Supplementary data

Multiple hit hypotheses for dopamine neuron loss in Parkinson's disease

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Table S1. Genes determined and/or suggested to cause or be a susceptibility factor underlying inherited 'primary parkinsonism'[a,b]

PARK designation / OMIM accession	Protein	Mode of inheritance	Initial gene identification	Currently known prevalence	Suggested normal function
PARK1 168601	α-Synuclein	Autosomal dominant	[1]	13 families from Italy, Germany, and Greece; three pathogenic mutations to date	Inhibits synaptic vesicle priming [2]
PARK2 600116	Parkin	Autosomal recessive in early onset forms, susceptibility factor in adult	[3]	Very common in juvenile PD	Ubiquitin E3 ligase [4]; it might be involved in Lewy body formation, as these are absent in recessive juvenile form
PARK3 602404	2p13 Strongly suspected to be sepiapterin	Autosomal dominant	Sepiapterin mutation causes a DOPA-responsive dystonia [5]	Six families from Denmark and Germany	Sepiapterin converts 6-pyrovyl-tetrahydropterin into tetrahydrobiopterin
PARK4 163890	α-Synuclein duplications	Autosomal dominant	[6]	Seven families in	Inhibits synaptic vesicle priming

				Europe, USA and Japan	and fusion [2]
PARK5 191342	Ubiquitin c-terminal hydrolase L1 (UCHl1)	Possibly autosomal dominant	[7]	Single sibling pair in Germany	Hydrolyzes polyubiquitin
PARK6 605909	PTEN-induced putative kinase 1 (PINK1)	Autosomal recessive early onset	[8]	Three related families in Sicily	Mitochondrial serine/threonine kinase [9]
PARK7 606324	DJ-1	Autosomal recessive	[10]	Families in Holland, Italy and Uruguay	Sumoylation pathway; endogenous antioxidant [11]
PARK8 609007 607060	LRRK2: dardarin protein	Autosomal dominant	[12,13]	Very common in north African and mideastern populations	Kinase with GTPase activity [14,15]
PARK9 610513 606693	ATP13A2	Autosomal recessive	[16]	One Jordanian and one Chilean family	Lysosomal transporter and ATPase of unknown substrate [17]
PARK10 606852	Unknown: 1p32	Autosomal susceptibility factor; suggested to affect age of onset	Not identified	Based on large population studies in Iceland: unclear	Not known
PARK11 607688	Unknown: 2q36-q37	Autosomal dominant	Not identified	Identified in sib pair, but might be common in familial PD	Not known
PARK12 300557	Unknown: Xq21-q25	X-linked	Not identified	Unclear	Not known
PARK13 610297	Omi/HtrA2; serine protease-25 (PRSS25)	Autosomal dominant	[18]	Detected in four patients in Germany	Serine protease targeted to mitochondria
230800	β-Glucocerebrosidase	Autosomal susceptibility factor; recessive for Gaucher's	Associated with Gaucher disease type 1, the most common	Many families, particularly Askenazi families	Hydrolase (breakdown of glucosylceramide) within lysosomal

		disease	lysosomal storage disorder [19]		degradation
174763	Mitochondrial polymerase gamma (POLG)	Autosomal susceptibility factor	Often associated with progressive external ophthalmoplegia [20,21]	Eight families in northern Europe and the USA	Replication of mitochondrial DNA
603779	Synphilin-1	Autosomal dominant	[22]	Two patients from Germany with apparent sporadic disease	Interacting factor with α-syn [23] and is ubiquitinated by parkin [24]
601828	NR4A2; NURR1	Autosomal susceptibility factor	[25]	Unclear	Development of DA neurons
124030	Cytochrome P450, subfamily IID, piolypeptide 6 (CPD6)	Risk factor associated with pesticide exposure	[26]	Mutations might require pesticide exposure for toxic properties	First phase in the metabolism and elimination of numerous endogenous and exogenous molecules
157140	Tau: MAPT H1	Autosomal susceptibility factor	Associated with multiple diseases by multiple studies, associated with frontotemporal dementia with parkinsonism [27]	Unclear	Organization and assembly of microtubules
605558	Fibroblast growth factor 20 (FGF20)	Risk factor	Strong association in a large family study [28]	Unclear	Growth factor that might regulate oxidative stress in dopamine neurons [29]
556500	Mitochondrial mutations (?)	Mitochondrial inheritance	Unclear	Unclear	Unclear

[a]Please note that this table lists suggested genes whether or not the current evidence supporting a particular gene is convincing.

[b]A current list of genes designated as “PARK” genes is at Online Mendelian Inheritance in Man website (OMIM: `www.ncbi.nlm.nih.gov/omim/ -`) accession `168600.`

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