:0055102	0.008072	0.041049	SNCB
Phospholipase Inhibitor Activity	GO:0004859	0.008072	0.041049	SNCB
Purine Ribonucleoside Triphosphate Binding	GO:0035639	0.008377	0.041049	SYN1;HSPA1B;HSPA1A
Sodium:Phosphate Symporter Activity	GO:0005436	0.009858	0.043913	SLC17A6
R-SMAD Binding	GO:0070412	0.01697	0.066991	FOS
Metal Cation:Proton Antiporter Activity	GO:0051139	0.01874	0.066991	SLC17A6

Microtubule Binding	GO:0008017	0.019183	0.066991	NEFM;NEFH
Disordered Domain Specific Binding	GO:0097718	0.020507	0.066991	HSPA1A
Ubiquitin Protein Ligase Binding	GO:0031625	0.024261	0.072447	HSPA1B;HSPA1A
Ubiquitin-Like Protein Ligase Binding	GO:0044389	0.027336	0.072447	HSPA1B;HSPA1A
Kinesin Binding	GO:0019894	0.027547	0.072447	NEFH
Hsp70 Protein Binding	GO:0030544	0.030174	0.072447	DNAJB1
Solute:Sodium Symporter Activity	GO:0015370	0.030174	0.072447	SLC17A6
Core Promoter Sequence-Specific DNA Binding	GO:0001046	0.031049	0.072447	FOS
Tubulin Binding	GO:0015631	0.03336	0.074303	NEFM;NEFH
Calcium Ion Binding	GO:0005509	0.038042	0.081046	CALB2;SNCB
Copper Ion Binding	GO:0005507	0.039751	0.081158	SNCB
Monoatomic Anion Channel Activity	GO:0005253	0.04666	0.0878	SLC17A6
Serine-Type Endopeptidase Inhibitor Activity	GO:0004867	0.04666	0.0878	SERPINH1
Chloride Transmembrane Transporter Activity	GO:0015108	0.04838	0.0878	SLC17A6

Cellular Component:

GO Terms		P-value	Adjusted P-value	Genes
Exocytic Vesicle Membrane	GO:0099501	1.39E-05	1.77E-04	SLC17A6;SYNGR3;SYN1
Synaptic Vesicle Membrane	GO:0030672	1.48E-05	1.77E-04	SLC17A6;SYNGR3;SYN1
Neuron Projection	GO:0043005	1.04E-04	8.35E-04	CALB2;NEFL;SLC17A6;NEFM;NEFH
Aggresome	GO:0016235	4.47E-04	0.002683	HSPA1B;HSPA1A
Axon	GO:0030424	7.73E-04	0.00371	NEFL;NEFM;NEFH
Intermediate Filament	GO:0005882	0.001732	0.006927	NEFL;NEFM
Intermediate Filament Cytoskeleton	GO:0045111	0.002376	0.008148	NEFL;NEFM
Ficolin-1-Rich Granule Lumen	GO:1904813	0.005382	0.016145	HSPA1B;HSPA1A
Ficolin-1-Rich Granule	GO:0101002	0.011691	0.031177	HSPA1B;HSPA1A
Cytoskeleton	GO:0005856	0.015598	0.037436	NEFM;NEFH;SYN1
Vesicle	GO:0031982	0.018584	0.040547	HSPA1B;HSPA1A
Excitatory Synapse	GO:0060076	0.02139	0.04278	SLC17A6
Polymeric Cytoskeletal Fiber	GO:0099513	0.02327	0.042961	NEFL;NEFM
Neuromuscular Junction	GO:0031594	0.034538	0.059209	SYNGR3
Intracellular Organelle Lumen	GO:0070013	0.039456	0.063129	SERPINH1;HSPA1B;HSPA1A
Focal Adhesion	GO:0005925	0.046588	0.068235	HSPA1B;HSPA1A
Cell-Substrate Junction	GO:0030055	0.048333	0.068235	HSPA1B;HSPA1A

KEGG Pathways:

Term	P-value	Adjusted P-value	Genes
Estrogen signaling pathway	2.38E-04	0.005666	FOS;HSPA1B;HSPA1A
Measles	2.48E-04	0.005666	FOS;HSPA1B;HSPA1A
Amyotrophic lateral sclerosis	2.70E-04	0.005666	GPX3;NEFL;NEFM;NEFH
Protein processing in endoplasmic reticulum	4.56E-04	0.007181	DNAJB1;HSPA1B;HSPA1A
Pathways of neurodegeneration	7.38E-04	0.009296	GPX3;NEFL;NEFM;NEFH
Lipid and atherosclerosis	8.87E-04	0.009317	FOS;HSPA1B;HSPA1A
Legionellosis	0.001186	0.010671	HSPA1B;HSPA1A
MAPK signaling pathway	0.002178	0.015443	FOS;HSPA1B;HSPA1A
Antigen processing and presentation	0.002206	0.015443	HSPA1B;HSPA1A
Longevity regulating pathway	0.003736	0.023538	HSPA1B;HSPA1A
Toxoplasmosis	0.004485	0.025686	HSPA1B;HSPA1A
Dopaminergic synapse	0.006172	0.032403	CALY;FOS
Spliceosome	0.007901	0.038292	HSPA1B;HSPA1A

Table S7. List of key genes (KGs) from the PPI network based on different topological measures.

SN	KGs	Betweenness	Closeness	Degree	EPC	MCC	Stress
1	CALB2	11.09	15	13	5.73	87360	70
2	NEFL	16.64	15.5	14	5.73	87390	92
3	DNAJB1	16.71	9.3	9	4.45	368	74
4	HSPA1A	20.39	13.5	10	4.83	1106	92
5	SYN1	3.27	13.83	11	5.33	86400	26
6	BAG3	3.07	12	7	4.13	150	24

Table S8. List of Disease-KGs Interaction

Disease Name	P-value	Adjusted P-value	Number of KGs	Associated KGs
Schizophrenia	4.51E-05	0.009926	5	CALB2, DNAJB1, NEFL, SYN1, HSPA1A
Alzheimer's Disease	5.24E-05	0.009926	5	CALB2, BAG3, NEFL, SYN1, HSPA1A
Axonal neuropathy	2.12E-04	0.020006	2	BAG3, NEFL
Distal sensory impairment	2.29E-04	0.020006	2	BAG3, NEFL
Infection	2.80E-04	0.020006	3	DNAJB1, BAG3, NEFL
Major Depressive Disorder	3.17E-04	0.020006	**3**	CALB2, NEFL, HSPA1A
Congenital myopathy (disorder)	4.43E-04	0.021301	2	BAG3, NEFL
Neurologic Symptoms	5.27E-04	0.021301	2	DNAJB1, SYN1
Huntington Disease	5.71E-04	0.021301	3	CALB2, NEFL, SYN1
Central neuroblastoma	6.12E-04	0.021301	**4**	BAG3, NEFL, SYN1, HSPA1A
Congenital pes cavus	6.18E-04	2.13E-02	2	BAG3, NEFL
Neuroblastoma	6.75E-04	2.13E-02	4	BAG3, NEFL, SYN1, HSPA1A
Amyloidosis	0.00131	3.49E-02	3	CALB2, NEFL, HSPA1A
Transient Ischemic Attack	0.001327	3.49E-02	2	NEFL, HSPA1A
Decreased tendon reflex	0.001383	3.49E-02	2	BAG3, NEFL
Carcinogenesis	0.001726	3.59E-02	5	CALB2, DNAJB1, BAG3, NEFL, HSPA1A
Atrial myxoma	0.001799	3.59E-02	1	CALB2
Snowflake vitreoretinal degeneration	0.001799	3.59E-02	1	NEFL
Subcortical Vascular Dementia	0.001799	3.59E-02	1	NEFL
Sarcoidosis	0.002016	3.79E-02	2	BAG3, HSPA1A
Charcot-Marie-Tooth disease, Type 1C	0.002098	0.037871	1	NEFL
Adenofibroma	0.002398	0.039318	1	CALB2
Parkinson Disease	0.00266	0.039318	3	DNAJB1, NEFL, HSPA1A
Respiratory Paralysis	0.002697	0.039317	1	BAG3
Hand muscle atrophy	0.002697	0.039317	1	NEFL

Table S9. Collection of Parkinson's Disease (PD), Alzheimer's Disease (AD), Multiple Sclerosis (MS), Huntington's Disease (HD), and Dementia with Lewy Bodies (DLB) related 170 meta-candidate drugs from published articles and different online web tools.

Disease type	Paper title with reference	Drug List
PD	Emerging drugs for Parkinson's disease [1]	Amantadine, Apomorphine, Benzatropine, Bromocriptine, Carbidopa, Entacapone, Pergolide, Pramipexole, Procyclidine, Ropinirole, Selegiline, Tolcapone, Trihexyphenidyl, levodopa,
PD	Medications for Parkinson's Disease [2]	Pimavanserin, rotigotine, rasagiline, Safinamide, opicapone,
PD	Amantadine in the Treatment of Parkinson's Disease [3]	Amantadine
PD	Identification of potential natural neuroprotective molecules for Parkinson's disease by using chemoinformatics and molecular docking [4]	Amphetamine, Cocaine, Methamphetamine, Rotenone, Baicalein, Caffeine, Curcumin, Epigallocatechin gallate, Metformin, Myricetin, Nordihydroguaiaretic acid, Nortriptyline, Scutellarein
PD	Anti-Parkinson's disease drugs and pharmacogenetic considerations [5]	Benztropine, Biperiden, Diphenhydramine, Ethopropazine, Orphenadrine, Procyclidine, Trihexyphenidyl, Levodopa, Carbidopa, Benserazide, Bromocriptine, Lisuride, Pergolide, Cabergoline, Ropinirole, Pramipexole, Rotigotine, Apomorphine, Selegiline, Rasagiline, Entacapone, Tolcapone
PD	NOVEL DRUGS FOR PARKINSON'S DISEASE [6]	Apomorphine, SIB-1508Y, OPC-14117, L-dopa
PD	Muscarinic receptor binding changes in postmortem Parkinson's disease [7]	pirenzepine, 4DAMP, and, AF-DX 384
PD	DSigDB: drug signatures database for gene set analysis [8]	Tanespimycin, disulfiram, alvespimycin, monorden, securinine, 1,4-chrysene-quinone, Elesclomol, tanespimycin, geldanamycin, raloxifene, Radicicol, thimerosal, thiostrepton, cycloheximide, Cadmium-sulfate, Zinc acetate dihydrate, lomustine, parthenolide, Aluminium sulfate, minocycline, CROTONALDEHYDE, puromycin, LY-294002, MG-132, valproic-acid, etacrynic-acid, levonorgestrel, MG-262, N-Acetyl-L-cysteine, albendazole, mometasone, 2-Methylcholine, Mehp, spiperone, withaferin A, mesalazine, sanguinarine, gefitinib, ellipticine, trichostatin-A, vorinostat, clotrimazole, celastrol, beta-carotene, metoprolol, azacitidine, irinotecan, fisetin, GW-8510, mebendazole, phenoxybenzamine, benzene, staurosporine, scriptaid, Latrepirdine, 1,9-Pyrazoloanthrone, meclofenoxate, 8-azaguanine, flunixin, mirtazapine, emetine, Bortezomib, cyclophosphamide, propanil, PYRENE, anisomycin, ABT-737, Ginsenoside-Re, cyclosporin-A, doxorubicin, thapsigargin, Ezetimibe, REMIFENTANIL, Sirtinol,
AD	Bioinformatics methods in drug repurposing for Alzheimer's disease [9]	Rottlerin, Dapsone, Biperiden, Skimmianine, Bupropion, Milrinone, Pioglitazone, Rucaparib, Nifedipine, BRD-K05331696, SN-38, Isoliquiritigenin, Forskolin, Vorinostat, Trichostatin-a, HC-toxin, THM-I-94, Panobinostat, Dacinostat, KM-00927,

		Bisindolylmaleimide, THZ-2-98-01, Enzastaurin, PKCbeta-inhibitor, Inhibitor BEC, SB-216763
AD	Recent advances on drug development and emerging therapeutic agents for Alzheimer's disease [10] Scutellarein derivatives with histamine H3 receptor antagonism and cholinesterase inhibitory potency as multi target-directed ligands for possible Alzheimer's disease therapy [11]	Lanabecestat, Umibecestat, Tramiprosate, ALZ-801, Verubecestat, Elenbecestat, Atabecestat, Semagacestat, Avagacestat, Etazolate, Acitretin, Epigallocatechin-gallate, Tarenflurbil, GV 971, Colostrinin, Bapineuzumab, Solanezumab, Gantenerumab, Aducanumab, Lecanemab, LMTM, Scutellarein, Blarcamesine, Saracatinib, Thiamet G, Telmisartan, ALZT-OP1, Atuzaginstat, Masitinib, Azeliragon, Encenicline, J-147
AD	Treatment of Alzheimer's Disease with the GSK-3 Inhibitor Tideglusib: A Pilot Study [12]	glycogen synthase kinase-3, tideglusib
AD	Recent Progress in the Drug Development for the Treatment of Alzheimer's Disease Especially on Inhibition of Amyloid-peptide Aggregation [13]	Tramiprosate, Troriluzole, Verubecestat
MS	Comparison of fingolimod, dimethyl fumarate and teriflunomide for multiple sclerosis [14]	Glatiramer acetate, Dimethyl fumarate, Fingolimod, Teriflunomide
MS	Comparative effectiveness of dimethyl fumarate versus fingolimod and teriflunomide among MS patients switching from first-generation platform therapies in the US [15]	Glatiramer acetate, Dimethyl fumarate, Fingolimod, Teriflunomide, Interferon β-1b, interferon β-1a, and glatiramer acetate, natalizumab, Ozanimod
HD	Pharmacogenetics in the Treatment of Huntington's Disease: Review and Future Perspectives [16]	Tetrabenazine, Deutetrabenazine, haloperidol, chlorpromazine, pluphenazine, aripiprazole, olanzapine, quetiapine, risperidone, citalopram, escitalopram, fluoxetine, paroxetine, sertraline, amitriptyline, desipramine, doxepin, imipramine, nortriptyline, trimipramine, diazepam, etizolam, quazepam, desmethylclobazam, alprazolam, midazolam, clonazepam, lorazepam, Clozapine, Aripiprazole, Haloperidol
DLB	Clozapine for Management of Neuropsychiatric Symptoms in Dementia with Lewy Bodies: Case Report and Literature Review [17]	Rivastigmine,Quetiapine,Olanzapine,Risperidone,Melatonin,Clonazepam,Lorazepam,

Table S10. Docking scores (binding affinities, kcal/mol) between the proposed receptors and top-ordered 30 candidate drugs (out of 170)

Drug/Protein	HSPA1A	HINFP	CALB2	SYN1	SREBF1	NEFL	DNAJB1	BAG3	YY1
Celastrol	-9.1	-9.2	-7.2	-8.4	-7.1	-7.4	-7.1	-7.5	-7.5
Withaferin A	-8	-9.1	-7.2	-8.1	-7.6	-8	-7.3	-7.3	-7.4
Apomorphine	-8.6	-8	-7.4	-7.4	-7.3	-7.3	-7.6	-7.3	-7.1
Masitinib	-9.1	-9.8	-7.2	-6.8	-6.3	-6.9	-7.2	-7	-7.1
Beta-carotene	-8.3	-7.4	-6.9	-7.8	-7.6	-7.6	-7.2	-7.3	-6.7
Staurosporine	-8.7	-8.4	-7.3	-7.6	-6.1	-7.4	-7	-6.9	-6.9
Latrepirdine	-8.2	-8.3	-7.3	-7.1	-7.2	-7.2	-6.7	-7	-6.4
Pyrene	-8.2	-7.9	-7.5	-8.8	-6.6	-6.8	-6.1	-6.9	-6.2
Tideglusib	-7.5	-7.3	-7	-8.4	-6.2	-6.7	-7.6	-6.9	-6.7
Ellipticine	-9.1	-8.5	-6.7	-6.7	-6.5	-7.2	-6.4	-6.5	-6.6
Scutellarein	-8.1	-8.2	-7.2	-7.5	-7.1	-7.4	-6.7	-6.1	-5.9
Ozanimod	-7.5	-7	-7.2	-7.3	-6.3	-7.5	-7.8	-6.6	-6.6
Rotenone	-7.4	-7.8	-7.6	-8.2	-6.1	-6.9	-7.4	-6.1	-6.1
Doxorubicin	-7.3	-8.1	-7.4	-7.2	-6.9	-7.5	-7	-6.1	-5.9
Benzatropine	-8.6	-7.8	-6.8	-6.6	-7.1	-7.1	-6.4	-6.6	-6.3
OPC-14117	-7.5	-8	-7.3	-6.3	-6.8	-7.4	-6.8	-6.8	-6.3
Mirtazapine	-8.8	-7.8	-6.7	-7.2	-7.1	-7.1	-6	-6.4	-6
Elenbecestat	-8	-8.7	-7.5	-7.3	-5.8	-6.5	-7.3	-5.9	-6
Mebendazole	-7.9	-6.6	-7.5	-6.7	-6.9	-7.5	-6.8	-6.8	-6.3
Gedunin	-7.4	-8.1	-6.9	-7.6	-6.3	-6.9	-7	-6	-6.7
Carbamazepine	-8	-8	-7.5	-7	-6.8	-7	-6.3	-6.4	-5.9
Scriptaid	-7	-8.2	-7	-6.8	-8.1	-7.1	-6.9	-6	-5.7
Siponimod	-8.8	-7.3	-6.7	-6.1	-6.4	-6.9	-7.2	-6.8	-6.6
Hydrocortisone-acetate	-7.1	-8.2	-7.3	-9.1	-5.5	-6.4	-6.8	-6.1	-6.2
Risperidone	-7.6	-8.4	-7	-6.4	-5.8	-6.7	-6.7	-7	-6.7
1,9-Pyrazoloanthrone	-8	-7.9	-7.4	-6.7	-6.8	-6.8	-6.5	-6.3	-5.9
Pimavanserin	-8.4	-7.4	-6.8	-7.4	-5.2	-7.3	-6.7	-6.4	-6.1
Pirenzepine	-8.7	-7.9	-7.5	-7.5	-4.9	-6.7	-6.5	-6.1	-5.9
Intepirdine	-7.8	-8	-7.4	-5.3	-5.6	-7.8	-7.1	-6	-6.2
Epigallocatechin-gallate	-8.1	-7.8	-7.4	-7.9	-5.4	-6.2	-6.5	-5.7	-6.1

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