|  |  |
| --- | --- |
| Panel type | Genes |
| Panel A (144 genes) | ADSL, ALDH5A1, ALDH7A1, ALG13, ANKRD11, ARG1, ARHGEF9, ARX, ASNS, ATP1A2, ATP1A3, ATP6AP2, ATRX, BRAT1, C12ORF57, CACNA1A, CACNA1E, CACNA1G, CASK, CDKL5, CHD2, CHRNA2, CHRNA4, CHRNA7, CHRNB2, CLCN4, CLN3, CLN5, CLN6, CLN8, CNTNAP2, CSTB, CTSD, CTSF, CUL4B, DCX, DDX3X, DEPDC5, DNAJC5, DNM1, DOCK7, DYRK1A, EEF1A2, EHMT1, EPM2A, FGF12, FLNA, FOLR1, FOXG1, FRRS1L, GABBR2, GABRA1, GABRB2, GABRB3, GABRG2, GAMT, GATM, GLDC, GNAO1, GOSR2, GRIN1, GRIN2A, GRIN2B, HCN1, HNRNPU, IQSEC2, KANSL1, KCNA2, KCNB1, KCNC1, KCNH1, KCNJ10, KCNMA1, KCNQ2, KCNQ3, KCNT1, KCTD7, KDM6A, KIAA2022 (NEXMIF), LGI1, MAGI2, MBD5, MECP2, MEF2C, MFSD8, NALCN, NGLY1, NHLRC1, NPRL3, NR2F1, NRXN1, PACS1, PAFAH1B1, PCDH19, PHGDH, PIGA, PIGG, PIGN, PIGO, PIGT, PIGV, PLCB1, PNKP, PNPO, POLG, PPP2R5D, PPT1, PRRT2, PURA, QARS, SATB2, SCARB2, SCN1A, SCN1B, SCN2A, SCN8A, SHANK3, SLC13A5, SLC19A3, SLC25A22, SLC2A1, SLC35A2, SLC6A1, SLC6A8, SLC9A6, SMARCA2, SMC1A, SNAP25, SPATA5, SPTAN1, STX1B, STXBP1, SYNGAP1, SZT2, TBC1D24, TBL1XR1, TCF4, TPP1, TSC1, TSC2, TUBB2A, UBE3A, WDR45, WWOX |
| Panel B (127 genes) | ADSL, ALDH5A1, ALDH7A1, ALG13, ARHGEF9, ARX, ASNS, ATP1A2, ATP1A3, ATP6AP2, ATRX, BRAT1, CACNA1A, CASK, CDKL5, CHD2, CHRNA2, CHRNA4, CHRNA7, CHRNB2, CLCN4, CLN3, CLN5, CLN6, CLN8, CNTNAP2, CSTB, CTNNB1, CTSD, CTSF, DDX3X, DEPDC5, DNAJC5, DNM1, DYRK1A, EEF1A2, EHMT1, EPM2A, FLNA, FOLR1, FOXG1, FRRS1L, GABBR2, GABRA1, GABRB2, GABRB3, GABRG2, GAMT, GATM, GLDC, GNAO1, GOSR2, GRIN1, GRIN2A, GRIN2B, HNRNPU, IQSEC2, KANSL1, KCNA2, KCNB1, KCNC1, KCNH1, KCNJ10, KCNMA1, KCNQ2, KCNQ3, KCNT1, KCTD7, KDM6A, LGI1, MAGI2, MBD5, MECP2, MEF2C, MFSD8, NALCN, NEXMIF, NGLY1, NHLRC1, NPRL3, NR2F1, NRXN1, PACS1, PCDH19, PIGA, PIGN, PIGO, PIGV, PLCB1, PNKP, PNPO, POLG, PPP2R5D, PPT1, PRRT2, PURA, QARS, SATB2, SCARB2, SCN1A, SCN1B, SCN2A, SCN8A, SLC13A5, SLC19A3, SLC25A22, SLC2A1, SLC6A1, SLC6A8, SLC9A6, SMC1A, SPATA5, SPTAN1, STX1B, STXBP1, SYNGAP1, SZT2, TBC1D24, TBL1XR1, TCF4, TPP1, TSC1, TSC2, UBE3A, WDR45, WWOX, ZEB2 |
| Panel C (87 genes) | ADSL, ALDH7A1, ALG13, ARHGEF9, ARX, ATP1A2, ATP6AP2, CACNA1A, CDKL5, CHD2, CHRNA2, CHRNA4, CHRNA7, CHRNB2, CLN3, CLN5, CLN6, CLN8, CNTNAP2, CSTB, CTSD, DNAJC5, DNM1, DYRK1, EEF1A2, EPM2A, FOLR1, FOXG1, GABRA1, GABRB2, GABRB3, GABRG2, GAMT, GATM, GOSR2, GRIN1, GRIN2A, GRIN2B, IQSEC2, KANSL1, KCNB1, KCNJ10, KCNQ2, KCNQ3, KCNT1, KCTD7, LGI1, MAGI2, MBD5, MECP2, MEF2C, MFSD8, NHLRC1, NR2F1, NRXN1, PCDH19, PIGA, PIGO, PIGV, PNKP, PNPO, POLG, PPT1, PRRT2, QARS, SCARB2, SCN1A, SCN1B, SCN2A, SCN8A, SLC13A5, SLC25A22, SLC2A1, SLC6A8, SLC9A6, SPTAN1, STXBP1, TBC1D24, TCF4, TPP1, TSC1, TSC2, UBE3A, WDR45, WWOX, ZEB2 |
| Panel D (36 genes) | ALDH7A1, CACNA1A, CASR, CHRNA2, CHRNA4, CHRNB2, CSTB, DEPDC5, EFHIC1, EPM2A, GABRA1, GABRB3, GABRD, GABRG2, GRIN2A, KCNMA1, KCNQ2, KCNQ3, KCNT1, KCTD7, LGI1, MBD5, ME2, NHLRC1, PCDH19, PRICKLE1, PRICKLE2, PRRT2, SCARB2, SCN1A, SCN1B, SCN2A, SCN9A, SLC2A1, SLC4A10, TBC1D24 |
| Panel E (141 genes) | ADGRG1, ALDH7A1, ARFGEF2, ARHGEF9, ARX, ATP1A2, ATP2A2, ATP6AP2, ATP6V0A2, ATRX, CACNA1A, CASK, CASR, CCDC88C, CDKL5, CHRNA2, CHRNA4, CHRNB2, CLCNKA, CLCNKB, CLN3, CLN5, CLN6, CLN8, CNTNAP2, COL18A1, COL4A1, CPT2, CSTB, CTSD, CUL4B, DCX, DEPDC5, DNAJC5, EFHC1, EMX2, EPM2A, FGD1, FGFR3, FKRP, FKTN, FLNA, FOXG1, GABRA1, GABRB3, GABRD, GABRG2, GPC3, GRIA3, GRIN2A, HSD17B10, KCNA1, KCNJ1, KCNJ10, KCNMA1, KCNQ2, KCNQ3, KCNT1, KCTD7, KDM5C, KIF1BP, KMT2D, LAMA2, LARGE, LBR, LGI1, MBD5, ME2, MECP2, MEF2C, MFSD8, NHLRC1, NIPBL, NOTCH3, NRXN1, OFD1, OPHN1, PAFAH1B1, PAK3, PANK2, PAX6, PCDH19, PEX7, PHF6, PIGV, PLA2G6, PLP1, PNKP, POLG, POMGNT1, POMT1, POMT2, PPT1, PQBP1, PRICKLEI, PRICKLE2, PRRT2, RAB39B, RtAB3GAP1, RAI1, RELN, RNASEH2A, RNASEH2B, RNASEH2C, SAMHD1, SCARB2, SCN1A, SCN1B, SCN2A, SCN8A, SCN9A, SERPINI1, SETBP1, SLC25A22, SLC2A1, SLC4A10, SLC9A6, SMC1A, SMC3, SMS, SNAP29, SPTAN1, SRPX2, STXBP1, SYNGAP1, SYP, TBC1D24, TBX1, TCF4, TPP1, TREX1, TSC1, TSC2, TUBA1A, TUBA8, TUBB2B, UBE3A, VPS13A, VPS13B, WDR62, ZEB2 |
| Panel F (202 genes) | AAR52, ABCB7, ACAD9, ACO2, ADCK4, AFG3-21 AUK, AlFM1, ALAS2, APOFTI ATP5A1, ATP5E, ATP7B, ATPAF2, AUH, BCSIL, BOLA3, C100RF2, Cl20RF65, C190RF121 C200RF7, C8ORF38, CARS2, CLPB, COA5, COA6, COASY, C002, COQ4, COOS, COW, C0O8A, COOS, COX10, COX14, COX15, COX20, COX6A1, COX6B1, COX8A, CYC1, DARS2, DGUOK, DLAT, DLD, DNA2, DNAJC19, DNM1Lp EARS2, ECHS1, ELAC2, ETFA, ETFB, ETFDH, ETHEL FARS2. FASTKD2, FBXL4, FDX1L, FH, FLAD1, FOXRED1, GARS, GCDH, GFER, GFM1, GFM2, GLRX5, GTPBP3, GYG2, HARS2, HMGCL, HTRA2, IARS2, IBA57, ISCA2, ISCU, LAMP2, LARS, LARS2, LIAS, LIPT1, LRPPRC, LYRM4, LYRM7, MARS2, MFF, MFN2, MGME1, MICU1, MPC1, MPV17, MRPLI2, MRPL3, MRPL44, MRPS16, MRPS22, MRPS7, MT-ATPS, MT-ATP8, MT-COI, MT-0O2, MT-0O3, MT-CYB, MT-DLOOP, MTFMT, MT-ND1, MT-NDZ MT-ND3, MT-ND4, MT-ND4L, MT-ND5, MT-NDS, MT01, MTPAP, MT-RNR1, MT-RNR2, MT-TA, MT-TC, MT-TD, MT-TE, MT-TF, MT-TG, MT-TH, MT-TI, MT-TKI MT-TL1, MT-TL2, MT-TM, MT-TN, MT-TP, MT-TO, MT-TR, MT-TS1, MT- TS2, MT:TT, MT-N, MT-TW, MT-TY, NARS2, NDUFA1, NDUFA10 NDUFA11, NDUFAl2, NDUFA2, NDUFA4, NDUFA9, NDUFAF1, NDUFAF2, NDUFAF3, NDUFAF4, NDUFAF7, NDUFB11, NDUFB3, NDUFB9, NDUFS1, NDUFS2, NDUFS3, NDUFS4, NDUFS6, NDUFS7, NDUFSB, NDUFVI, NDUFV2, NFS1, NFU1, NR2F1, NUBPL, OPA1, OPA3, OTC, PARS2, PC, PCCA, PCCB, PDHA1, PDHB, PDHX, PDP1, PDSS1, PDSS2, PET100, PNPT1, POLG, POLG2, PRKAG2, PUS1, OARS, RARS, RARS2, RMND1, RNASEH1, RRM2B, SARSZ SCOT, SCO2, SDHA, SDHAF1, SERACI, SFXN4, SLC19A2, SLCI9A3, SLC22A5, SLC25A26, SLC25A3, SLC25A38, SLC25A4, SLC25A46, SPAST, SPG7, SUCLA2, SUCLG1, SURF1, TACO1, TARS2, TAZ, TFAM, TIMM8A, TK2, TMEM126A, TMEM126B, TMEM70, TPK1, TRIT1, TRMTICC, TRMU, TRNT1, TSFM, TTC19, TUFM, TWNK, TYMP, UOCC2, UOCC3, UOCRB, UOCRC2, UQCRQ, VARS2, WDR45, WFS1, YARS2 |
| Panel G (18 genes) | ADRA2B, ASAH1, CLN3, CLN5, CLN6, CLN8, CSTB, EPM2A, GOSR2, GRN, IRF2BPL, KCTD7, MFSD8, NHLRC1, PPT1, PRICKLE1, SCARB2, TPP1 |
| Panel H (91 genes) | ADSL, ALDH7A1, ARHGEF9, ARX, ATP6AP2, ATRX, CACNA1A, CACNA1H, CACNB4, CASK, CASR, CDKLS, CHD2, CHRNA2, CHRNA4, CHRNB2, CLCN2, CNTN2, CNTNAP2, CPAS, CSTB, CUL4B, DCX, DEPDCS, DHFR, DNAJCS, DYNC1H1, EFHC1, CPM2A, FGO1, FOXG1, GABRA1, GABRB3, GABRD, GABRG2, GOSR2, GPC3, GRIA3, GRIN2A, HSD17B10, KANSL1, KCNC1, KCNJ10, KCNMA1, KCNQ2, KCNQ3, KCNT1, KCTD7, KOMSC, LGI1, MBD5, ME2, MECP2, MEF2C, NHLRC1, NIPA2, NPRL2, NPRL3, NRXN1, OFD1, OPHN1, PAK3, PCDH19, PHF6, PIGA, PLP1, PQBP1, PRICKLE1, PRICKLE2, PRRT2, RAB39B, ROGDI, SCARB2, SCN1A, SCN1B, SCN2A, SCN8A, SCN9A, SLC2A1, SLC9A6, SMC1A, SRPX2, STX1B, STXBP1, SYN1, SYNGAP1, SYP, TBC1D24, TCF4, UBE3A, ZED2 |

**Table S1: Description of genetic panel types.**

Panels A – E were comprehensive epilepsy panels. Panel F was a mitochondrial nuclear gene panel. Panel G was a progressive myoclonic epilepsy panel. Panel H was an idiopathic generalized epilepsy panel.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Identi-fication | InterprE-tation | Finding | Gene | Coding DNA | Variant | Zygosity | Panel type |
| GA | U | VUS | CLN3 | c.358 C>T | p.H120Y | Heterozygous | C | |
| PA | N | N |  |  |  |  | C | |
| SA | U | VUS | BRAT1 | c.424 G>A | p.D142N | Heterozygous | B | |
|  |  | VUS | POLG | c.488 C>T | p.P163L | Heterozygous |  | |
| MA | N | N |  |  |  |  | C | |
| FA | U | VUS | NPRL3 | c.1199 G>A | p.R400H | Heterozygous | B | |
|  |  | VUS | NRXN1 | c.259 G>T | p.A87S | Heterozygous |  | |
|  |  | VUS | PNKP | c.1381 A>C | p.N461H | Heterozygous |  | |
| AG | U | VUS | TCF4 | c.1318 G>A | p.G440S | Heterozygous | B | |
| AF | U | VUS | SLC13A5 | c.970 T>C | p.F324L | Heterozygous | B | |
|  |  | BV | POLG | c.3428 A>G | p.E1143G | Heterozygous |  | |
| AA | N | BV | POLG | c.3428 A>G | p.E1143G | Heterozygous | B | |
| MA2 | N | N |  |  |  |  | C | |
| LB | N | N |  |  |  |  | B | |
| JB | U | VUS | CNTNAP2 | c.1138 G>A | p.A380T | Heterozygous | A | |
| CB | N | N |  |  |  |  | B | |
| EC | U | VUS | CNTNAP2 | c.2945 A>G | p.E982G | Heterozygous | C | |
| PB | U | VUS | CACNA1A | c.3043 G>A | p.E1015K | Heterozygous | D | |
|  |  | VUS | SCN9A | c.2215 A>G | p.I739V | Heterozygous |  | |
| RB | U | VUS | GLDC | c.13 G>C | p.A5P | Heterozygous | A | |
| MB | U | VUS | KCNH1 | c.1022 G>A | p.R341K | Heterozygous | B | |
| NB | N | N |  |  |  |  | B | |
| KB | N | BV | POLG | c.3708 G>T | p.Q1236H | Heterozygous | C | |
| MB2 | U | VUS | MEF2C | c.752 G>A | p.R251H | Heterozygous | B | |
|  |  | VUS | NALCN | c.5164 C>T | p.R1722W | Heterozygous |  | |
| FB | **P** | **P** | POMT2 | c.1863\_1864:2 bp deletion of AG | Codon:621-622 deletion | Heterozygous | E | |
|  |  | VUS | CACNA1A | c.2283-5 (Isoform 1) T>A | | Heterozygous |  | |
|  |  | VUS | COL4A1 | c.553-10 T>C |  | Heterozygous |  | |
|  |  | VUS | LAMA2 | c.2289 G>A |  | Heterozygous |  | |
|  |  | VUS | ZEB2 | c.74-3 C>T |  | Heterozygous |  | |
| MB3 | N | N |  |  |  |  | B | |
| HB | N | N |  |  |  |  | B | |
| NB2 | N | N |  |  |  |  | C | |
| CB | U | VUS | CACNA1A | c.4646 C>T | p.P1549L | Heterozygous | B | |
| PB2 | U | VUS | POLG | c.752 C>T | p.T251I | Heterozygous | C | |
|  |  | VUS | POLG | c.1760 C>T | p.P587L | Heterozygous | | |
| EB | U | VUS | SLC2A1 | c.877 T>C | p.Y293H | Heterozygous | A | |
| BC | N | N |  |  |  |  | A | |
| MC | U | VUS | TCF4 | c.1489 A>G | p.M497V | Heterozygous | C | |
|  |  | BV | POLG | c.3708 G>T | p.Q1236H | Heterozygous | | |
| DC | N | N |  |  |  |  | C | |
| MC2 | N | BV | POLG | c.3708 G>T | p.Q1236H | Heterozygous | A | |
| MC3 | **P** | **LPV** | SZT2 | c.7702+5 G>A |  | Heterozygous | B | |
|  |  | VUS | POLG | c.3667 A>G | p.I1223V | Heterozygous | | |
| GC | N | N |  |  |  |  | B | |
| MC4 | U | VUS | CDKL5 | c.1850 G>T | p.R617L | Hemizygous | B | |
|  |  | VUS | KCNH1 | c.889 G>A | p.V297M | Heterozygous | | |
|  |  | VUS | SLC13A5 | c.1372 G>A | p.V458M | Heterozygous | | |
| CC | **P** | **PV** | SCARB2 | c.862 C>T | P.Q288X | Heterozygous | G | |
|  |  | VUS | SCARB2 | c.1187+2dupT | | Heterozygous | | |
| TC | N | N |  |  |  |  | B | |
| SC | N | BV | POLG | c.3708 G>T | p.Q1236H | Heterozygous | A | |
| NC | N | N |  |  |  |  | B | |
| NC2 | N | N |  |  |  |  | C | |
| MC5 | N | N |  |  |  |  | B | |
| MC6 | U | VUS | CACNA1A | c.3043 G>A | p.E1015K | Heterozygous | D | |
|  |  | VUS | TBC1D24 | c.554\_559: 6 bp deletion | Codon:185-187 deletion | Heterozygous | | |
| DC | N | N |  |  |  |  | B | |
| CC2 | U | VUS | EPM2A | c.488 A>G | p.N163S | Heterozygous | B | |
|  |  | BV | POLG | c.3708 G>T | p.Q1236H | Heterozygous | | |
| DP | U | VUS | UBE3A | c.2342 T>A | p.L781H | Heterozygous | B | |
|  |  | VUS | CTSD | c.353-8 C>G |  | Heterozygous | | |
|  |  | BV | POLG | c.3428 A>G | p.E1143G | Heterozygous | | |
| DB | N | N |  |  |  |  | C | |
| ND | U | VUS | POLG | c.3667 A>G | p.I1223V | Heterozygous | C | |
| JD | U | VUS | SCARB2 | c.445 G>A | p.V149M | Heterozygous | D | |
| JD2 | U | VUS | SCN1B | c.38 T>C | p.L13P | Heterozygous | B | |
| SD | N | N |  |  |  |  | B | |
| JD3 | U | VUS | ALDH7A1 | c.1567 A>G | p.T523A | Heterozygous | D | |
| AD | N | N |  |  |  |  | B | |
| MD | N | N |  |  |  |  | B | |
| CD | N | BV | POLG | c.3428 A>G | p.E1143G | Heterozygous | C | |
| RD | U | VUS | NPRL3 | c.858 G>A | p.G320S | Heterozygous | A | |
|  |  | VUS | BRAT1 | c.1451 C>G | p.T484S | Heterozygous | | |
| SD | N | N |  |  |  |  | B | |
| DD | U | VUS | ME2 | c.1230 C>T |  | Heterozygous | D | |
| FD | U | VUS | POLG | c.3436 C>T | p.R1146C | Heterozygous | C | |
| JD3 | U | VUS | PIGV | c.1369 C>T | p.L457F | Heterozygous | C | |
| TD | U | VUS | GABRB2 | c.1061 G>A | p.R354H | Heterozygous | C | |
|  |  | VUS | WWOX | c.1178 C>T | p.T393M | Heterozygous | | |
| AF2 | N | N |  |  |  |  | C | |
| AF3 | U | VUS | SCN2A | c.1421 T>A | p.F474Y | Heterozygous | B | |
| MF | N | N |  |  |  |  | B | |
| AF4 | N | N |  |  |  |  | A | |
| MG | U | VUS | DEPDC5 | c.3780 A>G | p.Il260M | Heterozygous | B | |
| NG | N | N |  |  |  |  | D | |
| AG2 | **P** | **PV** | CSTB | c.67-1 G>C | IVS1-1 G>C | Heterozygous | B | |
|  |  | VUS | KNCT1 | c.2713 G>A | p.V905M | Heterozygous | | |
|  |  | VUS | POLG | c.830 A>T | p.H277L | Heterozygous | | |
|  |  | VUS | SPATA5 | c.398 C>T | p.P133L | Heterozygous | | |
| DG | N | N |  |  |  |  | B | |
| SG | N | BV | POLG | c.3708 G>T | p.Q1236H | Heterozygous | B | |
| MG2 | N | N |  |  |  |  | C | |
| MG3 | U | VUS | DEPDC5 | c.1265 G>A | p.R422Q | Heterozygous | D | |
| SG2 | N | N |  |  |  |  | B | |
| SG3 | U | VUS | EHMT1 | c.3686 C>G | p.T1229S | Heterozygous | B | |
| SG4 | U | VUS | GABRD | c.1105 G>A | p.G369S | Heterozygous | D | |
| NG2 | U | VUS | ATP1A2 | c.1474 G>A | p.E492K | Heterozygous | B | |
| BG | U | VUS | HNRNPU | c.1369 T>C | p.F457L | Heterozygous | B | |
| FG | **P** | **LPV** | NALCN | Exon 27 deletion |  | Heterozygous | B | |
| MG4 | U | VUS | CACNA1A | c.3625 G>A | p.D1209N | Heterozygous | A | |
| VG | U | VUS | PNKP | c.1252 C>T | p.R418W | Heterozygous | B | |
| CG | U | VUS | SPTAN1 | c.5281 C>T | p.R1761W | Heterozygous | B | |
| AG | N | N |  |  |  |  | B | |
| MG5 | N | N |  |  |  |  | D | |
| DG | N | N |  |  |  |  | D | |
| RH | P | **PV** | ADSL | c.1342 T>C | p.S448P | Heterozygous | C | |
| SH | **P** | **LPV** | DEPDC5 | c.2527 C>T | p.R843X | Heterozygous | A | |
|  |  | VUS | CUL4B | c.1000 G>A | p.A334T | Heterozygous | | |
| DH | U | VUS | SCARB2 | c.995-7 A>G | IVS7-7 A>G | Heterozygous | C | |
| AH | U | VUS | WWOX | c.928 C>T | p.R310C | Heterozygous | C | |
|  |  | VUS | SLC13A5 | c.485\_487dupCAA | p.T162dup | Heterozygous | | |
| TH | **P** | **PV** | PCDH19 | Whole gene deletion |  | Heterozygous | A | |
| SH | N | N |  |  |  |  | B | |
| MJ | U | VUS | NALCN | c.1276 A>T | p.T426S | Heterozygous | B | |
|  |  | VUS | CSTB | c.167 A>G | p.K56R | Heterozygous | | |
|  |  | VUS | PIGO | c.2929 G>A | p.G977R | Heterozygous | | |
| GJ | N | N |  |  |  |  | A | |
| JJ | U | VUS | BRAT1 | c.1012 C>T | p.P338S | Heterozygous | B | |
|  |  | VUS | CNTNAP2 | c.136 G>A | p.V46M | Heterozygous | | |
|  |  | VUS | POLG | c.1837 C>T | p.H613Y | Heterozygous | | |
| ML | U | VUS | NRXN1 | c.262 C>G | p.R88G | Heterozygous | B | |
| JL | U | VUS | POLG | c.1772 T>G | p.L591R | Heterozygous | A | |
| ML2 | N | N |  |  |  |  | C | |
| RL | N | N |  |  |  |  | A | |
| ML3 | N | N |  |  |  |  | D | |
| GL | U | VUS | NALCN | c.4940 T>C | p.L1647P | Heterozygous | B | |
| DL | U | VUS | CACNA1A | c.6128 C>T | p.T3043M | Heterozygous | B | |
|  |  | BV | POLG | c.3708 G>T | p.Q1236H | Heterozygous | | |
| SL | N | N |  |  |  |  | C | |
| ML4 | N | N |  |  |  |  | B | |
| GL | **P** | **LPV** | LGI1 | c.388delA | p.I30FfsX9 | Heterozygous | C | |
| ML5 | N | N |  |  |  |  | B | |
| TL | U | VUS | TSC2 | c.4256 A>G | p.Q1419R | Heterozygous | B | |
|  |  | VUS | BRAT1 | c.1765 C>T | p.R589W | Heterozygous | | |
| PL | P | **PV** | ADSL | c.1342 T>C | p.S448P | Heterozygous | B | |
| YL | **P** | **LPV** | SZT2 | c.6553 C>T | p.R2185W | Heterozygous | B | |
| GL2 | U | VUS | SLC13A5 | c.1366 G>A | p.V456I | Heterozygous | C | |
| SL2 | N | N |  |  |  |  | D | |
| IL | U | VUS | GABRA1 | c.188 A>C | p.E63A | Heterozygous | C | |
|  |  | VUS | CNTNAP2 | c.2945 A>G | p.E982G | Heterozygous | | |
| DM | U | VUS | CACNA1A | c.1902 (Isoform 1) A>G | | Heterozygous | C | |
| SM | N | N |  |  |  |  | B | |
| CM | N | N |  |  |  |  | B | |
| LM | U | VUS | PNKP | c.1510delC | p.R504GfsX? | Heterozygous | B | |
|  |  | BV | POLG | c.3428 A>G | p.E1143G | Heterozygous | | |
| EM | N | N |  |  |  |  | B | |
| GM | N | N |  |  |  |  | C | |
| BM | N | VUS | DYRK1A | c.1471 A>C | p.N491H | Heterozygous | C | |
|  |  | VUS | ADSL | c,56 C>G | p.S19C | Heterozygous | | |
| MB4 | N | N |  |  |  |  | B | |
| AN | U | VUS | SZT2 | c.8207 A>G | p.H2736R | Heterozygous | B | |
|  |  | BV | POLG | c.3708 G>T | p.Q1236H | Heterozygous | | |
| AO | U | VUS | SCN2A | c.2046 G>T | p.K682N | Heterozygous | B | |
|  |  | VUS | TPP1 | c.1598 G>A | p.G533D | Heterozygous | | |
| UO | U | VUS | SCN2A | c.2046 G>T | p.K682N | Heterozygous | A | |
| VP | N | N |  |  |  |  | A | |
| SP | U | VUS | KCNB1 | c.2180 C>G | p.T727S | Heterozygous | C | |
|  |  | VUS | PNPO | c.322 C>T | p.R108C | Heterozygous | | |
| NP | U | VUS | CLN5 | c.434 G>A | p.R145Q | Heterozygous | B | |
|  |  | VUS | NHLRC1 | c.713 C>T | p.S238F | Heterozygous | | |
| PP | U | VUS | SCN2A | c.3412 A>G | p.T1138A | Heterozygous | C | |
| BP | **P** | **LPV** | GLDC | Deletion of exon(s) 12-16 | | Heterozygous | A | |
| BP2 | U | VUS | KCNQ2 | c.1505 C>T | p.A502V | Heterozygous | C | |
| CP | U | VUS | PIGV | c.808 C>T | p.R270C | Heterozygous | C | |
| EP | **P** | **PV** | CSTB | c.671 G>C | IVS1-1 C>G | Heterozygous | B | |
| AP | N | BV | POLG | c.3708 G>T | p.Q1236H | Heterozygous | B | |
| JP | U | VUS | ADSL | c.1016 T>A | p.I339N | Heterozygous | B | |
| JP2 | U | VUS | PIGN | c.1117 G>T | p.V373L | Heterozygous | B | |
|  |  | VUS | SLC13A5 | c.1052 C>A | p.T351K | Heterozygous | | |
| VP | N | N |  |  |  |  | B | |
| LP | U | VUS | WWOX | c.928 C>T | p.R310C | Heterozygous | C | |
| FP | U | VUS | CHRNB2 | c.1336 A>G | p.S446G | Heterozygous | D | |
| SR | N | N |  |  |  |  | C | |
| CR | P | **PV** | ALDH7A1 | c.1513 G>C | p.G505R | Heterozygous | C | |
| JR | U | VUS | SLC6A1 | c.1717 C>T | p.P573S | Heterozygous | A | |
|  |  | BV | POLG | c.3708 G>T | p.Q1236H | Heterozygous | | |
| LR | N | BV | POLG | c.3428 A>G | p.E1143G | Heterozygous | C | |
| SR2 | U | VUS | CACNA1A | c.3439 (Isoform 1) G>A | p.V1147I | Heterozygous | D | |
|  |  | VUS | GRIN2A | c.1675 G>A | p.V559M | Heterozygous | | |
|  |  | VUS | KNCMA1 | c.1224-4 T>A |  | Heterozygous | | |
| NS | U | VUS | BRAT1 | c.2029 G>A | p.V557M | Heterozygous | B | |
|  |  | VUS | GLDC | c.446 G>A | p.R149Q | Heterozygous | | |
| LS | **P** | **PV** | SCN1A | c.3985 C>T | p.R1329X | Heterozygous | B | |
|  |  | VUS | MFSD8 | c.931 A>G | p.I311V | Heterozygous | | |
|  |  | VUS | GLDC | c.2299 A>G | p.M767V | Heterozygous | | |
| PS | N | N |  |  |  |  | B | |
| CS | N | BV | POLG | c.3708 G>T | p.Q1236H | Heterozygous | B | |
| SS | U | VUS | KCNT1 | c.2388 C>T |  | Heterozygous | D | |
| DS | U | VUS | COL18A1 | c.1341\_1358 (Isoform 2): 18 bp deletion | Codon:447-453 | Heterozygous | D | |
|  |  | VUS | COL18A1 | c.2623 (Isoform 2) A>G | p.N875D | Heterozygous | | |
| SS2 | U | VUS | BRAT1 | c.1354 G>C | p.V452L | Heterozygous | A | |
|  |  | VUS | DOCK7 | c.1254 T>A | p.D418E | Heterozygous | | |
|  |  | VUS | MFSD8 | c.206 C>T | p.P69L | Heterozygous | | |
| GS | **P** | **PV** | MT-TL1 | m.3243 A>G |  |  | F | |
| DS2 | N | BV | POLG | c.3708 G>T | p.Q1236H | Homozygous | B | |
| SS3 | U | VUS | NRXN1 | c.2495-10 T>A | IVS13-10 T>A | Heterozygous | B | |
|  |  | VUS | ASNS | c.904-6 A>G | IVS7-6 A>G | Heterozygous | | |
| MT | U | VUS | KCNT1 | c.1911 C>G | p.F637L | Heterozygous | B | |
| AT | U | VUS | FLNA | c.1114 G>T | p.V372L | Heterozygous | A | |
|  |  | VUS | SMARCA2 | c.2082 T>G | p.S694R | Heterozygous | | |
| ST | N | BV | POLG | c.3428 A>G | p.E1143G | Heterozygous | B | |
| ST2 | U | VUS | CHRNA2 | c.247 G>A | p.V83M | Heterozygous | B | |
|  |  | VUS | NALCN | c.5185 G>T | p.D1729Y | Heterozygous | | |
| TV | P | **PV** | POLG | c.2890 C>T | p.R964C | Heterozygous | C | |
| EV | N | N |  |  |  |  | A | |
| PV | U | VUS | STX1B | c.428 G>A | p.R143H | Heterozygous | B | |
| TW | **P** | **PV** | CHRNA7 | 15q13.3 deletion | | Heterozygous | A | |
| GZ | N | N |  |  |  |  | B | |
|  |  |  |  |  |  |  |  | |
|  |  |  |  |  |  |  |  | |
| JC | U | VUS | FRRS1L | c.893 C>T | p.P298L | Heterozygous | A | |
|  |  | VUS | NHLRC1 | c.730 G>T | p.V244F | Heterozygous | | |
| ML6 | N | N |  |  |  |  | A | |
| HU | N | N |  |  |  |  | B | |
| EC | U | VUS | EHMT1 | c.2791 G>A | p.D931N | Heterozygous | A | |
|  |  | VUS | GLDC | c,698 T>C | p.V233A | Heterozygous | | |
| MG6 | U | VUS | DEPDC5 | c.233G>C | p.R78P | Heterozygous | H | |
| KV | U | VUS | SLC4A10 | c.766+8 T>C |  | Heterozygous | D | |
| SB | U | VUS | ME2 | c.1230 C>T |  | Heterozygous | D | |
| AC | U | VUS | SCN1A | c.4002+6 A>G |  | Heterozygous | D | |

**Table S2: All genetic panel findings and interpretations**

BV = benign variant; LPV = likely pathogenic variant; N = negative; P = positive; PV = pathogenic variant; VUS = variant of unknown significance.

Panels A – E were comprehensive epilepsy panels. Panel F was a mitochondrial nuclear gene panel. Panel G was a progressive myoclonic epilepsy panel. Panel H was an idiopathic generalized epilepsy panel.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Authors | Year | Sample description | Sample size | Intellectual disability | Positive family history | Refractory epilepsy | Yield of positive results | Diagnostic yield | Clinical actionability |
| Li et al.  (our study) | 2022 | Adults with epilepsy of unknown etiology followed by an epileptologist at a tertiary care center who consented to an epilepsy gene panel | 164 | 10% | 11% | 80% | 11% | 4.3% | 71% of diagnoses |
| McKnight et al. (1) | 2022 | Adults referred to genetic testing using the Invitae Epilepsy Panel from October 2015 through March 2020 | 2,008 | ≥ 21.8% | ≥ 29.8% | ≥ 39.7% | - | 10.9% | 55.5% of diagnoses |
| Johannesen et al. (2) | 2020 | Adults referred for genetic testing at the Danish Epilepsy Center from 2013 to 2018 | 200 | 91% | - | - | 23% (unclear if positivity yield or diagnostic yield) | | 17% of positive findings |
| Borlot et al. (3) | 2019 | Patients reported in this study were included in the newer study by McKnight et al. | | | | | | | |

**Table S3: Summary description of studies reporting on the usage of genetic panels in adults with epilepsy**

Only three studies describing the yield of genetic panels in adults with epilepsy exist to our knowledge (without counting our study). McKnight et al.’s study cohort contained the individuals reported in Borlot et al.’s study, so information on Borlot et al.’s study was omitted to avoid redundancy.

1. McKnight D, Bristow SL, Truty RM, et al. Multigene Panel Testing in a Large Cohort of Adults With Epilepsy: Diagnostic Yield and Clinically Actionable Genetic Findings. Neurol Genet. 2022;8(1):e650.

2. Johannesen KM, Nikanorova N, Marjanovic D, et al. Utility of genetic testing for therapeutic decision-making in adults with epilepsy. Epilepsia. 2020;61(6):1234-9.

3. Borlot F, de Almeida BI, Combe SL, Andrade DM, Filloux FM, Myers KA. Clinical utility of multigene panel testing in adults with epilepsy and intellectual disability. Epilepsia. 2019;60(8):1661-9.