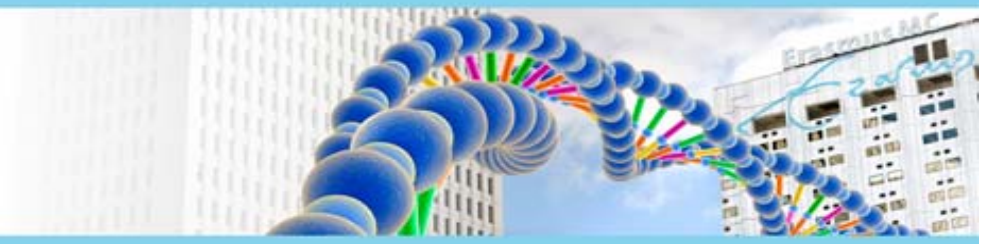
Whole Exome Sequencing
Gene package Neurodegeneration, version 3, 30-7-2018



Technical information
DNA was enriched using Agilent SureSelect Clinical Research Exome V2 capture and paired-end sequenced on the Illumina platform (outsourced). The aim is to obtain 8.1 Giga base pairs per exome with a mapped fraction of 0.99. The average coverage of the exome is ~50x. Duplicate reads are excluded. Data are demultiplexed with bcl2fastq Conversion Software from Illumina. Reads are mapped to the genome using the BWA-MEM algorithm (reference: http://bio-bwa.sourceforge.net/). Variant detection is performed by the Genome Analysis Toolkit HaplotypeCaller (reference: http://www.broadinstitute.org/gatk/). The detected variants are filtered and annotated with Cartagenia software and classified with Alamut Visual. 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 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	% covered >30x
AAAS	Achalasia-addisonianism-alacrimia syndrome, 231550	605378	88	100	100	100
ABCD1	Adrenoleukodystrophy, 300100 Adrenomyeloneuropathy, adult, 300100	300371	75	85	76	72
ALS2	Amyotrophic lateral sclerosis 2, juvenile, 205100 Primary lateral sclerosis, juvenile, 606353 Spastic paralysis, infantile onset ascending, 607225	606352	62	100	99	93
ANG	Amyotrophic lateral sclerosis 9, 611895	105850	110	100	100	100
ANXA11	Amytrophic lateral sclerosis 23, 617839	602572	74	100	100	95
APP	Alzheimer disease 1, familial, 104300 Cerebral amyloid angiopathy, Dutch, Italian, Iowa, Flemish, Arctic variants, 605714	104760	70	100	100	98
ARHGEF28	No OMIM phenotype	612790	54	100	97	86
ATP13A2	Kufor-Rakeb syndrome, 606693 Spastic paraplegia 78, autosomal recessive, 617225	610513	107	100	100	98
ATP1A3	Alternating hemiplegia of childhood 2, 614820 CAPOS syndrome, 601338 Dystonia-12, 128235	182350	134	100	100	100
ATP6AP2	Mental retardation, X-linked, syndromic, Hedera type, 300423 ?Parkinsonism with spasticity, X-linked, 300911	300556	41	100	87	60

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AUH	3-methylglutaconic aciduria, type I, 250950	600529	84	100	100	95
C19orf12	Neurodegeneration with brain iron accumulation 4, 614298 ?Spastic paraplegia 43, autosomal recessive, 615043	614297	166	100	100	100
C9orf72	Frontotemporal dementia and/or amyotrophic lateral sclerosis 1, 105550	614260	47	100	99	90
CAV1	?Lipodystrophy, congenital generalized, type 3, 612526 ?Partial lipodystrophy, congenital cataracts, and neurodegeneration syndrome, 606721 Pulmonary hypertension, primary, 3, 615343	601047	74	100	100	98
CBS	Homocystinuria, B6-responsive and nonresponsive types, 236200 Thrombosis, hyperhomocysteinemic, 236200	613381	122	100	100	100
CHCHD10	Frontotemporal dementia and/or amyotrophic lateral sclerosis 2, 615911 ?Myopathy, isolated mitochondrial, autosomal dominant, 616209 Spinal muscular atrophy, Jokela type, 615048	615903	35	87	68	54
CHCHD2	Parkinson disease 22, autosomal dominant, 616710	616244	59	100	88	62
CHMP2B	Amyotrophic lateral sclerosis 17, 614696 Dementia, familial, nonspecific, 600795	609512	75	100	100	94
CISD2	Wolfram syndrome 2, 604928	611507	132	100	100	100
CLCN2	{Epilepsy, idiopathic generalized, susceptibility to, 11}, 607628 {Epilepsy, juvenile absence, susceptibility to, 2}, 607628 {Epilepsy, juvenile myoclonic, susceptibility to, 8}, 607628 Leukoencephalopathy with ataxia, 615651	600570	95	100	100	99
CLN3	Ceroid lipofuscinosis, neuronal, 3, 204200	607042	101	100	100	99
CLN5	Ceroid lipofuscinosis, neuronal, 5, 256731	608102	62	100	100	99
CLN6	Ceroid lipofuscinosis, neuronal, 6, 601780 Ceroid lipofuscinosis, neuronal, Kufs type, adult onset, 204300	606725	117	100	100	99
CLN8	Ceroid lipofuscinosis, neuronal, 8, 600143 Ceroid lipofuscinosis, neuronal, 8, Northern epilepsy variant, 610003	607837	123	100	100	100
COASY	Neurodegeneration with brain iron accumulation 6, 615643	609855	129	100	100	100
COL4A1	Angiopathy, hereditary, with nephropathy, aneurysms, and muscle cramps, 611773 Brain small vessel disease with or without ocular anomalies, 607595 {Hemorrhage, intracerebral, susceptibility to}, 614519 Porencephaly 1, 175780 ?Retinal arteries, tortuosity of, 180000 Schizencephaly, 269160	120130	80	100	100	96
COL4A2	{Hemorrhage, intracerebral, susceptibility to}, 614519 Porencephaly 2, 614483	120090	97	100	100	98
CP	Cerebellar ataxia, 604290 Hemosiderosis, systemic, due to aceruloplasminemia, 604290 [Hypoceruloplasminemia, hereditary], 604290	117700	54	100	99	89

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CRAT	?Neurodegeneration with brain iron accumulation 8, 617917	600184	92	100	100	98
CSF1R	Leukoencephalopathy, diffuse hereditary, with spheroids, 221820	164770	92	100	100	99
CST3	Cerebral amyloid angiopathy, 105150 {Macular degeneration, age-related, 11}, 611953	604312	90	100	100	96
CTSA	Galactosialidosis, 256540	613111	118	100	100	100
CTSD	Ceroid lipofuscinosis, neuronal, 10, 610127	116840	138	100	100	100
CTSF	Ceroid lipofuscinosis, neuronal, 13, Kufs type, 615362	603539	86	100	96	92
CYP27A1	Cerebrotendinous xanthomatosis, 213700	606530	126	100	100	100
DARS2	Leukoencephalopathy with brain stem and spinal cord involvement and lactate elevation, 611105	610956	53	100	100	92
DCAF17	Woodhouse-Sakati syndrome, 241080	612515	66	100	98	91
DCTN1	{Amyotrophic lateral sclerosis, susceptibility to}, 105400 Neuropathy, distal hereditary motor, type VIIB, 607641 Perry syndrome, 168605	601143	85	100	100	99
DNAJC13	No OMIM phenotype	614334	61	100	98	90
DNAJC5	Ceroid lipofuscinosis, neuronal, 4, Parry type, 162350	611203	218	100	100	100
DNAJC6	Parkinson disease 19a, juvenile-onset, 615528 Parkinson disease 19b, early-onset, 615528	608375	72	100	100	97
DNMT1	Cerebellar ataxia, deafness, and narcolepsy, autosomal dominant, 604121 Neuropathy, hereditary sensory, type IE, 614116	126375	87	100	99	95
EIF4G1	{Parkinson disease 18}, 614251	600495	89	100	100	99
ERBB4	Amyotrophic lateral sclerosis 19, 615515	600543	57	100	99	89
FA2H	Spastic paraplegia 35, autosomal recessive, 612319	611026	73	100	100	95
FBXO7	Parkinson disease 15, autosomal recessive, 260300	605648	74	100	100	96
FIG4	Amyotrophic lateral sclerosis 11, 612577 Charcot-Marie-Tooth disease, type 4J, 611228 ?Polymicrogyria, bilateral temporooccipital, 612691 Yunis-Varon syndrome, 216340	609390	53	100	99	88
FOLR1	Neurodegeneration due to cerebral folate transport deficiency, 613068	136430	96	100	100	100
FTL	Hyperferritinemia-cataract syndrome, 600886 L-ferritin deficiency, dominant and recessive, 615604 Neurodegeneration with brain iron accumulation 3, 606159	134790	137	100	100	100
FUS	Amyotrophic lateral sclerosis 6, with or without frontotemporal dementia, 608030 Essential tremor, hereditary, 4, 614782	137070	65	100	100	97
GBE1	Glycogen storage disease IV, 232500 Polyglucosan body disease, adult form, 263570	607839	55	100	97	83
GFAP	Alexander disease, 203450	137780	79	100	100	99
GIGYF2	{Parkinson disease 11}, 607688	612003	54	100	99	89

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GLA	Fabry disease, 301500 Fabry disease, cardiac variant, 301500	300644	88	100	100	100
GRN	Aphasia, primary progressive, 607485 Ceroid lipofuscinosis, neuronal, 11, 614706 Frontotemporal lobar degeneration with ubiquitin-positive inclusions, 607485	138945	148	100	100	100
GSN	Amyloidosis, Finnish type, 105120	137350	92	100	100	97
HEXA	GM2-gangliosidosis, several forms, 272800 [Hex A pseudodeficiency], 272800 Tay-Sachs disease, 272800	606869	79	100	100	96
HEXB	Sandhoff disease, infantile, juvenile, and adult forms, 268800	606873	106	100	100	95
HNRNPA1	Amyotrophic lateral sclerosis 20, 615426 ?Inclusion body myopathy with early-onset Paget disease without frontotemporal dementia 3, 615424	164017	56	100	98	94
HNRNPA2B1	?Inclusion body myopathy with early-onset Paget disease with or without frontotemporal dementia 2, 615422	600124	54	100	100	94
HTRA1	CARASIL syndrome, 600142 Cerebral arteriopathy, autosomal dominant, with subcortical infarcts and leukoencephalopathy, type 2, 616779 {Macular degeneration, age-related, 7}, 610149 {Macular degeneration, age-related, neovascular type}, 610149	602194	87	94	86	80
HTRA2	3-methylglutaconic aciduria, type VIII, 617248 {Parkinson disease 13}, 610297	606441	137	100	100	97
ITM2B	Dementia, familial British, 176500 Dementia, familial Danish, 117300 ?Retinal dystrophy with inner retinal dysfunction and ganglion cell abnormalities, 616079	603904	72	100	100	97
KCTD7	Epilepsy, progressive myoclonic 3, with or without intracellular inclusions, 611726	611725	156	100	100	100
LMNB1	Leukodystrophy, adult-onset, autosomal dominant, 169500	150340	57	100	99	91
LRP10	No OMIM phenotype	609921	137	100	100	100
LRRK2	{Parkinson disease 8}, 607060	609007	68	100	99	92
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	106	100	100	99
MATR3	Amyotrophic lateral sclerosis 21, 606070	164015	54	100	99	91
MED20	No OMIM phenotype	612915	137	100	100	100
MFSD8	Ceroid lipofuscinosis, neuronal, 7, 610951 Macular dystrophy with central cone involvement, 616170	611124	56	100	99	89
MMACHC	Methylmalonic aciduria and homocystinuria, cblC type, 277400	609831	115	100	100	100

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NOTCH3	Cerebral arteriopathy with subcortical infarcts and leukoencephalopathy 1, 125310 Lateral meningocele syndrome, 130720 ?Myofibromatosis, infantile 2, 615293	600276	108	99	95	91
NPC1	Niemann-Pick disease, type C1, 257220 Niemann-Pick disease, type D, 257220	607623	74	100	100	97
NPC2	Niemann-pick disease, type C2, 607625	601015	87	100	100	100
OPTN	Amyotrophic lateral sclerosis 12, 613435 Glaucoma 1, open angle, E, 137760 {Glaucoma, normal tension, susceptibility to}, 606657	602432	71	100	99	93
PAH	[Hyperphenylalaninemia, non-PKU mild], 261600 Phenylketonuria, 261600	612349	57	100	98	91
PANK2	HARP syndrome, 607236 Neurodegeneration with brain iron accumulation 1, 234200	606157	72	100	100	96
PARK7	Parkinson disease 7, autosomal recessive early-onset, 606324	602533	62	100	98	83
PDGFB	Basal ganglia calcification, idiopathic, 5, 615483 Dermatofibrosarcoma protuberans, 607907 Meningioma, SIS-related, 607174	190040	97	100	100	100
PDGFRB	Basal ganglia calcification, idiopathic, 4, 615007 Kosaki overgrowth syndrome, 616592 Myeloproliferative disorder with eosinophilia, 131440 Myofibromatosis, infantile, 1, 228550 Premature aging syndrome, Penttinen type, 601812	173410	112	100	100	99
PFN1	Amyotrophic lateral sclerosis 18, 614808	176610	180	100	100	100
PINK1	Parkinson disease 6, early onset, 605909	608309	99	99	95	91
PLA2G6	Infantile neuroaxonal dystrophy 1, 256600 Neurodegeneration with brain iron accumulation 2B, 610217 Parkinson disease 14, autosomal recessive, 612953	603604	115	100	100	100
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, autosomal dominant 1, 157640 Progressive external ophthalmoplegia, autosomal recessive 1, 258450	174763	103	100	100	98
PPT1	Ceroid lipofuscinosis, neuronal, 1, 256730	600722	75	100	100	97
PRKAR1B	No OMIM phenotype	176911	86	100	97	89
PRKN	Adenocarcinoma of lung, somatic, 211980 Adenocarcinoma, ovarian, somatic, 167000 {Leprosy, susceptibility to}, 607572 Parkinson disease, juvenile, type 2, 600116	602544	84	100	100	98

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PRKRA	Dystonia 16, 612067	603424	64	100	99	96
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	135	100	100	100
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	50	100	99	89
PSEN2	Alzheimer disease-4, 606889 Cardiomyopathy, dilated, 1V, 613697	600759	106	100	100	99
PSENEN	Acne inversa, familial, 2, with or without Dowling-Degos disease, 613736	607632	68	100	100	100
PTRHD1	No OMIM phenotype	617342	109	100	100	98
QARS	Microcephaly, progressive, seizures, and cerebral and cerebellar atrophy, 615760	603727	92	100	100	98
SERPINI1	Encephalopathy, familial, with neuroserpin inclusion bodies, 604218	602445	63	100	100	94
SETX	Amyotrophic lateral sclerosis 4, juvenile, 602433 Spinocerebellar ataxia, autosomal recessive 1, 606002	608465	60	100	99	94
SIGMAR1	?Amyotrophic lateral sclerosis 16, juvenile, 614373 ?Spinal muscular atrophy, distal, autosomal recessive, 2, 605726	601978	121	100	100	100
SLC17A5	Salla disease, 604369 Sialic acid storage disorder, infantile, 269920	604322	73	100	100	94
SLC20A2	Basal ganglia calcification, idiopathic, 1, 213600	158378	90	100	99	92
SLC33A1	Congenital cataracts, hearing loss, and neurodegeneration, 614482 Spastic paraplegia 42, autosomal dominant, 612539	603690	60	100	96	81
SLC39A14	Hypermanganesemia with dystonia 2, 617013 ?Hyperostosis cranalis interna, 144755	608736	85	100	99	95
SLC6A3	{Nicotine dependence, protection against}, 188890 Parkinsonism-dystonia, infantile, 613135	126455	99	100	100	100
SMPD1	Niemann-Pick disease, type A, 257200 Niemann-Pick disease, type B, 607616	607608	130	100	100	98

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SNCA	Dementia, Lewy body, 127750 Parkinson disease 1, 168601 Parkinson disease 4, 605543	163890	42	100	100	88
SNCB	Dementia, Lewy body, 127750	602569	130	100	100	100
SOD1	Amyotrophic lateral sclerosis 1, 105400	147450	67	100	100	99
SORL1	No OMIM phenotype	602005	78	100	99	94
SPG11	Amyotrophic lateral sclerosis 5, juvenile, 602099 Charcot-Marie-Tooth disease, axonal, type 2X, 616668 Spastic paraplegia 11, autosomal recessive, 604360	610844	72	100	99	95
SPR	Dystonia, dopa-responsive, due to sepiapterin reductase deficiency, 612716	182125	100	100	100	100
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	126	100	100	95
SYNJ1	Epileptic encephalopathy, early infantile, 53, 617389 Parkinson disease 20, early-onset, 615530	604297	53	100	98	88
TAF1	Dystonia-Parkinsonism, X-linked, 314250 Mental retardation, X-linked, syndromic 33, 300966	313650	43	100	94	75
TANGO2	Metabolic encephalomyopathic crises, recurrent, with rhabdomyolysis, cardiac arrhythmias, and neurodegeneration, 616878	616830	87	100	100	99
TARDBP	Amyotrophic lateral sclerosis 10, with or without FTD, 612069 Frontotemporal lobar degeneration, TARDBP-related, 612069	605078	108	100	100	90
TBK1	{Encephalopathy, acute, infection-induced (herpes-specific), susceptibility to, 8}, 617900 Frontotemporal dementia and/or amyotrophic lateral sclerosis 4, 616439	604834	70	100	97	84
TH	Segawa syndrome, recessive, 605407	191290	92	100	99	94
TPP1	Ceroid lipofuscinosis, neuronal, 2, 204500 Spinocerebellar ataxia, autosomal recessive 7, 609270	607998	87	100	100	99
TREM2	Nasu-Hakola disease, 221770	605086	101	100	100	100
TREX1	Aicardi-Goutieres syndrome 1, dominant and recessive, 225750 Chilblain lupus, 610448 {Systemic lupus erythematosus, susceptibility to}, 152700 Vasculopathy, retinal, with cerebral leukodystrophy, 192315	606609	217	100	100	100
TTR	Amyloidosis, hereditary, transthyretin-related, 105210 Carpal tunnel syndrome, familial, 115430 [Dystransthyretinemic hyperthyroxinemia], 145680	176300	75	100	100	100
TUBA4A	Amyotrophic lateral sclerosis 22 with or without frontotemporal dementia, 616208	191110	179	100	100	100
TYMP	Mitochondrial DNA depletion syndrome 1 (MNGIE type), 603041	131222	92	100	100	100
TYROBP	Nasu-Hakola disease, 221770	604142	93	100	100	100

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UBQLN2	Amyotrophic lateral sclerosis 15, with or without frontotemporal dementia, 300857	300264	68	100	100	100
UCHL1	{?Parkinson disease 5, susceptibility to}, 613643 Spastic paraplegia 79, autosomal recessive, 615491	191342	74	100	100	100
VAPB	Amyotrophic lateral sclerosis 8, 608627 Spinal muscular atrophy, late-onset, Finkel type, 182980	605704	64	100	100	94
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	81	100	100	96
VPS13C	Parkinson disease 23, autosomal recessive, early onset, 616840	608879	43	100	94	76
VPS35	{Parkinson disease 17}, 614203	601501	59	100	99	91
WDR45	Neurodegeneration with brain iron accumulation 5, 300894	300526	80	100	100	99
XPR1	Basal ganglia calcification, idiopathic, 6, 616413	605237	54	100	100	94

- Gene symbols according HGCN
- OMIM release used: 4-7-2018
- "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 95 samples
- Median depth is the median of the mean sequence depth over the protein coding exons (±10bp flanking introns) of the longest transcript
- % Covered 10x describes the percentage of a gene's coding sequence (±10bp flanking introns) that is covered at least 10x
- % Covered 20x describes the percentage of a gene's coding sequence (±10bp flanking introns) that is covered at least 20x
- % Covered 30x describes the percentage of a gene's coding sequence (±10bp flanking introns) that is covered at least 30x