

Table 1 – General information of patients genetics, walking ability and the presence of cortical malformation, intellectual disability an epilepsy – Supplementary data

| P  | DOB        | Sex | First variant                      | ACMG              | Second variant                            | ACGM              | Cortical malformation | LG domain ? | Walks | Intellectual disability | Epilepsy | Type of variant | Missense predictors      |
|----|------------|-----|------------------------------------|-------------------|---|-------------------|-----------------------|-------------|-------|-------------------------|----------|-----------------|--------------------------|
| 1  | 08/11/2011 | F   | c.1255del p.(Ile419Leufs*4)        | Pathogenic        | c.4740_4741insG p.(Leu1581Profs*5)        | Pathogenic        | No                    | No          | No    | No                      | No       | LOF/LOF         |                          |
| 2  | 01/06/2015 | F   | c.3235T>C p.(Cys1079Arg)           | Likely Pathogenic | c.3976C>T p.(Arg1326*)                    | Pathogenic        | No                    | No          | No    | No                      | No       | LOF/MIS         | CADD Polyphen pathogenic |
| 3  | 03/09/2013 | F   | c.7581C>A p.(Tyr2506*)             | Pathogenic        | NA  | NA                | No                    | Yes         | Yes   | No                      | No       | LOF/NA          |                          |
| 4  | 30/07/2012 | F   | c.2049_2059del p.(Arg683Serf*21)   | Pathogenic        | c.2461A>C p.(Thr821Pro)                   | Pathogenic        | No                    | No          | Yes   | No                      | No       | LOF/MIS         | CADD, Polyphen uncertain |
| 5  | 03/11/1994 | F   | c.1255del p.(Ile419Leufs*4)        | Pathogenic        | c.1255del p.(Ile419Leufs*4)               | Pathogenic        | No                    | No          | Yes   | No                      | No       | LOF/LOF         |                          |
| 6  | 23/08/2013 | F   | c.1255del p.(Ile419Leufs*4)        | Pathogenic        | c.1255del p.(Ile419Leufs*4)               | Pathogenic        | No                    | No          | No    | No                      | No       | LOF/LOF         |                          |
| 7  | 25/02/2013 | M   | c.4960-17C>A                       | Likely Pathogenic | c.4960-17C>A                              | Likely Pathogenic | Yes                   | No          | No    | Yes                     | No       | LOF/LOF         |                          |
| 8  | 27/01/2006 | F   | c.2049_2059del p.(Arg683Serf*21)   | Pathogenic        | c.4960-17C>A                              | Likely Pathogenic | No                    | No          | No    | No                      | No       | LOF/NA          |                          |
| 9  | 27/02/1998 | M   | c.3976C>T p.(Arg1326*)             | Pathogenic        | c.1128_1129insG p.(Tyr2527Ter)            | Pathogenic        | Yes                   | No          | No    | No                      | Yes      | LOF/LOF         |                          |
| 10 | 03/03/2014 | F   | c.3235T>C p.(Cys1079Arg)           | Pathogenic        | Exons 2-9 deletion                        | Pathogenic        | No                    | No          | Yes   | Yes                     | No       | LOF/CNV         |                          |
| 11 | 12/06/2014 | F   | c.2049_2059del p.(Arg683Serf*21)   | Pathogenic        | c.8244+1G>A                               | Pathogenic        | No                    | Yes         | No    | No                      | No       | LOF/LOF         |                          |
| 12 | 08/08/2018 | M   | c.4536_4537del p.(Thr1514Trpfs*14) | Likely Pathogenic | Exon 11 c.1590delins32 p.(Tyr531Glyfs*27) | Pathogenic        | No                    | No          | No    | No                      | No       | LOF/LOF         |                          |
| 13 | 25/09/2007 | F   | c.3085C>T p.(Arg1029*)             | Pathogenic        | c.4176+1G>A                               | Likely Pathogenic | No                    | No          | No    | No                      | No       | LOF/LOF         |                          |
| 14 | 12/04/1    | F   | c.1255del                          | Pathogenic        | c.1255del                                 | Pathogenic        | No                    | No          | No    | No                      | No       | LOF/LO          |                          |

|    |            |   |                                  |                   |                                       |                   |     |     |     |     |     |     |         |                             |
|----|------------|---|----------------------------------|-------------------|---------------------------------------|-------------------|-----|-----|-----|-----|-----|-----|---------|-----------------------------|
|    | 999        |   | p.(Ile419Leufs*4)                | c                 | p.(Ile419Leufs*4)                     | c                 |     |     |     |     |     |     | F       |                             |
| 15 | 05/07/2012 | M | c.3976C>T<br>p.(Arg1326*)        | Pathogenic        | c.8244+1G>A                           | Pathogenic        | No  | Yes | Yes | No  | No  | No  | LOF/LOF |                             |
| 16 | 22/01/2009 | M | c.1255del<br>p.(Ile419Leufs*4)   | Pathogenic        | c.5651G>A<br>p.Arg1884Lys             | VUS               | No  | No  | No  | No  | No  | No  | LOF/MIS | CADD,<br>Polyphen<br>benign |
| 17 | 01/10/2009 | M | c.8556_8558del<br>(p.Ile2852del) | Likely Pathogenic | c.8556_8558del<br>(p.Ile2852del)      | Likely Pathogenic | Yes | Yes | No  | Yes | Yes | Yes | LOF/LOF |                             |
| 18 | 24/03/2017 | F | c.3976C>T<br>p.(Arg1326*)        | Pathogenic        | c.5234+1G>A                           | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/LOF |                             |
| 19 | 30/10/2011 | F | c.3085C>T<br>p.(Arg1029*)        | Pathogenic        | c.4960-17C>A                          | Likely Pathogenic | No  | No  | No  | No  | No  | No  | LOF/NA  |                             |
| 20 | 23/10/2008 | F | c.7732C>T<br>p.(Arg2578*)        | Pathogenic        | c.7732C>T<br>p.(Arg2578*)             | Pathogenic        | No  | Yes | No  | No  | Yes | Yes | LOF/LOF |                             |
| 21 | 24/03/2010 | M | c.5234+1G>A                      | Pathogenic        | Exon 56 deletion                      | Pathogenic        | Yes | No  | No  | Yes | Yes | Yes | LOF/CNV |                             |
| 22 | 24/04/1998 | F | c.3085C>T<br>p.(Arg1029*)        | Pathogenic        | c.5234+1G>A                           | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/LOF |                             |
| 23 | 01/06/2015 | F | Exon 56 deletion                 | Pathogenic        | Exon 15 deletion                      | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/CNV |                             |
| 24 | 02/01/2009 | F | c.1255del<br>p.(Ile419Leufs*4)   | Pathogenic        | c.1854_1861dup<br>p.(leu621fs)        | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/LOF |                             |
| 25 | 17/02/2009 | M | c.5234+1G>A                      | Pathogenic        | 117bpDUP (Exon 38)                    | Pathogenic        | No  | No  | No  | No  | Yes | Yes | LOF/LOF |                             |
| 26 | 23/04/2017 | F | c.8244+1G>A                      | Pathogenic        | c.6191del<br>p.(Gly2064fs*2)          | Pathogenic        | No  | Yes | No  | No  | No  | No  | LOF/LOF |                             |
| 27 | 17/10/2011 | M | c.5234+1G>A                      | Pathogenic        | c.391C>T<br>p.(Gln131*)               | Pathogenic        | No  | No  | No  | Yes | No  | No  | LOF/LOF |                             |
| 28 | 29/09/2006 | F | Exon 56 deletion                 | Pathogenic        | Exon 56 deletion                      | Pathogenic        | No  | No  | Yes | No  | No  | No  | CNV/CNV |                             |
| 29 | 17/06/2008 | F | c.1255del<br>p.(Ile419Leufs*4)   | Pathogenic        | c.4740_4741insG<br>p.(Leu1581Profs*5) | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/LOF |                             |
| 30 | 11/06/2012 | F | c.1255del<br>p.(Ile419Leufs*4)   | Pathogenic        | c.8244+1G>A                           | Pathogenic        | Yes | Yes | No  | No  | Yes | Yes | LOF/LOF |                             |
| 31 | 21/03/2009 | F | c.3372dup<br>p.(Cys1125Metfs*)   | Pathogenic        | c.9168_9169dup<br>p.(Ser3057Tyrfs*23) | Pathogenic        | No  | Yes | No  | No  | No  | No  | LOF/LOF |                             |
| 32 | 22/04/2014 | M | c.363C>A<br>p.(Tyr121*)          | Pathogenic        | c.4739dup<br>p.(Leu1581Profs*)        | Pathogenic        | No  | No  | No  | Yes | No  | No  | LOF/LOF |                             |

|    |            |   |                                    |            |                                  |                   |     |     |     |     |     |     |         |                          |
|----|------------|---|------------------------------------|------------|----------------------------------|-------------------|-----|-----|-----|-----|-----|-----|---------|--------------------------|
|    |            |   |                                    |            | 5)                               |                   |     |     |     |     |     |     |         |                          |
| 33 | 21/08/2012 | M | c.4739dup p.(Leu1581Profs*5)       | Pathogenic | Exon 1 deletion                  | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/CNV |                          |
| 34 | 30/08/2010 | M | c.5234+1G>A                        | Pathogenic | c.2461A>G p.(Thr821Pro)          | Pathogenic        | No  | No  | Yes | No  | No  | No  | LOF/MIS | CADD, Polyphen uncertain |
| 35 | 13/10/2009 | M | c.3976C>T p.(Arg1326*)             | Pathogenic | c.5234+1G>A                      | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/LOF |                          |
| 36 | 09/02/2016 | M | c.1255del p.(Ile419Leufs*4)        | Pathogenic | c.8556_8558del p.(Ile2852del)    | Likely Pathogenic | No  | Yes | No  | No  | No  | No  | LOF/LOF |                          |
| 37 | 03/02/1995 | M | c.4348C>T p.(Arg1450*)             | Pathogenic | c.9223C>T p.(Gln3075*)           | Pathogenic        | Yes | Yes | No  | No  | Yes | Yes | LOF/LOF |                          |
| 38 | 15/02/1998 | F | c.2461A>G p.(Thr821Pro)            | Pathogenic | c.5578C>T p.(Gln1860*)           | Likely pathogenic | No  | No  | Yes | No  | No  | No  | LOF/MIS | CADD, Polyphen uncertain |
| 39 | 07/07/2007 | F | c.8244+1G>A                        | Pathogenic | c.8244+1G>A                      | Pathogenic        | Yes | Yes | No  | No  | Yes | Yes | LOF/LOF |                          |
| 40 | 21/03/2012 | M | c.1255del p.(Ile419Leufs*4)        | Pathogenic | Exon 56 deletion                 | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/CNV |                          |
| 41 | 15/03/2004 | M | c.1255del p.(Ile419Leufs*4)        | Pathogenic | c.4888G>T p.(Glu1630*)           | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/LOF |                          |
| 42 | 09/09/2015 | M | c.363C>A p.(Tyr121*)               | Pathogenic | Lacks second variant             | NA                | No  | No  | No  | No  | No  | No  | LOF/NA  |                          |
| 43 | 15/08/2019 | F | c.3976C>T p.(Arg1326*)             | Pathogenic | c.3976C>T p.(Arg1326*)           | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/LOF |                          |
| 44 | 02/01/2015 | F | c..2486_2489del p.(Leu830Serfs*57) | Pathogenic | Exon 1 deletion                  | Pathogenic        | Yes | No  | No  | Yes | Yes | Yes | LOF/CNV |                          |
| 45 | 05/08/2019 | M | c.3976C>T p.(Arg1326*)             | Pathogenic | c.3976C>T p.(Arg1326*)           | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/LOF |                          |
| 46 | 12/10/2017 | F | c.2049_2059del p.(Arg683Serf*21)   | Pathogenic | c.8164G>A p.Ala2722Thr           | VUS               | No  | Yes | No  | No  | No  | No  | LOF/MIS | CADD, Polyphen benign    |
| 47 | 15/12/2017 | F | c.4739dup p.(Leu1581Profs*5)       | Pathogenic | c.2049_2059del p.(Arg683Serf*21) | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/LOF |                          |
| 48 | 08/04/2019 | F | c.3976C>T p.(Arg1326*)             | Pathogenic | c.3235T>C p.(Cys1079Arg)         | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/MIS |                          |
| 49 | 08/01/2    | F | c.2049_2059del                     | Pathogenic | Exons 3-4                        | Pathogenic        | No  | No  | No  | No  | No  | No  | LOF/CN  |                          |

|    |            |   |                                  |            |                                 |            |     |     |    |     |     |         |                                |  |
|----|------------|---|----------------------------------|------------|---------------------------------|------------|-----|-----|----|-----|-----|---------|--------------------------------|--|
|    | 020        |   | p.(Arg683Serf*21)                | c          | deletion                        | c          |     |     |    |     |     |         | V                              |  |
| 50 | 14/12/2020 | M | c.4739dup<br>p.(Leu1581Profs*5)  | Pathogenic | c.4739dup<br>p.(Leu1581Profs*5) | Pathogenic | No  | No  | No | No  | No  | No      | LOF/LOF                        |  |
| 51 | 01/02/2020 | M | c.7147C>T<br>p.(Arg2383*)        | Pathogenic | c.4523G>A<br>p.(Arg1508Lys)     | Pathogenic | Yes | Yes | No | No  | No  | LOF/MIS | CADD,<br>Polyphen<br>uncertain |  |
| 52 | 03/07/2008 | M | c.8775del<br>p.(His2926Metfs*35) | Pathogenic | c.3955C>T<br>p.(Arg1319*)       | Pathogenic | Yes | Yes | No | Yes | Yes | LOF/LOF |                                |  |