

**Supplementary Fig. S1. Distribution of other craniofacial dysmorphisms in the patients**

The number of patients with positive genetic results is presented as the red bar, and the number of patients with negative genetic results is presented as the blue bar.

**Supplementary Table S1. Single nucleotide variants in 24 patients**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Casenumber | Gene | Gene category | Variant | Zygosity | Inheritancemode | Source | Reported |
| 1 | *ATRX* | Syndromic | NM\_000489.5:c.6254G>A(p.Arg2085His) | Hemi | XL/XLD/XLR | Maternal | 16813605 |
| 6 | *TUBA1A* | Lissencephaly | NM\_006009.4:c.790C>T(p. Arg264Cys) | Het | AD | De novo | 17218254 |
| 7 | *KIF11* | Microcephaly | NM\_004523.4:c.2922G>A(p.Pro974Pro) | Het | AD | De novo | 25934493 |
| 9 | *FOXRED1* | Mitochondrial | NM\_017547.3:c.1054C>T(p. Arg352Trp)NM\_017547.3:c.606\_607delAG | Het/het | AR | MaternalPaternal | 20858599NO |
| 10 | *TAF2* | ID | NM\_003184.4:c.2119A>G(p.Asn707Asp);NM\_003184.4:c.2216\_2219delACAA | Het/het | AR | Paternal Maternal | NONO |
| 11 | *NIPBL* | Syndromic | NM\_015384.4:c.1660C>T(p.Gln554Ter) | Het | AD | De novo | NO |
| 16 | *ASPM* | Microcephaly | NM\_018136.5:c.4795C>T(p. Arg1599Ter);NM\_018136.5:c.3741+1\_3741+5delGTAAG | Het/het | AR | Paternal Maternal | 14574646NO |
| 17 | *ABCC8* | Metabolic | NM\_000352.4:c.1108A>G(p. Arg370Gly) | Het | AD/AR | Maternal | 18596924 |
| 21 | *DDX3X* | Syndromic | NM\_001193416.2:c.1490C>A(p.Ala497 Asp) | Het | XL/XLD/XLR | De novo | NO |
| 22 | *CHD7* | Syndromic | NM\_017780.4:c.2572C>T(p. Arg858Ter) | Het | AD | De novo | 16155193 |
| 26 | *BSND* | Syndromic | NM\_057176.3:c.22C>T(p. Arg8Trp) | Hom | AR | Paternal Maternal | 11687798 |
| 29 | *NIPBL* | Syndromic | NM\_133433.4:c.3562\_3563insG | Het | AD | De novo | NO |
| 31 | *DYRK1A* | ID | NM\_001396.4:c.951+4\_951+7delAGTA | Het | AD | NA | 26922654 |
| 32 | *ASPM* | Microcephaly | NM\_018136.5:c.1592\_1595delTAATNM\_018136.5:c.561\_562delAG | Het/het | AR | MaternalPaternal | NONO |
| 33 | *RECQL4* | Syndromic | NM\_004260.3:c.994A>T(p.Lys332Ter)NM\_004260.3:c.1770\_1807del | Het/het | AR | Maternal Paternal | NONO |
| 34 | *TUBA1A* | Lissencephaly | NM\_006009.4:c.818C>A(p.Ala273 Asp) | Het | AD | De novo | 31965297 |
| 35 | *NIN* | Syndromic | NM\_020921.3:c.4152\_4152delinsCATANM\_020921.3:c.4410\_4410delinsAG | Het/het | AR | PaternalMaternal | NONO |
| 39 | *DYRK1A* | ID | NM\_001396.4:c.1301dupC | Het | AD | NA | NO |
| 44 | *SCN2A* | Epileptic | NM\_021007.2:c.2629T>G(p.Ser877Ala) | Het | AD | De novo | NO |
| 51 | *CASK* | ID | NM\_003688.3:c.1668+1G>C | Het | XLD | De novo | NO |
| 52 | *ASPM* | Microcephaly | NM\_018136.5:c.9557C>G(p.Ser3186Ter)NM\_018136.5:c.5470C>T(p. Gln1824Ter) | Het/het | AR | MaternalPaternal | 14574646NO |
| 54 | *FOXG1* | Syndromic | NM\_005249.4:c.506delG | Het | AD | De novo | 24836831 |
| 57 | *HNRNPH2* | ID | NM\_019597.5:c.616C>T(p.Arg206Trp) | Het | XL/XLD | De novo | 27545675 |
| 59 | *OSGEP* | syndromic | NM\_017807.4:c.740G>A(p. Arg247Gln);NM\_017807.4:c.560G>T(p.Gly187Val) | Het/het | AR | Paternal Maternal | 28805828NO |

ID: intellectual disability.

**Supplementary Table S2. Copy number variants in 11 patients**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Case number | Region | CNV type | Position-start | Position-end | Size(Kb) |
| 8 | 22q11.21 | DEL | 18893540 | 21418453 | 2524.913 |
| 15 | 3q27.1-28 | DEL | 183205338 | 189456563 | 6251.225 |
| 25 | 18p11.31-18q22.3 | DUP | 2916991 | 73001905 | 70084.914 |
| 27 | 4p16.3-4p16.1 | DEL | 619372 | 10027630 | 9408.258 |
| 28 | 12q13.13 | DEL | 53701239 | 54340328 | 639.089 |
| 37 | 3p26.3-3p25.3 | DEL | 361365 | 10452499 | 10091.134 |
| 43 | 21q21.1-21q22.3 | DUP | 19641432 | 47865682 | 28224.25 |
| 45 | 18p11.31-18q23 | DUP | 2916991 | 77514510 | 74597.519 |
| 46 | 9p24.3-9p13.2 | DUP | 213107 | 37785061 | 37571.954 |
| 47 | 15q23-15q24.1 | DEL | 72635774 | 75191798 | 2556.024 |
| 58 | 17p12 | DUP | 14110126 | 15492541 | 1382.415 |

**Supplementary Table S3. 19 *ASPM* P/LP variants detected in patient and parent samples from the CCGT and 151 *ASPM* P/LP variants recorded detrimental in both the HGMD and ClinVar databases**

|  |  |
| --- | --- |
| **Site** | **Variants** |
| Site 1\* | NM\_018136.5: c.10168C>T(p.Arg3390Ter) |
| Site 2\* | NM\_018136.5: c.9557C>G(p.Ser3186Ter) |
| Site 3\* | NM\_018136.5: c.9319C>T(p.Arg3107Ter) |
| Site 4\* | NM\_018136.5: c.8987+1G>A |
| Site 5\* | NM\_018136.5: c.8133\_8136del(p.Lys2712LeufsTer16) |
| Site 6\* | NM\_018136.5: c.7782\_7783del(p.Lys2595SerfsTer6) |
| Site 7\* | NM\_018136.5: c.6232C>T(p.Arg2078Ter) |
| Site 8\* | NM\_018136.5: c.5149del(p.Ile1717Ter) |
| Site 9\* | NM\_018136.5: c.4795C>T(p.Arg1599Ter) |
| Site 10\* | NM\_018136.5: c.3811C>T(p.Arg1271Ter) |
| Site 11\* | NM\_018136.5: c.3741+1\_3741+5del |
| Site 12\* | NM\_018136.5: c.3055C>T(p.Arg1019Ter) |
| Site 13\* | NM\_018136.5: c.2936+1G>A |
| Site 14\* | NM\_018136.5: c.2791C>T(p.Arg931Ter) |
| Site 15 | NM\_018136.5: c.5470C>T(p.Gln1824Ter) |
| Site 16 | NM\_018136.5: c.5188G>T(p.Glu1730Ter) |
| Site 17 | NM\_018136.5: c.4720C>T(p.Gln1574Ter) |
| Site 18 | NM\_018136.5: c.1592\_1595del(p.Val531GlufsTer17) |
| Site 19 | NM\_018136.5: c.561\_562del(p.Arg187SerfsTer2) |
| **Site** | **Variants** |
| Site 1 | NM\_018136.5: c.10168C>T(p.Arg3390Ter) |
| Site 2 | NM\_018136.5: c.10060C>T(p.Arg3354Ter) |
| Site 3 | NM\_018136.5: c.10059C>A(p.Tyr3353Ter) |
| Site 4 | NM\_018136.5: c.9961C>T(p.Gln3321Ter) |
| Site 5 | NM\_018136.5: c.9910C>T(p.Arg3304Ter) |
| Site 6 | NM\_018136.5: c.9841A>T(p.Arg3281Ter) |
| Site 7 | NM\_018136.5: c.9789T>A(p.Tyr3263Ter) |
| Site 8 | NM\_018136.5: c.9730C>T(p.Arg3244Ter) |
| Site 9 | NM\_018136.5: c.9697C>T(p.Arg3233Ter) |
| Site 10 | NM\_018136.5: c.9595A>T(p.Lys3199Ter) |
| Site 11 | NM\_018136.5: c.9557C>G(p.Ser3186Ter) |
| Site 12 | NM\_018136.5: c.9492T>G(p.Tyr3164Ter) |
| Site 13 | NM\_018136.5: c.9454C>T(p.Arg3152Ter) |
| Site 14 | NM\_018136.5: c.9319C>T(p.Arg3107Ter) |
| Site 15 | NM\_018136.5: c.9286C>T(p.Arg3096Ter) |
| Site 16 | NM\_018136.5: c.9238A>T(p.Lys3080Ter) |
| Site 17 | NM\_018136.5: c.9190C>T(p.Arg3064Ter) |
| Site 18 | NM\_018136.5: c.9178C>T(p.Gln3060Ter) |
| Site 19 | NM\_018136.5: c.9104T>A(p.Leu3035Ter) |
| Site 20 | NM\_018136.5: c.9091C>T(p.Arg3031Ter) |
| Site 21 | NM\_018136.5: c.8903G>A(p.Trp2968Ter) |
| Site 22 | NM\_018136.5: c.8668C>T(p.Gln2890Ter) |
| Site 23 | NM\_018136.5: c.8273T>A(p.Leu2758Ter) |
| Site 24 | NM\_018136.5: c.8266C>T(p.Gln2756Ter) |
| Site 25 | NM\_018136.5: c.8017C>T(p.Gln2673Ter) |
| Site 26 | NM\_018136.5: c.7894C>T(p.Gln2632Ter) |
| Site 27 | NM\_018136.5: c.7825C>T(p.Gln2609Ter) |
| Site 28 | NM\_018136.5: c.7761T>G(p.Tyr2587Ter) |
| Site 29 | NM\_018136.5: c.7612C>T(p.Gln2538Ter) |
| Site 30 | NM\_018136.5: c.7491T>G(p.Tyr2497Ter) |
| Site 31 | NM\_018136.5: c.7324C>T(p.Arg2442Ter) |
| Site 32 | NM\_018136.5: c.7129C>T(p.Gln2377Ter) |
| Site 33 | NM\_018136.5: c.6994C>T(p.Arg2332Ter) |
| Site 34 | NM\_018136.5: c.6928C>T(p.Gln2310Ter) |
| Site 35 | NM\_018136.5: c.6568C>T(p.Gln2190Ter) |
| Site 36 | NM\_018136.5: c.6232C>T(p.Arg2078Ter) |
| Site 37 | NM\_018136.5: c.6189T>G(p.Tyr2063Ter) |
| Site 38 | NM\_018136.5: c.5196T>A(p.Cys1732Ter) |
| Site 39 | NM\_018136.5: c.5136C>A(p.Tyr1712Ter) |
| Site 40 | NM\_018136.5: c.4795C>T(p.Arg1599Ter) |
| Site 41 | NM\_018136.5: c.4732C>T(p.Arg1578Ter) |
| Site 42 | NM\_018136.5: c.4363G>T(p.Glu1455Ter) |
| Site 43 | NM\_018136.5: c.4250\_4251del(p.Tyr1417Ter) |
| Site 44 | NM\_018136.5: c.4074G>A(p.Trp1358Ter) |
| Site 45 | NM\_018136.5: c.3978G>A(p.Trp1326Ter) |
| Site 46 | NM\_018136.5: c.3811C>T(p.Arg1271Ter) |
| Site 47 | NM\_018136.5: c.3796G>T(p.Glu1266Ter) |
| Site 48 | NM\_018136.5: c.3710C>G(p.Ser1237Ter) |
| Site 49 | NM\_018136.5: c.3527C>G(p.Ser1176Ter) |
| Site 50 | NM\_018136.5: c.3327T>G(p.Tyr1109Ter) |
| Site 51 | NM\_018136.5: c.3188T>G(p.Leu1063Ter) |
| Site 52 | NM\_018136.5: c.3055C>T(p.Arg1019Ter) |
| Site 53 | NM\_018136.5: c.2967G>A(p.Trp989Ter) |
| Site 54 | NM\_018136.5: c.2938C>T(p.Arg980Ter) |
| Site 55 | NM\_018136.5: c.2863C>T(p.Gln955Ter) |
| Site 56 | NM\_018136.5: c.2791C>T(p.Arg931Ter) |
| Site 57 | NM\_018136.5: c.2389C>T(p.Arg797Ter) |
| Site 58 | NM\_018136.5: c.1990C>T(p.Gln664Ter) |
| Site 59 | NM\_018136.5: c.1386del(p.Tyr462Ter) |
| Site 60 | NM\_018136.5: c.1366G>T(p.Glu456Ter) |
| Site 61 | NM\_018136.5: c.1138C>T(p.Gln380Ter) |
| Site 62 | NM\_018136.5: c.577C>T(p.Gln193Ter) |
| Site 63 | NM\_018136.5: c.349C>T(p.Arg117Ter) |
| Site 64 | NM\_018136.5: c.9084+5G>A |
| Site 65 | NM\_018136.5: c.9084+5G>T |
| Site 66 | NM\_018136.5: c.3390+3\_3390+6del |
| Site 67 | NM\_018136.5: c.2936+5G>T |
| Site 68 | NM\_018136.5: c.2936+5G>A |
| Site 69 | NM\_018136.5: c.9984+1G>T |
| Site 70 | NM\_018136.5: c.8987+1G>A |
| Site 71 | NM\_018136.5: c.3741+1G>A |
| Site 72 | NM\_018136.5: c.3082+1G>C |
| Site 73 | NM\_018136.5: c.2936+1G>A |
| Site 74 | NM\_018136.5: c.2419+2T>C |
| Site 75 | NM\_018136.5: c.297+1G>C |
| Site 76 | NM\_018136.5: c.3082G>A(p.Gly1028Arg) |
| Site 77 | NM\_018136.5: c.2761-25A>G |
| Site 78 | NM\_018136.5: c.9754del(p.Arg3252GlufsTer10) |
| Site 79 | NM\_018136.5: c.9747\_9748del(p.Tyr3250GlnfsTer14) |
| Site 80 | NM\_018136.5: c.9686\_9690del(p.Ile3229SerfsTer10) |
| Site 81 | NM\_018136.5: c.9685del(p.Ile3229LeufsTer6) |
| Site 82 | NM\_018136.5: c.9677\_9678insG(p.Cys3226TrpfsTer5) |
| Site 83 | NM\_018136.5: c.9507del(p.Ile3170LeufsTer9) |
| Site 84 | NM\_018136.5: c.9309\_9310del(p.Arg3103SerfsTer20) |
| Site 85 | NM\_018136.5: c.9159del(p.Lys3053AsnfsTer5) |
| Site 86 | NM\_018136.5: c.9118\_9119insCATT(p.Tyr3040SerfsTer3) |
| Site 87 | NM\_018136.5: c.8844del(p.Lys2949ArgfsTer7) |
| Site 88 | NM\_018136.5: c.8711\_8712del(p.Gln2904ArgfsTer15) |
| Site 89 | NM\_018136.5: c.8702del(p.His2901LeufsTer37) |
| Site 90 | NM\_018136.5: c.8508\_8509del(p.Lys2837MetfsTer34) |
| Site 91 | NM\_018136.5: c.8378del(p.Met2793ArgfsTer27) |
| Site 92 | NM\_018136.5: c.8200\_8201del(p.Asn2734LeufsTer16) |
| Site 93 | NM\_018136.5: c.8195\_8198del(p.Arg2732LysfsTer4) |
| Site 94 | NM\_018136.5: c.8191\_8192del(p.Glu2731LysfsTer19) |
| Site 95 | NM\_018136.5: c.8133\_8136del(p.Lys2712LeufsTer16) |
| Site 96 | NM\_018136.5: c.8131\_8132del(p.Lys2711GlufsTer12) |
| Site 97 | NM\_018136.5: c.7860\_7861del(p.Gln2620HisfsTer16) |
| Site 98 | NM\_018136.5: c.7857\_7858insA(p.Gln2620ThrfsTer17) |
| Site 99 | NM\_018136.5: c.7783\_7786del(p.Lys2595TyrfsTer20) |
| Site 100 | NM\_018136.5: c.7782\_7783del(p.Lys2595SerfsTer6) |
| Site 101 | NM\_018136.5: c.7665del(p.Ala2556LeufsTer4) |
| Site 102 | NM\_018136.5: c.7491\_7495del(p.Thr2499SerfsTer18) |
| Site 103 | NM\_018136.5: c.7308\_7309insT(p.Val2437CysfsTer14) |
| Site 104 | NM\_018136.5: c.6920\_6921del(p.Gln2307LeufsTer10) |
| Site 105 | NM\_018136.5: c.6852\_6855del(p.Leu2285ArgfsTer6) |
| Site 106 | NM\_018136.5: c.6852\_6855del(p.Leu2285ArgfsTer6) |
| Site 107 | NM\_018136.5: c.6732del(p.Tyr2245ThrfsTer15) |
| Site 108 | NM\_018136.5: c.6686\_6689del(p.Arg2229ThrfsTer10) |
| Site 109 | NM\_018136.5: c.6651\_6654del(p.Thr2218TyrfsTer8) |
| Site 110 | NM\_018136.5: c.6513\_6514insA(p.Val2172SerfsTer7) |
| Site 111 | NM\_018136.5: c.6337\_6338del(p.Ile2113SerfsTer11) |
| Site 112 | NM\_018136.5: c.5590\_5591del(p.Leu1864SerfsTer2) |
| Site 113 | NM\_018136.5: c.5149del(p.Ile1717Ter) |
| Site 114 | NM\_018136.5: c.5064del(p.Val1689LeufsTer3) |
| Site 115 | NM\_018136.5: c.4858\_4859del(p.Ile1620PhefsTer24) |
| Site 116 | NM\_018136.5: c.4728\_4729del(p.Arg1576SerfsTer7) |
| Site 117 | NM\_018136.5: c.4583del(p.Lys1528ArgfsTer24) |
| Site 118 | NM\_018136.5: c.3960\_3961insA(p.Val1321SerfsTer29) |
| Site 119 | NM\_018136.5: c.3945\_3946del(p.Arg1315SerfsTer2) |
| Site 120 | NM\_018136.5: c.3853\_3854del(p.Asp1285SerfsTer32) |
| Site 121 | NM\_018136.5: c.3663del(p.Arg1221SerfsTer13) |
| Site 122 | NM\_018136.5: c.3506\_3507del(p.Val1169GlyfsTer15) |
| Site 123 | NM\_018136.5: c.3477\_3481del(p.Ala1160MetfsTer23) |
| Site 124 | NM\_018136.5: c.3185\_3189del(p.Asn1062ArgfsTer28) |
| Site 125 | NM\_018136.5: c.2968del(p.Asp990ThrfsTer11) |
| Site 126 | NM\_018136.5: c.1959\_1962del(p.Asn653LysfsTer14) |
| Site 127 | NM\_018136.5: c.1896\_1897del(p.Lys633IlefsTer8) |
| Site 128 | NM\_018136.5: c.1729\_1730del(p.Ser577ArgfsTer33) |
| Site 129 | NM\_018136.5: c.1726\_1729del(p.Lys576AlafsTer10) |
| Site 130 | NM\_018136.5: c.1631\_1635del(p.Tyr544SerfsTer9) |
| Site 131 | NM\_018136.5: c.1615\_1616del(p.Glu539ArgfsTer15) |
| Site 132 | NM\_018136.5: c.1590del(p.Val531Ter) |
| Site 133 | NM\_018136.5: c.1406\_1413del(p.Asn469IlefsTer9) |
| Site 134 | NM\_018136.5: c.1260\_1266del(p.Gln421HisfsTer32) |
| Site 135 | NM\_018136.5: c.1235\_1239del(p.Lys412ThrfsTer5) |
| Site 136 | NM\_018136.5: c.1179del(p.Asn394IlefsTer4) |
| Site 137 | NM\_018136.5: c.1154\_1155del(p.Glu385ValfsTer3) |
| Site 138 | NM\_018136.5: c.1002del(p.Val335Ter) |
| Site 139 | NM\_018136.5: c.972\_973del(p.Asn324LysfsTer5) |
| Site 140 | NM\_018136.5: c.803\_804del(p.Lys268SerfsTer4) |
| Site 141 | NM\_018136.5: c.719\_720del(p.Ser240CysfsTer16) |
| Site 142 | NM\_018136.5: c.688del(p.Glu230AsnfsTer30) |
| Site 143 | NM\_018136.5: c.637del(p.Ile213TyrfsTer47) |
| Site 144 | NM\_018136.5: c.440del(p.Lys147ArgfsTer54) |
| Site 145 | NM\_018136.5: c.117\_118del(p.Leu41GlnfsTer30) |
| Site 146 | NM\_018136.5: c.77del(p.Gly26AlafsTer42) |
| Site 147 | NM\_018136.5: c.8700\_8702delinsCC(p.Lys2900AsnfsTer38) |
| Site 148 | NM\_018136.5: c.8598dupA(p.Gln2867ThrfsTer5) |
| Site 149 | NM\_018136.5: c.6916\_6919del(p.Leu2306SerfsTer20) |
| Site 150 | NM\_018136.5: c.3741+1\_3741+5del |
| Site 151 | NM\_018136.5: c.1726\_1727del(p.Lys576GlufsTer34) |

\* overlapped with the 151 *ASPM* P/LP variants recorded detrimental in both the HGMD and ClinVar databases