**Comprehensive Neurogenetics Panel Description**

The neurogenetics panel tests for several genetic conditions with overlapping phenotypes, such as **dystonia, early-onset dementia or cognitive regression, psychosis, ataxia or a combination of these symptoms**. Disorders spectrum encompasses in particular several neurodegenerative disorders and inborn errors of metabolisms.

**Overview of genetic disorders tested**

* Aicardi-Gouttieres syndrome
* Cerebellar ataxias
* Early-onset dementia (Alzheimer, frontoteporal dementia, cerebral amyloid angiopathy, others)
* Episodic ataxias
* Joubert syndrome
* Leukodystrophies
* Lysosomal disorders (Niemann-Pick type C, ceroid lipofuscinosis, Krabbe, MLD, San Fillipo, others)
* Neurodegeneration with brain iron accumulation (NBIA)
* Primary familial brain calcifications
* Primary and combined dystonia
* Paroxysmal dystonia
* Other inborn errors of metabolism (aminoacids catabolism disorder, copper metabolism disorder, creatine synthesis defect, nuclear mitochondrial disorders, peroxisomal disorders, porphyria, organic acidurias, urea cycle defects, vitamins metabolisms (B12).

**Gene panel and subpanels**

**All neurogenetics subpanels combined (290 genes):** AAAS, AARS2, ABCB7, ABCD1, ABHD12, ACO2, ADAR, ADCK3, AFG3L2, AHI1, ALDH5A1, ALG6, ANO10, ANO3, APP, APTX, ARG1, ARL13B, ARSA, ASL, ASS1, ATCAY, ATM, ATP13A2, ATP1A3, ATP2B3, ATP7B, BCKDHA, BCKDHB, BTD, C10ORF2, C12ORF65, C19ORF12, C5ORF42, CA8, CACNA1A, CACNA1B, CACNB4, CAMTA1, CASK, CBS, CC2D2A, CEP290, CEP41, CHMP1A, CHMP2B, CLCN2, CLN3, CLN5, CLN6, CLN8, COASY, COL4A1, COQ2, COQ4, COQ6, COQ9, CP, CPS1, CSF1R, CSPP1, CST3, CTSA, CTSD, CTSF, CUL4B, CYP27A1, DARS2, DBT, DCAF17, DDB2, DDC, DKC1, DLAT, DLD, DNAJC19, DNAJC5, DNMT1, DRD2, EEF2, EIF2B1, EIF2B2, EIF2B3, EIF2B4, EIF2B5, ELOVL4, ELOVL5, EPM2A, ERCC1, ERCC2, ERCC3, ERCC4, ERCC5, ERCC6, ERCC8, EXOSC3, FA2H, FBXO7, FGF14, FOXG1, FTL, FUCA1, FUS, GALC, GAMT, GATM, GBA, GBA2, GBE1, GCDH, GCH1, GFAP, GLA, GLB1, GNAL, GNS, GOSR2, GRID2, GRM1, GRN, HEXA, HEXB, HGSNAT, HMBS, HPRT1, HSD17B4, HTRA1, INPP5E, ITM2B, ITPR1, IVD, KCNA1, KCNC3, KCND3, KCNJ10, KCTD7, KIF7, LAMA1, LIAS, LMNB1, LRRK2, MAN2B1, MAPT, MARS2, MCEE, MECP2, MFSD8, MMAA, MMAB, MMACHC, MMADHC, MRE11A, MTHFR, MTPAP, MUT, NAGLU, NEU1, NHLRC1, NOP56, NOTCH3, NPC1, NPC2, NPHP1, OFD1, OPA1, OPHN1, OTC, PANK2, PARK2, PARK7, PCCA, PCCB, PCNA, PDE6D, PDGFB, PDGFRB, PDHA1, PDHB, PDHX, PDP1, PDSS1, PDSS2, PDYN, PHYH, PIK3R5, PINK1, PLA2G6, PLP1, PMM2, PNKD, PNPLA6, POLG, POLG2, POLR3A, POLR3B, PPT1, PRICKLE1, PRKCG, PRKRA, PRNP, PRPS1, PRRT2, PSAP, PSEN1, PSEN2, PTS, RARS2, RNASEH2A, RNASEH2B, RNASEH2C, RNF216, RPGRIP1L, RRM2B, SACS, SAMHD1, SCARB2, SEPSECS, SERPINI1, SETX, SGCE, SGSH, SIL1, SLC17A5, SLC19A3, SLC1A3, SLC20A2, SLC25A15, SLC25A4, SLC2A1, SLC30A10, SLC6A19, SLC6A3, SLC6A8, SLC9A6, SNCA, SNCB, SPR, SPTBN2, SQSTM1, STUB1, SUCLA2, SUMF1, SYNE1, SYNJ1, SYT14, TARDBP, TCTN1, TCTN2, TCTN3, TDP1, TGM6, TH, THAP1, TIMM8A, TMEM138, TMEM216, TMEM231, TMEM237, TMEM240, TMEM67, TOR1A, TPK1, TPP1, TREM2, TREX1, TSEN2, TSEN34, TSEN54, TTBK2, TTC21B, TTPA, TTR, TUBB4A, TYROBP, UBE3A, UBQLN2, VAMP1, VCP, VLDLR, VPS13A, VPS53, VRK1, WDR45, WDR81, WFS1, WWOX, XK, XPA, XPC, ZNF423.

**1.Episodic ataxia (31 genes):** ARG1, ASL, ASS1, BCKDHA, BCKDHB, BTD, CACNA1A, CACNB4, CPS1, DBT, DLAT, DLD, IVD, KCNA1, LIAS, MCEE, MMAA, MMAB, MMACHC, MMADHC, MUT, OTC, PCCA, PCCB, PDHA1, PDHB, PDHX, PDP1, SLC1A3, SLC25A15, SLC6A19.

**2.Progressive and non-progressive ataxia (170 genes):** AAAS, AARS2, ABCB7, ABHD12, ACO2, ADCK3, AFG3L2, AHI1, ALDH5A1, ALG6, ANO10, APTX, ARL13B, ARSA, ATCAY, ATM, ATP2B3, C10ORF2, C12ORF65, C19ORF12, C5ORF42, CA8, CAMTA1, CASK, CC2D2A, CEP290, CEP41, CHMP1A, CLCN2, CLN3, CLN5, CLN6, CLN8, COASY, COQ2, COQ4, COQ6, COQ9, CP, CSPP1, CTSA, CTSD, CUL4B, CYP27A1, DARS2, DDB2, DKC1, DNAJC19, DNAJC5, DNMT1, EEF2, EIF2B1, EIF2B2, EIF2B3, EIF2B4, EIF2B5, ELOVL4, ELOVL5, ERCC1, ERCC2, ERCC3, ERCC4, ERCC5, ERCC6, ERCC8, EXOSC3, FA2H, FGF14, FTL, GALC, GBA2, GBE1, GLB1, GOSR2, GRID2, GRM1, GRN, HEXA, HEXB, HSD17B4, INPP5E, ITPR1, KCNC3, KCND3, KCNJ10, KIF7, LAMA1, MAN2B1, MARS2, MFSD8, MRE11A, MTPAP, NEU1, NOP56, NPC1, NPC2, NPHP1, OFD1, OPA1, OPHN1, PANK2, PCNA, PDE6D, PDSS1, PDSS2, PDYN, PHYH, PIK3R5, PLA2G6, PLP1, PMM2, PNPLA6, POLG, POLG2, POLR3A, POLR3B, PPT1, PRICKLE1, PRKCG, PRPS1, RARS2, RNF216, RPGRIP1L, RRM2B, SACS, SCARB2, SEPSECS, SETX, SIL1, SLC17A5, SLC19A3, SLC25A4, SLC9A6, SPTBN2, STUB1, SYNE1, SYT14, TCTN1, TCTN2, TCTN3, TDP1, TGM6, TIMM8A, TMEM138, TMEM216, TMEM231, TMEM237, TMEM240, TMEM67, TPK1, TPP1, TSEN2, TSEN34, TSEN54, TTBK2, TTC21B, TTPA, TTR, UBE3A, VAMP1, VLDLR, VPS53, VRK1, WDR45, WDR81, WFS1, WWOX, XPA, XPC, ZNF423.

**3.Joubert syndrome (22 genes):** AHI1, ARL13B, C5ORF42, CC2D2A, CEP290, CEP41, CSPP1, INPP5E, KIF7, NPHP1, OFD1, RPGRIP1L, TCTN1, TCTN2, TCTN3, TMEM138, TMEM216, TMEM231, TMEM237, TMEM67, TTC21B, ZNF423.

**4.Dystonia (78 genes):** ADAR, ANO3, ATP13A2, ATP1A3, ATP7B, BTD, C19ORF12, CACNA1B, COASY, COL4A1, CP, CTSF, DCAF17, DDC, DLAT, DRD2, EIF2B1, EIF2B2, EIF2B3, EIF2B4, EIF2B5, FA2H, FBXO7, FTL, GALC, GAMT, GATM, GCDH, GCH1, GLB1, GNAL, HEXA, HPRT1, LIAS, LRRK2, NPC1, NPC2, PANK2, PARK2, PARK7, PDGFB, PDGFRB, PDHA1, PDHB, PDHX, PDP1, PINK1, PLA2G6, PLP1, PNKD, POLG, PRKRA, PRRT2, PTS, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, SGCE, SLC19A3, SLC20A2, SLC2A1, SLC30A10, SLC6A3, SLC6A8, SPR, SUCLA2, SYNJ1, TH, THAP1, TIMM8A, TOR1A, TPK1, TREX1, TUBB4A, VPS13A, WDR45, XK.

**5.Adult onset dementia & psychosis (36 genes)\*:** APP, CHMP2B, COL4A1, CP, CSF1R, CST3, DNAJC5, DNMT1, FGF14, FTL, FUS, GLA, GRN, ITM2B, LMNB1, MAPT, NOTCH3, PDGFB, PDGFRB, PRNP, PSEN1, PSEN2, SERPINI1, SLC20A2, SNCA, SNCB, SQSTM1, TARDBP, TTR, TREM2, TYROBP, UBQLN2, VCP, VPS13A, WDR45, XK.

**\*Include disorders of primary adult onset, which are mainly autosomal dominant. It is not recommended to include this subpanel for pediatric patients.**

**6.Developmental regression/dementia/psychosis (109 genes)\*\*:** AARS2, ABCD1, ADAR, ALDH5A1, ARG1, ARSA, ASL, ASS1, ATP13A2, ATP7B, BCKDHA, BCKDHB, C10ORF2, C12ORF65, C19ORF12, CBS, CLN3, CLN5, CLN6, CLN8, COASY, CPS1, CTSA, CTSD, CTSF, CYP27A1, DBT, DLAT, DLD, EIF2B1, EIF2B2, EIF2B3, EIF2B4, EIF2B5, EPM2A, ERCC1, ERCC2, ERCC3, ERCC4, ERCC5, ERCC6, ERCC8, EXOSC3, FA2H, FOXG1, FUCA1, GALC, GAMT, GATM, GBA, GBE1, GFAP, GLB1, GNS, HEXA, HEXB, HEXB, HGSNAT, HMBS, HSD17B4, HTRA1, IVD, KCTD7, LIAS, MAN2B1, MECP2, MFSD8, MMAA, MMAB, MMACHC, MMADHC, MTHFR, MUT, NAGLU, NEU1, NHLRC1, NPC1, NPC2, OTC, PANK2, PCCA, PCCB, PCNA, PDHA1, PDHB, PDHX, PDP1, PLA2G6, PLP1, POLG, POLR3A, POLR3B, PPT1, PSAP, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, SGSH, SLC17A5, SLC25A15, SLC6A8, SLC9A6, SUCLA2, SUMF1, TIMM8A, TPP1, TREX1, WFS1.

     \*\*Include disorders of primary pediatric onset, some being known for adult presentations.

**7.Leukodystrophies (29 genes)\*\*\*:** ABCD1, ADAR, ARSA, CLCN2, CSF1R, CYP27A1, DARS2, EIF2B1, EIF2B2, EIF2B3, EIF2B4, EIF2B5, FUCA1, GALC, GBE1, GFAP, HSD17B4, LMNB1, POLR3A, POLR3B, PSAP, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, SLC17A5, SUMF1, TREX1, TUBB4A.

**\*\*\*Other disorders affecting cerebral white matter, but not fulfilling leukodystrophy criteria, are included in subpanels 5 and 6 above.**