Whole Exome Sequencing
Gene package Neurodegeneration, version 2, 1-7-2017

Technical information
After DNA was enriched using Agilent Sureselect Clinical Research Exome (CRE) Capture, samples were run on the Illumina Hiseq platform. The aim is to obtain 50 million total reads per exome with a mapped fraction >0.98. The average coverage of the exome is ~50x. Data are demultiplexed by Illumina software bcl2fastq. Reads are mapped to the genome using BWA (reference: http://bio-bwa.sourceforge.net/). Variant detection is performed by Genome Analysis Toolkit (reference: http://www.broadinstitute.org/gatk/). Analysis is performed in Cartagenia using The Variant Calling File (VCF) followed by filtering. Additionally, MPLA analysis was performed for *APP* (SALSA P170 APP; MRC Holland) and several (fragments of) Parkinson genes (SALSA P051/P052 Parkinson probemix). For *ATN1* and *C9orf72* a repeat expansion test was performed. *PRNP* was also tested by Sanger sequencing. It It is not excluded that pathogenic mutations are being missed using this technology. At this moment, there is not enough information about the sensitivity of this technique with respect to the detection of deletions and duplications of more than 5 nucleotides and of somatic mosaic mutations (all types of sequence changes).

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HGNC approved gene symbol	Phenotype description including OMIM phenotype ID(s)	OMIM gene ID	median depth	% covered >10x	% covered >20x
ABCA7	{Alzheimer disease 9, susceptibility to}, 608907	605414	57	98	91
ALS2	Amyotrophic lateral sclerosis 2, juvenile, 205100 Primary lateral sclerosis, juvenile, 606353 Spastic paralysis, infantile onset ascending, 607225	606352	77	100	98
ANG	Amyotrophic lateral sclerosis 9, 611895	105850	70	100	100
APP	Alzheimer disease 1, familial, 104300 Cerebral amyloid angiopathy, Dutch, Italian, Iowa, Flemish, Arctic variants, 605714	104760	75	100	99
ARHGEF28	No OMIM phenotype	612790	40	95	77
ATP13A2	Kufor-Rakeb syndrome, 606693 Spastic paraplegia 78, 617225	610513	67	100	99
ATP1A3	Alternating hemiplegia of childhood 2, 614820 CAPOS syndrome, 601338 Dystonia-12, 128235	182350	96	100	99
ATP6AP2	Mental retardation, syndromic, Hedera type, 300423 ?Parkinsonism with spasticity, 300911	300556	39	100	90
C19orf12	Neurodegeneration with brain iron accumulation 4, 614298 ?Spastic paraplegia 43, 615043	614297	71	100	100
C9orf72	Frontotemporal dementia and/or amyotrophic lateral sclerosis 1, 105550	614260	no coverage data, repeat expansion		

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CAV1	?Lipodystrophy, congenital generalized, type 3, 612526 ?Partial lipodystrophy, congenital cataracts, and neurodegeneration syndrome, 606721 Pulmonary hypertension, primary, 3, 615343	601047	78	100	100
CHCHD10	Frontotemporal dementia and/or amyotrophic lateral sclerosis 2, 615911 ?Myopathy, isolated mitochondrial, 616209 Spinal muscular atrophy, Jokela type, 615048	615903	14	55	27
CHCHD2	Parkinson disease 22, 616710	616244	33	89	67
CHMP2B	Amyotrophic lateral sclerosis 17, 614696 Dementia, familial, nonspecific, 600795	609512	60	100	97
CLN3	Ceroid lipofuscinosis, neuronal, 3, 204200	607042	68	100	100
CLN5	Ceroid lipofuscinosis, neuronal, 5, 256731	608102	73	100	94
CLN6	Ceroid lipofuscinosis, neuronal, 6, 601780 Ceroid lipofuscinosis, neuronal, Kufs type, adult onset, 204300	606725	72	100	91
CLN8	Ceroid lipofuscinosis, neuronal, 8, 600143 Ceroid lipofuscinosis, neuronal, 8, Northern epilepsy variant, 610003	607837	100	100	100
COASY	Neurodegeneration with brain iron accumulation 6, 615643	609855	74	100	100
CP	Cerebellar ataxia, 604290 Hemosiderosis, systemic, due to aceruloplasminemia, 604290 [Hypoceruloplasminemia, hereditary], 604290	117700	50	87	77
CSF1R	Leukoencephalopathy, diffuse hereditary, with spheroids, 221820	164770	81	100	99
CTSD	Ceroid lipofuscinosis, neuronal, 10, 610127	116840	83	100	96
CTSF	Ceroid lipofuscinosis, neuronal, 13, Kufs type, 615362	603539	43	82	70
DCAF17	Woodhouse-Sakati syndrome, 241080	612515	71	100	98
DCTN1	{Amyotrophic lateral sclerosis, susceptibility to}, 105400 Neuropathy, distal hereditary motor, type VIIB, 607641 Perry syndrome, 168605	601143	84	100	98
DNAJC13	No OMIM phenotype	614334	44	95	80
DNAJC5	Ceroid lipofuscinosis, neuronal, 4, Parry type, 162350	611203	111	100	100
DNAJC6	Parkinson disease 19a, juvenile-onset, 615528 Parkinson disease 19b, early-onset, 615528	608375	88	100	100
EIF4G1	{Parkinson disease 18}, 614251	600495	92	100	99
ERBB4	Amyotrophic lateral sclerosis 19, 615515	600543	95	100	99
FA2H	Spastic paraplegia 35, 612319	611026	55	98	87
FBXO7	Parkinson disease 15, 260300	605648	100	100	95
FIG4	Amyotrophic lateral sclerosis 11, 612577 Charcot-Marie-Tooth disease, type 4J, 611228 ?Polymicrogyria, bilateral temporooccipital, 612691 Yunis-Varon syndrome, 216340	609390	86	100	99

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FOLR1	Neurodegeneration due to cerebral folate transport deficiency, 613068	136430	94	100	100
FTL	Hyperferritinemia-cataract syndrome, 600886 L-ferritin deficiency, dominant and recessive, 615604 Neurodegeneration with brain iron accumulation 3, 606159	134790	62	94	76
FUS	Amyotrophic lateral sclerosis 6, with or without frontotemporal dementia, 608030 Tremor, hereditary essential, 4, 614782	137070	79	100	99
GIGYF2	{Parkinson disease 11}, 607688	612003	65	100	97
GRN	Aphasia, primary progressive, 607485 Ceroid lipofuscinosis, neuronal, 11, 614706 Frontotemporal lobar degeneration with ubiquitin-positive inclusions, 607485	138945	95	100	100
HNRNPA1	Amyotrophic lateral sclerosis 20, 615426 ?Inclusion body myopathy with early-onset Paget disease without frontotemporal dementia 3, 615424	164017	25	75	51
HNRNPA2B1	?Inclusion body myopathy with early-onset Paget disease with or without frontotemporal dementia 2, 615422	600124	53	96	93
HTRA1	CARASIL syndrome, 600142 Cerebral arteriopathy, with subcortical infarcts and leukoencephalopathy, type 2, 616779 {Macular degeneration, age-related, 7}, 610149 {Macular degeneration, age-related, neovascular type}, 610149	602194	76	83	78
HTRA2	3-methylglutaconic aciduria, type VIII, 617248 {Parkinson disease 13}, 610297	606441	86	100	100
ITM2B	Dementia, familial British, 176500 Dementia, familial Danish, 117300 ?Retinal dystrophy with inner retinal dysfunction and ganglion cell abnormalities, 616079	603904	70	100	100
KCTD7	Epilepsy, progressive myoclonic 3, with or without intracellular inclusions, 611726	611725	90	100	100
LRRK2	{Parkinson disease 8}, 607060	609007	75	100	97
MAPT	Dementia, frontotemporal, with or without parkinsonism, 600274 {Parkinson disease, susceptibility to}, 168600 Pick disease, 172700 Supranuclear palsy, progressive, 601104 Supranuclear palsy, progressive atypical, 260540	157140	55	97	91
MATR3	Amyotrophic lateral sclerosis 21, 606070	164015	56	91	80
MFSD8	Ceroid lipofuscinosis, neuronal, 7, 610951 Macular dystrophy with central cone involvement, 616170	611124	75	100	97
NOTCH3	Cerebral arteriopathy with subcortical infarcts and leukoencephalopathy 1, 125310 Lateral meningocele syndrome, 130720 ?Myofibromatosis, infantile 2, 615293	600276	66	95	90
NPC1	Niemann-Pick disease, type C1, 257220 Niemann-Pick disease, type D, 257220	607623	83	100	96

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OPTN	Amyotrophic lateral sclerosis 12, 613435 Glaucoma 1, open angle, E, 137760 {Glaucoma, normal tension, susceptibility to}, 606657	602432	69	100	93
PANK2	HARP syndrome, 607236 Neurodegeneration with brain iron accumulation 1, 234200	606157	90	100	100
PRKN	Adenocarcinoma of lung, somatic, 211980 Adenocarcinoma, ovarian, somatic, 167000 {Leprosy, susceptibility to}, 607572 Parkinson disease, juvenile, type 2, 600116	602544	69	100	99
PARK7	Parkinson disease 7 early-onset, 606324	602533	63	100	99
PDGFB	Basal ganglia calcification, idiopathic, 5, 615483 Dermatofibrosarcoma protuberans, 607907 Meningioma, SIS-related, 607174	190040	73	100	100
PDGFRB	Basal ganglia calcification, idiopathic, 4, 615007 Kosaki overgrowth syndrome, 616592 Myeloproliferative disorder with eosinophilia, 131440 (4) Myofibromatosis, infantile, 1, 228550 Premature aging syndrome, Penttinen type, 601812	173410	92	100	99
PFN1	Amyotrophic lateral sclerosis 18, 614808	176610	127	100	100
PINK1	Parkinson disease 6, early onset, 605909	608309	65	94	90
PLA2G6	Infantile neuroaxonal dystrophy 1, 256600 Neurodegeneration with brain iron accumulation 2B, 610217 Parkinson disease 14, 612953	603604	88	100	99
POLG	Mitochondrial DNA depletion syndrome 4A (Alpers type), 203700 Mitochondrial DNA depletion syndrome 4B (MNGIE type), 613662 Mitochondrial recessive ataxia syndrome (includes SANDO and SCAE), 607459 Progressive external ophthalmoplegia 1, 157640 Progressive external ophthalmoplegia 1, 258450	174763	86	100	100
PPT1	Ceroid lipofuscinosis, neuronal, 1, 256730	600722	81	100	100
PRKAR1B	No OMIM phenotype	176911	53	100	91
PRKRA	Dystonia 16, 612067	603424	55	100	97
PRNP	Cerebral amyloid angiopathy, PRNP-related, 137440 Creutzfeldt-Jakob disease, 123400 Gerstmann-Straussler disease, 137440 Huntington disease-like 1, 603218 Insomnia, fatal familial, 600072 {Kuru, susceptibility to}, 245300 Prion disease with protracted course, 606688	176640	51	100	97

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PSEN1	Acne inversa, familial, 3, 613737 Alzheimer disease, type 3, 607822 Alzheimer disease, type 3, with spastic paraparesis and apraxia, 607822 Alzheimer disease, type 3, with spastic paraparesis and unusual plaques, 607822 Cardiomyopathy, dilated, 1U, 613694 Dementia, frontotemporal, 600274 Pick disease, 172700	104311	71	100	98
PSEN2	Alzheimer disease-4, 606889 Cardiomyopathy, dilated, 1V, 613697	600759	87	100	100
PSENEN	Acne inversa, familial, 2, 613736	607632	101	100	100
SERPINI1	Encephalopathy, familial, with neuroserpin inclusion bodies, 604218	602445	71	100	100
SETX	Amyotrophic lateral sclerosis 4, juvenile, 602433 Spinocerebellar ataxia 1, 606002	608465	76	100	99
SIGMAR1	?Amyotrophic lateral sclerosis 16, juvenile, 614373 ?Spinal muscular atrophy, distal, 2, 605726	601978	56	100	100
SLC20A2	Basal ganglia calcification, idiopathic, 1, 213600	158378	83	100	97
SLC33A1	Congenital cataracts, hearing loss, and neurodegeneration, 614482 Spastic paraplegia 42, 612539	603690	62	100	96
SLC39A14	Hypermanganesemia with dystonia 2, 617013	608736	51	96	83
SLC6A3	{Nicotine dependence, protection against}, 188890 Parkinsonism-dystonia, infantile, 613135	126455	87	100	100
SNCA	Dementia, Lewy body, 127750 Parkinson disease 1, 168601 Parkinson disease 4, 605543	163890	82	100	100
SNCB	Dementia, Lewy body, 127750	602569	70	100	100
SOD1	Amyotrophic lateral sclerosis 1, 105400	147450	51	100	100
SORL1	No OMIM phenotype	602005	90	100	99
SPG11	Amyotrophic lateral sclerosis 5, juvenile, 602099 Charcot-Marie-Tooth disease, axonal, type 2X, 616668 Spastic paraplegia 11, 604360	610844	73	100	99
SPR	Dystonia, dopa-responsive, due to sepiapterin reductase deficiency, 612716	182125	98	100	94
SQSTM1	Frontotemporal dementia and/or amyotrophic lateral sclerosis 3, 616437 Myopathy, distal, with rimmed vacuoles, 617158 Neurodegeneration with ataxia, dystonia, and gaze palsy, childhood-onset, 617145 Paget disease of bone 3, 167250	601530	96	100	100
SYNJ1	Epileptic encephalopathy, early infantile, 53, 617389 Parkinson disease 20, early-onset, 615530	604297	42	96	79

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TAF1	Dystonia-Parkinsonism, 314250 Mental retardation, syndromic 33, 300966	313650	78	100	100
TANGO2	Metabolic encephalomyopathic crises, recurrent, with rhabdomyolysis, cardiac arrhythmias, and neurodegeneration, 616878	616830	52	100	91
TARDBP	Amyotrophic lateral sclerosis 10, with or without FTD, 612069 Frontotemporal lobar degeneration, TARDBP-related, 612069	605078	75	100	100
TBK1	Frontotemporal dementia and/or amyotrophic lateral sclerosis 4, 616439	604834	69	100	95
TH	Segawa syndrome, recessive, 605407	191290	55	100	95
TPP1	Ceroid lipofuscinosis, neuronal, 2, 204500 Spinocerebellar ataxia 7, 609270	607998	79	100	98
TREM2	Nasu-Hakola disease, 221770	605086	79	100	100
TUBA4A	Amyotrophic lateral sclerosis 22 with or without frontotemoral dementia, 616208	191110	75	100	99
TYROBP	Nasu-Hakola disease, 221770	604142	44	100	92
UBQLN2	Amyotrophic lateral sclerosis 15, with or without frontotemporal dementia, 300857	300264	47	100	100
UCHL1	?{Parkinson disease 5, susceptibility to}, 613643 Spastic paraplegia 79, 615491	191342	70	100	99
VAPB	Amyotrophic lateral sclerosis 8, 608627 Spinal muscular atrophy, late-onset, Finkel type, 182980	605704	85	100	89
VCP	Amyotrophic lateral sclerosis 14, with or without frontotemporal dementia, 613954 Charcot-Marie-Tooth disease, type 2Y, 616687 Inclusion body myopathy with early-onset Paget disease and frontotemporal dementia 1, 167320	601023	84	100	99
VPS13C	Parkinson disease 23, early onset, 616840	608879	37	90	72
VPS35	{Parkinson disease 17}, 614203	601501	52	89	79
WDR45	Neurodegeneration with brain iron accumulation 5, 300894	300526	32	89	78
XPR1	Basal ganglia calcification, idiopathic, 6, 616413	605237	50	97	84

- Gene symbols according HGCN
- OMIM release used: 2-6-2017
- "No OMIM phenotypes" indicates a gene without a current OMIM association
- OMIM phenotypes between "[ ]", indicate "nondiseases," mainly genetic variations that lead to apparently abnormal laboratory test values
- OMIM phenotypes between "{}", indicate risk factors
- OMIM phenotypes with a question mark, "?", before the disease name indicates an unconfirmed or possibly spurious mapping.
- The statistics above are based on a set of 50 samples
- Median depth is the median of the mean sequence depth over the protein coding exons of the transcript
- % Covered 10x describes the percentage of a gene's coding sequence that is covered at least 10x
- % Covered 20x describes the percentage of a gene's coding sequence that is covered at least 20x