SUPPLEMENTAL FIGURE LEGENDS

Supplemental Figure 1: The workflow of the whole exome sequencing (WES) data analysis.

We applied WES to 48 families with clinical sign of arthrogryposis. We identified likely pathogenic variants in 10 known genes in 17 families (35.4%). In 8 families we observed an arthrogryposis mutational burden. These 8 families with oligogenic model have another homozygous or compound heterozygous deleterious variant in an additional known gene (6 families, 12.5%) or in a novel gene (2 families, 4.2%) in addition to a homozygous variant in a known gene. Moreover, in 3 families (6.2%) we identified variants in potential novel candidate genes.

Supplemental Figure 2: Pedigrees of all solved cases in our study

Supplemental Figure 3: (A) Pedigrees and Sanger sequencing results showing the segregation of the patients with phenotypic expansion. (B and C) Photographs of the patient BAB3931 at age 10 months and 6 years, respectively. Note the low-set ears, retromicrognathia, crowded and decayed teeth, flexion contractures of the elbows, and the distinct finding of abnormal wound healing on the dorsum of left foot.
Screening of ~220 known genes in 52 patients from 48 families

Potential oligogenic model
8 families (16.7%)

Variant in a single known gene
17 families (35.4%)

Variants in 2 known genes
6 families (12.5%)

Variants in 1 known and 1 novel gene
2 families (4.2%)

Variants in a novel gene
3 families (6.2%)

- Segregation in family
- Variant pathogenicity according to computational algorithms
- Interactome analysis with known genes
- Function and the expression pattern of the gene
- Database review: no other deleterious variants in other cohorts

Top Candidates
28 Families (58.3%)

Unsolved
20 Families (41.7%)