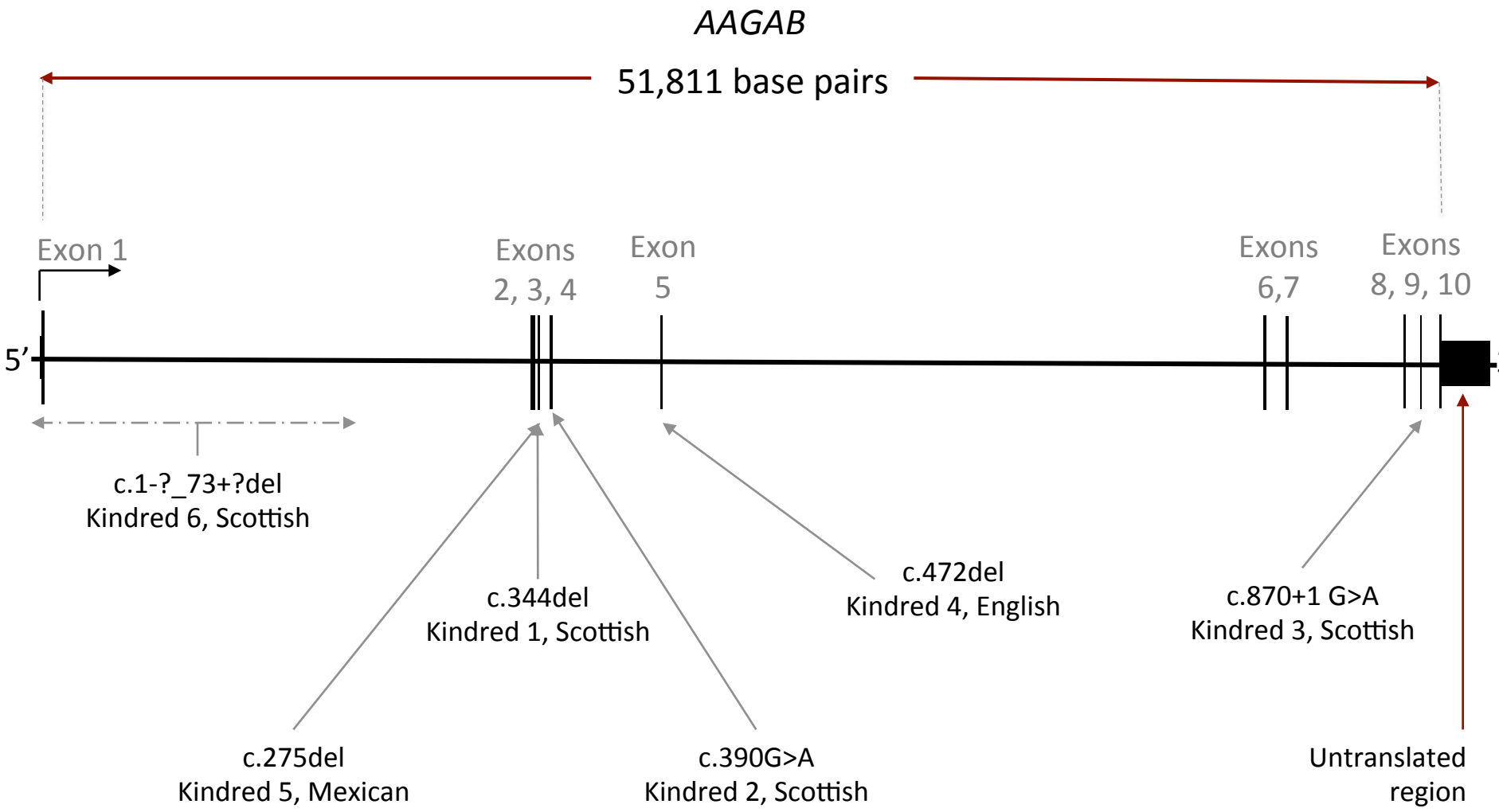


Figure S1. Diagrammatic representation of *AAGAB* showing sites of the mutations associated with PPKP1.

AAGAB is located on chromosome 15q22.33-15q23; gene annotation from RefSeq NM_024666.3

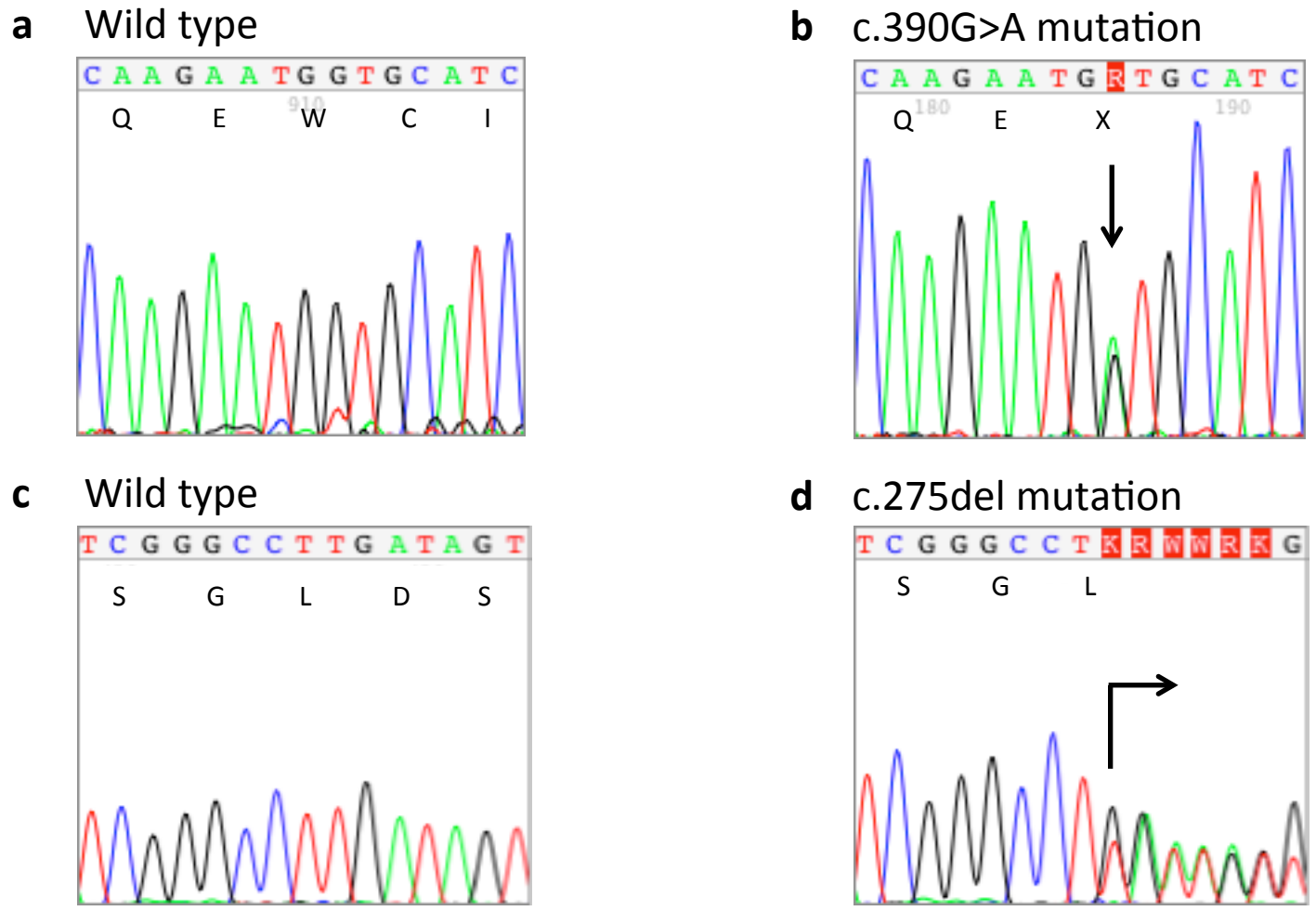
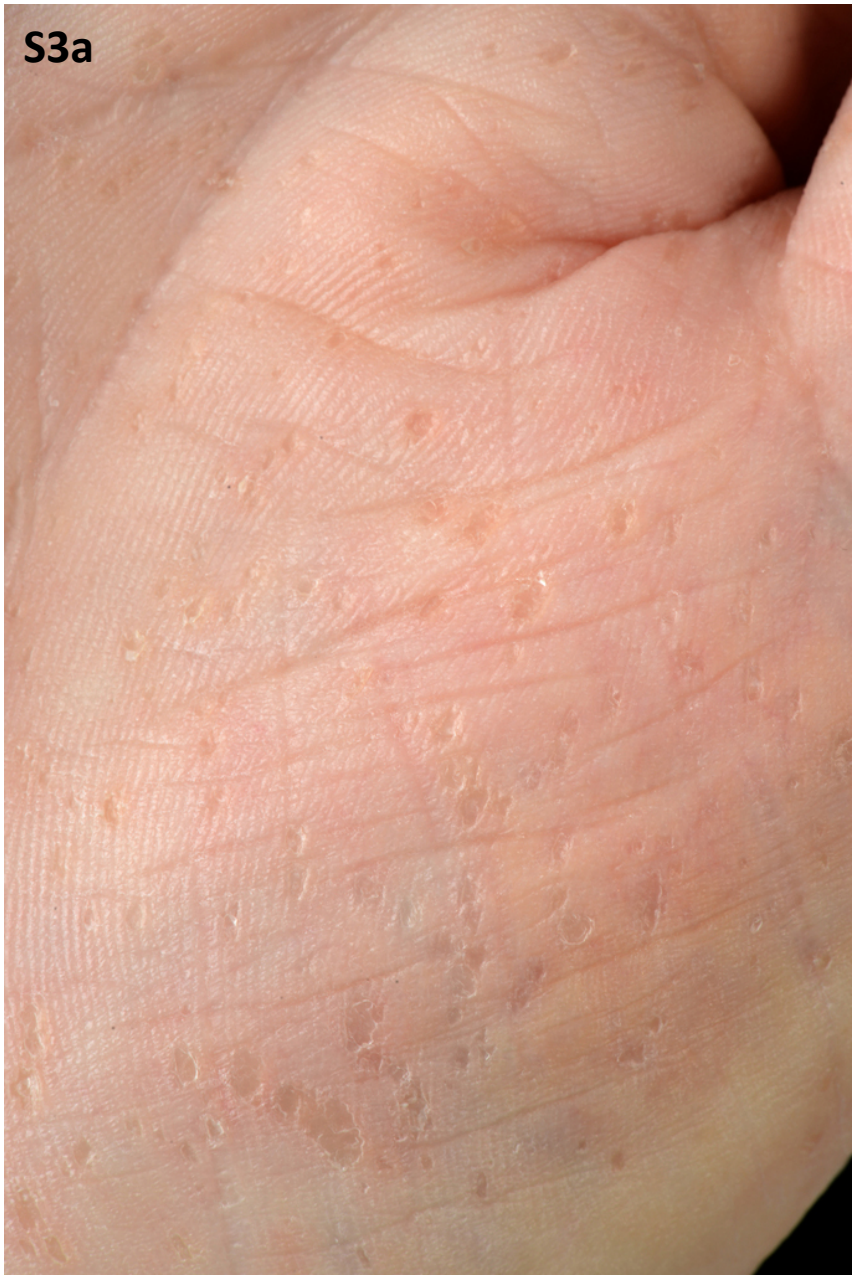


Figure S2. DNA sequencing showing two previously unreported mutations in *AAGAB*

AAGAB exon 4 showing wild-type DNA sequence for codons 128 to 132 (Figure 2a) and mutant sequences (Figure 2b) from kindred 2 showing c.390G>A, a nonsense mutation resulting in the protein change p.Trp130*0. *AAGAB* exon 4 showing wild-type DNA sequence for codons 90 to 94 (Figure 2c) and mutant sequences (Figure 2d) from kindred 5 showing the single base-pair deletion c.275del which results in a frameshift and protein change p.Leu92Leufs*0



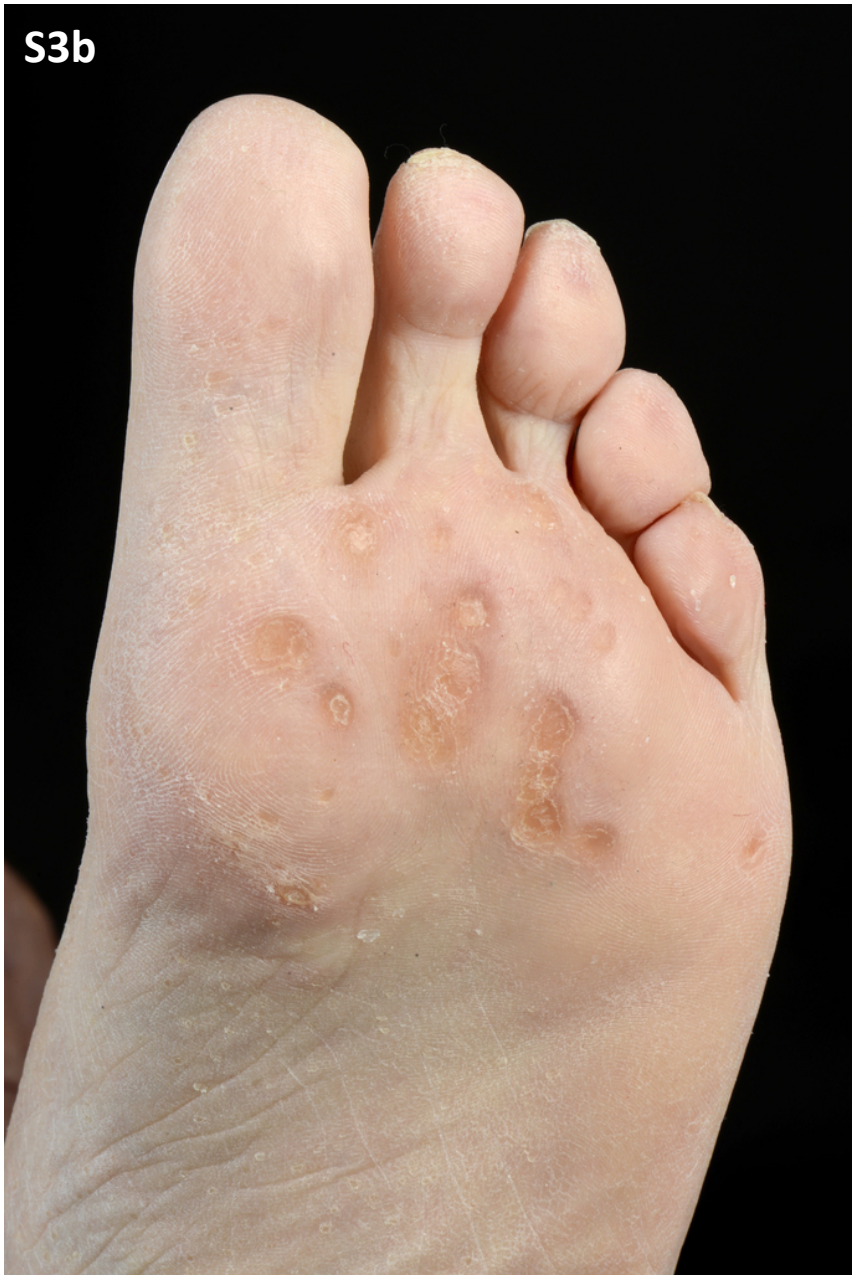
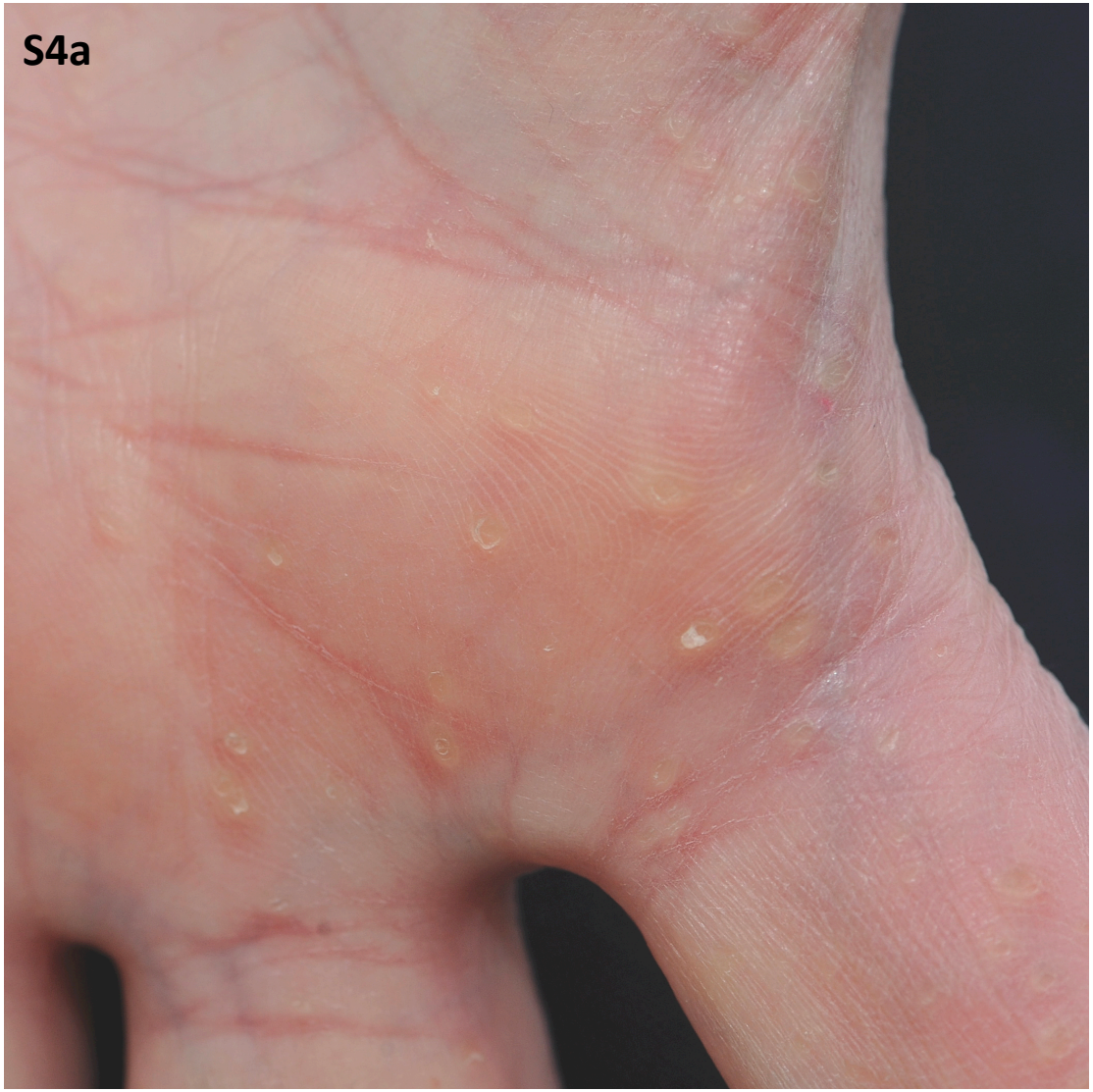


Figure S3a and S3b. Clinical photos of patient from Kindred 3



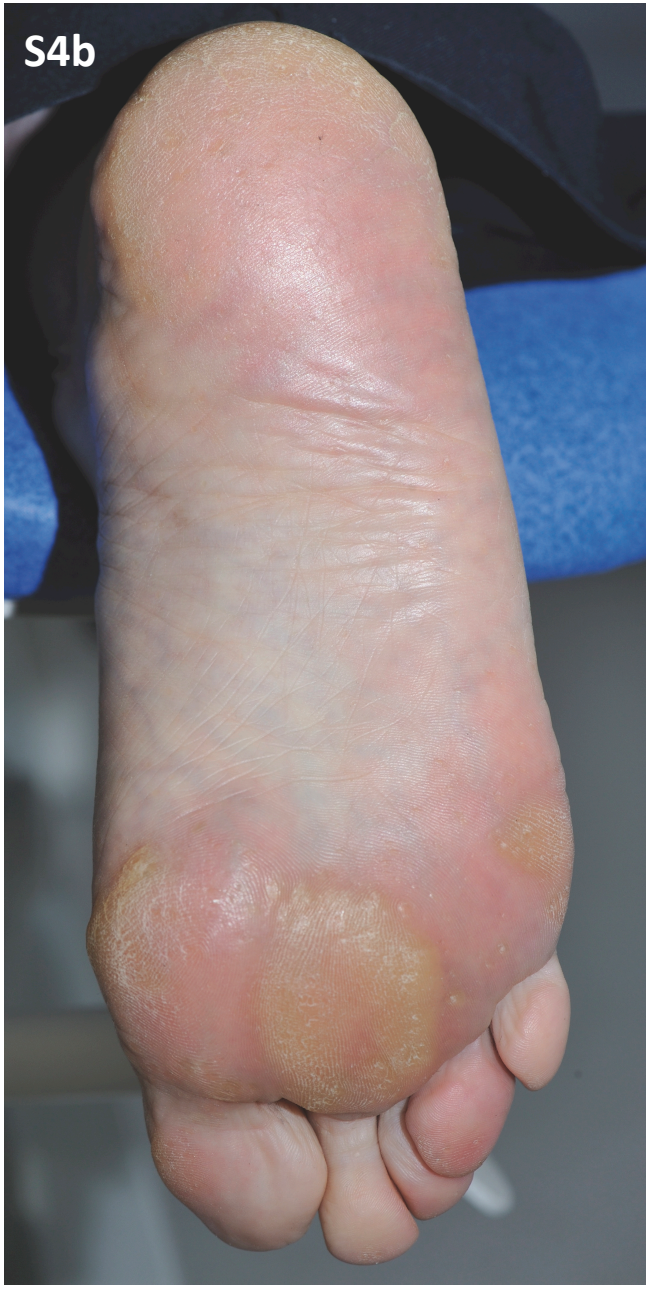


Figure S4a and S4b. Clinical photos of patient from Kindred 4

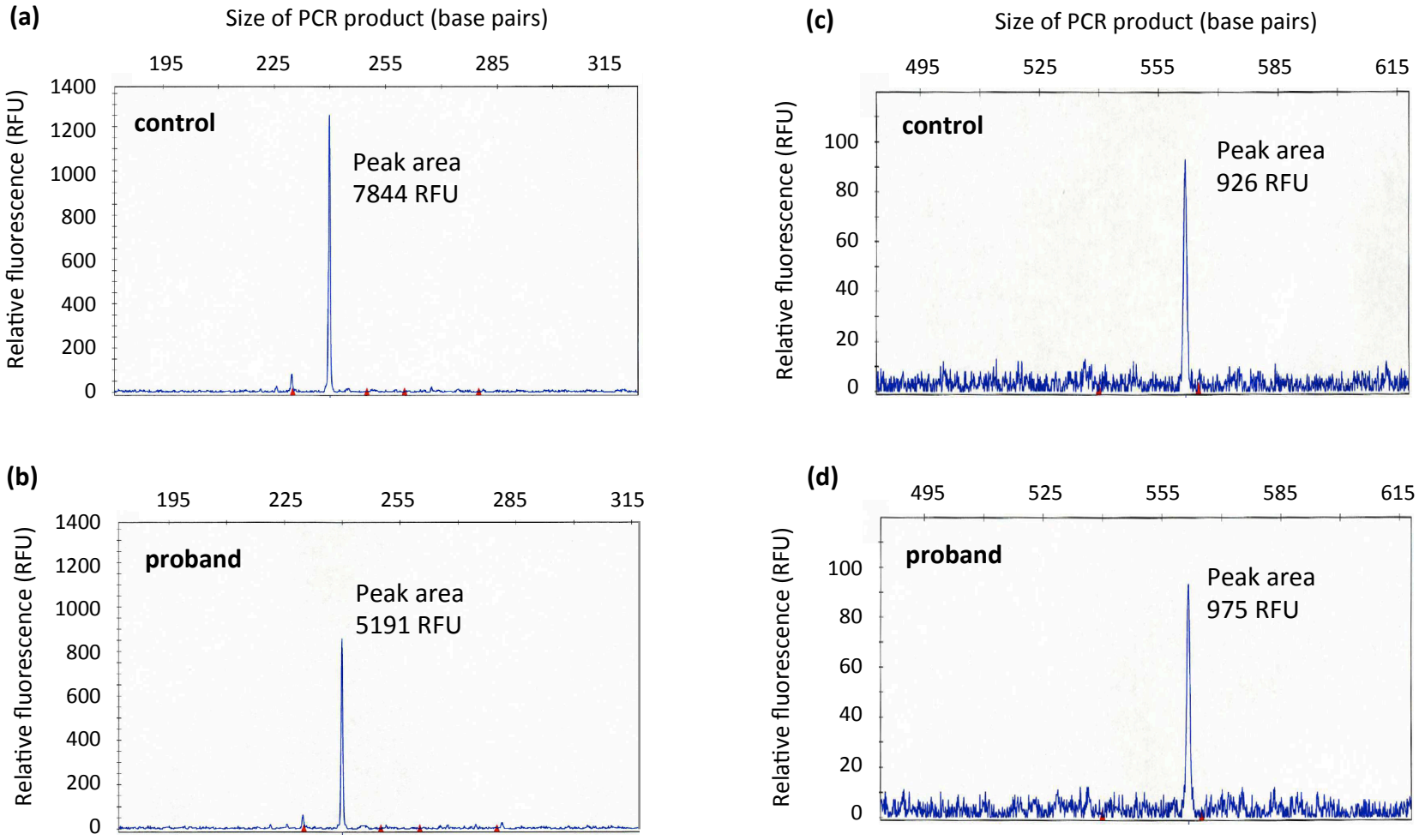

(a)
Size of PCR product (base pairs)
195
225
255
285
315
Relative fluorescence (RFU)
1400
1200
1000
800
600
400
200
0
control
Peak area
7844 RFU
(c)
Size of PCR product (base pairs)
495
525
555
585
615
Relative fluorescence (RFU)
100
80
60
40
20
0
control
Peak area
926 RFU
(b)
195
225
255
285
315
Relative fluorescence (RFU)
1400
1200
1000
800
600
400
200
0
proband
Peak area
5191 RFU
(d)
495
525
555
585
615
Relative fluorescence (RFU)
100
80
60
40
20
0
proband
Peak area
975 RFU

Figure S5.

Figure S5. Size estimation and quantification of PCR products of *AAGAB* exons in the proband and unaffected family member from kindred 6.

Fluorescently-labeled PCR product spanning exon 1 from unaffected father is shown as a control (**Fig 5a**); the equivalent PCR product from the proband is shown in **Fig 5b**. PCR products from DNA spanning exons 2 and 3 are shown in the unaffected father (**Fig 5c**) and proband (**Fig 5d**). Qualification analysis was performed using GeneMapper® (Applied Biosystems, UK), to estimate the area under each curve in relative fluorescence units (RFU). The proband has approximately half the quantity of PCR product from exon 1 compared with the control, consistent with hemizygosity. In contrast the quantities of PCR product from exons 2-3 are approximately equal in proband and control.

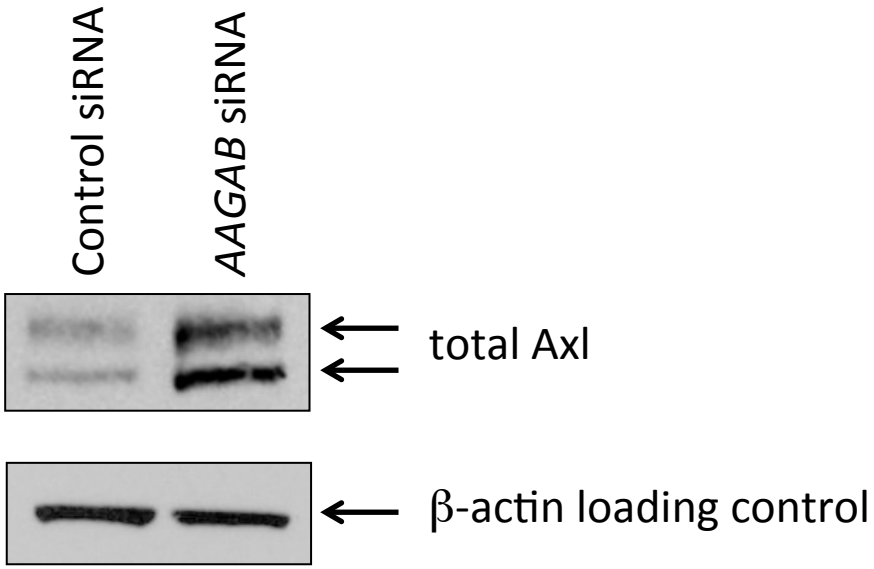


Figure S6. Western blot analysis showing an increase in expression of Axl protein following siRNA knockdown of *AAGAB* expression in HaCaT cells.

Keratinocyte cell line HaCaT (Boukamp et al., 1988) was grown in a monolayer in 5% CO_2 in DMEM (Invitrogen, Paisley, UK) supplemented with 10% Fetal Bovine Serum (Thermo Fisher Scientific, Loughborough, UK). The cells were then transfected with *AAGAB* siRNA 1239 or scrambled control siRNA and protein extraction and Western blotting were performed as described previously (Pohler *et al*., 2012). Blots were probed with mouse anti-rabbit monoclonal antibody C89E7 (Cell Signalling Technology, Danver, MA) and detected with Immobilon™ Western Chemiluminescent HRP substrate (Millipore, Billerica, MA). Antibody against total Axl reveals two distinct bands, suggesting the presence of Axl with different post-translational modification which is consistent with its activity in a signaling pathway.

Primer	Sequence (5' to 3')	Binding site
Ex1f-FAM	[6FAM]CTC TCC GGC CTG TCT CC	Exon 1
G/S1rev	GTT TCT TGT GGT GCT GGG TCC GTC	Intron 1
Ex2f-FAM	[6FAM]TGG TAT CTG ACT GAG AAA ATC AAC C	Intron 1
G/S3rev	GTT TCT TTT TAT CAA GGA ATG GCA AAT G	Intron 3

Table S1. Primer sequences for GeneMapper® analysis

The forward primer was labeled with 6-FAM and the sequence 'GTTTCTT' was added to the 5' end of the reverse primer to improve adenylation of the 3' end of PCR product. The primers were synthesized commercially (Sigma Aldrich, Dorset, UK). 50 ng of genomic DNA was used in PCR with Expand High Fidelity buffer (Roche Diagnostics, Mannheim, Germany) containing 1.5 mM $McCl_2$, 0.4 µM of each primer and 0.5 U of Expand High Fidelity Polymerase (Roche Diagnostics). PCR conditions were as follows: 1 cycle at 94°C for 2min; 35 cycles at 94°C for 30s, 55°C for 30s, 72°C for 30s; 1 cycle at 72°C for 5 min. The size of PCR products was determined using a 3730 DNA Analyser (Applied Biosystems) and data interpreted using GeneMapper® v3.7 software (Applied Biosystems, UK).

Primer	Sequence (5' to 3')	Binding site
AAGABM1F	[6FAM]GAC TTC CAC TCT CCT CTT TTT AGC	Intron 5
AAGABM1R	GTT TCT TAA GGG AGG AGG TAG CGT TAG GAT T	Intron 5
AAGABM2F	[6FAM]AAT AAG GCC TTT GAG TGA CA	Intron 1
AAGABM2R	GTT TCT TAA ATT AGC CGG GCA TAG TGG TA	Intron 1

Table S2. Primer sequences for microsatellite analysis

Primers were designed to amplify regions of microsatellite repeats within intron 1 and intron 5. The forward primer was labeled with 6-FAM and the sequence 'GTTTCTT' was added to the 5' end of the reverse primer to improve adenylation of the 3' end of PCR product. The primers were synthesized commercially (Sigma Aldrich, Dorset, UK). 50 ng of genomic DNA was used in PCR with Expand High Fidelity buffer (Roche Diagnostics, Mannheim, Germany) containing 1.5 mM $McCl_2$, 0.4 µM of each primer and 0.5 U of Expand High Fidelity Polymerase (Roche Diagnostics). PCR conditions were as follows: 1 cycle at 94°C for 2min; 35 cycles at 94°C for 30s, 55°C for 30s, 72°C for 30s; 1 cycle at 72°C for 5 min. The size of PCR products was determined using a 3730 DNA Analyser (Applied Biosystems) and data interpreted using GeneMapper® v3.7 software (Applied Biosystems, UK).

DNA mutation	Protein change	Number of families with this mutation	Ancestry	References
c.370C>T	p.Arg124Ter	1	German	Giehl *et al.*, 2012
c.481C>T	p.Arg161Ter	2	Croatian	Giehl *et al.*, 2012
c.2del	p.0?	1	Scottish	Pohler *et al.*, 2012
c.140G>A	p.Trp47Ter	2	Scottish, Irish	Pohler *et al.*, 2012
c.200_203del	p.Phe67Leufs*41	2	Japanese	Pohler *et al.*, 2012
c.348_349del	p.Arg116Serfs*1	3	Tunisian	Pohler *et al.*, 2012
c.481C>T	p.Arg161Ter	1	Scottish	Pohler *et al.*, 2012
c.344del	p.Asp115Valfs*7	3	Scottish	Pohler *et al.*, 2012 and the current study
c.472del	p.Gly158Glufs*0	6	Scottish	Pohler *et al.*, 2012 (called c.473del) and the current study
c.870+1G>A	p.?	3	Scottish	Pohler *et al.*, 2012 and the current study
c.390G>A	p.Trp130*0	1	Scottish	The current study
c.275del	p.Leu92Leufs*0	1	Mexican	The current study
c.1-?_73+?del	p.?	1	Scottish	The current study

Table S3. ***AAGAB*** **mutations in PPKP1 cases identified to date**