|  |  |
| --- | --- |
| 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.