**Table S1.** Molecular and electrophysiological findings of patients without PMP22 duplication (n=34).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **No** | **Clinical** | **Type** | **Gene** | **Reference Sequence** | **Nucleotide  change** | **Amino acid  change** | **Zygosity** | **Parental Mutation Status** | **Inheritance** | **ACMG classificationa** | **Affected  family  member** | **MNCV  ulnar/  median  nerve** | **CMAP  ulnar/ median  nerve** | **SNAP  ulnar/ median  nerve** | **SNAP  radial nerve** | **SNAP  sural nerve** |
| 1 | HSMN | De | *EGR2* | NM\_000399.5 | c.925C>T | p.Arg309Trp | heterozygous | Not confirmed | AD | Pathogenic | No | 24/14 | 1/1 | NR/NR | NR | NR |
| 2\* | HSMN | De | *HK1* | NM\_000188.3 | c.1A>G | p.(Met1?) | homozygous | Not confirmed | AR | Likely pathogenic | No | 30/28 | 2/2 | 40.8/- | - | - |
| 3 | HSMN | De | *MPZ* | NM\_000530.8 | c.245A>G | p.Tyr82Cys | heterozygous | *De novo* | AD | Pathogenic | No | 11/15 | 1/0.8 | -/- | - | NR |
| 4 | HSMN | De | *MPZ* | NM\_000530.8 | c.551del | p.Leu184Hisfs\*68 | heterozygous | *De novo* | AD | Pathogenic | No | 6/6 | 3/1 | NR/- | NR | NR |
| 5 | HSMN | De | *NEFL* | NM\_006158.5 | c.293A>G | p.Asn98Ser | heterozygous | *De novo* | AD | Pathogenic | No | 30/31 | 3/6 | -/- | NR | NR |
| 6 | HSMN | De | *NEFL* | NM\_006158.5 | c.280C>T | p.Leu94Phe | heterozygous | *De novo* | AD | Likely pathogenic | No | 29/33 | 3/5 | NR/NR | - | NR |
| 7 | HSMN | De | *NEFL* | NM\_006158.5 | c.280C>T | p.Leu94Phe | heterozygous | *De novo* | AD | Likely pathogenic | No | 26/30 | 3/3 | 7.5/5 | - | NR |
| 8 | HSMN | De | *PMP2* | NM\_002677.5 | c.155T>C | p.Ile52Thr | heterozygous | *Assume de novo* (only maternal confirmed) | AD | Pathogenic | Yes | 21.2/20.3 | 3.6/1.9 | -/- | 20.3 | - |
| 9\* | HSMN | De | *SH3TC2* | NM\_024577.4 | c.929dup | p.Ser312Valfs\*18 | homozygous | Paternal and maternal allele | AR | Pathogenic | No | 23.2/21.9 | 2.5/28 | NR/NR | - | NR |
| 10 | HSMN | De | unknown |  |  |  |  |  |  |  | No | 33/28 | 0.3/1.5 | NR/NR | - | - |
| 11 | HSMN | Ax | *GDAP1* | NM\_018972.4 | c.368A>G | p.His123Arg | heterozygous | Not confirmed | AD | Pathogenic | No | 55/- | 5/- | -/- | 28 | 6 |
| 12 | HSMN | Ax | *GDAP1* | NM\_001040875.4 | c.563A>G | p.His188Arg | heterozygous | Paternal allele | AD | Pathogenic | No | 47/67 | 1/3 | 32.2/16.6 | - | - |
| 13 | HSMN | Ax | *IGHMBP2* | NM\_002180.3 | c.547+1G>A | p.? | heterozygous | Not confirmed | AR | Pathogenic | No | NR/36 | NR/0.2 | NR/NR | - | NR |
| 14 | HSMN | Ax | *IGHMBP2* | NM\_002180.3 | c.983\_987del | p.Lys328Thrfs\*46 | heterozygous (trans phase) | Not confirmed | AR | Pathogenic | No | -/- | -/- | -/- | - | - |
| 15 | HSMN | Ax | *IGHMBP2* | NM\_002180.3 | c.2773del | p.His925Thrfs\*53 | heterozygous (trans phase) | Maternal allele | AR | Pathogenic | No | 44/- | 0.3/- | NR/NR | - | - |
| NM\_002180.3 | c.2362C>T | p.Arg788Ter | Paternal allele | Pathogenic |
| 16 | HSMN | Ax | *MFN2* | NM\_014874.4 | c.272T>G | p.Val91Gly | heterozygous | Assume *de novo* (only paternal confirmed) | AD | Likely Pathogenic | No | -/- | -/- | 5.9/43.2 | - | - |
| 17 | HSMN | Ax | *MFN2* | NM\_014874.4 | c.280C>T | p.Arg94Trp | heterozygous | Not confirmed | AD | Pathogenic | Yes | 50.5/51.4 | 4.6/4.4 | 4.3/- | - | - |
| 18 | HSMN | Ax | *MFN2* | NM\_014874.4 | c.430G>A | p.Ala144Thr | heterozygous (trans phase) | Maternal allele | AD/  AR | VUS | No | 46/41 | 5/3 | NR/NR | - | - |
| NM\_014874.4 | c.707C>T | p.Thr236Met | Not confirmed | Pathogenic |
| 19 | HSMN | Ax | *MFN2* | NM\_014874.4 | c.617C>T | p.Thr206Ile | heterozygous | Inherited from mother | AD | Pathogenic | Yes | -/48 | -/1 | -/- | - | NR |
| 20 | HSMN | Ax | *MFN2* | NM\_014874.4 | c.1090C>T | p.Arg364Trp | heterozygous | *De novo* | AD | Pathogenic | No | 53/42 | NR/1 | NR/NR | NR | NR |
| 21 | HSMN | Ax | *MFN2* | NM\_014874.4 | c.1091G>C | p.Arg364Pro | heterozygous | Not confirmed | AD | Pathogenic | Yes | 50/51 | 0.6/1.3 | 8/7 | - | NR |
| 22 | HSMN | In | *GDAP1* | NM\_018972.4 | c.368A>G | p.His123Arg | heterozygous | *Assume de novo* (only maternal confirmed) | AD | Pathogenic | No | 37/45 | 4/4 | NR/NR | NR | NR |
| 23 | HSMN | In | *GJB1* | NM\_000166.6 | c.223C>T | p.Arg75Trp | hemizygous | Not confirmed | XR | Pathogenic | No | 36/41 | 3/6 | 14/15.9 | - | NR |
| 24 | HSMN | Ax | unknown |  |  |  |  |  |  |  | No | 46/41 | 2/1 | 8/NR | - | 7 |
| 25 | HSMN | Ax | unknown |  |  |  |  |  |  |  | No | 56/53 | 4.5/8.1 | 48/47 | 59 | 19 |
| 26 | HSMN | Ax | unknown |  |  |  |  |  |  |  | Yes | 65/53 | 2.2/1.5 | NR/NR | 12 | NR |
| 27 | HSMN | Ax | unknown |  |  |  |  |  |  |  | No | 46/51 | 1.5/3.7 | 34/33 | 55 | 34 |
| 28 | HSMN | Ax | unknown |  |  |  |  |  |  |  | Yes | 191/32 | 0.1/0.1 | 6.9/6.7 | - | 2.4 |
| 29 | HSMN | UD | *MFN2* | NM\_014874.4 | c.472A>C | p.Lys158Gln | heterozygous | Maternal allele | AD | VUS | No | NR/NR | NR/NR | NR/NR | - | NR |
| 30 | HSMN | UD | *PMP22* | NM\_000304.4 | c.251\_253del | p.Phe84del | heterozygous | Not confirmed | AD | Pathogenic | No | NR/NR | NR/NR | NR/NR | - | NR |
| 31 | HSMN | UD | *PMP22* | NM\_000304.4 | c.215C>T | p.Ser72Leu | heterozygous | *De novo* | AD | Pathogenic | No | NR/NR | NR/NR | NR/NR | NR | NR |
| 32\* | HSN | Ax | *PRDM12* | NM\_021619.3 | c.570+2T>G | p.? | heterozygous (*trans* phase) | Paternal allele | AR | Pathogenic | No | -/50 | -/3 | 12/NR | - | NR |
| NM\_021619.3 | c.796A>C | p.Thr266Pro | Maternal allele | Likely pathogenic |
| 33b | HSN | Ax | unknown |  |  |  |  |  | AR |  | Yes | 67/51 | 12/9 | 21/16.9 | - | 15 |
| 34b | HSN | Ax | unknown |  |  |  |  |  | AR |  | Yes | 54/54 | 11/11 | 28.1/18.2 | - | 12.7 |

Abbreviations: AD: autosomal dominant; AR: autosomal recessive; Ax: axonal; CMAP: compound motor action potential; De: demyelinating; HSMN: hereditary sensorimotor neuropathy; HSN: hereditary sensory neuropathy; In: intermediate; MNCV: motor nerve conduction velocity; NP: not performed; SNAP: sensory action potential; UD: undetermined.

aAccording to the American College of Medical Genetics and Genomics interpretation guidelines ([**Genet Med. 2015 May; 17(5): 405–424.**](https://www.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&retmode=ref&cmd=prlinks&id=25741868))

bSibling relationships

\*Indicate novel variant

**Table S2.** Comparison of genetic distribution of pediatric CMT patients in diverse populations.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Author  Study period | This study  2017-2021 | Argente-Escrig H, et al.[1]  2017-2020 | Hsu YH, et al.[2]  1996-2018 | Hoebeke C, et al.[3]  1992-2016 | Fernandez- Ramos et al.[4] 2003-2015 | Cornett KMD, et al.[5]  2009-2014 |
| Patients  Number  Age at enrolment  Age of onset (range) | Thai  N=35  1-26Y  mean 2Y  (0-12Y) | Spanish  N=99  2-20Y  Average 3.2 ± 3.0  (0-13.8Y) | Chinese Han  N=177a (427)  N/A  (0-19Y) | France  N=75  15.4Y  mean 4.1Y  (0-18Y) | Spanish  N=36  Pediatric  N/A | 8 sites, 4 countriesb  N=520  3-20Y  N/A |
| Method  Diagnostic yield | ES  68.6% | GP and ES  79.5% | GP 124 genes  70.6% | GP 2,742 genes  80.6% | 66.7% | N/A  76.4% |
| Common causative genes | | | | | | |
|  | *MFN2* 17.1% | *PMP22* dup 37.4% | *PMP22* dup 36.7% | *PMP22* dup 61.3% | *PMP22* dup 44.4% | *PMP22* dup 48.5% |
| *NEFL* 8.6% | *GDAP* 10.1% | *GJB1* 10.7% | *MFN2* 14.7% | *HINT1* 8.3% | *MFN2* 6.0% |
| *GDAP1* 8.6% | *GJB1* 8.1% | *MFN2* 6.7% | *GJB1* 6.7% | *MFN2*, *GJB1*, *TRPV4*, *NDRG1* 2.8%c | *MPZ* 2.9% |
| *MPZ* 5.7% | *MFN2*, *MPZ*, *HK1*, *BICD2* 3%c | *MPZ* 4.5% | *HK1* 4.0% | *SH3TC2* 2.5% |
| *PMP22* 5.7% | *NEFL* 3.3% | *MPZ*, *GDAP1* 2.7% c | *PMP22* 1.7% |
| Most common causative genes according to electrophysiologic subtype | | | | | | |
| Demyelinating | *NEFL* | *PMP22* dup | *PMP22* dup | *PMP22* dup | *PMP22* dup | *PMP22* dup |
| Axonal | *MFN2* | *GDAP1* | *MFN2* | *MFN2* | *HINT1* | *MFN2* |
| Most common causative genes according to age of onset | | | | | | |
| Infantile (≤2Y) | *MFN2*, *NEFL* | N/A | *MFN2* | N/A | N/A | N/A |
| Childhood (3-19Y) | *MFN2*, *GDAP1* | N/A | *PMP22* dup | N/A | N/A | N/A |

Abbreviations: ES: exome sequencing; GP: gene panel; Y: year(s).

a This study was conducted in patients with age of onset 1-72 years. The data presents only the combination of infancy (0-2 years) and Childhood/Adolescent (3-19 years) onset groups.  
b This study enrolled patients across 8 sites in 4 countries: Australia, the United States (Iowa City, Michigan, Pennsylvania, Florida, New York), Italy, and England.

c Present percent per each gene.

References:

1. Argente-Escrig H, Frasquet M, Vázquez-Costa JF, Millet-Sancho E, Pitarch I, Tomás-Vila M, et al. Pediatric inherited peripheral neuropathy: a prospective study at a Spanish referral center. Ann Clin Transl Neurol. 2021;8(9):1809-16.

2. Hsu YH, Lin K-P, Guo YC, Tsai YS, Liao Y-C, Lee Y-C. Mutation spectrum of Charcot‐Marie‐Tooth disease among the Han Chinese in Taiwan. Annals of Clinical and Translational Neurology. 2019;6.

3. Hoebeke C, Bonello-Palot N, Audic F, Boulay C, Tufod D, Attarian S, et al. Retrospective study of 75 children with peripheral inherited neuropathy: Genotype–phenotype correlations. Archives de Pédiatrie. 2018;25(8):452-8.

4. Fernández-Ramos JA, López-Laso E Fau - Camino-León R, Camino-León R Fau - Gascón-Jiménez FJ, Gascón-Jiménez Fj Fau - Jiménez-González MD, Jiménez-González MD. Experience in molecular diagnostic in hereditary neuropathies in a pediatric tertiary hospital. Rev Neurol. 2015.

5. Cornett KMD, Menezes MP, Bray P, Halaki M, Shy RR, Yum SW, et al. Phenotypic Variability of Childhood Charcot-Marie-Tooth Disease. JAMA Neurology. 2016;73(6):645-51.