Table S1: Information of Parkinson's Disease associated genes selected from KEGG pathway database and literature resources

S.NO	GENE SYMBOL	ACCESSION NO.	GENE POSITION	CDS POSITION	CHROMOSOME NO. AND LOCATION OF GENES	FUNCTION OF GENES*
1.	CASP3	NM_032991	1-2522	97-930	chromosome: 4; Location: 4q34	This gene encodes a protein which is a member of the cysteine-aspartic acid protease (caspase) family. Sequential activation of caspases plays a central role in the execution-phase of cell apoptosis. Caspases exist as inactive proenzymes which undergo proteolytic processing at conserved aspartic residues to produce two subunits, large and small, that dimerize to form the active enzyme. This protein cleaves and activates caspases 6, 7 and 9, and the protein itself is processed by caspases 8, 9 and 10. It is the predominant caspase involved in the cleavage of amyloid-beta 4A precursor protein, which is associated with neuronal death in Alzheimer's disease. Alternative splicing of this gene results in two transcript variants that encode the same protein.
2.	CASP9	NM_032996	1-1584	96-896	chromosome: 1; Location: 1p36.3-p36.1	This gene encodes a member of the cysteine-aspartic acid protease (caspase) family. Sequential activation of caspases plays a central role in the execution-phase of cell apoptosis. Caspases exist as

						inactive proenzymes which undergo proteolytic processing at conserved aspartic residues to produce two subunits, large and small, that dimerize to form the active enzyme. This protein is processed by caspase APAF1; this step is thought to be one of the earliest in the caspase activation cascade. Alternative splicing results in two transcript variants which encode different isoforms.
3.	COX6B2	NM_144613	1-1679	184-450	chromosome: 19; Location: 19q13.42	Cytochrome c oxidase subunit VIb polypeptide 2 (testis)
4.	CYCS	NM_018947	1-5518	146-463	chromosome: 7; Location: 7p15.2	This gene encodes cytochrome c, a component of the electron transport chain in mitochondria. The heme group of cytochrome c accepts electrons from the b-c1 complex and transfers electrons to the cytochrome oxidase complex. Cytochrome c is also involved in initiation of apoptosis. Upon release of cytochrome c to the cytoplasm, the protein binds apoptotic protease activating factor which activates the apoptotic initiator procaspase 9. Many cytochrome c pseudogenes exist, scattered throughout the human genome.
5.	GPR37	NM_005302	1-3058	652-2493	chromosome: 7; Location: 7q31	GPR37 is an orphan G protein-coupled receptor expressed in mammalian brain, and its insoluble aggregates are found in the brain samples of juvenile Parkinson's

						disease patients
6.	HTRA2	NM_013247	1-2550	603-1979	chromosome: 2; Location: 2p12	This gene encodes a serine protease. The protein has been localized in the endoplasmic reticulum and interacts with an alternatively spliced form of mitogen-activated protein kinase 14. The protein has also been localized to the mitochondria with release to the cytosol following apoptotic stimulus. The protein is thought to induce apoptosis by binding the apoptosis inhibitory protein baculoviral IAP repeat-containing 4. Nuclear localization of this protein has also been observed. Alternate splicing of this gene results in two transcript variants encoding different isoforms. Additional transcript variants have been described, but their full-length sequences have not been determined.
7.	APAF1	NM_181861	1-7204	578-4324	chromosome: 12; Location: 12q23	This gene encodes a cytoplasmic protein that initiates apoptosis. This protein contains several copies of the WD-40 domain, a caspase recruitment domain (CARD), and an ATPase domain (NB-ARC). Upon binding cytochrome c and dATP, this protein forms an oligomeric apoptosome. The apoptosome binds and cleaves caspase 9 preproprotein, releasing its mature, activated form. Activated caspase 9 stimulates the subsequent caspase cascade that commits the cell to

						apoptosis. Alternative splicing results in several transcript variants encoding different isoforms.
8.	LOC100128525 (UQCRFSL1)	XM_001716642	1-1070	1-789	chromosome: 22; Location: 22q13.1	
9.	LOC100133737 (similar to hCG1809973)	XM_001722336	1-435	1-435	chromosome: 9	
10.	LRRK2	NM_198578	1-9234	121-7704	chromosome: 12; Location: 12q12	This gene is a member of the leucine-rich repeat kinase family and encodes a protein with an ankryin repeat region, a leucine-rich repeat (LRR) domain, a kinase domain, a DFG-like motif, a RAS domain, a GTPase domain, a MLK-like domain, and a WD40 domain. The protein is present largely in the cytoplasm but also associates with the mitochondrial outer membrane. Mutations in this gene have been associated with Parkinson disease-8.
11.	NDUFS7	NM_024407	1-787	21-662	chromosome: 19; Location: 19p13.3	This gene encodes a protein that is a subunit of one of the complexes that forms the mitochondrial respiratory chain. This protein is one of over 40 subunits found in complex I, the nicotinamide adenine dinucleotide (NADH):ubiquinone oxidoreductase. This complex functions in

						the transfer of electrons from NADH to the respiratory chain, and ubiquinone is believed to be the immediate electron acceptor for the enzyme. Mutations in this gene cause Leigh syndrome due to mitochondrial complex I deficiency, a severe neurological disorder that results in bilaterally symmetrical necrotic lesions in subcortical brain regions.
12.	PARK2	NM_013988	1-2513	102-1052	chromosome: 6; Location: 6q25.2-q27	The precise function of this gene is unknown; however, the encoded protein is a component of a multiprotein E3 ubiquitin ligase complex that mediates the targeting of substrate proteins for proteasomal degradation. Mutations in this gene are known to cause Parkinson disease and autosomal recessive juvenile Parkinson disease. Alternative splicing of this gene produces multiple transcript variants encoding distinct isoforms. Additional splice variants of this gene have been described but currently lack transcript support.
13.	PARK7	NM_007262	1-906	85-654	chromosome: 1; Location: 1p36.23	The product of this gene belongs to the peptidase C56 family of proteins. It acts as a positive regulator of androgen receptor-dependent transcription. It may also function as a redox-sensitive chaperone, as a sensor for oxidative stress, and it apparently protects neurons against oxidative stress and cell death. Defects in

						this gene are the cause of autosomal recessive early-onset Parkinson disease 7. Two transcript variants encoding the same protein have been identified for this gene.
14.	PINK1	NM_032409	1-5828	1021-4749	chromosome: 1; Location: 1p36	This gene encodes a serine/threonine protein kinase that localizes to mitochondria. It is thought to protect cells from stress-induced mitochondrial dysfunction. Mutations in this gene cause one form of autosomal recessive early-onset Parkinson disease.
15.	SDHA	NM_004168	1-2405	116-2110	chromosome: 5; Location: 5p15	This gene encodes a major catalytic subunit of succinate-ubiquinone oxidoreductase, a complex of the mitochondrial respiratory chain. The complex is composed of four nuclear-encoded subunits and is localized in the mitochondrial inner membrane. Mutations in this gene have been associated with a form of mitochondrial respiratory chain deficiency known as Leigh Syndrome. A pseudogene has been identified on chromosome 3q29.
16.	SEPT5	NM_002688	1-3525	126-1235	chromosome: 22; Location: 22q11.21	This gene is a member of the septin gene family of nucleotide binding proteins, originally described in yeast as cell division cycle regulatory proteins. Septins are highly conserved in yeast, Drosophila, and mouse and appear to regulate cytoskeletal organization. Disruption of septin function disturbs cytokinesis and

						results in large multinucleate or polyploid cells. This gene is mapped to 22q11, the region frequently deleted in DiGeorge and velocardiofacial syndromes. A translocation involving the MLL gene and this gene has also been reported in patients with acute myeloid leukemia. Two transcripts of this gene, a major one of 2.2 kb and a minor one of 3.5 kb, have been observed. The 2.2 kb form results from the utilization of a non-consensus polyA signal (AACAAT). In the absence of polyadenylation from this imperfect site, the consensus polyA signal of the downstream neighboring gene (GP1BB; platelet glycoprotein Ib) is used, resulting in the 3.5 kb transcript. An alternatively spliced transcript variant with a different 5' end has also been identified, but its full-length nature has not been completely determined.
17.	SLC6A3	NM_001044	1-3925	122-1984	chromosome: 5; Location: 5p15.3	The dopamine transporter (DAT1) mediates the active reuptake of dopamine from the synapse and is a principal regulator of dopaminergic neurotransmission. The DAT1 gene has been implicated in human disorders such as parkinsonism, Tourette syndrome, and substance abuse
18.	SLC18A1	NM_003053	1-2749	268-1845	chromosome: 8;	The vesicular monoamine transporter acts to accumulate cytosolic monoamines into

					Location: 8p21.3	vesicles, using the proton gradient maintained across the vesicular membrane. Its proper function is essential to the correct activity of the monoaminergic systems that have been implicated in several human neuropsychiatric disorders. The transporter is a site of action of important drugs, including reserpine and tetrabenazine.
19.	SLC25A4	NM_001151	1-1340	130-1026	chromosome: 4; Location: 4q35	Solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 4
20.	SNCA	NM_000345	1-1543	47-469	chromosome: 4; Location: 4q21	Alpha-synuclein is a member of the synuclein family, which also includes beta- and gamma-synuclein. Synucleins are abundantly expressed in the brain and alpha- and beta-synuclein inhibit phospholipase D2 selectively. SNCA may serve to integrate presynaptic signaling and membrane trafficking. Defects in SNCA have been implicated in the pathogenesis of Parkinson disease. SNCA peptides are a major component of amyloid plaques in the brains of patients with Alzheimer's disease. Two alternatively spliced transcripts of SNCA have been identified. Additional splicing may be present but the full-length nature of these variants has not been determined.

21.	SNCAIP	NM_005460	1-3569	207-2966	chromosome: 5; Location: 5q23.1-q23.3	This gene encodes a protein containing several protein-protein interaction domains, including ankyrin-like repeats, a coiled-coil domain, and an ATP/GTP-binding motif. The encoded protein interacts with alpha-synuclein in neuronal tissue and may play a role in the formation of cytoplasmic inclusions and neurodegeneration. A mutation in this gene has been associated with Parkinson's disease. Alternatively spliced transcript variants encoding different isoforms of this gene have been described, but their full-length nature has yet to be determined.
22.	TH	NM_199292	1-1910	20-1606	chromosome: 11; Location: 11p15.5	The protein encoded by this gene is involved in the conversion of tyrosine to dopamine. It is the rate-limiting enzyme in the synthesis of catecholamines, hence plays a key role in the physiology of adrenergic neurons. Mutations in this gene have been associated with autosomal recessive Segawa syndrome. Alternatively spliced transcript variants encoding different isoforms have been noted for this gene.
23.	UBE1	NM_153280	1-3483	91-3267	chromosome: X; Location: Xp11.23	The protein encoded by this gene catalyzes the first step in ubiquitin conjugation to mark cellular proteins for degradation. This gene complements an X-linked mouse temperature-sensitive

						defect in DNA synthesis, and thus may function in DNA repair. It is part of a gene cluster on chromosome Xp11.23. Alternatively spliced transcript variants that encode the same protein have been described.
24.	UBE2J2	NM_194457	1-2136	215-838	chromosome: 1; Location: 1p36.33	The modification of proteins with ubiquitin is an important cellular mechanism for targeting abnormal or short-lived proteins for degradation. Ubiquitination involves at least three classes of enzymes: ubiquitin-activating enzymes, or E1s, ubiquitin-conjugating enzymes, or E2s, and ubiquitin-protein ligases, or E3s. This gene encodes a member of the E2 ubiquitin-conjugating enzyme family. This enzyme is located in the membrane of the endoplasmic reticulum. Multiple alternatively spliced transcript variants have been found for this gene, but the full-length nature of some variants has not been defined.
25.	UBE2L3	NM_198157	1-3016	215-838	chromosome: 22; Location: 22q11.21	The modification of proteins with ubiquitin is an important cellular mechanism for targeting abnormal or short-lived proteins for degradation. Ubiquitination involves at least three classes of enzymes: ubiquitin-activating enzymes (E1s), ubiquitin-conjugating enzymes (E2s) and ubiquitin-protein ligases (E3s). This gene encodes a

						member of the E2 ubiquitin-conjugating enzyme family. This enzyme is demonstrated to participate in the ubiquitination of p53, c-Fos, and the NF-kB precursor p105 in vitro. Two alternatively spliced transcript variants encoding distinct isoforms have been found for this gene.
26.	ubiquitinB	NM_018955	1-971	139-828	chromosome: 17; Location: 17p12-p11.2	This gene encodes ubiquitin, one of the most conserved proteins known. Ubiquitin is required for ATP-dependent, nonlysosomal intracellular protein degradation of abnormal proteins and normal proteins with a rapid turnover. Ubiquitin is covalently bound to proteins to be degraded, and presumably labels these proteins for degradation. Ubiquitin also binds to histone H2A in actively transcribed regions but does not cause histone H2A degradation, suggesting that ubiquitin is also involved in regulation of gene expression. This gene consists of three direct repeats of the ubiquitin coding sequence with no spacer sequence. Consequently, the protein is expressed as a polyubiquitin precursor with a final amino acid after the last repeat. Aberrant form of this protein has been noticed in patients with Alzheimer's and Down syndrome.
27.	UCHL1	NM_004181	1-1110	66-737	chromosome: 4;	UCHL1 is a member of a gene family

					Location: 4p14	whose products hydrolyze small C-terminal adducts of ubiquitin to generate the ubiquitin monomer. Expression of UCHL1 is highly specific to neurons and to cells of the diffuse neuroendocrine system and their tumors. It is present in all neurons (Doran et al., 1983 [PubMed 6343558]).[supplied by OMIM]
28.	GBA	NM_001005741	1-2432	261-1871	chromosome: 1; Location: 1q21	The GBA gene provides instructions for making an enzyme called beta-glucocerebrosidase. This enzyme is active in lysosomes, which are structures inside cells that act as recycling centers. Lysosomes use digestive enzymes to break down toxic substances, digest bacteria that invade the cell, and recycle worn-out cell components. Based on these functions, enzymes in the lysosome are sometimes called housekeeping enzymes. Beta-glucocerebrosidase is a housekeeping enzyme that helps break down a large molecule called glucocerebroside into a sugar (glucose) and a simpler fat molecule (ceramide).
29.	NR4A2	NM_006186	1-3447	336-2132	chromosome: 2; Location: 2q22-q23	NR4A2 mRNA levels were significantly decreased in transfected cell lines with the mutation compared with those without the mutation, as well as in the lymphocytes of the affected individuals. Expression levels of the dopamine biosynthesis enzyme tyrosine hydroxylase were also markedly

						decreased in the transfected cells with the mutations compared to the wild type. These data suggest that dopaminergic dysfunction can result from mutations in NR4A2. Thus far, the role of orphan nuclear receptor NR4A2 in Parkinson disease susceptibility appears to be limited

***Source: NCBI**

Table S2: Distribution of target sites in 5` UTR, CDS and 3` UTR as predicted using miRanda

S. No.	Genes	5'	CDS	3'
1	CASP3	10	9	62
2	CASP9	39	88	43
3	COX6B2	33	38	154
4	CYCS	8	6	87
5	GPR37	66	183	0
6	HTRA2	98	142	13
7	APAF1	46	14	26
8	LOC100128525	0	75	0
9	LOC100133737	0	16	0
10	LRRK2	23	75	2
11	NDUFS7	4	141	16
12	PARK2	30	88	37
13	PARK7	16	29	2

14	PINK1	272	118	0
15	SDHA	32	162	15
16	SEPT5	22	95	367
17	SLC6A3	10	178	184
18	SLC18A1	24	135	22
19	SLC25A4	62	93	0
20	SNCA	1	24	10
21	SNCAIP	22	121	1
22	TH	3	287	58
23	UBE1	7	294	9
24	UBE2J2	46	50	230
25	UBE2L3	9	16	164
26	UbiquitinB	19	61	3
27	UCHL1	5	81	11
28	GBA	49	144	58
29	NR4A2	59	135	14
	Total	1015	2898	1588

Table S3: Distribution of hotspots prone to action of multiple miRNAs in 5` UTR, CDS and 3` UTR of considered genes.

S. No	Gene symbol	Hotspots at 5′ region	Hotspots at CDS region	Hotspots at 3′ region	Total
1.	CASP3	1	0	3	4

2.	CASP9	3	6	1	10
3.	COX6B2	1	2	11	14
4.	CYCS	-	-	-	-
5.	GPR37	2	12	-	14
6.	HTRA2	9	8	-	17
7.	APAF1	1	-	-	1
8.	LOC100128525 (UQCRFSL1)	6	-	-	6
9.	LOC100133737 (similar to hCG1809973)	-	-	-	-
10.	LRRK2	3	1	-	4
11.	NDUFS7	-	11	3	14
12.	PARK2	3	6	2	11

13.	PARK7	2	1	-	3
14.	PINK1	23	3	-	26
15.	SDHA	2	6	-	8
16.	SEPT5	1	5	17	23
17.	SLC6A3	1	3	4	8
18.	SLC18A1	0	5	1	6
19.	SLC25A4	6	4	-	10
20.	SNCA	-	2	-	2
21.	SNCAIP	-	4	2	6
22.	TH	-	18	2	20
23.	UBE1	1	11	1	13
24.	UBE2J2	4	1	19	24
25.	UBE2L3	-	-	6	6

26.	ubiquitinB	1	5	-	6
27.	UCHL1	-	6	2	8
28.	GBA	5	5	3	13
29.	NR4A2	6	5	-	11
	Total Clusters	**81**	**130**	**77**	**288**

Where – denotes no target site clusters were predicted

Table S4: miRNAs showing single hit and target Genes

S. No	Gene Symbol	miRNA showing single hit in the target gene
1	CASP3	hsa-miR-630
2	CASP9	hsa-miR-891a,hsa-miR-377*,hsa-miR-340*,hsa-miR-202
3	COX6B2	hsa-miR-320b,hsa-miR-299-3p,hsa-miR-217,hsa-miR-1284,hsa-miR-1201
4	CYCS	hsa-miR-518e,hsa-miR-380*,hsa-miR-329
5	GPR37	hsa-miR-424,hsa-miR-379,hsa-miR-26b*
6	HTRA2	hsa-miR-421,hsa-miR-1912
7	APAF1	hsa-miR-1304
8	LOC100128525	hsa-miR-371-5p

9	LOC100133737	hsa-miR-567,hsa-miR-516b
10	LRRK2	hsa-miR-588,hsa-miR-373*,hsa-miR-30d*,hsa-miR-302c,hsa-miR-105,hsa-let-7b*
11	NDUFS7	hsa-miR-342-5p
12	PARK2	hsa-miR-720,hsa-miR-600,hsa-miR-184
13	PARK7	hsa-miR-892a
14	PINK1	hsa-miR-654-3p,hsa-miR-628-3p,hsa-miR-506,hsa-miR-487a,hsa-miR-30a*,hsa-miR-17
15	SDHA	hsa-miR-584,hsa-miR-520d-3p,hsa-miR-518d-3p,hsa-miR-206,hsa-miR-1285,hsa-miR-1274a
16	SEPT5	hsa-miR-885-5p,hsa-miR-595,hsa-miR-372,hsa-miR-204,hsa-miR-16-1*,hsa-miR-154,hsa-miR-138-2*,hsa-miR-136
17	SLC6A3	hsa-miR-922,hsa-miR-604,hsa-miR-513c,hsa-miR-30b,hsa-miR-302c*,hsa-miR-1826,hsa-miR-107
18	SLC18A1	hsa-miR-24-2*,hsa-miR-24-1*,hsa-miR-142-3p,hsa-miR-1305
19	SNCA	hsa-miR-181d,hsa-miR-1185
20	TH	hsa-miR-220c,hsa-miR-1263
21	UBE1	hsa-miR-875-3p,hsa-miR-610,hsa-miR-589*,hsa-miR-488*,hsa-miR-383,hsa-miR-181b,hsa-miR-132,hsa-miR-1205,hsa-let-7c*
22	UBE2J2	hsa-miR-487b,hsa-miR-323-3p,hsa-miR-17*
23	UBE2L3	hsa-miR-647,hsa-miR-502-5p,hsa-miR-223,hsa-miR-183*
24	UCHL1	hsa-miR-525-5p,hsa-miR-376b,hsa-miR-376a
25	GBA	hsa-miR-585,hsa-miR-519e,hsa-miR-199b-5p,hsa-miR-191,hsa-miR-140-5p,hsa-miR-1276,hsa-miR-1272,hsa-miR-1258
26	NR4A2	hsa-miR-938,hsa-miR-645,hsa-miR-181c,hsa-miR-135b,hsa-miR-135a

Table S5: Sequence composition features of top 10 miRNAs

miRNA	%GC content	%AT content	%G content	%C content	%A content	%T content
hsa-miR-638	80	20	56	24	8	12
hsa-miR-1226*	69	31	53.84	15.39	15.38	15.39
hsa-miR-612	64	36	36	28	8	28
hsa-miR-1469	91	9	50	40.9	0	9.1
hsa-miR-939	71	29	58.33	12.5	8.33	20.84
hsa-miR-661	71	29	37.5	33.33	0	29.17
miR-1538	74	26	34.78	39.14	0	26.08
hsa-miR-663	91	9	54.54	36.36	9.1	0
hsa-miR-663b	82	18	50	31.82	4.54	13.64
hsa-miR-608	64	36	48	16	12	24

Table S6: Comparative account of target sites predicted in 3` UTR using miRanda and TargetScan

S.NO	Genes	miRanda	Target Scan
1	CASP3	62	17
2	CASP9	43	85
3	COX6B2	154	115
4	CYCS	87	202
5	GPR37	0	3
6	HTRA2	13	11
7	APAF1	26	248
8	LOC100128525	0	0
9	LOC100133737	0	0
10	LRRK2	2	10

11	NDUFS7	16	4
12	PARK2	37	257
13	PARK7	2	23
14	PINK1	0	69
15	SDHA	15	39
16	SEPT5	367	73
17	SLC6A3	184	219
18	SLC18A1	22	69
19	SLC25A4	0	27
20	SNCA	10	13
21	SNCAIP	1	2
22	TH	58	41
23	UBE1	9	14
24	UBE2J2	230	14
25	UBE2L3	164	190
26	ubiquitinB	3	12
27	UCHL1	11	2
28	GBA	58	56
29	NR4A2	14	159
	Total	1588	1974

Table S7: A comparison between miRanda and Target Scan

S.No.	Gene	miRNA target sites that were predicted by both algorithms	miRNA target sites similar in location
1	CASP9	7	1
2	COX6B2	20	7
3	CYCS	18	8
4	APAF1	4	1
5	PARK2	6	3
6	SE PT5	25	8
7	SLC6A3	26	8
8	TH	7	4
9	UBE2J2	3	0
10	UBE2L3	16	0
11	GBA	9	7
12	NR4A2	1	0
	TOTAL	142	47