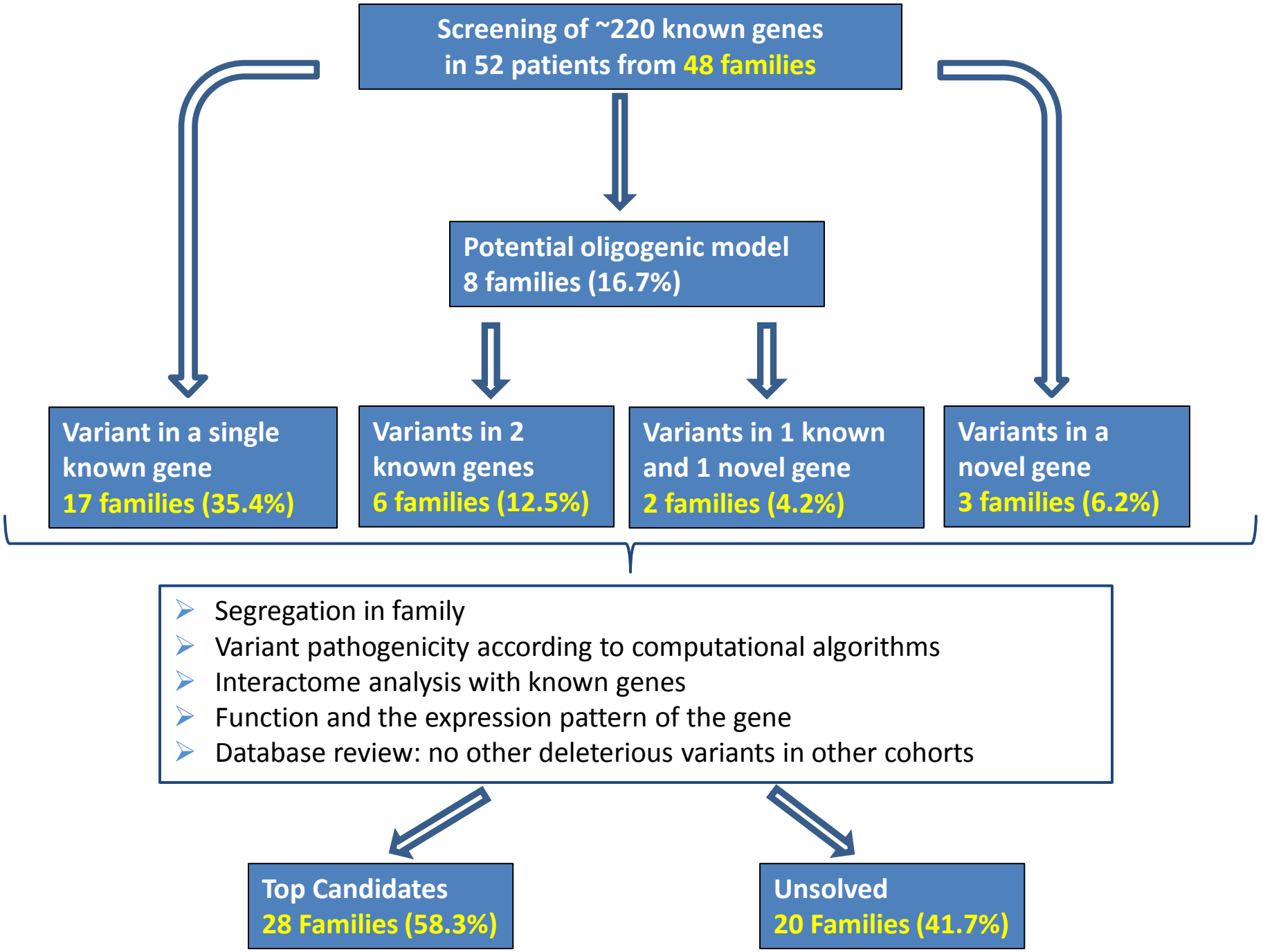
SUPPLEMENTAL FIGURE LEGENDS

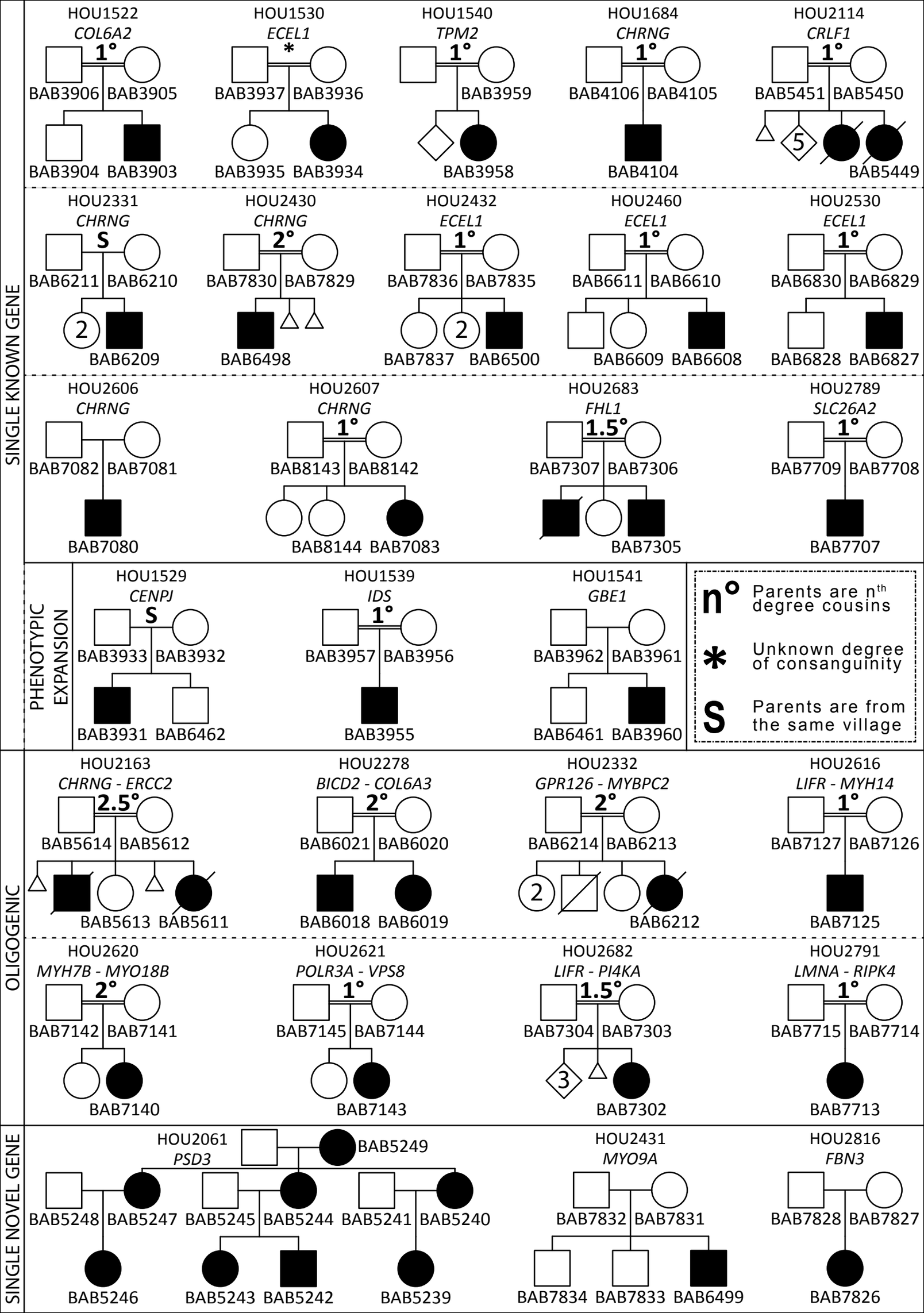
Supplemental Figure 1: **The workflow of the whole exome sequencing (WES) data analysis.**

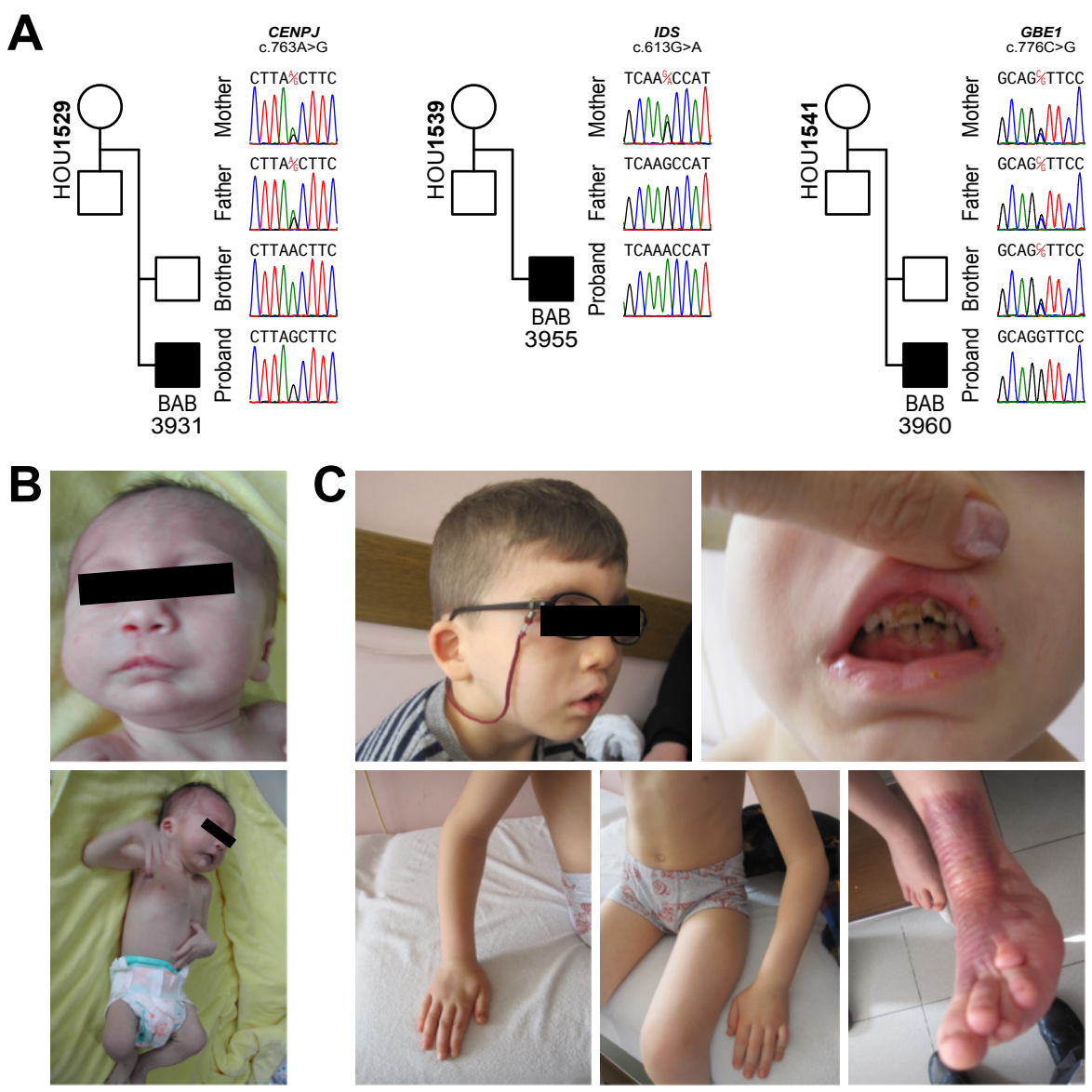
We applied WES to 48 families with clinical sign of arthrogryposis. We identified likely pathogenic variants in 10 known genes in 17 families (35.4%). In 8 families we observed an arthrogryposis mutational burden. These 8 families with oligogenic model have another homozygous or compound heterozygous 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%)


SINGLE KNOWN GENE
HOU1522
COL6A2
1°
BAB3906 BAB3905
BAB3904 BAB3903
HOU1530
ECEL1
*
BAB3937 BAB3936
BAB3935 BAB3934
HOU1540
TPM2
1°
BAB3959
BAB3958
HOU1684
CHRNG
1°
BAB4106 BAB4105
BAB4104
HOU2114
CRLF1
1°
BAB5451 BAB5450
5
BAB5449
HOU2331
CHRNG
S
BAB6211 BAB6210
2
BAB6209
HOU2430
CHRNG
2°
BAB7830 BAB7829
BAB6498
HOU2432
ECEL1
1°
BAB7836 BAB7835
2
BAB7837 BAB6500
HOU2460
ECEL1
1°
BAB6611 BAB6610
BAB6609 BAB6608
HOU2530
ECEL1
1°
BAB6830 BAB6829
BAB6828 BAB6827
HOU2606
CHRNG
BAB7082 BAB7081
BAB7080
HOU2607
CHRNG
1°
BAB8143 BAB8142
BAB8144 BAB7083
HOU2683
FHL1
1.5°
BAB7307 BAB7306
BAB7305
HOU2789
SLC26A2
1°
BAB7709 BAB7708
BAB7707
PHENOTYPIC EXPANSION
HOU1529
CENPJ
S
BAB3933 BAB3932
BAB3931 BAB6462
HOU1539
IDS
1°
BAB3957 BAB3956
BAB3955
HOU1541
GBE1
BAB3962 BAB3961
BAB6461 BAB3960
n° Parents are nth degree cousins
* Unknown degree of consanguinity
S Parents are from the same village
OLIGOGENIC
HOU2163
CHRNG - ERCC2
2.5°
BAB5614 BAB5612
BAB5613 BAB5611
HOU2278
BICD2 - COL6A3
2°
BAB6021 BAB6020
BAB6018 BAB6019
HOU2332
GPR126 - MYBPC2
2°
BAB6214 BAB6213
2
BAB6212
HOU2616
LIFR - MYH14
1°
BAB7127 BAB7126
BAB7125
HOU2620
MYH7B - MYO18B
2°
BAB7142 BAB7141
BAB7140
HOU2621
POLR3A - VPS8
1°
BAB7145 BAB7144
BAB7143
HOU2682
LIFR - PI4KA
1.5°
BAB7304 BAB7303
3
BAB7302
HOU2791
LMNA - RIPK4
1°
BAB7715 BAB7714
BAB7713
SINGLE NOVEL GENE
HOU2061
PSD3
BAB5249
BAB5248 BAB5247 BAB5245 BAB5244 BAB5241 BAB5240
BAB5246 BAB5243 BAB5242 BAB5239
HOU2431
MYO9A
BAB7832 BAB7831
BAB7834 BAB7833 BAB6499
HOU2816
FBN3
BAB7828 BAB7827
BAB7826


A
CENPJ
c.763A>G
HOU1529
Mother
CTTA[A/G]CTTC
Father
CTTA[A/G]CTTC
Brother
CTTAACTTC
Proband
CTTAGCTTC
BAB
3931
IDS
c.613G>A
HOU1539
Mother
TCAA[A/G]CCAT
Father
TCAAGCCAT
Proband
TCAAACCAT
BAB
3955
GBE1
c.776C>G
HOU1541
Mother
GCAG[C/T]TTCC
Father
GCAG[C/T]TTCC
Brother
GCAG[C/T]TTCC
Proband
GCAGGTTCC
BAB
3960
B
C