# Additional File 2: Supplementary files

The phenotypic spectrum of terminal 6q deletions based on a large cohort derived from social media and literature: a prominent role for *DLL1*

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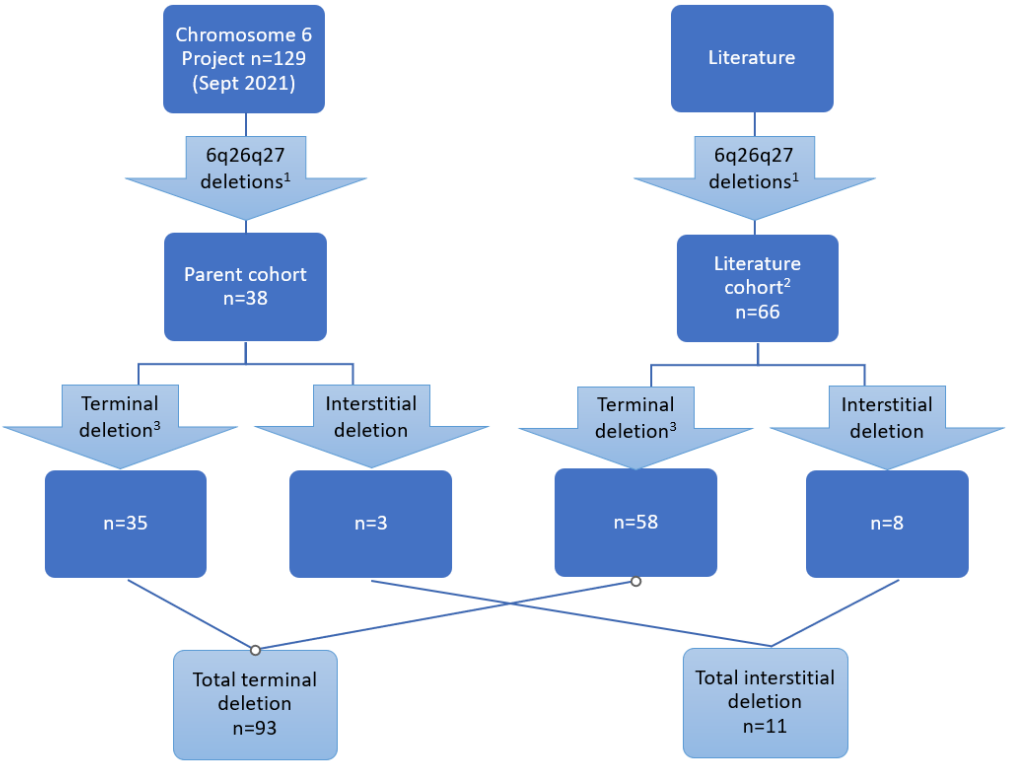
**Supplementary Figures**



**Supplementary Table**

**Figure S1. Case collection from the Chromosome 6 Project and literature**



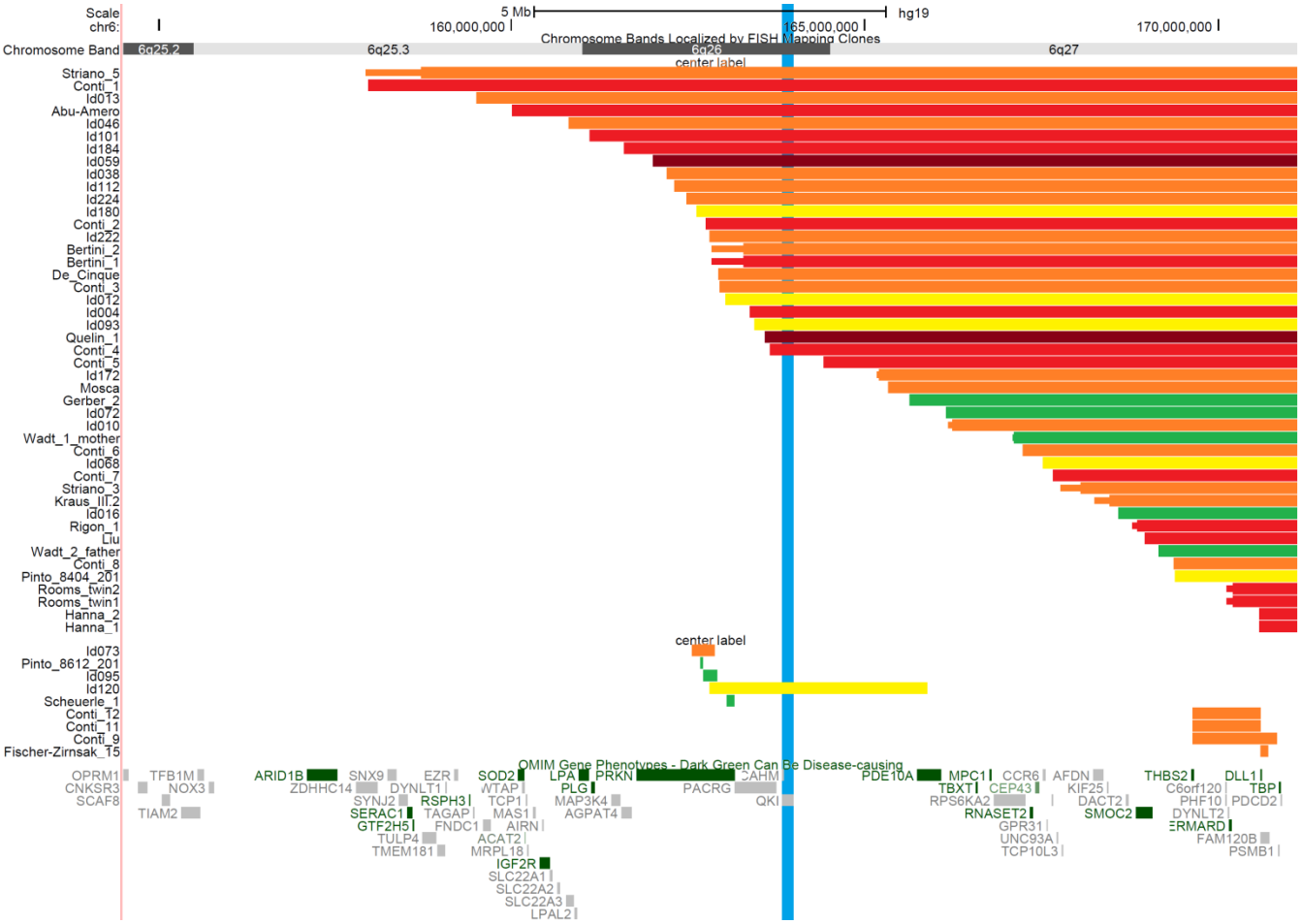

The number of terminal and interstitial 6q deletion cases derived from the Chromosome 6 Project and the literature.

[1] Defined as a deletion within the 6q26q27 region (161,000,001–171,115,067).

[2] Case reports involving terminal 6q deletions collected using PubMed with the search criteria (deletion or monosomy) and (6q26 or 6q27 or terminal 6q). References were checked for additional relevant case reports. Publications reporting detailed clinical information and microarray results or comparably detailed breakpoint analyses were included.

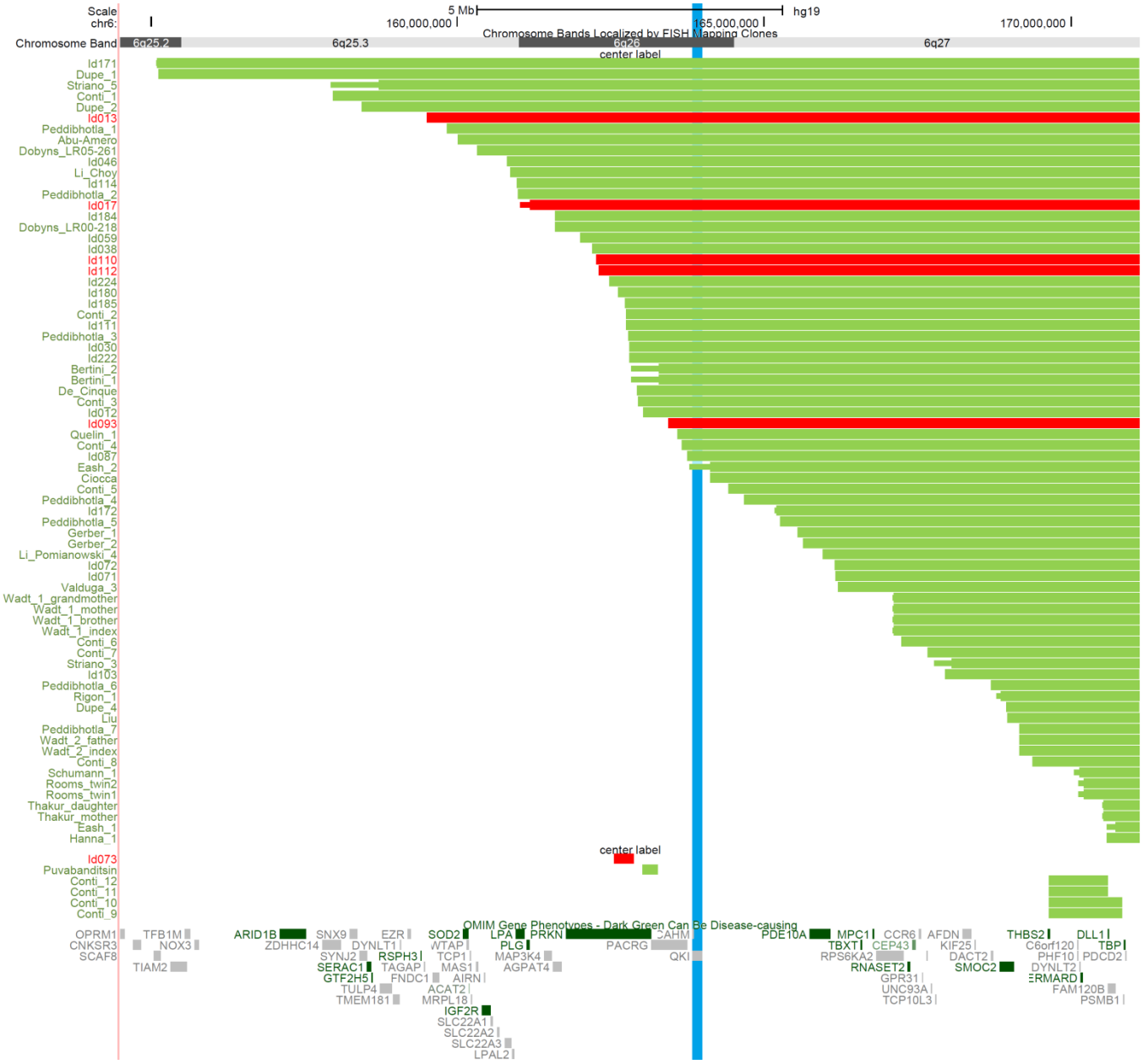
[3] Defined as a deletion including the most distally located gene (*PDCD2,* MIM*600866).

**Figure S2. Developmental delay in children older than 2 years of age**



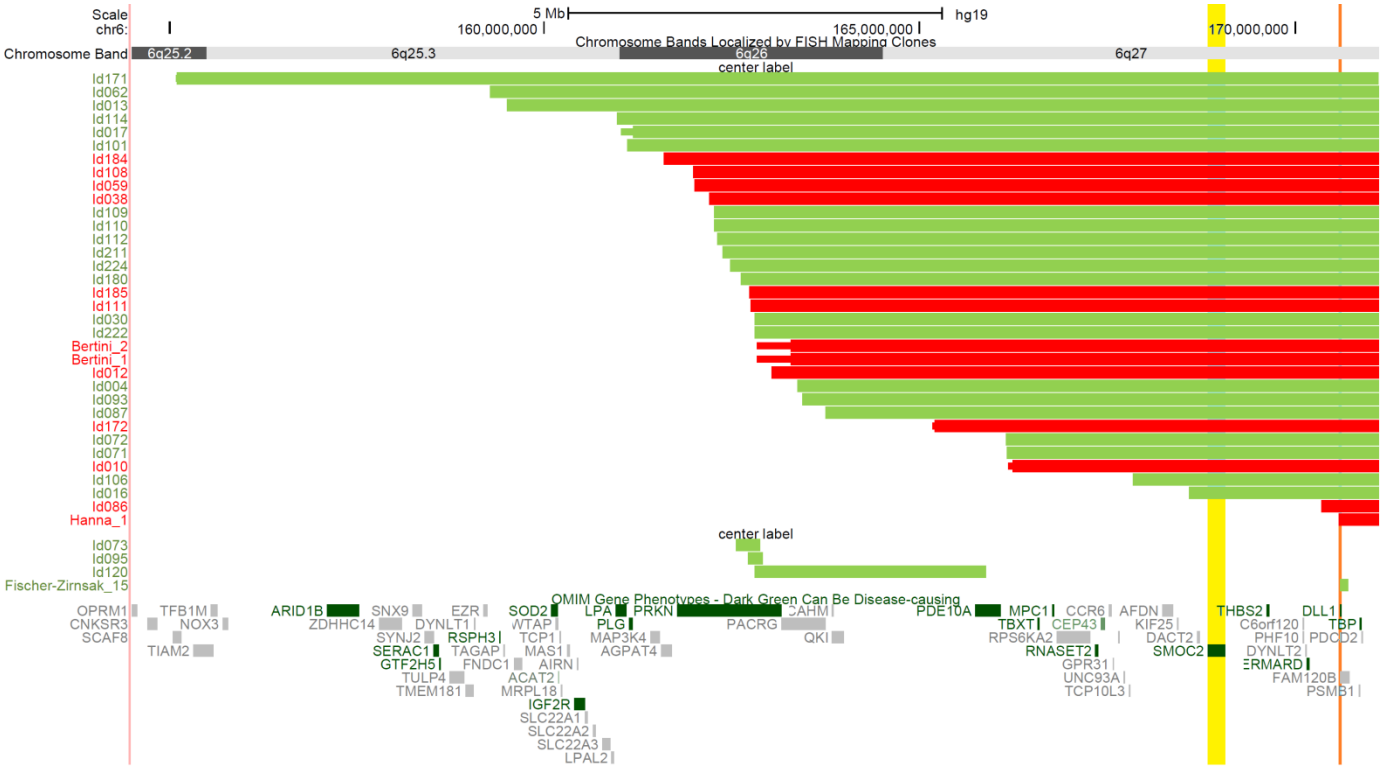

The deletion in each patient for whom development could be categorised is represented by a horizontal bar. Development is categorised as normal (IQ >85, green bar), borderline (IQ 70-85, yellow), mild (IQ 50-70, orange), moderate (IQ 30-50, red) or severe (IQ <30, dark red) delay. The gene *QKI* is represented by a vertical blue bar (see manuscript Discussion).

## Figure S3. Delayed Myelination




The deletion in each patient for whom delayed myelination was present (red) or absent (green) is represented by a horizontal bar. The gene *QKI* is represented by a vertical blue bar (see manuscript Discussion).

## Figure S4. Dental problems




The deletion in each patient for whom dental problems were present (red) or absent (green) is represented by a horizontal bar. The gene *SMOC2* is represented by a vertical yellow bar and the gene *DLL1* is represented by a vertical orange bar. *SMOC2* is related to dental abnormalities in pathogenic homozygous variants (see manuscript Results and Discussion).

**Table S2. HI and pLI scores**

| Location | Gene | MIM* | % HI | pLI |
|---|---|---|---|---|
| 6q27 | *PDCD2* | 600866 | 69.48 | 0.00 |
| | ***TBP*** | 600075 | 6.48 | 0.02 |
| | ***PSMB1*** | 602017 | 33.38 | 0.97 |
| | *FAM120B* | 612266 | 80.03 | 0.00 |
| | ***DLL1*** | 606582 | 4.65 | 1.00 |
| | *ERMARD (C6orf70)* | 615532 | 84.86 | 0.00 |
| | *DYNLT2* | 186977 | - | 0.00 |
| | *PHF10* | 613069 | 18.13 | 0.00 |
| | *C6orf120* | 616987 | 92.18 | - |
| | *THBS2* | 188061 | 59.96 | 0.56 |
| | *SMOC2* | 607223 | 55.41 | 0.00 |
| | *DACT2* | 608966 | 93.50 | 0.01 |
| | *KIF25* | 603815 | 95.70 | 0.00 |
| | ***AFDN*** | 159559 | - | 1.00 |
| | *TCP10L3* | 187020 | - | 0.00 |
| | *UNC93A* | 607995 | 85.97 | 0.00 |
| | *GPR31* | 602043 | 91.50 | 0.02 |
| | *CCR6* | 601835 | 84.13 | 0.01 |
| | *CEP43* | 605392 | - | 0.00 |
| | *RNASET2* | 612944 | 88.27 | 0.00 |
| | *RPS6KA2* | 601685 | 64.44 | 0.02 |
| | *MPC1* | 614738 | 49.44 | 0.04 |
| | *TBXT* | 601397 | - | 0.06 |
| | ***PDE10A*** | 610652 | 52.14 | 1.00 |
| 6q26 | ***QKI*** | 609590 | 4.10 | 0.75 |
| | *CAHM* | 615930 | - | - |
| | *PACRG* | 608427 | 10.61 | 0.00 |
| | ***PRKN*** | 602544 | 0.77 | 0.00 |
| | *AGPAT4* | 614795 | 61.98 | 0.10 |
| | ***MAP3K4*** | 602425 | 59.19 | 1.00 |
| | *PLG* | 173350 | 40.11 | 0.01 |
| | *LPA* | 152200 | 78.22 | 0.00 |
| 6q25.3 | *LPAL2* | 611682 | - | - |
| | *SLC22A3* | 604842 | 49.06 | 0.00 |
| | *SLC22A2* | 602608 | 63.53 | 0.00 |
| | *SLC22A1* | 602607 | 75.70 | 0.00 |
| | *AIRN* | 604893 | - | - |
| | ***IGF2R*** | 147280 | 53.96 | 1.00 |
| | *MAS1* | 165180 | 28.09 | 0.00 |
| | *MRPL18* | 611831 | 49.78 | 0.00 |
| | ***TCP1*** | 186980 | 5.10 | 1.00 |
| | *ACAT2* | 100678 | 53.11 | 0.00 |
| | ***WTAP*** | 605442 | 6.76 | 1.00 |
| | ***SOD2*** | 147460 | 0.99 | 0.15 |
| | *FNDC1* | 609991 | 75.28 | 0.00 |
| | *TAGAP* | 609667 | 82.32 | 0.85 |

| | | | | |
|---|---|---|---|---|
| | *RSPH3* | 615876 | 86.62 | 0.00 |
| | ***EZR*** | 123900 | 8.64 | 0.18 |
| | *DYNLT1* | 601554 | 66.63 | 0.00 |
| | *TMEM181* | 613209 | 67.29 | 0.01 |
| | *GTF2H5* | 608780 | 30.21 | 0.05 |
| | *SERAC1* | 614725 | 61.19 | 0.00 |
| | *SYNJ2* | 609410 | 63.42 | 0.00 |
| | *SNX9* | 605952 | 40.36 | 0.71 |
| | *ZDHHC14* | 619295 | 29.53 | 0.72 |
| | ***ARID1B*** | 614556 | 14.17 | 1.00 |
| | *NOX3* | 607105 | 38.77 | 0.00 |
| | *TFB1M* | 607033 | 53.74 | 0.00 |
| 6q25.2 | *TIAM2* | 604709 | 53.43 | 0.68 |
| | ***SCAF8*** | 616024 | 25.56 | 1.00 |

All the OMIM genes studied, extending from 6q27 to 6q25.2 (16 Mb). Predicted HI-genes are highlighted in bold. HI and pLI scores were derived from https://decipher.sanger.ac.uk in May 2021

**Table S4. Genes mentioned in the Discussion and the clinical characteristics to which they may contribute**

| Gene | May contribute to |
|---|---|
| *DLL1* | **small head size, dysplastic outer ears, hypertelorism, vision problems, abnormal eye movements, dental abnormalities, feeding problems, recurrent infections, respiratory problems,** congenital heart defects, **spinal cord abnormalities, abnormal vertebrae, scoliosis, joint hypermobility, brain abnormalities (ventriculomegaly/hydrocephaly, corpus callosum abnormality and cortical dysplasia),** PNH, **seizures, hypotonia, ataxia, torticollis, balance problems, developmental delay, sleeping problems, hyperactivity,** autism spectrum disorder |
| *ERMARD (C6orf70)* | PNH |
| *PHF10* | structural brain abnormalities |
| *THBS2* | congenital heart defects, structural brain abnormalities |
| *SMOC2* | dental problems |
| *TBXT* | hemivertebrae |
| *QKI* | cardiomyopathy, **delayed myelination**, **developmental delay** |

PNH = periventricular nodular heterotopia

A clinical characteristic is depicted in bold when haploinsufficiency of the associated gene is expected to be causal for the characteristic.