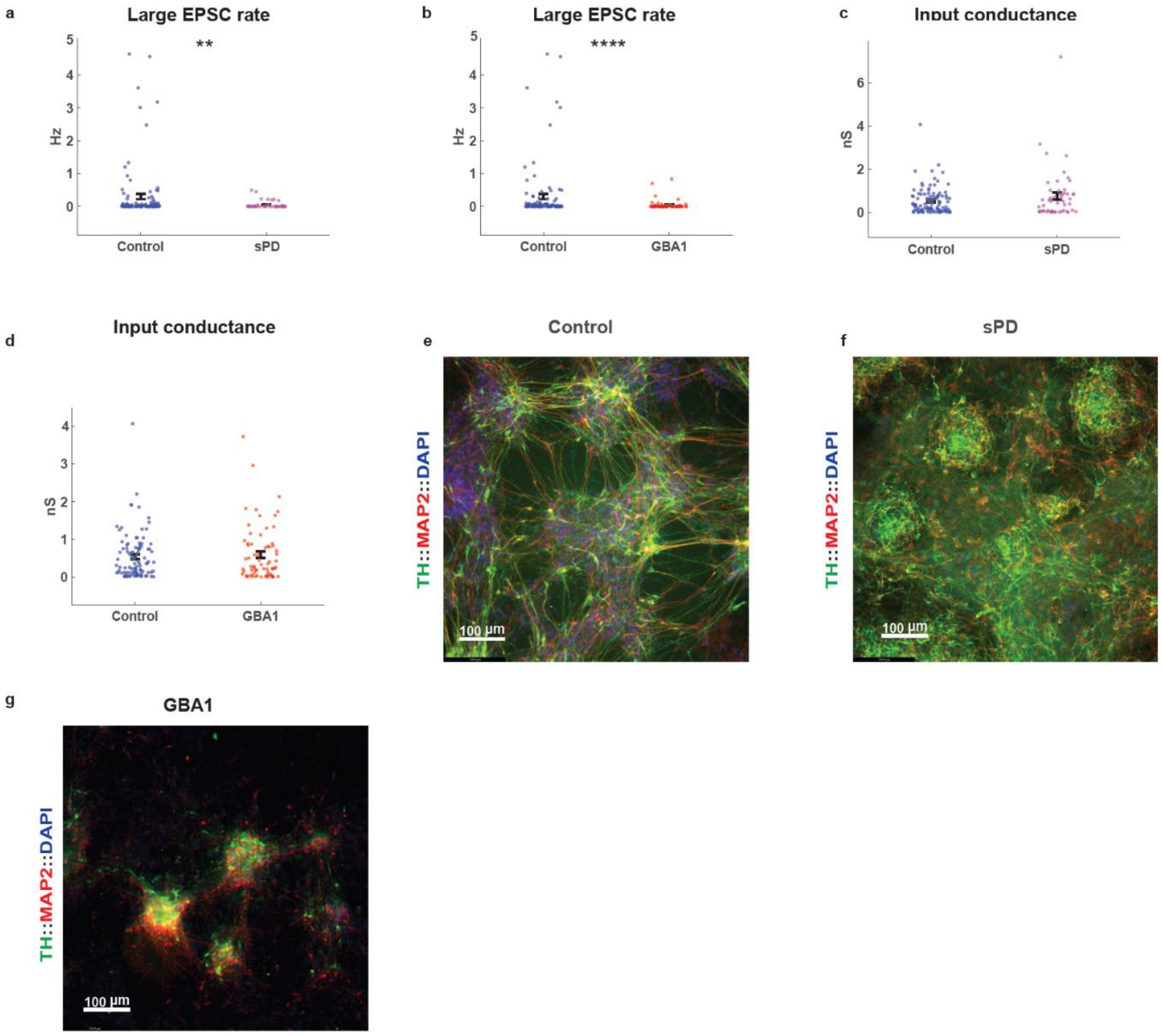
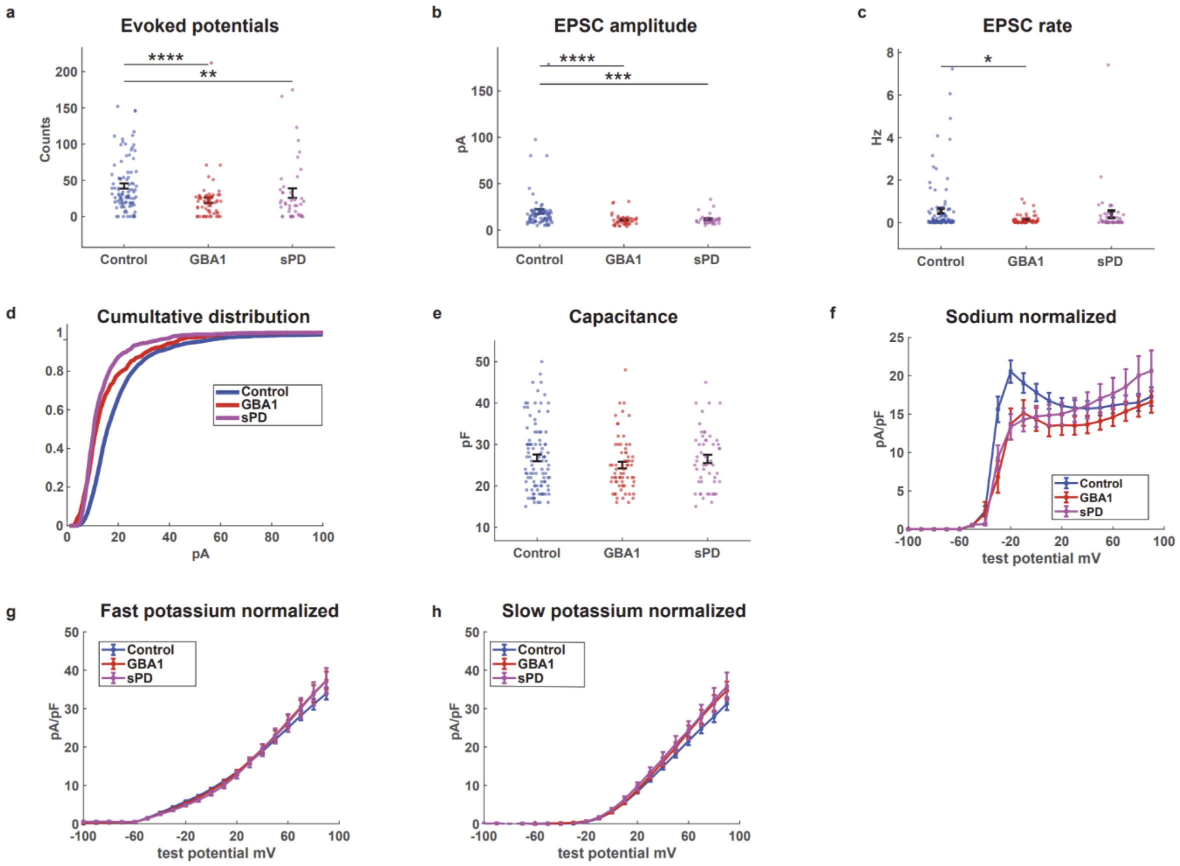
Supplementary Figure Legends



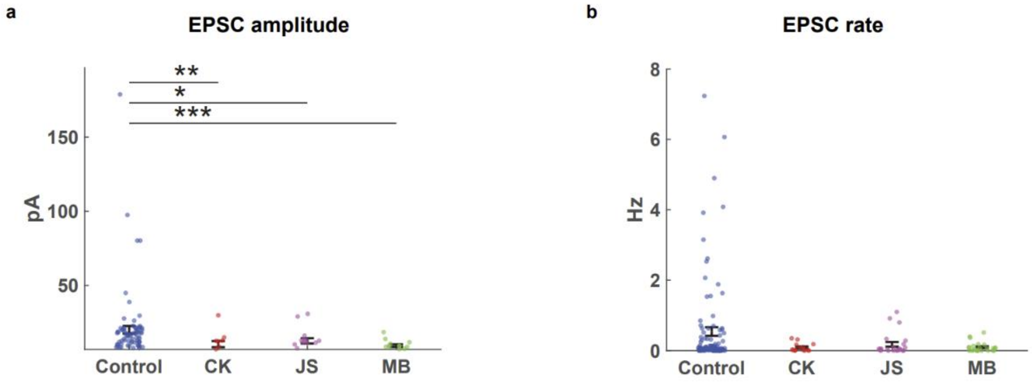
Supplementary Figure 1

(a) The large EPSC rate was significantly decreased in sPD neurons compared to control neurons. (b) The large EPSC rate was also significantly decreased in E326K-*GBA1* neurons compared to control neurons. (c) The input conductance was not significantly different between control and sPD neurons. (d) The input conductance was not significantly different between control and E326K-*GBA1* neurons. An example image of DA neurons with ICC for Tyrosine Hydroxylase (TH) (green), MAP2 (red), DAPI (blue) in a (e) control (f) sPD, and (g) E326K-*GBA1* DA neuronal cultures.



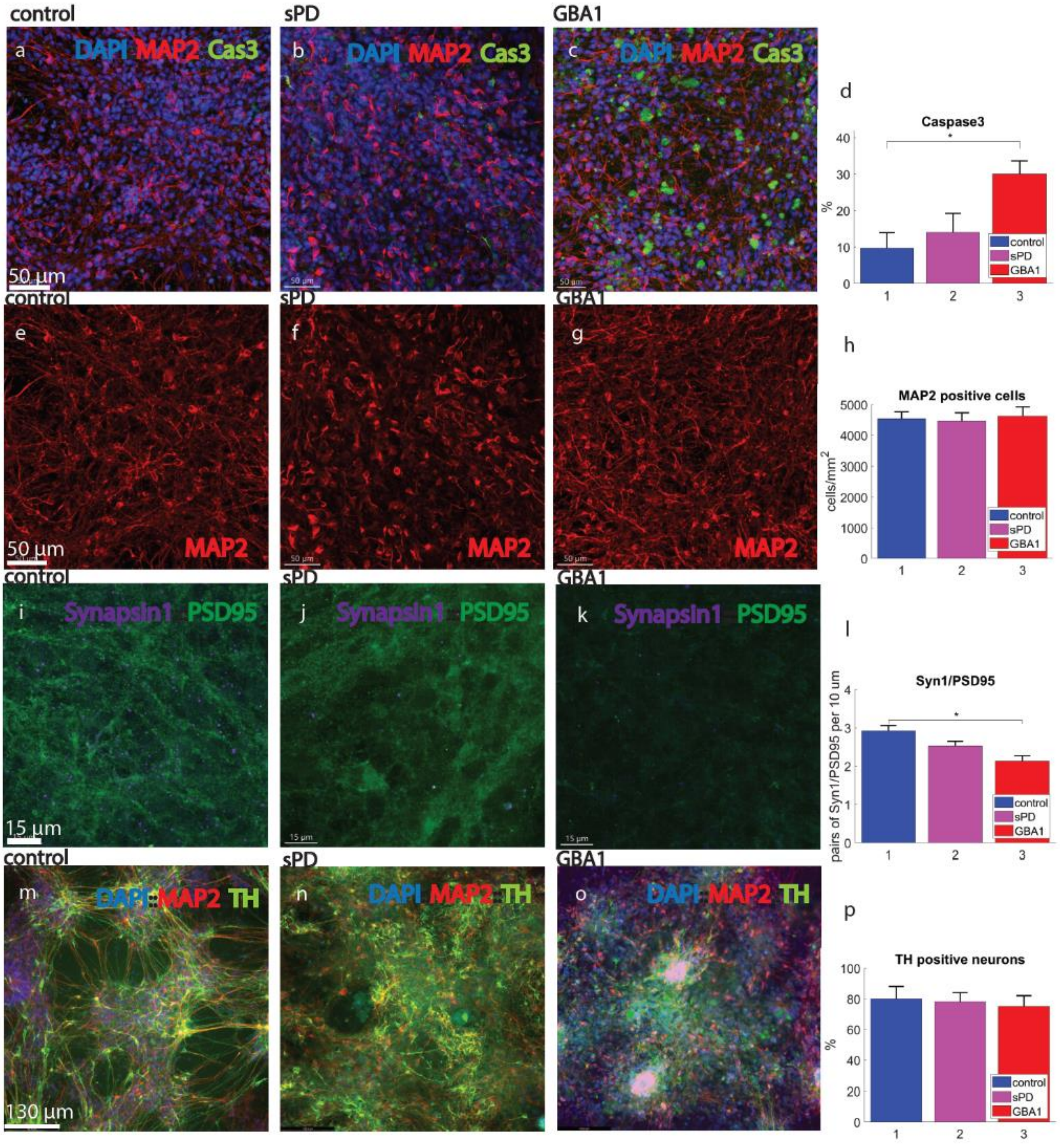
Supplementary Figure 2

This figure shows a comparison between Control, E326K-*GBA1*, and sPD neurons together. (a) Both E326K-*GBA1* and sPD neurons were hypoexcitable compared to control neurons. (b) The EPSC amplitude was decreased in both E326K-*GBA1* and sPD compared to control neurons. (c) The EPSC rate in E326K-*GBA1* neurons was significantly reduced compared to control neurons (d) The cumulative distribution of EPSC amplitudes was left shited in both sPD and E326K-*GBA1* neurons indicating smaller amplitudes. (e) The capacitance was similar between all groups. (f) The sodium currents were reduced in both E326K-*GBA1* and sPD neurons compared to control neurons. (g) The fast potassium and (h) slow potassium currents were not significantly different between E326K-*GBA1*, sPD, and control neurons.



Supp. Figure 3

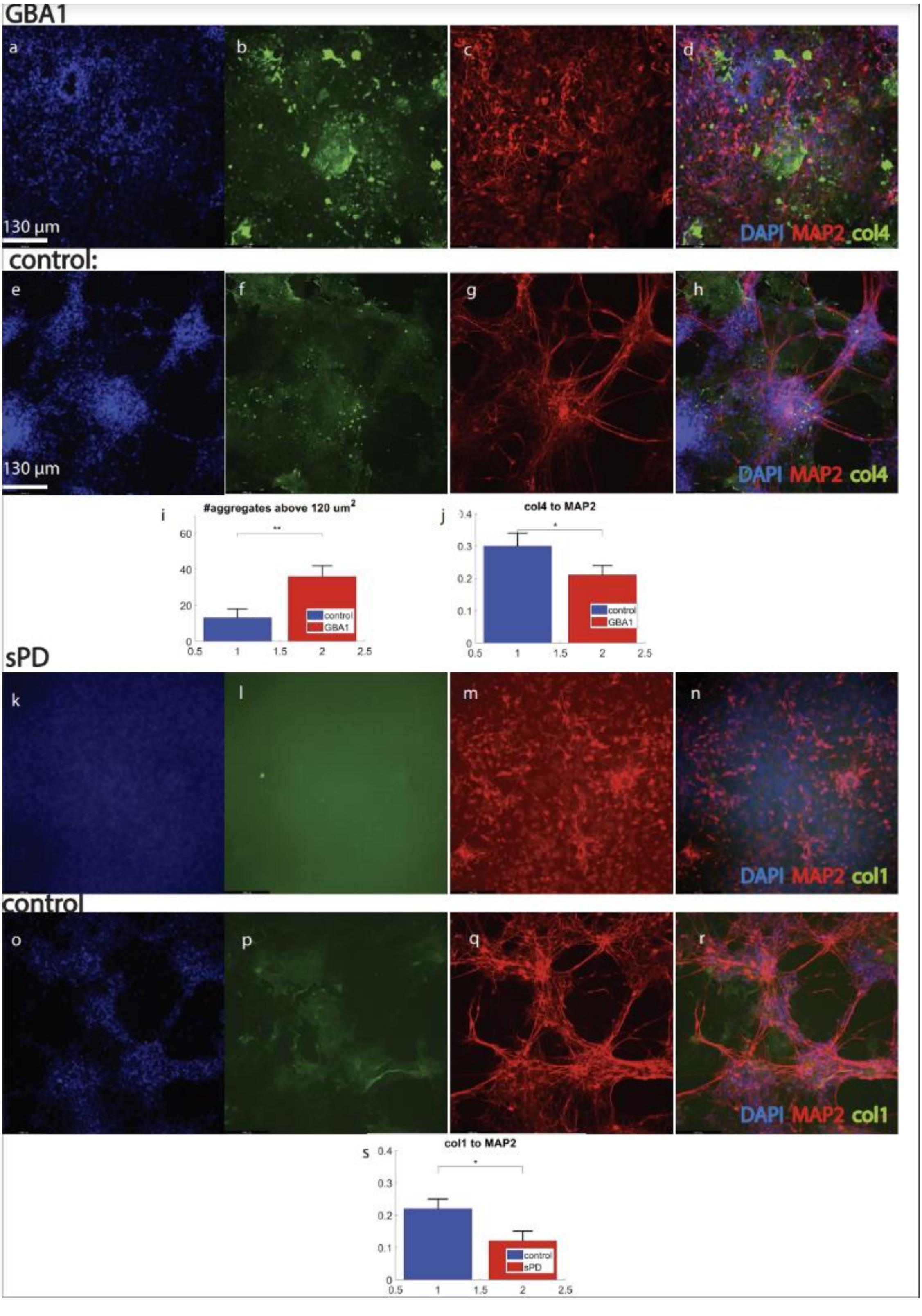
This figure shows comparisons among individual E326K-*GBA1* patients compared to the control group. (a) The EPSC amplitude was significantly decreased in all E326K-*GBA1* lines compared to the controls. (b) The EPSC rate in all E326K-*GBA1* lines showed a trend of a decreased mean value compared to controls (but not significantly).



Supplementary Figure 4, ICC

(a-d) Caspase3 protein expression is elevated in E326K-*GBA1* neuronal cultures. Representative traces (a-c) and the averages (d) are shown. (e-h) Despite more Caspase3 positive cells in the E326K-*GBA1* cultures, the density of MAP2 positive neurons was the same between the three groups. Representative images (e-g) and the averages (h) are presented. (i-l)

A reduction in the density of Synapsin1::PSD95 pairs was observed in the E326K-*GBA1* neuronal cultures. Representative images (i-k) and the averages (l) are presented. (m-p) The percentage of TH positive neurons was more than 80% on average in all the three groups. Representative images (m-o) and the averages (p) are presented.



Supplementary Figure 5, ICC

ICC images for DAPI (blue), MAP2(red), and collagen 4 (green) in the 2 upper rows and collagen1 (green) in the 2 bottom rows. (a-d) Example ICC images for a E326K-*GBA1* culture. (e-h) Example ICC images for a control culture. (i) E326K-*GBA1* DA neuronal cultures exhibited more aggregation of the collagen 4 protein compared to control DA neurons culture. (j) However, the diffuse background of collagen 4 in the E326K-*GBA1* DA neuronal cultures had a lower intensity compared to control DA neuronal cultures. (k-n) Example ICC images for an sPD culture. (o-r) Example ICC images for a control culture. (s) The diffuse background of collagen 1 in the sPD DA neuronal cultures had a lower intensity compared to control DA neuronal cultures.

Supplementary tables

Enrichment_kegg_GBA1_vs_Control					
Pathway	Total	Expected	Hits	P.Value	FDR
Basal cell carcinoma	63	2.28	10	7.67E-05	0.0176
ECM-receptor interaction	82	2.97	11	0.000163	0.0176
Pathways in cancer	530	19.2	36	0.000166	0.0176
Hypertrophic cardiomyopathy (HCM)	85	3.08	11	0.000226	0.0179
Focal adhesion	199	7.2	17	0.00085	0.0541
Arrhythmogenic right ventricular cardiomyopathy (ARVC)	72	2.61	9	0.00108	0.0571
Hippo signaling pathway	154	5.57	14	0.00133	0.0605
Dilated cardiomyopathy	91	3.29	10	0.00158	0.0629
Phenylalanine metabolism	17	0.615	4	0.00275	0.0972
Sulfur metabolism	9	0.326	3	0.00335	0.106
Signaling pathways regulating pluripotency of stem cells	139	5.03	12	0.00442	0.114
PI3K-Akt signaling pathway	354	12.8	23	0.00455	0.114
Regulation of actin cytoskeleton	214	7.74	16	0.00464	0.114
Breast cancer	147	5.32	12	0.00689	0.156
Mannose type O-glycan biosynthesis	23	0.832	4	0.00863	0.183
Wnt signaling pathway	158	5.72	12	0.0119	0.237
Melanoma	72	2.61	7	0.0149	0.279
Protein digestion and absorption	90	3.26	8	0.0159	0.28
Transcriptional misregulation in cancer	186	6.73	13	0.0173	0.289
FoxO signaling pathway	132	4.78	10	0.0211	0.336
AGE-RAGE signaling pathway in diabetic complications	100	3.62	8	0.028	0.425
Proteoglycans in cancer	201	7.27	13	0.0304	0.439
Arginine and proline metabolism	50	1.81	5	0.0337	0.446
N-Glycan biosynthesis	50	1.81	5	0.0337	0.446
Neuroactive ligand-receptor interaction	338	12.2	19	0.0372	0.465
Adipocytokine signaling pathway	69	2.5	6	0.0381	0.465
Insulin resistance	108	3.91	8	0.0416	0.477
Other types of O-glycan biosynthesis	22	0.796	3	0.0434	0.477
African trypanosomiasis	37	1.34	4	0.0435	0.477
Purine metabolism	130	4.7	9	0.0458	0.483
TGF-beta signaling pathway	92	3.33	7	0.0486	0.483
Proximal tubule bicarbonate reclamation	23	0.832	3	0.0487	0.483

Supplementary Table 1. KEGG pathway enrichment analysis of differentially expressed genes (DEGs) in E326K-*GBA1* versus control neurons. The table lists significantly enriched pathways, the number of genes in each pathway, the expected number of DEGs in the pathway, the actual number of DEGs observed in the pathway, p-values from the performed enrichment test, and Benjamini-Hochberg adjusted FDR p-values (q-values). Pathways are ordered by statistical significance.

enrichment_kegg_GBA1_downregulated_vs_Control					
Pathway	Total	Expected	Hits	P.Value	FDR
Pathways in cancer	530	13.2	29	4.14E-05	0.0132
Focal adhesion	199	4.94	15	0.000119	0.0189
PI3K-Akt signaling pathway	354	8.78	20	0.000471	0.0488
Jak-STAT signaling pathway	162	4.02	12	0.000673	0.0488
Regulation of actin cytoskeleton	214	5.31	14	0.000848	0.0488
ECM-receptor interaction	82	2.03	8	0.000921	0.0488
Hypertrophic cardiomyopathy (HCM)	85	2.11	8	0.00117	0.0531
Arrhythmogenic right ventricular cardiomyopathy (ARVC)	72	1.79	7	0.00196	0.0779
Proteoglycans in cancer	201	4.99	12	0.0042	0.144
Th17 cell differentiation	107	2.66	8	0.00498	0.144
Insulin resistance	108	2.68	8	0.00527	0.144
FoxO signaling pathway	132	3.28	9	0.00544	0.144
Dilated cardiomyopathy	91	2.26	7	0.00726	0.178
Melanoma	72	1.79	6	0.00868	0.197
AGE-RAGE signaling pathway in diabetic complications	100	2.48	7	0.0119	0.237
African trypanosomiasis	37	0.918	4	0.0128	0.237
EGFR tyrosine kinase inhibitor resistance	79	1.96	6	0.0134	0.237
Complement and coagulation cascades	79	1.96	6	0.0134	0.237
Transcriptional misregulation in cancer	186	4.62	10	0.0172	0.288
Basal cell carcinoma	63	1.56	5	0.0196	0.312
Adipocytokine signaling pathway	69	1.71	5	0.0279	0.422
Prolactin signaling pathway	70	1.74	5	0.0295	0.422
Malaria	49	1.22	4	0.0327	0.422
Adherens junction	72	1.79	5	0.0328	0.422
Hematopoietic cell lineage	97	2.41	6	0.0332	0.422
Bacterial invasion of epithelial cells	74	1.84	5	0.0363	0.444
Pancreatic cancer	75	1.86	5	0.0381	0.449
Pertussis	76	1.89	5	0.04	0.454
Kaposi's sarcoma-associated herpesvirus infection	186	4.62	9	0.0417	0.457

Supplementary Table 2. Downregulated and upregulated (separately) KEGG pathways in E326K-*GBA1* versus control neurons. Significantly enriched pathways for downregulated DEGs, with stats and enrichment analysis results displayed as in Supplementary Table 1.

enrichment_go_bp_GBA1					
Pathway	Total	Expected	Hits	P.Value	FDR
Muscle organ development	389	13.7	34	1.07E-06	0.000878
Skeletal muscle tissue development	197	6.95	21	6.43E-06	0.00263
Regulation of anatomical structure morphogenesis	702	24.8	47	1.79E-05	0.00398
Positive regulation of epithelial cell proliferation	120	4.23	15	2.07E-05	0.00398
Gland development	303	10.7	26	2.75E-05	0.00398
Negative regulation of developmental process	674	23.8	45	2.91E-05	0.00398
Negative regulation of cell differentiation	540	19	38	4.06E-05	0.00476
Tissue morphogenesis	566	20	39	5.10E-05	0.00523
Central nervous system development	784	27.7	49	6.92E-05	0.0063
Morphogenesis of an epithelium	440	15.5	32	8.97E-05	0.00735
Positive regulation of transcription from RNA polymerase II promoter	800	28.2	49	0.000114	0.00823
Vasculature development	652	23	42	0.00012	0.00823
Tissue remodeling	126	4.44	14	0.000142	0.00856
Striated muscle tissue development	354	12.5	27	0.000146	0.00856
Regulation of cell differentiation	1290	45.5	70	0.00017	0.00927
Skeletal system development	459	16.2	32	0.000195	0.00942
Cell development	1840	65	93	0.000195	0.00942
Regulation of developmental process	1880	66.2	94	0.000234	0.0107
Negative regulation of response to stimulus	967	34.1	55	0.000292	0.0126
Anatomical structure formation involved in morphogenesis	2090	73.7	102	0.000308	0.0126
Regulation of sequence_specific DNA binding transcription factor activity	372	13.1	27	0.000325	0.0126
Growth	839	29.6	49	0.000348	0.0126
Brain development	559	19.7	36	0.00037	0.0126
Endothelial cell proliferation	92	3.25	11	0.000384	0.0126
Negative regulation of transferase activity	189	6.67	17	0.000385	0.0126
Regulation of endothelial cell proliferation	79	2.79	10	0.000442	0.0139
Organ morphogenesis	966	34.1	54	0.000504	0.0148
Positive regulation of cell proliferation	786	27.7	46	0.000506	0.0148
Developmental growth	290	10.2	22	0.000633	0.0179
Cell fate commitment	254	8.96	20	0.000694	0.019
Positive regulation of peptidyl_tyrosine phosphorylation	134	4.73	13	0.000906	0.0239
Tissue development	1680	59.4	83	0.000942	0.0239
Tube development	506	17.8	32	0.00105	0.0239
Sensory organ development	485	17.1	31	0.00105	0.0239
Positive regulation of cell migration	263	9.28	20	0.00107	0.0239
Positive regulation of signal transduction	998	35.2	54	0.00107	0.0239
Regulation of peptidyl_tyrosine phosphorylation	171	6.03	15	0.00108	0.0239
Negative regulation of sequence_specific DNA binding transcription factor activity	121	4.27	12	0.00116	0.0251
Neurogenesis	1390	49.1	70	0.00142	0.0291
Positive regulation of lymphocyte activation	250	8.82	19	0.00142	0.0291
Cell morphogenesis involved in differentiation	827	29.2	46	0.00146	0.0291
Generation of neurons	1300	46	66	0.0017	0.0331
Neuron differentiation	1190	41.8	61	0.00176	0.0335

Positive regulation of binding	79	2.79	9	0.00181	0.0337
Positive regulation of cell differentiation	571	20.1	34	0.00204	0.0371
Regulation of lymphocyte activation	360	12.7	24	0.00218	0.0384
Regulation of neurogenesis	444	15.7	28	0.0022	0.0384
Embryonic morphogenesis	581	20.5	34	0.00269	0.0453
Regulation of cell morphogenesis	325	11.5	22	0.00272	0.0453
Regulation of cell proliferation	1430	50.4	70	0.00276	0.0453
Tube morphogenesis	347	12.2	23	0.00287	0.0456
Regulation of binding	189	6.67	15	0.00289	0.0456
Negative regulation of cell proliferation	585	20.6	34	0.003	0.0464
Negative regulation of signal transduction	790	27.9	43	0.00309	0.0469
Regulation of cell migration	456	16.1	28	0.00321	0.0479
Nervous system development	2190	77.4	100	0.00341	0.0494
Regulation of T cell proliferation	120	4.23	11	0.00343	0.0494
Pattern specification process	503	17.7	30	0.00357	0.0505
Neuron development	945	33.3	49	0.00425	0.0584
Negative regulation of growth	197	6.95	15	0.00427	0.0584
Angiogenesis	426	15	26	0.0048	0.0645
Cell_substrate adhesion	241	8.5	17	0.00529	0.07
Positive regulation of developmental process	817	28.8	43	0.0056	0.0729
Hematopoietic or lymphoid organ development	679	24	37	0.00577	0.074
Glycoprotein metabolic process	458	16.2	27	0.00646	0.0789
Development of primary sexual characteristics	246	8.68	17	0.00647	0.0789
Bone remodeling	63	2.22	7	0.00654	0.0789
Glycoprotein biosynthetic process	393	13.9	24	0.00655	0.0789
Hemopoiesis	640	22.6	35	0.00679	0.0806
Regulation of response to external stimulus	461	16.3	27	0.00703	0.0813
Peptidyl_tyrosine phosphorylation	228	8.04	16	0.00704	0.0813
Regionalization	353	12.5	22	0.00718	0.0818
Peptidyl_tyrosine modification	230	8.11	16	0.00763	0.0857
Cell migration	1050	37.2	52	0.00856	0.0949
B cell activation	194	6.84	14	0.00895	0.0966
Immune system development	722	25.5	38	0.00895	0.0966
Regulation of T cell activation	279	9.84	18	0.0102	0.109
Cell_matrix adhesion	159	5.61	12	0.0107	0.111
Protein processing	140	4.94	11	0.0107	0.111
Positive regulation of transport	570	20.1	31	0.0113	0.116
Regulation of growth	548	19.3	30	0.0116	0.117
Anatomical structure morphogenesis	2820	99.3	120	0.0119	0.119
Regulation of cell shape	106	3.74	9	0.0126	0.124
Peptidyl_amino acid modification	739	26.1	38	0.0127	0.124
Hormone metabolic process	203	7.16	14	0.013	0.125
Embryo development	1080	38.2	52	0.0142	0.136
Response to external stimulus	1510	53.3	69	0.0145	0.136
Regulation of intracellular transport	290	10.2	18	0.0147	0.136
T cell proliferation	147	5.19	11	0.0151	0.136
Regulation of endocytosis	128	4.52	10	0.0152	0.136
Negative regulation of immune system process	207	7.3	14	0.0152	0.136

Organ development	3290	116	137	0.0153	0.136
Positive regulation of T cell proliferation	75	2.65	7	0.0164	0.143
Cell proliferation	1900	67.1	84	0.0164	0.143
Leukocyte differentiation	404	14.3	23	0.0167	0.143
Regulation of angiogenesis	169	5.96	12	0.0167	0.143
Negative regulation of hydrolase activity	253	8.92	16	0.0177	0.149
Negative regulation of transport	318	11.2	19	0.0179	0.149
Positive regulation of cell cycle	113	3.99	9	0.0184	0.149
Regulation of signal transduction	2440	85.9	104	0.0186	0.149
Protein autophosphorylation	192	6.77	13	0.0187	0.149
Myoblast differentiation	44	1.55	5	0.0187	0.149
Glucan metabolic process	95	3.35	8	0.0189	0.149
Regulation of nucleocytoplasmic transport	172	6.07	12	0.0189	0.149
Protein maturation	153	5.4	11	0.0197	0.154
Positive regulation of phosphate metabolic process	789	27.8	39	0.0208	0.161
Regulation of homeostatic process	324	11.4	19	0.0213	0.163
Neuron projection development	816	28.8	40	0.0218	0.166
Gliogenesis	176	6.21	12	0.0222	0.167
Acute inflammatory response	118	4.16	9	0.0237	0.177
Extracellular structure organization	242	8.54	15	0.0249	0.184
Rhythmic process	200	7.05	13	0.0252	0.184
Positive regulation of protein phosphorylation	681	24	34	0.0261	0.19
Enzyme linked receptor protein signaling pathway	1180	41.4	54	0.0265	0.191
Positive regulation of T cell activation	202	7.13	13	0.027	0.193
JAK_STAT cascade	121	4.27	9	0.0274	0.193
Response to steroid hormone stimulus	267	9.42	16	0.0276	0.194
Negative regulation of phosphorylation	246	8.68	15	0.0282	0.196
Regulation of multicellular organismal process	2480	87.4	104	0.0292	0.199
"Positive regulation of transcription DNA_dependent"	1260	44.4	57	0.0293	0.199

Supplementary Table 3. Gene Ontology Biological Process enrichment analysis of DEGs in E326K-*GBA1* versus control neurons. The table displays significantly enriched terms with stats and enrichment analysis results displayed as in Supplementary Table 1.

enrichment_go_cc_GBA1					
Pathway	Total	Expected	Hits	P.Value	FDR
Extracellular region part	1320	42.9	75	1.31E-06	0.000294
Proteinaceous extracellular matrix	398	12.9	31	6.85E-06	0.000771
Extracellular space	901	29.3	54	1.04E-05	0.000782
Receptor complex	189	6.15	18	4.63E-05	0.0026
Extracellular matrix part	204	6.63	17	0.000374	0.0168
Extracellular matrix	570	18.5	34	0.000511	0.0191
Endoplasmic reticulum lumen	175	5.69	15	0.000606	0.0195
Cell surface	518	16.8	31	0.000845	0.0218
Collagen	93	3.02	10	0.000873	0.0218
Basement membrane	100	3.25	10	0.00153	0.0344
Basolateral plasma membrane	162	5.27	13	0.00247	0.0506
Integral to plasma membrane	1270	41.3	59	0.00343	0.0558
Intrinsic to plasma membrane	1320	43	61	0.00347	0.0558
Integrin complex	32	1.04	5	0.00347	0.0558
Integral to Golgi membrane	47	1.53	6	0.00398	0.0597
Intrinsic to Golgi membrane	50	1.63	6	0.00543	0.0763
Extracellular region	2860	92.9	113	0.0131	0.173
Acetylcholine_gated channel complex	17	0.553	3	0.0165	0.207
Actin cytoskeleton	430	14	22	0.0247	0.293
Secretory granule	276	8.97	15	0.0367	0.401
Cytoplasmic vesicle	1110	36.1	47	0.0374	0.401
Vesicle	1210	39.3	50	0.0467	0.478

Supplementary Table 4. Gene Ontology Cellular Component enrichment analysis of DEGs in E326K-*GBA1* versus controls. The table displays significantly enriched terms with stats and enrichment analysis results displayed as in Supplementary Table 1.

enrichment_go_mf_GBA1					
Pathway	Total	Expected	Hits	P.Value	FDR
Transferase activity, transferring hexosyl groups	237	8.31	19	0.000707	0.192
Transferase activity, transferring glycosyl groups	333	11.7	23	0.00159	0.192
Heparin binding	130	4.56	12	0.00206	0.192
Pattern binding	17	0.596	4	0.00247	0.192
Polysaccharide binding	17	0.596	4	0.00247	0.192
Glycosaminoglycan binding	178	6.24	14	0.00406	0.263
RNA polymerase II distal enhancer sequence_specific DNA binding transcription factor activity	110	3.86	10	0.00527	0.292
Growth factor activity	170	5.96	13	0.00696	0.338
Metalloendopeptidase activity	123	4.31	10	0.0113	0.487
Double_stranded DNA binding	149	5.23	11	0.0159	0.565
G_protein coupled receptor binding	232	8.14	15	0.017	0.565
Calmodulin binding	171	6	12	0.0175	0.565
UDP_glycosyltransferase activity	153	5.37	11	0.019	0.568
Acetylglucosaminyltransferase activity	47	1.65	5	0.0238	0.66
Positive regulation of transcription, DNA_dependent	1260	44.1	57	0.0268	0.692
Acetylcholine_activated cation_selective channel activity	21	0.737	3	0.0357	0.865
GTPase activity	241	8.45	14	0.0451	0.954
Structure_specific DNA binding	242	8.49	14	0.0464	0.954
Cytokine activity	220	7.72	13	0.0467	0.954

Supplementary Table 5. Gene Ontology Molecular Function enrichment analysis of DEGs in E326K-*GBA1* versus controls. The table displays significantly enriched terms with stats and enrichment analysis results displayed as in Supplementary Table 1.

enrichment_GO_CC_sPD				
Pathway	Total	Hits	Enrichment	FDR
Neuron projection	1444	71	2.259790233	5.29E-08
External encapsulating structure	601	39	2.982408352	2.12E-07
Extracellular matrix	600	39	2.987379032	2.12E-07
Synapse	1443	68	2.165806005	2.12E-07
Collagen-containing extracellular matrix	446	32	3.297555331	4.87E-07
Receptor complex	422	28	3.04945727	1.95E-05
Plasma membrane region	1323	58	2.014861142	2.52E-05
Integral component of plasma membrane	1881	74	1.808089383	3.22E-05
Intrinsic component of plasma membrane	1965	76	1.77757531	3.78E-05
Synaptic membrane	401	26	2.979929209	4.94E-05
Postsynapse	682	36	2.426024028	5.49E-05
Somatodendritic compartment	913	43	2.164585026	9.18E-05
Postsynaptic membrane	297	21	3.249674161	0.000112
Plasma membrane signaling receptor complex	194	16	3.790488859	0.000237
Postsynaptic specialization membrane	121	12	4.557984537	0.000514
Fibrillar collagen trimer	16	5	14.36239919	0.000544
AMPA glutamate receptor complex	26	6	10.6060794	0.000544
Banded collagen fibril	16	5	14.36239919	0.000544
Synaptic vesicle	213	16	3.452370135	0.000564
Neuronal cell body	535	28	2.405366295	0.000564
Axon	691	33	2.194890528	0.000641
Postsynaptic specialization	376	22	2.689130062	0.000767
Integral component of postsynaptic specialization membrane	74	9	5.589690497	0.000797
Postsynaptic density	352	21	2.741912573	0.000801
Synaptic vesicle membrane	114	11	4.434705716	0.000819
Asymmetric synapse	358	21	2.695958731	0.000819
Cell body	614	30	2.245586845	0.000819
Glutamatergic synapse	358	21	2.695958731	0.000819
Neuron to neuron synapse	385	22	2.626267281	0.000819
Exocytic vesicle membrane	114	11	4.434705716	0.000819
Intrinsic component of postsynaptic specialization membrane	78	9	5.303039702	0.000904
Exocytic vesicle	234	16	3.142542046	0.001051
Dendrite	674	31	2.113872404	0.001433
Excitatory synapse	49	7	6.565668203	0.001433
Dendritic tree	676	31	2.107618343	0.001433
Complex of collagen trimers	25	5	9.191935484	0.002814
Postsynaptic density membrane	95	9	4.354074703	0.003523
Presynapse	527	25	2.180250352	0.003789
Dendrite membrane	43	6	6.412978245	0.004649
Secretory vesicle	1150	43	1.718492286	0.005866
Collagen trimer	105	9	3.939400922	0.006406
Neuron projection membrane	64	7	5.026839718	0.006406
Plasma membrane protein complex	712	30	1.936503262	0.006406
Ionotropic glutamate receptor complex	47	6	5.867192862	0.006745

Synaptic cleft	18	4	10.21326165	0.006758
Neurotransmitter receptor complex	49	6	5.627715602	0.0081
Integral component of postsynaptic density membrane	51	6	5.407020873	0.009843
Dendritic spine	193	12	2.857596523	0.013227
GABA-ergic synapse	74	7	4.347537053	0.013227
Golgi apparatus	1812	59	1.496479563	0.013477
Cell projection membrane	368	18	2.2480277	0.013477
Neuron spine	196	12	2.813857801	0.013477
Integral component of postsynaptic membrane	119	9	3.47594199	0.013477
Intrinsic component of postsynaptic density membrane	55	6	5.013782991	0.013477
Intrinsic component of postsynaptic membrane	125	9	3.309096774	0.01742
Endoplasmic reticulum lumen	328	16	2.241935484	0.024315
Basolateral plasma membrane	240	13	2.489482527	0.024382
Parallel fiber to Purkinje cell synapse	13	3	10.6060794	0.024544
Collagen type V trimer	4	2	22.97983871	0.026696
Leading edge membrane	189	11	2.67490186	0.028219
Basal part of cell	283	14	2.273623618	0.035371
G protein-coupled receptor complex	15	3	9.191935484	0.035371
Calcitonin family receptor complex	5	2	18.38387097	0.041069
Neuron projection terminus	147	9	2.813857801	0.044432
Ion channel complex	324	15	2.127762843	0.045651
Basement membrane	97	7	3.316677752	0.045814
Catenin complex	33	4	5.57086999	0.046928
Basal plasma membrane	265	13	2.254625685	0.047111

Supplementary Table 6. Gene Ontology Cellular Component enrichment analysis of DEGs in sporadic versus controls. The table lists significantly enriched pathways, the number of genes in each pathway, the actual number of DEGs in the pathway, fold enrichment, and the Benjamini-Hochberg adjusted FDR p-values (q-values). Pathways are ordered by statistical significance.

enrichment_GO_upregulated_CC_sPD				
Pathway	Total	Hits	Enrichment	FDR
Collagen-containing extracellular matrix	446	18	3.739910314	0.000838
External encapsulating structure	601	20	3.083749307	0.001366
Extracellular matrix	600	20	3.088888889	0.001366
Plasma membrane region	1323	28	1.961199295	0.057905
Synaptic vesicle	213	8	3.480438185	0.111835
Neuron projection	1444	28	1.796860572	0.111835

Supplementary Table 7. Upregulated Gene Ontology Cellular Component in sporadic versus controls. Enriched Cellular Components for upregulated genes with layout as Supplementary Table 6.

enrichment_kegg_sPD				
Pathway	Total	Hits	Enrichment	FDR
Steroid biosynthesis	20	6	13.7879	0.000859
Protein digestion and absorption	103	10	4.462105	0.011724
Neuroactive ligand-receptor interaction	350	19	2.494954	0.018706
Arrhythmogenic right ventricular cardiomyopathy	77	8	4.775031	0.018706
Metabolic pathways	1527	53	1.595195	0.029583
Hypertrophic cardiomyopathy	90	8	4.085305	0.035943
Nicotinate and nicotinamide metabolism	35	5	6.565668	0.036069
Terpenoid backbone biosynthesis	22	4	8.356305	0.039046
AMPK signaling pathway	120	9	3.446976	0.039046
Dilated cardiomyopathy	96	7	3.351226	0.139387

Supplementary Table 8. KEGG pathway enrichment analysis of DEGs showing dysregulated pathways in sporadic versus controls. Enriched Cellular Components for upregulated genes with layout as Supplementary Table 6.

enrichment_GO_BP_sPD				
Pathway	Total	Hits	Enrichment	FDR
Cholesterol biosynthetic process	59	13	10.12670858	8.99E-07
Secondary alcohol biosynthetic process	59	13	10.12670858	8.99E-07
Sterol biosynthetic process	66	13	9.052663734	2.64E-06
Circulatory system development	1127	55	2.242930131	2.59E-05
Cell adhesion	1639	70	1.962890433	4.16E-05
Biological adhesion	1646	70	1.954542782	4.16E-05
Extracellular matrix organization	450	30	3.063978495	4.16E-05
Extracellular structure organization	451	30	3.057184751	4.16E-05
Supramolecular fiber organization	919	47	2.350494928	4.16E-05
External encapsulating structure organization	454	30	3.036983089	4.33E-05
Central nervous system development	1105	52	2.162808349	6.85E-05
Generation of neurons	1624	68	1.92441999	6.85E-05
Lipid biosynthetic process	838	43	2.358312803	8.08E-05
Export from cell	1545	65	1.933578662	9.24E-05
Regulation of neurotransmitter receptor activity	88	12	6.267228739	0.000159
Anatomical structure formation involved in morphogenesis	1183	53	2.059055709	0.000179
Alcohol biosynthetic process	145	15	4.754449388	0.000197
Organic hydroxy compound biosynthetic process	250	20	3.676774194	0.000197
Cholesterol metabolic process	146	15	4.721884666	0.000204
Secretion	1636	66	1.854119016	0.000226
Head development	856	42	2.255030901	0.000226
Sterol metabolic process	169	16	4.351212063	0.000228
Neuron differentiation	1473	61	1.90328603	0.000232
Neurogenesis	1757	69	1.804904805	0.000273
Brain development	811	40	2.266815162	0.000295
Secretion by cell	1489	61	1.882834333	0.000295
Locomotion	1982	75	1.739140165	0.000317
Secondary alcohol metabolic process	156	15	4.419199752	0.000322
Collagen fibril organization	121	13	4.937816582	0.000441
Lipid metabolic process	1555	62	1.832475884	0.000498
Regulation of transport	1910	72	1.7325114	0.000528
Vasculature development	748	37	2.273406503	0.000562
Forebrain development	411	25	2.795600816	0.000699
Regulation of secretion by cell	611	32	2.407053482	0.000773
Cellular lipid metabolic process	1178	50	1.950750315	0.000799
Response to endogenous stimulus	1769	67	1.740700049	0.000898
Response to organonitrogen compound	1121	48	1.967943369	0.000922
Regulation of locomotion	1056	46	2.002031403	0.000922
Cell-cell signaling	1885	70	1.706725421	0.000953
Regulation of cellular component movement	1092	47	1.978117984	0.000953
Tube development	1094	47	1.974501681	0.00097
Trans-synaptic signaling	776	37	2.191376372	0.000981
Blood vessel development	717	35	2.243498898	0.001027
Neuron development	1203	50	1.910211032	0.001124
Steroid biosynthetic process	202	16	3.640370489	0.001137

Cell motility	1776	66	1.707960985	0.001496
Localization of cell	1776	66	1.707960985	0.001496
Chemical synaptic transmission	767	36	2.157168692	0.001537
Anterograde trans-synaptic signaling	767	36	2.157168692	0.001537
Regulation of plasma membrane bounded cell projection organization	644	32	2.283710679	0.001537
Response to nitrogen compound	1231	50	1.866761877	0.001788
Response to organic cyclic compound	1034	44	1.955730954	0.001874
Small molecule biosynthetic process	623	31	2.286918138	0.001874
Positive regulation of developmental process	1373	54	1.8075911	0.001874
Muscle structure development	627	31	2.272328549	0.002071
Synaptic signaling	815	37	2.086512963	0.002147
Regulation of cell motility	1010	43	1.956699138	0.002147
Regulation of cell projection organization	661	32	2.224976819	0.002188
Regulation of cation channel activity	197	15	3.499467824	0.002603
Regulation of secretion	670	32	2.195089071	0.002749
Response to oxygen-containing compound	1832	66	1.655752571	0.003029
Cholesterol biosynthetic process via desmosterol	4	3	34.46975806	0.003378
Cholesterol biosynthetic process via lathosterol	4	3	34.46975806	0.003378
Hindbrain development	160	13	3.73422379	0.004139
Regulation of ion transmembrane transporter activity	282	18	2.933596431	0.004139
Cellular component morphogenesis	815	36	2.03012072	0.004139
Tube morphogenesis	886	38	1.971182553	0.004717
Organophosphate metabolic process	1121	45	1.844946908	0.004743
Muscle organ development	340	20	2.703510436	0.004785
Regulation of neuron projection development	453	24	2.434949797	0.004785
Blood vessel morphogenesis	635	30	2.171323343	0.004987
Fluid transport	33	6	8.356304985	0.005076
Regulation of system process	606	29	2.199390504	0.005116
Animal organ morphogenesis	1133	45	1.825406429	0.005506
Cell migration	1590	58	1.676516535	0.005506
Regulation of transmembrane transporter activity	293	18	2.823461411	0.005795
Heart development	583	28	2.207325845	0.006066
Cartilage condensation	22	5	10.44538123	0.006273
Neuron projection development	1045	42	1.847183207	0.00703
Ion transport	1720	61	1.629965304	0.007196
Regulation of cell migration	946	39	1.894743572	0.007196
Water transport	23	5	9.991234222	0.007398
Telencephalon development	274	17	2.851512833	0.007398
Regulation of ion transmembrane transport	533	26	2.241935484	0.007708
Intestinal epithelial cell development	13	4	14.14143921	0.008415
Regulation of transporter activity	306	18	2.703510436	0.008841
Regulation of membrane potential	451	23	2.343841642	0.009447
Regulation of ion transport	763	33	1.987771107	0.009447
Regulation of lipid metabolic process	394	21	2.449627477	0.009713
Muscle tissue development	394	21	2.449627477	0.009713
Proteoglycan metabolic process	92	9	4.4960554	0.010243
Cell aggregation	25	5	9.191935484	0.010243

Regulation of cell adhesion	837	35	1.92185031	0.010668
Negative regulation of response to stimulus	1940	66	1.563576654	0.010668
Negative regulation of protein targeting to mitochondrion	6	3	22.97983871	0.010815
Regulation of cation transmembrane transport	399	21	2.41893039	0.010815
Cell adhesion mediated by integrin	74	8	4.968613775	0.011004
Plasma membrane bounded cell projection organization	1649	58	1.616532014	0.011004
Cellular response to endogenous stimulus	1505	54	1.649051549	0.011226
Cell projection organization	1690	59	1.604509448	0.011519
Striated muscle tissue development	376	20	2.444663693	0.01256
Metencephalon development	117	10	3.928177557	0.01256
Response to growth factor	750	32	1.960946237	0.012831
Regulation of transmembrane transport	622	28	2.068924385	0.013116
Anterior/posterior pattern specification	214	14	3.006707869	0.013346
Cell part morphogenesis	721	31	1.976074896	0.013617
Regionalization	352	19	2.480778043	0.013837
Steroid metabolic process	352	19	2.480778043	0.013837
Modulation of chemical synaptic transmission	470	23	2.249090597	0.013837
Regulation of trans-synaptic signaling	471	23	2.244315458	0.014085
Ossification	416	21	2.32007987	0.016364
Phospholipid metabolic process	479	23	2.20683211	0.017528
Cell projection morphogenesis	704	30	1.958508981	0.018471
Organic hydroxy compound metabolic process	607	27	2.04433491	0.018471
Angiogenesis	544	25	2.112117528	0.018525
Visual learning	45	6	6.127956989	0.018586
Glycerolipid metabolic process	484	23	2.184034258	0.019319
Positive regulation of transport	1013	39	1.769424896	0.019319
Response to lipoprotein particle	30	5	7.659946237	0.019319
Behavior	611	27	2.030951375	0.019413
Cell morphogenesis	1085	41	1.736725138	0.019607
Cytoskeleton organization	1553	54	1.598082795	0.019607
Chondrocyte development	31	5	7.412851197	0.021666
CGMP-mediated signaling	31	5	7.412851197	0.021666
G protein-coupled receptor signaling pathway, coupled to cyclic nucleotide second messenger	65	7	4.949503722	0.021893
Low-density lipoprotein particle remodeling	18	4	10.21326165	0.022283
Alcohol metabolic process	403	20	2.280877291	0.02432
Cellular response to lipoprotein particle stimulus	32	5	7.181199597	0.024435
Cellular response to growth factor stimulus	722	30	1.909681887	0.024485
Cerebellum development	109	9	3.79483575	0.025718
Positive regulation of cell differentiation	897	35	1.79329845	0.027101
Visual behavior	50	6	5.51516129	0.029078
Circulatory system process	632	27	1.963467232	0.029199
Regulation of cell differentiation	1738	58	1.533752181	0.029819
Regulation of signaling receptor activity	211	13	2.831638893	0.029859
Plasma membrane bounded cell projection morphogenesis	700	29	1.904043779	0.029859
Positive regulation of cholesterol esterification	9	3	15.31989247	0.030065
Cardiac muscle cell development	70	7	4.595967742	0.031113

Positive regulation of cellular component organization	1192	43	1.657941383	0.032158
Pallium development	188	12	2.933596431	0.033225
Developmental growth	640	27	1.938923891	0.033225
Organophosphate catabolic process	163	11	3.101573323	0.033736
Cardiac muscle tissue development	215	13	2.778957239	0.033736
Protein phosphorylation	1678	56	1.533815218	0.034035
Negative regulation of G1/S transition of mitotic cell cycle	115	9	3.59684432	0.034035
Locomotory behavior	191	12	2.887519	0.036817
Regulation of exocytosis	219	13	2.728200029	0.037593
Signal release	518	23	2.040680658	0.037593
Sterol import	10	3	13.78790323	0.037593
Wound healing	583	25	1.970826647	0.037593
Cholesterol import	10	3	13.78790323	0.037593
Sensory organ morphogenesis	274	15	2.516040735	0.037593
Cellular response to oxidised low-density lipoprotein particle stimulus	10	3	13.78790323	0.037593
Negative regulation of establishment of protein localization to mitochondrion	10	3	13.78790323	0.037593
Negative regulation of cell cycle G1/S phase transition	118	9	3.505399125	0.038115
Response to wounding	718	29	1.856310091	0.038206
Muscle organ morphogenesis	74	7	4.347537053	0.038206
Positive regulation of cell projection organization	365	18	2.26650464	0.038792
Regulation of cellular component biogenesis	1032	38	1.692313703	0.038792
Pattern specification process	460	21	2.098159187	0.041031
Cellular carbohydrate metabolic process	308	16	2.38751571	0.041258
Cardiac cell development	76	7	4.233128183	0.043236
Pre-B cell allelic exclusion	3	2	30.63978495	0.044712
Lymphatic endothelial cell fate commitment	3	2	30.63978495	0.044712
Regulation of kainate selective glutamate receptor activity	3	2	30.63978495	0.044712
Intestinal epithelial cell differentiation	23	4	7.992987377	0.044908
Actin filament organization	467	21	2.066709263	0.04674
Visual perception	227	13	2.632052011	0.04674
Regulation of NMDA receptor activity	39	5	5.892266336	0.04674
Regulation of nervous system process	149	10	3.084542109	0.049896

Supplementary Table 9 Gene Ontology Biological Processes enrichment analysis of DEGs in sporadic versus controls. Enriched Cellular Components for upregulated genes with layout as Supplementary Table 6.

enrichment_GO_MF_sPD				
Pathway	Total	Hits	Enrichment	FDR
Extracellular matrix structural constituent	186	21	5.188995838	7.81E-07
Extracellular matrix structural constituent conferring tensile strength	45	8	8.170609319	0.002426
Structural molecule activity	784	36	2.110393351	0.005572
Lipid binding	811	37	2.096804025	0.005572
Calcium ion binding	770	35	2.089076246	0.007124
Phosphatidylinositol-5-phosphate binding	20	5	11.48991935	0.009065
Phosphotransferase activity, alcohol group as acceptor	742	33	2.04402878	0.012828
Kinase activity	848	35	1.896920648	0.029172
Cell adhesion molecule binding	577	26	2.070973333	0.044748
Integrin binding	152	11	3.326029287	0.04622
Lysophosphatidic acid binding	8	3	17.23487903	0.04622

Supplementary Table 10. Gene Ontology Molecular Function enrichment analysis of DEGs in sporadic versus controls. Enriched Cellular Components for upregulated genes with layout as Supplementary Table 6.

Code	Mutation	Gender	age
JS48753	GBA1 E326K	M	59
MB240649	GBA1 E326K	M	63
CK290347	GBA1 E326K (HomoZ)	M	65
Control1		M	71
Control2		M	43
Control3		F	66
sPD 1		M	51
sPD 2		M	55
sPD 3		M	46
sPD 4		M	65

Supplementary Table 11. A description of PD patients and controls that participated in the study.

Enriched_CC_sPD				
Pathway	Enrichment FDR	nGenes	Pathway Genes	Fold Enrichment
Neuron projection	5.29473030811923e-08	71	1444	2.259790233
External encapsulating structure	2.11690474787198e-07	39	601	2.982408352
Extracellular matrix	2.11690474787198e-07	39	600	2.987379032
Synapse	2.11690474787198e-07	68	1443	2.165806005
Collagen-containing extracellular matrix	4.86618297337138e-07	32	446	3.297555331
Receptor complex	1.95233736374745e-05	28	422	3.04945727
Plasma membrane region	2.52289546973582e-05	58	1323	2.014861142
Integral component of plasma membrane	3.21771471059385e-05	74	1881	1.808089383
Intrinsic component of plasma membrane	3.77688878259881e-05	76	1965	1.77757531
Synaptic membrane	4.94196055440749e-05	26	401	2.979929209
Postsynapse	5.49151847425893e-05	36	682	2.426024028
Somatodendritic compartment	9.17552470013141e-05	43	913	2.164585026
Postsynaptic membrane	0.000111842	21	297	3.249674161
Plasma membrane signaling receptor complex	0.000236805	16	194	3.790488859
Postsynaptic specialization membrane	0.000514373	12	121	4.557984537
Fibrillar collagen trimer	0.000544	5	16	14.36239919
AMPA glutamate receptor complex	0.000544	6	26	10.6060794
Banded collagen fibril	0.000544	5	16	14.36239919
Synaptic vesicle	0.000563779	16	213	3.452370135
Neuronal cell body	0.000563779	28	535	2.405366295
Axon	0.000641308	33	691	2.194890528
Postsynaptic specialization	0.000767229	22	376	2.689130062

Enriched_CC_GBA1				
Pathway	Enrichment FDR	nGenes	Pathway Genes	Fold Enrichment
External encapsulating structure	0.000778125	36	601	2.334161014
Extracellular matrix	0.000778125	36	600	2.338051282
Endoplasmic reticulum lumen	0.006597521	22	328	2.613675214
Basal plasma membrane	0.006597521	19	265	2.793897758
Internode region of axon	0.006597521	3	4	29.22564103
Receptor complex	0.006597521	26	422	2.400842549
Collagen trimer	0.006988459	11	105	4.082311762
Podosome	0.009318753	6	33	7.085003885
Basal part of cell	0.009318753	19	283	2.616194014
Plasma membrane signaling receptor complex	0.009318753	15	194	3.012952683
Glutamatergic synapse	0.009318753	22	358	2.394652151
Collagen-containing extracellular matrix	0.012199488	25	446	2.184278104
Postsynapse	0.018865127	33	682	1.885525227
Basolateral plasma membrane	0.020220106	16	240	2.597834758
Synapse	0.020220106	58	1443	1.56626212
Basement membrane	0.029145175	9	97	3.61554322
Intrinsic component of plasma membrane	0.029145175	73	1965	1.447648377
Neuron projection	0.029145175	57	1444	1.538191633
Integrin complex	0.037748097	5	32	6.088675214
Basement membrane collagen trimer	0.037748097	3	9	12.98917379
Plasma membrane region	0.043672287	52	1323	1.531603259
Integral component of plasma membrane	0.045396107	69	1881	1.429430608

Supplementary Table 12. The top 22 dysregulated pathways in DA neurons derived from PD patients with E326K-*GBA1* mutations compared to control DA neurons and from sPD patients compared to control neurons. The highlighted pathways are shared between these 2 PD groups.

DEGs_GBA1	
Gene ID	**Fold change**
FZD10-AS1	-6.219631314
TMEM132D	-4.859769902
FZD10	-4.783255274
A2M	-3.148072168
LINC02228	-3.015944299
ZFP42	-2.840491192
LINC00906	-2.78224874
PTH2R	-2.66523942
STYXL2	-2.651384589
TLX1	-2.607025957
IGF2-AS	-2.595644756
IGF2	-2.592744497
XAF1	-2.55996299
PTPRC	-2.540601438
A2M-AS1	-2.535904127
FGF10-AS1	-2.509438847
ASNSP1	-2.498889595
PRAL	-2.483678851
NECTIN3-AS1	-2.478304297
HRH1	-2.462200449
DGAT2L6	-2.368540165
LINC02211	-2.323216726
HLA-F	-2.275000152
FOXD2	-2.244346811
NT5E	-2.235040009
KLHL41	-2.204416616
FGF10	-2.149258651
SGCG	-2.14685133
RPL23P8	-2.13322205
IL6	-2.099670388
PTPRT-DT	-2.086833539
VCAM1	-2.016045756
GDA	-2.013158691
THORLNC	-1.970951235
CTHRC1	-1.965397986
PTPRT	-1.953346799
STRIT1	-1.951272205
DAPK2	-1.946777879
UNC5B	-1.945272034
ADAM32	-1.940112185
SEMA3D	-1.930448139
INSRR	-1.912759731
C4A	-1.907964261
PTPRE	-1.906169695
F2RL1	-1.889008801
B3GNT7	-1.866717125

LRRK1	-1.866392781
RPL10P6	-1.863297619
COX20P1	-1.859845782
SFRP4	-1.84819034
CDCP1	-1.845022405
TMEM158	-1.842429288
TNFRSF9	-1.824689378
MMP1	-1.812595383
COL15A1	-1.808055739
RBM46	-1.807043227
PTGDS	-1.785274479
WNT2	-1.783946321
IL20RA	-1.772177062
DES	-1.770689366
TBX15	-1.762615346
SCRG1	-1.756716631
LAMC3	-1.752563202
RNASE1	-1.752115388
LGALS3	-1.744625635
AGAP7P	-1.739069066
AGT	-1.71487689
HPR	-1.711794996
RUNX1	-1.710864359
SOCS3	-1.706667366
HS3ST3A1	-1.705258479
IFI16	-1.700997257
ARHGEF35	-1.694218364
MMP13	-1.692793713
FBXO32	-1.692586413
HGF	-1.690364272
A2MP1	-1.690357751
TBX18	-1.68746758
TNN	-1.681277771
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GIPR	1.002251248
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LDB2	1.003818557
AOX1	1.008079357
SLC8A1-AS1	1.016369182
AC003986.1	1.019771565
CNTLN	1.02309808
RGS9	1.024101387
F13A1	1.024238048
PRSS54	1.026681885
CAMK1D	1.026740195
AL139398.1	1.029705109
GHDC	1.03428059
UFSP2	1.040595376
CDO1	1.054440753
SERPINF2	1.056029518
CERNA1	1.062032646
RPS26	1.070512581
ZNF518A	1.078988152
AP000688.1	1.079654721
BOC	1.079665686
AC016597.1	1.082302474
LMAN1	1.094270342
CBLN1	1.102847227

CCDC13-AS1	1.105910734
ENPP2	1.109114827
AGPS	1.113765639
LRRK2	1.117634522
SESTD1	1.124239781
AL033397.2	1.12991896
SGSM1	1.133138102
AC069444.1	1.141724322
CFTR	1.145089003
AC078795.3	1.145406973
AL078601.2	1.145992418
PITPNM3	1.155592447
AC099795.1	1.156753566
NEK7	1.169628458
ENPP1	1.171113552
MAP7	1.17405496
AC098851.1	1.181519658
AC012485.1	1.181946771
AC104964.4	1.182197684
TPT1-AS1	1.191267991
TAGLN2	1.196683888
PRRG3	1.201319166
ARHGEF26	1.201685539
AC073869.1	1.205167094
CLCN5	1.205872017
IMPA2	1.206951495
SYNE1-AS1	1.209514327
UBXN10	1.212162358
HCG11	1.216720169
GPR37	1.223946314
AC078883.1	1.22761555
PISD	1.228235695
CCDC114	1.230285914
CDH23	1.230609653
LYST	1.233354945
AC079385.2	1.236565767
AL133367.1	1.239252143
RAB38	1.241961403
AC126755.1	1.243512859
SERPINI1	1.245927232
ATPAF2	1.246643962
IL1RAP	1.251000634
DMD	1.254644293
AC067930.5	1.256939402
MYO3A	1.272284791
PIAS1	1.280701164
DLC1	1.282209653
NF1	1.285944703

FAM196A	1.294109232
PPP1R1B	1.297429402
AL050331.2	1.307909251
SRPX2	1.310721104
NEK9	1.311458998
AL137804.1	1.313663757
SNRPCP3	1.31391476
FHIT	1.327661589
TUSC1	1.333463067
STARD5	1.336522925
SLC29A1	1.339732287
AC007255.1	1.340435974
GALK2	1.344535009
CEP126	1.349177878
SPATA17-AS1	1.349676489
AC010969.1	1.357255739
HMGN5	1.357257863
AC093535.1	1.35795144
KCNH5	1.35841936
GAS8-AS1	1.362144543
JPH1	1.362733322
MS4A8	1.373829359
KLF5	1.376901457
SLC37A1	1.380998939
LINC00602	1.390274936
ROR2	1.390649001
VILL	1.390846164
AC233296.1	1.391230104
CD200	1.412054634
MPPED2	1.416981704
HCG4P5	1.420913868
KCNH2	1.427642807
TAF1C	1.430864308
SPOCK2	1.438576888
KCNH7	1.440124928
PHEX	1.445302196
OTX2	1.448993838
RASA4B	1.454917778
AC104964.1	1.458453811
LRP1B	1.46266518
MYO1D	1.466027247
TMC5	1.467466516
AC097515.1	1.471739118
ADAMTS2	1.472682441
NR4A2	1.472916944
AL354733.2	1.474988082
ITGA11	1.486227703
CFAP44-AS1	1.486759925

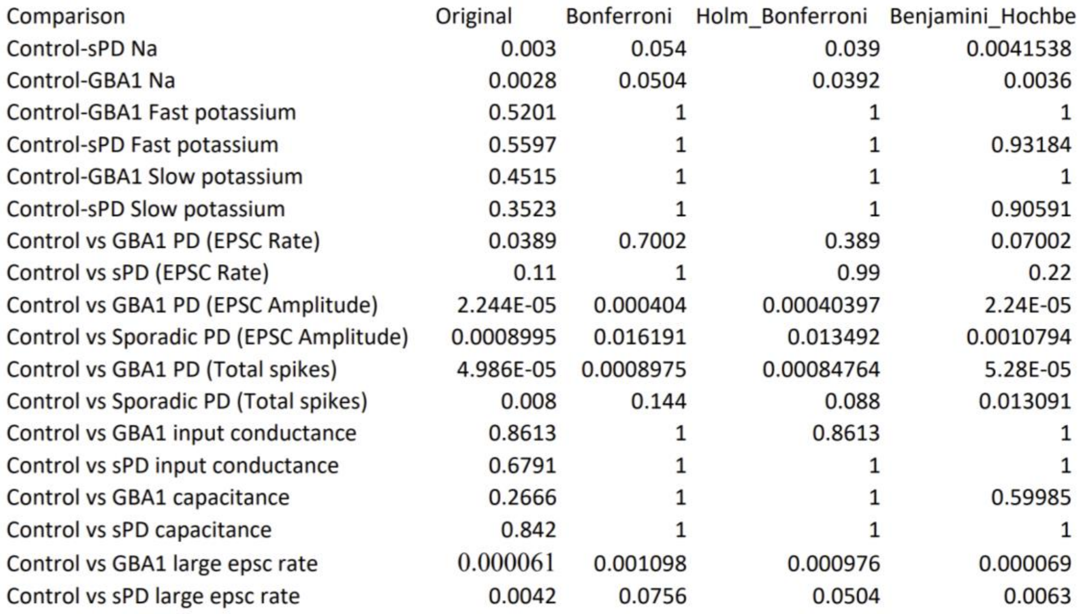
HNMT	1.491436871
MMRN1	1.491732151
PPP1R3C	1.495001375
AC002398.2	1.497403645
TC2N	1.497788917
ADAMTS12	1.499765402
AC027097.2	1.503260122
SELENBP1	1.507321747
IQCA1	1.511702041
AC092134.1	1.513957005
AC002064.2	1.518778872
LINC00954	1.519534811
TBX18	1.526559965
AQP3	1.526900324
AC008011.2	1.539609663
CHN2	1.545029116
LURAP1L-AS1	1.547407329
AC092641.1	1.555924014
AC079385.3	1.56132382
GPR156	1.568226846
AL354733.1	1.573696039
AC078883.3	1.574769398
LGI3	1.57785541
ATP8B4	1.588996452
RSPO2	1.58950254
C3orf67	1.593567654
AC078883.2	1.596349699
MARCHF7	1.607444219
PTCHD1	1.618098879
CFC1	1.623884056
AC078882.1	1.634189337
KLHL41	1.642882832
TPPP3	1.674907251
LRMP	1.676757499
AC027097.1	1.678203913
AC130456.3	1.682145314
NPAS2	1.69039847
LPIN3	1.705654797
DISP1	1.715665786
LINC02381	1.735066527
ALK	1.739713786
IQCA1-AS1	1.742394106
CR392000.1	1.74977857
ARHGEF11	1.751183968
HTR2C	1.757666734
MMP11	1.760325686
TTC14	1.764491913
AP003032.2	1.779615827

KCTD12	1.787129069
RBFADN	1.796527465
FGL2	1.813646845
EDARADD	1.822491378
INHA	1.824553995
CDCA7L	1.824877737
CTNNA3	1.829503353
AP000320.1	1.842662689
COL16A1	1.849028175
AC092142.1	1.853481738
AC008114.1	1.863672584
FER1L4	1.87711173
LINC01123	1.880077703
AL590560.2	1.887538935
ZNF385B	1.898970048
SBSPON	1.914715543
CDH7	1.923237802
AC008073.2	1.925210985
NUDT7	1.929231415
ADTRP	1.936343765
ACCS	1.943975274
PABPC4L	1.944952776
HHATL-AS1	1.953087025
DEPTOR	1.955550048
SIX3	1.96131923
ZXDC	1.967047594
AP000560.1	1.974976266
MYO7A	1.997942984
DCAF12L1	2.005836151
SERPINA12	2.014251562
RPL21P43	2.015186346
SLC17A9	2.015909681
AL049697.3	2.02148983
ELN	2.035668623
AC010255.2	2.041999071
DGKG	2.069764721
SCGB1B2P	2.073074629
UNC13C	2.089156192
HIST1H2BC	2.102336041
LINC02052	2.106057637
AGTR1	2.109983123
MUC5B	2.119744076
BCAS1	2.119984266
AC005682.1	2.137416298
KAAG1	2.153158255
ABCB1	2.158917745
RIMS1	2.160244779
FYB2	2.162022742

LINC00467	2.17869866
IL1A	2.182675625
AC005209.1	2.187028314
PDZD3	2.196396857
AL512625.1	2.201508388
MUC15	2.220391179
HTR1E	2.239222995
ALPK3	2.246628959
AC016757.1	2.259080379
HEY2	2.260432402
C1orf158	2.26272048
PTCHD1-AS	2.264691523
LTBR	2.272686489
CALCRL	2.274508779
AL353572.1	2.28814172
GABRG1	2.319465926
AC097468.1	2.332943279
CYP11A1	2.384275767
AC025038.1	2.385697248
NNMT	2.392031337
AC130456.4	2.413236239
TTR	2.415955986
SMOC1	2.431529766
SLC38A4	2.432177856
SLAMF9	2.434916421
OTOF	2.438065045
COL8A2	2.440391242
CILP	2.4429999
PI16	2.453284328
TRIM58	2.466120317
NKX3-1	2.477162127
AL021391.1	2.497245462
AL355812.1	2.514887682
AP005120.1	2.517407272
GZMA	2.5435967
CNMD	2.569256265
EGFL6	2.601010737
SLC22A8	2.653853247
AC104809.1	2.682449831
PRKAG3	2.743168102
CCRL1P1	2.784860628
AC126323.6	2.795811377
AL392003.2	2.827602631
LINC02020	2.827769923
AC005871.2	2.853124899
LINC02389	2.854986809
SSTR5-AS1	2.899796755
CLDN5	2.901522745

AC079360.1	2.908736275
HSPA8P7	2.912099073
SLC28A3	2.92667504
EPS15P1	2.935332514
RAB37	2.966696327
SPDEF	2.985989169
LINC02056	3.012624473
LINC01361	3.074152935
RF00019	3.081729229
LINC01257	3.088816575
AC061979.1	3.096446458
AL356134.1	3.10434782
ACAN	3.105117014
NPFFR2	3.142334439
LINC00654	3.167403489
AC138819.1	3.200121296
AL512625.3	3.202513781
AC098476.1	3.217874585
FER1L6	3.33832231
TTLL10-AS1	3.348024901
AC005281.1	3.443988178
PZP	3.460660282
CRACR2A	3.465026778
AC005831.1	3.671035995
CCDC68	3.723613334
AL161618.1	3.749869823
LINC01537	3.891135409
DGAT2L6	3.9650696
LINC02208	3.975688856
MUC5AC	4.086899719
AC091062.1	4.458167326
AP001999.1	4.715998118
CYP26C1	4.852844974
AC097493.2	4.895581365
PRPH2	5.390830869
SMIM31	5.725410845
MYO5BP2	6.307212632

Supplementary Table 13. DEGs between DA neurons derived from PD patients with E326K-*GBA1* mutations compared to control neurons and DEGs between DA neurons derived from sPD patients compared to control neurons.



Comparison	Original	Bonferroni	Holm_Bonferroni	Benjamini_Hochbe
Control-sPD Na	0.003	0.054	0.039	0.0041538
Control-GBA1 Na	0.0028	0.0504	0.0392	0.0036
Control-GBA1 Fast potassium	0.5201	1	1	1
Control-sPD Fast potassium	0.5597	1	1	0.93184
Control-GBA1 Slow potassium	0.4515	1	1	1
Control-sPD Slow potassium	0.3523	1	1	0.90591
Control vs GBA1 PD (EPSC Rate)	0.0389	0.7002	0.389	0.07002
Control vs sPD (EPSC Rate)	0.11	1	0.99	0.22
Control vs GBA1 PD (EPSC Amplitude)	2.244E-05	0.000404	0.00040397	2.24E-05
Control vs Sporadic PD (EPSC Amplitude)	0.0008995	0.016191	0.013492	0.0010794
Control vs GBA1 PD (Total spikes)	4.986E-05	0.0008975	0.00084764	5.28E-05
Control vs Sporadic PD (Total spikes)	0.008	0.144	0.088	0.013091
Control vs GBA1 input conductance	0.8613	1	0.8613	1
Control vs sPD input conductance	0.6791	1	1	1
Control vs GBA1 capacitance	0.2666	1	1	0.59985
Control vs sPD capacitance	0.842	1	1	1
Control vs GBA1 large epsc rate	0.000061	0.001098	0.000976	0.000069
Control vs sPD large epsc rate	0.0042	0.0756	0.0504	0.0063

Supplementary Table 14. Multiple hypothesis corrections for the electrophysiological data.