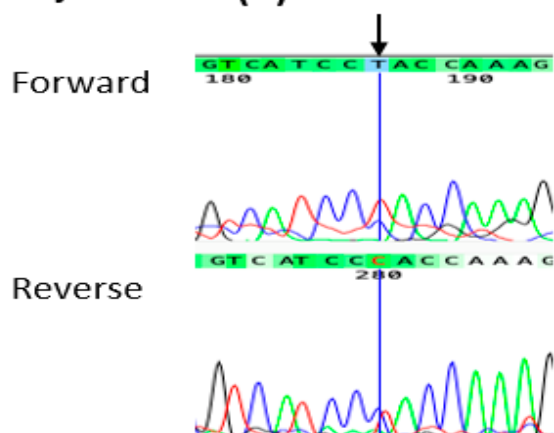


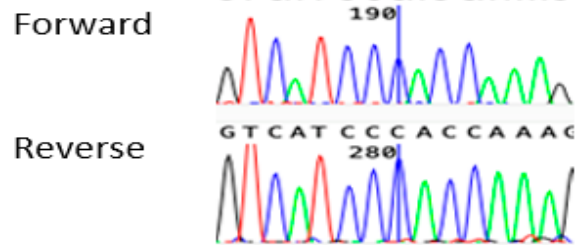
Figure S2. Validation of the candidate variations in the five subjects by Sanger sequencing.

- (A) Sanger sequencing confirmed a *de novo* heterozygous missense c.293C>T SNV in the *USP46* gene in subject 23, resulting in p.Pro98Leu.
- (B) Sanger sequencing confirmed a homozygous missense c.1860A>C SNV in the *SLITRK4* gene in subject 23 inherited from the mother, resulting in p.Leu620Phe.
- (C) Sanger sequencing confirmed a hemizygous missense c.1954G>A SNV in the *FLNA* gene in subject 23 inherited from the mother, resulting in p.Glu652Lys.
- (D) Sanger sequencing confirmed a *de novo* heterozygous missense c.1022G>A SNV in the *KRT2* gene in subject 45, resulting in p.Arg341His.
- (E) Sanger sequencing confirmed a *de novo* heterozygous frameshift c.471delA deletion in the *MIS18BP1* gene in subject 45, resulting in p.Lys157AsnfsTer24.
- (F) Sanger sequencing confirmed a homozygous missense c.371T>C SNV in the *HAAO* gene in subject 45 inherited from both parents, resulting in p.Met124Thr.
- (G) Sanger sequencing confirmed a hemizygous missense c.1804A>G SNV in the *PTCHD1* gene in subject 64, resulting in p.Thr602Ala.
- (H) Sanger sequencing confirmed a hemizygous missense c.2590G>T SNV in the *FLNA* gene in subject 64, resulting in p.Val864Phe.
- (I) Sanger sequencing confirmed a homozygous missense c.5560G>A SNV in the *ASXL3* gene in subject 70 inherited from both parents, resulting in p.Val1854Ile.
- (J) Sanger sequencing confirmed a *de novo* heterozygous missense c.97G>T SNV in the *LSMEM2* gene in subject 73, resulting in p.Gly33Trp.

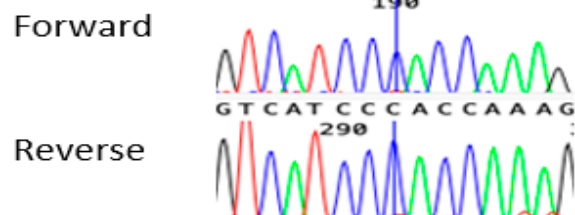
Subject 23 (A) *USP46*: c.293C>T



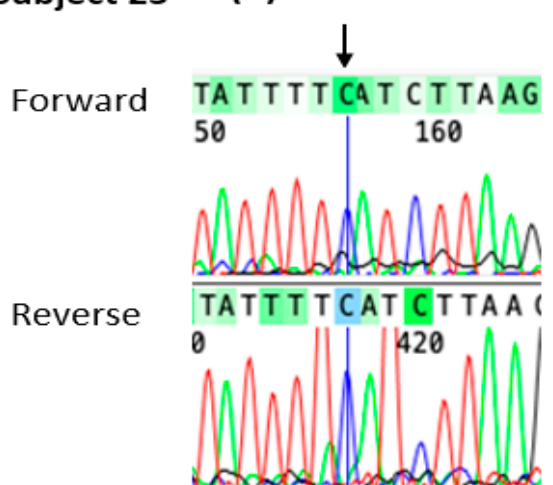
Mother 24



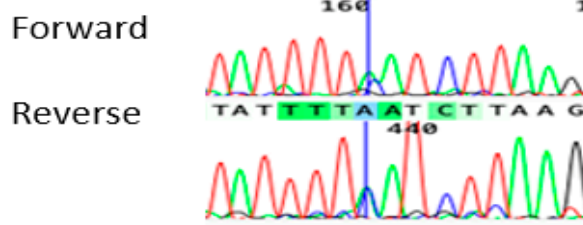
Father 25



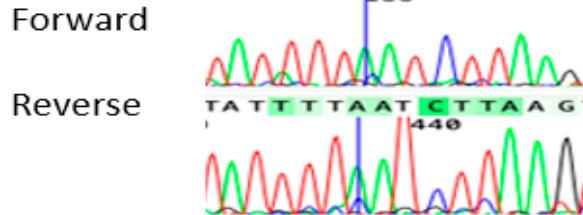
Subject 23 (B) *SLITRK4*: c.1860A>C



Mother 24



Father 25



Subject 23 (C) *FLNA*: c.1954G>A

Forward

ACAGCAAAGACATC
80 90

Reverse

ACAGCAAAAGACATC
420

ACAGCAAAGACATC
80 90

Mother 24

Forward

ACAGCAAAGACATC
240 250

Reverse

ACAGCAAAGACATC
80 90

Father 25

Forward

ACAGCAAAGACATC
200

Reverse

Subject 45 (D) *KRT2*: c.1022G>A

Forward

CAGCCCAACCTGG
130

Reverse

CAGCCGCAACCTGG
330

Mother 24

Forward

CAGCCGCAACCTGG
130

Reverse

CAGCCGCAACCTGG
420

Father 25

Forward

CAGCCGCAACCTGG
130

Reverse

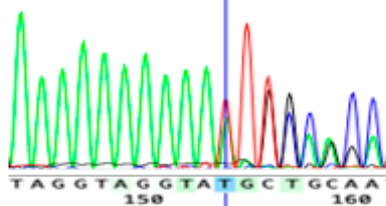
CAGCCGCAACCTGG
360 370

Subject 45 (E) *MIS18BP1*: c.471delA

Forward



Reverse

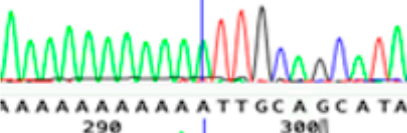


Mother 24

Forward



Reverse

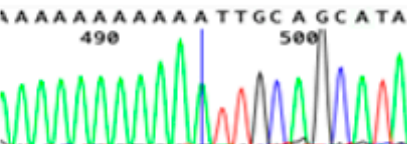


Father 25

Forward



Reverse

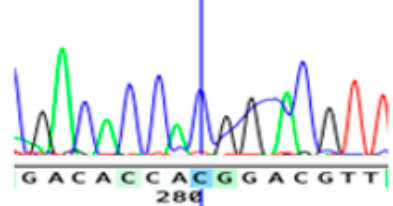


Subject 45 (F) *HAAO*: c.371T>C

Forward



Reverse

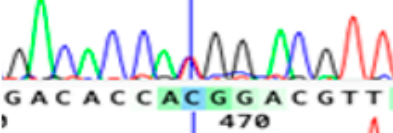


Mother 24

Forward



Reverse

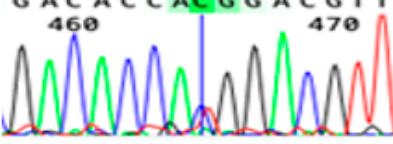


Father 25

Forward



Reverse



Subject 64 (G) PTCHD1: c.1804A>G

Forward

ATGTATCCGCTGGC
240

Reverse

ATGTATCCGCTGGC
60 270

Father 63

Forward

ATGTATCCACTGGC
240

Reverse

ATGTATCCACTGGC
340 350

Subject 64 (H) FLNA: c.2590G>T

Forward

ATCCGATTCAAGG
70 80

Reverse

ATCCGATTCAAGG
70 180

Father 63

Forward

ATCCGAGTCAAGG
70 80

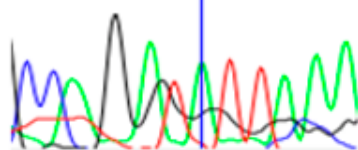
Reverse

ATCCGAGTCAAGG
0 220

Subject 70 (I) ASXL3: c.5560G>A

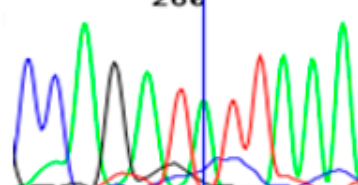
Forward

CCA G AT ATTA AA
220



Reverse

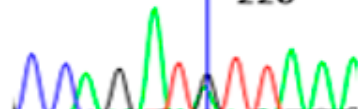
CC AG A TATTA AA
260



Mother 69

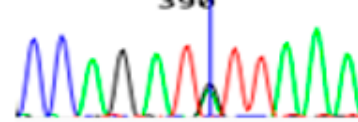
Forward

C CA G ATGT TAA A
220



Reverse

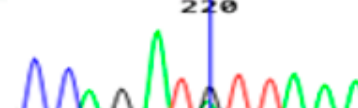
CC AG A TGT TAA A
390



Father 68

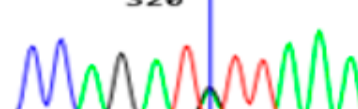
Forward

C CA G ATGT TAA A
220



Reverse

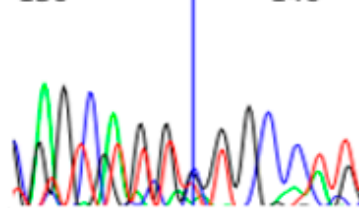
CC AG A TGT TAA A
320



Subject 73 (J) LSMEM2: c.97G>T

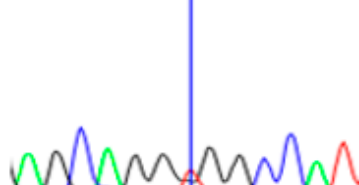
Forward

AGC AGG C GGC CTT
130 140



Reverse

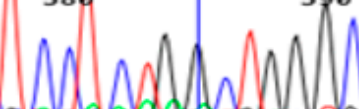
AGC AGG TGG C CAT
160



Mother 71

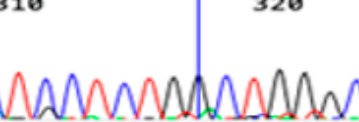
Forward

T C CT CTG G C TG G GC
580 590



Reverse

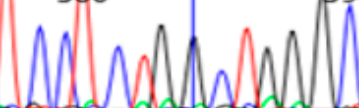
TC CT CTGG C TG G GC
310 320



Father 72

Forward

T C CT CTG G C TG G GC
580 590



Reverse

TC CT CTGG C TG G GC
310 320

